George Christakos
Ricardo A. Olea · Marc L. Serre
Hwa-Lung Yu · Lin-Lin Wang

Interdisciplinary Public Health Reasoning and Epidemic Modelling:

The Case of Black Death

Springer

George Christakos
Ricardo A. Olea
Marc L. Serre
Hwa-Lung Yu
Lin-Lin Wang
Interdisciplinary Public Health Reasoning and Epidemic Modelling: The Case of Black Death

George Christakos, Ricardo A. Olea,
Marc L. Serre, Hwa-Lung Yu,
Lin-Lin Wang

Interdisciplinary Public Health Reasoning and Epidemic Modelling: The Case of Black Death

With 79 Figures

Springer

Prof. Dr. George Christakos

4 Promitheos St
Athens 112-54, Greece

Dr. Ricardo A. Olea

507 Abilene Street
Lawrence, KS 66049 , USA

Asst. Prof. Dr. Marc L. Serre

108 Noble Street
Chapel Hill, NC 27516 , USA

Mr. Hwa-Lung Yu

212-19 Conner Drive
Chapel Hill, NC 27514, USA

Ms. Lin-Lin Wang

303 Giverly Pl.
Cary, NC 27513 , USA

ISBN 10 3-540-25794-2 **Springer Berlin Heidelberg New York**
ISBN 13 978-3-540-25794-3 **Springer Berlin Heidelberg New York**

Library of Congress Control Number: 2005926287

Springer is a part of Springer Science+Business Media
springeronline.com

Printed in The Netherlands

Cover design: E. Kirchner, Heidelberg
Production: A. Oelschläger
Typesetting: Camera-ready by the Authors

Printed on acid-free paper 30/2132/AO 5 4 3 2 1 0

To my little daughter, Maria-Stephania, who is doing what many of us fail to do--constantly looking at the world with fresh eyes--wishing her to realize her own legacy with a winged heart.
GC

For Lucila with all my love.
RAO

To my wife Leslie, for her love and support.
MLS

To my parents Po-Lung Yu and Lung-Gan Wang, for their love and support.
HLY

To my lovely daughter Erika
LLW

Preface

> If you want to achieve something, if you want to write a book, paint a picture, be sure the center of your existence is somewhere else and that it's solidly grounded; only then will you be able to keep your cool and laugh at the attacks that are bound to come."
> *P. Feyerabend*

This is a book about interdisciplinary public health reasoning and epidemic modelling, in general, and the study of the infamous 14th century AD Black Death disaster, in particular. We focus on the intellectual context in which epidemic modelling takes place, in a way that accounts for the present-day interdisciplinary and multicultural trends in scientific inquiry. Like most scientific fields, public health research defines itself based on knowledge, which raises serious epistemic and cognitive issues. Therefore, we maintain that for public health modellers to function in an often complex environment, they should be aware of the divergent conceptions of knowledge and the technological changes that these imply, the multiple sources of information commonly available and their reliability, the different styles of thinking adopted by the disciplines involved, and the importance of developing sound interdisciplinary knowledge integration skills.

A unique feature of the book is that it takes the reader through all four major phases of interdisciplinary inquiry: adequate conceptualization (in terms of metaphors, methodology, epistemic rules, and argumentation modes), rigorous formulation (involving sophisticated mathematical models), substantive interpretation (by means of correspondence principles between form and meaning), and innovative implementation (using advanced systems technology and multi-sourced real world databases).

If the interdisciplinary effort is going to succeed, it must be based on critical intelligence and take place at a research grassroots level rather than at an institutionalized level. Critical intelligence and new ideas cannot be developed in accordance with the dictates of an institution or the established "elite" that is usually behind it. Instead, some level of detachment is necessary to allow creativity to flourish and to gain a new perspective. A case in point is that, despite pompous institutional announcements, genuinely interdisciplinary environmental health research is often confused with cosmetic pseudo-interdisciplinarity that has a superficial and *ad hoc* interdisciplinary character, allowing disciplinary business to proceed as usual.

In view of the above considerations, our discussion of a synthetic public health paradigm and its implementation in the case of the Black Death epidemic is by no

means “the complete story”. It is rather “a call for research” in the field of disease modelling that ought to include new ways of thinking and interdisciplinary perspectives. Our research approach in this book is to open possibilities for consideration. The proposed theses and ideas are launched for exploration, and we do not pretend that we have demonstrated decisively that they are the best ones possible. In a similar vein, our criticism of existing paradigms and competing approaches is not intended to refute them conclusively. Rather its goal is to open scientific space in which new perspectives and ideas concerning a synthetic epistemic paradigm can breathe and grow.

The research presented in this book was supported in part by a grant from the National Institute of Environmental Health Sciences[1]. We are grateful to NIEHS, although one should not necessarily hold the institute responsible for the views expressed in the book. We are indebted to Mr. Christopher Windolph for his editorial acumen. He did a superb job, and if the text does not possess an Apollonian perfection of form, it is due to the interdisciplinary nature of the subject and the limitations of the authors. We also express our appreciation to Dr. Alexander Kolovos for reviewing the final copy of the book and Mr. Ulrich Schirov for his voluntary research on Black Death at his state of Mecklenburg-Vorpommern (Germany).

We would like to thank Drs. Jiu-Chiuan Chen and John Chasteen for their valuable comments and criticism. The criticism is welcomed and not feared, because one should be assured that the centers of our gravities are outside our professions. More to the point, every researcher must possess enough reserves of humor. Let us not forget that in life and in scientific inquiry there are significant parallels between the Ha-ha! and the Aha! experience. In the end, some subjects are so serious that one can only joke about them.

George Christakos
Ricardo A. Olea
Marc L. Serre
Hwa-Lung Yu
Lin-Lin Wang

January 2005

[1] NIEHS Grant No. P42 ES05948

Contents

"The devil pales beside a man who owns a truth, *his* truth."
E.M. Cioran

Note:

The following notation is used throughout the book:

- **Section A** denotes section A of the same chapter.
- **Section II.A** denotes section A of Chapter II. This notation is used when we refer to a section that is from within a different chapter.
- **Fig. 3** denotes the 3rd figure of the same chapter.
- **Fig. II.3** denotes the 3rd figure of Chapter II. This notation is used when we refer to a figure that is from within a different chapter.
- **Table 3** denotes the 3rd table of the same chapter.
- **Table II.3** denotes the 3rd table of Chapter II. This notation is used when we refer to a table that is from within a different chapter.
- **Eq. (3)** denotes the 3rd equation of the same chapter.
- **Eq. (II.3)** denotes the 3rd equation of Chapter II. This notation is used when we refer to an equation that is from within a different chapter.
- **Ziegler (1969: 127-128)** denotes that the reader is referred to pages 127-128 of Ziegler (1969).

Chapter I – Toward an Interdisciplinary Methodology

"Lacking the role of criticism, science would be reduced
to a witches' sabbath of adventurous ideas."
E. Mach

A. Concerning the Current Paradigm—In Search of Bohemians

Public health is viewed as the science and practice of protecting and improving the health of a human population, as by preventive medicine, health education, control of communicable diseases, application of sanitary measures, and monitoring of environmental hazards. Within this framework, the term "epidemic" is usually applied to the occurrence and space-time evolution of a disease (infectious or non-infectious) in a human population. Generally speaking, the aims of *epidemic modelling* are to understand, control, and when possible prevent the distribution of disease in the population. Epidemic modelling may address questions related to the factors that influence or determine this distribution, including the cause of the disease (genetic trait, environmental exposure, life style, etc.). In the case of environmental effects, epidemic modelling is closely related to human exposure-health impact research. Another group of questions may be concerned with the rate of disease transmission within the population, the geographical evolution of the epidemic, a description of the contact process, or the distribution of mortality and other epidemic variables[1].

In certain circumstances, a temporal distinction could be made between epidemic modelling occurring *before* the event (when certain measures may be taken to avoid a disastrous outbreak), *during* the event (in which case, there is the possibility of "on-line" intervention, effective containment of the epidemic, etc.), and *after* the event (in which case, understanding the space-time distribution character-

[1] While "epidemic" focuses on phenomena in the distribution of disease in space-time, "epidemiologic" refers to things pertaining to the study of such phenomena. Today the discipline of epidemiology is often understood to include the study of non-epidemic diseases, so things that are epidemiologic could pertain to epidemiology without pertaining to epidemics (Savitz, 2004).

istics of the specific disease can provide valuable knowledge concerning future outbreaks of the disease or about other kinds of epidemics).

For modelling purposes, epidemics may be categorized in different ways. One categorization distinguishes between two kinds of epidemics of communicable disease (Haggett, 2000: 11-12): (*a*) The *propagated* epidemic, which results from the chain transmission of some infectious agent. Transmission may occur directly from person-to-person (e.g., measles), or indirectly via an intermediate vector (e.g., malaria) or a microparasite. In some situations, transmission takes place through humans (e.g., typhus fever), whereas in some others the parasite survival is independent of man (e.g., bubonic plague). (*b*) The *common-vehicle* epidemic that is due to the dissemination of a causative agent. The epidemic may result from a group of individuals being infected from a common medium (e.g., water or food) that has been contaminated by a disease-causing organism (see, e.g., the cases of cholera and typhoid). In fact, as a result of the emerging environmental pollution problems and their health effects, many epidemiologic techniques have been extended and applied to study the effects on human population health of physical, chemical, and biological agents within the environment. This effort led to the development of the discipline of *environmental epidemiology* (e.g., Terracini, 1992; Moeller, 1997). By examining specified populations exposed to a variety of ambient environments, the general goal of environmental epidemiology is to investigate exogenous determinants of disease distributions and clarify the relationships between physical, chemical, or biological factors and human health.

Discussions of the current *paradigm*[2] of epidemiology can be found, e.g., in Gordis (1996), Rothman and Greenland (1998), and Rothman (2002). Basically, this paradigm provides little motivation for directing research toward seeking basic knowledge. Instead, it encourages research activities that are built mainly on the discipline's empirical basis. Its focus is *technical* practices rather than *theoretical* achievements[3]. Moreover, part of the difficulty of the current epidemiologic paradigm is that it persists in talking about modern interdisciplinary problems in an outmoded vocabulary. These are crucial elements of the current paradigm, because they may indicate a culture that equates *intellectual* debate with the banal exchange of technical opinions. Such a paradigm, of course, may be the influence of a predominantly anti-intellectual climate characterizing many institutional and social environments nowadays (see, e.g., Furedi, 2004, and references therein). Intellectuals, people who *wonder* (i.e., practice theoretical thinking, search for meaning and truth, seek to improve the ways of scientific reasoning, and try to build new concepts and models), are often considered pariahs and ir-

[2] Generally, the term "paradigm" is used to describe a particular way of looking at things. The paradigm includes a set of theories, techniques, applications, and instrumentation together (Christakos *et al.*, 2002: 13).

[3] Unfortunately, as many junior faculty members will admit, those who are proactively accepting the "brute force" application of new technologies in epidemiologic problems are much more likely to get federal research support than those who are interested in a theoretical type of work.

relevant. Thus, it is hardly surprising that theoretical modelling in epidemiology and public health often falls victim to this climate.

In the current paradigm, public health data gathering and processing avoids facing the fact that innovative experimentation and observation are theory laden, i.e., they are not possible without strong theoretical support and interaction between different *modes of reasoning*. This was a hard-learned lesson in a recent case of grossly inaccurate health effect estimates that resulted from the "brute force" implementation of commercial statistical packages without a deeper understanding of the underlying assumptions and theoretical parameters (see, Knight, 2002; Revkin, 2002). As a matter of fact, it is theoretical knowledge--and not just observation or data gathering--that *distinguishes* humans from other animals and that is responsible for major advances in the history of mankind (Tomkinson, 1999). Given the strong historical evidence about these matters, it is safe to predict that a continuing backlash against intellectuals cannot be without repercussions in the future of epidemiology and public health, among other fields.

The gap between data gathering and theoretical thinking is, indeed, widening[4]. In his study of the plague in 17th century AD Italy, Cipolla (1981: 14) maintains, "Paradoxically as it may sound, the lesson of history is that all too often people find it easier to manipulate the facts to fit their theories than to adapt their theories to the facts observed". In "Epidemiology Faces Its Limits", Gary Taubes warned that modern epidemiology was reaching a crisis point and was in danger of becoming a "pathological science" because it had devolved into a data dredging exercise, mindlessly searching an ever-expanding pool of danger for marginally significant associations unpredicted by any *a priori* hypothesis (Taubes, 1995). Also, Phillips *et al*. (2004) emphasized the need for greater perspective and innovation in epidemiology, pointing out that "the desire for new information means that the health science literature is overwhelmingly devoted to reporting new findings, leaving little opportunity to improve the quality of the science" and that "current discussions of advanced statistical methods, the nature of random error, sensitivity analysis and uncertainty quantification, and proper interpretation of results, to name just a few, show that most current epidemiologic research uses methodology[5] in need of improvement".

In view of the profound asymmetries of the current paradigm, new ways of thinking are needed to establish an improved public health methodology based on

---

[4] It seems that data gathering often seeks isolation, avoiding interaction not only with theoretical knowledge but with crucial developments in different disciplines as well. Moreover, it is not uncommon that the inability of data gathering to produce the necessary experimental results lies behind an institutionalized agenda aiming at preventing theoretical thinking from developing improved models that could lead to deeper understanding of the epidemic system and the associated human health risks. This agenda may serve someone-sometime-somewhere, but it is profoundly against scientific progress in the global effort to fight disease.

[5] In general, methodology refers to concepts and ideas about when and how to use various methods to develop knowledge and solve problems, and about what each method really *means* (underlying conceptions, presumptions, normative rules, reasoning modes, etc.); (see, Christakos *et al*., 2002: 189).

genuine interdisciplinary interactions and intellectual exchanges. Indeed, we now have the opportunity to study infectious and other onset diseases in a more substantive and rigorous manner. The following is a brief summary of certain significant limitations of the current epidemic paradigm that a new methodology should take into consideration in the new Conceptual Age[6]:

a. Little attention has been given to the *interdisciplinary* nature of epidemic research and development. In this manner, important sources of knowledge available in the physical and life disciplines are ignored at the cost of profoundly inadequate epidemic and human exposure studies. The *status quo* of disciplinary attitudes needs to change in the current epidemic research paradigm so that interdisciplinary *knowledge integration* becomes a genuine scientific inquiry and not a cosmetic process having a superficial and *ad hoc* interdisciplinary character allowing disciplinary business to go on as usual.

b. The fundamental *spatiotemporal* character of an epidemic under conditions of uncertainty has been mostly neglected. Intrinsically spatiotemporal phenomena, like disease propagation, are often modelled with "aspatial" and "aspatiotemporal" theories. Mathematically rigorous and epidemically meaningful stochastic tools (e.g., spatiotemporal random field theory) have been ignored in favor of deterministic methods and classical statistics techniques that neglect vital cross-correlations and laws of change on space-time manifolds[7]. This neglect has resulted in unsatisfactory analyses of major issues such as space-time prediction of disease distribution, epidemic explanation, and causation. Holmes (1997: 111), e.g., poses the plausible question: "A key question is to what extent do we lose insight or are quantitatively misled by modeling the intrinsically spatial process of disease spread with nonspatial theory". In the present book we go beyond that and argue that the process is fundamentally spatiotemporal, i.e., it develops within a composite space-time domain.

c. The solution of mathematical models of epidemics has been viewed as a purely *ontologic* affair that focuses on abstract and dry formulas, whereas crucial factors—such as modes of perception and reasoning, and their integration—are neglected. Thus, what the current perspective is missing is that these models are imperfect constructs of the human mind, often they do not account for essential site-specific knowledge, and they constitute an uncertain representation of reality. Since public health research defines itself based on

[6] We are certainly aware of the difficulties that such a view will be probably confronted with. The majority of professional scientists are strongly committed to the paradigm of their subject. But, as Ziman (1991: 90) maintains, "…there is a price to pay for this commitment. Each generation of scientists gives too much credence to its own paradigm. By his education, and by participation in 'normal science', the average research worker is heavily indoctrinated and finds great difficulty in facing the possibility that his world picture might be wrong".

[7] Although the discussion focuses on infectious diseases and acute onset diseases following point exposures, even chronic disease modelling (e.g., childhood leukemia) could benefit considerably from stochastic space-time analysis (say, advanced clustering techniques).

knowledge, the solution of an epidemic model is likely to be more realistic if its derivation invokes *epistemic cognition*[8] notions and insights concerning the validity and legitimacy of knowledge (e.g., what are the "grounds of knowledge", what the mind considers to be the goal of a solution of a public health problem, or how it reaches this solution). Also, since the solution of an epidemic model often refers to the future, it should account for the fact that the future is accessible neither observationally nor physically, but only cognitively (the future is ontologically nonexistent).

d. In many cases of public health research, the emphasis is solely on *data gathering*[9] (experimental, observational, surveillance, etc.) and the black-box operation of the *techniques/instruments* employed for this purpose, without any appreciation of the kind of substantive *theoretical* modelling that underlies these techniques/instruments and gives voice to the data. In fact, there is nothing inspiring or intellectually satisfying in the flood of undigested data, mistaken for knowledge in the current paradigm[10]. Public health researchers become data managers (and guardians), and in order to work efficiently, they often use tools that they do not understand. Naturally, issues linked to the question of the *reliability* of the generated information naturally arise in this context. Moreover, in epidemic sciences with little theoretical modelling basis, the *indetermination* principle[11] can cause considerable problems.

An in depth study of the above limitations of the current epidemic paradigm could potentially produce a paradigm change in certain constructive ways. In view of this possibility, we find it reasonable and timely that the goal of the present book be twofold:

i. Bring to the fore a significant challenge in public health research, namely, the possibility of developing a *synthetic epidemic paradigm* (SEP) that provides an integrated methodology able to account for the major issues *a-d* above in a mathematically tractable and epidemiologically thoughtful fashion. Key concepts and tools are needed to open new areas of epidemiology to detailed understanding in an integrated manner. The SEP should play a creative role in

[8] The term "epistemic" refers to the construction of models of the processes (perceptual, intellectual and linguistic) by which knowledge and understanding are achieved and communicated. In the epistemic cognition framework, the contribution of cognition is to identify basic knowledge-assimilation, belief-forming and problem-solving processes, which are then examined by means of the evaluative standards of epistemology. The meaning of these terms will be clarified further in subsequent sections.

[9] Data gathering but not sharing might be closer to the mark (see, also, Section B.a below).

[10] Unfortunately, the dictum that "data do not speak for themselves, and when they do they tell different stories, depending on the audience" has gone unnoticed in these cases. Directly relevant to the Black Death study of this book, is the remark of a medieval scholar: "Medieval data are like children; they do not talk to strangers."

[11] Indetermination principle: Every set of data can be associated, in principle, with an infinite number of possibilities. Thus, sound theoretical modelling is needed to eliminate all but a few meaningful choices.

this context, containing novel ideas as well as concrete suggestions on how existing ideas fit into new frameworks.

ii. Implement SEP in the case of the major 14th century AD *Black Death* epidemic. Although this epidemic has been a major disaster in human history (in terms of the mortality it caused and the speed with which it spread), and as such has been discussed extensively in the literature, neither rigorous modelling of its main epidemic features nor systematic mapping of its space-time evolution exist (including mortality maps, space-time correlation functions, areal spread and epidemic velocities). The SEP can produce useable models of the way the epidemic propagated through geographical space and time. Since Black Death had grave societal, public health, and financial effects (Fig. 1), the study of these models can offer valuable insight about these effects, as well as about similar effects of potential contemporary epidemics[12].

Figure 1. One of the effects of the Black Death epidemic was the frequent use of extremely morbid imagery in art. Death incarnate made many appearances in paintings of the period, like the apocalyptic composition of Pieter Bruegel's "The Triumph of Death". Death--a skeletal figure on an emaciated horse at the center of the painting--is the leveler. Its legions and horsemen--all skeletons--drive humanity toward the final trapdoor (Roberts-Jones and Roberts-Jones, 2002).

[12] Today, many experts believe that the majority of infectious diseases have not gone away, but lie in wait until their chance comes. The re-emergence of Black Death several times in the past is an example of this situation.

But before we start our long promenade through the methodological and empirical affairs of public health interdisciplinarity, we briefly introduce our readers to some technological, intuitive, intellectual, and philosophical features that should be incorporated into an SEP.

A main characteristic of SEP should be the *innovative description* of the composite geographical and temporal distribution of a disease (propagation characteristics, space-time correlation structure, etc.). The description should be the product of a sound theory of knowledge rather than an *ad hoc* combination of purely empirical techniques (pattern fitting, etc.). This kind of description can generate valuable information that would optimally allow containing the epidemic spread (by means of control strategies, infection breaks, isolation, or eradication), assessing potential socioeconomic effects, etc. Furthermore, in the case of environmental epidemiology, the adequate description of the geographical and temporal distribution of the exposures (toxic chemicals, radioactive materials, etc.) to which the population has been subjected is a crucial component of any modelling study. As Moeller (1997: 39) has pointed out, "Regardless of the complexity, valid environmental monitoring measurements and accurate estimates of exposures are essential if confidence is to be placed in the associations that are developed between exposures and observed adverse consequences to human health."

Another characteristic of SEP is that it should be *flexible* and *versatile*. It could rely directly on measurable infection parameters, environmental quantities and health variables (incident rate, mortality, contaminant concentration, infection agent and path, etc.) and the models relating them; it may utilize a group of epistemic vectors drawn from interdisciplinary areas of human thought and experience; or it may involve a complete causal chain based on a certain course of events. In the latter case, the chain may start with ambient sources of environmental risk (e.g., contaminated water or air pollution), followed by population exposure to environmental risk factors and health damage, which can result in an epidemic[13].

The SEP focus should not be limited to the implementation of computational technologies (informatics, sophisticated numerical schemes, etc.) with experimental techniques. The use of these valuable technologies should not be a cut-and-dry subject but an *intellectual* effort in a conceptually sound and creative background context. Sound interdisciplinary knowledge is the result of the careful integration of the underlying concepts and critical reasoning modes, and not merely the integration of the vast sequences of numbers generated by the computational technologies[14]. In a similar vein, SEP should seek a balance between *form* and *substance* that accounts for the facts that humans can develop sophisticated formal tools because they possess very effective capabilities to construct meaning and

[13] In this case, the SEP description of the epidemic would depend on the environmental chain of events that precedes it.

[14] Noticeably, recent publications (e.g., Kanehisa, 2000) emphasize the critical role of conceptual links between different disciplines toward understanding basic principles of life vs. informatics technologies that merely cope with the vast amount of data generated by the genome projects.

that the correlation of form and meaning is a highly desirable feature of creative thinking.

When disciplinary boundaries are successfully crossed, new arrangements are emerging. The SEP could confront the challenge by adopting a change from the traditional view of a human health community consisting merely of experts with their technological tools and specialist interpretations, to a new view of a community possessing an *epistemic culture* that is certainly run on expert processes and systems epitomized by science, but which is also structured into various areas of life and their concepts of theory and practice. This raises the issue of the transition of the contemporary public health community to a knowledge community, of which epistemic culture is a structural feature. One of the real consequences of such a culture underlying SEP is that it would be preferable to debate about hypotheses before debating about results. It is a common practice that different teams of public health scientists are brought together at the final stage of their research projects in order to debate their results and attempt an "after the event" dialogue that focuses mostly on rhetoric and has little effect on scientific progress[15]. On the contrary, in the SEP context these research groups will have to debate their hypotheses and resolve the relevant issues (theoretical, experimental, institutional, social, etc.) at the early research stages.

As we mentioned in the Preface of this book, our discussion of the SEP and its application in the Black Death situation is by no means "the complete story". It should be rather viewed as "a call for research" in the field of public health research, in general, and epidemic modelling, in particular, which should include novel ways of thinking and rational interdisciplinary perspectives. As a matter of fact, the above considerations seem to point toward the creation of a Bohemian style of an epidemic modeller[16]. According to the *Bohemian Manifesto* (Stover, 2004; 11): "Bohemians start movements. They break the rules, set the trends. Bohemians change thinking and sometimes they write manifestos. Bohemians cross cultures and integrate mantras, philosophies, substances and clothing seamlessly into everyday life. Bohemians tenderly and violently create new work and change paradigms." What could be closer to the mark in the emerging Conceptual Age?

---

[15] This kind of a "dialogue" is certain to fail, as the aftermath of the World Trade Center (WTC) disaster amply demonstrated (Dalton, 2003): Two groups of researchers came to diametrically opposing conclusions concerning how much of the lower Manhattan pollution could be ascribed to the WTC-generated plume and how much was native. Typically, such cases are characterized by: (i) the lack of understanding of the different scientific theories underlying the instruments used, thus leading to contradictory interpretations of the measurements obtained; (ii) the unwillingness to share information obtained by the different groups at the early stages of the research; and (iii) the subsequent absence of constructive criticism, knowledge reliability assessment, and methodology evaluation (all of which constitute violations of fundamental principles of scientific reasoning). Issues such as i-iii should have been dealt with at an early stage of the WTC study and not at the late stage of presenting the final results.

[16] This would be a Ha-ha! or an Aha! moment.

B. Methodological and Empirical Issues of Interdisciplinary Epidemic Research

In the context of scientific development, public health scientists try to make sense of the real world by developing a set of *mental* frameworks about it. A fundamental constituent of such an effort is the establishment of an adequate *methodology*, i.e., a coherent step-by-step procedure for thinking critically about scientific development and acting upon it. Methodological standards act like teachers: they give marks to one's epidemiologic theories. Although a considerable deal of *ad hoc* interdisciplinary activity may be happening on an everyday basis (e.g., in the form of complimentary health professions and skills within a common space, partnerships, or as a management tool), no systematic methodological framework exists for integrated epidemic modelling in a realistic space-time domain under conditions of multi-sourced uncertainty. As a result, even with a group comprised of the best experts, there is no guarantee for a successful public health outcome (i.e., the sum total of competencies is not necessarily competence). Edward Bender, an expert on artificial intelligence, notices (Bender, 2000: 192), "One approach to inaccurate estimates is to consult several experts and then create a reasonable compromise based on their estimates".[17]

In the meantime, the number of interdisciplinary research cases continues to grow at an increasing pace. The need to develop integration frameworks incorporating individual- and population-level dynamics of a disease, as well as within-host dynamics, has been emphasized in recent studies (Grenfell *et al.*, 2004). Panels of experts acknowledge that the environment plays a contributing role in the etiology of most diseases (e.g., reproductive, immune competence, pulmonary/cardiovascular, cancer, or neurodevelopment), and urge that (DHHS, 2003), "the long-term improvement of public health requires an interdisciplinary approach that integrates biomedical, geochemical and engineering sciences." While numerous techniques of cluster detection exist in the epidemiologic literature, a sound interdisciplinary methodology is not yet available (Millikan, 2004). The need for an interdisciplinary approach in the context of the genome project is emphasized by Kanehisa (2000: 19-23): "The genome certainly contains the information on the building blocks, but it is premature to assume that the genome also contains the information on how to connect or relate the building blocks… the information in the genome is not sufficient to make up life… The ultimate objective of post-genome informatics is therefore to unite life and matter and to establish a grand-unification theory of the physical and biological worlds". Decision-makers who need to combine information from different disciplines agree that "there is no commonly accepted methodology for combining multiple expert judgments" (Webster, 2003: 4). The National Institute of Health proposed its Roadmap initia-

[17] Many speak of the growing problem of experts who are no longer able to understand one another and communicate effectively. Disciplinary territoriality, ignorance of basic findings in scientific domains other than one's own, and occasional arrogance, all contribute to this lack of understanding between experts.

tive in 2003 as "an integrated vision to deepen our understanding of biology, stimulate interdisciplinary[18] research teams, and reshape clinical research to accelerate medical discovery and improve people's health." At the same time, the development of a genuinely interdisciplinary public health approach is necessary, especially since information processing sciences give rise to new objects of study, new instruments of collective practices, and new forms of human interactions (Web forums, etc.), which challenge disciplinary boundaries. In his book *How Scientists Explain Disease*, Paul Thagard studies the three major kinds of explanations of the development of scientific knowledge--logical, cognitive, and social[19]--and comes out in favor of the view that health scientists will have to bring these three schemas together to form an integrated explanation of scientific change (Thagard, 1999: 4): "But we can appreciate science as a product of individual minds *and* as a product of complex social organizations. Not only can we see cognitive and social explanations as providing complementary accounts of different aspects of science, but we can also look for ways of integrating those explanations, bringing them together into a common approach."

As far as Black Death is concerned, the interdisciplinarity of the various information sources (documents, accounts, reports, etc.) has been noticed, although its impact has not been adequately assessed (Bleukx, 1995: 72). This is not a small matter, since the case of Black Death is unique in the sense that it deeply affected life at all levels--social, economic, demographic, political, religious, and artistic.

a. Quis Custodiet Ipsos Custodies?

We have already said that the development of an SEP aiming at the integration of different life support fields across space-time for public health purposes will have to deal with the salient methodological and empirical aspects of interdisciplinary sciences. But the outcome is certainly worth the effort, in our view. A broadly conceived SEP would bring data and explanation into a coherent whole, merge cross-disciplinary dynamics and logics of inquiry, and offer opportunities for space-time epidemic prediction, infection risk assessment, health policy and damage control. E.g., in order to identify infectious agents and toxicants, assess factors that may affect their transmission, transport, and bioavailability, and determine the critical pathways resulting in exposures to human populations, SEP needs to rely on a synthesis of methods and tools utilized by biomedical, ecological, toxicological, and biological specialties. Although SEP provides an integrated public health modelling methodology that is generally applicable, for illustration

[18] Although in this initiative interdisciplinarity seems to be conceived as the integration of data and techniques from different disciplines rather than conceptual frameworks and thinking modes.

[19] According to logical explanations, new knowledge derives logically from previous knowledge; for cognitive explanations the growth of knowledge derives from the mental structures and procedures of scientists; and in social explanations factors such as the organization, power relations, social connections and interests of scientists are used to explain scientific change.

purposes its implementation in this book involves the specific case of the Black Death epidemic. This epidemic has been studied in the past by different disciplines, which have missed important parts of the picture and did not come together to form a coherent whole.

Naturally, the development of an SEP should reside on *organized connectedness* between the various scientific disciplines involved in a public health study. Many names have been given to the making (or finding) of such connections: integration, organization, patterning, development of schemata. These connections may apply to processes, objects, symbols, ideas, and actions. Moreover, the SEP requires the consideration of certain conceptual and technical products (e.g., models, algorithms and computer codes, and experimental techniques) developed during cross-disciplinary research. In this respect, the study of the elements that contribute to the segregation of science into isolated units called *disciplines* can provide valuable guidance in one's effort to successfully integrate these units in the human health context. The SEP should also account for the fact that most of the public health processes and disease variables involved in cross-disciplinary integration vary across space and time. In addition to efficiently coordinating events and processes, the *space-time* domain of SEP may provide the means for establishing connections between different disciplines.

Besides, the need for a close *collaboration* between theory and experiment/observation is an inescapable necessity. By arbitrarily isolating phenomena for experimentation, one seeks to give them a beginning and an end. Yet phenomena are no more isolated in nature than are notes isolated in a melody, which is why theoretical modelling is the soul of science. When theory and experiment/observation are well-balanced and work in concert, progress is made by means of an public health research program that manages careful shifts from empirical investigation to explanatory theory, from ontologic description to epistemic interpretation, and from epidemic prediction to confirmatory evidence. In the end, the question "Quis custodiet ipsos custodies"[20] has a deeper meaning in the context of a scientific inquiry aiming at a realistic representation of the epidemic system that can best serve the needs of public health. The current public health paradigm that allows the practice of "data gathering but not sharing" serves neither the ultimate goals of scientific research nor the long-term interests of the public that finances it. The institutional encouragement of a misguided experimental culture that systematically avoids any constructive criticism by means of theoretical thinking and critical intelligence should be reconsidered.

Data sharing and scientific criticism can drastically prevent the data gathering process from heading into a blind alley. As Lewis Thomas has remarked (Thomas, 1995: 91): "If the funds for a particular research project are coming in over his head in cascades, the scientist may be misled into thinking that he is on to a good thing, no matter what his data show… If he is in possession of sophisticated instruments of great power, and if he is being assured that whatever other new instruments he can think of will be delivered to the door of his laboratory tomorrow, he may find it difficult to stop himself on a dead road of inquiry, even if he knows

[20] "Who will observe the observers?"

it to be dead. I have long believed that there is no scientist alive whose career could not be terminated by an enemy, if the enemy were capable of increasing the laboratory's budget by ten fold or any-fold overnight and, as well, assuring access immediately to any instrument within reach of the victim's imagination". If Thomas is right, there seem to be cases in which the research administration and bureaucracy system seriously corrupt scientific inquiry.

The rush to collect data before the phenomenon is sufficiently understood is the approach of Deweyan pragmatism, which seems to be a dominant worldview in modern America. For Dewey's pragmatism, human action precedes the invention of human forms of thought needed to satisfy the needs of the action. In this case, reality is expected to adapt itself accordingly (of course, there is no historical evidence that reality has made any such commitment to pragmatists--on the contrary). Besides, pragmatists would be surprised how hard it can often be to translate an action into an idea. Deweyan pragmatism is strongly opposed by the Aristotelian worldview. For Aristotle, human thought always precedes human action: first grasping the appropriate facts of reality in an adequate thought mode, on the basis of which the goals and the necessary course of action are set.

The main objectives of SEP should include the development of integrated epidemic *systems*[21] for innovative problem solving and inquiry, and the advancement of public health interdisciplinary efforts to join communities of scholars from a range of disciplines. The SEP, of course, assumes that practicing scientists and scholars and public health research administrators are interested in creating and working in environments that help researchers traverse intellectual, cultural, and organizational boundaries. Remarkably, rather obvious connections with other disciplines are not always adequately appreciated in the context of an epidemic study. Human exposure-health effects is one of these disciplines. The linkage between epidemiology and human exposure-health effects is undoubtedly very strong, especially when the cause of the disease is environmental exposure[22]. As a matter of fact, serious challenges emerge from attempts to link epidemiology-relevant research taking place in a range of scientific disciplines. One of the chief issues is that researchers from different fields approach health problems with different conceptual tools and methodological orientations. No systematic framework exists to synthesize the diverse reasoning modes and knowledge sources of scientists working, e.g., in the fields of infection analysis, environmental transport, contaminant bioavailability, physiological compartmental systems, biochemical transformations, demography dynamics, and population risk assessment, in a way that is more than juxtaposition, more than laying one discipline along side another. At the same time, important notions, such as "exposure", may not be well under-

[21] Generally, a system is viewed as a collection of related elements organized according to a plan and forming a unity. In the case of epidemics, the system may include the infection agents, the exposure pattern, the population (infecteds, susceptibles, removed, etc.), the medium within which an epidemic may propagate, lines of infection, contact processes, as well as their relations and interdependencies in a space-time domain.

[22] In some cases, this strong linkage makes the two disciplines essentially indistinguishable (Haining, 2003).

stood (conceptually and operationally), or their meaning may differ from one discipline to another. In the end, one should not forget that what can count more in these cases is integration of concepts rather than data.

Concerning the public's preparation for future epidemics, a serious effort is dedicated to combining and communicating information from different disciplines to *decision-makers*. Such an effort gives rise to a number of challenges, as well. Due to other non-epidemiologic factors at play (economic growth, technological change, climate variations, etc.), one cannot rely only on past disease data to predict future epidemic distributions; decision-making can be aided by calculating how epidemic uncertainties change with new interdisciplinary knowledge and how they impact potential choices; although certain types of epidemiologic data are often too sparse, valuable information can be transferred from other disciplines, assuming that adequate techniques become available for this purpose; biases exist in the way the human brain forms judgments under conditions of uncertainty, and these biases may be of different kinds depending on the discipline; and there is currently no established methodology for combining multiple expert judgments, especially when these come from various disciplines.

The above are some of the interdisciplinarity issues that deserve to be studied in a wider SEP context. Such a study can potentially produce a paradigm change in certain ways. Next, with the reader's permission, we will make a modest attempt to investigate a few of these ways.

b. Crossing Disciplinary Boundaries

As already mentioned, a number of cases exist in public health, in particular, and in life sciences in general, in which researchers have been actively engaged in endeavors that take them across disciplinary boundaries (e.g., White *et al.*, 1998; Christakos and Vyas, 1998; Pennington *et al.*, 2001; Pybus *et al.*, 2001; Serre *et al.*, 2003; BenMap, 2003; Law *et al.*, 2004). In special circumstances, it may be possible to apply a kind of an isolation condition claiming that the properties of the components of the structured whole can be identified by studying them when they are not incorporated into the structured whole. Their behavior in the structured whole can be then derived from this condition plus statements describing the organized structure in which they are bound and the prevailing epidemic conditions. In the most interesting situations, however, a connection condition applies, in that it is impossible to understand how the components function when bound into structured wholes by simply studying their properties in an isolation condition[23]. These situations are ripe for investigation by those interested in the process of interdisciplinary public health inquiry.

[23] The paramount importance of the connection condition is also demonstrated in the case of the genome project. As was mentioned above, while the genome contains the information on the building blocks of life, it is unlikely that it contains the information on how to connect or relate the building blocks.

It is a well-known fact that major scientific progress often comes from researchers who have crossed conventional disciplinary boundaries, and who had no established authority in the particular discipline. Generally, cognitive reasons that motivate crossing disciplinary boundaries include the recognition that either the public health problem of interest cannot be adequately studied within one discipline, or the problem requires--by its nature--the synthesis of knowledge sources from different scientific disciplines. Epidemic prediction across space-time, e.g., entails blending information from the fields of mathematics, systems engineering, molecular biology, toxicology, climate change, and demography (Christakos and Hristopulos, 1998). Also, Pybus *et al*. (2001) developed a model that builds a bridge between the disciplines of population genetics and mathematical epidemiology by using pathogen gene sequences to infer the population dynamic history of an infectious disease. Several other examples can be found in the relevant literature.

Albert Einstein famously said, "The significant problems we face cannot be solved at the same level of thinking we were at when we created them". Indeed, the reader may agree that, it is not unusual to find out that a public health problem cannot be solved with the same kind of thinking that gave rise to that problem. Therefore, of considerable interest is the development of a paradigm that merges intellectual discourse, ideas, and techniques from different disciplines to produce a new structure, which shows the influence of the ancestor ideas without being a mere "cut-and-paste" combination. In this context, adequate human health assessment is not achieved solely from knowledge of its component parts--it will emerge from the integrated whole. Subsequently, what one seeks from the integrated whole is sound epistemic ideals that can be expressed in terms of mathematical equations for theoretical modelling and applied technology purposes. More to the point, the SEP involves four major phases--adequate *conceptualization*, rigorous *formulation*, substantive *interpretation*, and innovative *implementation*--and every one of these phases requires a group effort of experts from different disciplines who share the integration goal of SEP[24].

c. Inter- and Intra-

If the development of SEP is going to produce rigorous rules for the integrated modelling of knowledge from different disciplines and levels of organization, it must rely on an adequate understanding of scientific intradisciplinarity and interdisciplinarity in an epidemic assessment context. One should point out that:

- *Intradisciplinarity* usually refers to integration activities between sub-fields of the same domain (e.g., genetic and molecular epidemiology; or obstetrics, gynaecology, and paediatrics).

[24] While they will not be discussed in due detail in this book, we are aware that when attempts to cross the disciplinary boundaries are successful, important sociological and political arrangements are emerging as well (Latour, 1988, Thagard, 1999).

- *Interdisciplinarity* involves the synthesis of different scientific domains (e.g., physics, cognitive science, toxicology, systems theory, and epidemiology).

It is worth noticing that, while intradisciplinarity is a rather familiar precept among most scientists, interdisciplinarity is not always a clearly understood and widely accepted concept. As a matter of fact, it is not uncommon for scientists to refer to the latter when what they really mean is the former.

First, for epidemic modelling purposes interdisciplinarity should not be viewed in the same context as the so-called *unification* of science, which refers to the pyramidal hierarchy that reduces one domain of science to another, seeking the unity of science and searching for the ultimate scientific truth (Galison and Stump, 1993). While many scientists oppose the idea of unification (for a variety of scientific, social, political, and economic reasons), the vast majority of them support the cooperation of different domains of inquiry.

Second, one may distinguish between interdisciplinarity producing a new discipline (e.g., biochemistry) and interdisciplinarity involving the *continuing interaction* of a variety of disciplines without leading to a separate discipline (e.g., evolutionary biology). In the former case a group of individuals coming together from different disciplines feed into the same research enterprise, whereas in the latter case individuals are able to successfully develop cross-disciplinary programs through their own research efforts (Bechtel, 1986).

Third, a distinction must be made between interdisciplinarity viewed as a merely *practical activity* happening on an everyday basis (e.g., studying the components of structured whole in isolation and applying arbitrary combinations to yield the final result) and interdisciplinarity considered for scientific research purposes. Interdisciplinarity is considered valid and even necessary in the context of pressing practical public health problems that need attention from experts from a variety of scientific fields to be dealt with effectively. For scientific research purposes, however, interdisciplinarity is usually handled with considerable caution. E.g., some scientists often argue that their discipline is either too incomplete or too non-reductively autonomous to be blended with another one. On the other hand, nothing will ever be attempted if all possible objections must be first overcome.

Fourth, genuinely interdisciplinary and innovative epidemic research should not be confused with *cosmetic* inderdisciplinarity, the latter having a superficial and *ad hoc* interdisciplinary character allowing disciplinary business to proceed as usual at the cheap price of some interdisciplinary rhetoric. E.g., the lack of genuine interdisciplinarity has often led to human exposure research that is based on poor interaction with physical sciences, even when it is obvious that the latter play a vital role in the causal chain leading to the disease.

d. The Interdisciplinarity Argument of SEP

Public health scientists have long struggled with conceptual and methodological issues occurring when the enormous variation of environmental data is juxtaposed with the biological, kinetic and infection processes leading to the generation and

spread of an epidemic across space-time. It seems natural that in the SEP context the interdisciplinarity argument is three-fold:

(*a*) On occasion, it is a fruitful approach to look at one discipline through the lens of another, thus revealing similar, analogical, or conflicting *patterns* between them. E.g., by using differential equations theory, epidemiologists may represent the disease distribution in an exposed population. Or by using models from stochastic physics, toxicologists can predict the fate of toxicants in the human body and make useful epidemiologic inferences.
(*b*) The network of interacting disciplines of space-time epidemiology should be *holistic*, i.e. considered as a whole. E.g., the biological and physiological characteristics of human populations must be blended with the physical, chemical, and biological properties of environmental media to obtain a better understanding of the factors that increase the risk of a disease becoming an epidemic.
(*c*) While disciplinary research concerns one level of reality, interdisciplinarity concerns the *dynamics* engendered by the action of several levels of reality at once. E.g., part of the task in achieving epidemic synthesis is to bring together analyses at different physical, biomedical, and demographic levels to provide a coherent account of a potential epidemic and to assess the factors that can improve scientists' ability to control an outbreak once it has begun.

Beyond the three-fold argumentation, an adequate SEP should account for the two processes operating in parallel:

(*i*) One aiming at increasing what we *know* (by means of experimentation, observation, surveys, computer simulation, theorization, etc.).
(*ii*) One aiming at rectifying the *logical geography* of the knowledge that we already possess. In this context one must be able to talk sense with concepts as well as to talk sense about them (i.e., to know by practice how to operate with concepts inside familiar fields, and to also be able to state the logical relations governing their use).

Bringing together diverse teams of scientists for brainstorming plays a crucial role in implementing the threefold epidemic argument and the two parallel processes above. Through collaboration, consensus building, regular and open communication, and expanding roles across discipline boundaries, the SEP team members could plan and provide synthetic epidemic science.

e. Integrating Modes of Reasoning

Reasoning plays a vital role in all forms of human activities. Nothing expresses the power of reason to transfigure human suffering better than a sentence from the classic French novel *La Princesse De Clèves*: "I told him that as long as his suf-

fering had had limits, I had approved of it and shared it; but that I would pity him no longer if he gave way to despair and lost his reason."[25]

It could be a constructive approach, indeed, that the SEP views interdisciplinarity as a *reasoning* process that entails rigorously formulated logical and cognitive mechanisms (scientific argumentation modes, conceptual metaphors, epistemic principles, mathematical techniques, etc.) in a composite space-time manifold (in which space and time are intimately connected). This proposition contrasts previous views of interdisciplinarity, such as the *ad hoc* multidisciplinary activity precept (i.e., studying the components of structured whole in isolation and applying arbitrary combinations to yield the final result), and the unification of science metaphysical construct (i.e., in the sense of the unity of science and search for scientific truth). Instead, the SEP should refer to a higher-level synthesis process, which defines the means, or the way of working and acting, that produces holistic, integrative knowledge.

The interdisciplinary genre of public health research is problem-centered, participatory, and could involve multiple stakeholders. SEP should contribute, e.g., to the emergence of a cognitive science of human health that involves the application of the science of the mind to epidemiologic ideas and methods. At the center of this effort is learning to *think about thinking* in an interdisciplinary arena. More to the point, the SEP will be confronted with different *modes of reasoning* (or *styles of scientific thinking*) including:

- The Taxonomic
- The Analogical
- The Mathematical
- The Statistical
- The Experimental

While being well aware that epidemic assessments resulting from each one of these different modes of reasoning are not necessarily consistent with each other (e.g., an epidemic assessment may be valid in terms of taxonomic but invalid in terms of analogical reasoning), SEP should nevertheless seek an appropriate integration of the component modes. By focusing on integrated modelling in the methodological sense, the term "integration" covers possible links that can be developed between different physical and life science disciplines, i.e., SEP will be viewed as disunified but interconnected seeking integrated (theoretical and empirical) links and laws. In this manner the SEP can include, e.g., many biological characteristics that link exposure with dose and subsequent disease.

f. The Role of Uncertainty

We cannot think of a better introduction to this section than by quoting Sir Arthur Eddington (1958: 1): "If 'to know' means 'to be certain of', the term is of little use to those who wish to be undogmatic." Indeed, for a variety of reasons dis-

[25] "Je luis dis que tant que son affliction avait eu des bornes, je l'avais approuvée, et que j'y étais entré; mais que je ne le plaindrais plus s'il s'abandonnait au désespoir et s'il perdait la raison" (Lafayette, 1980: 150).

cussed elsewhere (Christakos and Hristopulos, 1998; Christakos, 2001, 2003a), there is not logical certainty in public health sciences. Instead, uncertainty characterizes a plethora of phenomena, such as the space-time distribution of toxicants or the precise molecular effects of environmental factors in relation to the DNA of genes. The future spread and threat to human populations of known pathogens (linked, e.g., to malaria and AIDS) are highly uncertain, as is the case with yet to be discovered pathogens. Considerable uncertainty also characterizes the transmission process of pathogens among humans, their adaptability, the links between pathogen evolution and epidemic processes (within and among hosts), and the potential to infect humans of pathogens found in animals (Grenfell *et al.*, 2004).

Despite the crucial role that the term "uncertainty" plays in public health sciences, no clear insight is available that accounts for its essential conceptual and technical features associated with various scales and levels of organization (e.g., Wimsatt, 1976). In the view of many, it is the "model concept" that is the main source of uncertainty[26], whereas others are concerned with uncertainty introduced by empirical relationships. Actually, most of the natural variables and biomedical systems involved in cross-disciplinary integration are connected and vary in *synergy* across space and time, rather than being isolated and space-time separable, as is often assumed. The concept of synergy has connotations that may determine the meaning of uncertainty associated with the epidemic system. In view of the above considerations, one of the SEP priorities is to examine an *integrated uncertainty* framework through which cross-disciplinary epidemic research can proceed, uncertainty sources (conceptual, empirical, etc.) can be meaningfully interpreted and taken into account with rigor, and valid predictions can be made across space-time. In fact, how to develop and implement efficiently such an integrated uncertainty framework is one of the most important outstanding questions in current public health modelling, one that involves deep and challenging conceptual and methodological issues.

On occasion, exposure studies have used the *organization* inherent in *deterministic* mathematics to represent and predict the behavior of rather simple physical systems, but this approach has basically failed to provide predictive models in life sciences. Instead, the SEP view is that one cannot underestimate the importance of uncertainty in health studies, for its consequences transcend the domains of the two most significant constituents of scientific development: *explanation* and *prediction*. When uncertainty describes a state of incomplete knowledge (due, e.g., to poor understanding of the integrated behavior of bioavailability across disciplines, the factors affecting host susceptibility, intra- and inter-subject variability, biological noise, or mixtures of chemicals acting in synergy) it can serve an inspirational purpose, for it makes it possible to study the role of human conceptualization in creating empirical knowledge across different life support disciplines. Hence, the SEP view is that the rigorous study of epidemic systems should be based on the power of the *stochastic* mathematical theory (Chapter II) that accounts for various sources of uncertainty emerging from cross-disciplinary inte-

[26] E.g., uncertainty due to inadequate model structure (conceptualization) may be far more detrimental to its predictive ability than parameter and data uncertainty.

gration in composite space-time manifolds. In stochastic theory, the physical and life variables of an epidemic system (exposure concentration, fate and transport, incidence rate, mortality, infecteds, susceptibles, etc.) are represented in terms of *spatiotemporal random fields* (S/TRF) in the sense of Christakos and Hristopulos (1998). Briefly, a S/TRF $X(\boldsymbol{p})$ is a collection of possible realizations x for the distribution of the field at space-time points $\boldsymbol{p} = (\boldsymbol{s}, t)$, where the vector $\boldsymbol{s}$ denotes spatial location and the scalar t time (the realizations x are asumed to be consistent with the data available). The uncertainty inherent in the determination of the space-time structure of the epidemic variables of interest is taken into consideration by S/TRF theory in a rigorous mathematical manner. E.g., stochastic characterization of $X(\boldsymbol{p})$ is provided by the probability density function (pdf) f_{KB}, where the subscript KB denotes the *knowledge base* used to construct the pdf. The f_{KB} describes the comparative likelihoods of the various realizations and not the certain occurrence of a specific realization. Accordingly, the pdf unit is probability per realization unit. Further discussion of S/TRF follows in Section II.C.

Stochastic theory accounts in an integrative manner for uncertainty sources and variations arising from multiplicative interactions between factors like imprecision of assays, inter-individual fluctuations in uptake rates, elimination rates, biotransformation, and repairs among persons. Interdisciplinary uncertainty analysis is also crucial in comprehending the mechanisms whereby toxicants induce adverse health effects. By focusing on scientific reasoning processes and cognitive machineries of knowledge integration, distinct features of the theoretical models, empirical approaches, instrumentations and institutional contexts of the disciplines involved in human health studies can be revealed, complex nonlinear interactions can be dissected and analyzed, and a solution of the epidemic problem can be sought that provides a good fit to the cognitive description of the real system incorporating all relevant knowledge sources and associated uncertainties.

g. Epistemic Cognition

Since not all information generated during a scientific study is necessarily correct, recourse to epistemic standards evaluating the "grounds of information" is unavoidable, in most cases[27]. Thus, the role of epistemology in scientific inquiry is often linked to the question of information *reliability*. Cognition, on the other hand, is concerned with the mechanisms of acquiring knowledge, including perception, intuition, and reasoning. It focuses on mental processes that include thinking, learning, judging, and problem solving[28]. In view of the above, another potentially significant departure of SEP from the traditional epidemic paradigm is

[27] "Very practically, in matters of life and death, our grounds for decision and action may eventually depend on understanding what science can tell us, and how far it is to be believed" (Ziman, 1991: 2).

[28] For those readers seeking a detailed presentation of topics like epistemology, cognition, and styles of scientific thinking, good references are Goldman (1986), Harre (2002), and Keller (2002).

the thesis that an *epistemic cognition* solution (which assumes that the relevant models describe incomplete knowledge about the epidemic and focuses on cognitive mechanisms) can lead to more adequate results than the conventional *ontologic* solution (which assumes that the models describe nature as is and focuses on form manipulations). In the epistemic cognition framework, the contribution of cognition is to identify basic knowledge-assimilation, belief-forming, and problem-solving processes, which are then examined by means of the evaluative standards of epistemology. Scientific thinking is viewed as a critical process that is as objective as possible, has a deep appreciation of the various sources of uncertainty, and is versatile enough to change commonly held views and established beliefs as new ideas and evidence call previous views and beliefs into question.

In many public health situations, form manipulations and technical operations by themselves will not suffice (as was noticed before, their mathematical organization structure has been of limited use in life sciences). Often, there is neither a good cognitive reason why a formal fit will be the best representation of the public health data available (even if the fit looks perfect in some "technical" sense) nor any evidence that human minds operate in this way. This situation is, in part, due to the fact that in reality one is hardly ever dealing with an ideal epidemic situation in which all health and physical inputs are perfectly known, the models available constitute an exact representation of the system under consideration, and there are no serious sources of uncertainty present. Unfortunately, these important considerations have escaped the attention of many epidemic modellers. In mathematical epidemiology (e.g., Daniels, 1995; Diekmann and Heesterbeek, 2000) the analysis focuses on deriving ontologic solutions for closed systems that merely satisfy a set of mathematical equations in the purely technical sense mentioned above, thus ignoring the facts that these equations, abstract and dry, provide an incomplete representation of reality and are imperfect constructs of the *human mind*.[29] Since all models in physical and life sciences are constructs of the mind, their solution is likely to be more realistic if its derivation invokes open systems and epistemic cognition notions (e.g., what the mind considers to be the goal of the solution, or how it produces an optimal solution under conditions of uncertainty). It is in an improved understanding of our mental relations to nature that the permanent contribution of the epistemic solution is to be found[30].

To confront these challenges, the SEP proposes to set up a powerful and versatile quantitative public health framework that accounts for clear scientific intuitions, represents multi-scale uncertainties and variabilities that transcend the disciplinary knowledge sources involved, accounts for toxicants acting in synergy, and is capable of extracting and generalizing critical principles of the epistemic cognition process. Several proposals could be made regarding a set of adequate SEP principles. Two of the principles that can potentially play an important role are:

---

[29] Genetics researchers, e.g., are aware of the fact that so much emphasis is often placed on the solution of ontologic models that they are eclipsing careful consideration of what the organism is actually *doing* and what its *goals* are (Cherfas, 1986).

[30] Metaphorically speaking, the matter is "not only to learn to dance, but to learn to judge who is a better dancer".

(*i*) *Teleologic* principle applied at the interdisciplinary core knowledge level (i.e., the knowledge processing level that includes scientific theories, physical and biological laws, statistical relationships, etc., from scientific fields relevant to the system of interest).
(*ii*) *Adaptation* principle applied at the specificatory level (i.e., the knowledge processing level that consists of case-specific details about the system, like hard exposure data, uncertain infection agents, experimental toxicogenomics variables, and secondary biomedical information).

Both the "teleologic" and the "adaptation" principles are viewed by SEP in an epistemic cognition sense rather than as ontologic and evolutionary concepts, respectively, which is the case in the traditional approach. Epistemic cognition may be interested about the unrefined, everyday practices of the laymen as well as the refined, highly specialized methods of the scientists and engineers. In this sense, it involves the entire range of our intellectual efforts to understand our environment and make meaningful predictions about future health risks. After all, whatever meaning one assigns to the term "solution" of a public health problem, the term has far-reaching implications for one's knowledge of the public health situation and, thus, a strong epistemic element.

An attraction of the epistemic cognition component of SEP lies in perceiving the conceptual structure of the subject. In addition, it guarantees the consistency between the *formal* part (mathematical theory, statistical techniques, etc.) and the *interpretive* part (biophysical interpretation of mathematical terms, goal-based cognitive processes, justifications of formal toxicogenomics assumptions, and testable genetic arguments and infection hypotheses)[31]. On theoretical grounds, public health scientists may prefer, e.g., that the SEP includes an epidemic theory that spans disciplines rather than several theories related by a derivation relation.

A constant *interplay* between theory and data (including data from modern technologies, such as genomics and proteomics) could occur in the SEP, where the former plays a central role in illuminating the latter. Theory will also provide us with a means of epidemic assessment and with space-time prediction not directly suggested by compilations of data. Several remarkable issues can be investigated in the SEP framework, such as the case that biomarkers can potentially control for the different exposure routes and give a true integrated measure of exposure, taking into consideration that time constants for biomarkers range from minutes to years and are subject to inter-individual factors related to uptake, elimination, damage and repair, and thus add additional layers of complexity. Experimental and field studies at these different layers will be integrated with abstract mathematical accounts offered by theoreticians (systems analysis, stochastics, multivariable mathematics, fields theory, etc.) and with computational tools provided by the technologists. The SEP is made *operational* by specification and elaboration. As we shall see in the following sections, the principles *i* and *ii* above offer interest-

[31] See also Section II.B.a.

ing suggestions about how to proceed with the mathematical analysis and establish an integrated operational SEP approach[32].

C. Conceptual Components of SEP

In this section we turn our attention to the three main conceptual components of SEP. The discussion involves some abstraction that can actually make things more transparent and simpler, and it can also lead to powerful quantitative tools.

a. Theoretical Construct

Consider an epidemic system representing a public health situation. In SEP, the solution of the system in uncertain space-time environments is neither a fixed nor an absolute matter in the ontologic sense. Instead, an adequate solution has no independent status of its own, but is the theoretical construct of the epistemic cognition process as described in the previous section. This line of thought elicits the first thesis, as follows:

> *Epistemic Thesis*: The intellectual process leading to the solution of an epidemic system should be viewed as the theoretical construct of epistemic cognition.

Indeed, the solution of such a system should follow certain rules of reasoning. But these rules are, in the final analysis, propositions about one's epistemic cognition process. The reasoning rules leading to a solution in uncertain space-time domains do not constitute an independent ontologic entity, but they are rather implicit in the epistemic cognition process that enforces them. It is actually an aid in the search for knowledge about epidemics and their public health consequences to understand the nature of knowledge we seek, which is an epistemic task. According to critical conceptualism (Christakos, 2003a), concepts and knowledge sources are linked by sound reasoning to provide rational support to scientific modelling. Conceptual difficulty is directly related to logical complexity (Feldman, 2000), in which case a lucid logical structure could be essential in the solution of the epidemic problem, as well. Remarkably, the epistemic cognition schema is more general than the logical one, because it involves representations and procedures (diagrams, visual images, mental metaphors, etc.) that may be not found in formal logic. The mental tools of epistemic cognition can also explain the discovery of

[32] It is worth noticing that the SEP could be conceived as dealing with the integration of epistemic cultures, and not only with the integration of interdisciplinary knowledge sources. At present, however, the mathematical formulation of the epidemic problem is mainly concerned with the latter.

new concepts and offer solid support to assumptions concerning the epidemic system.

If one continues to indulge the traditional habit of regarding the ontologic approach as absolute and independent of any cognitive influences, one may miss the opportunity to look at the frontiers of scientific research (cognitive science, system theories, stochastics, neurosciences, epistemology, etc.) for a better understanding of the epidemic solution process or for the means of real-world validation and refinement.

b. Knowledge Bases: General and Specificatory

Knowledge is a relationship between the knower and the known (e.g., knowledge may denote a mental state that bears a specific relationship to some feature of the world). The acquisition, categorization and processing of the various types of knowledge available to humans are major issues in public health. Thus, a specified type of knowledge is often intimately linked with the method used to acquire it from a relevant source (e.g., physical knowledge is the kind of knowledge acquired by the methods of physical science). The existence of a plethora of distinct information sources and data (physical, biological, demographic, etc.) to be accounted for during an epidemic assessment process makes it plausible to categorize them in terms of knowledge bases (KB), as follows:

> *Categorization Thesis*: One can distinguish between two major categories of knowledge, viz. the general or core KB ($\mathcal{G}$) and the specificatory or site-specific KB ($\mathcal{S}$).

This is a fundamental SEP thesis that may need some additional interpretation and justification. In *neurosciences*, one of the three major properties of cortical memory in humans is the "invariant" representation, which refers to the fact that the human brain preserves the core knowledge of the world (*mutatis mutandis*, the $\mathcal{G}$-KB of the Categorization Thesis), independent of the specific details ($\mathcal{S}$-KB). As Hawkins (2004) points out, memories are stored in a form that captures the essence of relationships. Then, a human understands the world by finding invariant structures on the basis of its stored knowledge. However, this invariant structure alone is not sufficient to use as a basis for making predictions. In order to make predictions the brain must blend knowledge of the invariant structure (vis-à-vis, $\mathcal{G}$-KB) with specific details about the situation under consideration ($\mathcal{S}$-KB). Similarly, the distinction between general and site-specific KB may find considerable support in *sociobiological* studies, which have demonstrated that at a very fundamental level the goal of human behavior is to distinguish between sensory data ($\mathcal{S}$) and stored knowledge ($\mathcal{G}$) of the structure of the world, and then to use them to generate motor responses that are adaptive, i.e., they seek high inclusive fitness for an organism (Wilson, 1975). Furthermore, the Categorization Thesis may find an interesting metaphor in the field of modern *evolutionary epistemol-*

ogy[33]. Indeed, both Darwinian evolutionary theory and traditional epistemology are accounts of the growth of knowledge. Evolution is itself a knowledge process in which information regarding the environment is incorporated in surviving organisms through the adaptation process (Radnitzky and Bartley, 1993). Two kinds of knowledge are assumed in an evolutionary epistemology context: *Endosomatic* knowledge, as incarnated in organisms through adaptation (corresponding to $\mathcal{G}$-KB); and *exosomatic* knowledge, as encoded in new experiences with the environment ($\mathcal{S}$-KB). In the former case there is an increasing fit or adaptation between the organism and the environment when its stored templates model stable features of the environment, whereas in the latter case there is an increasing fit between theory and fact. In the evolutionary epistemology context, $\mathcal{G}$-KB is combined with $\mathcal{S}$-KB in an appropriate manner--in evolutionary epistemology terms this means that the two kinds of knowledge are adaptationally continuous.

What KB will be synthesized to solve a public health problem is contingent on the nature of the solution as well as the current stage of development of the various disciplines involved. Since our focus is the realm of quantitative public health science, the Categorization Thesis is mostly concerned with KB that can be expressed in mathematical terms. The $\mathcal{G}$-KB may include human constructs like scientific theories, physical and biological laws, and primitive equations developed in various disciplines of physical and life sciences. The $\mathcal{S}$-KB consists of site-specific details of the real-world epidemic system, like hard data, uncertain observations, and secondary information sources. The $\mathcal{G}$-KB refers to all those information sources that are relevant to the public health situation under consideration but their domain of application far transcends the specified situation. The $\mathcal{S}$-KB, on the other hand, refers solely to the specified epidemic system. The union of these two major KB is often denoted by $\mathcal{K}$, which is the total KB available regarding the epidemic system, i.e. $\mathcal{K} = \mathcal{G} \cup \mathcal{S}$.

Example C.1. The variety and diversity of the disciplines involved in an epidemic study can be quite astonishing. In the historic case of Black Death, integrated epidemic modelling involves knowledge bases from quite a few different disciplines and levels of organization, such as:

Epidemiology	Zoology	History	Linguistics
Public Health	Entomology	Literature	Sociology
Geography	Biology	Arts	Economics
Demography	Genetics	Religion	Politics
Agronomy			

Clearly, in the case of the Black Death epidemic other sources of insight must be sought in addition to those generated by scientific techniques. In Chapter III we visit the various interdisciplinary information sources above in considerable detail.

[33] In simple terms, evolutionary epistemology is concerned with the study and understanding of knowledge through the use of evolutionary theory.

c. Knowledge Synthesis

We are now ready to focus on the third main conceptual component of SEP. In view of the above considerations, it would be reasonable to use an adaptive approach, in the sense that it provides a good fit to the cognitive description of the real-world epidemic system and accounts for all relevant knowledge sources ($\mathcal{G}$- and $\mathcal{S}$-KB) and their associated uncertainties. In accordance to what has been said in more than one places of the preceding text, the crux of this view is that the SEP solution to the epidemic problem cannot be achieved solely from knowledge of its parts--it emerges from the integrated whole itself. This insight leads to the following fundamental thesis, from a methodological viewpoint:

> *Synthesis Thesis*: The study of an epidemic system is reducible to a knowledge synthesis problem.

This thesis resides on organized connectedness between the various elements involved. In the SEP context, we consider the meaning of such a connectedness that is conferred by what might be described as *operational* or *functional* connectedness. This is the kind of connectedness that elevates a collection of parts into a functioning whole--i.e. a whole capable of functioning. In other words, the SEP solution to an epidemic problem evolves out of knowledge synthesis principles, the latter understood in a cognitive sense subject to epistemic standards.

Example C.2. A simple but sufficiently instructive knowledge synthesis situation may be the following. In the circumstances shown in Fig. 2 the $\mathcal{G}$-KB consists of: (i) the light travels in straight lines, and (ii) the laws of trigonometry. The $\mathcal{S}$-KB includes: (a) the wall casts a shadow $s = 40$ meters long, and (b) the angle of the sun's elevation is $\theta = 26.6$ degrees. A rather straightforward synthesis of the two KB allows one to predict that the wall's height is $h = 20$ meters.

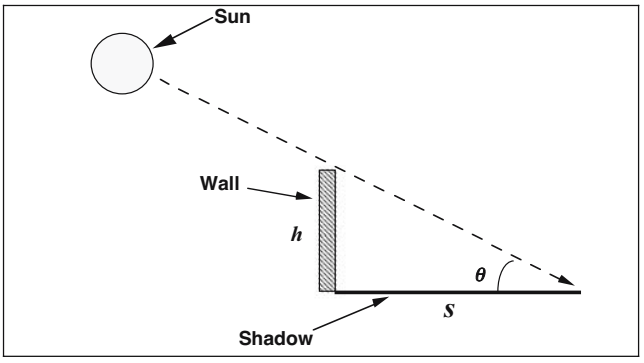


Figure 2. A case of knowledge synthesis leading to valid predictions.

Without question, in real world epidemics the situation is much more complicated than the example of Fig. 2--although remarkably some of the basic principles remain the same. The real world KB are more sophisticated, there are various forms of uncertainty involved, a probabilistic assessment of the epidemic system is sought, etc. Nevertheless, taking into consideration the preceding theses, the mathematical formulation of knowledge synthesis involves *teleologic* (in the human teleology or teleology of reason sense) and *adaptation* (in the human cognition sense) principles, which can embrace diverse phenomena and interdisciplinary descriptions in a single scheme, as follows:

$$\left.\begin{matrix} \mathcal{G} \xrightarrow{\mathcal{T}} PF_{\mathcal{G}} \\ \mathcal{S} \end{matrix}\right\} \xrightarrow{\mathcal{A}} PF_{\mathcal{K}} \qquad (1)$$

At this point, our aim is to give an abstract yet informative representation of the conceptual SEP components in terms of Eq. (1). The $\mathcal{T}$ and $\mathcal{A}$ denote the teleologic and the adaptation principles, respectively; the former operates on the $\mathcal{G}$-KB, whereas the latter involves the $\mathcal{S}$-KB (these two KB refer to all relevant interdisciplinary variables across space-time under conditions of uncertainty); $PF_{\mathcal{G}}$ is a probability function derived teleologically from the $\mathcal{G}$-KB, and $PF_{\mathcal{K}}$ is a probability function that updates $PF_{\mathcal{G}}$ in view of $\mathcal{A}(\mathcal{S})$. The $PF_{\mathcal{K}}$ accounts for the total $\mathcal{K}$–KB, $\mathcal{K} = \mathcal{G} \cup \mathcal{S}$, and constitutes the final outcome of the knowledge synthesis process.

To some of our readers Eq. (1) may seem as a strange-looking equation that stares at the reader like a hieroglyph. It will acquire, however, significant meaning when a more detailed mathematical analysis is attempted in Section II.D and following chapters. Indeed, the conceptual scheme underlying Eq. (1) is both meaningful and powerful. It can integrate all relevant public health information sources, generate a collection of rigorous formulas, and provide useful insight. We are not only concerned with utilizing these formulas (in terms of mathematical techniques, computer libraries, etc.), but also with the *meaning* we can attach to them. This meaning is intimately connected with the human mind and its cognitive powers, and is not necessarily an ontologic feature of the real world.

D. Epidemic Causality as an Interdisciplinary Affair

a. The Chain Concept

In an integrated public health situation, a central role is often played by the concept of *epidemic causality* or *causation*[34]. This concept links potential causal factors (infectious agents, environmental exposures, etc.) and the resulting health ef-

[34] Relevant terms in epidemiology are “etiology” or “aetiology”.

fects (mortality, incidence rate, etc.) One can clearly distinguish between causation at the *individual* level and causation at the *population* level (large scale), which is the main interest of most epidemic studies. There are at least two expressions of the epidemic causation concept, as follows:

- An expression is the typical *disease transmission chain*, in which the group of hosts is exposed to an environment carrying the disease-causing organism; then this group transmits the organism to other hosts, and the process continues eventually leading to an epidemic (e.g., Anderson and May, 1995).
- Another expression is the *environmental causal chain* (Buringh, 2002). This chain involves a complete course of events, starting with a variety of ambient sources (generating emissions, transformations, and dispersions), followed by ambient concentrations and levels of exposure which, in turn, lead to personal exposures and body burden (by way of pharmacodynamics-toxicokinetics) and which, eventually, can cause significant physiological changes and possibly a serious epidemic.

In both the disease transmission and the environmental chains the underlying process is basically interdisciplinary. Furthermore, in many causality studies, another important factor is the so-called *confounding*. Loosely speaking, confounding refers to the confusion or mixing of various (possibly interdisciplinary) effects. Confounding is an important parameter in the determination of a disease causation, in the sense that it can mix the main cause of the disease with some other effects. In environmental epidemiology, confounding may refer to a situation in which a measure of the effect of an exposure on risk is distorted because of the association of the exposure with other factors that influence the outcome of interest (Last, 1995: 35).

b. Some Important Features

There are fundamental differences (conceptual and technical) between the existing views about causality. As a matter of fact, any adequate causation analysis should seek answers to a long list of questions. Critical conceptual and methodological questions include the following:

- Is disease causality logical or physical?
- Does disease causality links events, facts, or processes?
- Is epidemic causality a mechanistic (efficient) or a teleologic (final) type of causation.
- What is the conceptual distinction between theoretical and empirical probability in public health.
- Should an epidemic causality approach use the epistemic, the ontologic, or the modal conception of scientific explanation?

- Are the causal laws of nature more basic than the causal relations between events?
- Under what conditions can prediction serve as causal explanation of diseases?
- What is the relationship between causal and non-causal state of affairs?

Among a plethora of decisive technical questions concerning disease causality are the ones listed below:

- How meaningful are the causal inference checklists and statistical techniques?
- What part of the environment might be to blame for carrying an infectious agent?
- Which are the different exposure factors causing/influencing an infection? Are these factors interrelated?
- Which are the possible confounding factors, and how is it possible to adjust for them?
- Under what conditions does a contact lead to transmission, and which is the contact process?
- What are the relevant contributions of multi-causality, strength of a cause, interaction between causes, sum of attributable functions, and induction time?

In this section we will be limited to a very brief discussion of some of the above considerations[35]. Some scholars view disease causality as a mental (logical) construct, whereas some others suggest that it is an objective part of the structure of the real world (see, e.g., Mackie, 1974). A group of health scientists (e.g., Aickin, 2002; and references therein) have suggested that epidemic causation can be analysed in terms of necessary and/or sufficient conditions. While Mellor (1995: xi) maintains that "causation links not events but facts", Aickin (2002: 13) agrees with Mackie that "causation is a relationship that holds between events". On the other hand, Salmon (1998: 16) proposed to us "to focus our attention on processes instead of events (or facts)".

Epistemic conception views causal explanations as arguments (i.e., mental constructs), *ontologic* conception sees explanations as fitting in to patterns and regularities of the real world, and *modal* conception assumes that causal explanations show that what did happen had to happen (see, e.g., Hempel and Oppenheim, 1948; Scriven, 1975; Mellor, 1995). In life sciences, in general, there are cases in which one is talking about efficient causation (i.e., having a rather mechanistic character) vs. teleologic causation (i.e., involving reference to purposes), see Allen *et al.* (1998).

A conceptual distinction between two different effective uses of probability in public health sciences could be as follows: a theoretical definition of probability

[35] The interested reader is encouraged to study the original references and form his/her own view of the causality problem.

at the level of individuals, and an empirical definition at the population level. The former involves a theoretical meaning enrooted in its epistemic context, whereas the latter has a practical meaning expressing results of observations, surveys, etc.

Methodologically, causality has been associated with *explanation* and *prediction*. In most cases, indeed, to explain a disease is to find its cause. There are, however, some other situations in which the concepts of explanation and causation can have different ranges of applicability (e.g., one may explain the spread of an epidemic in non-causal space-time terms). Nevertheless, while not all explanations in public health sciences are causal, in most cases knowledge of the relevant causal relations can help us explain important phenomena and gain a better understanding of the epidemic system.

The situation is not so clear as far as the relationship between causal explanation and prediction is concerned. It seems rather appropriate to bring to the fore the often *asymmetric* character of this relationship, as follows. In some cases, it is true that the same KB that generates sound predictions may be used to produce meaningful causal explanations of the phenomenon. E.g., suppose that epidemiologists predict the spread of a disease on the basis of knowledge about the environmental conditions, and these predictions turn out to be correct. Obviously, some argue, the same environmental knowledge that was used to predict the spread of disease before it happened, will serve to explain the same event after it has happened. Anyone with a soul can feel the elegance of this obvious symmetry. But the problem with the obvious is that it sometimes can make one overlook the evidence. Indeed, as it turns out, the symmetric character of the relationship between causal explanation and prediction is not always the case. In fact, there are situations in which the KB that serve to predict a phenomenon (before it occurs) may not be able to explain it as well (after it has occurred).

Example D.1. Let us revisit the case of Fig. 2. As we saw, the $\mathcal{G}$- and $\mathcal{S}$-KB available made it possible to predict that the wall's height is $h = 20$ meters. However, these KB cannot provide an explanation of it. Instead, a plausible causal explanation would be that the wall was *built* to be 20 meters high, which is independent of the $\mathcal{G}$- and $\mathcal{S}$-KB above.

Some efforts have been made to apply a list of causation criteria discussed in Hill (1965), although with limited success[36]. As a consequence, many epidemiologists have concluded that the causation problem cannot be solved simply by means of causal inference checklists or statistical techniques (e.g., Rothman, 2002: 15).

As it turned out to be the case, an efficient detection of potential confounders should study the exposure variables causing or merely influencing an infection, assess if and how these factors are related with the potential confounders, characterize the nature of the relationship in a causality context, etc. At the individual level, a definite proof of the actual cause of the disease is a task that should in-

[36] This checklist is essentially based on certain philosophical considerations of causality suggested by Hume and Mill.

volve the scientific study of the biological characteristics of the disease, among other things[37]. According to Thagard (1999) the causal explanations of many diseases may fall under a set of basic patterns or organized schemas. This different kind of unification may be necessary, since health science is not like physical science, in which a set of mathematical equations and the associated boundary/initial conditions in many cases can provide unified causal explanations for a considerable variety of phenomena.

Example D.2. Fig. 3 outlines the causal explanations of infectious (germ), noninfectious (nutritional), and molecular (multifactorial) diseases. The germ theory suggests that some diseases are caused by microorganisms (e.g., cholera and tuberculosis). Other diseases are caused by vitamin deficiencies (beriberi, rickets, etc.). Yet a large variety of multifactorial diseases may be caused by the interaction of inherited genes and environmental factors (e.g., cancer). More involved molecular genetics schemes of causal explanation are also used, such as the following (Thagard, 1999: 28): genes encoded in DNA → DNA specifies RNA synthesis → RNA specifies polypeptides synthesis forming proteins → mutations producing DNA changes → mutated DNA altering protein production → abnormal functioning of the individual → symptoms and disease. E.g., a mechanism has been identified by which smoking causes lung cancer (benzo[a]pyrene produces mutations in the tumor suppresser gene *p53*, etc.; Denissenko *et al.*, 1996).

In most public health circumstances the determination of causation is, indeed, a very important but technically difficult problem[38]. Large scale epidemic modelling cannot offer, in general, a definite proof of the actual cause of the disease, although on occasion it could provide valuable clues regarding the possible cause of a disease (suggesting causal hypotheses, etc.). In principle, the concept of causation in an epidemiologic context involves the study of a multitude of factors, such

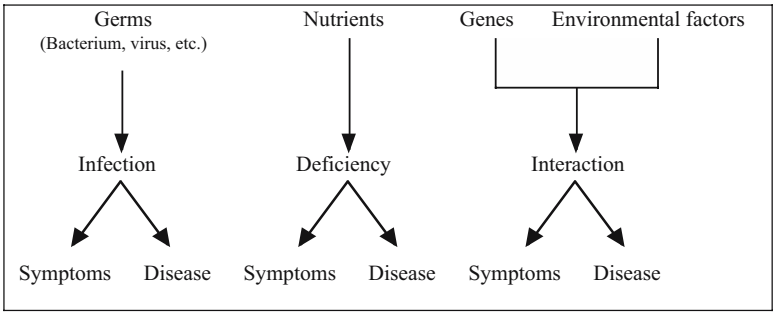


Figure 3. Examples of causal explanation schemes for germ, nutritional, and multifactorial diseases.

[37] See, e.g., Schulte and Perera (1993).

[38] Certainly, not a problem to be solved by means of a "causal pie" approach (Rothman, 2002: 9ff).

as: the combined action of several processes contributing to the cause-effect mechanism (certain of these processes may lie outside the boundaries of epidemiology)[39]; the characterization of cause-effect in association with populations rather than individuals; the space-time domain of causation; and the underlying scientific reasoning providing a mental representation of causality that is consistent with real world evidence.

c. A Brief Categorization of Causality Approaches

By way of a summary, a critical study of epidemic causality should take into consideration four important theoretical characteristics of the causation concept: *deterministic* causation (effects are completely determined by causes) vs. *indeterministic* causation (effects are not completely determined by causes, e.g., they are characterized as *stochastic*); and *mechanistic* causation (efficient causes are involved) vs. *teleologic* causation (final causes are involved). Different epidemic causation approaches involve different combinations of these characteristics. Below we briefly discuss some examples of such approaches.

Deductive-Nomological Approach

This is an essentially deterministic view of epidemic causality according to which the causal explanation of an effect is obtained by means of valid deductive arguments (Hempel and Oppenheim, 1948). This kind of an explanation would be possible only if all the relevant mechanistic laws (physical, biological, etc.) linking exposure and health effect were perfectly known for each individual in the population. Although very desirable, such an approach is very rarely materialized in public health practice. Other kinds of difficulties also exist. According to the deductive-nomological approach, explanation and prediction are symmetric processes. However, as we saw above (Example D.1), this is not always the case in real world applications. Also, in some other cases causal explanations rest on mechanisms that may be insufficient to warrant prediction. A thorough discussion of the serious hidden difficulties of the deductive-nomological approach can be found, e.g., in Salmon (1998).

Thus, although in theory the highest level of causal order is certainly offered by the traditional determinism, due to the serious problems of the deterministic approach (insufficient knowledge, complex mechanisms at work, luck of empirical support at the population level, etc.), the majority of modern epidemic studies focus on indeterministic interpretations of causality.

Inductive-Statistical Approach

This is an indeterministic approach that replaces the deductive-nomological concept by a scheme in which causality is manifested in terms of an almost perfect

[39] Some factors may cause things, whereas some others may merely affect them.

statistical correlation between exposure and effect. Clearly, the inductive-statistical approach is not free of some serious complications. One problem with correlation-based approaches is that, while correlation is a symmetric relation (e.g., if cigarette smoking is correlated with cancer, then cancer is correlated with smoking as well), causation is basically non-symmetric (e.g., the fact that cigarette smoking causes cancer does not imply that cancer causes smoking). It is worth-noticing that, while statisticians favor Fisher's randomized experiment as the main approach to causal inference, this approach has serious problems when applied to life science problems. E.g., Shipley (2000: 14) suggests that, "the randomized experiment is unsuited to much of biological research". Another important issue is the relationship between causality referred to single events (aleatory causality) and causality related to populations of events (property causality), see Galavotti *et al.* (2001).

Another variant of the inductive-statistical approach seeks to determine associations by comparing separate maps of health effects and environmental exposures across geographic areas or over time, using multivariate statistics to establish correlations between health effects and exposures. There are certain problems with this technique as well (e.g., several cases are reported in the scientific literature in which the technique led to incorrect conclusions; Krewski *et al.*, 1989).

Difficulties with the previous techniques have led to the development of improved procedures that establish a more drastic break with the deductive-nomological concept, as follows.

Probabilistic Conditioning Approach

In a certain context, this indeterministic approach replaces the notion of statistical inference with that of statistical *relevance* (Suppes, 1970). The approach assumes that the presence, or the introduction, of a genuine cause (exposure or infection) must make the occurrence of its health effect more likely than if it had not been present. This means that this approach associates the causes and the health effects with a probability distribution, which is the most complete information attainable. Then, the approach is formalized in terms of conditional probabilities (e.g., the probability of the effect given the occurrence of the specified exposure or infection is greater than the probability of the effect given that the exposure or infection did not occur). Some of the fundamental difficulties of the probabilistic-conditioning approach are discussed in Dupre (1993).

An interesting variant that has received considerable attention in recent years is the so-called *Bayesian network* method (sometimes also called causal network method). The network consists of a structural component that represents causal relationships and a probabilistic component that assess the strength of these relationships. A detailed presentation of the method and its range of potential applications can be found in Pearl (2000).

A rigorous application of the probabilistic conditioning approach generally should account for important factors, such as the different causally relevant contexts in which an exposure or infection may occur, physical and biological con-

nections between events and facts, intermediate causes, and the different paths that may link an exposure or infection to an effect.

Integrative Prediction Approach

This is a stochastic approach that differs from the previous ones in certain subtle ways. Firstly, it assumes that causation is an interdisciplinary affair that can be adequately studied as an integrated *knowledge* process (Christakos and Hristopulos, 1998; Christakos, 2001). It is well known that a causal mechanism often involves the combined action of several component causes. The human mind seeks to construct a cause-effect model that integrates the component causes associated with different disciplines and scientific fields in order to reach a sound conclusion regarding causation.

Secondly, the cognitive meaning of causation lies in its potential for improved *integrative prediction*. This kind of prediction combines logical and natural laws, and assumes that the existence of a cause-effect association should lead to more accurate disease predictions when information about both (a) the potential causal factors (physical, ecological, environmental, etc.) and (b) the health effects (disease distribution, epidemic observations, etc.) is integrated than when only health effect data is used (see, Example D.3 below).

Knowledge integration is a crucial factor that distinguishes this approach from some previous causality methods based on predictability. Indeed, integrative prediction does not have certain of the difficulties of these methods (such as, the effects of the possible explanation/prediction asymmetry in the deductive-nomological method). Another important feature of this approach is that prediction is understood as a product of human teleology (teleology of reason), in which case prediction is likely to be more realistic if it is derived via a theory of knowledge. By blending physical, ecological, and biological measurements of potential causes with general and specificatory epidemic features of the effects in a space-time manifold, prediction accounts for various sources of uncertain knowledge, as well as for inter- and intra-subject variations of the specified populations. In view of the above considerations, epidemic causality is not merely a relation between a potential causal factor and a health effect, but a knowledge synthesis process involving potential causal factors[40], health effects, and a specified population (which, in a public health context, usually refers to a group of representative receptors).

Example D.3. This example is from a study by Christakos and Serre (2000). Let the S/TRF X_p denote cold temperature exposure (in ^{o}F) and D_p denote death rate (in deaths per 100,000 people per day) in the state of North Carolina. An integrative prediction measure of the X_p-D_p association is as follows:

[40] Depending on its form, a potential cause may be described in terms of information concerning its biological features, level, duration, frequency, contact process, and a set of possibly interrelated factors (e.g., acting in synergy).

$\beta_{DX} = (E_{DX} - E_D)/E_D$ (in %), where E_{DX} is the death rate prediction error based on D_p and X_p data, and E_D is the death rate prediction error based on D_p data only[41]. In Fig. 4a the β_{DX} is plotted as a function of time (days) for the 1996 winter season (E_{DX} and E_D are spatial prediction error averages over North Carolina). The β_{DX} is consistently negative, which according to the integrative prediction theory above supports a X_p-D_p association during this time period. The β_{DX} magnitude is indicative of the strength of the X_p-D_p association; as is shown in Fig. 4a the association is of varying magnitude in time. In Fig. 4b the spatial distribution of the X_p-D_p association at the population level is represented by the β_{DX} map (in this case, the E_{DX} and E_D are temporal prediction er-

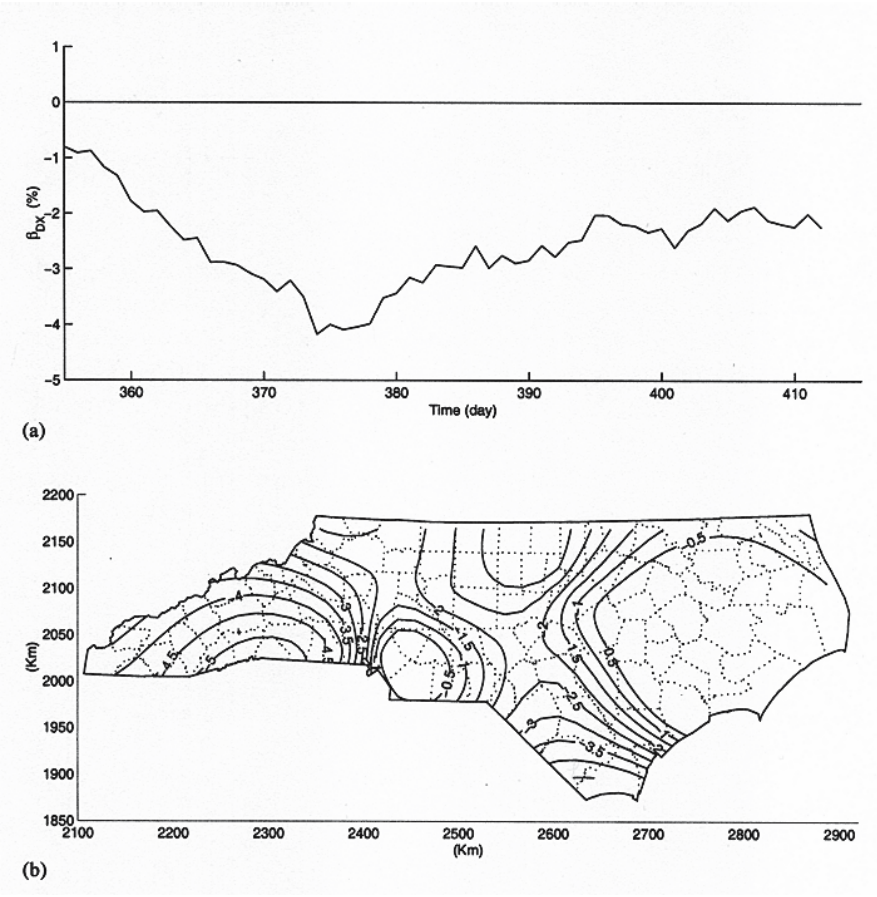


Figure 4. (a) Time profile and (b) spatial map of β_{DX} (in %); winter of 1996.

[41] Space-time predictions and prediction errors can be calculated using random field techniques, see Chapter II.

ror averages calculated for each one of the state counties). The map of Fig. 4b shows a stronger X_p-D_p association in the mountainous area (south-west part of North Carolina), whereas a weaker association occurs at the eastern part of the state (near the ocean) and, also, in the urban area near the city of Charlotte (south-central part of the state). These geographical differences may be due to two factors: the moderating influence of the ocean on cold temperatures (less fluctuations and milder cold temperature peaks), which probably explains the weaker effect of the latter along the coastline; the living conditions (exposure to cold temperature is usually higher in mountainous, rural areas, than in urban areas near large cities, due to the impact of environmental conditions, transportation, etc.). Next, a possible con-founder P_p was been identified, viz. PM_{10} exposure (particulate matter is a possible confounding factor as it may have causal associations with D_p while being correlated with X_p data). To incorporate this confounding effect in the analysis we let $\beta_{DXP} = (E_{DXP} - E_{DP})/E_D$ (in %), where E_{DXP} is the death rate prediction error based on the combination of D_p, P_p, and X_p data, and E_{DP} is the death rate prediction error based on D_p and P_p data only. The β_{DXP} measures the improvement in D_p predictability from knowledge of X_p when the confounding effect of P_p has been removed. Then, by comparing β_{DXP} vs. β_{DX} one can assess the importance of P_p in the X_p-D_p causal association[42]. The β_{DXP}, which accounts for the composite X_p-D_p-P_p distributions, is plotted in Fig. 5a vs. time. Also plotted in the same figure is the β_{DX} (which did not account for the confounding effect of P_p). These plots show that accounting for the potential confounder PM_{10} results only in a slightly different strength in the reported association between the X_p-D_p distributions for the winter period (the β_{DXP} and β_{DX} values show small differences). Moreover, the spatial β_{DXP} map, plotted in Fig. 5b, is almost identical to that obtained for β_{DX} (Fig. 4b). Both Figs. 5a and b seem to support the view that knowledge of the PM_{10} distribution does not have a significant confounding effect on the association between cold temperature exposure and death rate distributions in space-time.

We conclude this section by suggesting that a serious interdisciplinary research effort is needed to comprehend the "Tower of Babel" character of epidemic causation. Any adequate causality analysis should seek answers to long lists of questions that may span a variety of scientific disciplines and could account for multi-sourced knowledge in a rigorous integrative manner.

[42] The same approach may serve to evaluate competing causal theories by means of prediction accuracy at a set of critical observation points.

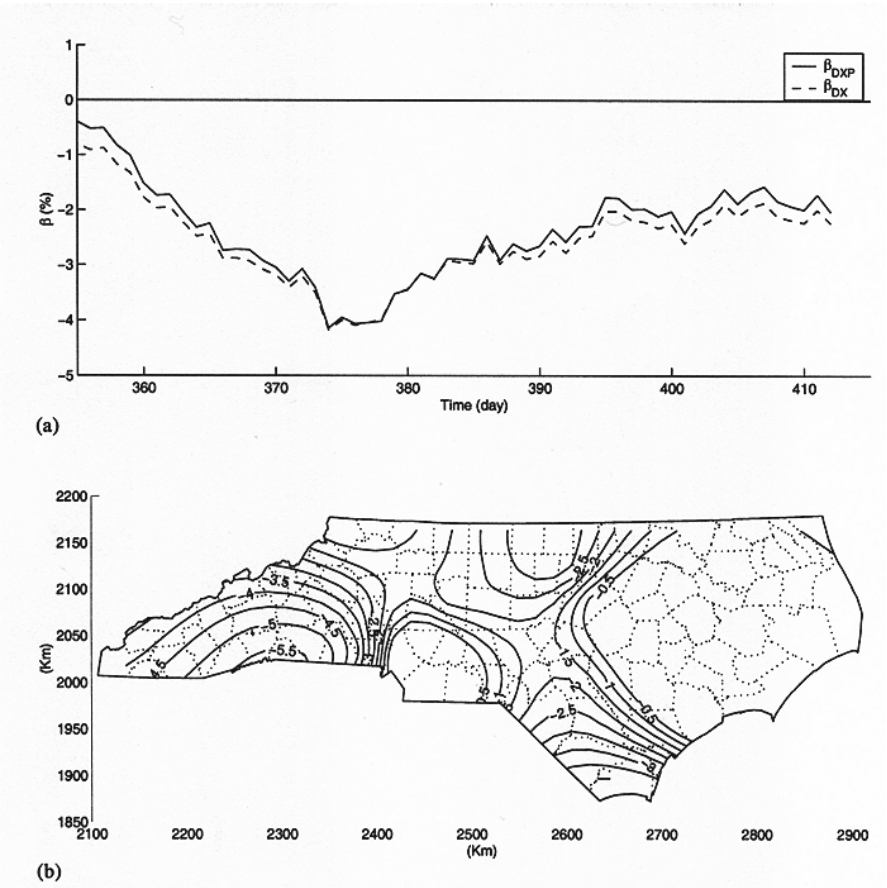


Figure 5. (a) Time profiles of β_{DX}, β_{DXP} and (b) spatial map of β_{DXP} (%); winter season.

E. Focusing on Black Death

In *The Grand Inquisitor* the cardinal warned his prisoner (Dostoevsky, 2003: 10), "For the secret of man's being is not only to live but to have something to live for." For most of the people living in Europe during the times of Black Death, neither of the above seemed to be an option.

a. Lunch with Friends and Dinner with Ancestors

Perhaps, one of the most imaginative and at the same time succinct descriptions of the severity and the terrible speed with which Black Death struck its victims is that

of the famous Italian writer Boccaccio: "The victims of Black Death often ate lunch with their friends and dinner with their ancestors in Paradise". Also, "La Danse Macabre" (or the "Dance of Death") is a late-medieval allegory on the universality of death that was produced under the impact of the Black Death epidemic. It was expressed in the form of woodcuts, paintings, or frescos in churches, which usually consisted of the personified Death leading a row of dancing figures from all walks of life to the grave (Fig. 6). These images reminded people of how fragile their lives were and, also, how vain the glories of earthly life were. Before we proceed with the details of our Black Death study, it may be instructive to briefly review the situation in Europe by the time of arrival of Black Death.

Several changes in 14th century AD Europe were driven by a climatic change called the "Little Ice age" that brought to the continent wetter and colder weather (Gottfried, 1983: 23-24). The change resulted in bad crops, thus paving the way for famine. The situation was most critical between 1309 and 1325. The crisis resulted in a debilitated population that saw unprecedented levels of massive mortality (which, nevertheless, paled in comparison to the Black Death mortality that was to follow). Some scholars have argued that several of the survivors of the famines were ill prepared to fight a serious disease like Black Death because their bodies received improper nutrition at a critical stage of childhood development. Another cause contributing to the high mortality of Black Death was certainly the state of medical science, which at the time was far from having a correct under-

Figure 6. An image of "La Danse Macabre" by Hans Holbein. It shows Death leading a row of dancing figures (typically a king, pope, monk, youngster, beautiful girl, all in skeleton-state).

standing of human physiology and disease etiology, even for the simplest of diseases. The result was inadequate treatments. Moreover, the living and sanitary conditions were favorable for the transmission of diseases. Houses of ordinary people were crowded (Fig. II.5); their floors were dirty; the quarters were shared with all kinds of animals; bathing was rare; and the water supply was frequently drawn from contaminated sources. Streets were narrow, without pavement, serving simultaneously as roads, sewers, and unsanitary fills for refuse and dead animals. The plague crisis proved to be instrumental for cities to start enforcing some minimum public sanitary codes.

The study of the Black Death epidemic of 1347-51 in Europe has regained considerable interest nowadays (Naphy and Spicer, 2000; Cantor, 2001; Cohn, 2002a and b; Wheelis, 2002; de Hahn, 2002; Orent, 2004; Scott and Duncan, 2004). Since Black Death had grave consequences (societal, public health, and financial), a quantitative understanding of the epidemic distribution characteristics across space-time can offer valuable insight regarding these consequences, as well as about similar situations with potential contemporary epidemics. Furthermore, several experts argue that the plague was a virus similar to AIDS and Ebola that has only lain dormant, waiting to emerge again--perhaps in another form (Scott and Duncan, 2004). Taking into consideration the periodic occurrence of plagues throughout history, these researchers predict its inevitable re-emergence sometime in the future, transformed by mass mobility and bioterrorism into an even more devastating killer. Scott and Duncan (2004) also maintain that the explosive increase of adventure traveling to exotic places is increasing the exposure of people to high biodiversity environments that in the past have been the source of serious diseases.

One should admit that modellers can be spoiled by data abundance: waiting until vast amounts of data become available, hoping to make the application of mathematical techniques a rather trivial procedure. However, genuine scientific progress often depends on the scientist's choice to develop creative theories and models in view of limited and highly uncertain information, rather than to proceed in a routine fashion by collecting large amounts of data and then applying mathematical techniques mechanically[43]. In view of the above considerations, we will restrain from rhapsodizing on the matter, apart from noticing that we selected Black Death as the main SEP case study specifically to consider a hard nut to crack. Indeed, any attempt to model the Black Death epidemic is seriously limited by the fact that most of the evidence lies far in the past. Hence, unlike modern epidemic databases, which often include a significant amount of hard scientific evidence and can readily use a host of modern tools[44], the Black Death databases lack any of the above, instead being fundamentally historical. These databases are notoriously uncertain, inherently heterogeneous, and usually based on indirect ac-

[43] Not to mention that in several applications a huge collection of data must be confronted, little of which is really relevant to the problem. In these cases theoretical modelling can be a valuable tool in the effort to find meaningful patterns that will make sense out of shapeless heaps of data.

[44] See, e.g., Schulte and Perera (1993).

counts and information sources that are limited and highly variable across space-time (see, also, Sections III.C and D). Nevertheless, these limitations of historical databases constitute a challenge for the SEP theory and technology to demonstrate their intellectual value and practical usefulness--and this challenge must be treated very seriously.

b. Limitations of Previous Studies and Advantages of SEP

Being one of the worst in history, the Black Death epidemic has been extensively studied from demographic, anthropological, epidemiological, historical, etc., perspectives (Creighton, 1891; Gasquet 1893; Sticker, 1908; Deaux, 1969; Ziegler, 1969; Gottfried, 1983; Twigg, 1984; Kohn, 1995; Hirshleifer, 1996; Scott and Duncan 2001, 2004; Cohn, 2002a and b; Benedictow, 2004). However, as far as we know, no systematic analysis and mapping of the spatiotemporal evolution of the epidemic exists, let alone one based on sophisticated stochastic mathematics and methodological principles of interdisciplinary integration. The reasons for this scarcity may be linked to a variety of factors, including the serious uncertainty of the available databases (which makes a conventional deterministic analysis extremely difficult or even impossible), the mathematical difficulties associated with the study of the complex spatiotemporal distribution of the disease, an insufficient appreciation of the interdisciplinary nature of the problem[45], the lack of sufficiently precise hypotheses about the spread of the epidemic suitable for expression in quantitative terms, and the aspatial/aspatiotemporal tradition of most biomathematical and epidemiological works.

Although the need for a rigorous space-time representation of the Black Death epidemic has been acknowledged in a number of past and recent publications (e.g., Wood *et al.*, 2003), currently there exist neither models successfully incorporating explicit space and time components into Black Death studies nor techniques that account for integrated geographical-temporal variations, uncertainty sources, individual- and population-level dynamics in a mathematically tractable manner (Cliff, 1995; Scott and Duncan, 2001).

In this book we suggest the implementation of SEP as an adequate response to these needs, especially given the plethora of uncertainty sources involved in the predominantly historical Black Death databases available. More to the point, SEP possesses a battery of sophisticated stochastic techniques to efficiently assess the spatiotemporal characteristics of the Black Death distribution (correlations between spatial and temporal mortality structures, heterogeneity patterns, large-scale trends connected with the disease, etc.) and generate substantive predictions in a dynamic manner that accounts for the various uncertainty sources and spatiotemporal characteristics of the epidemic.

---

[45] Even though the interdisciplinary character of the disease has not gone unnoticed in some previous studies (e.g., Bleukx, 1995: 72), nevertheless, it has not been adequately considered.

A study of the Black Death epidemic based on sound methodological principles and rigorous mathematical modelling could shed light on certain important aspects of the epidemic (e.g., transmission and spread of the infectious disease, space-time course and life-cycle of the epidemic). Such a study may also provide some insight concerning Black Death aspects that are currently under debate, such as the cause of the epidemic (Cohn, 2002a). Furthermore, as already mentioned, it is conceivable that by understanding the serious Black Death effects in a geographical-temporal context (societal, financial, etc.), valuable insight can be gained regarding similar effects of potential contemporary epidemics (e.g., AIDS and Ebola) or biological warfare.

It was stressed that interdisciplinarity is valid and even inescapable in the context of public health problems that need experts from a variety of fields of knowledge in order to be dealt with effectively. Accordingly, the epidemic modelling of Black Death as viewed in this work is based on the integrated modelling of knowledge from different disciplines and levels of organization (see Example C.1 above). Note that the Black Death epidemic has also played an important role in the evolution of many of these disciplines[46]. While disciplinary research concerns one level of reality, cross-disciplinary modelling concerns the dynamics engendered by the action of several levels of reality at once (e.g., bringing together information at different experiential levels, from a variety of sources to provide a coherent account of the Black Death epidemic).

The integration methodology may need to be confronted with different modes of reasoning (Section B.e above). In this context, the term "integration" covers possible forms of relationship that can be developed between different disciplines, i.e., SEP will seek integrated links between the various information sources. Rigorous spatiotemporal Black Death epidemic representation and mapping requires the consideration of certain conceptual and technical tools developed in the SEP context (e.g., spatiotemporal models, prediction algorithms, and mapping technology). These technical tools provide powerful and efficient means for rectifying the logical geography of the Black Death knowledge available and for extracting and generalizing critical principles of the epidemic propagation process. The SEP tools also provide the means of summarizing, modelling, and visualizing the differences between digital representations of Black Death epidemic patterns and variations.

A considerable part of the current epidemic state of knowledge about Black Death is summarized in the map of Fig. III.1 (Chapter III). This map serves to emphasize the following:

- A rather poor time resolution is displayed. Our study aims at improving it by one order of magnitude and go from a resolution of semesters to a resolution of months.
- Nothing has been mapped beyond the plot of Fig. III.1. E.g., there are no maps of mortality at any scale.

[46] Some examples are discussed in Chapter III.

- Salient space and time cross-correlations and interdisciplinary dependencies have not been taken into consideration in the existing epidemic analyses of Black Death.
- There exist serious discrepancies regarding the nature of the Black Death epidemic.

Being aware of the above limitations of previous modelling efforts, among the realizable objectives of the present Black Death study were the following:

(*a*) Using state of the art electronic bibliographical research to exhaust sources of published material about the Black Death epidemic. This endeavor is complicated by the interdisciplinary nature of the epidemic data sources that is behind the dispersion of information in books, websites, and papers, which is far higher than the dispersion for other topics.
(*b*) Creating a database with current knowledge about population and mortality. This database should guide future research by our SEP group or others and point to information bases suspected to be in error.
(*c*) Preparing, for the first time, detailed geographical-temporal maps of monthly mortality, infected areal propagation, etc., thus providing the powerful means for representing critical features of the dynamics of the epidemic.
(*d*) Deriving and representing visually important parameters and characteristics of the epidemic's evolution across space and time (centroid paths, epidemic velocities, elasticity index etc.).
(*e*) Anticipating that more serious efforts will be compensated along the way leading to unexpected insight about the disease. Initial objectives may be linked with our research findings (quantitative determination of space-time correlations between urban population and duration of the epidemic, stochastic generalization of conventional epidemic models in a composite space-time domain under conditions of uncertainty, etc.).
(*f*) Carefully analyzing any findings of the present space-time modelling effort that could potentially throw some light on the long-lasting controversy about the nature and the origins of the Black Death epidemic. Making comparisons between the spatiotemporal characteristics of the Black Death and the bubonic plague, thus contributing to the debate concerning the nature of Black Death: bacterial or viral[47].

The generation of new ideas and critical attitudes should go hand by hand in a new paradigm. In the following chapters we will make an effort to communicate to our readers what we view as the two major strengths of SEP in the context of the Black Death study:

- Its *conceptual* strength, which lies in its emphasis on intellectual work and creativity (which are the background context of critical thinking, reliable

[47] The main issues of this debate are discussed in Section III.B.

knowledge, and the integration of ideas) rather than on merely gathering information and applying it mechanically [48].

- Its *technical* strength, which lies in its organized attempt to understand the space-time evolution of the Black Death disease in considerable detail based on uncertain city-level data[49] generated from a variety of interdisciplinary information sources.

The powerful combination of the above two elements provides SEP with significant advantages over previous public health approaches. While epidemiologic statistics, e.g., focuses mainly on the uncertainty of the disease data and parameter values, SEP accounts for this kind of uncertainty as well as for the uncertainty resulting from the structure (conceptual and mathematical) of the models representing the epidemic system. This is a serious issue. In many cases, inadequate model structure (conceptualization) has far more important consequences in the prediction of disease distribution across space-time than data or parameter uncertainty. Also, SEP accounts for the critical space-time dependence of mortality values--which classical statistics assumes to be independent--and it possesses powerful techniques that allow it to generate substantive predictions of the relevant disease variables. As a result, SEP can process content-rich information about the epidemic system. This information cannot be conveyed by statistics, because the *form* of the latter excludes the *content* of the former.

[48] Hofstadter (1986: 526) remarked: "People like Mozart are held to be somehow divinely inspired, to have magical insights for which they could no more be expected or be able to account for than spiders for the wondrous webs they weave. It is all felt to be somehow too deep down, too hidden, too occult a gift, to be mechanical in any sense. Creativity, in fact, is perhaps one of the last refuges of the soul."

[49] I.e., population, numbers of deaths, and epidemic duration.

Chapter II - Stochastic Modelling

"... a probability is a reputable proposition ... A probability is that which happens for the most part."
Aristotle

A. Why Stochastics?

Albert Camus expressed, with great clarity, the role of *uncertainty* in our lives (Camus, 1970: 230-231): "we can name things only with uncertainty, and our words become certain only when they cease to refer to actual things". Uncertainty, in its various forms, is at the center of many scientific investigations and debates. Indeed, in the last few decades scientists have moved from seeing nature as inherently stable and deterministic to viewing it as uncertain, subject to unexpected shifts and changes, which can suddenly create huge opportunities for the prepared and sometimes fatal threats for the slow movers[1]. The issue of uncertainty and its consequences transcend the domains of the two most significant constituents of scientific development: *explanation* and *prediction*. Therefore, no serious public health scientist can afford to ignore uncertainty without paying a price. Sooner or later one will have to devise the necessary tools (strategies, heuristics, and technologies) to deal with uncertainty as adequately as possible.

As we shall see in the remaining of the present section, uncertainty is an integral part of one's critical thinking process. Epidemic models often start with a description of the relevant parameters (incidence rate, mortality rate, susceptibles, migration rate, etc.). Uncertainty can enter these models because parameters vary in unpredictable ways. Moreover, public health research in SEP is concerned with a variety of issues, including the possible origin of an infectious disease outbreak and the conditions that led to the epidemic, the geographical shape and extent of the epidemic, its temporal evolution features, and ways to control it. Uncertainty assessment plays a vital role in the study of all these issues.

---

[1] Naturally, nobody wants to be left behind as far as uncertainty assessment and its consequences are concerned. "As we know, there are known knowns--there are things we know we know. We also know there are known unknowns--that is to say we know there are some things we do not know. But there are also unknown unknowns, the ones we don't know we don't know. And it is the latter category that tend to be the difficult ones," as was maintained by D. Rumsfeld (US Defense Secretary) during a 2004 news briefing.

We argue that *stochastic* theory provides the most solid theoretical background and useable set of tools for studying uncertainty and its consequences in public health science. As a matter of fact, when it comes to Black Death the information sources in existence today about the epidemic of 1347-51 are notoriously scarce and uncertain (see, e.g., Twigg, 1984; Scott and Duncan, 2001; Cohn, 2002b), which makes a stochastic approach to the problem most appropriate. In view of the considerable uncertainties and variations, stochastic modelling suggests that one should give up the futile attempts to make exact (deterministic) predictions in favor of conditional (stochastic) predictions of epidemics (see also Chapter V). Here the meaning of the term "conditional" is that the predictions generated by stochastic theory are conditioned on a number of factors: the space-time variation features of the disease spread, the conceptual and technical uncertainty associated with epidemic modelling, the knowledge bases available, the prediction accuracy sought, the objectives of the study, etc. Celebrated early stochastic modelling approaches in sciences include Maxwell's and Boltzmann's development of the kinetic theory of gases (1860 and 1896), Planck's derivation of the radiation law (1900), Gibbs' formulation of statistical mechanics (1901), Einstein's and Langevin's analyses of Brownian motion (1905 and 1908), Taylor's and von Karman's theories of turbulent motion (1921 and 1937), and Heisenberg's and Born's approaches to modern quantum mechanics (1925 and 1926)[2].

Before proceeding any further with the presentation of stochastic theory, let us first spend a little more time thinking about its main concern, i.e. uncertainty, in a public health modelling context.

a. Thinking About Uncertainty—Public Health Reasoning Modes

In his epic poem *Satyricon*[3] the ancient Roman author Caius Petronius (Petronius Arbiter) wrote: "suam habet fortuna rationem", i.e., "chance has its reason". From a modern public health perspective this implies that thinking about uncertainty and its consequences involves a particular *mode of reasoning*. With this is mind, our introduction to stochastic theory focuses on the subject of public health reasoning modes under conditions of uncertainty.

It is customary to start with a brief review of the most commonly encountered interpretations of uncertainty. Some public health policy studies assume a purely *subjective* interpretation of uncertainty and associate it with preferences, subjective decisions, beliefs, and linguistic imprecision (Morgan and Henrion, 1990). In the case of a potentially harmful exposure, e.g., the permitted maximum exposure level is considered as a decision variable that has no true value. From a more pragmatic point of view, in the eyes of many practicing public health scientists the uncertainty encountered in real-world situations should be described as a *technical* notion linked with measurement errors, heterogeneous data bases, erratic fluctua-

[2] Interesting reviews of these historic stochastic modelling works may be found in Beran (1968), Gardiner (1990), and Sklar (1993).

[3] See, Allinson (1930).

tions of the underlying processes, etc. (a discussion of possible sources of uncertainty and their estimation in practice can be found in Taylor, 1982). As a consequence, it should not come as a surprise that most common definitions of uncertainty are technical. Coleman and Steele (1999: 4), e.g., define uncertainty as "an estimate of experimental error". In our view, however, a sound public health model should go beyond these common uses of the uncertainty concept. Uncertainty is of far greater importance in scientific thought than merely a technical notion reflecting error measurements and observation biases or a subjective kind of a variable associated with decisions and preferences. This thesis may invite debates on a number of issues. E.g., some readers may ask whether the uncertainty we are dealing with in public health sciences is really a concept or a belief (Section A.b below). Many researchers support the notion of *conceptual* uncertainty, i.e., uncertainty related to model structure. The issue of epistemic vs. ontologic uncertainty arises in several public health problems (Section A.d). Another major issue is how important is conceptual uncertainty vs. data uncertainty (Section A.c). Also, under what conditions inferences concerning the origin, propagation or etiology of a disease can be considered as logically sound and scientifically meaningful? It is this kind of questions that immediately brings on the table some serious knowledge-theoretic issues. Therefore, it is worth going through a brief yet critical review of the meanings of terms such as "sound reasoning", "concept", "belief", and "model", especially in the light of the present investigation of public health uncertainties. Understanding these terms can be very helpful in scientific communications and in scientific consensual determination of health risk under conditions of uncertainty[4]. For instructional purposes, in this section we focus on reasoning, postponing until the next section an explicit consideration of the terms concept, belief, and model.

The vital role of the thinking process in scientific inquiry is underlying Einstein's famous statement: "I want to know how God created this world. I am not interested in this or that phenomenon, in the spectrum of this or that element. I want to know His *thoughts*; the rest are details." Generally, *reasoning* is a thought process that involves arguments (e.g., Tomassi, 1999; Shand, 2000). An *argument* is a mental construction that starts with specific *premises* or *hypotheses* (assumptions, epidemic laws, data, facts, etc.) and develops certain *conclusions* or *consequences* (predictions, evaluations, new laws, etc.). An argument, in turn, involves *statements*, i.e., the kind of sentences that make definite factual claims. There is a list of so-called *indicator words*, which point out which part of the argument is the premises and which the conclusions. E.g., words like "therefore", "thus", "hence", "so", "consequently", and "it follows that" indicate the beginning of conclusions. On the other hand, words like "assuming that", "if", "because", "since" and "by virtue of" indicate the beginning of premises. An epidemic argument may be concerned with a number of things, e.g., it could be for or against a specific thesis or it may lead to a novel result. In evaluating an argument, one is basically interested in two elements: *(i)* Are the premises true? *(ii)* Assuming that the premises are

[4] See, e.g., Klim McPherson's commentary on "epidemiology on trial-confessions of an expert witness" (McPherson, 2002: 889-890).

true, what kind of support do they offer to the conclusion? Although element *i* is not the business of logic, it is of great concern in scientific reasoning. Element *ii*, on the other hand, is definitely the business of logic.

On Valid Reasoning

Valid argument is an argument in which one cannot have epidemiologically true premises followed by wrong conclusions. In practice, individual public health arguments are considered valid when they are instances of valid forms of argument. Three classical valid argument-forms are shown in Table 1. The word "possible" in the title of Table 1 is meant to emphasize that, e.g., true premises and true conclusion is not enough to have a valid argument; it must also hold that to assert the premises and deny the conclusion would involve a contradiction (i.e., it will be logically inconsistent). Generally, for public health purposes it is customarily to assume the existence of two kinds of reasoning:

(i) *Deductive* reasoning, i.e. reasoning from the general to the particular or less general. It evaluates the arguments on the basis of validity (it allows only valid arguments). In this case, the premises, if they were true, guarantee the truth of the conclusion.

(ii) *Inductive* reasoning, i.e. reasoning from the particular to the general. It evaluates the arguments on the basis of probability (it allows invalid arguments that are, though, highly probable arguments on the basis of the premises). In this case, the premises, if they were true, make probable the truth of the conclusion.

In the case of deduction, the conclusion asserts no more information than is asserted in the premises, whereas in the case of induction, the conclusion goes beyond, i.e. "amplifies", the content of premises. In other words, deductive reasoning is defined in a very precise way: it is the kind of reasoning in which it is logically impossible for the premises to be true and the conclusion false. Generally, every variety of acceptable reasoning that is not deductive may be considered as inductive. These include all forms of argument in which the conclusion does not follow necessarily from the premises, as in valid deductive reasoning, but instead is inferred as likely. Inductive reasoning assures us that the conclusion is likely, but not that it is certain. Inductive reasoning analyzes risky arguments using probabilistic statements.

Let H and C denote, respectively, the hypothesis (antecedent) and the conclusion (consequence) of an argument. Table 2 displays certain rules of reasoning, which involve the following *logical operators*:

Table 1. Possible valid argument forms

(*a*) True premises - True conclusion
(*b*) False premises - False conclusion
(*c*) False premises - True conclusion

Table 2. A summary of reasoning rules.

Deductive Rules		Inductive Rules	
$H \to C$ $\neg C$ $\therefore \neg H$	Modus Tollens, *MT*	$H \to C$ C $\therefore$ It is likely that H is valid	Partial Confirmation, *PC*
$H \to C$ H $\therefore C$	Modus Ponens, *MP*	$H \to C$ $\neg H$ $\therefore$ It is likely that $\neg C$ is true	Partial Rejection, *PR*
$H \to C_1$ $C_1 \to C_2$ $\vdots$ $C_{n-1} \to C_n$ $\therefore H \to C_n$	Hypothetical Syllogism, *HS*	$\langle \Theta_i \vert a_i, b_i \rangle \quad i = 1,2,...,N-1$ $\langle \Theta_N \vert a_N \rangle$ $\therefore$ It is likely that $\langle \Theta_N \vert b_N \rangle$	Analogy, *An*
$H \vee C$ $\neg H$ $\therefore C$	Disjunctive Syllogism, *DS*	$\langle \Theta \vert a_i \rangle \quad \begin{cases} a_i \in A \\ (i = 1,2,...,N) \end{cases}$ $\therefore$ It is likely that $\langle \Theta \vert A \rangle$	Simple Enumeration, *SE*
H C $\therefore H \wedge C$	Conjunction, *Co*	$\langle \Theta \vert S_i \rangle \quad \begin{cases} S_i \subset \Omega \\ (i = 1,2,...,N) \end{cases}$ $\therefore$ It is likely that $\langle \Theta \vert \Omega \rangle$	Statistical Generalization, *SG*
$(H_1 \to C_1) \wedge (H_2 \to C_2)$ $H_1 \vee H_2$ $\therefore C_1 \vee C_2$	Constructive Dilemma, *CD*	C follows H $\therefore$ It is likely that H is the cause of C	Causal Generalization, *CG*
$H \to C$ $\therefore H \to (H \wedge C)$	Absorption, *A*	Appeal to Authority, *AtA*	
H $\therefore H \vee C$	Addition, *Add*	Appeal to Utility, *AtU*	
$H \wedge C$ $\therefore H$	Simplification, *Si*	Appeal to Experience, *AtE*	
$H \to C$ $\neg H \to C$ $\therefore C$	Excluded Middle, *EM*		
$H \to C$ $H \to \neg C$ $\therefore \neg H$	Contradiction, *Co*		
$\langle \Theta \vert A \rangle$ $a \in A$ $\therefore \langle \Theta \vert a \rangle$	Direct Generalization, *DG*		

- *Negation*, which is represented by the symbol "$\neg$". E.g. $\neg H$ represents the negation of hypothesis H, which means that it is not the case that H is true.
- *Conjunction*, represented by the symbol "$\wedge$". E.g., the $H \wedge C$ means that both H and C are true.
- *Disjunction*, represented by the symbol "$\vee$". E.g., the $H \vee C$ means that either H or C is true.
- *Implication*, represented by the symbol "$\rightarrow$". E.g., the $H \rightarrow C$ means that if H is true then C is true. What is asserted by implication is precisely that $\neg(H \wedge \neg C)$, i.e. it is not the case that H and not C.

Yet another logical operator--not shown in Table 2, but which will play a role in the following--is:

- *Equivalence*, represented by the symbol "$\leftrightarrow$". E.g., the $H \leftrightarrow C$ means that H is true if and only if C is true. Equivalence is a strong logical operator that means the same thing as "$(H \rightarrow C) \wedge (C \rightarrow H)$".

Furthermore, the symbol "$\therefore$" means "therefore" (or "as a result of the above"). The *MT* (see Table 2) is a deductive rule that denotes the disconfirmation of a hypothesis, whereas *MP* denotes the confirmation of a consequence. The *HS* is extremely useful in public health inferences. This kind of argumentation, i.e. creating and following through a chain of conditional thoughts linked together logically by hypothetical syllogism, is a very common form of reasoning in public health situations. The *EM*-rule is based on Aristotle's law of the excluded middle: $H \vee (\neg H)$ is always true. The *Co* rule is based on the simple fact that the consequence C cannot be both true and false; hence the hypothesis H is false or, equivalently, $\neg H$ is true. The *DG* refers to elements as members of a set. The symbol "$\langle \cdot | \cdot \rangle$" denotes that whatever is on the right of the vertical line has the property on the left of the line. E.g., $\langle \Theta | a \rangle$ denotes that the element a has the property Θ; $\langle \Theta | a, b \rangle$ implies that both elements a and b have the property Θ; etc. A is a set of elements to which a belongs.

Inductive reasoning by *generalization* is a reasoning operation of paramount importance in scientific reasoning, as well as one that can be a source of serious errors. A typical case of generalization is the *SG* rule of Table 2 (S_i denotes subclasses of the larger class Ω.). The *AtA* is the kind of reasoning relying on the views expressed by an authority in the field (e.g., Dr. Watson's views on DNA research). *AtU* is the reasoning that relies on the fact that the suggested reasoning works (e.g., analytical or numerical approximations to complex mathematical problems). Finally, *AtE* is based on the experience of recognized experts in the field of interest.

The reasoning rules are indispensable in the case of contemporary Black Death evidence (Sections III.C and D), in which the epidemic modeller needs to extract and evaluate complex and important arguments found in chronicles, accounts, reports, etc. Next we discuss a few illustrative examples from the Black Death experience aiming at illustrating some of the reasoning rules of Table 2.

Example A.1. Detractors of the bubonic plague theory of Black Death (Section III.B.d) use the deductive *MT* rule to promote their views. Let $H =$ *Black Death is bubonic plague*, and $C =$ *Y. pestis is found on skeletons of Black Death victims*. It is known that the bacillus *Y. pestis* is a characteristic of bubonic plague, in which case $H \rightarrow C$ makes sense. However, since $\neg C$ is valid (based on experimental findings of the Oxford University researchers[5]), the $\neg H$ must be valid according to *MT*, i.e., it is not the case that H is true.

Example A.2. Proponents of the bubonic plague theory of Black Death (Section III.B.d) use the inductive *PC* syllogism. Let H be as in Example A.1 above, and $C =$ *clinical symptoms of Black Death and bubonic plague are the same*. Then, it is likely that H is valid. One could also argue that, if C is true then the probability of H is larger than that of $\neg H$, i.e. $P[H] > P[\neg H] \geq 0$.

Example A.3. In our study of the contemporary evidence, we often employ *SG* rules (Table 2). For illustration, consider the case of the city of Lübeck (Germany), in which $\Theta =$ *death rate due to Black Death is roughly 1 in 3*; $S_1 =$ *subpopulation of property owners in Lübeck*; $S_2 =$ *subpopulation of city clerks in Lübeck*; $S_3 =$ *subpopulation of city councilors in Lübeck*; $\Omega =$ *population of about 25,000 residents in Lübeck*. Then, there is a reasonably high probability that the population death rate in Lübeck was roughly 1 in 3 (see, also, Section III.C.b).

Public health argumentation is often a combination of the rules of Table 2. For illustration, consider the following situation.

Example A.4. Assume that $H \rightarrow C_1$, $C_1 \rightarrow C_2$, and $\neg C_2$. The question is whether under these conditions the hypothesis H is valid. By using the *HS* and *MT* rules of Table 2 we obtain the following deductive reasoning mode:

$$\left.\begin{array}{l} H \rightarrow C_1 \\ C_1 \rightarrow C_2 \end{array}\right\} \xrightarrow{HS} H \rightarrow C_2 \qquad \left.\begin{array}{l} H \rightarrow C_2 \\ \neg C_2 \end{array}\right\} \xrightarrow{MT} \neg H \text{; i.e., the } \neg H \text{ is valid.}$$

The careful study of reasoning sometimes reveals certain *fallacies*. Some of the most well known are listed in Table 3. The *AtC* leads to a reasoning mode that makes no deductive sense. I.e., we can never deduce that a hypothesis is true by showing that some consequence following from it is true, or even that several consequences that follow from it are true. In these cases, it only makes sense to use the *PC* inductive reasoning form. *SiG* implies that if certain elements a_i of A have the property Θ, then all elements of A do have this property; this form of

[5] See, Section III.B.d.

Table 3. Fallacies of reasoning.

Deductive Fallacies		Inductive Fallacies	
$H \to C$ C $\therefore H$	Affirming the Consequent, *AtC*	$\langle \Theta \mid a_i \rangle \quad a_i \in A \quad (i = 1,2,...,N)$ $\therefore \langle \Theta \mid A \rangle$	Simple Generalization, *SiG*
$H \to C$ $\neg H$ $\therefore \neg C$	Denying the Antecedent, *DtA*	C follows H $\therefore H$ is the cause of C	Causal Generalization, *CG*
H and $\neg H$	Inconsistency, *Inc*	Regularity: $x_i \quad (i = 1,2,...,N)$ $\therefore$ Regularity: x_{N+1}	Projectible Regularity, *PR*

induction is not necessarily true. In these cases one can use the probabilistic *SE* form (Table 2), instead. Inductive generalization has some serious problems in the context of prediction, such as the famous *Hume's riddle of induction*, which underlies the *PR* fallacy: prediction should be based on projection of data regularity into the future (i.e., a regularity established on the basis of the data x_i, $i = 1,2,...,N$, is supposed to be projectible to future values, such that x_{N+1}). The problem, however, is that there is no definite rule to determine which regularities induction considers to be projectible in the future. Indeed, naive characterization of generalization as a system that projects observed data regularities in the future is pointless unless we can say which regularities it projects. Let us consider a few examples.

Example A.5. The detractors of the bubonic plague explanation of Black Death (Section III.B.c) on occasion use the *AtC* syllogism to attack its proponents: let H=*Black Death is bubonic plague*, and C=*clinical symptoms of Black Death and bubonic plague are the same*; even if C is true (which may be questionable), it is a mistake to conclude with certainty that H is true.

Example A.6. We are given the dataset $x_i = i$ ($i = 1,2,...,100$) and we want to predict the future value x_{101}. Obviously, one model that fits all data values is $x_i = i$ ($i = 1,2,...,100$), in which case the prediction is $x_{101} = 101$. But it may be *PR* fallacy to accept this result. Indeed, another model that fits the data equally well is $x_i = \prod_{j=1}^{100}(i-j) + i$, which predicts $x_{101} = 100!+101 \approx 9.3 \times 10^{157} >> 101$, i.e. a much larger number than the first model's prediction. Induction offers no definite rules to choose between the two models above. In a similar vein, the statement that inductive logic presupposes the uniformity of nature is equally pointless unless we are able to say in what respects nature is presupposed to be uniform. Induction-based prediction models are problematic when a record event beyond past experience occurs--a problem that vexes experience-based models.

The Role of Probability

We already pointed out the role of probability in inductive reasoning. Probability may be used, e.g., in most inductive rules in Table 2 in order to quantify the likelihood of the arguments involved. When probability assessments are made under conditions of incomplete knowledge, the resultant probability is a measure of one's ignorance, in which case the probability is called epistemic (see, also, Example A.16 below). Deduction is a different story. It must be stressed that, in theory, deductive reasoning *assumes* that the premises are true. In real-world public health applications, however, one may be not able to verify beyond any doubt the truth of the premises[6]. Therefore, we maintain that it makes sense to consider the *probability* of a deductive argument. This may sound like a strange proposal, for most people are accustomed to probability being a feature of inductive reasoning. Probability formulations, however, are possible in the case of deductive reasoning as well, when it is applied in real world public health situations. In fact, on the basis of this postulate a detailed theory of *stochastic deduction* has been developed by Christakos (2002a and b) with a wide range of applications in life sciences. This proves that in the modern public health paradigm the research and development efforts do not need to be guided only by what is available "off the shelf" but by careful and innovative theoretical considerations, as well.

These matters are of considerable interest in public health research and development. As far as space-time epidemic modelling is concerned, one may distinguish between two modes of uncertain reasoning, as follows:

(*a*) Statistical induction.
(*b*) Stochastic deduction.

A remarkable difference exists between statistical induction in the form of a *Bayesian conditional* (*bc*, symbolized by " $\mid$ "), which belongs to mode *a* above, vs. stochastic deduction in the form of a *non-Bayesian* conditional (e.g., *material conditional*, *mc*, symbolized by the implication operator " $\rightarrow$ "; and *material biconditional*, *mb*, symbolized by the equivalence operator " $\leftrightarrow$ "), which belongs to mode *b* above (see, also the stochastic theory of epidemics in Sections C.b, D.c, and IV.D). As before, consider a hypothesis H and a conclusion C. The corresponding probability functions are defined as follows[7].

[6] The reason for this limitation is intimately linked to the problem of reliability of knowledge.

[7] For a mathematical introduction to inductive and deductive probabilities, see also Christakos (2002a) and Christakos *et al*. (2002).

Inductive Conditional Probability:

$$P(C|H) = P(H \wedge C) / P(H), \tag{1}$$

Deductive (Material) Conditional Probability:

$$P(H \rightarrow C) = 1 - P(H) + P(H \wedge C), \tag{2}$$

Deductive (Material) Bi-Conditional Probability:

$$P(H \leftrightarrow C) = 2P(H \wedge C) + 1 - P(H) - P(C). \tag{3}$$

In all three cases above, the probability functions do not determine what will happen, they only provide information about the comparative likelihoods of what might happen. However, while the non-Bayesian conditionals (2) and (3) are based on a reasoning that investigates which scenarios linking the events under consideration are epidemiologically possible at the specific hierarchical and/or organizational level, the Bayesian conditional (1) concentrates on an explicitly statistical reasoning regardless of any such epidemic scenarios. The issue may be illustrated by means of some simple examples.

Example A.7. To clarify the statistical reasoning involved in the various modes of conditionalization consider a set of 52 water samples brought in the laboratory for testing. Only 4 of these samples are over-contaminated, i.e., the contamination exceeds a specific threshold and can be harmful to human receptors. Assuming that the samples are selected at random, let $H =$*The first sample is over-contaminated*, and $C =$*The second sample will be over-contaminated*. It is easily seen that, $P(H) = P(C) = \frac{1}{13}$ and $P(H \wedge C) = \frac{4}{52} \times \frac{3}{51}$. The *bc*, *mc*, and *mb* probabilities are calculated as follows: $P(C|H) = \frac{4}{52} \times \frac{3}{51} \times (\frac{4}{52})^{-1} \approx 0.059$; $P(H \rightarrow C) = 1 - \frac{1}{13} + \frac{4}{52} \times \frac{3}{51} \approx 0.928$; and $P(H \leftrightarrow C) = 2 \times \frac{4}{52} \times \frac{3}{51} + 1 - \frac{1}{13} - \frac{1}{13} \approx 0.86$, respectively. As should be expected for random selection situations, the purely statistical nature of the *bc* probability seems to be the most intuitive.

Example A.8. A different situation arises in this example. Consider the events, $H =$*An individual has been exposed to an agent that 93% of the time is infectious*, and $C =$*The individual has been infected*. Assume that the following a priori probabilities are assigned to the relevant events $P(H) = P(C) = 0.3$; and $P(H \wedge C) = 0.001$, reflecting the fact that, a priori, there may exist reasons other than H for the occurrence of C. The *bc* probability is $P(C|H) = \frac{0.001}{0.3} \approx 0.003 << P(C) = 0.3$, which implies that the fact that H occurred does not provide any evidence for C. This is clearly counter-intuitive. On the other hand, $P(H \rightarrow C) = 1 - 0.3 + 0.001 \approx 0.701 > P(C) = 0.3$. The *mc* analysis implies that on non-Bayesian principles, H does provide considerable evidence for

C. This result is consistent with the existing knowledge. Indeed, the use of the *mc* concept makes sense here, since, by definition, it calculates the probability that "it is not the case that H occurs and C does not occur", which is what we study in this example. Finally, $P(H \leftrightarrow C) = 2 \times 0.001 + 1 - 2 \times 0.3 \approx 0.402 > P(C) = 0.3$. The *mb* probability demonstrates the fact that the *mb* includes the scenarios that "both H and C occur" and "both H and C do not occur", whereas it ignores the scenario that "H does not occur but C still occurs", which was taken into account by the *mc*. If the last scenario is a public health possibility, it may be more appropriate to choose the *mc* approach in the situation studied in this example. If it is not, then the *mb* may be preferred.

These two examples support the view that there is not a unique knowledge-based conditional that is universally valid. Instead, the choice of a conditional depends on the public health characteristics of the situation, rather than merely on purely statistical arguments[8]. As we saw in Examples A.7 and A.8 above, the calculus of probability teaches us how to manipulate probabilities in a formal manner, but it does not give us a definite answer as to what these probabilities correspond *operationally*. Nevertheless, in public health applications we may need to assign an operational meaning to assertions such as "the probability of hypothesis H concerning an epistemic system is 0.3". A possible operational meaning of this kind of assertion could be that we assign a probability to an element of our *description* of the epidemic system rather than to an element of the system itself. To express this epistemic interpretation of probability in formal terms we often use the subscript "*KB*", i.e. $P_{KB}(H) = 0.3$ in the above case, which denotes the knowledge base utilized to generate the probability value 0.3 concerning the occurrence of H (see, also, Section I.C.b). In some cases, we may be able to provide an operational meaning to this assertion by generating on a computer a large number of numerical simulations that are compatible with the KB about the epidemic system and finding that the proportion of realizations in which H occurs is equal to 0.3.

On Sound Reasoning and Inference

Sound (or *good*) public health reasoning requires one more feature for the arguments involved, that of *true premises*--e.g., in Table 1 above only the argument form *a* is sound. The difference between valid and sound (or good) arguments is subtle and can have severe consequences in epidemic inquiry. Similar is the case with Black Death: many differences of opinion are concerned with the accuracy of the premises rather than with the validity of the logical structure involved.

Example A.9. To demonstrate the matter, one may refer to the etiology of the plague in 17th century AD Italy in terms of "venomous atoms" and "miasmatic air" (see, e.g., Ayliffe and English, 2003). The etiologic system developed by the

[8] This salient issue is revisited in Section III below.

Renaissance doctors was logically valid but not sound, in the sense described above, and therefore it turned out to be epidemically meaningless[9].

Without delving into further details, *deductively sound* public health reasoning is the thought process that starts from *true* premises and derives conclusions on the basis of *valid* arguments, whereas *inductively sound* epidemic reasoning is the thought process that starts from *true* premises and derives conclusions on the basis of *probable* arguments. While the study of the principles of reasoning is the domain of logic, the study of the principles of sound reasoning requires knowledge of the relevant science, as well. Clearly, inductive reasoning can never attain the high standards of deduction. Inductive reasoning relies considerably on experience, which is often a hard teacher: it gives the test first, and the lesson afterwards. Nevertheless, inductive reasoning can be very valuable in public health studies. In certain epidemiologic situations, e.g., induction in terms of statistical modelling may be attainable in practice (e.g., Clayton and Hills, 1993). These issues can be further clarified by means of an example.

Example A.10. As we saw in Example A.1 above, detractors of the bubonic plague theory of Black Death used the deductive *MT* syllogism that is based on the belief that the following premise is not valid: "*Y. pestis* is found on skeletons of Black Death victims". This belief was based on the experimental findings of a British team of researchers. On the other hand, proponents of the theory use the same H and C as in Example A.1 but employ, instead, the inductive *PC* syllogism, which is based on the belief that the above premise is valid. The validity of the premise--which is critical in the *PC* syllogism--is supported by the experimental findings of a French team of researchers (Section III.B.d). There are two important points here: The first is that in both kinds of syllogism the validity or not of the premise is not a matter of logic but of experimental science (biology, etc.); the second is that, regardless of the experimental validity of the premise or not, *MT* is a logically stronger kind of syllogism than *PC*.

One may need to assess an existing hypothesis in the light of the emerging interdisciplinary evidence (physical, ecological, historical, demographic, epidemiologic, etc.). As we see in the following example, Black Death modelling often encounters situations in which the testing of a hypothesis may involve evidence from different disciplines.

Example A.11. In Section V.C.b we want to test the existing hypothesis H = *The pre-plague population of Florence was about twice that of Bologna.* The available evidence includes: (1) *In both cities the area inside the city walls was approximately the same: 420 ha.* (2) *There were no dwellings adjacent to the city walls.* (3) *Duration of epidemic in both cities was 8 months.* (4) *Pre-plague population of Bologna was 40,000 residents.* (5) *Duration and population are linked*

[9] One should not laugh too much with the Renaissance doctors. *Mutatis mutandis*, similar reasoning styles are not so rare even nowadays.

through Eq. (IV.1). In this case, the hypothesis H is contradicted by the evidence (1)-(5) and, thus, needs to be revised.

At the heart of sound public health reasoning is the kind of a thought process called *inference*. This is the thought process whereby one passes from the premises to the conclusions, on the grounds that if the former are true then the latter may be or must be true, as well. In other words, the essence of inference is the *justification* of terms like "therefore", "thus", "hence", "consequently", "it follows that", etc., which connect premises with conclusions. In this sense, inferences may be of a deductive or an inductive form, depending on whether they are associated with deductive or inductive reasoning. Typically, scientific inference involves both the *logical* construction of the epidemic system and several *non-logical* factors (e.g., system content and context). In view of the above considerations, it is not enough to understand the data, facts, concepts, and beliefs making up the premises, but one must also understand how these premises are combined by means of inference to lead to novel and interesting results and accurate predictions about future events associated with an epidemic. Facts, concepts, and beliefs in themselves may be of limited value in epidemic reasoning; only when they are linked in terms of inference they do obtain rational force.

By way of a summary, one can hardly overestimate the importance of the argumentation modes and styles of reasoning under conditions of uncertainty, for they form an essential part of the background intellectual context of public health inquiry. Argumentation modes and styles of reasoning have two roles:

- They are indispensable concepts and tools of the *scientific inference* (*detective work*[10]) that an epidemic modeller needs to perform when it comes to handling historical evidence of infectious diseases (i.e., uncertain evidence that lies far in the past), such as in the case of the Black Death epidemic during Middle Ages (Sections III.C and V.C).
- They are at the heart of the mathematical formulation of *random field* models, which provide the necessary means for studying the space-time distribution of infectious diseases and epidemic outbreaks (Sections B.b and C).

In view of these considerations, the claim made by a certain epidemiology school that "…we need epidemiologic discipline to prevent our inferences from going astray" (Rothman, 2002: vii) rather trivializes and obscures the real issue. In fact, it is not the isolated epidemiologic discipline (with its often outmoded concepts, vocabulary, and tools) that can prevent inferences from failing, but rather the intellectual process based on integration of knowledge from different disciplines (including epidemiology) guided by sound epistemic principles and scientific reasoning modes that can achieve such an important task. Unfortu-

[10] A public health researcher, in general, and an epidemic modeller, in particular, often may find themselves in the position of a detective, such as Sherlock Holmes, only things usually do not look so "elementary", as was the case with the great detective. See, also, Section V.C.b.

nately, the current epidemiologic paradigm lacks these crucial elements and, hence, it is an inadequate one in need of immediate replacement.

b. Thinking About Uncertainty—Concepts, Beliefs, and Models

On Concepts

A *concept* is a basic mental structure. This structure acquires its meaning on the basis of its function or use or role in thought processes (Harman, 1999). Generally, concepts have a function in reasoning that is relevant to their content, which, in turn, may depend on connections with perception and inference (e.g., a fundamental cognitive role of concepts is to serve as a bridge between perceptions and actions). However, cognition is often dominated by other more indirect modes that are not triggered by perception alone, i.e., the concepts have a function in reasoning and acting that can be independent of perception (Gardenfors, 2000). Concepts have a direct relation with human *creativity*; according to Hofstadter (1986: 528), "Having creativity is an automatic consequence of having the proper representation of concepts in mind".

It is not uncommon to allow words to guide our thinking, instead of using language to express our thoughts consciously and critically. Becoming conscious of the meaning of words is not as straightforward as learning a factual subject such as biology. The analysis of concepts teaches us how to avoid certain pitfalls of language that can be dangerous if we are not aware of them. Scientific concepts, in particular, require a definition based on actual or thought experiments[11]. The color "red", e.g., is a perceptual concept that describes a specific characteristic of a person, say, the color of his face. In addition, on the basis of the "redness" concept, one could also make some interesting inferences. From his "red" colored face one may infer, e.g., that a person experiences high fever. In fact, several concepts in modern science possess only an inferential function (this is the case, e.g., of the theoretical concept "electron").

For illustration, in Fig. 1 we consider some basic epidemic concepts associated with the different stages in the evolution of an infectious disease transmitted person-to-person (such as measles or chickenpox): incubation period (the time between a person's infection and the appearance of the first symptoms), infectious period (the time during which a person can transmit the disease to others), and latent period (time between infection of a person and his becoming infectious). Concepts such as the above are at the heart of epidemic science. Also, epidemiologic laws may describe an infinite set of possible events in a concise way, using a small number of such concepts. Moreover, one of the most significant benefits of theoretical concepts is that they allow new predictions. Finally, the analysis of

[11] Heisenberg, e.g., pictured a microscope that did not exist, but it could be constructed in principle. He then imagined using this microscope to see an electron and to measure its position. He found that the electron's position and momentum did indeed obey the uncertainty relation he had derived mathematically.

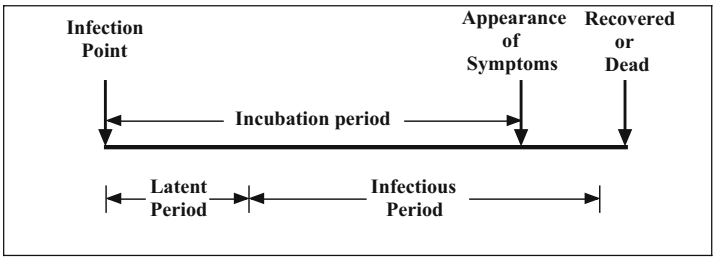


Figure 1. Different stages in the evolution of an infection disease transmitted person-to-person (reproduced from Scott and Duncan, 2004: 141).

concepts can cultivate the important skill of how to communicate.

On Beliefs

Probably, most people would agree with the following definition of what constitutes a belief: A *belief* is a state of thought that involves concepts organized in a certain way. E.g., without the concepts of "homogeneity", "stationarity", and "space ", a public health scientist cannot form the belief that "the space-time distribution of influenza in the state of California is spatially homogeneous". Macintyre *et al.* (2002) have expressed certain beliefs concerning the “place effects” on health in industrial countries. It is possible that a belief formed within the context of the Newtonian conceptual framework of absolute place and time will be fundamentally different than a belief established within Einstein’s framework of relative place-time.

Wilson (1963) argues plausibly that there may exist numerous possible beliefs regarding a situation. Some of these beliefs may be erroneous or useless, even if they have a certain content and use meaningful concepts. The belief, e.g., that the earth is flat involves meaningful concepts, but it is nevertheless incorrect and of no practical use whatsoever. It is, therefore, worth emphasizing that the content of a belief does not derive from its own role in reasoning, but rather from *its uses* of the concepts it exercises[12].

Furthermore, according to Einstein, the advancement of sciences depends on the development of concepts that extend intuition into realms beyond daily life, beliefs, and raw experiences. All this points towards the thesis that concepts play the primary role in public health reasoning involving uncertainty, and not merely

[12] When thinking about concepts, one of the oldest and yet most powerful examples that comes to mind is the concept of the "wheel", which was first conceived as a mental structure by our ancestors several thousands years ago. The "wheel" was not just a belief shared by a group of people and opposed by some others, but a powerful new concept that changed the history of human kind. Perhaps, some people appreciated its importance more than others who were thus left behind, or it was used by different people in different ways, but the conceptual image of "wheel" was clear to everybody.

the various possible beliefs in which those concepts could occur[13]. A fundamental element of the problem of epidemic prediction, e.g., is to decide which concepts to use in inductive generalizations across space-time.

On Models and Model Selection

When asked to summarize his creative process, Peter Ilich Tchaikovsky remarked (Garden and Gotteri, 1993: 299): "It's only by persistent hard work that I've finally reached the stage where the *form* in my compositions more or less corresponds to the *content*." Similarly, formal tools (mathematical equations and calculations) should not be used uncritically, but always in accord with a well defined and rich in content contextual background.

Like all kinds of models, public health models ought to be built around concepts. As it turns out, the conceptual model can be one of the main contributors of uncertainty in scientific studies. Although the role of mathematics is very important in modelling, one must learn not only *how* to use mathematics but also *when* to use it. Once the conceptual framework for an epidemic situation has been established, theories in the form of *mathematical equations* can be proposed and tested. These mathematical equations may provide powerful concise expressions to reasoning rules of the form presented in Table 2 above.

Example A.12. Consider the simple population exposure-response equation (Christakos and Hristopulos, 1998: 76),

$$H_P = \alpha E^c, \tag{4}$$

where H_P is the population health effect, E is the exposure, and α and c are empirical coefficients. For simplicity, let $c = 1$ (linear case) and $\alpha = 0.5$; then Eq. (4) is a concise expression for statements expressed by the equivalence reasoning rule, as follows

$$\left.\begin{array}{l} E = 0.00 \leftrightarrow H_P = 0.00 \\ E = 0.10 \leftrightarrow H_P = 0.05 \\ E = 0.50 \leftrightarrow H_P = 0.25 \\ \vdots \end{array}\right\} \tag{5}$$

in suitable units. I.e., in this case each value of E is a necessary and sufficient condition for a unique value of H_P.

[13] This being the case with the predominant role of concept vs. belief in scientific reasoning, the claim made by a certain school of statistical thought that reasoning is belief revision, the latter being simply a matter of changing probability distributions in light of new evidence independently of any conceptual structure considerations (e.g., Bernardo and Smith, 1994), could be problematic.

The formulation of laws of nature in terms of mathematical equations may have more than one *interpretation*[14]. Consider, e.g., a law that is mathematically represented by the model ($i = 1,2,...,N$)

$$\mathcal{L}[X_i] = 0, \tag{6}$$

where X_i ($i = 1,2,...,N$) are variables (physical, biological, epidemic, etc.) and $\mathcal{L}[\cdot]$ is a suitable operator (algebraic, differential, etc.). One can think of law (6) in two ways:

(*i*) As an *interactive relationship* between the variables X_i. The law (6) is interpreted as expressing a proportionality relationship between the variables, in which case one can ask questions of the basic forms "to what factors is X_1 related" or "to what extent is X_1 interacting with X_j ($j = 2,...,N$)."

(*ii*) As a *cause-effect association* between the variables X_i. The law (6) is interpreted as expressing the sequence of X_i, in which case one can ask questions of the form "what variable is the cause of which variable" or "what causes X_1".

In some cases the interpretation *ii* may be more problematic yet more informative than the interpretation *i*. For demonstration, it is best to use some examples from general physical sciences, as follows.

Example A.13. Consider Newton's second law: $F = ma$ (m denotes the mass of an object and a its acceleration, and F is the force applied on the object). According to the interpretation *i*, the law simply states that for a given m, a is proportional to F. According to the interpretation *ii*, however, the law states that if a known force F is applied to a given mass m, it will cause that mass to change its state of motion in a specified way. Interpretation *i* is certainly shorter and less ambiguous than interpretation *ii*, but the latter offers more information about the kind of physical associations involved and their consequences. Furthermore, causality (Section I.D) may function in both directions. Consider Boyle's law for a given mass of gas, at a constant temperature: $PV = constant$ (P is the absolute pressure and V is the volume of the gas). According to interpretation *ii*, the law states that changes in P cause contractions and expansions, but also that changes in V cause compressions or refractions. According to interpretation *i*, on the other hand, the law simply states that P is inversely proportional to V.

In theory, the choice of considering an epidemic model is critical, because it includes salient conceptual issues, such as which particular biological, physical, and demographic processes are included in the model, which are the underlying assumptions and mechanisms, what is the conception of the space-time environ-

[14] See, also, the distinction between formal and interpretive components considered in Section B.a later in this chapter; and the discussion on form vs. substance in Section I.A.

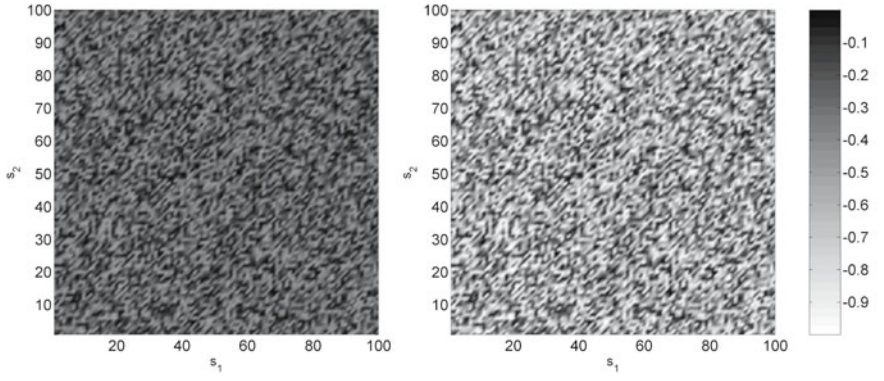
ment, what connections can be established between different domains, etc. In the case of environmental epidemiology, Christakos and Hristopulos (1998: Chapter VIII) have considered a number of models in a stochastic context, including multi-compartmental toxicokinetics, population exposure-response relationships, and health damage indicators.

The conventional solution of a mathematical model often does not suffice in real world situations. On occasion, epidemic modelling may not be as straightforward as one might expect it to be, in which case caution must be exercised. This is demonstrated in the case of *model selection*. In practice, SEP may be confronted with epidemic models of varying complexity (e.g., Anderson and May, 1995; Mollison, 1995), in which case the choice of the most appropriate model for the situation depends on a number of factors including the availability of good quality data for parameter estimation, the resulting prediction accuracy, and the intended use of the model. Complex models, e.g., usually offer a better representation of uncertainty and better prediction for cleaner data. Simpler yet epidemically meaningful models may yield more accurate predictions in case of rather noisy data[15].

A criterion used by a large class of model selection approaches is the accuracy of the predictions obtained on the basis of each model (Walters, 1986): among a series of candidate models, a particular model is chosen, which leads to the most accurate predictions of the epidemic variables of interest. However, in some situations the choice of the appropriate model may depend on the choice of the disease variable to be predicted. Such a situation is described in the following example.

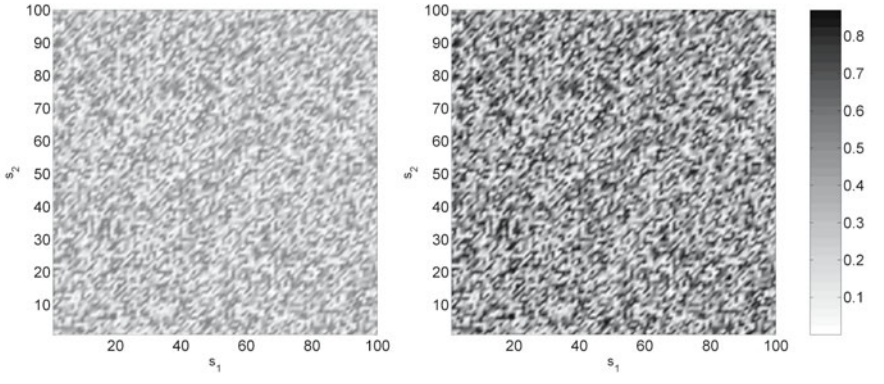
Example A.14. For illustration purposes, let us consider a controlled (simulated) environment in which two models M_q ($q = 1,2$) are available for the epidemic system under consideration. Predictions are obtained in terms of the disease variables $X_{i,\boldsymbol{s}}$ ($i = 1,2$), where the vector $\boldsymbol{s} = (s_1, s_2)$ denotes coordinates within a spatial domain D. The actual (true) realizations of the two variables over D are assumed known and are denoted by x_i^a ($i = 1,2$), whereas the predicted realizations generated by the models M_1 and M_2 are denoted by x_i^1 and x_i^2, respectively. Given the x_i^a and x_i^q ($q = 1,2$), the prediction errors $e_{x,i}^q = x_i^a - x_i^q$ ($i, q = 1,2$) between the actual and the predicted realizations (generated by each one of the two epidemic models) were calculated. Then, the spatial distributions of the relative errors $\Delta e_{x,i} = \left|e_{x,i}^1\right| - \left|e_{x,i}^2\right|$ ($i = 1,2$) over D were plotted in Fig. 2. Clearly $\Delta e_{x,i} < 0$ ($i = 1,2$) throughout D and, hence, model M_1 should be selected. But we are not done yet. Next, assume that the initial variables $X_{i,\boldsymbol{s}}$ of the

[15] Gauch (1993) has argued that in certain circumstances models can be more accurate than the data used to build them, for they are capable of amplifying hidden patterns and ignoring noise.



(a) (b)

Figure 2. Relative predictive errors for the two models: (a) $\Delta e_{x,1}$, and (b) $\Delta e_{x,2}$.



(a) (b)

Figure 3. Relative predictive errors for the two models: (a) $\Delta e_{y,1}$, and (b) $\Delta e_{y,2}$.

same disease system are related to another set of disease variables $Y_{i,\boldsymbol{s}}$ via the relationships

$$\left.\begin{aligned} Y_{1,\boldsymbol{s}} &= 6.93\,X_{1,\boldsymbol{s}} + 4.04\,X_{2,\boldsymbol{s}} \\ Y_{2,\boldsymbol{s}} &= 12.12\,X_{1,\boldsymbol{s}} + 6.93\,X_{2,\boldsymbol{s}} \end{aligned}\right\}. \tag{7}$$

The new errors $e^{q}_{y,i} = y^{a}_{i} - y^{q}_{i}$ $(i,q = 1,2)$ between the actual and predicted realizations generated by the two models were calculated, and the spatial distributions of the relative errors $\Delta e_{y,i} = \left|e^{1}_{y,i}\right| - \left|e^{2}_{y,i}\right|$ $(i = 1,2)$ over D are plotted in Fig. 3. Clearly $\Delta e_{y,i} > 0$ $(i = 1,2)$ throughout D and, hence, model M_2 should be selected in this case. By way of a summary, predictions in terms of the variables $X_{i,\boldsymbol{s}}$ $(i = 1,2)$ suggest that model M_1 is the better representation of the real epi-

demic system, whereas predictions in terms of the variables $Y_{i,s}$ $(i = 1,2)$ favor model M_2. Therefore, one should be aware that there may exist cases in which the selection of a model representing an epidemic system may not be uniquely determined by means of the predictions generated. In this sense, our choice of a model might need to be associated with our preference for a specific group of predicted variables. This is a rather open research problem, worthy of further investigation.

c. Questions of Concepts and Questions of Facts

In scientific inquiry it is essential to distinguish questions of *concept* from questions of *fact*. The question, e.g., "Is the West Nile virus epidemic likely to spread all over the world?" is a question of fact. The relevant evidence consists of facts about the Nile virus and about the world. Of course, we may not be able to give a definite answer to the question, but this is not due to any doubt we may have about the concepts involved. It is rather due to our inability to predict which way the facts point, or because the facts available are incomplete and inconclusive. On the other hand, the question "Is the West Nile virus epidemic adequately described by a random field?"[16] is a question of concept. Indeed, this question asks us to evaluate whether the Nile virus distribution fits or not into the random field concept. To answer the question we need to examine the epidemic characteristics of the West Nile virus distribution in space and time and compare them with the theoretical features of the random field in order to decide whether they are compatible or not. This may be a decision that depends on the interpretation of the random field concept we select, on our understanding of the Nile virus spatiotemporal variation, on the level of the relevant hierarchy, etc. Hence, questions of concept are distinguished from questions of facts. In the former, issues of meaning, use, and function arise and are at the center of the answers, whereas in the latter, thought processes provide answers on the basis of existing facts.

It goes without saying that, despite their fundamental differences, both types of questions are important in public health research and closely dependent on each other. A sense of symmetry is desirable here. While fact gathering (by observation and experimentation) is an indispensable component of scientific development, trying to understand uncertainty on the basis of observed facts alone will not get us far. It would reduce uncertainty evaluation to merely observation error analysis, lacking any explanatory or predictive power. All the public health facts are not of equal value, and we must have a hypothesis or a theoretical model to guide our error analysis, obtain the necessary insight about the existing uncertainties, integrate the various experimental results to obtain a holistic picture of the situation, and make credible predictions[17]. Also, we must always keep in mind

[16] The random field concept and its central role in the uncertainty analysis of epidemics are discussed in the following Section B.

[17] "With different instrumentation, people see different stuff. Any one individual data set gives a picture, but it's not the *whole* picture" was one of the critical assessments of the

that a central element of scientific interdisciplinarity is integration of concepts rather than of data (the latter being merely numbers that obtain meaning in the context of a sound theory). Actually, since observations are “theory laden”, they will be interpreted differently after a change of paradigm takes place that involves new concepts. Thagard (1999) refers to several scientific revolutions (in physics, biology, and psychology) to demonstrate the importance of concepts and conceptual changes in the development of scientific knowledge. Remarkably, in many of these revolutions the new concepts were based mainly on *thought experiments* and visual imagery abstracted from the world of sense perceptions.

More often than not, one's answer to a question of fact, may well depend on one's previous answer to a relevant question of concept. The way we conceptually conceive physical occurrences or facts of nature tempers the way we evaluate these occurences or facts. The way we look at, e.g., a set of tissue data depends on our relevant concept of tissue. Predictions of space-time distributions of Black Death mortality using modern stochastics, which involves a physical theory-dependent conceptual framework, can lead to more accurate and informative results than using the classical statistics framework, which is based on a theory-free interpretation of facts. Another historical example may be instructive here.

Example A.15. Tycho Brahe, a great astronomer of his time, had collected a set of superb observations concerning planetary positions. Although a very good gatherer of facts, he was lacking the necessary theoretical concepts that would allow him to make good use of his data and build a reasonable set of celestial laws (e.g., despite his excellent collection of facts, his poor conceptual formulation led to nonsensical conclusions). This task (and glory) was thus left to Johannes Kepler, who later derived and proved an adequate conceptual model of planetary motion using Brahe's data. Therefore, adequate answers to questions of concept may need to be given before meaningful answers to questions of facts can be obtained.

In most cases it is important to establish a sound conceptual understanding of the public health problem before gathering relevant facts by means of surveys, computational and experimental investigations, etc. This is the view advocated by the old dictum, "One really understands a problem when he can conceptually guess the answer before he does the calculations or performs the experiments". We will not go that far. We will argue, however, that conceptual understanding focuses on the really important aspects of the phenomenon and puts aside complexities that are completely beside the point[18]. Hence, the mathematical details are often secondary to the conceptual framework and logic of scientific inquiry. It is the understanding of the conceptual framework and principles, not the calculation, which is the primary issue in public health studies, as well. Mollison (1995:

situation concerning population health effects due to the World Trade Center disaster (Dalton, 2003).

[18] When Galileo, e.g., was trying to understand the fundamentals of objects in motion, he knew that the key issue was to conceptualize how objects fall through a vacuum, ignoring wind effects and other details.

17) is probably right to maintain that "The fundamental aim is to help understanding of the relation between assumptions and the related dynamics: because without such understanding even a model which fits [epidemic] data perfectly can be of no scientific value". In fact, in many cases, no new mathematical tools are involved, but it is rather the novel and innovative way in which old tools are combined that can lead to a new conceptual framework. Furthermore, a new conceptual framework may point to new kinds of facts that need to be gathered via innovative experimentation.

Uncertainty in concept formation will be reflected into a corresponding uncertainty in experimental results. An adequate representation of the uncertainty related to proposed concepts can improve the accuracy of the facts gathered through experimentation; similarly, a meaningful calculation of the uncertainty of the experimental facts can offer valuable information in our representation of the uncertainty of the corresponding concepts. This twofold argument is summarized as follows: concept-related uncertainty and fact-related uncertainty are closely linked and can enlighten each other.

The conclusion one draws from the preceding discussion is that *critical thinking* systems based on the close interaction between concepts and experimental fact may be more valuable in public health research and development than belief-based systems. In many cases, the latter are not concerned with scientific evidence except as it supports the belief. Also, belief is often associated with common sense, which frequently has been proven naive and inappropriate for extending our knowledge. Miller (1996) gives a fascinating account of historical incidents where common sense-based belief had pointed to the wrong direction. The theory of probability, in particular, is a field in which common sense has been frequently proven wrong. Time and again, rigorous mathematical calculations have led to results that were completely unexpected on the basis of common sense.

d. Epistemic and Ontologic Concepts

A major classification of public health concepts can be drawn in terms of *epistemic* (knowledge-theoretic) vs. *ontologic* considerations. While the latter is directly concerned about nature, the former rather focuses on information about nature (Weil, 1978). Traditionally, causal relationships have been considered to be ontologic, describing objective (physical, biological, etc.) constraints in our world (see, also, Section I.D). Probabilistic relationships, on the other hand, are epistemic, reflecting either the particular KB situation or the nature of the problem considered. The former case is concerned with a lack of detailed information, whereas the latter case is associated with the kind of public health problem we wish to solve. The probabilistic interpretation is necessary, e.g., when one seeks information about the mortality rate of NC hospital patients in the first 3 hours after the removal of one kidney rather than when one seeks to predict whether Mr. Karpenisiotis, whose kidney has just been removed in an NC hospital, will survive the next 3 hours.

To put it in a slightly different way, the properties of an ontologic concept are determined by nature itself. An epistemic concept, on the other hand, can possess whatever properties we decide to give it (often subject to the condition that the results of any calculations involving the concept agree with experiments). Analysis in terms of epistemic vs. ontologic concepts can lead to strikingly different answers to questions of facts. The long-standing quantum mechanics debate is a case in point. Looking at the same facts, Bohr's evaluation in terms of epistemic concepts implies that quantum mechanics is a complete theory, whereas Einstein's analysis in terms of ontologic concepts concludes that quantum mechanics is an incomplete theory (D'Espagnat, 1995).

In the context of the above distinction, uncertainty characterizing a public health system can be seen both as an epistemic concept describing one's state of incomplete knowledge regarding the system and an ontologic concept that reflects certain objective aspects of reality. The following simple example (modified from Jaynes, 1989) is quite instructive in this respect.

Example A.16. A population consists of M members possessing a specific gene G that makes them susceptible to a deadly disease, and $N-M$ members who do not possess the gene G. If members are selected at random for testing, and R_i denotes that a G member was selected on the i-th draw, then the uncertainty about R_1 is expressed by the probability function $P(R_1)=M/N$. If we know that a G member was selected at the first draw, the uncertainty of the second draw is represented by the conditional probability function $P(R_2|R_1)=(M-1)/(N-1)$, which expresses a kind of ontologic causal influence of R_1 on R_2. Suppose now that we are told that a G member was selected on the second draw. Then, given that the second draw cannot have a physical influence on the first, an ontologic interpretation of the situation would require that $P(R_1|R_2)=P(R_1)$. On the other hand, although R_2 cannot affect R_1 in an ontologic (physical) sense, an epistemic interpretation of the situation will imply that knowledge of R_2 does affect our inferences about R_1. Hence, the uncertainty about R_1 should be expressed by $P(R_1|R_2)=P(R_2|R_1)$ in epistemic terms.

As a consequence, whether uncertainty is viewed from an epistemic or an ontologic standpoint can affect the outcomes of the analysis of the epidemic system in question. Of course, this thesis begs the question: when should an epistemic vs. an ontologic concept of uncertainty be used? The answer to this question may depend on the hierarchical level of the analysis (see next section), the nature of the data available, the role of the observer (in modern science, e.g., it is often the epistemic aspect of observations that is of importance), and the cognitive accessibility of future events (which are, otherwise, physically and observationally inaccessible).

In the end, public health scientists may find themselves acting as a kind of *applied philosophers*[19]. The interdisciplinary, multi-cultural, and multi-objective nature of the world could leave them no choice. Indeed, regardless of how technical or formal their research may be, they will always need to gain intellectual access to issues such as the nature and reliability of knowledge, the conception of reality, the reasoning mode, and the underlying methodological assumptions.

e. Conceptual Hierarchies

The conception of a *hierarchy* is vital in many thought processes and intellectual mechanisms. It may be instructive to start with a few examples of conceptual hierarchies commonly encountered in science:

(*i*) Hierarchy of *biological scales*, from the microscopic scale (e.g., atoms) to the macroscopic scale of everyday life (e.g., humans).
(*ii*) Hierarchy of *animal types*, from super-types (e.g., animal) to sub-types (e.g., horse).
(*iii*) Hierarchy of *disease explanations*, from infectious disease (bacterial and viral) to molecular-genetics (e.g., multifactorial).

Viewed from the angle of similar hierarchies, many of the concepts characterizing an epidemic system are not absolute. Occasionally we may do better if we view public health uncertainty within the context of a certain conceptual hierarchy. At the macroscopic level (hierarchy *i*), e.g., uncertainty may be viewed as an epistemic concept describing one's state of incomplete knowledge regarding a situation, whereas at the quantum level uncertainty may be seen as an ontologic concept that describes certain objective aspects of reality[20]. The following example is also instructive.

Example A.17. While at the level of independent clinical trials an interpretation of data uncertainty in terms of frequencies seems to be adequate in many cases, at the level of epidemic processes that vary in space and time the same interpretation proves to be clearly inadequate, and a different theory-laden interpretation of uncertainty is needed. Furthermore, evaluating uncertainty on the basis of a *reductionist* approach (i.e., understanding the whole by learning about an hierarchy of its parts) has been very successful in the study of physical phenomena, whereas

[19] In his discussion of disease causation, Rothman (2002: 15-16) points out that, "How do we go about determining whether a given relationship is causal? Some scientists refer to checklists for causal inference, and others focus on complicated statistical approaches, but the answer to this question is not to be found either in checklists or is statistical methods. The question itself is tantamount to asking how we apply the *scientific method* to epidemiologic research. This question leads directly to the *philosophy of science*."

[20] The latter is the meaning of Heisenberg's uncertainty principle, at least in the context of the Copenhagen interpretation.

uncertainty evaluation on the basis of a *teleologic* approach (i.e., understanding an organism by learning about the purpose of its hierarchy of morphological and behavioral traits) may be more appropriate for certain biological phenomena[21].

The preceding analysis leads to the conclusion that the proper interpretation of uncertainty concerning a phenomenon (biological, epidemic, demographic, physical, etc.) may depend on the level of the hierarchy that the phenomenon is associated with. Often, it may be the *scale* of observation that creates the phenomenon. E.g., change in scale has consequences in most functions of living organisms (Schmidt-Nielsen, 1999). There exist biologic situations in which the study of humans can only be performed over a certain range of coarse scales, whereas an organism looks completely different seen through a microscope when individual cells become visible.

Example A.18. In Table 4, different human exposure scales are used to classify variables, such as space, time, age, exposure level, and health effects.

In epidemic investigations, an interesting situation of the hierarchy of scales is the so-called "change-of-scale effect", which has to do with the different degrees of disease variation associated with the same type of observation when the area within which the observation takes places changes (e.g., from state to county to city, etc.; Christakos *et al.*, 2002; Choi *et al.*, 2003). The implications of this effect in the case of Black Death are discussed in Section III.D.e. Also, in Section IV.B.a we introduce a scaling law which links the duration of the epidemic with the population scale (expressed in terms of the pre-plague city size). This kind of laws are usually expressed in the form of descriptive equations that can reveal connections that otherwise may remain obscure and can generate estimates of essential disease variables.

In light of the above considerations, a distinction between the concepts of uncertainty and space-time *variability* is usually called upon in scientific applications. In particular, the epistemic interpretation of uncertainty at the macroscopic level of our everyday lives (based on insufficient knowledge, incomplete understa-

Variable	Scale
Space	$\mu m \rightarrow Km$
Time	$m\,\mathrm{sec} \rightarrow years$
Age	$young \rightarrow old$
Exposure	$micro \rightarrow macro$
Health effect	$local \rightarrow global$

Table 4. Examples of scale variations in human exposure studies.

[21] For a fascinating discussion of the revival of Aristotle's teleologic approach in life sciences the reader is referred to Allen *et al.* (1998).

nding, inadequate cognition processes, etc.) distinguishes it from natural variability, which is rather an ontologic concept describing the actual space-time distribution of a real-world phenomenon (e.g., the distribution of ozone exposure values across space and time). Despite this distinction, however, we often need to resort to an epistemic representation of the natural variability in terms of uncertainty concepts due to our incomplete state of knowledge and inadequate data sets.

B. On Stochastic Modelling

a. Formal and Interpretive Components

Traditional public health studies mostly relied on standardized mortality ratio, life tables, and Mantel-Haenszel methods, among others. A defining feature of modern epidemiology was the more sophisticated use of quantitative methods (Susser 1985), which have been employed by public health researchers to relate the frequencies of diseases to the distribution of exposure and to control the potential confounding in non-experimental data (e.g., by comparing two standardized mortality ratios, by stratified tabular analyses). The introduction of statistical models into epidemiologic studies appealed to many researchers, mainly because of its considerable capacity to "statistically" adjust for multiple potential confounders (Rothman and Greenland, 1998). Advancement in computation and the availability of statistical software made statistical model-based inference more pervasive in epidemiologic research since the 1980s (Chen, 2005)[22]. However, many researchers have realized that real-world epidemic problems are much more complex to be handled by purely statistical methods. Speaking after the 1968 epidemic of Hong Kong flu, the epidemiologist Alexander Langmuir remarked, "Influenza predictions are like weather forecasts". If this is the case, a logical implication is that the appropriate mathematical tools to be used in the study of such epidemics are stochastic tools similar to those used in weather forecasting (random field models, stochastic differential equations, variational techniques, etc.). Indeed, in our view stochastic modelling is the primary conceptual and operational apparatus for studying fundamental uncertainties of the type happening in public health research, in general, and epidemics, in particular.

Beyond an initial view that the term *stochastic modelling* is associated with the study of uncertainty in public health situations, at a more substantial level perceptions regarding stochastic modelling's uses are not as uniform as one might think. This should not come as a surprise, in view of the interdisciplinary nature of science. Depending on the application considered, one may refer to stochastic models as environmental, weather forecasting, epidemiologic, genetic, ecological, etc. Nevertheless, a common factor in all these cases is that stochastic modelling is

[22] Air pollution studies are typical examples in which statistical software tools has been applied to address public health issues (unfortunately, not always without some serious problems; see Knight, 2002, and Revkin, 2002).

concerned with the mathematically rigorous and scientifically meaningful representation, explanation, and prediction of natural and life systems in uncertain environments (such uncertainties may be due to measurement errors, heterogeneous data bases, erratic fluctuations in the space-time variation of the underlying processes, insufficient knowledge, etc.).

In such a framework, the main goal of stochastic modelling may be to provide a realistic epidemic situation with *spatiotemporal continuity* and *internal consistency*. To achieve such a goal, stochastic modelling relies on the powerful blending of two essential components:

(*i*) A *formal* component that focuses on mathematical structure, logical process, and sophisticated theoretical representation.

(*ii*) An *interpretive* component concerned with applying the formal part in real-world situations, including the epidemiological content of mathematical structure, the physical meaning of specific observation methods, and the connections to other empirical phenomena.

Formal stochastic modelling deals with a large variety of mathematical topics, including random fields, probability theory, stochastic differential and integral equations, statistics, space-time geometries, logical reasoning under conditions of uncertainty, optimal estimation, and multi-objective optimization theories, among others. The challenge of applying sophisticated stochastic modelling in public health sciences is often not in the formal component itself, but in the appropriateness of the application and the validity of the interpretive component that goes beyond mathematics into the realms of logic, physical and biological knowledge, and empirical observation. Interpretation issues are relevant when one needs to establish *correspondence* rules (also called, *operational* or *duality* rules) between the disease variables and the formal mathematics that describe them, to measure and test the formal structure, or to justify certain methodological steps[23]. On the other hand, the adequate interpretation of experimental or survey data and the design of new experiments in component *ii* depend on the sophisticated theoretical analysis of the epidemic structure in component *i* that is consistent with the data.

The fruitful interaction of formal and interpretive investigations plays a crucial role in the successful application of stochastic modelling in public health sciences. The essential connection between the formal and the interpretive components of stochastic modelling has been astonishingly productive, in both ways: formal techniques have generated the means for understanding public health phenomena, like epidemics, beyond sense perceptions; and interpretive investigations have produced new and more powerful formal techniques. In fact, stochastic epidemic modelling differs significantly from the classical statistics approach in this respect: the former is founded on laws (physical, biological, etc.), phenomenological representations and scientific reasoning, whereas the latter mainly uses formal techniques of pattern fitting (trend projection, regression analysis, sampling theory,

[23] That is not to imply that the two components are totally independent, or merely linked by the correspondence rules. Instead, they form an integrated whole.

etc.). This remarkable feature of stochastic modelling enhances its scientific content and makes it a central force in the study of such diverse phenomena as contaminant transport in environmental media, turbulence, ionospheric scattering and electromagnetic wave propagation through the atmosphere, large-scale phenomena associated with disease and mortality, embryonal formative processes, and organic molecules organizing themselves into organisms of increasing complexity through random chemical processes.

Most public health phenomena and epidemic systems governed by mathematical equations include situations that need to be treated from a stochastic modelling viewpoint (e.g., Bailey, 1957; Mollison, 1995). In situations involving uncertain elements and random fluctuations, stochastic modelling formally casts the governing epidemic equations into a stochastic form that may involve random field realizations, probability distributions, or space-time moments. As a consequence of their biological basis, these stochastic equations provide public health scientists with the means for generating sound scientific inferences, as opposed to merely statistical inferences[24].

b. An Outline

An outline of the main stages of stochastic modelling is given in Fig. 4. Stochastic modelling in a public health context relies on the interaction between its formal and interpretive components, and involves a combination of interdisciplinary elements. Briefly, the main stages are as follows*: (a)* A *hard core* of fundamental concepts, constitutive hypotheses, and theoretical representations in terms of stochastic theory. *(b)* A set of *auxiliary tools* (model parameters, assumptions, correspondence or duality rules, etc.) linking formal theory with the observed public health phenomenon. *(c)* A *heuristic* (i.e., a group of guidelines for choosing auxiliary tools), which with the help of mathematical techniques, offer interpretations, explanations, and predictions about the real world public health situation. The methodology is successful when these explanations and predictions are corroborated. If they are refuted (e.g., falsified), one may need to go back to stage *b* and choose another set of auxiliary tools.

Fig. 4 offers a useful perpsective for describing the structure of scientific knowledge and the processes that advance it. Some important features include:

- Its *operational* character expressed by the dictum, "what one *does* determines what one *means*". In this context, concepts and tools acquire meaning from the operations we perform with them.
- Its *corroboration* property, which is materialized in terms of concise reports evaluating the stochastic modelling methodology.

[24] In terms of minimum variance, bias, efficiency, estimation, and confidence tests, etc.; Bury (1975). An interesting discussion of scientific vs. statistical inferences may be found in the little known book by Wang (1993: 160)

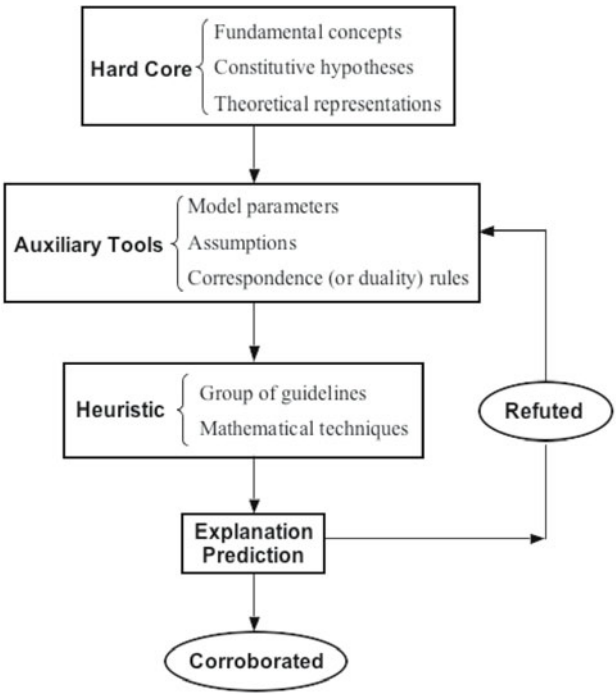


Figure 4. Outline of the main stochastic modelling stages.

- Its *progressive* character, i.e., the revised tools in stage *b* successfully anticipate previously refuted predictions, lead to novel results, etc. Space-time predictions may be deductions from generalizations (e.g., law statements) and singular statements (data or "circumstances").

Let us now briefly focus on the issues of *explanation* and *prediction*. A lot of what is going on in epidemic studies today has to do with *ad hoc* explanation. According to stochastic modelling, however, what does the explaining must be richer in *content* than the situation to be explained. In this sense, stochastic methodology is Aristotelian rather than Deweyan (see, also, Section I.B.a). Most studies of scientific methodology emphasize the salient role of prediction (expressed in terms of testable auxiliary tools) in conjunction with hypothesis making and model building. Epidemic predictions may be empirical generalizations based on unexplained correlations (e.g., statistical forecasting techniques), or theoretical predictions based on the knowledge of laws (physical, biological, demographic, etc.). In several situations epidemic predictions are uncertain and lack the desired level of accuracy, in which case rigorous stochastic analysis can increase the accuracy of these predictions by continuously improving our understanding of the uncertainties involved. As a matter of fact, when considered in the appropriate context the determining role of prediction in human affairs can hardly be overestimated. Modern neuroscience, e.g., strongly emphasizes the importance of prediction: as

we saw above (Section I.C.b), human brains make predictions on an everyday basis by integrating general or core knowledge (of the invariant structure stored in memory) with specificatory or site-specific knowledge (highly specific inputs and recent details). According to Hawkins (2004), prediction is the primary function of the neocortex, and the foundation of intelligence. If one seeks to understand what creativity is, how to make intelligent choices in any scientific field or in everyday activities, and even how to build intelligent machines, one must comprehend the nature of these predictions and how the cortex makes them. In the SEP context, predictions are visualized by means of space-time *maps*. The generation of these maps relies on the sound theoretical support provided by stochastic theory as well as the modern technological facilities supplied by temporal geographical information systems (Section E below). At this point, it may appropriate to remind the reader of the possibly asymmetric character of the relationship between explanation and prediction described in Section I.D.

In the SEP context, the stochastic modelling methodology outlined in Fig. 4 should be viewed as a continuously evolving project rather than a dogmatic, timeless, and unchanging framework. We would like to emphasize that the goal of the project is not to reject or suppress all novel forms of public health knowledge just because they do not happen to conform to its current framework or are subversive to the project's basic commitments, whatever they may happen to be. On the contrary, new viewpoints should be always considered when they offer objective opportunities for development and scientific growth. Skepticism and critical thinking, as well as open-mindedness, must be exercised tirelessly by the stochastic epidemic modeller in order to decide whether new evidence makes it necessary to have a shift in the current conception of stochastic modelling or to resist meaningless interventions to the project that are devoid of any scientific substance.

C. Theory of Spatiotemporal Random Fields (S/TRF)

a. Basic Notions

At a basic modelling level, accurate representation of the epidemic patterns across space and time relies on the adequate characterization of the distibutions of the relevant variables (e.g., variation of susceptibles or infecteds in the space-time domain), as well as the adequate processing of the uncertain information available regarding the essential parameters of the epidemic[25]. If such issues are not adequately addressed, erroneous public health decisions could be made having potentially serious consequences. The strong spatial element characterizing many epidemiologic concepts has not been unnoticed. Holmes (1997: 111), e.g., argues that: “It is obvious to any observer of epidemics that the spread of disease is un-

[25] This includes cases in which inaccurate results are obtained due to poor computational programming of the mathematical techniques employed.

avoidably spatial. Disease moves from individual to individual following the network of contacts between individuals within a population". We would like to go beyond that and claim that such a spread is essentially *spatiotemporal*, i.e., it propagates in a composite space-time manner. This being the case, stochastic theory comes to the rescue and proposes a powerful solution in terms of the *spatiotemporal random field* (S/TRF) model. For a rigorous mathematical discussion of the classical S/TRF theory in a life sciences context, the reader is referred to Christakos and Hristopulos (1998). Moreover, more recent conceptual formulations of S/TRF in terms of deductive logic can be found in Christakos (2002a)[26]. Here we restrict ourselves to a rather basic introduction to the S/TRF model and make the necessary connections with the public health phenomena it represents.

Let $\boldsymbol{p} = (\boldsymbol{s}, t)$ be a point in the space-time domain ($\boldsymbol{s}$ denotes the spatial location and t the time instant under consideration). A S/TRF model, $X_{\boldsymbol{p}} = X_{\boldsymbol{s},t}$, is viewed as the collection of all epidemically possible realizations of the phenomenon we seek to represent mathematically. The multiplicity of realizations allows S/TRF to account for the uncertainty sources and, at the same time, to adequately represent the spatiotemporal variation of a disease. These realizations have an epistemic quality: they do not correspond merely to all possible ways an epidemic system can be represented logically, but rather to the ways that are consistent with the *known* properties of the system (i.e., known by the modeller's brain). Hence, the S/TRF theory can produce disease distribution models that are mathematically rigorous and tractable while, at the same time, they are geographically and epidemiologically plausible. From a stochastic theory point of view, the S/TRF model is fully characterized by its probability density function (pdf), f_{KB}, which is generally defined as

$$P_{KB}[x_1 \le X_{\boldsymbol{p}_1} \le x_1 + dx_1,\, x_2 \le X_{\boldsymbol{p}_2} \le x_2 + dx_2,\, \ldots] = f_{KB}(x_1, x_2, \ldots)\, dx_1\, dx_2 \ldots \qquad (8)$$

where the subscript *KB* denotes the knowledge base utilized to construct the pdf ($KB = \mathcal{G}$, $\mathcal{S}$ or $\mathcal{K} = \mathcal{G} \cup \mathcal{S}$; Section I.C.b). By means of Eq. (8), the f_{KB} assigns probabilities to different $X_{\boldsymbol{p}}$-realizations and may involve multiple space-time points. The S/TRF (8) has many conceptual layers and salient features that tell a long story that all epidemiologists should be aware of:

(*a*) The model assumes a composite space-time manifold, i.e., it considers space and time as an integrated whole rather than as separate entities.

(*b*) It can incorporate spatiotemporal cross-correlations and interdependencies of the disease distribution, as well as laws of epidemic spread (e.g., expressed in terms of algebraic or differential equations).

(*c*) It is of immediate relevance to models that are mathematically rigorous and tractable while, at the same time, they are geographically and epidemiologically plausible.

---

[26] While the fundamental element of propositional logic is the proposition (Section A above), the fundamental element of the deductive S/TRF formulation is the stochastic event; for more details see references.

(*d*) It is capable of generating informative maps enabling the determination of several important characteristics of the disease as it moves from one geographical region to another, such as the direction and speed of epidemic spread, prevailing trends and patterns, as well as the relative significance of the different disease components.

These features of the S/TRF will eventually reveal themselves during the process of studying the Black Death epidemic in the following sections and chapters. At this point we would like to point out some important aspects of the S/TRF model that are sometimes misunderstood. When representing a public health phenomenon in terms of a S/TRF model we attribute to it a *random* character but, also, an equally important *structural* character. This is acknowledged, e.g., by the fact that a realization is allowed only if it is consistent with the knowledge available regarding the public health phenomenon the S/TRF represents--this is sometimes called the S/TRF *conditionalization* property. Conditionalization accounts for mathematical theories of large-scale phenomena as well as for purely empirical descriptions. Clearly, not all realizations of the S/TRF are equally probable. Depending on the underlying mechanisms, some realizations are more probable than others, and this is reflected in the pdf of the S/TRF, Eq. (8) above.

Example C.1. Consider the case of individuals organizing themselves into communities of increasing complexity through random processes of spatiotemporal movement and interaction. The possible arrangements of individuals into complex societies are realizations of an S/TRF with varying probabilities of occurrence. These probabilities depend on the characteristics of the interacting individuals and the laws that govern their dynamics.

The S/TRF model allows a rigorous characterization of complex epidemic variability and uncertain effects, and generates predictive space-time maps. Depending on the situation, random field representations of disease distribution can be combined with other types of information, such as environmental exposure concentration, frequency and duration, population density, lines of infection, contact processes, etc., in order to analyze sensitivity and assess the features of the epidemic. Random field models have led to considerable advances in the analysis and mapping of composite space-time heterogeneities, which are used in real world public health situations. For illustration purposes, in the following section we use the S/TRF theory to represent a few basic epidemic variables of the Black Death situation.

b. Expressing Black Death Uncertainty in Terms of S/TRF

As we saw above, the stochastic modelling of an epidemic such as Black Death starts by introducing a prime methodological assumption: the relevant disease variables will be mathematically represented as S/TRF. Mortality generally refers

to the proportion of a population that dies during a specific time period[27]. Mortality distribution across space and time is represented by the S/TRF $M_p = M_{s,t}$. This is a very important methodological step since, as it has been emphasized in the Black Death literature (e.g., Wood *et al.*, 2003), the Black Death mortality distribution is heterogeneous in space and time and, hence, the spatiotemporal random field theory is a most appropriate mathematical tool to handle this situation. As a matter of fact, most epidemic-related events are functions of space and time, i.e., they take place at some geographical location at a specified time, and they vary from one space-time point to another. Typically, the random field $M_{s,t}$ is mathematically described by the pdf f_{KB}, which assigns probabilities to the various possible mortality realizations, $m_{s,t}$, across space-time, see Eq. (8) above[28]. Loosely speaking, the S/TRF model frees data of their classical duty of determining directly mortality values at future times and allows them instead to determine the probability of these values.

Example C.2. For illustration purposes, let us consider the case of monthly mortality data or other proxies. Given the various uncertainties in the preparation of these sources of information, when we finally obtain a mortality value, say 18%, the number is likely to differ from the actual value, which we may never know. We would be surprised if the real value was, say, 60%, but we cannot disregard 15.6% or 20.9%. Practical situations like this are best handled in terms of stochastic theory. In contrast to a deterministic variable, which can only take a single value, random fields allow consideration of a range of values. Even better, the likelihood of each one of these values being the correct one does not have to be the same (every value can have a different probability of being the correct answer)[29]. Variations in the probability of delivering the correct answer define the shape of the pdf f_{KB}. There is a large number of possibilities regarding the shape of the pdf--SEP modelling is not restricted to any specific shape of the pdf.

The mortality S/TRF may be associated with different kinds of *conditional* probabilities, Eqs. (1)-(3) above. These probabilities are of particular interest when the S/TRF is implemented in a cause-effect context (see, also, the argument forms in Section A.a and the adaptation principles in Section D.c). Let F_{KB} denote the cumulative distribution function (cdf). Then, the

$$P_{KB}(M_{s',t'} \,|\, M_{s,t}) = F_{KB}(m_{s,t}, m_{s',t'})\, F_{KB}^{-1}(m_{s,t}), \tag{9}$$

---

[27] For the mortality definition used in Black Death modelling, see Eq. (III.1).

[28] As we will see in subsequent chapters, in view of the knowledge categorization thesis (Section I.C.b), the pdf may be also written as $f_{\mathcal{G}}$ or $f_{\mathcal{S}}$ to denote the fact that it has been constructed on the basis of the $\mathcal{G}$-KB or the $\mathcal{S}$-KB, respectively.

[29] These probabilities are important in a decision-making context. E.g., information on low-probability high-consequence epidemic events allows public health managers to better assess their decisions.

$$P_{KB}(M_{s,t} \rightarrow M_{s',t'}) = 1 - F_{KB}(m_{s,t}) + F_{KB}(m_{s,t}, m_{s',t'}) \tag{10}$$

and

$$P_{KB}(M_{s,t} \leftrightarrow M_{s',t'}) = 1 - F_{KB}(m_{s,t}) - F_{KB}(m_{s',t'}) + 2F_{KB}(m_{s,t}, m_{s',t'}) \tag{11}$$

are the statistical conditional, material conditional, and material bi-conditional probability functions, respectively; as before, $KB = \mathcal{G}$, $\mathcal{S}$, or $\mathcal{K} = \mathcal{G} \cup \mathcal{S}$.

For all practical public health purposes, space-time heterogeneity can be described in terms of (*i*) the mortality *mean* function (the bar denotes stochastic expectation)

$$\overline{M_{s,t}} = \int dm_{s,t}\, m_{s,t}\, f_{KB}(m_{s,t}), \tag{12}$$

at each space-time point $\boldsymbol{p} = (\boldsymbol{s}, t)$, (*ii*) the mortality *covariance* function,

$$c_{M;s-s',t-t'} = \overline{\tilde{M}_{s,t}\tilde{M}_{s',t'}} = \int\int dm_{s,t}\, dm_{s',t'} (m_{s,t} - \overline{M_{s,t}})(m_{s',t'} - \overline{M_{s',t'}}) f_{KB}(m_{s,t}, m_{s',t'}) \tag{13}$$

between pairs of points $\boldsymbol{p} = (\boldsymbol{s}, t)$ and $\boldsymbol{p}' = (\boldsymbol{s}', t')$, where

$$\tilde{M}_{s,t} = M_{s,t} - \overline{M_{s,t}}, \tag{14}$$

are mortality fluctuations, and (*iii*) the mortality semi*variogram* function

$$\gamma_{M;s-s',t-t'} = \tfrac{1}{2}\, \overline{M_{s,t} M_{s',t'}} = \tfrac{1}{2} \int\int dm_{s,t}\, dm_{s',t'} (m_{s,t} - m_{s',t'})^2 f_{KB}(m_{s,t}, m_{s',t'}). \tag{15}$$

The $\overline{M_{s,t}}$ represents structural trends of mortality, whereas the $c_{M;s-s',t-t'}$ and $\gamma_{M;s-s',t-t'}$ express space-time mortality dependence. This dependence is an inherent feature of mortality variation across geographical space and during different times. There exist, in fact, different forms of dependence that lead to distinct covariance shapes (specific covariance models of mortality are discussed in Section IV.B.c). The mortality variance, σ_M^2, is obtained from Eq. (13) if we let $\boldsymbol{s} = \boldsymbol{s}'$ and $t = t'$, in which case we get

$$\sigma_M^2 = \overline{\tilde{M}_{s,t}^2} = \int\int dm_{s,t}\, (m_{s,t} - \overline{M_{s,t}})^2\, f_{KB}(m_{s,t}). \tag{16}$$

Because it can investigate the different forms of space-time correlation that are allowed by the epidemic data and core knowledge available, the $M_{s,t}$ model can provide multiple permissible realizations (scenarios) and can also characterize their likelihood of occurrence.

Example C.3. For an illustration of the above formulas, consider the simple case of one *soft* (interval I; i.e., $m_1 \in I$) mortality datum at point $\boldsymbol{p}_1 = (\boldsymbol{s}_1, t_1)$ and one mapping point $\boldsymbol{p}_k = (\boldsymbol{s}_k, t_k)$ at which a mortality prediction is sought. First, only means (12) and variances (16) are assumed to constitute the general KB (i.e., no space-time mortality correlations are considered), in which case the $\mathcal{G}$-based pdf

is given by $f_{\mathcal{G}}(m_1, m_k) = e^{\mu_0+\mu_1 m_1+\mu_k m_k+\mu_2 m_1^2+\mu_3 m_k^2}$, where μ_i ($i = 0,1,2,3,k$) are functions of the known means and variances (in fact, they can be calculated in terms of the BME technique, see Section E.b below). The statistical conditional (*sc*) pdf is given by[30]

$$f_{\mathcal{G}}(m_k \,|\, m_1) = e^{\mu_0+\mu_k m_k+\mu_3 m_k^2} \int dm_1\, e^{\mu_1 m_1+\mu_2 m_1^2} = f_{\mathcal{G}}(m_k). \tag{17}$$

From Eq. (17), the *sc* mode estimate of the *S/TRF* at point $\boldsymbol{p}_k$ is the solution of

$$df_{\mathcal{G}}(m_k)/dm_k\big|_{m_k = m_{k,\mathrm{mode}}(sc)} = 0, \tag{18}$$

which gives $m_{k,\mathrm{mode}}(sc) = -\mu_k / 2\mu_3$. The material biconditional (*mb*) pdf, on the other hand, is given by

$$f_{\mathcal{K}}(m_k) = (2A-1)^{-1}[2\, A\, f_{\mathcal{G}}(m_k \,|\, m_1) - f_{\mathcal{G}}(m_k)], \tag{19}$$

where $A = \int_I dm_1\, f_{\mathcal{G}}(m_1)$. Eqs. (17) and (19) yield $\tilde{f}_{\mathcal{K}}(m_k) = f_{\mathcal{G}}(m_k \,|\, m_1)$, leading to the estimate $m_{k,\mathrm{mode}}(mb) = m_{k,\mathrm{mode}}(sc)$, in this case. Things are different if the space-time correlation term $m_1 m_k$ is included in the $\mathcal{G}$-based pdf, i.e., $f_{\mathcal{G}}(m_1, m_k) = e^{\mu_0+\mu_1 m_1+\mu_k m_k+\mu_2 m_1^2+\mu_3 m_k^2+\mu_4 m_1 m_k}$. Then,

$$f_{\mathcal{G}}(m_k \,|\, m_1) = A^{-1}\, B(m_k)\, f_{\mathcal{G}}(m_k), \tag{20}$$

where $B(m_k) = [\int dm_1\, e^{\mu_1 m_1+\mu_2 m_1^2+\mu_4 m_1 m_k}]^{-1} \int_I dm_1\, e^{\mu_1 m_1+\mu_2 m_1^2+\mu_4 m_1 m_k}$. As a consequence, the *sc* mortality estimate at point $\boldsymbol{p}_k$ is the solution of

$$f_{\mathcal{G}}(m_k)\, dB(m_k)/dm_k + B(m_k)\, df_{\mathcal{G}}(m_k)/dm_k\big|_{m_k = m_{k,\mathrm{mode}}(sc)} = 0. \tag{21}$$

Furthermore, for the *mb* density we get

$$f_{\mathcal{K}}(m_k) = (2A-1)^{-1}[2\, B(m_k) - 1] f_{\mathcal{G}}(m_k), \tag{22}$$

which differs from the *sc* (19); and the *mb* mode estimate at point $\boldsymbol{p}_k$ is the solution of

---

[30] The normalization condition $\int\int dm_1\, dm_k\, f_{\mathcal{G}}(m_1, m_k) = 1$ implies that $\int dm_k\, e^{\mu_k m_k+\mu_3 m_k^2} = (e^{\mu_0} \int dm_1\, e^{\mu_1 m_1+\mu_2 m_1^2})^{-1}$. By definition (Christakos, 2000), $f_{\mathcal{G}}(m_k \,|\, m_1) = e^{\mu_0+\mu_k m_k+\mu_3 m_k^2} \int_I dm_1\, e^{\mu_1 m_1+\mu_2 m_1^2}$ In view of the normalization condition, $(e^{\mu_0} \int_I dm_1\, e^{\mu_1 m_1+\mu_2 m_1^2} \int dm_k\, e^{\mu_k m_k+\mu_3 m_k^2})^{-1}$ reduces to Eq. (17).

$$f_{\mathcal{G}}(m_k)\,dB(m_k)/dm_k + B(m_k)\,df_{\mathcal{G}}(m_k)/dm_k - \tfrac{1}{2}\,df_{\mathcal{G}}(m_k)/dm_k\Big|_{m_k=m_{k,\mathrm{mode}}(mb)} = 0 \qquad (23)$$

By comparing the last equation with Eq. (21), we conclude that the *mb*-estimate is, generally, different than the *sc*-estimate in the case that space-time correlation is taken into account.

When implemented in the context of the Black Death epidemic, the S/TRF model should involve a number of critical empirical parameters, such as:

- Δ_s, Duration of epidemic in a community residing at geographical location s.
- $T_{s,o}$, Beginning of the epidemic.
- $T_{s,f}$, Ending of the epidemic (clearly, $\Delta_s = T_{s,f} - T_{s,o}$).
- τ, Serial generation time or serial interval (i.e., mean time interval between acquiring the disease to being able to transmit it).
- K_s, Average number of adequate contacts per individual per τ (the value of K_s will depend on the typical *lifestyle* characteristics of the susceptibles; see, e.g., Fig. 5).
- $P_{s,0}$, Population size at location s at the beginning of epidemic (time $t = 0$).
- G_s, Cumulative number of fatalities throughout the epidemic.
- f, Empirical Black Death conversion factor to convert from number of infecteds to number of deaths.

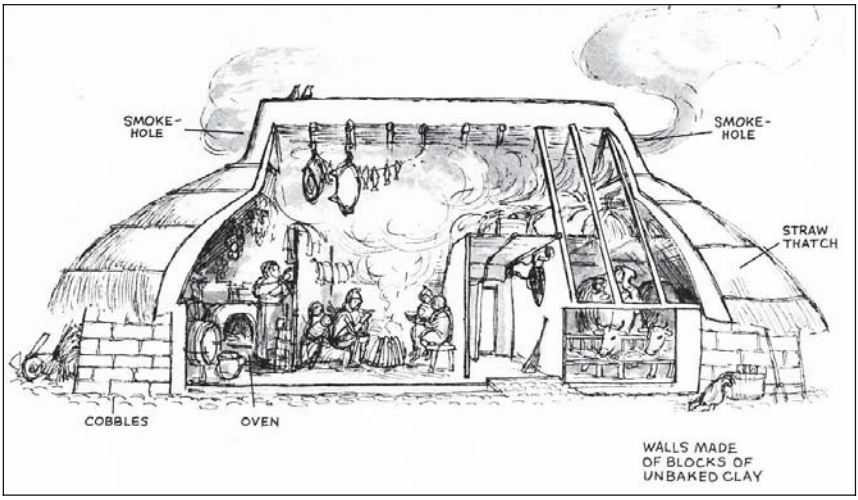


Figure 5. Typical lifestyle in an ordinary house in the village of Gerneham (UK) on a cold winter's morning in the year 1328 (Sancha, 1982).

In view of the above parameters, we assume that $t = k\tau$ ($k = 0,1,2,...$; τ is typically measured in days or months). Let $I_{s,(k+1)\tau}$ and $E_{s,(k+1)\tau}$ be two S/TRF that represent, respectively, infecteds (number of infected cases) and susceptibles (number of susceptible cases) between $t = k\tau$ and $t = (k+1)\tau$. The urban population size $P_{s,0}$ is measured in thousands of residents, and is such that $E_{s,0} = P_{s,0}$. The epidemic duration Δ_s at geographical location s is measured in months. The number of deaths between $t = k\tau$ and $t = (k+1)\tau$ is also a S/TRF given by

$$D_{s,(k+1)\tau} = f\, I_{s,(k+1)\tau}, \tag{24}$$

where the factor f expresses the proportion of fatalities among infecteds. The serial generation of $D_{s,(k+1)\tau}$ values depends on five parameters: τ, K_s, f, $P_{s,0}$, and $I_{s,\tau}$ (the number of infected cases between $t = 0$ and $t = \tau$). In light of the above considerations, we can also express mortality at each geographical location s and time period $t = (k+1)\tau$ as follows

$$M_{s,(k+1)\tau} = D_{s,(k+1)\tau} / P_{s,k\tau}, \tag{25}$$

where $P_{s,k\tau}$ (> 0) is the population at $t = k\tau$.

Essential space-time variability features of the disease parameters above are treated by S/TRF modelling in an integrated manner that accounts for non-linear geographical trends, temporal non-stationarity, random spatial fluctuations, and their cross-effects in epidemic propagation. S/TRF models can study large-scale population phenomena related to social and public health measures that may be proposed or applied. Since the book is concerned with the Black Death epidemic, our S/TRF analysis focuses on disease variables directly related to this study. However, the reader should be aware that the same analysis applies to any other epidemic variable or system.

D. Mathematical Formulation of the SEP Principles

In order to construct a rigorous and useable SEP, it does not suffice to have a clear conception of the goal. We must also develop a formal viewpoint that will sufficiently restrict an otherwise large variety of possibilities. Several suggestions usually exist concerning the development of such a formal framework in public health science that involves no logical paradoxes. The formal framework is made operational by specification and elaboration, and it consists of various models depending on the situation. By no means can one claim "one model fits them all"[31]. Remarkably, the exposition of the main elements of this framework involves some abstraction that can actually make things more transparent and simple, and it also leads to powerful quantitative tools.

[31] In view of considerable uncertainty, these models are often of a stochastic nature.

a. The SEP Stages: Structural, Site-specific, and Integration

Since theoretical SEP considers adaptation in an epistemic cognition sense rather than in a natural evolution sense (Section I.C), it is reasonable to associate $\mathcal{G}$- and $\mathcal{S}$-KB with distinct stages of the SEP process. As a matter of fact, the boundary lines between $\mathcal{G}$- and $\mathcal{S}$-KB should also be the boundary lines between the corresponding cognitive stages of knowledge acquisition, integration, and processing that lead to the solution of the public health problem. Briefly, this chain of reasoning distinguishes between the following epistemic cognition stages:

- *Structural* stage: It transforms the cross-disciplinary $\mathcal{G}$-KB into a set of structural equations that are solved *teleologically* for the corresponding probability model. In the teleology of thinking, integrated human health modelling starts by seeking quantitative solutions possessing high *information content* to express the interdisciplinary core knowledge available. In other words, we seek to maximize the information produced by our mental construction of the epidemic system.
- *Specificatory* stage: It examines the $\mathcal{S}$-KB and represents it in a form suitable for quantitative analysis and processing. The building blocks of reality are "throbs" of experience--*experiential representations*. In real world public health situations, e.g., a significant part of this experience is characterized by considerable uncertainty. As a result, the experiential representation is transformed into *operational forms* with the help of stochastic concepts and computational schemes.
- *Integration* stage: It blends the results of the previous stages, thus leading to the final solution in terms of an *integration* probability model. In other words, the core solution of the structural stage above is subsequently "adapted" (progressively modified) in order to account for the specificatory knowledge available and give better performance in its cognitive environment.

More specifically, the probability models at the structural and the integration stages are expressed in terms of the structural pdf ($f_{\mathcal{G}}$) and the integration pdf ($f_{\mathcal{K}}$), respectively[32]. The preceding structural solution ($f_{\mathcal{G}}$) is "adapted" at the integration stage in order to account for the $\mathcal{S}$-KB of the specificatory stage, thus evoking the final solution ($f_{\mathcal{K}}$). The solution to an epidemic problem, e.g., evolves out of SEP principles, the latter understood in a cognitive sense subject to epistemic standards. More to the point, the SEP involves a *teleologic action principle* $\mathcal{T}$ at the structural stage and an *adaptation principle* $\mathcal{A}$ at the integration

[32] The pdf $f_{\mathcal{G}}$ and $f_{\mathcal{K}}$ are linked to the probability functions $PF_{\mathcal{G}}$ and $PF_{\mathcal{K}}$, respectively, of Eq. (I.1).

stage[33]. Teleologic thinking is at the heart of several important scientific developments. Modern neurobiologists argue that in order to understand the relationship between human behavior and the biological brain, one must first understand the goal of that behavior (Glimcher, 2004). In behavioral ecology, a working premise is that animals generate efficient solutions to the problems their environments present in order to maximize the rate at which their genes are propagated (Krebs and Davies, 1991). Next, we discuss the SEP stages in more detail.

b. Teleologic Formulas: Maximum Expected Information Functions

Transformation in the structural stage is expressed in a formal way via a teleologic solution of the structural $\mathcal{G}$-equations. At this point, we must distinguish between the human teleology of SEP and the traditional natural teleology that assumes that material events are moving to an inevitable and discernible end (in which case common criticisms addressed at natural teleology clearly do not apply in human teleology). We may recall that in the traditional (Aristotelian) teleology of nature, a solution is sought in terms of a final cause expressed by an action principle. Well-known action principles considered in this sense include Aristotle's principle of minimum potential energy, Fermat's principle of least time, and Hamilton's principle of stationary principal function (Christodoulou, 1999). On the contrary, what is at issue in SEP is *teleology of reason* rather than natural teleology. According to human teleology, people behave for the sake of goals, purposes, and intentions rather than solely in response to impulsions of efficient causation. In the epistemic cognition context, science is about information rather than about ultimate reality (which is the ontologic view). As a consequence, the SEP employs a goal-based action principle $\mathcal{T}$: the principle of *maximum expected information*. We seek to maximize the information offered by our mental construction (i.e., the solution $f_{\mathcal{G}}$), in which case information is the means connecting reality and human brain, helping the latter shape our understanding of the former. E.g., the teleologic principle can merge toxicokinetics with multistage models of cancer formation to link biomarkers of exposure to cancer risks, in a manner such that the information offered by the resulting model is maximized. Random field-based techniques can properly transform the general KB into a set of $\mathcal{G}$-equations. A detailed review of these techniques is found in Christakos (2000) and Christakos *et al*. (2002). For illustration, consider the following example.

Example D.1. Table 5 gives an example of $\mathcal{G}$-equations in the case of an environmental exposure law representing advection-reaction fields along a river; X_p

[33] As was mentioned in Section I.B.g, both "teleologic action" and "adaptation" are viewed as epistemic cognition concepts rather than as an ontologic and an evolutionary concept, respectively.

Table 5. $\mathcal{G}$–equations of the environmental exposure law, $(\frac{\partial}{\partial t} + a_1 \frac{\partial}{\partial s}) X_p + a_2 X_p = 0$.

$\int\int dx_i\, dx_{i'}\, f_{\mathcal{G}} = 1$
$\int\int dx_i\, dx_{i'}\, x_i\, (\frac{\partial}{\partial t_i} + a_1 \frac{\partial}{\partial s_i} + a_2)\, f_{\mathcal{G}} = 0$
$\int\int dx_i\, dx_{i'}\, x_i^2\, (\frac{\partial}{\partial t_i} + a_1 \frac{\partial}{\partial s_i} + 2a_2)\, f_{\mathcal{G}} = 0$
$\int\int dx_i\, dx_{i'}\, x_i\, x_{i'}\, (\frac{\partial}{\partial t_i} + a_1 \frac{\partial}{\partial s_i} + a_2)\, f_{\mathcal{G}} = 0$
$\vdots$

Table 6. $\mathcal{G}$–equations of the modified Kermack-McKendrick law of communicable disease: $\frac{\partial}{\partial t} X_p = -\beta \eta_p X_p$, $\frac{\partial}{\partial t} Y_p = \beta \eta_p X_p - \lambda Y_p$, $\frac{\partial}{\partial t} Z_p = \lambda Y_p$.

$\int\int\int dx_i\, dy_i\, dz_i\, f_{\mathcal{G}} = 1$
$\int\int\int dx_i\, dy_i\, dz_i\, x_i\, (\frac{\partial}{\partial t} + \beta\eta_i)\, f_{\mathcal{G}} = 0$
$\int\int\int dx_i\, dy_i\, dz_i\, [y_i\, (\frac{\partial}{\partial t} + \lambda) - \square\square_i\, x_i]\, f_{\mathcal{G}} = 0$
$\int\int\int dx_i\, dy_i\, dz_i\, (z_i \frac{\partial}{\partial t} - \square y_i)\, f_{\mathcal{G}} = 0$
$\vdots$

denotes pollutant concentration at each space-time point $\boldsymbol{p}$, a_1 is the flow velocity, and a_2 is the reaction rate constant (Kolovos *et al.*, 2002). In Table 6 (see, also, Christakos *et al.*, 2002: 43) we set up the $\mathcal{G}$-equations linked to the modified Kermack- McKendrick law of communicable disease, where the random fields X_p, Y_p, and Z_p denote the proportions of susceptible, infected, and resistant (i.e., immune) individuals, respectively (η_p is a weighted function of the number of infecteds within a contact radius of a susceptible individual; λ denotes the rate at which individuals recover and become immune, whereas β expresses the rate at which susceptible individuals become infected).

Several other interesting situations of KB representation can be found in the relevant literature. Some useful references are the following:

- Beran (1968) discussed in detail methods that can be used to determine the $\mathcal{G}$-equations from the corresponding laws (Navier-Stokes law, continuity and energy principles, turbulence laws, etc.).
- Serre and Christakos (1999) derived $\mathcal{G}$-equations associated with the hydrogeologic Darcy's law.
- Christakos and Kolovos (1999) used $\mathcal{G}$-equations involving exposure-response-population damage models (see, also, Example D.4 below).
- Serre *et al.* (2003) considered multistage carcinogenesis models with variable repair rates (see, also, Example D.5).
- In Christakos *et al.* (2004), the $\mathcal{G}$-equations accounted for empirical laws of tropospheric ozone distribution in space-time.

It is worth noticing that space-time covariance or semivariogram models associated with public health systems can be also expressed in terms of $\mathcal{G}$-equations. These models are instrumental in understanding epidemic heterogeneities, assessing crucial correlations and laws of change, and explaining critical mechanisms and dependencies in a spatiotemporal manifold, which are factors that play an important role in disease propagation. A critical investigation of broad classes of space-time covariance models that are adequate for homogeneous/stationary as well as for non-homogeneous/non-stationary disease data is presented in Kolovos *et al*. (2004). These classes include non-separable spatiotemporal covariance and semivariogram models that are derived from epidemiologic laws or health effect relationships (in the form of differential equations, dynamic rules, etc.), spectral functions, and generalized representations. A detailed exposition of various of these models is given in Section IV.B.c.

Information is not a property of the epidemic system itself, but it is rather related to what we *know* about this system. I.e., *information* is not an absolute property of the epidemic system, but *relational*. The information concept may be described in various, equally meaningful, ways. In our view, one of the most appealing ones is presented in the following example in terms of one's *ignorance* concerning a future event.

Example D.2. Assume that the actual--but unknown to us--mortality value at the point $\boldsymbol{p} = (\boldsymbol{s}, t)$ of the disease system is $M_p = 5\%$. From an epistemic standpoint, the pdf model $f_{\mathcal{G}}(5\%)$ expresses our degree of expectation concerning the value $M_p = 5\%$ given the available $\mathcal{G}$-KB. If $f_{\mathcal{G}}(5\%)$ is initially considered to be small and later we found out that $M_p = 5\%$, we could say that our ignorance was large. Thus, it makes sense to use the monotonically decreasing function $log\, f_{\mathcal{G}}^{-1}(5\%)$ as a measure of our ignorance about the value $M_p = 5\%$ (*log* denotes the logarithm to any arbitrary base)[34]. In fact, we can consider two distinct states of ignorance: (a) *Before* the event (i.e., when we do not know the actual M_p value), in which case our expected ignorance concerning all possible M_p values is given by

$$Ignorance_{Before} = \overline{log\, f_{\mathcal{G}}^{-1}} = \int dm_p\, f_{\mathcal{G}}(m_p) log\, f_{\mathcal{G}}^{-1}(m_p). \tag{26}$$

(b) *After* the event (i.e., when we find out that $M_p = 5\%$), at which point our ignorance[35] is $Ignorance_{After} = 0$. Therefore, the information associated with the

[34] The logarithmic expression satisfies several important properties (it is zero when the probability is one; it obeys additivity requirements; when, for technical reasons, probabilities are very small, it is more convenient to work with logarithms, etc.; Aczel and Daroczy, 1975).

[35] Note that after the event the probability is $P_{\mathcal{G}}[M_p = 5\%] = 1$ and $P_{\mathcal{G}}[M_p \neq 5\%] = 0$.

model may be expressed as the decrease in ignorance expressed by $Ignorance_{Before} - Ignorance_{After} = \overline{log f_{\mathcal{G}}^{-1}}$. I.e., information could be meaningfully defined by Eq. (26).

Generally, the shape of the pdf $f_{\mathcal{G}}$ depends on the information measure used in the mathematical formulation of the teleologic principle $\mathcal{T}$. Christakos *et al.* (2002) have suggested Shannon and Fisher information-based formulations of the principle $\mathcal{T}$ in an uncertain space-time domain. In the Shannon case, the solution of the $\mathcal{G}$-equations with respect to $f_{\mathcal{G}}$ seeks to maximize the information contained in the structural pdf. As we saw above, a formal way to represent the expected information is in terms of Eq. (26), which is also called the *entropy* function $\mathcal{E}_{\mathcal{G}} = \overline{log(f_{\mathcal{G}}^{-1})}$. In this case, the principle can be written mathematically as

$$\mathcal{T}: \max_{f_{\mathcal{G}}} \overline{[log(f_{\mathcal{G}}^{-1})]}, \tag{27}$$

in a space-time environment. Another $\mathcal{E}_{\mathcal{G}}$-case is the so-called Fisherian information that involves Fisher's function $[\sum_i \frac{\partial}{\partial \chi_i} log(f_{\mathcal{G}})]^2$, but is not considered here. In light of Eq. (27), the issue is not reality itself (the meaning of which escapes our cognitive powers, anyway), but the available information about reality, quantified in terms of probabilities. Thus, information could be viewed as the means that connects objective reality with the human brain, helping the latter shape our understanding of the former. The $f_{\mathcal{G}}^{-1}$ is inversely proportional to the number of X_p realizations consistent with the KB available, which implies that the smaller the number of realizations allowed by the model $f_{\mathcal{G}}$, the larger the amount of information it provides (or, equivalently, the smaller our ignorance). This is essentially, the insight provided by the principle (27) above.

c. Adaptation Formulas: Statistical Induction and Stochastic Deduction

Depending on the public health situation, a large variety of interdisciplinary information sources ($\mathcal{S}$-KB) would become available to the modeller. The case of the Black Death epidemic is of special interest, for it includes surviving contemporary evidence from a variety of sources including hospital records, letters, edicts, financial transactions, ecclesiastical records, court rolls, chronicles, tax documents, etc. (for a detailed presentation, see Section III.C of the next chapter).

Several operational techniques (encoding, probablification, fuzzification, etc.) can be used to express $\mathcal{S}$-KB into useful forms (Christakos, 2000). In addition to *hard* data (exact evidence), uncertain site-specific information may be available in various *soft* data forms (interval data, probability functions, etc.) about an epidemic variable X_p (infecteds, mortality, etc.).

$x_j \in I$
$f_S(x_j)$
$P_S[g(x_j)]$
$P_S[g(x_j, x_{j'})]$

Table 7. Formulations of the soft $\mathcal{S}$-KB.

Example D.3. Some examples of site-specific information are presented in Table 7 (I is an interval of possible x_j-values, f_S is a site-specific pdf, P_S denotes a probability operator, and g is an empirical function relating field values between specified space-time points). Other interesting examples of $\mathcal{S}$-KB include remote sensing and satellite-based data, simulations, and secondary information (Christakos *et al.*, 2004). Kovitz and Christakos (2004a) introduced efficient operational techniques for incorporating $\mathcal{S}$-KB in the form of *fuzzy* data.

In epistemic cognition terms, the f_S of the specificatory stage is viewed as the site-specific knowledge environment of the structural solution f_G. In the integration stage, the structural solution is progressively modified through application of an adaptation rule $\mathcal{A}$ to yield an updated pdf model f_K that is consistent with the $\mathcal{S}$-KB of the specificatory stage, i.e.,

$$\mathcal{A} : f_K(X_p) = f_G(X_p \setminus \mathcal{S}), \tag{28}$$

where the symbol "\" denotes an epistemic adaptation formalism that can be expressed in terms of *conditionals*, such as follows:

(i) *Natural* conditional involves a causal connection between X_p and $X_{p'}$, i.e., the conditional is valid if and only if X_p causally implies $X_{p'}$ by means of a physical or biologic law (e.g., the \ is associated with a law of nature).

(*ii*) *Logical* conditional asserts that the X_p logically implies $X_{p'}$, i.e., the conditional issues from the nature of the entities involved and is not necessarily beholden by the laws of nature (e.g., the "\" means "$\rightarrow$" or "$\leftrightarrow$"; see, Section C.b above). These conditionals are sometimes referred to as *stochastic deductive* adaptation schemes.

(iii) *Statistical* conditional based on the assumption that the occurrence of X_p provides statistical evidence for the occurrence of $X_{p'}$, without necessarily involving any physical or logical connection between them (e.g., $\setminus = |$, where the "|" denotes "statistical/Bayesian conditional"). These conditionals are also known as *statistical inductive* adaptation schemes.

Consideration of the different operational forms *i-iii* above is needed because of the different nature of the environmental, ecological, disease, etc. processes contributing to an epidemic situation (some of these processes are causal, whereas some others are the products of logical schemes). Furthermore, one may need to

integrate models designed to operate at different geographical and temporal scales. In our view, the introduction of the "stochastic" element in the deductive adaptation of group *ii* is justified on the basis of the fact that in the purely deductive scheme there is no room for the "surprises" that nature has to offer (e.g., underlying mechanisms that differ from those we initially assumed as valid, uncertainty in initial and/or boundary conditions). These "surprises" are very important components of scientific inquiry and are taken into consideration seriously by SEP.

Once the f_K is known, different kinds of solutions in the form of field realizations across space-time can be generated to account for the relationships among the three SEP stages above in a space-time domain (e.g., Section E.b). Various real world SEP applications can be found in the relevant literature[36].

d. An Integrated Human Exposure Framework

Exposure analysis and mapping of spatiotemporal pollutants in relation to their health effects are important challenges facing public health research, in general, and *environmental epidemiology*, in particular. Stochastic modelling starts with exposure distributions (often producing the input to toxicokinetics laws) that are linked to exposure-response (health effect) models which, in turn, are integrated with relationships describing how population health damage is distributed across space and time. In view of the SEP analysis discussed in Sections D.a-c above, the main steps of integrated human exposure modelling are briefly outlined in Table 8. For illustration, two successful real world applications of the approach are reviewed in the following examples.

Example D.4. Christakos and Kolovos (1999) proposed a framework to study the impact of spatiotemporal ozone exposure distributions on the health of human populations in eastern US[37]. In light of the approach in Table 8, mathematical models were used expressing functional relationships between ozone exposure $E(\boldsymbol{p})$ [in *ppm*] at each space-time point $\boldsymbol{p} = (\boldsymbol{s}, t)$; toxicokinetics models of burden $B(\boldsymbol{p})$ on target organs and tissues of a receptor at $\boldsymbol{p}$ [in *ppm*][38]; health effect (response) $H(\boldsymbol{p})$ [e.g., in frequency of pulmonary function decrements]; and population damage indicator $\Psi(\boldsymbol{p})$ [number of receptors affected per km^2]. These models, which offer a meaningful representation of the processes that affect human exposure, are summarized in Table 9, where $\zeta_t = \int_0^t d\tau\, \lambda_e(\boldsymbol{s}, \tau)$, λ_α is the

[36] See, e.g., Christakos and Hristopulos, 1998; Christakos and Vyas, 1998; Christakos *et al*., 2002; Kolovos *et al*., 2002; Serre *et al*., 2003; Christakos and Kolovos, 1999; Christakos and Serre, 2000; Bogaert and D'Or, 2002; D'Or and Bogaert, 2003; Law *et al*., 2004; Christakos *et al*., 2004; Douaik *et al*., 2004; and references therein.

[37] The framework, however, is very general and can be used to study various other applications of environmental epidemiology.

[38] Assuming that the uptake rate is proportional to the exposure concentration.

Table 8. An outline of the integrated human exposure modelling.

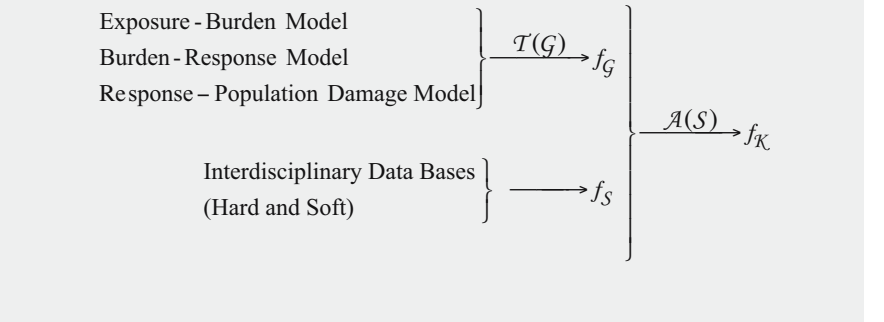


Table 9. Mathematical models of integrated human exposure.

Exposure-Burden (Toxicokinetics)	$B(\boldsymbol{p}) = \begin{cases} \int_0^t dt' \lambda_\alpha(\boldsymbol{s},t') E(\boldsymbol{s},t') \exp(-\zeta_t + \zeta_{t'}), \\ \qquad\qquad \text{during exposure } (t \le t_0) \\ B(\boldsymbol{s},t_0)\exp(-\zeta_t), \quad \text{after exposure } (t > t_0) \end{cases}$
Burden-Response	$H(\boldsymbol{p}) = \alpha(\boldsymbol{p}) B^c(\boldsymbol{p})$
Response-Population Damage	$\Psi(\boldsymbol{p}) = \lvert \upsilon(\boldsymbol{s}) \rvert^{-1} \int_{\upsilon(s)} d\boldsymbol{s}' \theta(\boldsymbol{s}-\boldsymbol{s}',t) H(\boldsymbol{s}-\boldsymbol{s}',t)$

absorption rate and λ_e the removal rate coefficient of the receptor, $\alpha(\boldsymbol{p})$ and c are empirical exposure-response coefficients, $\upsilon(\boldsymbol{s})$ is the region of interest at time t, and $\theta(\boldsymbol{p})$ is the density of receptors in the neighborhood of υ. In Fig. 6 we plot the semivariograms of the ozone exposure and burden profiles, $\gamma_E(\tau)$ and $\gamma_B(\tau)$, respectively, at various geographical locations. The rate coefficient λ_e or the half-life[39] $T_{1/2} = 0.693/\lambda_e$ are useful tools to describe how ozone exposure variability affects burden levels in the body. Remarkably, when $\lambda_e \ge 1.0$ the exposure and burden semivariograms show very similar behaviors. But they start to exhibit significant differences in their shapes when $\lambda_e \le 0.35$. Thus, the smaller the λ_e is (or, the larger the $T_{1/2}$ is), the less affected is the burden by changes in exposure (e.g., the longer it takes the burden to decrease when exposure ends, or to reach a steady-state when exposure is stable). For $\lambda_e \ge 1.0$, burden follows the daily exposure variations well and it is, therefore, a very good indicator of the exposure conditions. For $\lambda_e \le 0.35$, exposure fluctuations constitute a rather poor indicator of the burden levels in the body (note the differences in magnitude between burden profiles). The shape of the semivariograms at the origin and at large distances is of particular importance for it provides information about the behavior of the

[39] Which is equal to the time required for burden to be reduced to 50% of its original value after uptake.

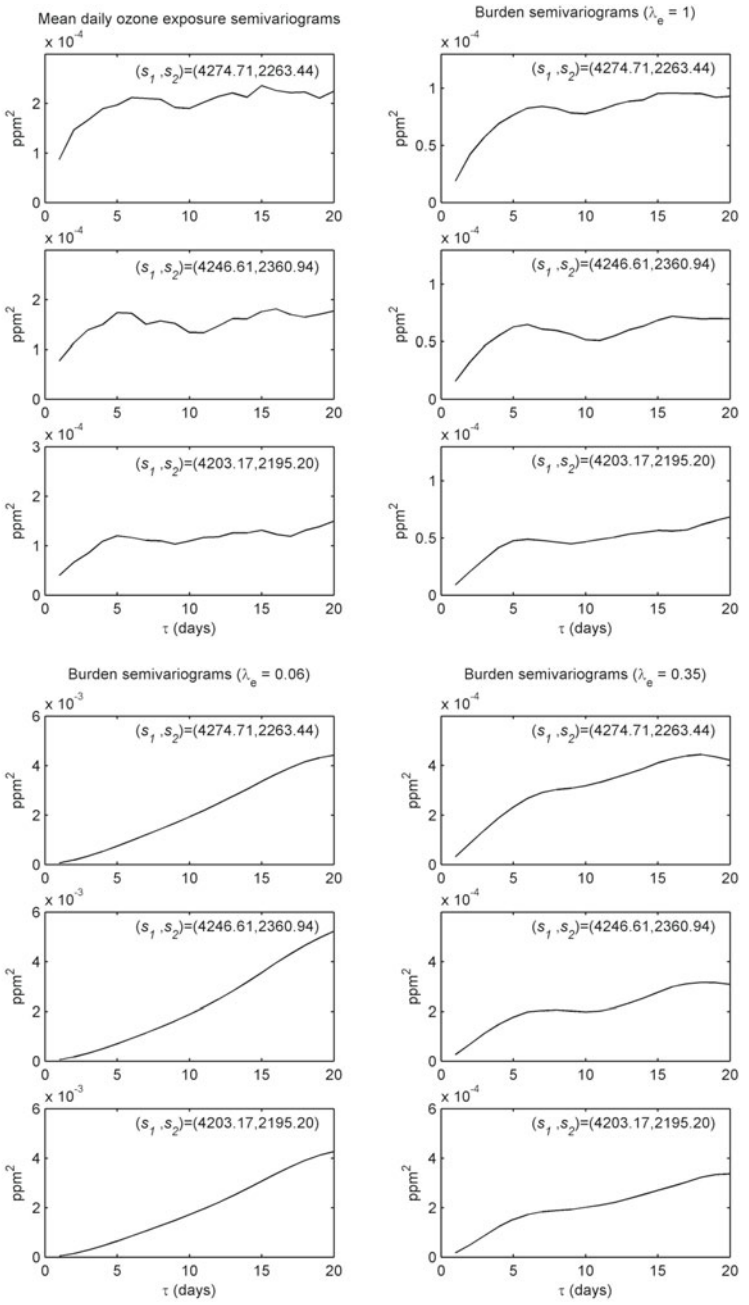


Figure 6. Semivariograms of ozone exposure and burden profiles (different λ_e) at certain geographical locations considered in Christakos and Kolovos (1999).

actual exposure and burden profiles. While a quadratic shape of the semivariogram at the origin implies a rather smooth temporal variation (as is the case, e.g., with $\lambda_e = 0.06$), a linear shape indicates a more irregular variation exhibiting significant fluctuations ($\lambda_e = 0.35$ and 1.0). An asymptotic behavior at large distance denotes a rather stationary profile fluctuating around a constant mean ($\lambda_e = 0.35$ and 1.0), but a linear shape implies a non-stationary profile with temporal trends ($\lambda_e = 0.06$). The ozone data set included 1228 monitoring stations east of 95 degrees west longitude and north of 25 degrees north latitude. The burden-response model in Table 9 is assumed valid for any receptor that belongs to a specific cohort (i.e., a group of individuals with similar time/activity profiles). In addition to the burden on the target organs, a number of cohort-related factors can potentially affect α and c including the exposure duration, the activities of the receptors during exposure, pre-existing conditions, biological or physiological characteristics, and age group of the receptors. In view of the considerable uncertainty implied by all the above factors, stochastic modelling represents certain variables in terms of random fields[40]. The health damage indicator, Ψ, for the eastern US geographical region can be calculated at any geographical location and time period. E.g., consider the New York City and Philadelphia areas with $c = 0.5$ and 1.5, i.e., both sublinear and supralinear exposure-response curves are used. Furthermore, it is assumed that α is randomly varying in the intervals 1.63 ± 0.05 (sublinear model) and 7.25 ± 0.25 (supralinear model). For illustration, the calculated Ψ values at the New York City and Philadelphia areas are tabulated in Table 10. Note the considerable effect of the different burden-health response curves assumed. Interpreted with judgment (i.e., keeping in mind the assumptions made concerning the exposure, biological, and health response parameters, the cohort characteristics, etc.), the Ψ values can offer useful insight regarding the possible population damage due to ozone exposure. In fact, one can generate various Ψ maps associated with different ozone exposure distributions and cohort characteristics. With the help of such maps, geographical areas where exposure has the highest probability to cause adverse health effects on the local population can be detected. Also, detailed space-time maps of exposure and burden can be generated (see, Christakos and Kolovos, 1999). Then, the sequence of maps--exposure, burden, and population health damage--provide the means to consider human exposure as a spatiotemporal system, by looking at the whole picture, not just certain isolated parts.

Example D.5. Serre *et al.* (2003) studied the lifetime population damage due to groundwater Arsenic (As) exposure in Bangladesh. The interdisciplinary mathematical models used are summarized in Table 11; $E(\boldsymbol{p})$ is the As concentration [in $\mu g/L$] at each space-time point $\boldsymbol{p} = (\boldsymbol{s}, t)$; $H(\boldsymbol{p})$ is the health effect (response) expressed in terms of the lifetime probability of a receptor at $\boldsymbol{p}$ to develop

[40] Stochastic analysis may involve the pdf of each one of the above cohort factors, thus generating a set of possible values for α and c. These pdf may be obtained from field studies and/or the relevant literature

Table 10. Health damage indicator values on July 20, 1995 for representative receptors (number of receptors affected per km^2).

Burden-Response coefficients	New York City area	Philadelphia area	Background region
$c = 0.5$ $\alpha = 1.63 \pm 0.05$	$300 < \Psi < 1500$	$200 < \Psi < 700$	$\Psi < 100$
$c = 1.5$ $\alpha = 7.25 \pm 0.25$	$60 < \Psi < 200$	$40 < \Psi < 100$	$\Psi < 20$

Table 11. Mathematical models of interdisciplinary environmental epidemiology.

Exposure-Response (Linear/Empirical)	$H(\boldsymbol{p}) = P_B + k\ E(\boldsymbol{p})$
Exposure-Response (Nonlinear/Mechanistic)	$H(\boldsymbol{p}) = N_t(t = life\ expectancy)$ $\frac{dN_n(t)}{dt} = -k_{ni}\ N_n(t) + [0.015 - 7 \cdot 10^{-4}\ E(\boldsymbol{p})^{0.3}] N_i(t)$ $\frac{dN_i(t)}{dt} = k_{ni}\ N_n(t) - [0.015 - 7 \cdot 10^{-4}\ E(\boldsymbol{p})^{0.3}] N_i(t)$ $- k_{it} N_i(t) + M\ N_i(t)$ $\frac{dN_t(t)}{dt} = k_{it}\ N_i(t)$
Response-Population Damage	$\Psi(\boldsymbol{p}) = \theta(\boldsymbol{p})[H_B + H_{As}(\boldsymbol{p})]$

bladder cancer. Two exposure-response models were used: An empirical (linear) model, where $k = 3.5 \times 10^{-5}\ [\mu g / L]^{-1}$ is a constant calculated by fitting the model to the data of Morales *et al.* (2000); $P_B = 0.005$ is the background bladder cancer probability not depending on *As* as a causing factor. And a (nonlinear) model[41], where $N_n(t)$, $N_i(t)$, and $N_t(t)$ are the numbers of normal, initiated, and tumor cells, respectively, at time *t*; k_{ni} and k_{it} are the rates of transition from normal to initiated cells, and initiated to tumor cells, respectively (in $probability \times T^{-1}$ units); $k_r = 0.015 - 7 \cdot 10^{-4}\ E(\boldsymbol{p})^{0.3}$ is the repair rate from initiated to normal cells ($probability \times T^{-1}$); M is the net growth rate for the pool of initiated cells (in $probability \times T^{-1}$ units)[42]. Fig. 7 depicts a map of the distribution of the population damage indicator $\Psi(\boldsymbol{p})$ [in number of people per km^2 with a lifetime bladder cancer development expectancy]; $\theta(\boldsymbol{p})$ is the geographical density of re-ceptors; H_B and $H_{As}(\boldsymbol{p})$ refer, respectively, to population damage due to background bladder cancer and due to the health effect caused by to the presence of *As*

[41] Based on a multistage carcinogenesis approach due to Moolgavkar *et al.* (1990).

[42] M refers to mitosis (cell division), therefore the total number of cells naturally increases with time.

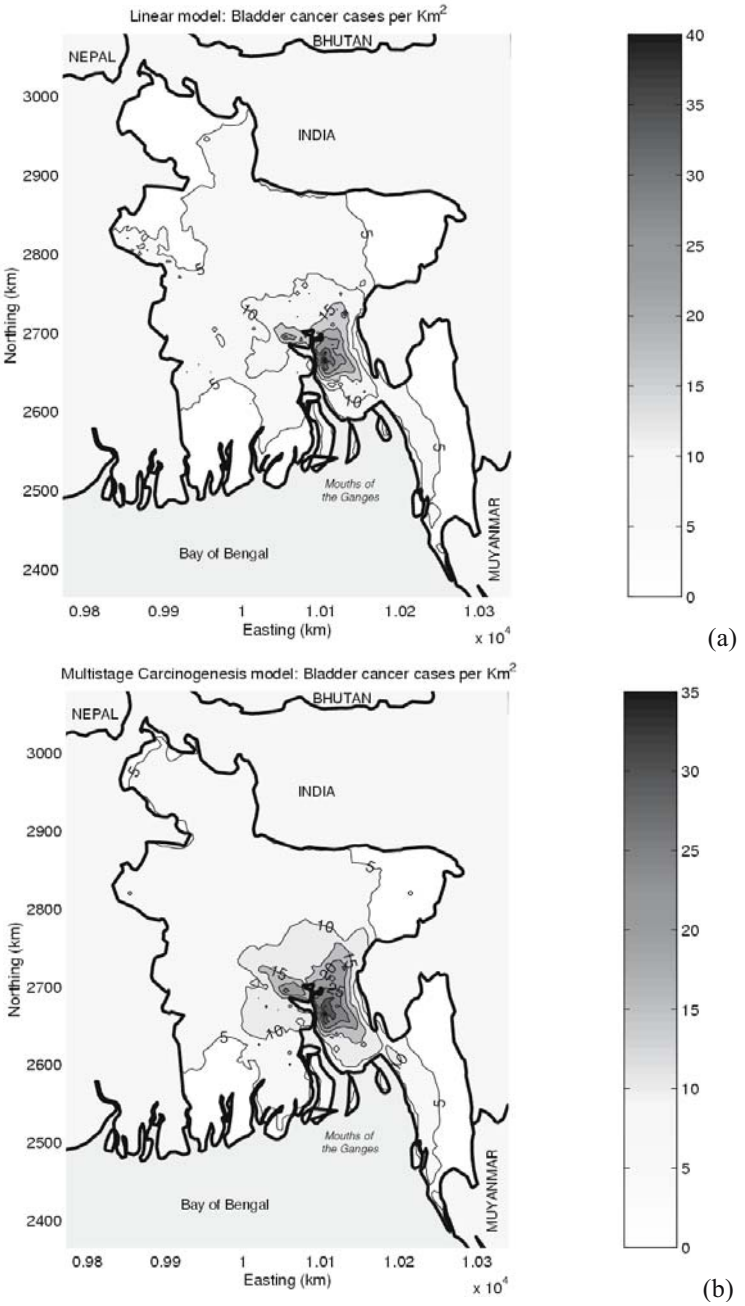


Figure 7. Maps of $\Psi(\boldsymbol{p})$ in Bangladesh for (a) the linear exposure-response model, and (b) the nonlinear (multistage carcinogenesis) model.

in drinking water. The maps identify areas in Bangladesh where it was estimated that as many as 45 lifetime cancer incidents are expected to occur per km^2 (roughly corresponding to 3 incidents every 4 years for a life span of 58 years). Such maps are very useful for the public health planner and policy maker, for they allow, e.g., to estimate the cost of treatment of population damage due to a particular health effect.

By way of a summary, the SEP can offer a multi-level, cross-discipline human exposure framework that allows the consideration of hierarchical causal relations among the natural processes and the public health systems of the various disciplines involved (e.g., a KB about gene mutations can offer information regarding causes leading to population changes). Interdisciplinary learning is often viewed as a logic of discovery and as a means of communication between the different realms of knowledge (without, necessarily, leading to a new discipline). The fact that there are many different disciplines of knowledge entails a diversity of approaches, none of which can claim to incorporate all the others. The idea of interdisciplinarity proposed in SEP does not necessarily mean a search for a lower common multiple or a highest common factor (which is the case of science unification). It is rather concerned with the entire epistemic space within which the separate kinds of knowledge are deployed like so many paths through the unknown. Loosely speaking, one would suggest that the SEP supports a picture of public health science like a *quilt* rather than a pyramid. In such a framework, the aim of the discussion of the SEP and its application in real world situations is to open possibilities for consideration. In some cases, certain new views and theses concerning public health reasoning and epidemic modelling are suggested in an attempt to launch them for exploration, without claiming that they are necessarily the best possible ones. Any occasional criticism of previous views and approaches is not necessarily intended to refute them conclusively, merely to clear scientific space in which newly proposed views can breathe and grow.

E. The Role of Temporal Geographical Information Systems (TGIS)

a. Epidemics and Human Geography

The close ties of epidemic modelling with human geography have been studied extensively in Peter Haggett's work (see, e.g., Haggett, 2000; and references therein). Furthermore, Christakos *et al*. (2002) have explored some of these ties in the context of *temporal geographical information systems* (TGIS). In the case of Black Death, scholars have suggested a link between the severity of the plague and geography; e.g., Black Death hit harder the ports and large cities along trade routes, mountainous areas had lower mortality than the valleys and plains, etc. (see, Section III.D).

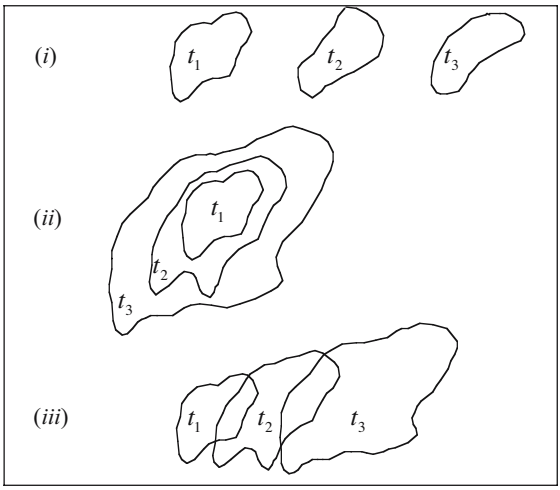


Figure 8. Three kinds of geographical diffusion of epidemics: (i) relocation, (ii) expansion, and (iii) combined relocation-expansion (modified from Haggett, 2000).

There is no doubt that human geography concepts and TGIS technology tools can be very helpful in a variety of epidemic modelling problems, including the location of the possible origin of an infectious disease outbreak and the conditions that led to the epidemic, the geographical shape and extent of the epidemic, its temporal evolution features, as well as ways to control the epidemic. In this section, we limit ourselves to a rather brief description of certain close relationships between human geography and epidemic modelling. As it turns out, several geographical concepts and techniques can be used in the study of epidemics.

Of particular usefulness in the description of the spatiotemporal propagation of a certain class of epidemics are the concepts of (*i*) *relocation*, (*ii*) *expansion*, and (*iii*) *combined relocation-expansion diffusion* (also known as advection, diffusion, and advection-diffusion, respectively; Fig. 8). Case *i* is characterized by a spatial spread process in which the epidemic leaves one area to move to another, whereas in case *ii* the disease occupies new areas without leaving the previous ones. In case *iii* one observes a blending of cases *i* and *ii*. The spatial spread process of the Black Death epidemic involves a combination of the above cases (see, Chapter V).

Another important epidemic issue to which human geography can throw some light is the question of the spatial and historical (temporal) *origin* of a disease. In many cases, including Black Death, the answer to the question lies far in the past, which may create some serious problems. The human geography's approach for determining the origins of an epidemic disease is essentially based on (*a*) deductive locational principles that can help identify candidate regions, and (*b*) the use of maps as hypotheses. The interested reader is refereed to Haggett (2000) for a more detailed discussion of this approach.

Diseases also spread within an *environmental* space-time manifold, meaning that the environmental features of the specified geographical/temporal domain can

influence the origins and the propagation of an epidemic disease. Environmental changes that can affect the epidemic usually are related to: the demography of the host population (growth, relocation, etc.); the land use (agricultural, forest, water, etc.); the global warming and related effects (higher temperatures would favor the endemic area expansion of certain diseases[43], the rapid replication of food-poisoning organisms, etc.); the increased geographical mobility in the human population (traveling public may be exposed to new diseases, migration of populations characterized by new genetic characteristics, etc.).

Unlike traditional epidemiologic research, which was mostly descriptive in nature, the majority of epidemiologic studies conducted since the 1970s have been characterized by a shift in the level of analysis from the population to the individual (e.g., Pearce 1996). This shift reflected not only the pervasive views of individual risk factors on disease causation, but also the refined conceptualization and methodological advancement in designing epidemiologic research (e.g. case-control studies). Ecological studies, for which the unit of observation and analysis is at the ecological level (e.g. workplace, zip-code area, or county), were often regarded as old-fashioned and methodologically less rigorous. However, since the 1990s there has been a gradual return of ecological studies. A few forces have contributed to this noticeable resurfacing of the population perspective (Chen, 2005). Among the most important is the increasing application of TGIS tools to public health research and practice (Christakos *et al*., 2002; Ricketts 2003), the public's attention to health disparity (Kawachi and Kennedy 2002), the availability of aggregated environmental and survey data linkable to population health data (Brooks *et al*., 2000; Jorgenson 2001; Nuckols *et al*., 2004), and emerging public health needs (e.g. re-emerging infectious diseases, disease surveillance to identify threats of bioterrorism; see, Pavlin *et al*., 2003). At present, however, there is no unified approach to an improved ecological inference. SEP-based TGIS may offer a promising approach in this regard. E.g., it might be used in individual-level studies, including the spatiotemporal modelling of a point process where a point represents multi-dimensional individual attributes, etc.

b. TGIS Technology and the BME Technique

TGIS technology plays a vital role in public health research and practice. To apply a rigorous stochastic modelling and epidemic prediction procedure, TGIS relies on the powerful theory and tools of SEP. There are a number of such tools. For illustration, Fig. 9 presents some of the various interdisciplinary integration techniques that are implemented by TGIS technology. The theoretical underpinnings of these techniques are combinations of the teleologic and adaptation SEP principles, which provide TGIS with the theoretical means to consider different information measures and conditionalization rules, whenever the emerging conditions make it appropriate.

[43] Such as malaria, leishmaniasis, and arboviral infections.

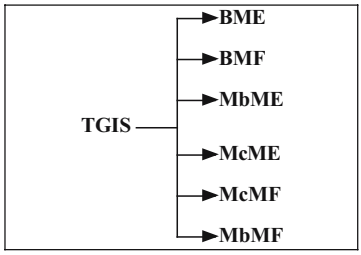


Figure 9. TGIS techniques. B=Bayesian, F=Fisherian, M=Maximum, E=Entropy, Mc=Material conditional, Mb=Material biconditional.

Although there exist a variety of theoretical and computational options, the information measure and conditionalization rule used by the *Bayesian Maximum Entropy* (BME) technique possess important analytical and computational virtues. As a consequence, BME is the most developed and popular SEP technique, at the moment (see, Christakos *et al*., 2002).

BME has several appealing features, indeed, its analytical and computational properties are well understood, and it has been applied in a variety of real world situations with considerable success. More to the point, BME is based on a powerful and versatile approach, which:

- Accounts rigorously for the uncertainty features of the epidemic system in a composite space-time domain.
- Imposes no restriction on the shape of the probability distributions and the form of the predictor (non-Gaussian disease distributions and non-linear epidemic predictors are automatically incorporated).
- Allows the consideration of multiple-point stochastic moments of the disease variables across space-time.
- Derives several previous techniques of epidemic modelling (e.g., statistical regression) as its limited cases.
- Incorporates databases that are not necessarily disease variables, thus resulting to the consideration of additional information sources.

Due to space limitations, for a detailed description of the mathematical BME theory, the relevant TGIS software, as well as the potential applications of the method, the reader is referred to Christakos (2000), Christakos *et al*. (2002, 2004) and references therein. Here we are limited to a brief description of the main steps of formal BME modelling and prediction. In particular, we illustrate these steps in terms of the mortality distribution, $M_{\boldsymbol{p}} = M_{s,t}$; but the approach is much more general and can consider several epidemic variables simultaneously. We are concerned with the prediction of the $M_{\boldsymbol{p}}$ distribution at a network of nodes $\boldsymbol{p}_k$ on a space-time grid, given core knowledge about the entire mortality domain and a set of site-specific data $\boldsymbol{m}_{\text{data}} = (m_1, ..., m_n)$ at geographical/temporal points

$\boldsymbol{p}_{\text{data}} = (\boldsymbol{p}_1, ..., \boldsymbol{p}_n)$[44]. In the stochastic theory context, one seeks to *derive* the pdf, $f_{\mathcal{K}}(\boldsymbol{m}_k)$, that characterizes $M_{\boldsymbol{p}}$ at every node of the mapping grid in light of the total epidemic-relevant knowledge available. The BME steps are briefly summarized below:

Step (i): The general KB is expressed in terms of mathematical $\mathcal{G}$-equations involving the corresponding pdf $f_{\mathcal{G}}$ (KB=$\mathcal{G}$, in this case) and a set of functions g_α so that ($\alpha = 1, .., N$)

$$\mathcal{G}[g_\alpha, f_{\mathcal{G}}] = 0. \tag{29}$$

The g_α are properly chosen to express the general KB considered in the epidemic system. Various examples of Eq. (29) can be found in the relevant literature. In applications in which theoretical and/or empirical equations in terms of $M_{\boldsymbol{p}}$ moments are available, Eq. (29) reduces to ($\alpha = 1, .., N$)

$$\overline{g_\alpha}(\boldsymbol{p}_{\text{map}}) = \int d\boldsymbol{m}_{\text{map}}\, g_\alpha(\boldsymbol{m}_{\text{map}})\, f_{\mathcal{G}}(\boldsymbol{m}_{\text{map}}) \tag{30}$$

where $\boldsymbol{p}_{\text{map}} = (\boldsymbol{p}_{\text{data}}, \boldsymbol{p}_k)$ and $\boldsymbol{m}_{\text{map}} = (\boldsymbol{m}_{\text{data}}, \boldsymbol{m}_k)$. By convention, $g_0 = \overline{g}_0 = 1$ (normalization constraint), and the total number N of equations is such that mortality moments are included that involve all the grid points $\boldsymbol{p}_i \in \boldsymbol{p}_{\text{map}}$ of the map. E.g., in the special case that the $\mathcal{G}$-KB includes the mean functions $\overline{M_{\boldsymbol{p}_i}} = \overline{M_i}$ and the covariance functions $c_M(\boldsymbol{p}_i, \boldsymbol{p}_j)$ throughout the space-time domain of the epidemic, the selected g_α-functions are shown in Table 12.

Step (ii): For BME, the teleologic principle $\mathcal{T}$ of choice is the expected information maximization in light of the $\mathcal{G}$-KB. The information measure assumed is that of Shannon (extended in the space-time manifold), in which case the solution of Eq. (27) has the general maximum entropy form

$$f_{\mathcal{G}}(\boldsymbol{\chi}_{\text{map}}) = e^{\mu_0 + \boldsymbol{\mu}^T \boldsymbol{g}}, \tag{31}$$

Table 12. Examples of a $\mathcal{G}$-KB.

$\mathcal{G}$	g_α	$\overline{g_\alpha}$
Mean functions	m_i	$\overline{M_i}$
Covariance functions	$(m_i - \overline{M_i})(m_j - \overline{M_j})$	$c_M(\boldsymbol{p}_i, \boldsymbol{p}_j)$

[44] At the points $\boldsymbol{p}_k$, either we have no observations at all, or the available data are considerably uncertain and cannot be used as reliable predictions of the actual $M_{\boldsymbol{p}}$ values at these points.

where $\boldsymbol{g} = \{g_\alpha;\ \alpha = 1,...,N\}$ is a vector of the g_α-functions, and $\boldsymbol{\mu} = \{\mu_\alpha;\ \alpha = 1,...,N\}$ is a vector of coefficients associated with $\boldsymbol{g}$. The $\boldsymbol{\mu}$ includes functions of the space-time coordinates and will be determined in the following step, whereas μ_0 is a coefficient that accounts for the normalization constraint, $\overline{g_0} = 1$.

Step (*iii*): Substitute Eq. (31) into (30) and solve for coefficients $\boldsymbol{\mu}$. Insert these coefficients back into Eq. (31) to find the exact form of the $\mathcal{G}$-based model $f_{\mathcal{G}}$ of the mortality $M_{\boldsymbol{p}}$ distribution.

Step (*iv*): The $\mathcal{S}$-KB may consist of hard $M_{\boldsymbol{p}}$ data at a set of points $\boldsymbol{p}_i$ ($i = 1,...,\rho_h$), and soft (uncertain or secondary) data at another set of points $\boldsymbol{p}_i$ ($i = \rho_h + 1,...,n$), i.e.,

$$\mathcal{S}: \begin{cases} \boldsymbol{m}_{\text{hard}} = (m_1,...,m_{\rho_h}) \\ \boldsymbol{m}_{\text{soft}} = (m_{\rho_h+1},...,m_n) \end{cases}, \tag{32}$$

such that $\boldsymbol{m}_{\text{data}} = (\boldsymbol{m}_{\text{hard}}, \boldsymbol{m}_{\text{soft}})$. Soft mortality data $\boldsymbol{m}_{\text{soft}}$ may be expressed in terms of intervals of varying lengths and probabilistic functions of arbitrary shapes (e.g., Table 7).

Step (*v*): The $\mathcal{G}$-based model $f_{\mathcal{G}}$ is adapted through application of the operational Bayesian conditionalization (*bc*) rule to yield the integration pdf that is consistent with the $\mathcal{S}$-KB available, as follows:

$$f_{\mathcal{K}}^{bc}(\boldsymbol{m}_k) = A^{-1} \int_D d\Xi_{\mathcal{S}}(\boldsymbol{m}_{\text{soft}})\, f_{\mathcal{G}}(\boldsymbol{m}_{\text{map}}), \tag{33}$$

where $\text{KB} = \mathcal{K} = \mathcal{G} \cup \mathcal{S}$, A is a normalization parameter independent of $\boldsymbol{m}_k$, and the forms of the operator $\Xi_{\mathcal{S}}$ and the domain D depend on the types of hard and soft data considered in the context of the epidemic problem of interest. For illustration, some examples are given in Table 13. This step essentially completes the central part of the procedure[45]. The following steps are concerned with the derivation of particular mortality predictors and the associated accuracy from $f_{\mathcal{K}}^{bc}(\boldsymbol{m}_k)$.

Step (*vi*): From Eq. (33) we select the appropriate mortality predictions, $\hat{\boldsymbol{m}}_k$, across space-time, depending on the goals of the study. The *BMEmode* prediction (34) in Table 14, e.g., represents the most probable $M_{\boldsymbol{p}}$ realization, whereas the *BMEmean* (35) minimizes the mean squared prediction error. Other forms of $M_{\boldsymbol{p}}$

[45] The underlying methodology is considerably versatile. In the case of MbME, e.g., Eq. (33) can be replaced by $f_{\mathcal{K}}^{mb}(\boldsymbol{m}_k) = (2A-1)^{-1}[2Af_{\mathcal{K}}^{bc}(\boldsymbol{m}_k) - f_{\mathcal{G}}(\boldsymbol{m}_k)]$; etc.

Table 13. Examples of Ξ_S and D (F_S denotes a cumulative distribution function derived on the basis of the S-KB).

S	Ξ_S	D
$\boldsymbol{m}_{\text{soft}} \in \boldsymbol{I} = (I_{\rho_h+1},...,I_n)$	$\boldsymbol{m}_{\text{soft}}$	$\boldsymbol{I}$
$P[\boldsymbol{m}_{\text{soft}} \le \boldsymbol{\zeta}] = F_S(\boldsymbol{\zeta})$	$F_S(\boldsymbol{m}_{\text{soft}})$	$\boldsymbol{I}$
$P[\boldsymbol{m}_{\text{soft}} \le \boldsymbol{\zeta}, \boldsymbol{m}_k \le \boldsymbol{\zeta}_k] = F_S(\boldsymbol{\zeta}, \boldsymbol{\zeta}_k)$	$F_S(\boldsymbol{m}_{\text{soft}}, \boldsymbol{m}_k)$	$\boldsymbol{I} \cup \boldsymbol{I}_k$

Table 14. Examples of space-time predictions $\hat{\boldsymbol{m}}_k$.

BMEmode	$\hat{\boldsymbol{m}}_{k,\text{mode}}$: $\max_{\boldsymbol{m}_k} f_{\mathcal{K}}^{bc}(\boldsymbol{m}_k)$	(34)
BMEmean	$\hat{\boldsymbol{m}}_{k,\text{mean}} = \int d\boldsymbol{m}_k \, \boldsymbol{m}_k \, f_{\mathcal{K}}^{bc}(\boldsymbol{m}_k)$	(35)

prediction can be derived so that they optimize an objective function. The predicted mortality values $\hat{\boldsymbol{m}}_k$ are used to create informative spatiotemporal maps, which can be scientifically interpreted to provide a useful picture of reality and generate science-based decisions.

Step (*vii*): Because of the inherent randomness of the M_p distribution and data inaccuracies, we can use pdf (33) to obtain an uncertainty assessment of the $\hat{\boldsymbol{m}}_k$ values. A popular accuracy measure is the prediction *error standard (std) deviation* of $f_{\mathcal{K}}^{bc}$, viz. $\sigma_{\mathcal{K}}(\boldsymbol{p}_k) = [\int dm_k \, (m_k - \overline{M_k})^2 \, f_{\mathcal{K}}^{bc}(m_k)]^{1/2}$, which is calculated at each map grid point of the epidemic domain. Other accuracy measures (including *confidence intervals* and *sets*) can be also calculated (Christakos *et al*., 2002).

The interdisciplinary analysis of an epidemic system may involve several space-time variables (physical, biologic, ecologic, demographic, epidemic, etc.), $X_{i,p}$ ($i = 1,...,l$). E.g., $X_{1,p} = M_p$, $X_{2,p} = I_p$, etc. In this case, the BME technique is expressed in terms of the *vector* S/TRF

$$\boldsymbol{X}_p = [X_{1,p},...,X_{l,p}]^T, \tag{36}$$

and the corresponding *cross-covariances* are

$$c_{X_i X_j}(\boldsymbol{p}, \boldsymbol{p}') = \overline{[X_{i,p} - \overline{X_{i,p}}][X_{j,p'} - \overline{X_{j,p'}}]}, \tag{37}$$

$i, j = 1,...,l$; see, *vector BME* in Christakos (2000: Chapter 9). The vectorial formulation can be also used to incorporate the study of cause-effect associations, including confounding variables (Section I.D). The $X_{i,p}$ may denote exposures, cohorts (age, sex, previous health status, etc.), life-styles, and social conditions, all acting in synergy to produce the specified health effect (e.g., exposure $X_{1,p}$ could be the triggering factor that completes a causal chain leading to the effect, while

variables $X_{2,p},...,X_{i,p}$ may constitute the standing conditions that allow the effect to be triggered).

Noticeably, the conceptual structure of BME is more than mathematical structure. It confronts the questions: When do we use the mathematics and what are we saying about the interpretation of the equations? It is in this pursuit--the pursuit of *meaning*--that both the difficulty and the pleasure lie. On implementation grounds, the computer programs of TGIS (BMElib, SANlib, etc.[46]) can generate detailed space-time disease maps that adequately assess the spatiotemporal characteristics of the Black Death epidemic (correlations between space and time mortality distributions, heterogeneity patterns, large-scale trends connected with disease, etc.). BME allows the integration of knowledge from different disciplines and levels of organization (see, e.g., Section I.C.b), and the underlying mathematics involve a set of versatile S/TRF models.

c. Some Salient Differences Between BME and Classical Techniques

There are several salient distinctions between the BME technique above and other techniques based on Bayesian rules and/or maximum entropy principles (e.g., Skilling, 1989; Jaynes, 2003). Indeed, as was pointed out by Christakos (2002b) there are significant differences (both in structure and function) between the standard Bayesian formulation and the operational formulation proposed by BME. Standard *bc* is based on the classical Bayesian formalism for updating the prior (original) probability $P_{\text{o}}(M_p)$ using the evidence provided by a database $\mathcal{S}$, thus leading to the posterior (new) probability $P_{\text{n}}(M_p)$ as follows (e.g., Starck *et al.*, 1998: 92),

$$P_{\text{n}}(M_p) = P_{\text{o}}(M_p)\,[P_{\text{o}}^{-1}(\mathcal{S})\,P_{\text{o}}(\mathcal{S}|M_p)] \tag{38}$$

where the $P_{\text{o}}(\mathcal{S}|M_p)$ and $P_{\text{o}}(\mathcal{S}) \neq 0$ are traditionally called the likelihood and the dataset probability, respectively. Eq. (38) offers a "decompositional" formulation of the posterior probability in which prior probability is the probability of M_p before the dataset is observed, dataset probability is the probability of observing $\mathcal{S}$, and likelihood is the probability of $\mathcal{S}$ when M_p is true. This formulation is commonly found in logical probability theory (e.g., Jaynes, 2003: 253) and in modern statistical learning from data (Cherkassky and Mulier, 1998). On the other hand, in several classical statistics references (e.g., Edwards, 1972) the likelihood is denoted as $l(M_p|\mathcal{S})$ so that $P_{\text{n}}(M_p) \propto P_{\text{o}}(M_p)l(M_p|\mathcal{S})$ is the expression traditionally used in place of Eq. (38). For a classical Bayesian, induction is just

[46] The reader is encouraged to visit the website of the Center for the Integrated Study of the Environment (UNC) at http://www.sph.unc.edu/envr/cise where these programs can be found and used.

the process of modifying the $P_o(M_p)$ assessment by conditionalizing on $\mathcal{S}$ via (38); e.g., Rosenkrantz (1977)[47].

Standard Bayesian methods, which basically establish evidential relevance, have been used in a variety of applications (see references above). The prior and dataset probabilities as well as the likelihood must be calculated before the standard *bc* formulation (38) can be used. In most applications, such a calculation is a rather difficult task. Indeed, the dataset is often the only KB considered in formulation (38) and the calculation of the prior probability and likelihood functions is made possible only with the help of some rather restrictive assumptions. Prior probability, e.g., is usually assumed to have a Gaussian shape and the likelihood cannot be calculated without making certain strong assumptions about the underlying probability distributions (all elements of $\mathcal{S}$ are assumed independent, a convenient model relating $\mathcal{S}$ and M_p is considered with additive deviations, the statistics of the deviations must be known a priori, etc.). Moreover, Eq. (38) assumes both that $\mathcal{S}$ is a certainty once it is acquired and that it is all the information that is acquired. These assumptions have been questioned on theoretical as well as on practical grounds by Jeffrey (1965) and others. In addition, Lewis (1976) has argued that standard *bc* can lead to certain triviality results. Shortcomings of formulation (38) in some environmental applications have been presented in Caselton and Luo (1992), although the Dempster-Shafer belief theory proposed in the same reference as an alternative to (38) is quite problematic when applied to environmental situations[48]. According to Vapnik (2000), a significant weakness of the standard *bc* formulation (38) in the context of statistical learning theory is that it is restricted to the case where the set of functions of the learning machine coincides with the set of problems that the machine has to solve. Finally, Mahner and Bunge (1997) point out that the interpretation of Eq. (38) in factual terms is not always a straightforward affair. E.g., in several cases the $P_n(M_p) = P_o(M_p|\mathcal{S})$ measures the probability that the phenomenon will undergo the transition from state $\mathcal{S}$ to state M_p. But the problem is that the $P_o(\mathcal{S}|M_p)$, which in formulation (38) refers to the probability of the reverse process "M_p to $\mathcal{S}$", has no meaning, because the reverse process may not occur in certain phenomena. Therefore, in such cases the use of Eq. (38) makes no sense.

The standard definition (38) above suggests one possible way to express conditionalization of the random field-related event M_p on the event $\mathcal{S}$. This definition is based on statistical reasoning and is not generally connected with causality or deductive validity (Glymour, 1981). In many applications, $\mathcal{S}$ and M_p belong to the same disease variable and, hence, they could be considered as causally connected through an epidemic law. This being the case, the problem is that the purely evidential character of standard *bc* is not able to express such a law in an

[47] As is well known, standard *bc* has no direct connection with causality.

[48] Very restrictive requirements are imposed for modelling prior information such as the *n*-monotonicity of the lower probabilities, inference relies on sampling information alone, a limited group of single parameter distributions is often considered, etc.

epidemiologically and geographically consistent manner. A satisfactory solution offered by BME is in terms of the *operational bc*, which does not involve the standard formulation (38), but instead the *bc* probability is expressed in terms of (physical, biological, epidemiologic, etc.) knowledge-based *operators*. More specifically, an operational *bc* of M_p has been proposed by Christakos (2000) as follows

$$P_{\mathcal{K}}^{bc}(M_p) = A^{-1} \int_{-\infty}^{m_p} d\upsilon \int_I d\Xi_{\mathcal{S}}(\boldsymbol{m}_{soft}) f_{\mathcal{G}}(\boldsymbol{m}_{data}, \upsilon), \tag{39}$$

which yields the pdf (33) above. Clearly, the notation introduced in Eq. (39) has a special meaning that differs from the standard meaning of Eq. (38): The subscript "$\mathcal{G}$" denotes that the probability model $P_{\mathcal{G}}$ and the pdf $f_{\mathcal{G}}$ of the epidemic system have been constructed taking into account the general KB, whereas the subscript "$\mathcal{K}$" denotes that the probability model is updated (conditionalized) on the site-specific knowledge $\mathcal{S}$, which may be uncertain. The symbol "$\cdot \,|\, \cdot$" does not stand for anything by itself, but it has a meaning in a conditional probability context. The site-specific KB, $\mathcal{S}$, is responsible for the different functional forms of $P_{\mathcal{G}}$ and $P_{\mathcal{K}}^{bc}$. Eq. (39) avoids the "decompositional" formulation of Eq. (38) in favor of a direct application of adaptational probability in scientific (physical, biologic, etc.) terms. Another difference is that while $P_o(M_p)$ is the prior probability in formulation (38), in the operational *bc* formulation a similar role is played by $P_{\mathcal{G}}(M_p)$. In standard *bc* practice, the $P_o(M_p)$ is often assessed by means of questionable subjective-probability techniques (Dickey and Chen, 1985; West, 1988). Walters' view concerning such subjective judgments is that (Walters, 1986: 170), "Too often they are based not on real physical constraints or past experience with other systems, but instead on accumulated folklore (wishful thinking) and earlier application of inappropriate estimation methods…" As a result, such approaches often lead to circular reasoning. On the contrary, in operational *bc* practice the $P_{\mathcal{G}}(M_p)$ is estimated by scientific knowledge-based methods involving epistemically sound information measures, and scientifically meaningful laws and theories. Therefore, the operational formulation has considerable interpretive power by expressing specific assertions about the empirical world in terms of the KB it assimilates and integrates in the SEP context[49].

F. The Man and the Hammer

The American philosopher and psychologist Abraham Maslow commented: "If the only tool you have is a hammer, you tend to see every problem as a nail." To avoid such a rather embarrassing situation, public health modellers must operate in

[49] For a more detailed discussion of the important difference between BME and classical techniques, the reader is referred to Christakos (2002b).

an intellectual environment and possess a wide selection of substantive tools. Such tools have been reviewed in the present chapter, and several references have been given for the interested reader who wishes to pursue further the theoretical and/or applied study of these tools.

We made an effort to evaluate the methodological viewpoint that public health modelling should be compatible with general principles of epistemic cognition and knowledge synthesis, which, if false, would impact scientific reasoning in fundamental ways. If the general principles are correct, the proposed modelling approach has to be correct as well. This allows considerable confidence in the correctness of the approach.

We hope that it has been demonstrated that the SEP provides both a variety of fundamental theories and models and a collection of powerful and versatile technologies. Their application in the case of the Black Death epidemic is the subject of the following chapters.

Chapter III - Black Death: The Background

"The medievalist who has to do with records finds
that he needs more than common sense and diligence
to extract their meaning. Records, like the little
children of long ago, only speak when they are spoken to,
and they will not talk to strangers."
C. Cheney

A. Introduction

The deep and long-lasting effect that Black Death had in the daily life, culture, and economy of Europe during the period 1347-51 AD has lured scholars from various disciplines who studied the Black Death from different perspectives, thus contributing to a bibliography that covers disciplines as diverse as history, art, medicine, ecology, economics, and law (e.g., Eamon, 1997). This book makes an attempt to advance the understanding of salient *spatiotemporal* features of the epidemic distribution under conditions of uncertainty. We intend to achieve this goal by means of four consecutive steps:

- Collecting information from a wide range of interdisciplinary sources and understanding its structure, which means understanding the ways information can be true.
- Converting multi-sourced evidence across geographical space to general and site-specific KB, including mortality values with 1-month resolution at each locality of interest.
- Studying the composite space-time mortality distributions in terms of the stochastic theory concepts and tools of SEP.
- Using modern TGIS technology to process the mortality KB and displaying the findings in the forms of substantive space-time maps and other forms of visual representation.

To achieve this multifold objective it was imperative to secure *interdisciplinary* data in a form that could be handled in a quantitative manner. There was neither the time nor the financial resources to implement an *ab initio* kind of an approach, i.e., starting directly from the original sources. Hence, the development of the necessary Black Death KB required data acquisition that involved meticulous bibliographical research, which made use of databases comprising conventional pub-

lications and the latest in electronic searches of the Internet. There was some doubt about the feasibility of the project at the outset given the scarcity and proverbial uncertainty of the data, but in the event of a success, the relevance of the results was assured. Also, to be engaged in rigorous inquiry, one must be capable of handling *uncertainty*, and must be ready to change his mind as newer research questions previous interpretations of the evidence. Therefore, the poor quality, uncertainty, and limited availability of direct information sources were incentives in our case rather than liabilities. We wanted to find ways to improve our understanding of the devastating epidemic, not to use the difficulties as an excuse to dismiss the whole idea. We realized that medieval research is an endless yet methodical quest, often leading to provisional and inconclusive results, because most information sources, in addition to being uncertain, more or less are related to each other[1]. We sought to develop a creative program of research rather than to offer a finished body of knowledge, while keeping in mind that man is always ahead of perfect knowledge in his demands for urging solutions to problems. It is in this spirit that we decided to implement some of the SEP concepts and techniques of modern public health research (e.g., reasoning modes, stochastic theory, and TGIS technology, including the BMElib) in a real yet highly non-trivial space-time data set, uncertain enough not to be adequately handled by other techniques and computer packages available for modelling and mapping spatial or spatiotemporal phenomena. That was the challenge.

At the time we decided to study the Black Death epidemic in a systematic manner, all previous studies that had been concerned with important modelling aspects of the epidemic (spatiotemporal dynamics of the disease, mapping, etc.) were shown to be inadequate. Our new findings have further confirmed our initial evaluation of the situation. It is noteworthy that with regards to the mapping of the propagation of the epidemic, several publications merely included slight modifications of the map of Fig. 1, which appeared for the first time 40 years ago. Fig. 2 is a variant of the previous map in which the emphasis is on its gradient. Recently, Benedictow (2004) merged the two types of maps, added some color, and in the process he reduced the contour interval to 1 year. Among the several Black Death publications, the books by Biraben (1975) and Benedictow (2004) are the two ones that have particularly focused on spatiotemporal aspects of the epidemic. Biraben did a pioneering historical research, indeed, that included not only the plague of 1347-53 AD, but also the numerous infectations that followed for more than three centuries and are considered as successive visitations of the same disease. Benedictow (2004), on the other hand, expanded the number of locations in which information about the date of the outbreak was available to about 320 localities, and provided a better coverage of issues related to death rate caused by the plague. However, information may have been misinterpreted or ignored in the process, leading to a biased account of the actual Black Death situation (e.g., systematic disregard of information reporting low values of mortality results in higher averages than those comprising all reliable sources). No much else is available

[1] In the sense of relationism rather than relativism.

regarding the quantitative Black Death modelling and mapping across space and time.

In our view, the scope and detail of the SEP-based data acquisition and stochastic modelling are superior to those of previous studies. Below we provide a list of initial assertions to support this claim. In particular:

- Acquisition of multi-sourced information relevant to Black Death is guided by theoretical modelling (data collection is part of an operational scheme capable of producing monthly mortality values, space-time dependence is taken into consideration, information sources are categorized according to methodological standards, internal consistency requirements are satisfied, etc.).
- Richer KB are constructed by collecting significantly more information about the spatiotemporal mortality of the 1347-51 Black Death, including the development of a database that includes 531 places.
- More attention is paid to the fairly neglected issue of the ending date of the epidemic at an infected locality. This allows us, at the same time, to obtain a better assessment of the duration of the epidemic.
- Demographic data is considered an integral part of the study, hence doubling the parameters of interest from two (epidemic start and mortality) to four (epidemic start and end, mortality, and population).
- We use epidemic models and improved data gathering to systematically downscale global mortality[2] figures to monthly values. This is a level of detail that prior to our study was available almost exclusively for the English counties.
- The collection and processing of multi-sourced evidence are designed in a way that permits the preparation of several types of useable space-time maps and plots (the maps describe different aspects of mortality, each type of map comprising a set of 40 monthly displays; the plots summarize global aspects of Black Death, such as its propagation speed, rate of areal expansion, and the average monthly mortality throughout Europe)[3].

From a methodological perspective, the developments in this chapter are summarized in Fig. 3. Multi-sourced contemporary evidence about Black Death is transformed into a mortality information base that can be examined and processed with the help of sophisticated quantitative techniques. The information base will include city-level data on population, numbers of deaths, and epidemic duration. There is, of course, plenty of work involved in passing from the beginning of the arrow in Fig. 3 to its ending. In the following sections of this chapter we will describe in considerable detail the numerous sources of information we had to analyze and evaluate--*decipher* may be a more appropriate word--in order to generate the required mortality KB across space and time. Deciphering is a fundamental element of epidemic reasoning. In some cases, e.g., one could see that something

[2] Global mortality refers to the total death rate from the beginning to the end of the epidemic.

[3] Which is a considerable improvement over previous studies that summarized their findings in terms of one map or no map at all.

Figure 1. Contours of the epidemic front sweeping Europe from 1347 to 1351 (Langer, 1964).

was wrong with the medieval evidence available, but, lacking any understanding of how this kind of evidence was built, one could not say what it was. In many cases, the detection of logical contradictions is a valuable tool of epidemic reasoning that can effectively eliminate inadequate hypotheses and poorly developed premises. Moreover, mathematical sensitivity analysis can be very helpful in some cases of information acquisition and processing by providing a deeper understanding of the connections between the various sources of evidence and the epidemic variable of interest (e.g., which piece of evidence is an important contributing factor in deriving accurate mortality maps in a space-time context).

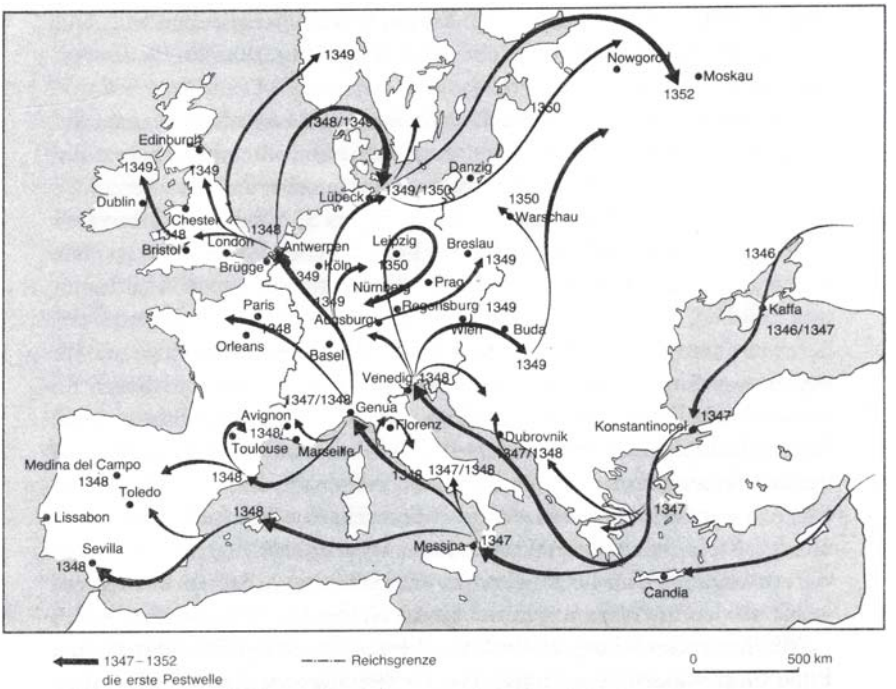


Figure 2. Spreading of the Black Death showing direction of propagation (Vasold, 1991:47).

Before we proceed with the systematic study of the interdisciplinary contemporary sources and their mathematical modelling under conditions of uncertainty (Sections C-E), in the following Section B we take a walk among the main elements of the major controversy concerning the epidemiologic nature and characteristics of the 14th century Black Death.

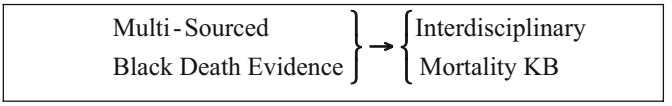


Figure 3. Developments in the present chapter from a modelling perspective (KB=knowledge base).

B. The Controversy About the Epidemiologic Nature of Black Death

a. Symptoms

Accounts from chroniclers, medical surgeons, and people thanking the Saints for miraculous recovery from the pest, offer a description of the typical symptoms of the notorious epidemic, presently known as the Black Death (Herlihy, 1997: Chapter 1; Scott and Duncan, 2004). By way of a summary, these symptoms can be described as follows:

- Formation of *buboes* in different parts of the body up to the size of a hen egg, particularly in the groins, armpits, and neck. There is no consensus as to the number of buboes per sick person. Based on testimonies from miraculous cures, Cohn (2002b: Appendix I) is of the opinion that the buboes were few in number. This, however, may be a biased account valid only for survivors of the plague. Buboes were painful inflamed lymphatic nodes that sometimes were opened to alleviate the suffering and increase the likelihood of survival (Fig. 4), but no cure really worked effectively. People displaying solely buboes had the best chance of survival, especially after the fifth day of displaying the symptoms; yet, somehow surprisingly, the mortality rate was still in the order of 60%.

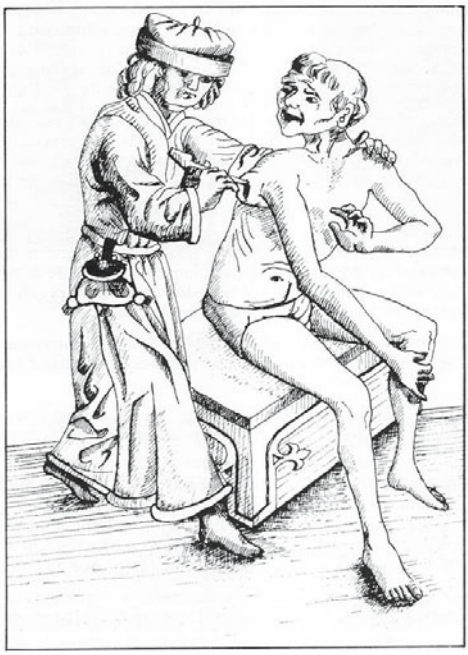


Figure 4. Piercing of a bubo depicted in a 1482 print from Nuremberg.

- Coughing of *blood* as a result of severe gangrenous inflammation of throat and lungs. This form of the disease was 100% lethal. Death usually came two days after showing symptoms.
- Darkish *blotches*, or "tokens," produced by subcutaneous hemorrhages and skin lesions in the form of skin eruptions covering large areas of the body. This form was also lethal within hours of showing symptoms and has been associated with the development of the term Black Death during the 18th century AD. Locally the epidemic received different names in the various languages and dialects (Reichborn-Kjennerud, 1948). *Magna pestilencia* and *magna mortalitas*[4] were the most common names among English chroniclers (Bleukx, 1995).

There is consensus that the above symptoms plus *prostration*, *high fever*, and *unbearable stench* from any matter exuding the body were different manifestations of the same disease. Combinations abound in terms of displaying more than one symptom simultaneously or in the prevalence of one form over the other throughout the course of the epidemic at a certain geographical locality. Take, e.g., the case of Avignon, which at the time of the plague was the residence of the Pope[5]. The head surgeon Guy de Chauliac (Fig. 5), who examined local victims, claimed that the plague started in the blood coughing form that was eventually replaced by the bubonic form. It is important to point out that none of these symptoms, not even the buboes, are unique to Black Death (e.g., syphilis, gonorrhea, and tuberculosis may include buboes among their symptoms).

Figure 5. Guy the Chauliac (c.1300-1368), the most eminent surgeon of the Middle Ages, physician to three popes in Avignon, eyewitness to an equal number of plague outbreaks, and author of *Chirurgia Magna*, a medical textbook published in 1361 that dealt extensively with Black Death and remained a standard reference for three centuries (Biraben, 1987: 185).

[4] Great Pestilence and Great Mortality, respectively.

[5] This is a time period centuries before the Reformation, and the Pope is a more powerful authority.

b. Contemporary Explanations

Contemporaries were not short of disease explanations, but all have been discarded as fantastic and devoid of scientific merit:

- God's punishments for sins.
- The plague was part of an apocalyptic event preceding the second coming of Jesus Christ.
- Planetary alignment of Saturn, Jupiter, and Mars.
- Rain of fire in an area between China and Iran.
- Great earthquakes in the Far East resulting in release of toxic substances to the atmosphere.
- A battle between the sun and the sea in the Indian Ocean.

In addition to the religious explanations, one cannot escape noticing a tendency to locate the source of devastation in the Far East and to enumerate events resulting in a corruption of the air.

c. Modern Etiology

In 1855, an epidemic of bubonic plague started to rage in southern China. Two teams of scientists eventually went to Hong Kong in 1894 to study the epidemic and try preventing its spreading. They succeeded in the former purpose, but still the plague spread to India. The first team was a Japanese commission headed by pathologist Shibasaburo Kitasato, a disciple of Robert Koch. The Swiss microbiologist Alexander Yersin, a student of Louis Pasteur, headed the second team. Within days, both groups were able to observe the bacillus now known as *Yersina pestis* (*Y. pestis*), a tribute to Yersin's more accurate report (Yersin, 1894). The next important laboratory results were those of M. Ogata, published in 1897, and those of P. L. Simonds, published in 1898, on the basis of which they independently launched the hypothesis that bubonic plague was a disease transmitted by fleas. Yet it took another 10 years of laboratory and field experimentation, primarily in India and Australia, to confirm the suspicion (Hirst, 1953: Chapter 7). About 10% of infected fleas develop esophagus and gizzard blockage by highly abnormal reproduction of the bacteria after sucking blood from infected rats. The result is biting at a higher than normal rate because the blockage makes them hungry since the blood cannot reach the intestines for digestion. The bubonic plague mechanism also requires at least one species of rodents that is resistant to the bacteria and another one that is not. The resistant rodents are responsible for keeping the disease endemic by hosting the infested fleas. The infection is passed from fleas to the victims by the blocked fleas that regurgitate infected blood at biting. As the sensitive rodents are infected, they die. The fleas, facing a shortage of their favorite host, move on to people, thus triggering the epidemic. Hence, bubonic plague is not a disease transmitted person-to-person, but one transmitted by fleas facing decreases in the rat population.

Gasquet (1893: 80) made the comment, a year ahead of Yersin's discovery, that the Black Death "would appear to have been some form of the ordinary Eastern or bubonic plague," thus proving that the extrapolation that Black Death was bubonic plague predates Yersin's first step on cracking the bubonic plague mechanism. Gasquet (1908: viii) was also the first Black Death scholar to accept the then recent findings about the epidemiology of the bubonic plague when he pointed out, in the preface of the second edition of his Black Death book, the analogy between the cause of malaria, transmitted by the bite of infested mosquitoes, and the propagation of bubonic plague by the bite of infested rat fleas. Having previously accepted that Black Death was bubonic plague, Gasquet initiated the blaming of rats and fleas for the Black Death epidemic, a dogma that would go unchallenged for decades.

There is one more remarkable fact about Black Death. Although the Black Death caught Europe by surprise, there have been previous outbreaks displaying similar symptoms. The earliest ones are mentioned in the Bible. Then there are descriptions of a form of plague that went around Athens from 430 BC to 427 BC, and more recently there was a longer epidemic—the Justinian plague—that devastated the Roman Empire from 541 AD to 700 AD (Scott and Duncan, 2004: 233-237). Early 20th century extrapolations of previous occurrences of bubonic plague included the Justinian plague, which became the 1st Pandemic, making the Black Death the 2nd Pandemic, whereas the one starting in China in the 1850s came to be the 3rd Pandemic. Thus, the bubonic plague became a kind of a "universal" explanation for a series of previous disasters. This is not so surprising, given that all-explanatory theories have an irresistible effect on the human mind.

d. Discrepancies

The bubonic plague theory of Black Death was accepted without serious opposition by a community of scholars consisting mostly of experts in Black Death aspects other than epidemiology. This is a remarkable fact, indeed, which may be partially explained in terms of the available evidence being mainly of a historical kind (referring to the distant past) rather in the form epidemiologists are accustomed to working with. The first scientist to come up with certain objections was the British bacteriologist J. F. D. Shrewsbury, who published in 1970 a detailed account of the 2nd Pandemic in the UK. Interestingly, Shrewsbury objected accounts of high mortality based on the notion that, given the population density of UK in the late Middle Ages, bubonic plague could not have been able to produce the death rates mentioned by the chroniclers, especially in the countryside. Shrewsbury stood by the bubonic plague theory and concluded, instead, that most contemporary accounts were gross exaggerations (Morris, 1971). The inconsistency between population density and mortality was later pursued by the English zoologist Graham Twigg. In 1984, Twigg published the first book objecting to the bubonic plague theory. In recent years, Samuel K. Cohn, Jr. (2002a and b), David Herlihy (1997), and Susan Scott and Christopher Duncan (2001, 2004) have joined the ranks of the "heretics", so to speak.

In the meantime, Ole Benedictow (2004) remains a leading defender of the bubonic plague interpretation of the epidemic. He and others basically claim that:

- The clinical symptoms of Black Death and bubonic plague are the same.
- There was a well-established black rat population in Europe, including Scandinavia.
- The epidemic propagation was facilitated by the transportation of infested fleas in commodities such as wheat.
- *Y. pestis* DNA found in the teeth of bodies buried in the cities of Marseille and Provence (France) prove that the same bacteria that produces bubonic plague was responsible for the outburst of the Black Death. Ancient and modern DNA sequences differed by at most a single base pair.

On the other hand, detractors of the bubonic plague as the cause of Black Death have counter argued that:

- Clinical symptoms are not unique; several diseases have similar external symptoms. Also some scholars (e.g. Cohn, 2002b: Chapter 4) allege significant phenomenological differences (different kinds of fevers, buboes, etc.).
- As Shrewsbury (1970) and Twigg (1984) have claimed, the rat population of Europe has never been dense and diverse enough to sustain a pandemic lasting for more than three centuries.
- Epidemic propagation through infected fleas traveling long distances hidden in commodities such as wool or grain (rather than attached to rats) is of minimal importance, if any.
- What was previously considered to be final evidence in support of the *Y. pestis* theory--tooth pulp tissue taken from a 14th century plague cemetery in Montpellier containing *Y. pestis* DNA--was never confirmed in any other cemetery. French tooth samples were probably contaminated by improper laboratory procedures, thus invalidating the DNA test. Noticeably, there were cases of true bubonic plague in the area. Moreover, in September 2003, researchers from Oxford University (UK) revealed the results of tests made on 121 teeth from 66 skeletons found in 14th century mass graves. The remains showed no genetic trace of *Y. pestis*, and the researchers suggested that the Montpellier study might have been flawed (Gilbert *et al*., 2004)[6].

As the above were not enough, the detractors of the bubonic plague theory of Black Death have added a myriad of other contradictions, including the following:

- There is not a single account of rats dying prior to any of the repeated visitations of Black Death to thousands of places between 1347 and 1670. On the

[6] "We cannot rule out *Y. pestis* as the cause of the Black Death," says Alan Cooper, head of the Ancient Biomolecules Centre at Oxford University (UK), whose team did the latest work. "But right now there is no molecular evidence for it."

contrary, epizootics were common during the modern pandemic in China and India.

- Temperatures are simply too cold for fleas in northern Europe to be responsible for flares of bubonic plague.
- Iceland suffered two Black Death epidemics in the 1400s, despite freezing temperatures and a complete lack of rodents on the island.
- Black Death advanced at rates up to 5 km/day during a pre-Industrial Revolution era without trains or steamboats. Modern bubonic plague is famous for its slow propagation, which has been documented to be as slow as 15 meters/week.
- There is no evidence of any resistant rodent species available in England or continental Europe during the Black Death period to establish a buffer epizootic through the metapopulation. A pre-infected rodent population throughout Europe would have been a prerequisite for the rapid spread of the Black Death.
- There is no comparison of the mortality rates of untreated patients. There are numerous documented cases of Black Death decimating half or more of the population of a city. The bubonic plague has a death rate one order of magnitude smaller than Black Death. Mortality is related to incubation period. The bubonic plague has an incubation period of 2-8 days and Black Death about 32 days.
- Endemic bubonic plague is essentially a rural disease because it is an infection of rodents. Black Death, in contrast, struck indiscriminately in the countryside and in the cities.
- Chroniclers consistently talked about Black Death being a contagious disease to the point that, starting in the 15th century AD, affluent families found effective protection by isolating themselves in the countryside.
- Black Death rarely hit a locality two years running, at least in epidemic proportions, and the interval separating plagues ranged between 5 and 15 years. By contrast, once modern plague flares up, it remains for the next 8-40 years (as in the case of India), with regular yearly bouts, before mysteriously disappearing.

Nevertheless, the detractors of the bubonic plague etiology of Black Death have been slow in coming up with constructive explanations of the disease cause. Shrewsbury (1970: 124-125) partly discarded bubonic plague by suggesting that many of the casualties may have been cases of *typhus*. Twigg (1984: 221) was the first scholar to deny bubonic plague any role in the 14th century AD epidemic and he blamed anthrax, instead. In a similar vein, the historian Norman F. Cantor (2001) suggested that Black Death might have been a combination of pandemics including a form of *anthrax*. Included in the evidence he cites are reported disease symptoms not in keeping with the known effects of either bubonic or pneumonic plague; the discovery of anthrax spores in a plague pit in Scotland, and the fact that meat from infected cattle was known to have been sold in many rural English areas prior to the onset of the plague. Nevertheless, none of the above explanations received wide acceptance.

In their latest book, Scott and Duncan (2004) have come up with the notion that Black Death was an *infectious* disease transmitted person-to-person. Given the symptoms, they called it *hemorrhagic* plague. There have not been reported cases

of the disease since 1670, which may imply that it has vanished or is dormant. The closest contemporary disease would be ebola. Based primarily on a detailed study of the epidemic at Penrith (UK) during the time period 1597-1598, Scott and Duncan managed to estimate specific values for the stages of the disease, as follows (see, also, Fig. II.1):

- Latent period before the sick person is contagious: 10 to 12 days.
- Period when the sick person is apparently normal but can transmit the disease: 20-22 days.
- Average time period between developing symptoms and death: 5 days.

Scott and Duncan (2004: 161) are confident that this disease is the same as the plague of 1347-51, despite the elapsed time of more than two centuries. Scott and Duncan (2004: 185-186), however, do not deny that while Black Death[7] devastated Europe during 1347-1670, there were occasional epidemics of bubonic plague[8] in Mediterranean ports. They were necessarily brief, because they were extinguished once all the local rodents had died. These localized, sporadic, and short-lasting epidemics of bubonic plague were of no significance in comparison with the terrible mortality and suffering that people had to endure from Black Death, but they have added to the confusion. Fifty years after the Black Death had completely disappeared from Europe, the Mediterranean port of Marseille suffered from a major bubonic plague epidemic that has been well documented.

There is no question that the controversy concerning the epidemiologic nature of Black Death is of considerable importance for the reasons mentioned in various parts of this book as well as in the relevant literature. In Chapter V we discuss the two opposing views in the light of the findings of spatiotemporal stochastic SEP analysis.

C. Interdisciplinary Sources

A primary objective of the study is to analyze the spatiotemporal evolution of the Black Death epidemic. Considering the availability of interdisciplinary information, the area of interest was restricted to the portion of Europe west of meridian 19E and south of parallel 65N. Chronologically the epidemic was active in this region between October 1347 and the beginning of 1351. Before we proceed with our review of the interdisciplinary sources, some modelling decisions need to be made as follows.

The *city* was selected as the minimum unit of study. In most cities, the epidemic lasted for less than a year. Hence, any attempt to observe the local evolution of the disease requires a smaller sampling interval in time. Because daily records are almost non-existent, we decided that a *month* unit was a realistic

[7] Or *major pest* as the Italians called it.
[8] *Minor pest.*

compromise. We, also, had to decide about the main epidemic variable of interest. The mapping accuracy of any such variable depends on spatiotempotal continuity; the higher the continuity, the more reliable the map. During Black Death, cities had populations up to 100,000 residents. Counts of fatalities, therefore, were expected to vary over several orders of magnitude. To smooth out the variability in death counts and to eliminate the influence that the city size by itself may have had on the counting of fatalities, we decided to make the *monthly mortality* rate the epidemic variable of our interest. Mortality was defined as the number of plague casualties during a calendar month divided by the number of resident at the beginning of the month. I.e.,

$$Mortality = \frac{\text{Number of Deaths During a Month due to Plague}}{\text{Number of Residents at Beginning of Month}} \times 10^2 \qquad (1)$$

(e.g., Last, 1995: 43). Whenever possible, Eq. (1) refers to cause-specific mortality, whereas in some other cases it refers to crude mortality. The reader may recall that a methodological postulate was made in Section II.C.b to represent mortality mathematically as a S/TRF, $M_{s,t}$. This postulate allows the efficient modelling of the multi-sourced uncertainty in its various forms. Another methodological assumption is that mortality among the laity is a case of mortality without replacement. If one ignores the possibility of migrations and the influence of births during the plague, the monthly population mortality is not equal to the monthly fatalities divided by the initial population, but to the plague fatalities divided by the residents alive at the beginning of the month.

Example C.1. For numerical illustration, the example in Table 1 demonstrates the various steps leading to the calculation of monthly mortality values at Givry (France). In Section IV.C.a we will present mathematical techniques for constructing the mortality pdf at any geographical location and time period on the basis of these values. Unfortunately, the calculation of population mortality directly from death databases as in Givry is by far the most rare case. As we will see be-

Table 1. Calculation of monthly population mortality at Givry (France), assuming $P_{s,0} = 2{,}000$ residents, $B = 3$ residents/month is the background number of deaths (i.e., due to causes other than plague), $T_o =$ July 28, 1348 and $T_f =$ November 15, 1348.

Month	Deaths (a)	Deaths minus background (b) = (a) − 3	Prior month survivors (c)	Standardized fatalities, % $100(b)/2000$	Monthly mortality $100(b)/(c)$
First	87	84	2,000	4.2	4.2
Second	308	305	1,913	15.8	15.9
Third	180	177	1,605	8.9	11.0
Fourth	42	39	1,425	2.0	2.7
Total	617	605		30.9	

low, in the vast majority of localities, mortality had to be calculated indirectly from a variety of surviving contemporary evidence sources.

Many researchers find it convenient to generally distinguish between two major categories of epidemic-related information sources:

(a) *Modern* epidemic database: relies on a battery of techniques for determining the nature of the infectious agent and the possible contaminant source (in-situ examination of the infected, access to blood samples and other tissues, tracing the lines of infection, estimating its potential lethality, etc.).
(*b*) *Historical* epidemic database: based on evidence that lies far in the past and is characterized by the limited, highly variable across space-time, and mostly uncertain amount of relevant information that has been recorded and preserved.

In view of the preceding discussion, the Black Death knowledge base belongs mainly to case *b* above (see, Sections A, B, and D and most of the present Section C), although some modern models are used as well (see, e.g., Section C.e). For a comprehensive summary of the Black Death databases and contemporary sources—which were produced from our systematic investigation of the matter—the reader is referred to Appendix A. There is, indeed, a considerable amount of effort behind the construction of the tables of Appendix A. In some cases, our scrutinizing search of the contemporary sources might have reminded one of Columbus attending the sea current carrying exotic plants, animal carcasses, and finely carved wooden objects, on the basis of which he visualized the far off and yet unknown land from which these objects came. Theoretical constructs were subsequently used to help classify or organize contemporary sources, integrate them, and translate them into meaningful mortality values.

With the above salient issues in mind, let us now proceed to review the main features of the interdisciplinary Black Death sources. The reasoning modes discussed in Section II.A (deductive and inductive patterns of argumentation, analogical reasoning, etc.) were explicitly or implicitly implemented as tools of *detective* work. Principles of logic were used, e.g. in the analysis, synthesis, and transformation of the contemporary evidence in Appendix A. Indeed, the deductive mode of reasoning has been used to eliminate alternative hypotheses about the Black Death characteristics (e.g., beginning or ending of the epidemic) by means of disjunctive arguments. Detecting logical contradictions in the available records or documents is an effective method of eliminating inadequate arguments and data. Mathematical sensitivity analysis is another useful tool that provides quantitative evaluations of linkages between various kinds of evidence and the disease variable under consideration. On occasion, the inductive mode has served to confirm the validity of a hypothesis (e.g., about the duration of the epidemic) on the grounds that some of its consequences are proved to be true. The reader may have noticed that we suggested using rules of reason to study the Middle Ages—a his-

torical epoch that has been characterized as an "era of unreason", an "age of superstition", and "times of dark forces" (i.e., the very opposites of reason).

a. Surviving Contemporary Evidence

Initially, information of various kinds about the Black Death casualties was collected at 531 places (for details, see Appendix A). At no place was the information directly available in the form of mortality values. In some cases, the information was too imprecise or incomplete to be of use, so the database was reduced to 359 localities. Some pre-processing was necessary for the close to 2,000 monthly mortality values that we ended up coding, starting from a variety of information sources. Preparing mortality data was not a trivial task, but we anticipated that (as a matter of fact, it was part of the challenge, as was previously mentioned). The often poor quality, limited availability, and multi-sourced character of the data were incentives, in our case, rather than liabilities.

When data are scarce and multi-sourced but one can make use of fuzzy evidence with the help of the modern stochastic techniques available, any piece of information counts. In our case, in a way, 100% of the data were uncertain if one considers only the values above zero. According to various authors (e.g., Scott and Duncan, 2004: 45), Black Death never came back to infect the same place twice, shortly after the end of a period of infection. The epidemic did recur in the same place, but in the course of decades and not immediately. For example, in most of Europe, e.g., after the visitation of 1347-51, the next epidemic came in 1361-62. For all practical purposes, this means that after determining the beginning and the end of the epidemic at a geographical location, one can be sure that the values of cause-specific mortality immediately before and after the devastation are exactly equal to zero; they are *hard* data for space-time modelling purposes. Yet, all the non-zero values during the visitation of the plague turned out to be *soft* data with varying degrees of uncertainty.

A census in the modern sense of the word had not been established by the mid-14th century AD; neither had printing been invented. Hence, there were not newspapers for the accurate preservation of major daily events. Most people were illiterate, the main exception being the clergy and the nobility. There were widespread rumors (about the disease, its causes, and its effects) based mainly on superstition and poor assessment of the real events, and, as it often happens in these cases, nothing was so firmly believed as what was least known. Much mold has grown in these six centuries, let alone wars, floods, and fires, all of which have taken a heavy toll on the scarce material that may have ever been prepared concerning Black Death casualties. This being the case with the geopolitical environment of the time, the main sources of surviving material are:

- *Ecclesiastical records*. Perhaps, these are the most numerous and accurate records, prepared at a time when the Catholic Church ruled the western Christian world. The records are most numerous in UK and Spain, but do not deal with the fatalities of the entire community; instead, they are concerned with re-

placements of benefited clergy[9]. A typical record contains the name of the new priest, the name of the person he was replacing, and the date of the appointment. Not exactly the death certificate needed for a mortality study, not even an indication that the vacancy was due to death. We will return to this subject in Section D.b. For illustration purposes, Fig. 6 summarizes the data in the case of the diocese of Barcelona (Spain).

- *Parish records*. Black Death scholars have found churches at four locations that indeed kept a record of fatalities among the parishioners, three of them in the French speaking world: the parishes of Bremen (Germany), the Saint-Nizier Church in Lyon (France), the parish of Saint Maurice in Switzerland, and the parish of Givry in Burgogne (France; Fig. 7). They are by far the most reliable and detailed records, some of them having a 1-day resolution. The only missing piece of information that keeps these places at a minimal soft data status (in the sense of Section II.D.c) is precise information about the total population. Unfortunately, the Saint-Nizier records stop in the middle of the plague. Nevertheless, these records certainly provide some of the most accurate accounts of the local effects of Black Death.
- *Testaments*. Last wills from notaries and hospitals are, within the precision limits of the Black Death studies, another good source of information. Like ecclesiastical records, their limitation is that they represent a minimal and biased segment of the population. In the case of testaments, it is expected that only affluent adults had any reasons to make arrangements in case of death. Considering that there were recoveries and people kept passing away from reasons other than the plague during the time of Black Death, a will was not necessarily a proof of pestilence death. Given prompt death after the development of plague

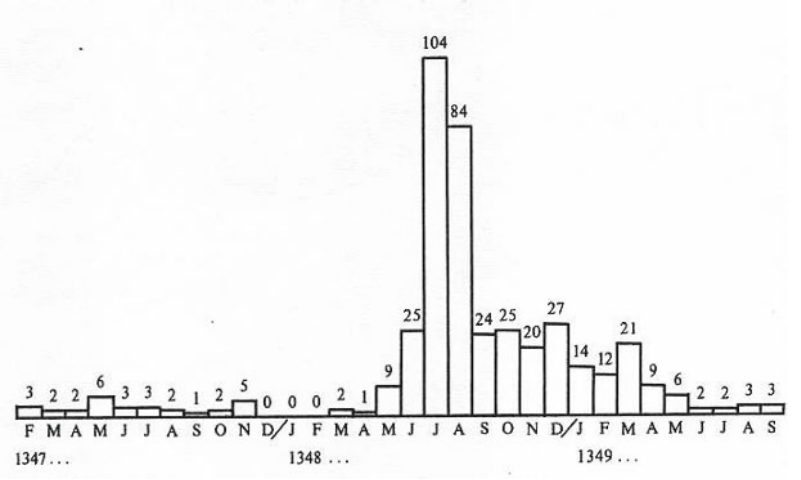


Figure 6. Temporal distribution of ecclesiastical appointments in the diocese of Barcelona during Black Death (Gyug, 1983: 388).

[9] Benefited clergy were high officials and senior priests who received compensation from the church for their services.

Figure 7. Two pages of parochial records at Givry (France) containing the date of death of epidemic victims (Gillot-Voisin, 1982: 18).

signs, the obvious lag between disease detection and actual death is not an important issue, in this case. The fact that a background can be commonly established (referring to the monthly number of wills under normal conditions) improves data reliability and makes it plausible for the SEP concepts and methods to consider cause-specific mortality calculations (Fig. 8).

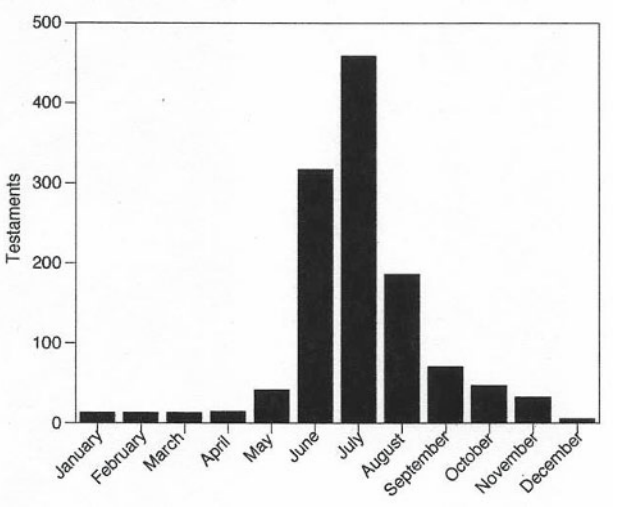


Figure 8. Number of last wills in the city of Bologna during 1348. Testaments in December and prior to May denote the monthly number of wills under normal conditions, and serve as the background (Cohn, 2002b: 149).

- *Tax records.* Like ecclesiastical records, tax records are more numerous in England, followed by Spain and France. Two of the English records are particularly important, both of them being indirectly connected to France: the Domesday Book and the Poll Tax of 1377. Twenty years after the Normans conquered England, King William decided that he needed to have a good idea about the wealth around his new territories. He sent out inspectors to assess every single property in the kingdom. The survey was later used to determine tax payments, for which there was no appeal; the owners were "doomed". The assessments provide today two books that can be used to estimate the population of England in 1086, even though in a strict sense the survey is closer to a census of affluent heads of households. Almost 300 years later, the English Parliament decided that the most fair way to collect funds in order to continue the Hundred Years War against France was to impose a tax of 4 pence on every man or woman 14 years of age or older. Such payment records are closer to being a real census and, in addition, they were collected at a time that is much closer to the Black Death occurrence, thus providing population estimates that constitute a useful source of information for SEP mortality calculations. The matter is discussed further in Section D.g below.
- *Court rolls.* The English feudal system is rich in another type of documents, called court rolls. They are the minutes of local court sessions regulating life in the rural villages. Although the cases are mostly related to breakings of the law, a fair amount of business is relevant to Black Death because they deal with death dues (heriots) and transfers of property after the passing away of tenants. In the England of the late Middle Ages, it has been estimated that approximately 90% of the population lived in the countryside, where most of the land was either the property of the king, the nobility, or the church. Life was regulated by well-established contracts that were obeyed by the time of the 1347-51 Black Death. Peasants had to pay to the landlord a levy usually proportional to the size of the lot. Upon the tenant's death, the family had to make a payment to the landlord, the heriot, which sometimes was not in cash but in kind, such as the family's best cow. Courts were in session several times a year depending on the amount of business, a frequency that goes well with the one-month resolution of our mortality data. Uncertainty about the extrapolation of tenant mortality to the rest of the community remains a problem similar to the significance of other sources of information.
- *Chronicles.* Contemporary accounts, though rare, do exist. Over the years, however, scholars have learned to use chroniclers' testimonies with caution (Coulton, 1929: Chapter 2). When Giovanni Villani declares that the population of Florence right before the Black Death epidemic was 90,000 residents and Giovanni Boccaccio writes that 100,000 people died, at least one of the two must be terribly wrong. One explanation for the frequent inaccuracies of chroniclers is that many times they wrote the accounts years after the event, often without being eyewitnesses to it (see, e.g., Fig. 9). Other explanations include deliberate misinterpretations and sheer carelessness (Cheney, 1956: 14-15). In view of the above considerations, chronicles were used with caution in

Figure 9. The Nüremberg Chronicle included this Black Death account, written and printed during the 15th-century (Naphy and Spicer, 2000: 34).

mortality calculations (cross-validation with other information sources is a necessity).

- *Donations to the church*. Considering that a vast majority of the population believed that most likely Black Death was a divine punishment for people's sins, the parishioners suddenly became generous with the church as a way to buy back absolution as the plague was approaching. Remarkably, Benedictow (2004: 175-176) came up with a history of the Black Death outbreak in Sweden based almost exclusively on an analysis of the abnormal increases on church donations.
- *Financial transactions*. Perpignan (France) offers unique records that have been used to date the outbreak and the end of Black Death epidemic. The city had an important Jewish community largely devoted to money lending, which was a common Jewish practice throughout Europe. Transactions occurred at a normal pace of 24 transactions per month during the first quarter of 1348. Subsequently, 8 transactions were registered during the first 11 days of April but only 3 for the rest of the month, whereas no more transactions took place until August 12 (Ziegler, 1969: 65). The most logical explanation for this gap is the raging of Black Death. Indeed, this explanation fits well with independent additional evidence for southern France.
- *Passing away of famous people*. Death of ordinary people goes without explanation or notice. Yet death of nobility or other influential persons goes into the annals of history, usually due to the writings of several authors. Although, in general, a single death is not sufficient evidence to determine the beginning or the end of an epidemic, it, nevertheless, serves as a point of reference for further investigation concerning the pestilence's evolution. One of the most remarkable examples is that of Princess Joan de la Tour of England. Engaged to Prince Pedro of Castile, the bride started a trip to Spain in the summer of 1348 escorted by a large group of people. The trip considered a stop for provisions in Bordeaux (at the time in the hands of England, as part of its initial success in

the Hundred Years War). They arrived in Bordeaux in early August of the same year, where the mayor informed them that the plague was causing serious trouble in the city. The princess and her entourage did not pay attention to the mayor's warning and went for a short stay at a castle overlooking the port. Within days, members of the party fell sick and died of the plague. Princess Joan died on September 2 (Cantor, 2001: Chapter 3).

- *Letters*. Accounts of the plague are preserved in personal or open letters narrating developments or sending warnings about its coming. Petrarch, the famous Italian poet, endured the plague in Verona, lamenting the mortality, especially after the death of his beloved Laura, most likely of plague, in Avignon in 1348, at exactly the same hour and the same day of April 6 that he had met her 21 years before (Ziegler, 1969: 65).
- *Edicts*. Authorities facing the effects of the Black Death produced numerous documents that today are useful to study reactions and assess fatalities. López de Meneses (1956), e.g., published a large collection of documents related to the Black Death that were prepared during the reign of King Pedro IV of Aragon.
- *Guild records*. The urban skilled workers of the Middle Ages were grouped in guilds, ordinarily powerful and well organized. The records of the guilds in Hamburg (Germany), e.g., allow us to know today that 12 of 34 master bakers and 18 of 40 butchers died from the plague.
- *Hospital records*. Some hospitals kept records of deceased personnel and patients, records that are significant in the presence of information about mortality during normal times. In Bruges (Belgium), e.g., 10 clerks died during the second semester of 1349, while the average rate for the following two years was less than 2.
- *New cemeteries*. Several communities run out of room in their cemeteries for burying the dead. Cemeteries were the property of the church. Enlargement of a cemetery or approval of a new one required special paperwork, which today can be used as an indication of high mortality. Given the high level of mortality, several places in Europe decided to bury plague victims in mass graves (Fig. 10).
- *Tombstones*. Jews in Toledo continued to bury family members in the traditional way, writing on the tombstones the death date and in some instances specifying that the cause was plague (León, 1977: 334).
- *Abnormal increases in adoptions*. Benedictow (2004: 115) has used abnormal increases in adoptions as a sign of the plague raging the city of Ghent in the summer of 1349.

It is worth-noticing that a significant proportion of the data we have collected for the purpose of our modelling study appears in recent publications without indicating the information source. A rather typical example is the monumental work of Biraben (1975). While the original source most likely is one of those listed above, there is much work that remains to be done in terms of source identification and reliability. Next we examine a number of issues of concern in the context of multi-sourced information assessment and processing.

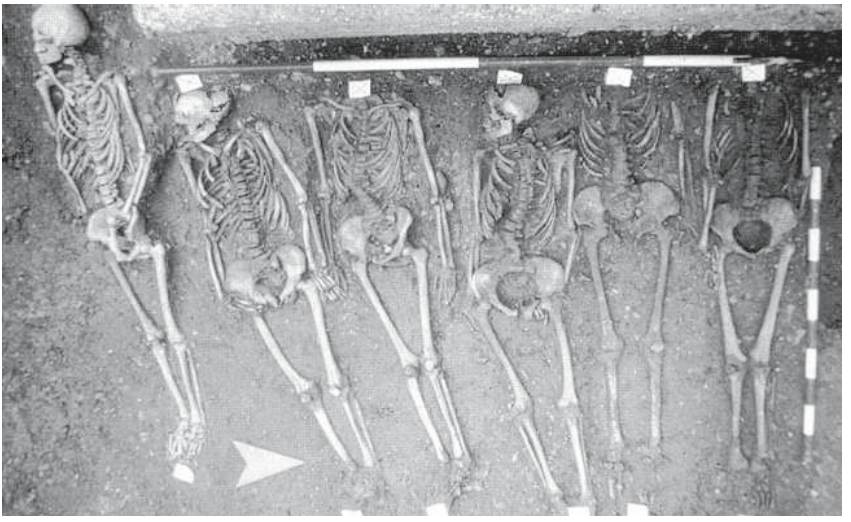


Figure 10. Detail of mass burial grave of victims of the plague during 1349, East Smithfield, just south of the Tower of London, UK (Kelly, 2003: Plate 20). Excavation took place between June 1986 and June 1988.

b. Reliability of Contemporary Sources

We have assigned special emphasis on the fact that the reliability of the available information is a major point in question with a strong epistemic component (Section I.B.g). A relevant question is the use of language in the chronicles and other written evidential sources. We know only by means of words. If they are proven useless, then we are blinded. There will always be a primary question about the value of the words the chroniclers use. Ideally, one would like to know when chroniclers' language is truth or falsehood, i.e., when they deliberately exaggerate to impress their readers and when their language is false at the very moment when they think they are telling the truth. Yet another issue is the consideration of numerical data. Some scholars have argued that numerical data from the Middle Ages are so corrupted and fragmentary that they do not deserve much attention. Serious problems with data of even more recent vintages are indeed unsatisfactory by modern standards of measurement and sampling. Most values were not even collected for the purposes for which they are used today. Also, there are errors in copying, reporting, and enumerating. Yet, it is the wrong decision to discard them completely. Spatiotemporal stochastic theory and statistical analysis offer today powerful enough tools, ones that have been developed exactly for the purpose of handling information that is known to be of poor quality. Indeed, we rather agree with Ohlin (1966: 69), who emphasized: "To abandon the scraps of quantitative insight into the past merely on the grounds of general suspicion would be as foolish as to regard them as wholly accurate. The question at all times must be how great the uncertainty is and how seriously it affects the conclusions at stake. In the

statistical, as in any empirical study of the world, 'a reasonable probability is the only certainty' ". Interestingly, in some cases a mathematical sensitivity analysis may demonstrate that the uncertainty concerning a contemporary piece of information has little effect in the final modelling outcome.

When it comes to mortality observations by chroniclers, Turner (1988: 19) has compared contemporary writers to modern reporters who often tend to purposely exaggerate the case of an extreme example in an effort to come up with a more sensational story. Shrewsbury (1970: 72) has gone even further suspecting that there was an element of competition and pride among the chroniclers, which motivated them to exaggerate in order to show to their readers that the event they narrated was more outrageous than those narrated by their competitors. This may well be the case of Lübeck (Germany), as follows.

Example C.2. In Lübeck (Germany) some chroniclers described a state of complete hysteria in the streets and about 90,000 casualties by the time the plague was over. Independent assessments give Lübeck a population of about 25,000 residents on the eve of the Black Death outbreak, and there are more credible but partial accounts reporting the passing away of 11 of the 30 city councilors, 2 out of the 5 town clerks and 27% of the property owners--roughly a death rate of 1 in 3. Therefore, most likely the actual casualties were in the order of 9,000 instead of 90,000.

Experts in the field have offered different explanations for this type of blunder, some of which are as follows:

- Large numbers should not be interpreted literarily. Instead of saying just that "many people died", chroniclers tended to pick any number that they thought was large enough to portray an image to the public, without trying to imply that there was some actual counting of fatalities. In these cases, it is the impression, not the number, that counts (Coulton, 1929: 29; Gottfried, 1983: 68). This problem with the overestimation of the numbers of victims has contributed to our decision to select mortality rates rather than the total number of casualties as our modelling variable of interest. Indeed, it was easier for a chronicler to make a reasonably accurate statement based on the proportion of neighbors killed by the plague in his surroundings than to come up with a figure for the total number of fatalities in a large city.
- Lack of scientific method and interest. Chroniclers were not used to gathering information in the field. Most of them were clerks spending a comfortable life close to the nobility, often preferring to rely on informants and hearsay without checking the facts. The main focus of chroniclers was to exalt military victories, a fairly different business than preparing long and detailed accounts about the misery of peasants (Benedictow, 2004: 207).
- There is the confusion caused by Roman numbers in use at the time. Even the simplest arithmetic operation is much harder to perform with Roman numbers than with the present decimal system of Arab numerals (Coulton, 1929: 29-30).

- Most assumed blunders may not be real blunders. In modern history one finds considerable changes in attitude concerning the Black Death mortality estimates. For a long period of time, the prevalent view was that mortality was high, as much as 35-45% (Ziegler, 1969: 230-231). Gasquet (1908: 135) commented that although the accounts of the Black Death horrors are hard to believe when read individually, they become more credible when one notices the remarkable coincidences in descriptions by chroniclers from distant places who had no way of communicating with each other. Russell (1948) and especially Shrewsbury (1970) claimed that contemporaries inflated the English mortality figures considerably. Shrewsbury (1970: 123) went on to postulate no more than 5% mortality for England. Today, the tendency is for the vindication of chroniclers. Benedictow (2004: 383) may have gone too far. He put his emphasis on places with high mortality but ignored others with low mortality, thus reaching an overall death rate of 60% for Europe.

When systematic error is likely to be significant and the sources are contradictory, it becomes important to use some kind of logical cross-validation (using, e.g., the reasoning rules of Tables II.2 and II.3), check original sources, get a deeper understanding of the underlying assumptions, and investigate the guesswork behind some of the numbers[10]. When gathering data for this study, we never ceased recording evidence at a given locality by assuming that there was enough information already. In this way, by the end of the information acquisition stage of the SEP method we collected approximately 2,500 typed literal transcriptions making more than 300 pages of text. When the time came to use the information bases, a systematic search for redundancies and logical inconsistencies was employed to discard questionable data and rigorously assess the reliability of the resulting mortality values. In the event of agreement among the produced numbers, our general tendency was to quote the original source, the first author to publish the original data, or the scholar who was most knowledgeable about the specific region (see *AtA* inductive rule in Table II.2). In France, e.g., we relied more on the word of Biraben than that of Benedictow, but the opposite happened in the case of Scandinavia.

c. Concerns About Time Accuracy

The official Julian calendar was only one of many devices available to keep track of time during the Black Death era (Tuchman 1978: xv). This calendar is behind by 10 days relative to its successor, nowadays Gregorian calendar introduced by Pope Gregory XIII in 1582 to take care of shifting in seasons because the rotation of earth does not take exactly 365.25 days. More common in the 14th century Europe was to keep track of time referring events to the day of crowning of the reign king; or in the case of the Julian calendar, it was employed only to keep

[10] In some cases, the final choice seemed to offer all the advantages of “honest theft” over “dishonest toil”; but it might be that "honest theft" is one’s only option in these cases.

track of the year, because instead on going by months or days the predominant practice was to name the saint of the day or the nearest church feast (Cheney 1996). This latter practice was valid particularly for vague events as is the beginning or the end of a plague. Local variations on these practices plus the fact that the year started on the moving feast of Easter have added to the existing confusion among scholars even to nowadays.

Example C.3. Givry (Bourgogne, France) has one of the best kept records of casualties during the Black Death period, with a 1-day resolution. Table 2 summarizes the entries during the days of the epidemic. As is the case in other places, the link to Black Death casualties is no more than a good presumption based on the absolutely abnormal number of casualties and the timing of the event. There are no annotations stating the cause of death. During normal times, there were 2-3 deaths a month. Hence, July is already an abnormal month. But, when exactly was the first passing away due to Black Death? Was it on July 17, i.e., the first day with deaths in consecutive days? Was it July 5 or 22, when there were 2 deaths in one day? Was it July 18 when the fatalities exceeded the background? Or was it on August 6, which marks the beginning of daily casualties? Yet, Biraben (1975: 74) believes that the plague started on July 28. Determining the end of the epidemic presents similar difficulties.

In other less organized communities or in cities larger than Givry, most likely the first Black Death casualties went undetected. Presumably, what we know today as the beginning of the epidemic would be the equivalent of August 8 in Givry, when things clearly went out of control, or even the feast of the Ascension of The Blessed Virgin Mary (August 15), the first religious holiday after the beginning of the crisis. Yet, considering our modelling decision to study mortality at the monthly level, all inaccuracies mentioned in this section are effectively blurred by the sampling frequency of the study.

In some cases, there are disagreements within and between cities that may be related to the same causes but go beyond a discrepancy of a few days. Two classic examples are the cities of London and Mühldorf.

Example C.4. The chronicler of the monastery of Bermondsey dated the beginning of the plague in London at the feast of Saint Michael (September 29, 1349), while clerk Robert the Avesbury at the service of the Canterbury archbishop declared that the pest arrived in London close to the feast of All Saints Day (November 1) of the same year.

Example C.5. The city of Mühldorf (Bavaria, Germany) offers a good example of dating not matching regional data. The *Annals of Mühldorf* reported that the plague arrived in town on June 29, 1348. The problem with this date is twofold: Our investigation found that Trent (Italy) was the closest infested place, 360 km to the south (on the other side of the Alps), where the plague had started on June 2, and no other place in Bavaria suffered from Black Death that year. Biraben (1975:

92) suggests that either the disease was not Black Death or that there is an error of one year in the dating, which should read June 29, 1349 instead.

Table 2. Daily number of fatalities in Givry during the plague year of 1348 (Gras, 1939: 305-306).

	July	August	September	October	November
1			6	7	3
2		4	9	6	4
3		4	8	7	3
4		1	8	7	4
5	2		4	8	
6		2	6	7	2
7		1	15	6	1
8		7	3	6	
9		5	11	4	4
10		3	24	4	3
11		1	7	7	2
12		1	10	9	1
13		4	15	3	
14		5	10	14	
15		3	14	5	5
16		3	11	5	
17	1	4	17	4	
18	1	1	8	8	
19		5	6	6	3
20		2	3	7	
21		4	17	3	
22	2	3	6	2	
23		6	11	5	
24		2	16	4	
25		2	7	4	
26		6	16	2	
27		3	12	3	
28	3	8	5	1	
29	2	4	10	3	
30		6	7		
31		10		6	
Total	11	110	302	168	35

d. Notorious Inconsistencies in Outbreak Dating

Of the several factors that have contributed to the perplexing situation with medieval data, surely one is the existence of inconsistencies in outbreak dating. The case of Mühldorf (Example C.5) is one of the most complex cases. A second chronicle from Matsee maintained that on September 29, 1348 there were 1400 plague casualties in Mühldorf. The number of fatalities is most likely another one of those examples in which the number of dead people is larger than the town population. In this case, a logical analysis of the evidence convinced us that Mühldorf, along with the rest of southern Bavaria, was struck by Black Death during the summer of 1349.

In addition to London, Marseille is another city with multiple dates assigned to the beginning of the plague. Biraben (1975: 91) makes a reference clearly stating that the pest was already raging the Rifle-Rafle street by November 1, 1347. Gasquet (1908: 39), on the other hand, maintains that Black Death did not start in Marseille until the beginning of 1348. Finally, Verlinden (1938: 116) suggested an intermediate position that the plague started during Christmas of 1347. In the absence of clear evidence one way or the other, we simply took the middle road (Verlinden's suggestion).

The beginning of the plague in Copenhagen (island of Zealand) has been assigned even more dates. Biraben (1975: 78-80), denoting insecurity, provides three dates. The first one is November 25, 1348, which he marks with a question mark. Then comes January 1349, and he ends up suggesting July 1350 for the island of Zealand. Fössel (1987: 6) postulates January of 1349, without giving any sources. Benedictow (2004: 164), based on just 3 donations annotated in the *Anniversary Book of Our Lady's of Copenhagen*, favours the summer of 1350 as the time when the Black Death reached Copenhagen, basically agreeing with the latest of Biraben's dates. Benedictow (2004: 163) reinforces his opinion on the basis of equally shaky donation evidence during October-November 1350 at Roskilde (which is located only 30 km west of Copenhagen). It is hard to come up with a definitive date for Copenhagen, as there are other places in northern Germany for which Biraben (1975: 78-80) provides two dates for the beginning of the plague. In Schleswig and Holstein (Germany), the beginning of the plague has been placed during July-August 1349 as well as during January-March 1350. Considering the opinion of Scott and Duncan (2004: 45) that the plague never came back to infect the same place twice during the same outbreak, the period 1347-51 in our case, one has to discard one of these dates. We ended up discarding the 1349 date. Nevertheless, this is an area that definitely needs further research of its original sources.

A similar situation exists with The Netherlands. Biraben (1975: 77) has Foswert (Friesland) as the only place in the country where Black Death started during 1349. This dating makes a big difference, because in this case Friesland was the source of infection for the rest of the country. Other authors (e.g., Blockmans, 1980: 843) maintain that the country, and specifically Friesland, were struck by Black Death in 1350 and 1351, thus reverting the flow and having the Black Death coming from Germany and infecting Friesland last, rather than the other way around. Either point of view is weak. The case calls for additional research.

Germany is a country short in data and rich in contradictions[11]. Hoeniger (1882: 25) found that the *Chronica Sampetrinum* states that Black Death reached Erfurt (Thuringia) on July 25, 1350. Biraben (1975: 77) changed the date to January-March, 1350, offering no source. We decided to use the earliest dating.

As was mentioned before, the detection of contradictions and inconsistencies in the writings of scholars can help eliminate possible dates. The city of Limburg is a typical example. Black Death started in Mainz (Germany) during July or August, 1349 (Biraben 1975: 77). The *Chronicle of Limburg* mentions that in the summer of 1349 the plague moved to Limburg (state of Hesse), about 50 km north of Mainz. Biraben (1975: 77), however, has Limburg listed among the places receiving Black Death during January-March 1350, which contradicts his own claim that the plague reached the Hesse during July-August 1349. Under these circumstances, we used the 1349 dating, despite Benedictow's "skepticism about the chronicler's horizon of knowledge and interest" (Benedictow, 2004: 194).

Biraben (1975) supplemented his magnificent Black Death account for Europe with a valuable update for France (Biraben, 1987). However, this supplemental book chapter presents some inconsistencies between the text and a color map summarizing the findings. These inconsistencies are shown in Table 3. More to the point, the map shows Black Death reaching the Givry area during July-September 1349. The city is either not displayed on the map or is placed at the wrong location, since none of the cities are labeled. We have seen in Table 2 that Black Death started in Givry during July-August of 1348. In Table 3 we also present our final choices of dates.

According to the site http://membres, the plague was at Quimper, Bretagne (France) between November 1348 and January 1349. Biraben (1987: 179) maintains that Black Death started in January of 1349. Neither party cites the sources. We gave the benefit of the doubt to the local and much more recent reference.

In a groundbreaking study, Ubieto (1975) considerably advanced the understanding of Black Death spread in Spain with his bold use of ecclesiastical records. On the basis of appointments of benefited bishops, he postulated that the predecessor had died of plague, to which he added the general knowledge that it took 1-6 months of paperwork to renew the appointment. Benedictow missed

Table 3. Inconsistencies concerning the beginning of the Black Death epidemic in some locations in France (Biraben, 1987).

City	Beginning in Text	Beginning in Map	Our Choice
Abbeville, Somme	April 1349	July-September 1349	April 1349
Amiens, Somme	January 1349	April-June 1349	January 1349
Auch, Gers	May, 1348	July-September 1348	May, 1348
Beaune, Côte d'Or	April 1349	July-September 1349	April 1349
Paray-le-Monial, Saône-et-Loire	April 1349	July-September 1349	April 1349

[11] Unlike Italy, which, among the countries with abundant information, is the one with the smallest number of inconsistencies, a fact attributed to its good chroniclers.

the delay element and, instead, he used the appointment dates as the dates of the bishops deaths. E.g., a new bishop for Cádiz was actually appointed on May 25, 1348. Nevertheless, Benedictow (2004: 82) wrongly assumed that the diseased bishop passed away "around June 1 or a few days later." Our own investigation of the matter (which included resorting to the original papers) concluded that these mistakes were probably due to translation problems. Valdeón and Martin (1996: 84) have objected Ubieto's findings primarily on the grounds that there is no evidence that any of the bishops who passed away in 1348-49 did so because of Black Death. We have found, however, a good fitting between these appointments and the raging of Black Death, assuming that the deaths took place 1-6 months before the appointment of a successor.

Ubieto's research has been instrumental in the study of the Black Death front that radiated from the city of Santiago de Compostela (Galicia), which is a famous Catholic center of pilgrimage in Spain. There was a bishop appointment for Santiago on June 14, 1348, and another one for Tuy, to the south, four days later. Benedictow (2004: 82) wrongly assumed that "the bishop of Santiago is mentioned alive for the last time on 14 June". He credits the information to Ubieto, which is a mistake, again probably due to the poor translation of Ubieto's work. Valdeón and Martin (1996: 84) strongly support the view that Black Death did not reach Galicia until after these appointments, most likely in October of 1348.

Amasuno (1996: 64), following Ubieto, suggests that Santiago de Compostela was visited by Black Death between March and July of 1348; then the plague spread to the south, reaching Coimbra (Portugal) on September 29, 1348, which seems a reasonable conclusion. The only problem is that Braga and Lamego (Portugal), half way between Santiago and Coimbra, had Black Death later. Ubieto (1975: 64) postulated that Black Death was in Lamego y Braga between January and May, 1349.

Another place with contradictory information is Seville. The bishop died during the second semester of 1348, being replaced in January 28, 1349. Ubieto (1975: 63), making an exception, clearly states that this appointment does not fit other data, a fact that would have allowed one to use the Seville appointment as an indication of the death of the previous bishop from the plague. Collantes (1977: 154) places the Black Death in Seville during 1349-50. Velásquez y Sánchez has Black Death reaching Seville in 1350 (Amasuno 1996: 70), but Phillips (1998: 49-50) emphatically declares that all forms of the Black Death disaster ended in the peninsula by March of 1350.

The websites http://www.ayto-puertollano.es/ and http://centros6.pntic.mec.es/ have Puertollano, Ciudad Real (Spain) suffering the effects of Black Death in the summer of 1348. Ubieto, however, maintained that the geographical regions in the sector defined by the imaginary lines going from Coimbra to Soria and from Soria to Valencia had Black Death beginning after the winter of 1348-49. Taken into account the above considerations, we concluded that Black Death was in Puertollano during the summer of 1349.

Crowland Abbey was about 10 km northwest of Cambridge (UK) in the diocese of Ely. Black Death was in the diocese of Ely between March and December of 1349 (Aberth, 1995: 279-280). The court rolls of October 1348 report 11 fatali-

ties, which Benedictow (2004: 133) considered as the onset of Black Death. Yet, at the December session of the court there was no report of deaths at any of the manors--the beginning of massive casualties is reported in the May 21, 1349 session. We have linked this generalized mortality with the beginning of the Black Death epidemic in the spring of 1349 and have assigned the October deaths to other causes.

Hoeniger (1882: 17) talks of evidence for the outbreak of Black Death at Rutwil, near Lucerne (Switzerland) on July 29, 1349. Biraben (1975: 77) reports March 1349 as the beginning of Black Death at both places. Given Biraben's consistency on the subject, we adopted his view, even though the 4-month delay seems to be in agreement with other regional information.

Concerning Geneva (Switzerland), we did not follow Biraben (1975: 75) who offers no source for his dating of the beginning of the outbreak in January of 1349. Working with testaments, Andenmatten and Morerod (1987) have reliably dated the duration of the epidemic from August 10 to October 11, 1348. This was our choice, as well.

Gasquet (1893: 63) states that Black Death reached Dissentis, Grisons (Switzerland) from northern Italy through the St. Gotthard Pass, and from there went northeast (down the Rhine river) to reach Pfäfers in May of 1349. Benedictow (2004: 119-120) has reservations about this sequence of events. He claims that the epidemic reached northern Italy in the summer of 1348, believing that there was not enough time for the plague to cross either the St. Bernard or the St. Gotthard pass and reach Dissentis by October-November 1348, which is the onset time suggested by Biraben (1975: 75) and Fössel (1987). Benedictow is tempted to suggest yet another case of misdating by one year, indicating that an October-November 1349 outbreak in Dissentis would be a better match to an infection from Engelberg to the northwest. Yet Benedictow himself rejects such a possibility a few sentences later when he remarks that Engelberg is at the foot of impassable mountains where the pestilence found a dead end. Benedictow has Pfäffers infected from Austria to the east, where Back Death reached in the fall of 1348. We followed Sticker (1908: 56), who dated the outbreak at Dissentis in December of 1348, and we left it to SEP space-time modelling to figure out the route of the Black Death on its way to Pfäffers (see the maps in Chapter V).

e. Epidemic Modelling

A salient interdisciplinary issue is the use of epidemic models (see, also, Section II.D.b). There exist numerous epidemic models in the modern literature that are mathematical representations of empirical or theoretical knowledge concerning the transmission of infectious disease (see, e.g., Anderson and May, 1995; Daley and Gani, 2001). Despite complications (some of which are discussed in other chapters of this book), mathematical models can provide valuable insight into the dynamics of the disease, predict its course with reasonable accuracy if used within an adequate methodological framework, and help policy makers to make useful decisions about a plethora of public health issues.

The majority of epidemic models are currently *deterministic* (they deal with conveniently closed systems having a limited number of theoretically definable units with properties that do not change as the thinking proceeds, etc.). However, due to a number of critical issues (in reality one is dealing with incompletely known open systems, characterized by the uncertainty of their parameters, observation inaccuracies, etc.), it is widely acknowledged that *stochastic* models of open systems offer much more adequate representations of an epidemic distribution across space and time. The predominant role of stochastics in the description of real-world phenomena is reflected in Einstein's views on the subject: "as far as the laws of mathematics refer to reality, they are not certain; and so far as they are certain they do not refer to reality." In a similar vein, stochastics creates the context that gives meaning to the various kinds of uncertain medieval data and converts them into useable knowledge.

Due to the mainly historical nature of the evidence about Black Death, employing epidemic models is far from being a straightforward mathematical exercise. Nevertheless, modelling based on sound theoretical and empirical underpinnings is vital for epidemic studies to be valid and reliable, and for the generated predictions to be substantive, they should possess a meaningful cognitive basis. We must not forget, that a cornerstone of the current modelling efforts is the decision to time mortality every month. Although English ecclesiastical records are rich in data with such a resolution, they are by far the exception. Most other places at best have some mortality for the overall period of infection. Therefore, we decided to extend the well-known epidemic model of Lowell J. Reed and Wade H. Frost (Maia, 1952; Scott and Duncan, 2001) to develop a satisfactory S/TRF-based methodology capable of downscaling global mortality figures into a sequence of monthly mortality values. The generalized model is stochastic and its parameters are distributed across space and time. We will revisit this important matter in Section IV.B.b, in which a detailed mathematical exposition of the Reed-Frost model suitably extended in a composite space-time manifold will be provided.

D. Data Processing and Interpretation Issues

a. Medieval Data are Like Children

The eminent historian Christopher Cheney commented, "It is an English habit to distrust method—still more, methodology—and English historians like to claim 'amateur status'. But the medievalist who has to do with records finds that he needs more than common sense and diligence to extract their meaning. Records, like the little children of long ago, only speak when they are spoken to, and they

will not talk to strangers."[12] In other words, the data talk only to those who have an adequate conceptual background and contextual expertise to understand them. Common sense approaches will not suffice, because they are often self-limited, proceed from an uninformed basis, lack context, and rely on unspoken assumptions. In this sense, Cheney's comment is crucial for appreciating the important role of theoretical modelling in the interpretation of medieval records.

The situation described above clearly implies that Black Death modelling has to use interdisciplinary data collection techniques and rigorous knowledge synthesis rules in order to adequately interpret and process contemporary evidence; evaluate a wide range of more recent sources, including experts in the corresponding fields; and offer a meaningful assessment of the associated uncertainties. As was mentioned above, principles of logic are used as tools of detective work, e.g., for appraising arguments, interpreting evidence, and creating chains of reasoning. In this sense, one of the most important detective tools is generalization. The epidemic modeller should be aware, however, that generalization is like a double-faced Janus[13]--a critical operation of creative thinking and, at the same time, a potentially serious source of errors. Also, since each word used in a record, account, chronicle, etc., means different things to different people in different contexts, we must carefully seek out an author's intended meaning, search for contradictions and inconsistencies, etc.

b. Time Series Deconvolution and Compensation Based on Ecclesiastical Appointments

As we mentioned in a previous section, ecclesiastical paperwork has left one of the most reliable documents for the study of Black Death mortality. The information is in the form of a list of appointments of benefited clergy. What would be more useful for our modelling purposes is a list that dates the passing away of all priests who died of plague. This section deals with differences between the two types of lists and its relevance in the temporal analysis of mortality. First of all, not all appointments were to replace plague victims. Appointments also took place because:

- The pay depended both on the merit and the wealth of the community. Priests had enough mobility to accept more advantageous positions in terms of benefits, proximity to family, or working conditions.
- People kept dying of other causes during the Black Death.
- Some priests stayed in the same place, but were reappointed to new responsibilities.
- In some cases priests simply retired.

[12] Cheney (1956: 11). The reader may see a close association of this comment with the earlier one: "the data do not speak for themselves…" (Section I.A).

[13] Janus is the Roman god of gates and doors, beginnings and endings, and hence represented with a double-faced head, each looking in opposite directions.

There are also examples of benefited clergy who died while temporarily working at a different parish, a situation that would distort the statistics if not taken into consideration properly. Moreover, there was the problem of a delay in the search procedure and the bureaucratic process culminating with the appointment. The first step was to issue a notification to the patron of the benefice, who then had the privilege to look for a replacement. Under normal circumstances, there may have been candidates waiting for an opening. If not, a search was necessary, a chore commonly delegated to an assistant. Once a suitable replacement was found, it took several days to go through the formalities and ceremonies proper to the benefice. Finally, the bishop communicated the good news to the candidate, who promised obedience to the bishop. The annotations that we have today were recorded in the bishop's official register at the time of institution. Appointments suffered additional delays if the bishop himself happened to die (Fig. 11).

Wood et al. (2003) have studied the bishop's register of the Coventry and Lichfield diocese, a register that is unique in the sense that it lists both the date of death and the institution. Dividing the records by archdeaconry, the authors were able to establish 5 subpopulations of acceptable sizes. They noticed increasing delays in the appointments as the plague went on, an effect that is diagrammatically displayed in Fig. 12 for the case of a constant rate of variation. The authors, however, noted differences in the distribution shapes for appointments vs. deaths that suggested a variable rate of change. This is a mathematically more complicated problem than the simple deconvolution required to correct an increasing lag at a

Figure 11. Death checkmates a bishop, St. Andrew's Church, Norwich (Platt, 1996: 161).

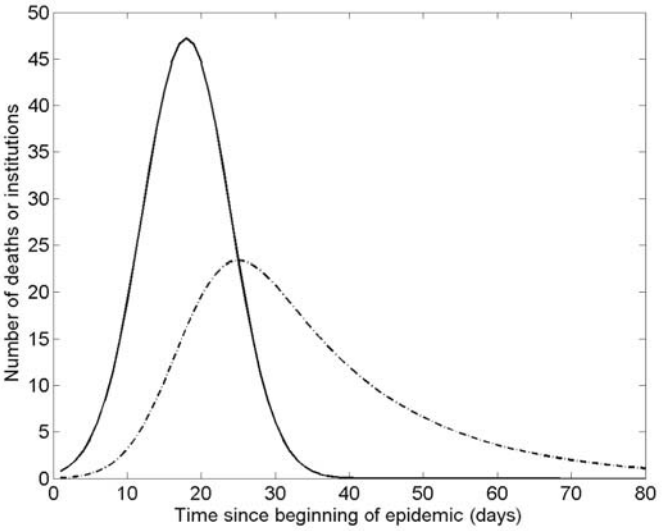


Figure 12. Hypothetical distribution of deaths--dashed line; and appointments--continuous line (reconstructed from Wood *et al*., 2003: 436).

constant rate. Lag variability among archdeaconries was high, suggesting that personal factors (such as the diligence of the bishop) overrode any other considerations. Under those circumstances, the authors came to the conclusion that was not possible to extrapolate the experience of Coventry and Lichfield to other places. Wood *et al.* (2003), however, found mean and median lags that are close to one month, i.e., in agreement with the older rule of thumb of correcting a lag in institution: subtract one month from the date of the annotation in order to obtain the date of death. Note that Church regulations allowed bishops six months to appoint a replacement to a vacated benefit.

Not even the most detailed registers mention the cause of death. Therefore, even after eliminating all institutions not related to fatalities, there is a still a small margin of error. Nevertheless, this margin can be minimized by considering fatalities in the same bishop's record before or after the plague, or both. Time shifting plus subtraction of this background mortality should provide of fairly accurate temporal distribution of mortality for any group of benefited priests, such as the ones in Fig. 13.

Considering that we are interested in mortality rates rather than total numbers of fatalities, we also need to know the total number of benefits. This information is available for all dioceses, thus the conversion is not a problem. Considering that priests were replaced as they passed away, as a first approximation the population size was assumed constant. The delays, however, made the exact number of benefited clergy on duty slightly smaller (by an amount that is not possible to calculate as long as there is no information about the temporal variation of delays in appointments). The approximation of keeping the number of benefits equal to its

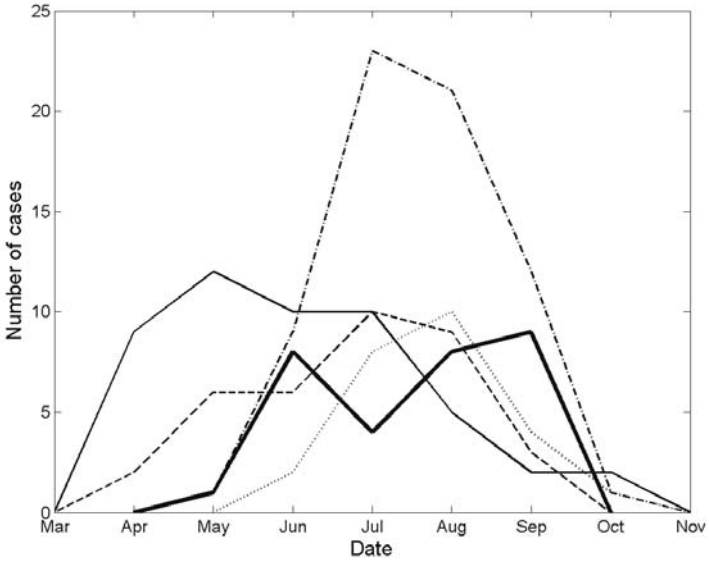


Figure 13. Benefited clergy mortality of Black Death during 1349 at the archdeaconries of the diocese of Coventry and Lichfield: Derby (dashed-dotted line), Stafford (dashed line), Coventry (thin continuous line), Chester (thick continuous line), Salop (dotted line); reconstructed from Wood *et al.* (2003: 443).

initial value has, in theory, the effect of producing conservative mortality values. In practice, the underestimation helps to compensate for the unknown number of institutions due to causes other than plague deaths.

Example D.1. For numerical illustration, Table 4 demonstrates the procedure that was followed in order to calculate the monthly mortality of benefited clergy for the diocese of Bath and Wells.

According to the plan outlined in Fig. 3, there is one more critical step: to establish a relationship between the benefited clergy mortality and that of the population at large, which will allow us to transfer the benefited clergy mortality data into monthly population mortality values. These two sections of the population have clear differences that can tilt the transfer function in either direction. In particular, factors favoring higher benefited clergy mortality than the rest of the population are:

- Assistance to the ill and administration of the last rites should have exposed the benefited clergy to epidemics more than the laity.
- The average age of benefited priests was higher than that of the general population.

Table 4. Calculation of monthly mortality of benefited clergy for the diocese of Bath and Wells based on institution according to de Hahn (2002: 83). Background=3 institutions per month (Gasquet, 1908: 192); number of benefits=475 (Ziegler, 1969: 128).

Date of Appointment (a)	Number of Appointments (b)	Appointments – Background $(c) = (b) - 3$	Monthly mortality $(d) = \frac{100 \times (c)}{475}$	Date of Death $(e) = (a) - 1$
November, 1348	9	6	1.3	October, 1348
December	32	29	6.1	November
January, 1349	47	44	9.2	December
February	43	40	8.4	January, 1349
March	36	33	7.0	February
April	40	37	7.8	March
May	36	33	7.0	April
June	7	4	0.8	May
Total	250	226	47.6	

On the other hand, factors in favor of a lower mortality among benefited clergy than among populations at large would be the following:

- Exposure was much lower than generally presumed because a disproportionate part of the dangerous work was passed to lower ranking priests. Benefited clergy tended to concentrate on bureaucratic work in the comfort and isolation of their offices.
- Benefited clergy were well fed and protected against the consequences of crop failures, thus having stronger immune systems.
- Frequently, servants attended and nursed benefited clergy in case of poor health. When the plague broke among laity, sometimes there was nobody left either able or daring to feed and nurse the sick.

Yet, other factors that are in dispute or that could very well turn out to be irrelevant are the following:

- Benefited priests were all males. Studies on difference on mortality by sex are inconclusive for lack of good data. Hence, as particular as this difference is, it is hard to say if it influenced clergy mortality one way or the other.
- Better housing. It has long been assumed that priests had better living conditions than ordinary people. Some recent archaeological excavations have put this claim in doubt.

The relevance of the above factors also depends on the nature of Black Death (bubonic vs. hemorrhagic). If Black Death was indeed transmitted by fleas, then housing conditions are of paramount importance. In the case it was a viral infection, contacting people is a more important factor than housing or working conditions. In the midst of all these arguments, we have found that Philip Ziegler (1969: 128) has been the only one to quantify the uncertainty: "No final answer to this conundrum [the representativity of ecclesiastical records] will ever be forthcoming. But it would be reasonable to state as a general rule that the proportion of benefited clergy who died in any given diocese could not possibly have been much smaller than the corresponding figure for the laity and is unlikely to have been very much bigger. Arbitrary limits of 10% less [mortality among benefited clergy] and 25% more [mortality among benefited clergy] seem to provide a reasonable bracket within which the correct figure must be encompassed." Taking into account the above considerations, in Section IV.C.b we will develop a rigorous quantitative method for transferring benefited clergy mortality to probability distributions of the mortality of the population at large.

c. Parameter Tabulation

As is described in Section D.a, one is dealing with numerous interdisciplinary information sources. For illustration purposes Appendix A tabulates the various sources used[14]. On the basis of these tables, a number of useful inferences are drawn about essential parameters of the Black Death epidemic such as G_s, Δ_s, $T_{s,o}$, $T_{s,f}$, τ, K_s, $I_{s,\tau}$[15]. As was mentioned in previous sections, these inferences were derived with the help of valid combinations of reasoning modes (e.g., we argued each case by presenting grounds of reasons for accepting some conclusion starting from the information sources tabulated in Appendix A). More to the point, an adequate space-time modelling of the epidemic should take into consideration the following summary data concerning Black Death:

(a) In some epidemic cases the observables are the Δ_s and G_s (a typical example is Wycombe, UK). In several other places only the beginning of the epidemic, $T_{s,o}$, was recorded, whereas the ending, $T_{s,f}$, remained unknown (Biraben, 1975: 103). In addition, there is significant knowledge about the exact or, at least, the order of magnitude of $P_{s,0}$ across Europe on the eve of the Black Death epidemic.

[14] The tables in Appendix A constitute a useful summary of more than 300 excerpts of notes collected during our bibliographical search of the Black Death epidemic, although this tabulation lacks the anecdotal details, etc. of the original notes.

[15] These parameters have already been defined in Section II.C.b.

(b) In a smaller number of cases the observables are $T_{s,o}$, G_s, and $P_{s,0}$ (e.g., Piacenza, Italy). And in an even smaller number of cases the observables are $T_{s,o}$, $T_{s,f}$, G_s, and $P_{s,0}$ (e.g., Canterbury, UK).

(c) The basic incremental time unit in the present Black Death study is one month. Very few places have monthly itemizations of data. In the vast majority of locations, we have at best a single number, G_s, to summarize the reduction in the population from beginning to the end of the epidemic (say, 50%).

A few examples may throw some light on these issues, which are essential from a modelling standpoint.

Example D.2. Values for G_s, Δ_s, τ, K_s, $I_{s,\tau}$, and f are displayed in the summary Table 5. As soon as the G_s and Δ_s values are known at a geographical location s, the corresponding values of τ, K_s, $I_{s,\tau}$, and f can be found from Table 5. Note that Appendix B includes a detailed list of the values of the above epidemic parameters. These values are calculated at all geographical localities throughout Europe in which the generation of monthly mortalities was required as part of the SEP modelling and space-time mapping process. In this sense, Table 6 is merely a summary of Appendix B containing only a small number of examples of places associated with a given duration and overall mortality[16]. Some geographical localities required spatial interpolation of the global mortality values. In Section IV.C.b we will discuss specific numerical examples.

d. Mortality in Germany

Germany was at the time of the Black Death epidemic part of the Holy Roman Empire (see map in Fig. 1), consisting of a loose conglomerate of cities and feudal territories. The instability of institutions and mainly the weak authority of the emperor may have something to do with the scarce number of Black Death documents that are available today.

The lack of German data is particularly true in the case of population mortality. Nevertheless, we realized that we could take advantage of another information source; Fig. 14 reproduces a map of degree of land desertion during the late Middle Ages constructed by Abel (1965). Abandonment of villages and farming land took place in Germany during a long period of time for a variety of reasons, of which the plague of 1349-51 was an important one. Admittedly, the plague's contribution is impossible to quantify precisely. Other causes were wars, fires, earthquakes, floods, geotechnical reasons, fertility of the land, as well as other visitations of the plague. As far as the last factor is concerned, however, it is well documented that no other epidemic was as devastating as the Black Death epi-

[16] In Chapter IV we discuss the steps leading to the preparation of Tables 5 and 6.

Table 5. Values of the parameters K_s, $I_{s,\bar{x}}$, and f (in all cases, $P_{s,0} = 100$ and $\tau = 20$).

Mortality, %	Duration of epidemic, Δ_s, in months							
	3	4	5	6	7	8	9	10
5		4, 5, 0.051						
10		4, 5, 0.1	4, 5, 0.102					
15		4, 4, 0.153	3, 7, 0.158	2, 6, 0.182				
20		4, 5, 0.203			2.2, 3, 0.233			
25	6, 10, 0.251	4, 5, 0.254	3, 7, 0.263	2.5, 6.5, 0.275	2.2, 3, 0.291	1.7, 7.5, 0.336		
30	6, 10, 0.301	4, 5, 0.305	3, 7, 0.316					1.4, 5.5, 0.505
35	6, 10, 0.351	4, 5, 0.356	3, 5, 0.369	2.7, 6.5, 0.377	2.3, 2.4, 0.4	2, 3, 0.421	1.5, 5, 0.506	
40	6, 10, 0.401	4, 6, 0.407	3, 6.5, 0.421	2.5, 6.5, 0.44	2.2, 3, 0.466	2, 3, 0.49	1.6, 5, 0.578	1.4, 5, 0.673
45	6, 10, 0.451	4, 6, 0.457	3.3, 5, 0.467	2.3, 7, 0.51	2.3, 3, 0.524	2, 3, 0.551	1.6, 5, 0.65	1.45, 5, 0.728
50	6, 10, 0.501	4, 5, 0.508	3, 6, 0.527	2.3, 7, 0.566	2.3, 3, 0.571	2, 3, 0.601	1.8, 3, 0.659	
55			3, 6, 0.579		2.3, 3, 0.628			
60			3, 6, 0.632	2.5, 6, 0.661	2.3, 3, 0.685			

demic of 1349-51. In Table 7 we give a list of all the geographical locations throughout Germany where we managed to find mortality data, their corresponding desertion values, and the ratio between the two. An analysis of Table 7 produced a triangular probability distribution for the scaling factor in Germany (the scaling factor is defined as the ratio mortality/desertion), which is plotted in Fig. 15 (see, also, the mathematical analysis of Section IV.C.b). More specifically, at geographical places without a mortality value, rather than estimating a value from those highly scattered places with mortality data, we decided to use the continuous coverage of the land desertion map to produce a desertion value. This value was then scaled by a factor generated from the triangular distribution with a minimum of 0.3, a mode of 1.2, and a maximum of 3.3[17].

[17] See Section IV.C.b for a detailed explanation of the mathematical techniques implemented for this purpose.

Table 6. Examples of places with different duration of Black Death and overall mortality.

Mortality, %	Duration of epidemic, months							
	3	4	5	6	7	8	9	10
5		Osnabrück						
10		Minden	Nuremberg					
15		Maubege	Kontanz	Lille				
20		Passau			Mainz			
25	Hamar	Hanover	Tournai	Angers	Reims	Bruges		
30	Camprodón	Morella	Calais					Ghent
35	Quimper	Borja	Badajóz	León	Evora	Forez	Pisa	
40	Villalobos	Santesteban	Basel	Béziers	Cádiz	Anjou	Toledo	Seville
45	Pto. Llano	Alès	Braga	Málaga	Rouen	Naples	Lund	Granada
50	Ste. Marie	Nîmes	Arles	Cagliari	Sardinia	Florence	Cologne	
55			Albi		Avignon			
60			Trapani	Estella	Marseille			

e. Aggregation and Scale Effects

In dealing with the Coventry and Lichfield diocese (UK), Wood *et al*. (2003) observed that by downscaling the diocese to its archdeaconries resulted in a reduction of the infection period for the different archdeaconries. The epidemic stayed in the diocese for about 8 months, but at the individual archdeaconries the duration time was 5-7 months. This finding can be explained in terms of the time that it took for Black Death to move from one place to another. The actual ground speed for Black Death ranged from less than 1 km/day to 5 km/day (Biraben, 1975: 90; Andenmatten and Morerod, 1987: 31). For a given ground speed, the disease duration in a large region depends on the urban mixture, topography, size, shape, and orientation of the region relative to the direction of the plague propagation. The effect of a decreasing geographical area on the disease duration is always to make it shorter. On the other hand, the effect that a decreasing study area has on mortality is more complex. This is demonstrated with the help of the following numerical example.

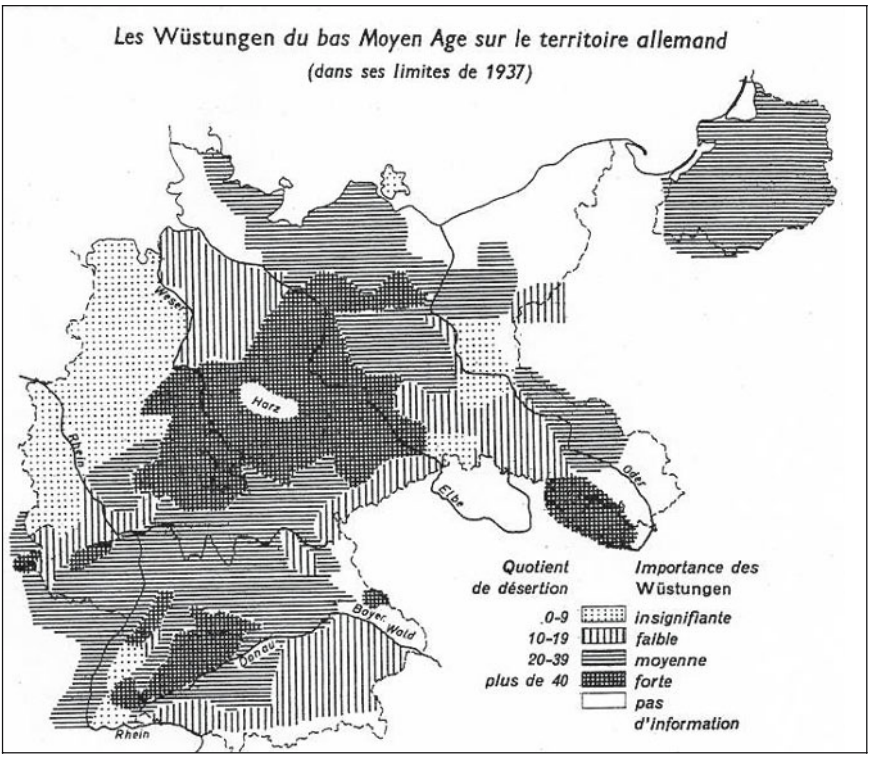


Figure 14. Land desertion map in Germany and Poland during the late Middle Ages (Abel 1965: 520). Title (translated from German): The Wustungen during the late Middle Age across the German territory (shown within the 1937 boundaries). Legend: Fraction of land desertion-Importance of the Wustungen: 0-19, not significant; 10-19, weak; 20-39, medium; greater than 40, high; blank, no information.

Table 7. German cities with mortality values and the corresponding land desertion values during the 1349 Black Death epidemic.

City	Mortality, %	Desertion, %	Mortality / Desertion
Bremen	50	15	3.3
Erfurt	40	40	1
Frankfurt	20	20	1
Güstrow	28	30	1
Hamburg	55	20	2.75
Lübeck	40	30	1.33
Lüneburg	36	15	2.4
Magdeburg	53	45	1.2
Nüremberg	10	30	0.33
Parchim	40	30	1.33

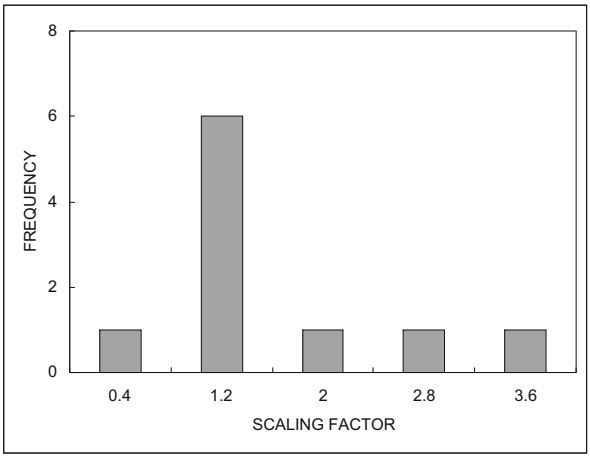


Figure 15. The histogram of the scaling factor defined as the ratio mortality/desertion (Germany).

Example D.3. Fig. 16 describes the situation in the county of Durham, UK. While the mortality for the study area (consisting of 28 townships) was 50%, the mortality for individual townships varied from 21% to 78% (Lomas, 1989). The increase in the range of values is nothing new in the stochastic analysis of spatio-temporal data (Christakos *et al.*, 2002; Choi *et al.*, 2003). It is often called the "change-of-scale effect"[18] and has to do with the different degrees of disease variability associated with the same type of observation when the area within which the observation takes places changes (from county to township in the case of this example).

Generally, the process of inferring the epidemic variation at small scales from that at a large scale is called *downscaling* and does not have a unique solution. At most, one can prepare realizations of an epidemic random field having the same moments as the observed data. A general rule is that the smaller the scale, the hi-

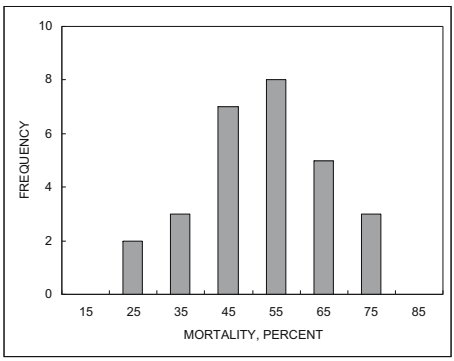


Figure 16. Black Death mortality rate for 28 parishes in eastern and central Durham county, UK (Lomas, 1989).

[18] See also Section II.A.e on *Conceptual Hierarchies*.

gher the variability; thus the lower the continuity. Shrewsbury (1970) provides numerous examples of extreme mortality variations at the parish level throughout the English dioceses.

To increase the data resolution, we followed the example of Wood *et al.* (2003) in downscaling dioceses to archdeaconries whenever possible. We were particularly pleased with our use of the information collected by Thompson (1911 and 1914) to downscale the two largest English dioceses of York and Lincoln, a procedure that we have not seen performed before. We were unable to go beyond the archdeaconry level for several reasons. One is that the existing publications rarely presented archdeaconry data downscaled to the parish level. Should that information were available, the samplings would be too small to be reliable. Thus, the potential of breaking ecclesiastical data for Black Death studies stops at the level of the archdeaconry. Archdeaconry data were used only for England, where they are the best source displaying a continuous coverage, despite the problems mentioned in Section D.b. Discarding ecclesiastical records for reasons of scale inconsistency would have resulted in the loss of most of the direct monthly mortality information provided by these records.

Given the need to use every available piece of reliable information available, we employed a combination of observation *scales*. In most cases the scale is the city, whereas in some others it is a province, an archdeaconry, or a diocese. Certain archdeaconries in UK have data both for the archdeaconry and for some manors. In those cases, we usually considered the more representative archdeaconry data (Appendix A); the manor information was employed only to verify its consistency with the archdeaconry data.

f. Correlation Between City Size and Epidemic Duration

It was clear from the outset of data collection that there are more documents dating the beginning of the plague than its ending (Biraben, 1975: 103). In Italy, e.g., we found that at only 1 in 3 cities an ending date for the plague is available. Our interest to assess the epidemic duration arose from the need to estimate these missing ending dates.

The local duration of Black Death is one of the many aspects of the epidemic that remains poorly known, more than six and a half centuries later. At the simplest level, some authors consider a fixed time for the duration of the epidemic, such as a little more than 2 months (Guilleré, 1984: 111), or 2-3 months (Chédeville, 1983: 131), or 3 months (Ubieto, 1975:53), or about 8 months (Scott and Duncan, 2004: 28). Tuchman (1978: 93) claims that, except for the larger cities, the pestilence generally lasted 4-6 months. Familiarization with the databases and the application of critical reasoning brought us to the conclusion that there was a connection, indeed, between the duration of the epidemic and the population size of the place under consideration. The number of cities in which information for both the population size and the duration of the epidemic was available ended up being approximately 1 in 10. These cities are displayed in Table 8. Interestingly, as we shall see in Section IV.B.a later in the book, a careful statistical analysis of

Table 8. Cities with data for both pre-plague population and duration of Black Death.

Austria	Vienna		
Belgium	Bruges		
France	Avignon	Caen	Givry
	Lille	Lyon	Marseille
	Millau	Paris	Perpignan
	Reims	Rouen	Ste Marie Laumont
	Strasbourg	Toulouse	
Germany	Erfurt	Frankfurt-am-Main	Lübeck
	Magdeburg		
Ireland	Dublin		
Italy	Arezzo	Bologna	Florence
	Naples	Orvieto	Padua
	Parma	Perugia	Pisa
	Reggio d'Emilia	Siena	Venice
Spain	Almería	Barcelona	Girona
	Murcia	Seu d'Urgell	Tarragona
	Teruel	Valencia	Vic
	Villalobos	Zaragoza	
United Kingdom	Bristol	Cambridge	Canterbury
	Cuxham	Fingreth	London
	Ruthin	Walsham	

the quantitative information associated with Table 8 reveals that the population size and the duration of the epidemic at a populated place are related by means of a scaling law.

g. Demographic Uncertainty

For reasons to be explained in detail in Chapter IV, the population size became an important part of SEP modelling. As with almost any medieval aspect that one wants to quantify, demography is full of uncertainties resulting from the fact that the counting of people in the modern sense of a census did not start for another century after the Black Death epidemic of 1347-51. Consequently, similar to other medieval variables of interest, what is available most of the time are proxies that one can use with caution to infer values about what we really want to know, such as the population of a port. Most common sources of information about medieval population during the Black Death era are:

- Direct references to the number of residents.
- Tax records. Prior to the preparation of censuses, the vast majority of counting of residents was done for the very profitable purpose of collecting taxes. Scholars have developed over time methods to try to derive counts of total numbers of residents starting from these tax sources that, in general, are the most comprehensive available.

- An assortment of sources that, even though originally not going into records for the purpose of counting people, have been scaled to provide useable assessments of contemporary populations.

Knowing that actual counts of all residents never took place in the 14th century AD, even direct values have to be used with caution because what we have today are at best educated guesses (although, often they are not explicitly mentioned as such). E.g., when a chronicler said that the population of Dublin on the eve of the Black Death was 14,000 residents (Kelly 2001: 95), the actual figure could have been 10,533 or 15,859. We will never know, of course, but at least we should be aware of the uncertainty. The mere mention of a round number should be taken as a warning that there was no actual population counting behind the figure. All numbers must be scrutinized. If possible, one should try to clarify some technicalities. Points of eternal contention among medieval demographics are:

- the counting or omission of children and beggars;
- for large cities, the counting inside the wall only, or including families in the contiguous vicinity, too; and
- strict urban counting, or including those in the surrounding countryside as well.

There are numerous indirect sources that can be employed to derive population estimates starting from numbers that sometimes have nothing to do with people. These estimates can be recent or contemporary. Merchant and chronicler Giovanni Villani, e.g., is credited with having derived estimates of the pre-plague Florence population based on his familiarity with business transactions (Day, 2002). Scholars have made several remarks about this otherwise ingenious method. Villani reported a daily wheat consumption of 140 *modia* in Florence around 1338, which is an amount that has been challenged to start with. The second reservation, common to all indirect methods, has to do with the accuracy of the scaling factor that he used to translate a volume of wheat, as is 140 *modia*, to mouths to feed. A common practice to rate cities was their capacity for contributing men to bear arms, a capacity that can be used to estimate populations when only the conscription is known. Creighton (1891: 126), e.g., used the conscription for Bodmin, England, to come up with an estimate of 3,000-4,000 residents based on the conscription and population for neighboring Gloucester, Hereford, and Shrewsbury. Other indirect sources include the number of baptisms, also used to estimate the Florence population (Day, 2002), and the number of weddings at Givry (Biraben, 1975: 160).

Tax records are particularly abundant for medieval England and in moderate numbers for Spain and France. England has several of these records both from before and after the Black Death period, but the most reliable and complete ones are the Domesday Book of 1086 and the Tax Poll of 1377, which were levied differently. The purpose of the Tax Poll of 1377 was to raise funds to continue the Hundred Years War against France. Parliament wanted to diffuse the load from the nobility, so lords went for a widespread tax, imposing a mandatory 4 pence

contribution from every man or women older than 13 years of age. Experts have been trying to convert the tax records into population counts for a long time. The first source of uncertainty is the inaccuracy of the records themselves, comprising a mixture of lost records, illegal appropriation by collectors, and evasion. All these factors are difficult to assess. However, if ignored, they lead to calculations biased toward low population estimates. Guesses for evasion range between 5-25% (Titow, 1969:68). The other factors are considered of secondary importance and normally are not even entered into the calculations.

Having corrected the tax records, the next task is to add the minors. Russell (1948: 143) is of the opinion that minors below 14 years of age were one-third of the total population; others see this estimate only as a minimum boundary, with the real proportion going as high as 45% (Postan, 1972: 30). For all these reasons, one reaches the conclusion that the total English population in 1377 was 1.58 to 1.81 times the number of taxpayers. The hardest part of the calculations is still ahead: the conversion from the 1377 Tax Poll to pre-plague population. Such a calculation is presumed to be able to estimate the population growth during normal years, and the effects of four rounds of plague: the major outbreaks of 1347-51 and 1361-62, plus the less catastrophic epidemics of 1369 and 1374. Here we face the common situation of medieval studies being capable, in theory, to account for a factor but having no data to actually perform the calculations. The only way to proceed ahead is in terms of educated guesswork, which in this case calls for an estimate of the net population shrinkage during the 30 years before the 1377 Tax Poll. The reductions most commonly mentioned are between 40% and 60%, implying a grand scaling factor of 2.8-4.53 to convert 1377 Tax Poll residents to 1347 residents in the same area.

Though important to Black Death studies, the 1377 Tax Poll is a very particular form of taxation. More commonly levies were based on counts of households, which typically included husband and wife, their children, some elderly parent or relative, and servants in the case of the most affluent. Calculations here are slightly simpler, involving a conversion factor from families to family members, and time extrapolation if the records significantly differ in date from the beginning of the Black Death. Post-plague extrapolation is always more difficult, because it involves considering mortality from the Black Death plus other causes if the gap is larger than a decade (in a similar manner as that described for the 1377 English Tax Poll). On the contrary, pre-plague corrections of population estimates after the year 1300 are minor or unnecessary, since Europe suffered from global wars, floods, and famines that tended to cancel out the normal rate of population growth (Tuchman 1978). Concerning the scaling factor (from number of households to number of people), demographers like to use slightly different numbers depending on spatiotemporal considerations and urban or rural conditions. Factors commonly vary between 3.5 and 5, and, contrary to other situations, they are based on data such as the counting in Fig. 17.

Some scholars can become frustrated with all these uncertainties associated with efforts to quantify medieval affairs, causing them to denounce the calculations as worthless (Postan, 1972: 30). We are definitely in the opposite camp, assured that the situation is less chaotic than it might look at first glance, and

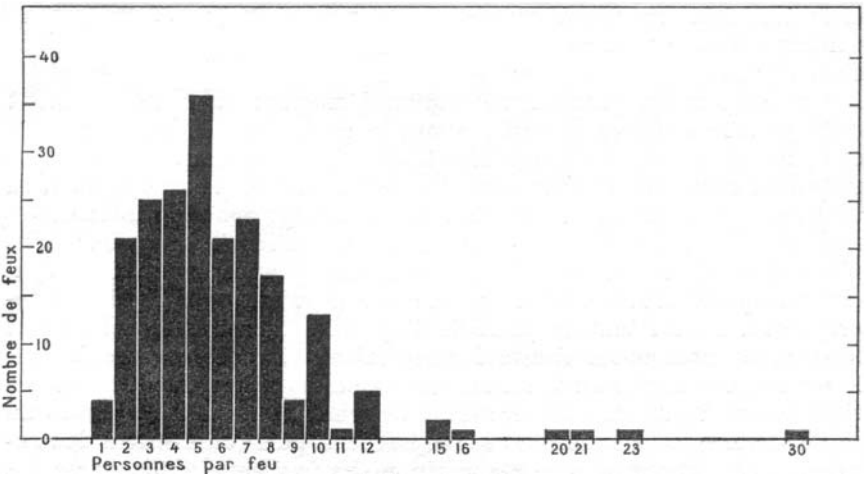


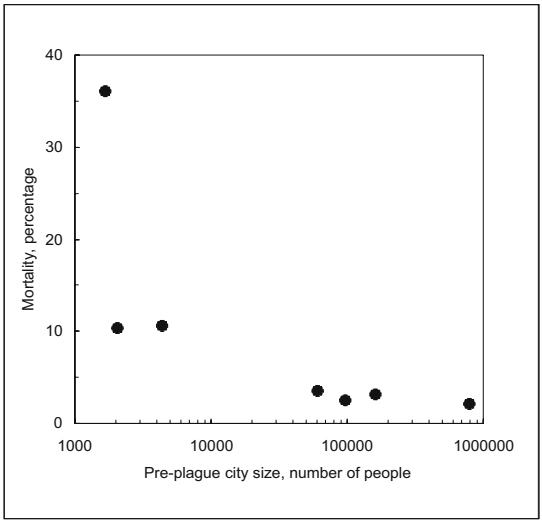
Figure 17. Number of resident per household for the Jewish community of Aix-en-Provence, France, in 1341 (Baratier, 1961: 60).

certainly within the realm of stochastic modelling to produce useful results. After all, for modelling purposes what we mostly need is rather the order of magnitude of the populations of interest, that is, whether it was a hamlet with a few houses, a modest village with a few hundred people, a town with a few thousand residents, or a major cathedral city. As we will see in Chapter V, e.g., considering that the population of a city was either 2,000 or 4,000 residents--a 100% discrepancy--will only have an 8% impact in the duration of the epidemic, which is the epidemic variable of interest, in this case.

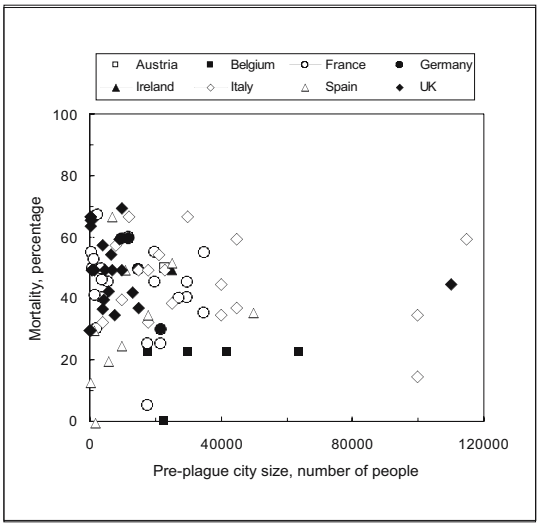
h. Other Possible Correlations, Links, and Dependencies

Success in relating city size to Black Death duration has opened the possibility to further advance medieval studies through multivariate regression modelling. In the past, certain remarks had been made linking mortality to several factors. Regrettably, we were not able to quantitatively study most of these remarks due to lack of data, contradictory remarks or, most frequently, both. In one case, however, some very interesting quantitative inferences were made as follows.

The plot of Fig. 18a reveals that in the case of the modern bubonic plague, the smaller the city, the more severe the mortality. Fig. 18b, on the other hand, displays a city size vs. mortality plot for 86 of the 14th century European cities included in Appendix A in which reliable information was available for both variables. The second plot is nothing like the first one: it shows a distinct absence of correlation between city size and mortality. In fact, the influence of city size has been cast in a different way by trying to investigate differences in Black Death mortality between urban centers and the countryside. We have not yet found any data for a documented opinion. There are no data about Black Death mortality



(a)



(b)

Figure 18. Disease and city size (a) Fluctuation of modern bubonic plague mortality in India vs. city size (Hankin, 1905: 56). (b) Fluctuation of mortality during the 1347-51 Black Death epidemic at 86 European cities.

among peasants living outside organized communities in rural districts. If one is willing to assume that small villages in Fig. 18b had similar death rates as the true countryside (in the sense of people living in non-organized communities), our conclusion would be that Black Death swept indiscriminately into both rural areas and urban centers. This result agrees with the opinion of some scholars (e.g., Creighton, 1891: 135; Baratier, 1961: 111-112; Wills, 1997: 64; Naphy and Spicer, 2000: 41) and contradicts the assertion that Black Death was more of an urban epidemic (e.g., Titow, 1969: 69; Shrewsbury, 1970: 109; Weyl, 1975: 247; Martin *et al.*, 1991: 595). Yet, there is a third group of researchers who assume a higher mortality in the countryside than in the cities (e.g., Davies, 1924: 199).

This may be a rather distorted vision influenced either by the kind of tendency displayed in Fig. 18a for modern bubonic plague or by an arbitrary comparison between places as far apart as Lovain and Sardinia (Kelly, 2001: 17).

Scholars have also tried to find a link between the severity of the plague and geography. Phillips (1998: 52), among others, argued that Black Death hit harder the ports and large cities along trade routes. Here, again, the generalization is logically valid at a regional level at best, in our view. Examples and counterexamples abound, making it impossible to reach any definite conclusion. In Italy, e.g., the port of Genoa had a mortality of about 35%, which is higher than that of inland Verona (45%) but lower than that of the even further east port of Venice (60%). While ports and trade centers were in many cases the focal point of the beginning of the epidemic in a region, once the plague had propagated, there is no evidence that receiving the epidemic first made it more virulent. Other scholars have promoted the view that mountainous areas had lower mortality than the valleys and plains (Cabrillana, 1968: 247; Latreille, 1975: 112-113; Kelly, 2001: 37), yet Gelting (1991: 8) has prepared a study showing that people in the mountains of Savoy were hit as hard as or harder than those in other locations in France. Santamaria (1969: 123), studying the Black Death in Majorca, concluded that mortality was proportionally higher in the mountainous area of the island than along the coast. In terms of the topography, we were limited to the information provided by Biraben (1987: 179), who maintained that the high mountain regions of the Pyrenees and the Alps were never affected by the plague, most likely for the obvious reason that nobody lives there to this day. The discussion above summarizes the topographical feedback used in SEP modelling.

Another topic of inconclusive debates has been the relationship between mortality and social status. Most scholars seem to agree that the poor suffered more than the rich, but the contention seems to be an extrapolation on the basis of the general observation that, throughout history, poor housing, sanitary conditions, and nutrition resulted in higher exposure to diseases. This remark looks more like a plausible statement rather than an independent scientific conclusion derived from the analysis of real Black Death data. In UK, e.g., Ecclestone (1999: 27) was surprised to observe that the mortality among poor peasants at Glastonbury (57%), was approximately the same as that reported for the wealthy tenants at neighboring Halesowen (46%). The contemporary chronicler Gilles Li Muisis, however, claimed that at Tournai the Black Death mortality was particularly high among the affluent and the powerful (Orent 2004: 129), and so does Bean (1982: 29) for English landowners.

Medieval information systematically ignores children and rarely includes women. This biased nature of the data has been a serious obstacle toward investigating any differences in death rates in terms of gender and age. The main findings are valid for England. Charles Creighton (1891) made the counterintuitive remark that "it was mostly the young and the strong who were cut off, the aged and weakly being commonly spared," but he does not back up his statement with data. On the other hand, Ohlin (1966: 79) and Cohn (2002b: 48) did not observe any age discrimination, nor did Razi (1980: 103-104) saw gender playing any role.

Cohn (2002b: 126) claims that the unusual virulence of the Black Death epidemic that started in Europe during 1347 left no room for special conditions. The effect was massive and indiscriminate, making no exception to factors such as personal hygiene, health, age, sex, or social class.

Stochastic modelling can be very helpful in the investigation of dependences between Black Death mortality and the various contemporary evidence sources. The existence of such dependences can be critical in generating informative mortality predictions, assessing the epidemic spread across space-time, etc. A possible situation is described in the following example.

Example D.4. Assume that the available evidence consists of a database $\mathcal{S}$ (land desertion data, exposure measurements, etc.) at a set of space-time points $\boldsymbol{p}_i$ ($i = 1,2,...,N$). A plausible measure of the predictability of mortality $M_{\boldsymbol{p}}$ at a point $\boldsymbol{p}$ ($\neq \boldsymbol{p}_i$) from the database $\mathcal{S}$ may be the difference $P[M_{\boldsymbol{p}}|\mathcal{S}] - P[M_{\boldsymbol{p}}]$. Multiplying the difference by $P[\mathcal{S}]$ yields $P[M_{\boldsymbol{p}},\mathcal{S}] - P[M_{\boldsymbol{p}}]P[\mathcal{S}]$. In this sense, the predictability of $M_{\boldsymbol{p}}$ from $\mathcal{S}$ is a measure of the stochastic dependence of $M_{\boldsymbol{p}}$ and $\mathcal{S}$. E.g., if the difference is zero--meaning that $M_{\boldsymbol{p}}$ and $\mathcal{S}$ are stochastically independent-- $M_{\boldsymbol{p}}$ is unpredictable on the basis of the database $\mathcal{S}$. In this case, the database is useless for mortality prediction purposes. If, on the other hand, the difference is non-zero, $M_{\boldsymbol{p}}$ and $\mathcal{S}$ are stochastically dependent and the former is predictable on the basis of the latter. This stochastic dependence may be linked to some natural dependence that is an inherent feature of mortality variation.

E. Si non è Vero, è Molto Ben Trovato

The mid-1300s AD were difficult times in a variety of ways (Gottfried, 1983; Kelly, 2003). Europe was inhabited by far fewer people than presently, who very rarely moved away from their hometowns, and life moved at a slower pace. Superstition played an important role in local communities (people were taught that diseases were punishment from God, etc.), poor hygiene conditions were common, and there were very few medical advances made during this period in history. The Hundred Years War began in 1337 and lasted about 120 years, despite the name. There was a great famine in Europe from 1315 to 1317. The economy spiraled downward and banks collapsed in the first few decades of the 1300s. The Catholic Church was already a powerful institution and served as the unifying force between many small kingdoms--as a center of learning, but also as a force of oppression. The Church gave standards on the levels of sexual sin, as well. Sex, it was taught, was a necessary (for reproductive reasons) evil introduced to humanity by the Devil[19]. It was in such an environment that Black Death arrived in Europe.

[19] Diverse views have been expressed about this historical epoch, including characterizations such as “an age of superstition”, “times of barbarism”, and an “era of unreason”.

In the previous sections of this chapter, we described the numerous sources of information we had to evaluate in order to generate the required mortality KB. The SEP aims at giving a logical and systematic account of historical Black Death sources[20], and at enabling us to predict from past experience to new circumstances. In doing so, we were reminded that scientific inquiry demands an element of creativity and an element of faith. Creativity comes in working up the appropriate SEP concepts and models (Chapters I and II) to associate with the multi-sourced evidence of the present chapter. Faith comes in thinking that these concepts and models, when shown to be useful or successful in some way, bear a relation to what one may call epidemic reality, as described in terms of the multi-sourced evidence. With regards to SEP, therefore, we are hopeful that "si non è vero, è molto ben trovato"[21].

Medieval studies are not alone in the pursuit of the distant and uncertain events that took place several centuries ago. By far, they are not even the most remote and distant events. The realm of archaeology is still a human activity, but dealing with events that happened in the order of thousands of years ago. Geologists and astronomers have developed their disciples around the pursuit of knowledge toward the dawn of time, billions of years ago. The odds against obtaining any information that distant are phenomenal, but at the same time, the fascination of learning anything about the universe in general and our planet in particular are also of such paramount significance that many still devote their lives to advance these sciences of the impossible. The likelihood of obtaining any information about the distant past is miniscule, and when found, the significance and inaccuracy of any speck of evidence may disappoint most scholars used to dealing with the precision, accessibility, and repetitiveness of, say, mass spectrometry. The scarcity and uncertainty of geological data make progress in the discipline slow and subject to change. On the other hand, despite the difficulties, it is undeniable that geology has made progress in the understanding of what has been happening from millions of years ago to now. Patient observation, careful verification of facts for consistency, and modelling based on critical thinking have been some of the crucial tools of success.

The SEP models constitute the formal basis for extracting and evaluating the main characteristics of epidemic distribution and generating informative predictions across space and time. These models need not be mathematical, but mathematics is one of the most powerful and general methods of reasoning that we possess. Therefore, in this chapter we attempted to secure data--wherever possible--in a form that can be handled mathematically. The last task is furthered in Chapters IV and V.

The Austrian writer Karl Kraus went as far as to maintain that "Mankind became hysterical in the Middle Ages because it poorly repressed the sexual impressions of its Greek boyhood".

[20] E.g., many of the tables presented in this chapter demonstrated that useful data can be produced by thinking things through--i.e. by using intellectual frameworks (reasoning modes, modelling, etc.) to organize and process contemporary evidence.

[21] "Even if it is not reality, it is a good invention" (Giordano Bruno).

Chapter IV - Mathematical Formulation of the Knowledge Bases

" The real truths are those that can be invented."
K. Kraus

A. Introduction

What we can measure, we can know. This precept has been recast as a formal mathematical statement. The weight of thought is in the words; the mathematics and its symbols enable one to probe the consequences of the thought. Thus, although this chapter deals mainly with the *formal* component of epidemic modelling (i.e., the mathematical formulation of the Black Death multi-sourced databases), the blending of form with content, theoretical with interpretive analysis, and conceptual with applied work will continue to be prominent and unavoidable. Robert Frost provides a picturesque description of this kind of blending in his poem *To a Thinker* (Lathem, 1979: 325-326, lines 10-14):

" From form to content and back to form
From norm to crazy and back to norm
From bound to free and back to bound
From sound to sense and back to sound
So back and forth. It almost scares
A man the way things come in pairs. "

In Chapter II we proposed that the modelling of the Black Death epidemic starts by introducing a first methodological assumption: the relevant disease parameters will be mathematically represented as S/TRF. Indeed, the information sources in existence today about the Black Death epidemic of 1347-51 AD are notoriously scarce and uncertain (Twigg, 1984; Scott and Duncan, 2001; Cohn, 2002a and b), which makes a *stochastics* approach to the problem most appropriate. As we saw in Chapter II, to understand stochastics we need to add to our language as well as to our imagination. The *spatiotemporal random field* (S/TRF) representing disease variables is a field of possibility, not a real field. It describes the probable structure of a disease variable in space-time, not its actual structure. It implicitly requires the consideration of that which probably does not exist in order to explain that which actually exists (but is unknown). The mind of any sen-

tient epidemic modeller should be capable of reaching into alternate realizations of reality and deriving conclusions about that reality.

Although the interdisciplinary structure of the various knowledge sources relevant to Black Death has not gone unnoticed, it has not been taken into consideration in previous studies of the epidemic[1]. Hence, a subsequent methodological assumption is the epistemic-based distinction between two major categories of interdisciplinary knowledge concerning the Black Death situation: the general knowledge base ($\mathcal{G}$-KB) that is discussed in Section B below, and the specificatory knowledge base ($\mathcal{S}$-KB) that is the topic of the following Section C[2]. The union of these two major KB is denoted by $\mathcal{K}$, which is the total KB available regarding the Black Death epidemic. The $\mathcal{G}$-KB may include human constructs like scientific theories, empirical laws, and relationships developed in various disciplines that are relevant to the Black Death epidemic. The $\mathcal{S}$-KB, on the other hand, consists of case-specific details (linked to the specified geographical area, time period, and human culture). This includes contemporary (but often highly uncertain) written records and a plethora of secondary information sources about Black Death (see, also, our discussion in Chapter III).

To put things in perspective for our readers, it may be helpful to provide a brief outline of the material considered in this chapter (Fig. 1). The mortality KB are viewed from several different angles: mathematically, logically, statistically, comparatively, etc. The $\mathcal{G}$-formulated knowledge includes space-time covariance functions, epidemic models, and city size-epidemic duration laws; the $\mathcal{S}$ base involves probability functions of various forms and shapes (Gaussian and non-

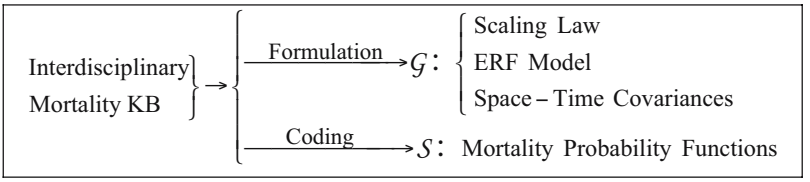


Figure 1. An outline of the process leading to the mathematical formulation of the interdisciplinary Black Death knowledge bases (KB). This figure is a continuation of Fig. III.3.

[1] In his treatise on Black Death, Bleukx (1995: 72) commented: "With this introduction I want to point out many problems of interpretation that arise when this issue is approached in a critical way. I have only discussed a few of them, some of which have hardly ever been taken into consideration, and certainly not on an interdisciplinary level."

[2] Under certain circumstances, one may draw an instructive parallel between the general vs. specificatory KB and the knowing by the mind (Latin *scire*) vs. knowing by the senses (Latin *noscere*), as discussed in Plotkin (1997). Knowing by the senses is knowledge of events that are temporally coincident with the act of knowing. Knowing by the mind, whether it is understood by invoking memory or thought or both (in this context, it includes logic and mathematics) refers to knowledge that is removed in time from the actual or possible experience of what is known.

Gaussian, etc.). As we saw in Section II.E.b, the $\mathcal{G}$-KB will be used to generate the pdf model $f_{\mathcal{G}}$, whereas the $\mathcal{S}$-coded data will be used to update $f_{\mathcal{G}}$, thus leading to the final model of the Black Death mortality, $f_{\mathcal{K}}$, across space and time ($\mathcal{K} = \mathcal{G} \cup \mathcal{S}$). Chapter V demonstrates how the various KB in Fig. 1 can be exploited by means of BME to yield a wealth of information in the form of $f_{\mathcal{K}}$.

B. Mathematical Formulation of the General Knowledge Base

In the present Black Death study, the $\mathcal{G}$-KB refers to knowledge that is relevant to the epidemic system under consideration, but its domain of application may far transcend the specified situation. Which kind of general knowledge elements will be synthesized to solve the Black Death epidemic problem should be contingent on the nature of the solution as well as on the status of the various knowledge disciplines involved and their relations.

The $\mathcal{G}$-KB of this section includes conceptual systems on the basis of which the Black Death datasets may be acquired, tabulated, and analyzed. As Carlo Cipolla highlighted in his treatise on plague, "Man cannot grasp new facts without reference to some existing concepts, and these concepts inevitably modify the kinds of facts he sees and how he sees them… The most induction-addicted investigator never starts from a *tabula rasa*" (Cipolla, 1981: 9). The covariance concept, e.g., expresses space-time mortality dependence. Since this dependence is implicit in any mortality dataset, it makes sense to look at the dataset with reference to the covariance concept, which provides the means to formalize mortality dependence in a convenient quantitative form. Theoretical covariance models are then constructed on the basis of the general knowledge about the epidemic (e.g., a class of epidemics is generally characterized by advancing wave-form covariance models; Section B.c below). With this in mind, we can now proceed with our discussion of certain of the main components of the Black Death $\mathcal{G}$-KB.

a. A General Scaling Law Between City Size and Epidemic Duration

A valuable piece of information in the context of the $\mathcal{G}$-KB is available in the form of a general *scaling law* between urban population at the beginning of the Black Death epidemic and its duration (Figs. 2), as follows:

$$\Delta_{\boldsymbol{s}} = 3.031 + 0.132 P_{\boldsymbol{s},0} \tag{1}$$

where $\Delta_{\boldsymbol{s}}$ denotes the duration of the epidemic (in months) and $P_{\boldsymbol{s},0}$ denotes urban population (in thousands of residents) immediately before the start of Black Death at each geographical location $\boldsymbol{s}$. The correlation coefficient is 0.97. In Fig. 2 the

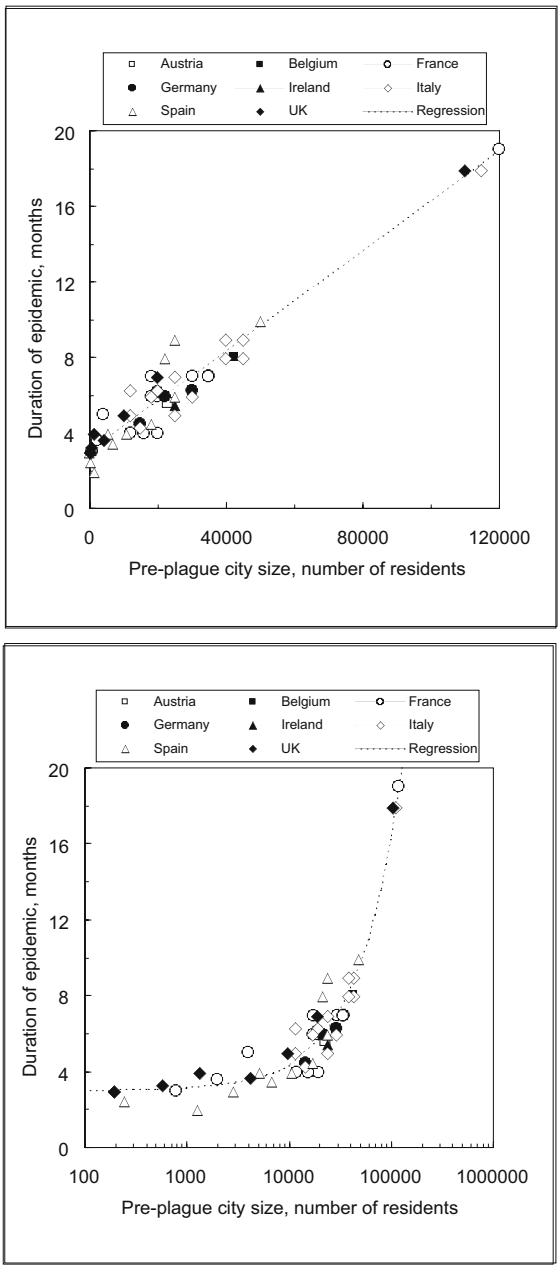


Figure 2. A scaling law of Black Death duration vs. pre-plague city size, (a) linear scale, (b) semilogarithmic scale.

scaling law is plotted in both a linear and a logarithmic population scale for better appreciation of the excellent fit for the entire range city size values. The equation is assumed valid for $P_{s,0} \geq 0.2$, the minimum size for which we have data. Ex-

trapolation of the line below the population point $P_{s,0} = 0.2$ should be avoided for epidemic reasons (e.g., on the basis of the minimum population required for an epidemic to occur), as well as for reasons having to do with the structure of the scaling equations: although very helpful in interpolation, one should be careful when using them for extrapolating purposes, for the constraints are unknown when one goes beyond the range of available data (Schmidt-Nielsen, 1999: 29).

The subtraction or addition of points—e.g. ignoring the three cities with the largest population—leaves Eq. (1) essentially unchanged, a sign of stability (Olea and Christakos, 2005). The regression is also fairly stable to variations in population size, which is good when there is some uncertainty in the population and the dependable variable of interest is epidemic duration. E.g., discrepancy in the population of a city between 2,000 to 4,000 residents--a hypothetical 100% fluctuation--will only have an 8% impact in the duration of the epidemic. As one might expect, the duration Δ_s increases with increasing city size. The fact that it increases linearly is an interesting and, perhaps, less-anticipated finding. A significant increase in the number of residents certainly implies more susceptibles in danger of being infected. Yet, the duration of the epidemic has been shown in practice and through the use of models (Scott and Duncan, 2001) to depend on the number of contacts, K_s, as well. Therefore, while our results are not counterintuitive, they do not offer an immediate etiologic explanation of the rate of increase of epidemic duration with population size. Due to uncertainty, the variables in Eq. (1) are represented in terms of random fields (Section II.C). In addition to $P_{s,0}$ and K_s, the serial generation of monthly Δ_s values depends on three parameters: τ, $I_{s,\tau}$, and f (these parameters have been defined in Section II.C.b).

Scaling equations (or the equivalent graphic regression lines) are convenient and useful tools in life sciences. Eq. (1) is a product of the careful analysis and theoretical interpolation of the data in Table III.8, which are highly atypical, in the sense that they lack the serious uncertainties of other records--with the exception of Florence, Paris, and London. Other than tax records, information also comes primarily from reliable chroniclers, and in the case of UK, mainly from ecclesiastical records and court rolls, which on average are the most reliable sources. Several cases demonstrating the empirical usefulness of the scaling law in the Black Death modelling and space-time mapping are discussed in Section V.C.b.

b. An Extended Reed-Frost Model for Increasing the Resolution of the Mortality Data

There is no shortage of epidemic models (e.g., Anderson and May, 1995; Mollison, 1995). Most of these models are mathematical representations of empirical or theoretical knowledge concerning the transmission of infectious disease. In many cases they are based on re-interpretations of models that have been used in other scientific disciplines. In the SEP context, epidemic models are considered as primary components of the $\mathcal{G}$-KB with reference to geographical regions of Europe.

Since a central decision was to time mortality every *month*, we needed an epidemic model that was adequate for this purpose. Hence, we extended the original *Reed-Frost* model (Maia, 1952) in a S/TRF context that was then used to temporally downscale global mortality (e.g., a 50%, global mortality is downscaled into a sequence of monthly values, say 4, 10.7, 22.9, 23.7, 8.7, 2.2, and 0.3).

Epidemics are generally characterized by a first stage during which the number of infecteds increases, followed by a stage with a decreasing number of cases until the process dies out due to exhaustion of susceptibles. While some generalizations of the original Reed-Frost model can be found in the literature (e.g., Picard and Lefevre, 1990), the stochastic behavior of the model in a *composite* space-time manifold has not been investigated[3]. In the latter case, the original Reed-Frost model can be expressed as ($k = 0, 1, 2, ...$)

$$I_{s,(k+1)\tau} = E_{s,k\tau}\,(1 - q^{I_{s,k\tau}}) \tag{2}$$

where τ is the total latent period plus half the infectious period, also called serial generation time, $I_{s,k\tau}$ is the infecteds field (number of infected cases) at location s and time $t = k\tau$, $E_{s,k\tau}$ is the susceptibles field (number of susceptible cases) at location s and time $t = k\tau$, and q is the probability of any given person to avoid contact with another person at $t = k\tau$. This probability is given by

$$q = 1 - K_s (P_{s,0} - 1)^{-1}, \tag{3}$$

where K_s is the average number of contacts at location s during time $t = k\tau$, and $P_{s,0}$ is the initial ($t = 0$) population size at location s.

Note that Eq. (2) depends on four parameters, τ, q (or K_s), $P_{s,0}$, and $I_{s,\tau}$ (the number of infecteds between $t = 0$ and $t = \tau$), which give the model flexibility to adapt to different diseases and population characteristics. We extended model (2) to make it reflect death rate rather than infecteds. The susceptibles field $E_{s,k\tau}$ is

$$E_{s,k\tau} = P_{s,0} - I^T_{s,k\tau} \tag{4}$$

($k = 0, 1, 2, ...$), $I^T_{s,k\tau} = \sum_{j=1}^{k} I_{s,j\tau}$. By inserting Eq. (4) into (2), the latter becomes

$$I_{s,(k+1)\tau} = (P_{s,0} - I^T_{s,k\tau})(1 - q^{I_{s,k\tau}}) \tag{5}$$

We have that $D_{s,k\tau} = f\, I_{s,k\tau}$ and $P_{s,k\tau} = P_{s,0} - D^T_{s,k\tau}$, where $D^T_{s,k\tau} = \sum_{j=1}^{k} D_{s,j\tau}$ and f is the proportion of fatalities among the infecteds. Then Eq. (5) is written as

[3] Despite their sophistication, many mathematical models seem to disregard the fact that in real world situations the epidemic variables are fundamentally spatiotemporal. Interestingly, little explanation for this omission is given in the mathematical epidemiology literature, even when sincere apologies are expressed on occasion, for less serious inadequacies of the proposed models (see, Diekmann and Heesterbeek, 2000: xi-xvi).

$$D_{s,(k+1)\tau} = (f P_{s,0} - D^T_{s,k\tau})(1 - q^{D_{s,k\tau}/f}). \quad (6)$$

and, as a consequence, mortality $M_{s,(k+1)\tau} = D_{s,(k+1)\tau} / P_{s,k\tau}$ at $t = (k+1)\tau$ is an S/TRF that can be expressed as

$$M_{s,(k+1)\tau} = f(P_{s,0} - I^T_{s,k\tau})(P_{s,0} - f I^T_{s,k\tau})^{-1}(1 - q^{I_{s,k\tau}}), \quad (7)$$

Note that now the model depends on a fifth parameter: f. Eq. (7) is the so-called *extended Reed-Frost* (ERF) model. Eq. (7) can be expressed as a function of the 5 initial parameters (τ, f, q, $P_{s,0}$, $I_{s,\tau}$), i.e., $M_{s,(k+1)\tau} = Funct(\tau, f, q, P_{s,0}, I_{s,\tau})$. For illustration, a few terms of the last expression are as follows:

$$M_{s,2\tau} = f(P_{s,0} - I_{s,\tau})(1 - q^{I_{s,\tau}})(P_{s,0} - f I_{s,\tau})^{-1},$$

$$M_{s,3\tau} = f(P_{s,0} - I_{s,\tau}) q^{I_{s,\tau}} (1 - q^{(P_{s,0} - I_{s,\tau})(1 - q^{I_{s,\tau}})})$$
$$[P_{s,0}(1 - f(1 - q^{I_{s,\tau}})) - f I_{s,\tau} q^{I_{s,\tau}}]^{-1}; \text{ etc.}$$

The explicit consideration of both the geographical location s and the time t is an important difference of the ERF vs. the original Reed-Frost model. The value of K_s (and, hence, of q) may change as a function of the location, depending on the community and the occasion under consideration. The theory behind the ERF model (7) is based on the assumption that the rise and fall of the epidemic depends on the number of susceptibles available and their depletion, due to infection or death, to a subliminal level or complete exhaustion. The ERF model accounts for composite space-time variations of mortality and their dependencies on other disease characteristics (population distribution, infected cases, etc.) as well as for important sources of uncertainty linked to a large-scale epidemic such as Black Death (which was not the case with the original model). Unlike the original RF model, the ERF model can include influences between different geographical locations in terms of space-time correlation functions. Model (7) is used to increase the resolution of the Black Death data. The model has the capability to decompose mortality into a period as short as the serial interval τ.

Because the $I_{s,\tau}$, K_s, and f are initial inputs to the ERF model, which may differ with geographical location s (e.g., when the locations are characterized by different G_s and Δ_s), a practical way to use the ERF model is by selecting the values of these 3 parameters in a way that the observables (i.e., Δ_s and G_s) of the Black Death epidemic are reproduced at each s. As was mentioned before, the value of K_s (and, hence, of q) may change, and initial estimates of the τ value are obtained on the basis of the knowledge available concerning the epidemic. It has been shown (Scott and Duncan, 2001) that, increasing the assumed number of contacts K_s markedly reduces the duration of the Black Death epidemic, a fact that could introduce an additional uncertainty element in our analysis. However,

because in all cases considered here the duration of the epidemic is given, the value of K_s is determined accordingly (although it differs from one geographical area to the other), thus reducing considerably this element of uncertainty.

One of the difficulties with the analytical treatment of the plague based on Eq. (7) is that the mortality field, $M_{s,(k+1)\tau}$, is a non-linear function of the corresponding infecteds field, $I_{s,k\tau}$. A straightforward solution to this problem is the linearization of Eq. (7) for easier application of the model in other aspects of the study. Some interesting formulas are derived if we define mortality as

$$M_{s,(k+1)\tau} = D_{s,(k+1)\tau} / E_{s,k\tau} = f\, I_{s,(k+1)\tau} / E_{s,k\tau}, \tag{8}$$

$E_{s,k\tau} > 0$, i.e., ignoring any immune cases. This is a reasonable assumption, since at that time Black Death was a new disease. E.g., Scott and Duncan (2004: 207) maintained that, "…almost everyone who made effective contact with an infectious person caught the disease and died. The reason for this was because nobody had been exposed to the disease before." Then, Eq. (7) reduces to a simpler expression of the space-time distribution of Black Death mortality, as follows

$$M_{s,(k+1)\tau} = f(1 - q^{I_{s,k\tau}}). \tag{9a}$$

Note that the initial population $P_{s,0}$ does not appear explicitly in Eq. (9). Eq. (9a) can be also written in a *recursive* form in terms of mortality

$$M_{s,(k+1)\tau} = f(1 - q^{f^{-1}E_{s,(k-1)\tau}M_{s,k\tau}}). \tag{9b}$$

Linearization of Eq. (9a) leads to the following ERF model

$$M_{s,(k+1)\tau} \approx f \begin{cases} -(\log q) I_{s,k\tau}, & M_{s,(k+1)\tau} < 0.3f \quad (10a) \\ -0.41(\log q) I_{s,k\tau} + 0.177, & M_{s,(k+1)\tau} \geq 0.3f, \quad (10b) \end{cases}$$

which suggests that the mortality at time $t = (k+1)\tau$ is a linear function of the infecteds at the previous time $t = k\tau$. In Fig. 3 we plot an example of $M_{s,(k+1)\tau}$ vs. $I_{s,k\tau}$ for both the non-linear model (9a) and its linearized version (10), assuming $f = 0.8$. This numerical comparison illustrates the good fit between the non-linear and the linearized ERF models. The good behavior of the model (10) is also demonstrated in real-world situations--see Section C.b and Fig. 24 below.

In some cases, it is useful to examine how changes in $I_{s,k\tau}$ may affect $M_{s,(k+1)\tau}$ by means of the *elasticity indicator* of the latter with respect to the former, i.e.,

$$\varepsilon_M = (\mathrm{d}M_{s,(k+1)\tau} / \mathrm{d}I_{s,k\tau})(M_{s,(k+1)\tau} / I_{s,k\tau})^{-1} = \mathrm{d}\log M_{s,(k+1)\tau} / \mathrm{d}\log I_{s,k\tau} \tag{11}$$

In view of Eq. (9a), definition (11) yields

$$\varepsilon_M = (\log q) q^{I_{s,k\tau}} I_{s,k\tau} / (q^{I_{s,k\tau}} - 1) = [(M_{s,(k+1)\tau} - f) / M_{s,(k+1)\tau}] \log(1 - M_{s,(k+1)\tau} / f) \tag{12}$$

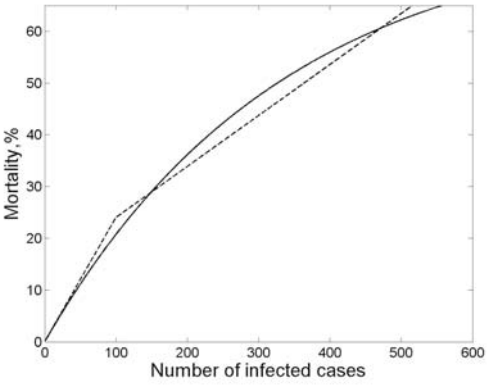


Figure 3. Plot of the non-linear ERF model (solid line) and the linearized ERF model (dashed line) vs. the number of infected cases ($f = 0.8$).

Elasticity ε_M is an indicator that measures the ratio of the fractional change in $M_{s,(k+1)\tau}$ over the fractional change in $I_{s,k\tau}$. Eq. (12) shows that when it is expressed as a function of infecteds, the ε_M depends on q (probability of no contact). But the ε_M is independent of q when it is expressed as a function of mortality. For illustration, ε_M vs. $I_{s,k\tau}$ is plotted in Fig. 4a. As might have been expected, as q increases (i.e., the probability of contact decreases), a change in the number of infecteds yields a smaller increase in mortality. In Fig. 4b we plot ε_M vs. mortality, assuming various f values throughout 14th century Europe. Using such plots in combination with the Black Death mortality maps of Chapter V allows one to obtain new maps of the corresponding ε_M distribution across space-time. These maps could offer another useful description of the geography and temporal evolution of disease dynamics. E.g., the larger the ε_M, the smaller the fractional increase in infecteds required to yield a specified fractional increase in mortality.

c. Space-Time Correlations of Mortality Distributions

Though stochastics (Chapter II) provides us with rather abstract notions, it is by no means "art pour l'art". On the contrary, these are of fundamental importance in developing applied epidemic systems. Such notions include the mean, $\overline{M}_{s,t}$, and the covariance $c_{M;r,\tau}$ ($r = |\boldsymbol{s} - \boldsymbol{s}'|$ and $\tau = |t - t'|$) of the mortality S/TRF $M_{s,t}$, which were mathematically defined in Section II.C.b[4]. In other words, inherent to the mortality space-time distribution are relationships seeking a *form*, which is materialized in terms of the theoretical mean and covariance functions.

[4] The reader may recall, e.g., that covariance is the quantitative representation of the idea of space-time dependence, which has roots with multiple branches that extend to diverse scientific fields.

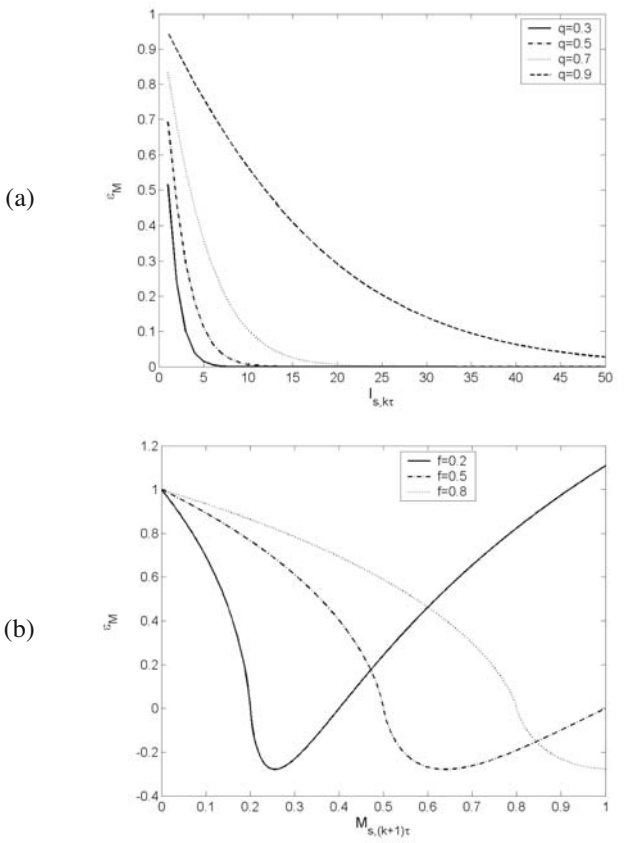


Figure 4. Mortality elasticity indicators as a function of (a) infecteds (b) mortality.

Theoretical Models and Their Interpretation

S/TRF theory offers rich classes of theoretical covariance models to represent dependence of Black Death mortality across space-time. Theoretical covariances are part of the $\mathcal{G}$-KB. One important class of covariance models is as follows

$$c_{M;r,\tau} = [0.7a_1 e^{-3r/b_1} + 0.3a_2 e^{-3r/b_2}][0.01a_3 e^{-3\tau/b_3} + 0.99a_4(1 - b_4\tau^2)e^{-c^2\tau^2}], \qquad (13)$$

where a_i and b_i ($i = 1,...,4$) are coefficients to be determined from the mortality dataset. Eq. (13) is a space-time *separable* covariance model, i.e., it is the product of purely spatial and purely temporal components: $c_{M;r,\tau} = c_{M;r}\, c_{M;\tau}$. In Fig. 5 we plot a three-dimensional perspective of the theoretical model (13), which offers a very good fit to the data available, as well. Concerning certain technical issues (space-time covariance fitting, parameter estimation, etc.), the reader is refereed to Christakos *et al.* (2002) and references therein. Each $c_{M;r,\tau}$ value estimates the dependence between Black Death mortalities at geographical distance r and time

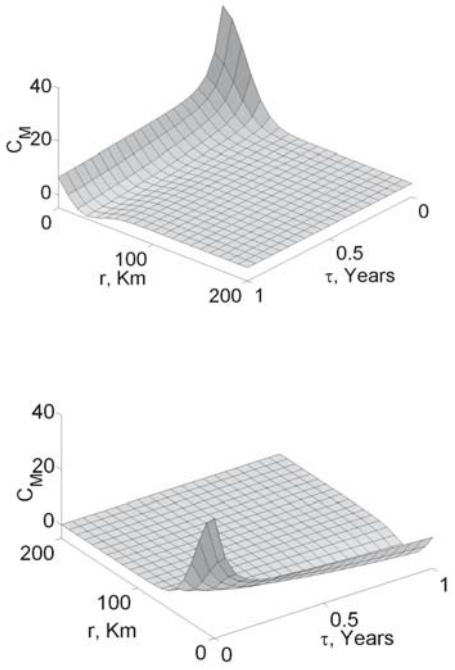


Figure 5. Three-dimensional representations of the mortality covariance model in space-time.

lag τ--larger $c_{M;r,\tau}$ values generally imply stronger mortality dependence)--in which case the plot of Fig. 5 offers a powerful visualization about how this dependence changes across space and time. One may observe a decreasing shape of the covariance and a strengthening of the dependency at certain space-time lags. Differences in correlation strength along space vs. time are also evident. The closer to zero is the $c_{M;r,\tau}$, the more dissimilar are the mortality values across space-time. Some spatial and temporal components of the mortality covariance (13) are plotted in Fig. 6 (experimental and model). The correlation between mortality values falls with increasing space and time lags, although in different fashions (e.g., the drop is faster along space than along time lags). For a fixed time lag the exponential drop of the covariance values may imply that similar mortality levels could be found in different geographical areas of Europe. Thus, the covariance plots help epidemiologists to comprehend the nature and extent of the effect that neighboring mortality values have on each other. These plots also reflect a number of peaks of the Black Death epidemic. The behavior of the covariance at the origin (small space and time lags) implies a smoother variation of mortality in time than along space. Also, the covariance *range* indicates the *predictability*

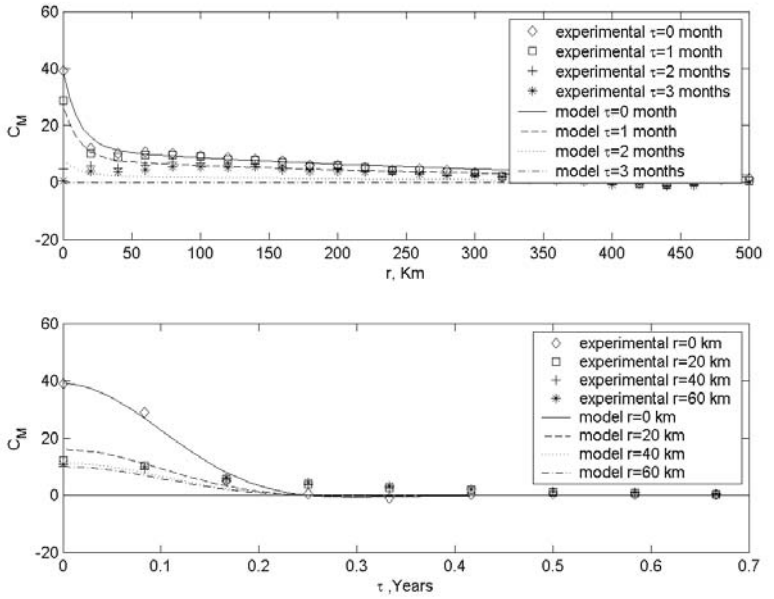


Figure 6. Spatial and temporal components of the separable mortality covariance.

horizon of the process, i.e. the space-time distances for which predictions can be made. A non-separable model is considered next.

Due to the advancing *waveform* of the epidemic, another plausible covariance model could be of the form $c_{M;r,\tau} = c_{M;\boldsymbol{r}+\boldsymbol{v}\tau}$. This model can be associated with mortality waves $M_{s,t} = M_{s+vt}$ traveling at speed $\boldsymbol{v}$. Covariance models of this type have been proposed by Kolovos *et al.* (2004), as follows

$$c_{M;\boldsymbol{r}+\boldsymbol{v}\tau} = \begin{cases} e^{-|\boldsymbol{r}+\boldsymbol{v}\tau|/a} & (14a) \\ e^{-(\boldsymbol{r}+\boldsymbol{v}\tau)^2/a^2} & (14b) \\ [1+(\boldsymbol{r}+\boldsymbol{v}\tau)^2/w^2]^{-\lambda/2} e^{-|\boldsymbol{r}+\boldsymbol{v}\tau|/a} & (14c) \end{cases}$$

where λ, w, and a are empirical parameters calculated from the data. Some examples of the spatial and temporal components of the mortality covariances (14) are plotted in Figs. 7-12 (experimental and model). These Black Death mortality covariances have been calculated along different geographical directions ($\alpha = 0$, $\pi/4$, $\pi/2$, and $3\pi/4$ is the angle between East and the estimation direction, whereas $\phi = 0.495\pi$ is the angle between East and the disease propagation direction). The symbols "◊", "□", and "+" denote the experimental values. The lines denote the fitted model: solid line (◊), dashed line (□), and dotted-dashed line (+).

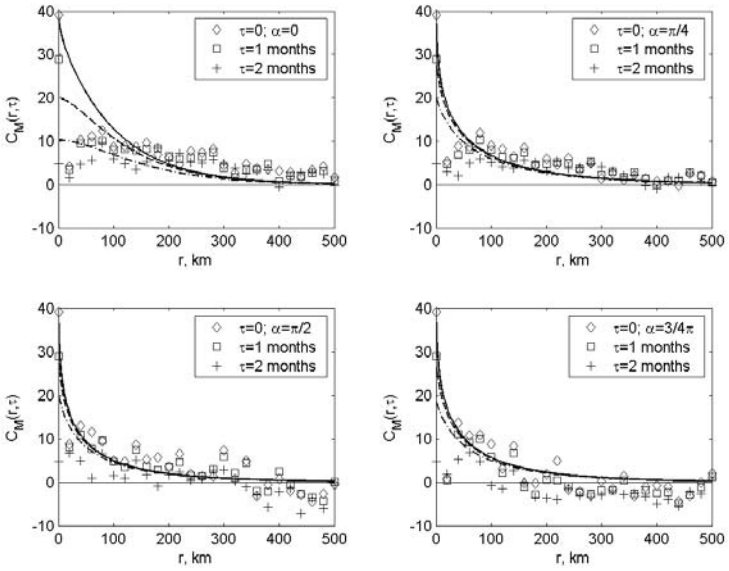


Figure 7. Spatial components of mortality covariance (14a)--experimental and model; $v = 800$, $\phi = 0.495\pi$, $a_0 = 100$, $a_{45} = a_{90} = 200$, and $a_{135} = 180$.

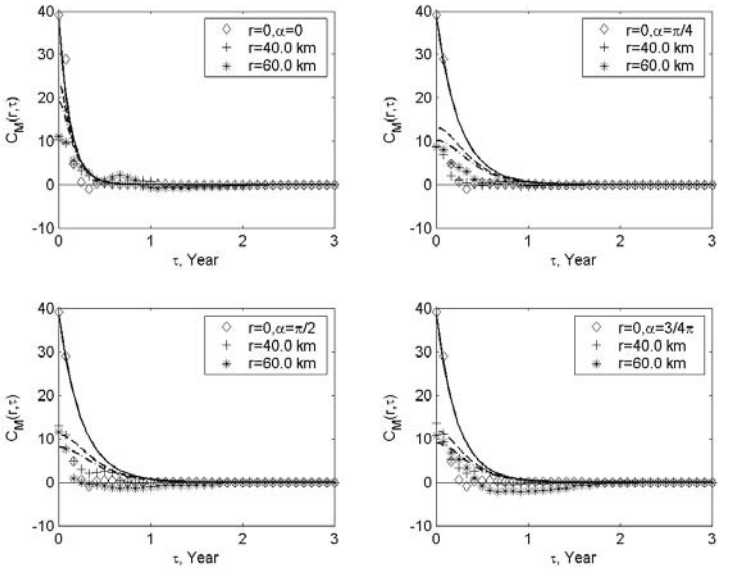


Figure 8. Temporal components of mortality covariance (14a)--experimental and model; v, ϕ, a_0, a_{45}, a_{90}, a_{135} are the same as in Fig. 7.

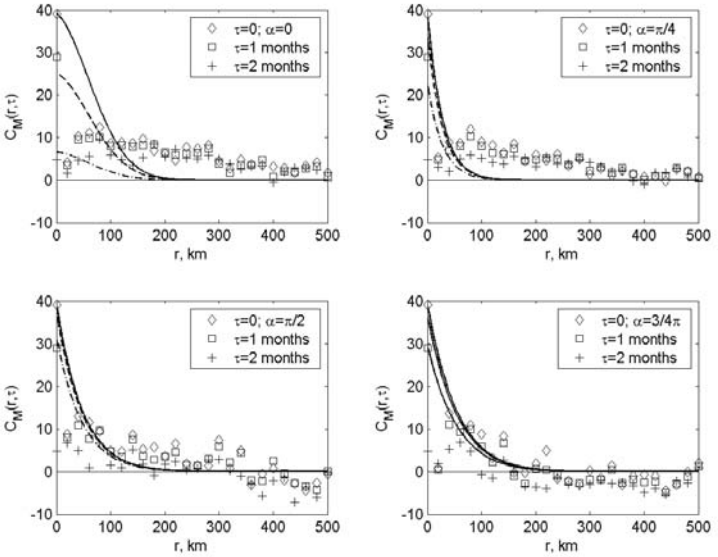


Figure 9. Spatial components of the mortality covariance (14b)--experimental and model; $v = 800$, $\phi = 0.495\pi$, $a_0 = 100$, $a_{45} = 180$, $a_{90} = 280$, $a_{135} = 250$.

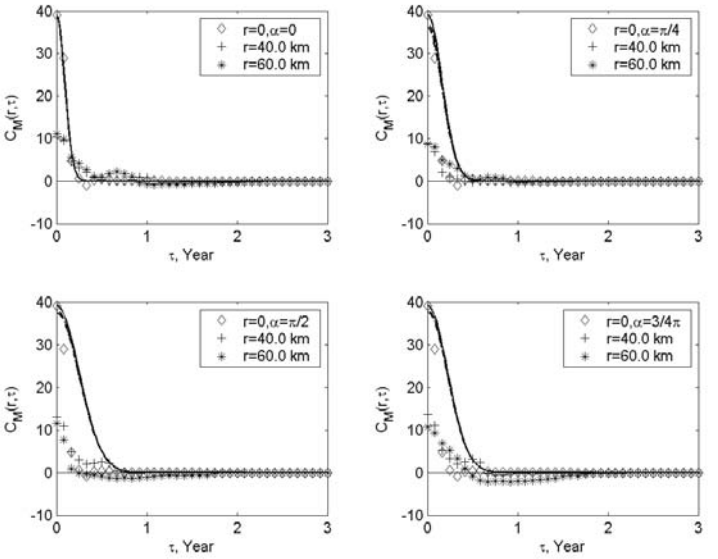


Figure 10. Temporal components of the mortality covariance (14b)--experimental and model; v, ϕ, a_0, a_{45}, a_{90}, a_{135} are the same as in Fig. 9.

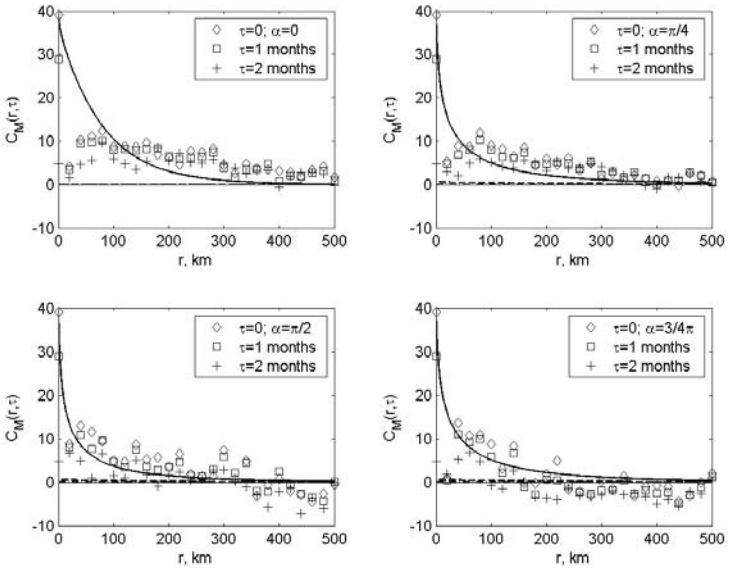


Figure 11. Spatial components of the mortality covariance (14c)--experimental and model; $v = 800$, $\phi = 0.495\pi$, $w = 100$, $\lambda = 0.5$, $a_0 = 100$, $a_{45} = a_{90} = a_{135} = 250$.

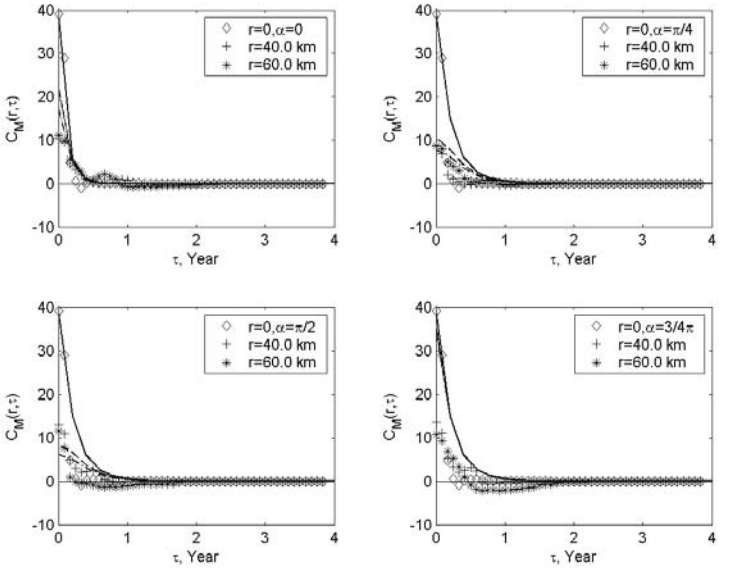


Figure 12. Temporal components of the mortality covariance (14c)--experimental and model; v, ϕ, a_0, a_{45}, a_{90}, a_{135} are the same as in Fig. 11.

Notice the different shapes of the theoretical mortality covariances (14) and the varying fits to the experimental covariances--which means that different models can be used for different epidemic directions and time periods. This flexibility is a considerable advantage of the class of models (14).

Continuously Distributed and Clustered Spatial Data Sets

If needed, efficient algorithms exist for the practical estimation of the theoretical covariance models above in both cases of data sets:

(*a*) *Continuously* distributed in space. Covariance estimators are available for spatially homogeneous/temporarily stationary as well as for spatially nonhomogeneous/temporarily nonstationary disease variables (Christakos and Hristopoulos, 1998; Kolovos *et al.*, 2004).

(*b*) *Clustered* in space. In this case, a coefficient of variation of the dimensionless spatial density of the point pattern of sample locations is introduced as a metric of the degree of clusteredness of the data set; then a modified form of the covariance estimator is used that incorporates declustering weights and proposes a scheme for estimating the declustering weights based on zones of proximity (Kovitz and Christakos, 2004b).

ERF-Based Models

Another advantage of the linearized ERF model (10) is that the temporal mortality mean, variance, and covariance can be expressed as linear functions of the infection statistics at any geographical location $\boldsymbol{s}$, i.e.,

$$\overline{M_{\boldsymbol{s},(k+1)\tau}} \approx f \begin{cases} -(\log q)\overline{I_{\boldsymbol{s},k\tau}}, & M_{\boldsymbol{s},(k+1)\tau} < 0.3f \quad (15a) \\ -0.41(\log q)\overline{I_{\boldsymbol{s},k\tau}} + 0.177, & M_{\boldsymbol{s},(k+1)\tau} \geq 0.3f, \quad (15b) \end{cases}$$

(which means that the expected mortality at time $t = (k+1)\tau$ is a linear function of the infection mean at time $t = k\tau$), and

$$\overline{M^2_{\boldsymbol{s},(k+1)\tau}} \approx f^2 \begin{cases} (\log q)^2 \overline{I^2_{\boldsymbol{s},k\tau}}, & M_{\boldsymbol{s},(k+1)\tau} < 0.3f \quad (16a) \\ 0.168(\log q)^2 \overline{I^2_{\boldsymbol{s},k\tau}} - 0.145(\log q)\overline{I_{\boldsymbol{s},k\tau}} + 0.031, & M_{\boldsymbol{s},(k+1)\tau} > 0.3f \quad (16b) \end{cases}$$

$$\overline{M_{\boldsymbol{s},(k+1)\tau} M_{\boldsymbol{s},(k+1)\tau}} \approx f^2 \begin{cases} (\log q)^2 \overline{I_{\boldsymbol{s},k\tau} I_{\boldsymbol{s},(k+1)\tau}}, & \text{if } M_{\boldsymbol{s},(k+1)\tau}, M_{\boldsymbol{s},(k+2)\tau} < 0.3f \quad (17a) \\ 0.41(\log q)^2 \overline{I_{\boldsymbol{s},k\tau} I_{\boldsymbol{s},(k+1)\tau}} - 0.177(\log q)\overline{I_{\boldsymbol{s},k\tau}}, & \\ \qquad \text{if } M_{\boldsymbol{s},(k+1)\tau} < 0.3f, M_{\boldsymbol{s},(k+2)\tau} \geq 0.3f \quad (17b) \\ 0.17(\log q)^2 \overline{I_{\boldsymbol{s},k\tau} I_{\boldsymbol{s},(k+1)\tau}} - 0.073(\log q)(\overline{I_{\boldsymbol{s},k\tau}} + \overline{I_{\boldsymbol{s},(k+1)\tau}}) & \\ \qquad + 0.031, \quad \text{if } M_{\boldsymbol{s},(k+1)\tau}, M_{\boldsymbol{s},(k+2)\tau} \geq 0.3f. \quad (17c) \end{cases}$$

For visualization purposes, Eqs. (15) and (17) are plotted in Fig. 13 (assuming $q = 0.99$ and $f = 0.4$). One notices a cyclic relationship between the mortality and the infection statistics, which is due to the fact that the infecteds field initially increases and then decreases with time (this is, in fact, a typical behavior of the infecteds field observed at geographical locations throughout the 14th century Europe).

The cross-covariance function of the mortality and infecteds fields is expressed as

$$\overline{M_{\boldsymbol{s},(k+1)\tau} I_{\boldsymbol{s},k\tau}} \approx f \begin{cases} -(\log q)\overline{I^2_{\boldsymbol{s},k\tau}}, & M_{\boldsymbol{s},(k+1)\tau} < 0.3f \\ -0.41(\log q)\overline{I^2_{\boldsymbol{s},k\tau}} + 0.177\overline{I_{\boldsymbol{s},k\tau}}, & M_{\boldsymbol{s},(k+1)\tau} \geq 0.3f \end{cases} \tag{18}$$

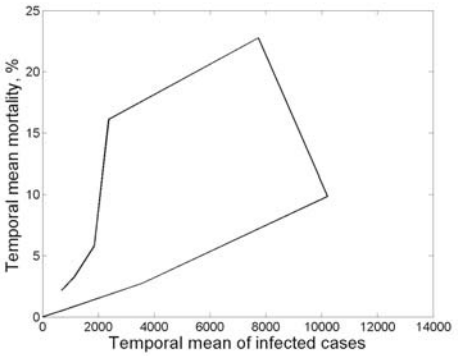
Interestingly, Eq. (18) implies that the dependence between mortality and infecteds at two different times $t = (k+1)\tau$ and $t = k\tau$ can be expressed in terms of the infecteds variance at time $t = k\tau$. In a similar manner, mortality covariances can be derived between any pair of geographical locations, $\boldsymbol{s}$ and $\boldsymbol{s}'$, in terms of infecteds mean and covariance, as follows

$$\overline{M_{\boldsymbol{s},(k+1)\tau} M_{\boldsymbol{s}',(k+1)\tau}} \approx f^2 \begin{cases} (\log q)^2 \overline{I_{\boldsymbol{s},k\tau} I_{\boldsymbol{s}',k\tau}}, & \text{if } M_{\boldsymbol{s},(k+1)\tau},\ M_{\boldsymbol{s}',(k+1)\tau} < 0.3f \quad (19a) \\ 0.41(\log q)^2 \overline{I_{\boldsymbol{s},k\tau} I_{\boldsymbol{s}',k\tau}} - 0.177\ \log q \overline{I_{\boldsymbol{s},k\tau}}, & \\ \qquad \text{if } M_{\boldsymbol{s},(k+1)\tau} < 0.3f,\ M_{\boldsymbol{s}',(k+1)\tau} \geq 0.3f \quad (19b) \\ 0.41(\log q)^2 \overline{I_{\boldsymbol{s},k\tau} I_{\boldsymbol{s}',k\tau}} - 0.177\ \log q \overline{I_{\boldsymbol{s}',k\tau}}, & \\ \qquad \text{if } M_{\boldsymbol{s},(k+1)\tau} \geq 0.3f,\ M_{\boldsymbol{s}',(k+1)\tau} < 0.3f \quad (19c) \\ 0.17(\log q)^2 \overline{I_{\boldsymbol{s},k\tau} I_{\boldsymbol{s}',k\tau}} - 0.073\ \log q(\overline{I_{\boldsymbol{s},k\tau}} + \overline{I_{\boldsymbol{s}',k\tau}}) + 0.031, & \\ \qquad \text{if } M_{\boldsymbol{s},(k+1)\tau},\ M_{\boldsymbol{s}',(k+1)\tau} \geq 0.3f \quad (19d) \end{cases}$$

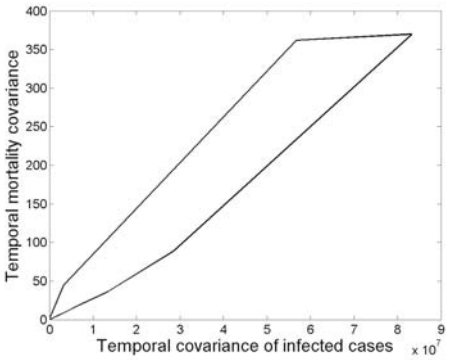
Higher order and multiple-point mortality correlation functions across space-time can be derived as well.

Other Classes of Space-Time Models

In Table 1 we present a summary of several rich classes of space-time correlation models $c_X = c_X(\boldsymbol{p}, \boldsymbol{p}')$ for an S/TRF $X(\boldsymbol{p})$. These models can be useful in public health research and disease modelling studies, including the Black Death epidemic. Time and space limitations did not allow us to test all models of Table 1 in the case of Black Death, which would be an interesting future research topic. Various methods have been used to generate the models of Table 1, including differential equations, spectral densities, dynamic rules, and linear superposition of permissible covariance models. A more detailed mathematical presentation of



(a)



(b)

Figure 13. Plots of temporal: (a) mortality mean vs. mean of infected cases; and (b) mortality covariance vs. covariance of infecteds ($q = 0.99$, $f = 0.4$).

these methods can be found in Christakos (1992, 2000), Christakos and Hristopulos (1998), and Kolovos *et al.* (2004). Spatially homogeneous/temporally stationary and non-homogeneous/non-stationary covariance models are included in Table 1. There are several possibilities regarding the way these covariance models can be used in public health practice, as follows:

i. Public health scientists may have at their disposal a well-established set of relationships to work with. In human exposure analysis, e.g., environmental laws in the form of mathematical equations are often available. Thus, if these equations are solved (exactly or to some approximation), the solution should definitely be used in the definition of the covariance model.[5]

ii. Epidemic laws may not be known completely, but some guidance regarding the functional dependence of the covariance can be gained from approximate empirical laws, which can be expressed either in terms of algebraic/differential equations or in terms of algorithmic rules that aim to emulate the real world epidemic system.

[5] In some cases, this may lead to exact specification of the covariance model parameters in terms of functions that can be determined from the available data.

Table 1. A summary of space-time covariance models in $R^n \times T$ (**continues**).[6]

c_X	n	Figure No.
$E_n(\beta\tau^{2\gamma}+1)^{-n/2}\int_0^1 du\,(1-u^2)^{(n-1)/2}e^{-(ur)^2/(\beta\tau^{2\gamma}+1)}$	1, 2, 3	14A, B
$e^{-0.5r^2/(1+b\tau^2)}\begin{cases}(1+b\tau^2)^{-3/2}\,[1-0.5r^2(1+b\tau^2)^{-1}]\\(1+b\tau^2)^{-5/2}\;\{1-r^2(1+b\tau^2)^{-1}\\\quad+r^4[8(1+b\tau^2)^2]^{-1}\}\end{cases}$	2	14C, D
$(\beta\tau^{2\gamma}+1)^{-n/2}e^{-r^2/(\beta\tau^{2\gamma}+1)}$	1, 2, 3	
$(4\alpha\pi\tau)^{-n/2}e^{-r^2/4\alpha\tau}$	1, 2, 3	15A, B
$B_n\int_0^1 du\,(1-u^2)^{(n-1)/2}e^{-(ur)^2/4\alpha\tau}$	2, 3	
$\frac{1}{8}\pi^{1/2}(\alpha\tau)^{-1/2}E_2\,KummerM[\frac{1}{2},2,-Z_A]$	2	15C
$\frac{1}{2}r^{-1}E_3\,[(1-\frac{1}{2}Z_A^{-1})\,Erf(Z_A^{1/2})+(\pi Z_A)^{-1/2}e^{-Z_A}]$	3	15D
$\frac{1}{2}\alpha\int_0^\infty dk\;k^{-3}(k^2+v^2)^{-2}e^{-\alpha^2k^2/2}\;J_0[k(r+v\tau)]$	2	
$\frac{1}{2}[e^{-ar}\,Erfc(a\sqrt{c^{-1}\tau}-\frac{1}{2}r\sqrt{c\tau^{-1}})$ $+e^{ar}\,Erfc(a\sqrt{c^{-1}\tau}+\frac{1}{2}r\sqrt{c\tau^{-1}})]$	1	16A, B
$\frac{1}{2}E_n\int_0^1 du\,(1-u^2)^{(n-1)/2}[\,e^{-aur}\,Erfc(a\sqrt{c^{-1}\tau}$ $-\frac{1}{2}ur\sqrt{c\tau^{-1}})+e^{aur}\,Erfc(a\sqrt{c^{-1}\tau}+\frac{1}{2}ur\sqrt{c\tau^{-1}})]$	1, 2, 3	16C, D
$A_PE_n\int_0^1 du\,(1-u^2)^{(n-1)/2}\sqrt{(ur)^{z-2\alpha}\tau^{-1}}\;e^{-(ur)^{-z}\tau}$	1, 2, 3	
$\beta_n r^{1-n/2}\int_0^\infty dk\,k^{n/2}e^{-c^{-1}(k^2+\alpha^2)^p\tau}(k^2+\alpha^2)^{-p}J_{n/2-1}(kr)$	1, 2, 3	17A, B
$E_n\beta_n\int_0^1\int_0^\infty du\,dk\,(1-u^2)^{(n-1)/2}(urk)^{1/2}$ $e^{-c^{-1}(k^2+\alpha^2)^p\tau}(k^2+\alpha^2)^{-p}J_{-1/2}(kur)$	1, 2, 3	17C, D
$(\frac{1}{2}\pi)^n\int d\boldsymbol{k}\,e^{i(\boldsymbol{k}\cdot\boldsymbol{r}+v\tau)}\,\tilde{c}_s(\boldsymbol{k})$	1, 2, 3	
$E_n\int_0^1 du\,(1-u^2)^{(n-1)/2}e^{-\sqrt{(ur/a)^2+(\tau/b)^2}}$	1, 2, 3	

[6] $E_n = 2\Gamma(n)\{\sqrt{\pi}\,\Gamma[\frac{1}{2}(n-1)]\}^{-1}$, $B_n = (4\alpha\pi\tau)^{-1/2}E_n$, $\tau,\alpha,z,D>0$, $A_P = e^{D/4}(4\sqrt{\pi D^3})^{-1}$, $Z_A = r^2(4\alpha\tau)^{-1}$, $\beta_n = [2(2\pi)^{n/2}c]^{-1}$, $0\le\beta\le 1$, $0<\gamma\le 1$; χ_{1j}, χ_{2j} are modes of the associated differential equation with amplitudes A_j (random or deterministic), $c_{jk} = \overline{A_jA_k}$, $c_{\chi(j,k)}$ denotes the mode correlation $\overline{\chi_{1j}(s)\chi_{1k}(s')}$; $f_v(r;u_c) = \Gamma(-v)^{-1}\int_0^{u_c} du\,\exp(-ur)\,u^{-(v+1)}$, $\hat{f}_v(r;u_c) = f_v(r;u_c)\,f_v^{-1}(0;u_c)$; for more details, see Kolovos *et al*. (2004).

Table 1. A summary of space-time covariance models in $R^n \times T$ (**concludes**).

$e^{-\lvert r \pm v\tau \rvert/\alpha}$ $e^{-(r \pm v\tau)^2/\alpha^2}$ $[1+(r \pm v\tau)^2/w^2]^{-1/2} e^{-\lvert r \pm v\tau \rvert/\xi}$	1, 2, 3	
$\sigma^2 \hat{f}_z(\tau/r^\beta; u_c) \hat{f}_\alpha(r; w_c)$	1, 2, 3	18
$\sum_{j,k=0}^{\infty} \left\{ \begin{array}{l} c_{jk}\, \chi_{1j}(s)\chi_{1k}(s')\chi_{2j}(t)\chi_{2k}(t') \\ A_j A_k\, c_{\chi(j,k)}(s,s')\chi_{2j}(t)\chi_{2k}(t') \\ \overline{A_j A_k\, \chi_{1j}(s)\chi_{1k}(s')}\chi_{2j}(t)\chi_{2k}(t') \end{array} \right\} - \overline{X(s,t)}\,\overline{X(s',t')}$	1	19
$r^{-1} g(r^z/\tau)$	1, 2, 3	
$r^{\alpha z-1}/\tau^\alpha \quad (r^z\tau^{-1} << 1)$ $\tau^b/r^{bz+1} \quad (r^z\tau^{-1} >> 1)$	2	

iii. Even if knowledge of the specific disease distribution law is unavailable, covariance models derived from general laws can be used as potential candidates, in which case their parameters are estimated from data sets.[7] Then, appropriate techniques can be used to decide among the possible candidates.

For illustration, some of the models in Table 1 are plotted in Figs. 14-19. In the end, it is the public health modeller who will decide which approach to follow, since each approach has its own merits and domain of applicability. The models in Table 1 are *non-separable*, in general, and cover a wide range of space-time correlation scenarios, which can be used to represent the variability of public health systems across space and time. It is interesting to investigate the properties (short-range and asymptotic behavior, shape of the covariance function, etc.) of these models in the context of the specific epidemic problem of interest and assess the space-time dependence for various model parameter values. As can be seen in Figs. 14-19, the different mathematical functions lead to distinct features. Hence, the visual representation of the covariance models is very helpful in selecting the appropriate model for the specific epidemic situation. Among the noticeable features of the covariance plots in Fig. 14C and D is the presence of "hole effects", mainly, along the space direction. The shape of the covariance in Fig. 15 changes with the *n*- and α values. Clearly, the same is true for the correlation ranges and the behavior near the space-time origin. A comparison of the sets A, B and C, D in Fig. 16 shows that one covariance decreases as a function of spatial distance more quickly than it does as a function of temporal distance, whereas the other covariance exhibits the reverse behavior. In Fig. 17 the covariance declines faster

[7] In the same manner that so-called "standard" models are employed to represent epidemic covariance functions.

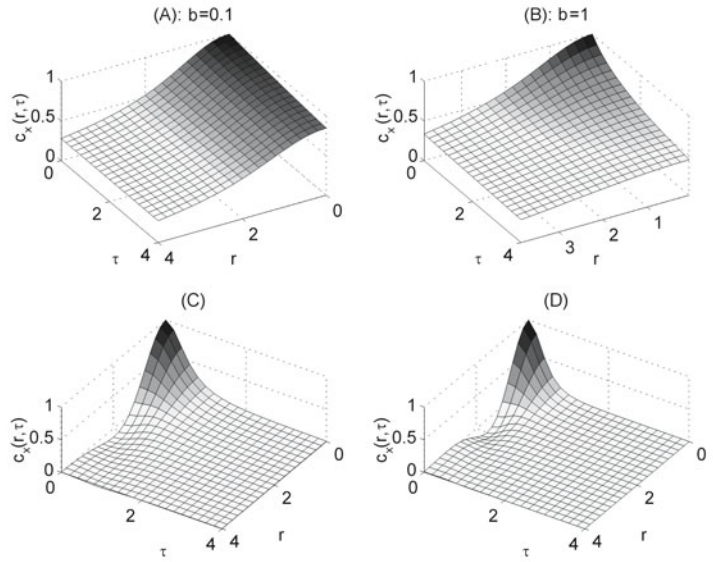


Figure 14. Top row shows covariance plots in $R^2 \times T$ (A) and $R^3 \times T$ (B) for selected b values. The bottom row shows covariance plots in $R^2 \times T$ (C, D) for $b = 2$.

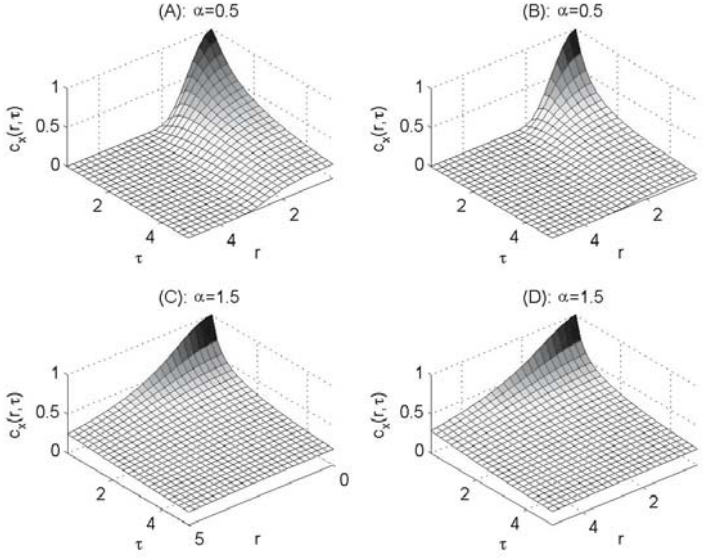


Figure 15. Plots of space-time covariance models: (A) $R^2 \times T$, (B) $R^3 \times T$; (C) $R^2 \times T$, (D) $R^3 \times T$ for selected α values.

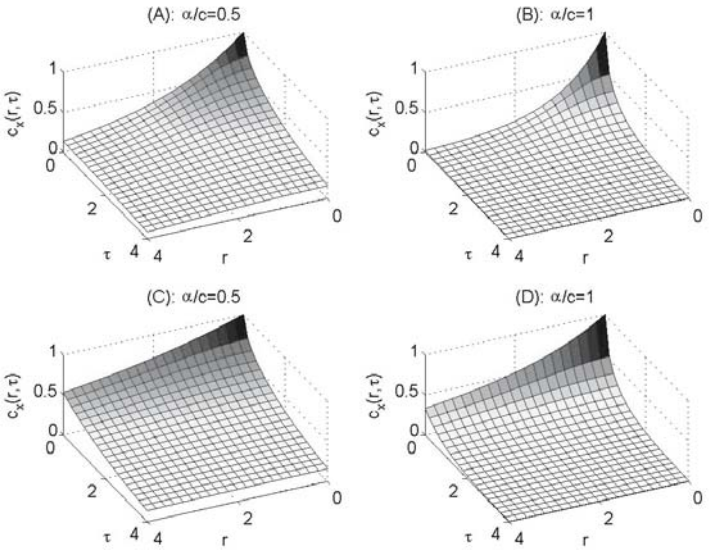


Figure 16. Plots of the covariance models in the $R^1 \times T$ (plots A and B), and in $R^3 \times T$ domain (plots C and D) for various values of the ratio α / c.

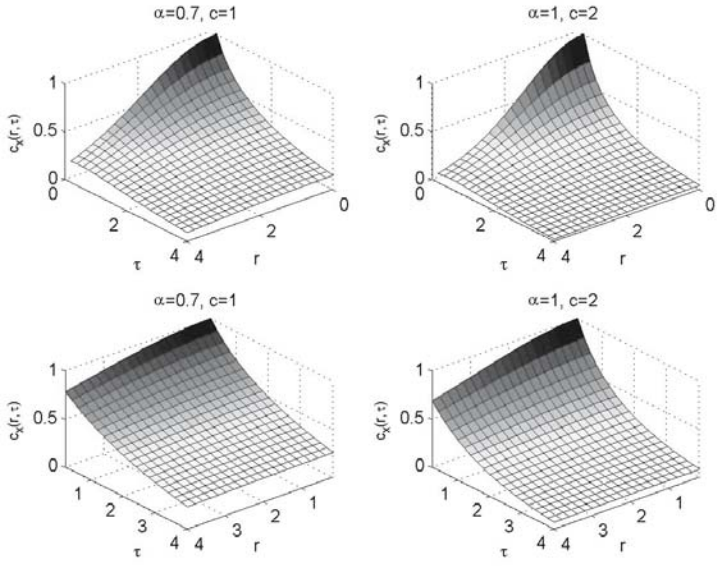


Figure 17. Covariance models in $R^2 \times T$ (top row) and in $R^3 \times T$ (bottom row) for varying values of the parameters α and c.

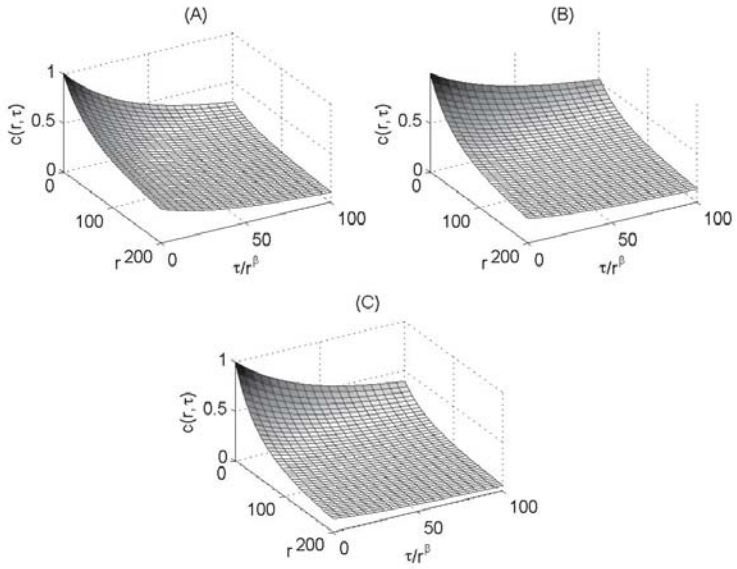


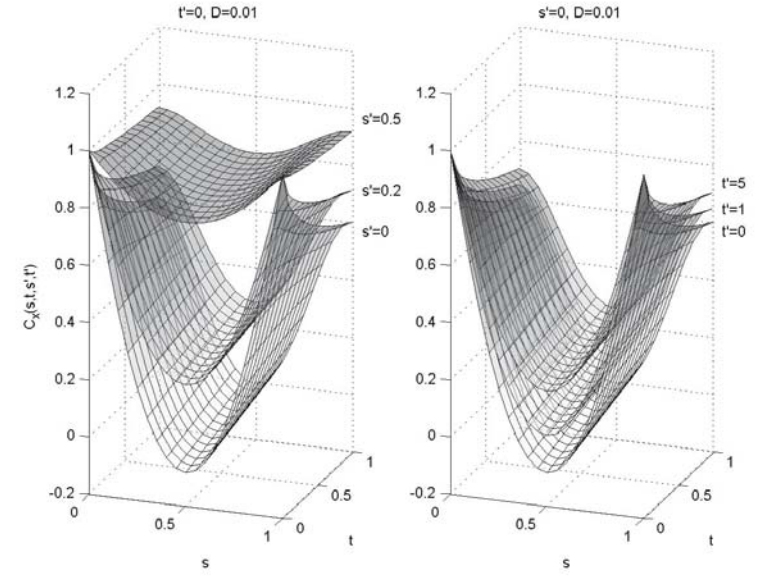
Figure 18. Covariance models in $R^n \times T$ for selected combinations of the parameters z, α, and β. (A) $z = -0.845$, $\alpha = -0.454$, $\beta = -0.35$; (B) $z = -0.385$, $\alpha = -0.615$, $\beta = -0.35$; (C) $z = -0.615$, $\alpha = -1.396$, $\beta = 1.05$.

along the time direction than along the space direction. In Fig. 18, a range of z- and β-values is assumed and the α is derived on the basis of the corresponding permissibility conditions. The covariance in Fig. 19 depends on the space-time coordinates of both points $\boldsymbol{p}$ and $\boldsymbol{p}'$, and not just on the space and time distances between the two points (this model may be nonhomogeneous/nonstationary due to a number of reasons, including the boundary and initial condition effects).

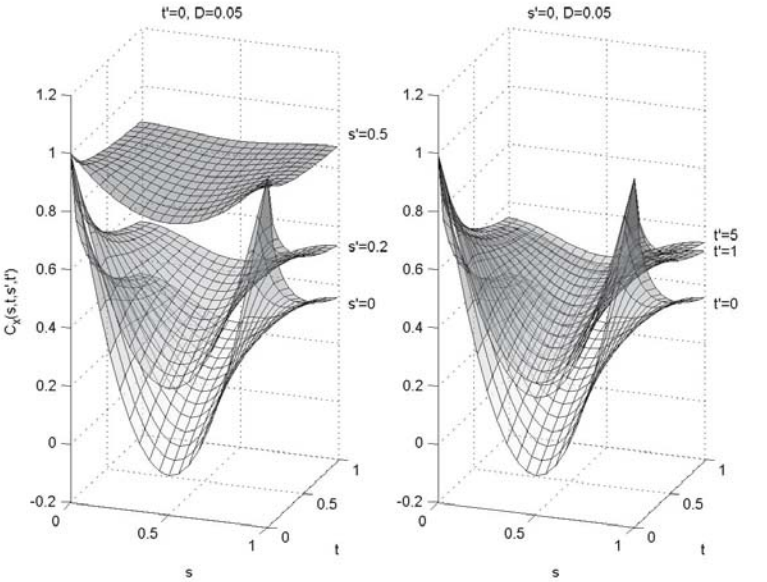
d. Space-Time Mortality PDF With Reference to the $\mathcal{G}$-KB

On the basis of Eqs. (15)-(19), the BME technique (Section II.E.b) can generate the pdf of the mortality field across space-time, thus enabling the determination of several important characteristics of the epidemic, such as the direction and speed of disease spread, prevailing trends and patterns, and the relative significance of the different epidemic components. In light of Eqs. (9a) and (15)-(18), BME formally expresses the mortality pdf as follows

$$f_{\mathcal{G}}(m_{s,(k+1)\tau}, m_{s,(k+2)\tau}) = \exp[\mu_0 + \mu_1 m_{s,(k+1)\tau} + \mu_2 \log(m_{s,(k+1)\tau}) + \mu_3 \log(m_{s,(k+2)\tau}) + \mu_4 m_{s,(k+1)\tau}^2 + \mu_5 \log(m_{s,(k+1)\tau})^2 + \mu_6\, m_{s,(k+2)\tau} \log(m_{s,(k+1)\tau}) + \mu_7 \log(m_{s,(k+1)\tau} + m_{s,(k+2)\tau}) + \mu_8 (m_{s,(k+1)\tau} m_{s,(k+2)\tau})], \quad (20)$$



(A)



(B)

Figure 19. (a) Plots of covariance model in $R^1 \times T$ with $L = 1$ and (A) $D = 0.01$, (B) $D = 0.05$.

where μ_i ($i = 0,1,...,8$) are coefficients expressing the relative weight of certain functions of the mortality values across space-time (the form of the functions de-

pends on the epidemic models, space-time correlations, Black Death databases, and other knowledge sources considered); as usual, the subscript G denotes that the pdf has been produced on the basis of a general KB. The vector of coefficients $\boldsymbol{\mu} = \{\mu_i;\ i = 0,1,...,8\}$ are parameters to be calculated from the solution of the so-called *BME system* of equations (for details, see Christakos *et al.*, 2002: 35). The solution $\boldsymbol{\mu}$ is substituted back into Eq. (20) to obtain the shapes of the different f_G across space and time (see, Section II.E.b).

For numerical illustration, in Fig. 20 we plot an example of a bivariate mortality pdf, f_G (for $f = 0.5$, $q = 0.85$). The f_G, which does not necessarily have a Gaussian form, offers a stochastic characterization of the mortality distribution; it allows the calculation of parameters like the joint probability of occurrence of the mortality values $M_{s,(k+1)\tau}$ and $M_{s,(k+2)\tau}$, the most probable mortality value, quantiles, etc.

C. Coding the Specificatory Knowledge Base

An epidemic concept is synonymous with the corresponding set of operations and assumptions by which it is determined. This is the case with the concept of Black Death mortality, as well. The operations leading to the calculation of monthly mortality values at each space-time point $\boldsymbol{p}$ were often based on the assumption that each one of them is random with a specified pdf, $f_S(m)$--see, Fig. 21; as usual, the subscript S denotes that the pdf is constructed using site-specific KB. The S-KB refers solely to the specified Black Death epidemic situation determined contextually (geographically, temporally, disciplinary, etc.). The series of

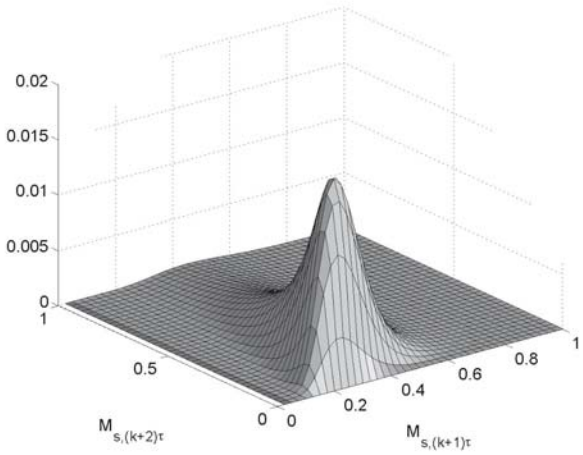


Figure 20. An example of a BME-derived bivariate mortality pdf $f_G(m_{s,(k+1)\tau}, m_{s,(k+2)\tau})$.

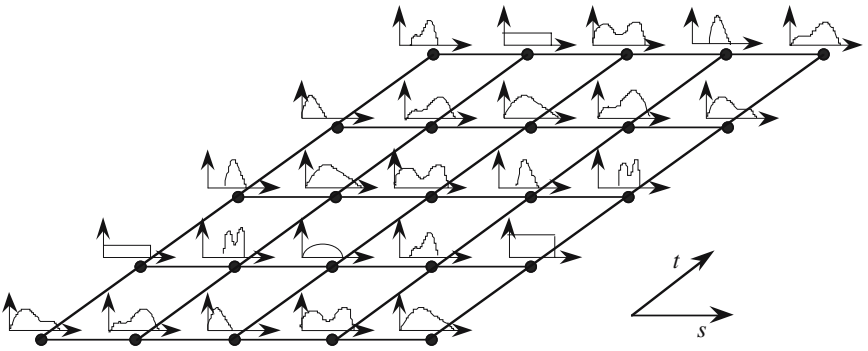


Figure 21. An illustration of mortality pdf $f_S(m)$ across space-time.

pdf in Fig. 21 structurally belong to the S/TRF representing mortality distribution across space-time. The S/TRF definition includes simultaneously all pdf that are considered spatiotemporally interconnected. The S/TRF governing rules are *consistent*--the realizations are the confluence of agreements concerning what is logically and epidemically consistent. Also, the S/TRF model allows for the existence of the so-called *observation-effect*: actualization of a specific potentiality (mortality realization), when a specific set of observations becomes available.

In SEP, the systematic collection and analysis of multi-sourced information was a critical part of a process aiming at increasing our understanding of the space-time characteristics of the Black Death epidemic distribution. In Table 2 we list the database locations where various kinds of data were available. In accordance with the epistemic approach discussed in previous chapters, the significance of the data depends on the way the human brain extracts meaning from them. Therefore, the data were properly evaluated (see, also, Chapter III), and depending on the situation (information reliability, minimal time uncertainty sources, downscaling considerations, valid inferences, and spatiotemporal variability), a decision was made to use the data that were available at a certain number of geographical locations and ignore the data available at others (Appendix A). The minimum time information for a place to be entered into the SEP modelling database consisted of the beginning of the epidemic, its end, or some event occurring during the outbreak. Dates such as September 29, 1348, September 1348, or fall of 1348 qualified a place for entering the database. Just mentioning outbreak during 1348 was considered too vague information to be of any value. If the place of plague interest had too many conflicting dates, such as Copenhagen, it was ignored. When information was available for both the town and its region, e.g., as was the case with Cuxham and Oxfordshire (UK), the better documented of the two was used.

As was discussed in previous chapters, important information sources concerning the spread of the epidemic include contemporaneous written records and the land topography of the infected region under consideration (e.g., the epidemic was absent in many mountainous areas). It was also mentioned with due emphasis that

Table 2. Number of locations in the database where information was available.

Country	Used	Not used	Total
Austria	7	1	8
Belgium	8	5	13
Croatia	3	0	3
Czech Republic	1	1	2
Denmark	4	2	6
France	92	27	119
Germany	35	8	43
Gibraltar	1	0	1
Ireland	13	7	20
Italy	43	6	49
Norway	15	1	16
Poland	2	2	4
Portugal	6	8	14
Spain	50	24	74
Sweden	10	1	11
Switzerland	18	2	20
The Netherlands	4	1	5
United Kingdom	47	76	124
Total	359	172	531

contemporaneous written records of the Black Death epidemic are scattered and scarce. As a result, in the context of the TGIS technology, a considerable amount of effort was dedicated to the acquisition, evaluation, and taxonomy of the information sources, and the subsequent formulation of the associated $\mathcal{S}$-KB. The specification of the pdf, $f_{\mathcal{S}}(m)$, across space and time is made possible with the help of the multi-sourced Black Death evidential support that has been outlined in Chapter III (and described in more detail in Appendix A). Depending on the discipline that generated the Black Death data, these pdf can be constructed using a variety of techniques. A few of these techniques are reviewed below.

a. Direct Techniques

The TGIS technology used by the SEP requires spatiotemporal input about epidemic casualties. The region of interest is Western Europe and the time period of concern is September 1347 to June 1351. As regards TGIS *coding*, each record is a vector of size 8: name, latitude, longitude, month, year, and three parameters to specify monthly mortality and its uncertainty. These parameters include: a code to indicate the type of distribution (spare place, monthly mortality, land desertion, or priest mortality); and two parameters for the distribution, e.g., the mean and the variance of a normal probability law (if the place was spared, the parameters were ignored). Information about casualties is scarce, usually of unknown accuracy,

and never in the form of monthly death rates relative to the local population at the beginning of the month. Hence, all mortality values had to be calculated from interdisciplinary information sources (Chapter III), the most favorable of them being records of monthly fatalities and population size (at the beginning or the end of the epidemic), which allow the straightforward calculation of monthly mortalities at every locality of interest. For numerical illustration, Table III.1 demonstrated the steps involved in the derivation of monthly mortality values at the city of Givry (France). The next step is the calculation of the mortality pdf, $f_S(m)$, from the preceding temporal mortality distributions.

The step-by-step procedure is outlined in Fig. 22. At each geographical locality $\boldsymbol{s}$ of interest we blend various interdisciplinary sources to generate monthly mortality values (such as those in Table III.1)--see box (*a*). From these values we construct the temporal mortality distribution, see box (*b*). At each time t_k the corresponding mortality random field is stochastically characterized by a pdf—see box (*c*). This pdf, say $f_S(m) = f_S(m; \boldsymbol{s}, t_k)$, is assumed to have a mean equal to the calculated value of the temporal mortality distribution at t_k and a standard (std) deviation[8] proportional to the mean. In practical applications we considered three levels of uncertainty, as follows:

- Minimal uncertainty: There is a reasonable amount of information about all the assumptions and values that are part of the calculations resulting in a monthly mortality value or a proxy. In this case, the std deviation--i.e. the square root of the variance--was assumed to be equal to $0.05 \times$ mean.
- Medium uncertainty: At least one parameter is not known, typically the global mortality $G_{\boldsymbol{s}}$, which may require borrowing a value from a neighboring place or using a global value for the specified region. In this case we set the std deviation equal to $0.1 \times$ mean.
- Maximum uncertainty: A minimum amount of information is available about the locality of interest, typically the date of the beginning of the epidemic, $T_{\boldsymbol{s},o}$,

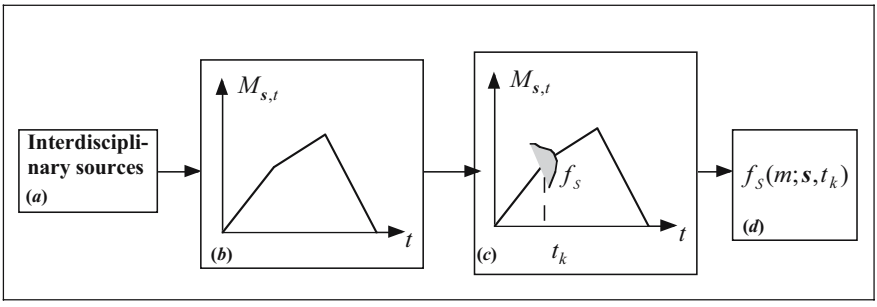


Figure 22. Direct generation of mortality pdf.

[8] Which expresses the uncertainty associated with the mortality value.

and the population size, $P_{s,o}$. In such cases, the std deviation was taken to be equal to $0.2 \times$ mean.

The reader may appreciate an illustration of the above procedure involving empirical techniques with the help of a few numerical examples. An important modelling element that these examples, as well as the ones which will follow, can help demonstrate is that, in order to mitigate our ignorance concerning certain aspects of the Black Death mortality distribution we must ask substantive questions, collect adequate information, and use the appropriate reasoning mode that will allow us to gain valuable insight and meaning.

Example C.1. Consider the city of Givry (France). Givry is one of the very few places in which there is information about the population level at the beginning of the epidemic and rather detailed accounts of all the deaths within the city boundaries[9]. According to the preceding discussion about uncertainty levels, the std deviation of mortality values was set equal to $0.05 \times$ mean, i.e., $\sigma_M(\boldsymbol{s},t) = 0.05\,\overline{M_{s,t}}$. In this case, Table 3 presents the steps that lead to the calculation of the mortality pdf across space-time (notice that the values in Table 3 are the ones that are coded into the TGIS/BMElib computer library; Section II.E.b). It is noteworthy that stochastic theory (Chapter II) allows the mortality pdf to have an arbitrary shape. However, in most localities the data available indicated a symmetric shape for $f_S(m)$, in which case a Gaussian pdf model was usually assumed at the specificatory stage.

Example C.2. This example is concerned with the trivial case of an epidemic-free region. E.g., the high elevations of the European continent never experienced

Month	Mortality, $M_{s,t}$		
	Pdf, f_S	Mean, $\overline{M}$	Std. Dev., σ_M
August	Gaussian	4.2	0.2
September	Gaussian	15.9	0.8
October	Gaussian	11.0	0.3
November	Gaussian	2.7	0.1

Table 3. Mortality pdf for Givry in 1348 (France; longitude=4.750 degrees, latitude = 46.783 degrees, T_o = August 1, 1348).

Month	Mortality, $M_{s,t}$
January	0

Table 4. Mortality for a high Maritime Alps mount in 1348 (longitude=7.2 degrees, latitude=44.05 degrees).

[9] For more historical details about the case of Givry the reader may want to review Chapter III and references therein.

the Black Death, because of the lack of population in place to be infected. SEP modelling restricted these cases to the Pyrenees region between France and Spain, and the Alps area from France to Austria. Table 4 depicts the trivial coding of mortality for one mount along the French Alps.

In all epidemic-free cases encountered, a utility computational algorithm automatically prepared the corresponding information bases for subsequent insertion into the TGIS computer library. Note that plague-free locations were not the onlyones to have mortality equal to zero in the computer coding. Considering that there existed a single infection period during the 1347-51 outbreak of the epidemic (Scott and Duncan 2004: 45), every infected place was plague-free before and after this period. E.g., in Givry (Example C.1 above), there was no infection prior to the month of August and after the month of November of the year 1348.

b. Indirect Techniques

One of the advantages of the TGIS software is that it can readily process interdisciplinary S-KB in the form of probability distributions, interval data, fuzzy sets, etc. In Chapter III it was pointed out that many of the Black Death information sources do not include *monthly* mortality data. Instead, some evidence is available in terms of total population or global mortality, some sources involves ecclesiastical records, some other databases involve land desertion rates, etc. Below we consider several representative situations of using ERF modelling to generate monthly mortality distributions, as well as transferring information about land desertion and clergy mortality into monthly population mortality in a spatiotemporal domain.

ERF-Based Techniques

In Black Death studies one can take advantage of the logical links that tie theoretical models to observations in order to gain valuable insight about the epidemic. Here we use these links to illustrate the implementation of the ERF models in the Black Death study to generate mortality pdf, $f_S(m)$, across space and time. Once more the step-by-step procedure is outlined in Fig. 23. The only difference with Fig. 22 is box (*a*), i.e., instead of calculating the monthly mortality values directly from the interdisciplinary evidence, we generate them with the help of ERF models. It should be noticed that the relevance of the ERF model within the data preparation is its capability to decompose global mortality into its monthly components, in the context of the mortality pdf generation process of Fig. 23.

First, we will use ERF models to generate mortality distributions—see box (*b*)--and to demonstrate the very good agreement between the linear ERF model of Eq. (9a) and the non-linear model of Eq. (10). In addition, an excellent fitting of both models to the mortality data was observed. In Fig. 24a we look again at the

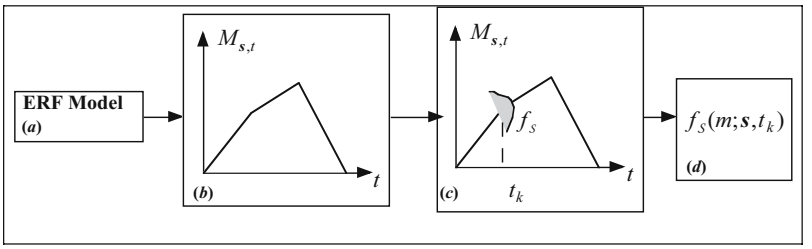


Figure 23. An outline of the procedure generating mortality pdf using ERF models.

case of Givry (France). The reason we consider Givry this time is that it can help us demonstrate that the ERF models can generate values of monthly mortality in close agreement with the actual ones. Let us be more specific. Givry has the advantage--as far as SEP modelling is concerned--of being the only city in Europe for which we obtained daily accounts of plague fatalities (Table III.2)--as we saw above, from these accounts one can prepare a realistic plot of monthly mortalities using 1-month periods starting on July 28, 1348 (Table III.1). This means that Givry does not really need the ERF models to derive monthly values of mortality. We run the models only to show that they can generate values of monthly mortality in close agreement with the actual ones. Of the five ERF model parameters, only two of them are known, in this case: the serial generation time $\tau = 20$ days was conveniently selected as a round up number close to the 22 days that characterize the hemorrhagic plague (Scott and Duncan, 2001: 30); and the pre-plague population has been estimated at $P_{s,0} = 2000$ residents. The other three parameters ($I_{s,\tau}$, K_s, and f) were determined by trial and error. The models' fitting to the data, see Fig. 24a, is remarkable. The agreement between models (9a) and (10) is so good that it is hard to distinguish between the two curves. Fig. 24b addresses another common situation: unknown pre-plague population, $P_{s,0}$. This figure shows the results obtained running the ERF model for the same city of Givry, this time ignoring the actual estimated population and using an arbitrary value of 100 residents. We could have used another city for which we really do not know the actual $P_{s,0}$, but, again, we did not do it because Givry offers the possibility of comparing synthetic results to actual data. Once more, there is excellent agreement between the linear and non-linear ERF models and between them and the real data. As was expected, a drop in the population by a factor of 20 (relative to the case in Fig. 24a) resulted in a drop of the number of infecteds during the first period, $I_{s,\tau}$, by the same factor, i.e. from 115 to $115/20 = 5.7$. The other parameters remained the same ($K_s = 3.9$ and $f = 0.315$). Because we are not interested in actual number of fatalities but in mortality rates per 100 residents, this is an important practical result that allows to considerably extent the applicability of the models even if the actual city population is unknown. As a whole, Fig. 24 brings to mind one of the characteristics of conditional modeling: usually there is a large combination of parameters to be considered. For convenience, we decided

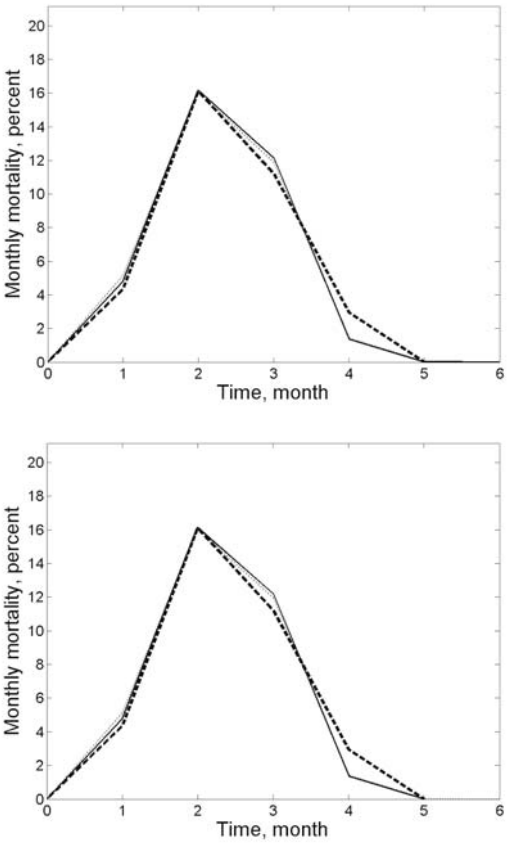


Figure 24. Modelling of Black Death monthly mortality distribution at Givry, France: (a) using the actual population $P_{s,0} = 2000$ residents; (b) ignoring the real population and using an arbitrary reference value $P_{s,0} = 100$ residents. The dashed line denotes the actual data, the solid line the prediction by the non-linear ERF model, and the dotted line the prediction by the linearized ERF model.

to use a *standardized* population of 100 residents for all places even if we knew their actual populations. We also set the serial generation number, $\tau = 20$ days, thus leaving three parameters to satisfy two constraints: the parameters are $I_{s,\tau}$, K_s, and f; and the constraints are Δ_s and G_s. The under-determined problem was solved each time by keeping the solution that led to an approximately symmetric monthly mortality distribution (the symmetric choice is in agreement with existing knowledge bases). The fact that SEP modelling is interested in the shape of the curve and not in the particular combination of the parameters producing equivalent distributions has played to our advantage.

Since, as was demonstrated above, the ERF modelling produces very good results for the box (*b*) of the procedure outlined in Fig. 23, we applied it to other localities that suffered from the Black Death epidemic to produce informative monthly mortality distributions, such as those in Fig. 24. In the following example additional insight is gained in terms of the disease situations in the cities of Piacenza (Italy) and Jérica (Spain). In this example we proceed beyond box (*b*) to boxes (*c*) and (*d*) of the procedure.

Example C.3. In the case of Piacenza (Italy), the available information is $T_{s,o}$ (July 1348), G_s (33%), and $P_{s,o}$ (about 20,000 residents). Following the steps described in Fig. 25, the plague duration Δ_s was estimated by employing the scaling law of Eq. (1), and then the Δ_s and G_s were used to condition the solution of the ERF models to generate the Black Death temporal mortality distribution displayed in Fig. 26. This last figure corresponds to the box (*b*) of the procedure in Fig. 23. Next, the boxes (*c*) and (*d*) of Fig. 23 correspond to the generation of the pdf, $f_S(m)$, in Table 5 for each month. A medium degree of uncertainty was assumed--which is used in the calculation of the mortality pdf $f_S(m)$ from the temporal mortality distributions above (see last two columns in Table 5). At time t the corresponding pdf is Gaussian with a mean equal to the calculated value of the temporal mortality distribution at time t and a std deviation (expressing the uncertainty associated with the value) proportional to the mean.

In the preparation of the entire database we did not run the ERF model for every single location. By rounding the duration to whole months and the mortality to multiples of 5%, the combination of possible (Δ_s, G_s) pairs was reduced to the finite number of cases listed in Table III.5. Mortalities for all other places were assumed equal to those with the same combination of (Δ_s, G_s) values. In this

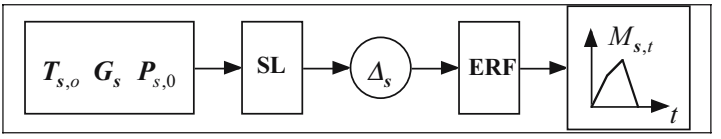


Figure 25. Procedure leading to the generation of monthly mortality values at a given locality; SL=scaling law of Eq. (1).

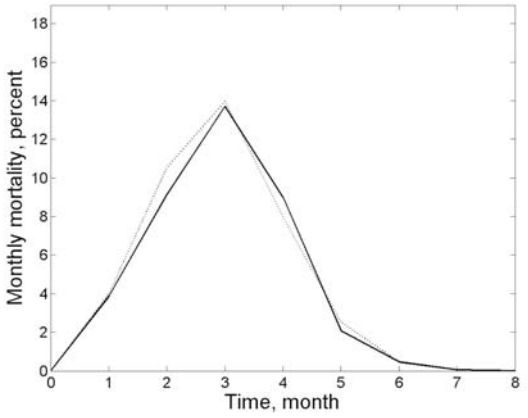


Figure 26. Modelling of Black Death temporal mortality distribution in Piacenza, Italy. The solid line denotes the prediction by the non-linear ERF model and the dotted line the prediction by the linearized ERF model.

Table 5. Database code for Piacenza, Italy in 1348 using ERF parameters $K_s = 2.7$, $I_{s,t} = 6.5$, and $f = 0.377$ and medium degree of uncertainty.

Month	Mortality, $M_{s,t}$		
	Pdf, f_S	Mean, $\overline{M}$	Std. Dev., σ_M
July	Gaussian	5.3	0.5
August	Gaussian	13.8	1.4
September	Gaussian	15.4	1.5
October	Gaussian	5.3	0.5
November	Gaussian	0.5	0.1
December	Gaussian	0.1	0.1

case, we favored simplicity (combined with epidemic consistency) over purposely preparing slightly different histograms satisfying no particular requirements [10].

Example C.4. While Givry (France) was the closest to ideal case for mortality modelling purposes, the city of Jérica (Spain) was at the other end of the spectrum, offering the minimum amount of information. What follows is a discussion of the reasoning process that led to the preparation of Table 6. The minimal information required for coding a place into the SEP database was to have a time reference with a precision of at least one season. Such is the case of Jérica where according to Ubieto (1997: 85) the plague arrived in October of 1348 ($T_{s,o}$). For SEP modelling purposes, coding at any place lacking monthly mortality values requires information about the parameters $P_{s,0}$ and G_s. Jérica was a provincial city, definitely not found in the comprehensive list of http://scholar, which includes localities with at least 15,000 residents. Nevertheless, assuming a population of $P_{s,0}$= 15,000 people for Jérica, the implementation of the SEP scaling law of Eq. (1) predicted that Black Death lasted $3.025 + 0.132 \times 15 \approx 5$ months. On the other hand, by comparison to other cities in the area, most likely Jérica had a population of at least $P_{s,0}$= 500 residents. For such a population, the scaling law predicted that Black Death lasted $3.025 + 0.132 \times 0.5 \approx 3.1$ months. Hence, a plague duration of $\Delta_s = 4$ months cannot be far from the truth, given the scattering in the regression scheme. Jérica was at the time part of the Kingdom of Aragon, for which Gottfried (1983: 52) gives a global mortality of $G_s = 30\%$ (from the beginning to end of the epidemic). Having values for the parameters Δ_s and G_s, we can now make use of the ERF model to generate monthly mortality values. According to

[10] In fact, we take simplicity into consideration always in a subordinate way to beauty.

Table 6. Database code for Jérica in 1348 and 1349 (Spain; longitude=-0.600 degrees, latitude=39.945 degrees)

Month	Mortality, $M_{s,t}$		
	Pdf, f_S	Mean, $\overline{M}$	Std. Dev., σ_M
October, 1348	Gaussian	4.0	0.8
November	Gaussian	16.4	3.9
December	Gaussian	17.1	3.4
January, 1349	Gaussian	2.3	0.5

Table III.5, the values of the remaining three parameters required by the model are $K_s = 4$, $I_{s,\tau} = 5$, and $f = 0.305$. Under these conditions, the predicted monthly mortality values are 4.0, 16.4, 17.1, and 2.3. Note that Jérica is definitely a place characterized by the highest uncertainty level, which, according to Section C.a above, implies that the std deviation for the Gaussian model of uncertainty should be $0.2 \times$mean. The procedure above is summarized in Table 6, which is the coding actually inserted into the BMElib. Other localities throughout Europe that possess more than the minimal temporal information required fewer calculations to derive the mortality pdf, $f_S(m)$. Note, also, that if the epidemic duration is given, information about $P_{s,0}$ becomes immaterial, and the use of Eq. (1) turns out to be unnecessary.

The Case of Ecclesiastical Records

We consider the important case in which specificatory information is available in the form of ecclesiastical records linked to the Black Death epidemic. More specifically, let $C_{s,t}$ be the space-time random field representing benefited clergy mortality in the region of interest. Assume that the pdf of $C_{s,t}$, $f_C(c)$, is Gaussian with given mean and std. deviation, i.e. $f_C(c) \sim N(\overline{C}, \sigma_C)$. On the basis of the literature (e.g., Ziegler, 1969: 127-128) and our own study of the available information, a conversion factor from clergy mortality to general population mortality was derived that is expressed as a random variable uniformly distributed between the values 0.75 and 1.1. Hence, the pdf of the regional population mortality $M_{s,t}$ given $C_{s,t}$ is $f_S(m|c) = \frac{1}{0.35c}$ (when $0.75c \le m \le 1.1c$), and $= 0$ (otherwise). In this case, the integral

$$f_S(m) = \int_{m/1.1}^{m/0.75} dc\, f_C(c)\, f_S(m|c) = \frac{1}{0.35} \int_{m/1.1}^{m/0.75} dc\, N(\overline{C}, \sigma_C)/c \qquad (21)$$

will be the monthly mortality pdf sought at each point $\boldsymbol{p} = (\boldsymbol{s}, t)$ in the spatiotemporal manifold under consideration. Next, let us study a specific numerical example involving an important set of ecclesiastical records.

Example C.5. In this example we consider the ecclesiastical mortality situation in Bath and Wells (UK)[11]. In Section III.D.b we discussed the precious information left to posterity by the English Church, and in Table III.4 we summarized the technical procedure generating mortality values for the benefited clergy. In light of this information, we assessed the uncertainty level in the calculation of the clergy mortality rates as minimal, i.e. $\sigma_M(\boldsymbol{s}, t) = 0.05\,\overline{M_{\boldsymbol{s},t}}$ (with a minimum value of 0.1%). In this case, the steps leading to the calculation of the clergy mortality pdf, $f_C(c)$, at various times are conveniently tabulated in Table 7 and plotted in Fig. 27 for the month of April. In the same figure we plotted the population mortality pdf, $f_S(m)$, which was calculated with the help of Eq. (21).

The Case of Land Desertion

This is primarily the case of land desertion data in Germany associated with the epidemic. In particular, let $A_{\boldsymbol{s},t}$ be the percentage of deserted area (cultivated land and villages) at the geographical region $\boldsymbol{s}$ during the month t. The $A_{\boldsymbol{s},t}$ is a random field that obeys a Gaussian law, $f_A(c) \sim N(\overline{A}, \sigma_A)$, whereas the ratio

Table 7. Clergy mortality for the diocese of Bath and Wells in 1348 and 1349 (UK; longitude= -2.859 degrees, latitude= 51.060 degrees).

Month	Clergy mortality, $C_{\boldsymbol{s},t}$		
	Pdf, f_C	Mean, $\overline{C}$	Std. Dev., σ_C
October, 1348	Gaussian	1.3	0.1
November, 1348	Gaussian	6.1	0.3
December, 1348	Gaussian	9.2	0.5
January, 1349	Gaussian	8.4	0.4
February, 1349	Gaussian	7.0	0.4
March, 1349	Gaussian	7.8	0.4
April, 1349	Gaussian	7.0	0.4
May, 1349	Gaussian	0.8	0.1

[11] Again, for more historical details about the case of Bath and Wells the reader is referred to Chapter III.

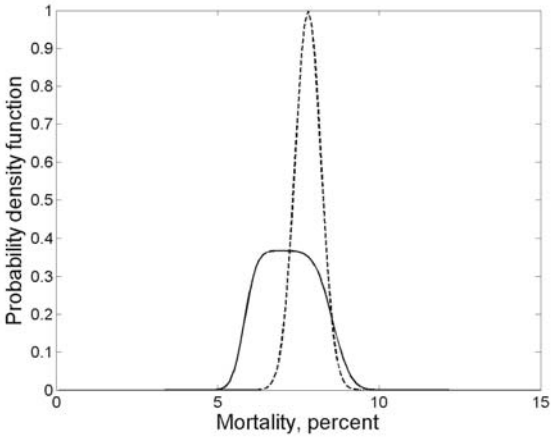


Figure 27. Mortality at the diocese of Bath and Wells (UK) in April 1349. The solid line denotes the population mortality pdf f_S of Eq. (21), and the dashed line the ecclesiastical mortality pdf f_C for the same month (see Table 7).

$R = M_{s,t} / A_{s,t}$ follows an asymmetric triangular distribution, $T(l,h,u)$, which is assumed space-time independent (Fig. 28) with a pdf of the form

$$f_R(r) = \beta \begin{cases} (r-l)/(h-l), & l \le r \le h \\ (u-r)/(u-h), & h < r \le u, \end{cases} \tag{22}$$

where $\beta = 2/(u-l)$. As a result, the pdf of $M_{s,t}$ is given by

$$f_S(m) = \beta(\sqrt{2\pi}\sigma_A)^{-1}\{\int_l^h dx\, e^{-(m/x-\bar{A})^2/2\sigma_A^2}(x-l)[(h-l)x]^{-1} + \int_h^u dx\, e^{-(m/x-\bar{A})^2/2\sigma_A^2}(u-x)[(u-h)x]^{-1}\} \tag{23}$$

which is a useful analytical formula that generates mortality pdf at any space-time point $\boldsymbol{p} = (s,t)$. For illustration, Eq. (23) is implemented in the case of the following numerical example.

Example C.6. This is the land desertion case of Erfurt (Germany). As was discussed in Section III.D.d, we employed land desertion as a proxy variable to compensate for the less abundant information about Black Death mortality in Germany. Table 8 presents the results of the ERF modelling process that was based

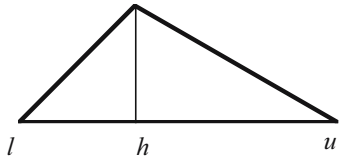


Figure 28. The pdf of the ratio R.

Table 8. Land desertion for the city of Erfurt in 1350 and 1351 (Germany; longitude=11.045 degrees, latitude=50.796 degrees).

Month	Land Desertion, $A_{s,t}$		
	Pdf, f_A	Mean, $\overline{A}$	Std. Dev., σ_A
August, 1350	Gaussian	2.9	0.3
September	Gaussian	7.9	0.8
October	Gaussian	14.9	1.5
November	Gaussian	15.1	1.5
December	Gaussian	5.9	0.6
January, 1351	Gaussian	1.7	0.2
February	Gaussian	0.3	0.1

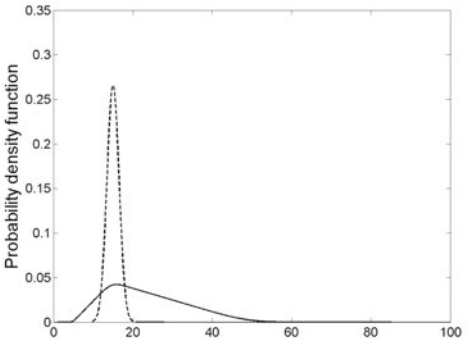


Figure 29. Erfurt, Germany (October, 1350). Land desertion pdf--dashed line (Gaussian with mean 15% and std. deviation 1.5%). Population mortality pdf according to Eq. (23)--solid line (non-Gaussian).

on the following assumptions: the epidemic lasted about 7 months contributing to a land desertion of 40%, and the level of uncertainty was ranked as medium, i.e. $\sigma_M(\boldsymbol{s},t) = 0.1\,\overline{M_{s,t}}$ (with a minimum value of 0.1%). Just as in the case of ecclesiastical mortality, the land desertion values in Table 8 require transformation to population mortality values. This transformation is done with the help of Eqs. (22) and (23), which made possible the calculation of the population mortality pdf, $f_S(m)$, across space and time. An example is shown in Fig. 29. Note that while the original land desertion pdf is Gaussian, the resulting mortality pdf is clearly non-Gaussian.

Plots like the one of Fig. 29 were produced at all places in Germany where values of global mortality G_s were not available.

D. Some Thoughts on the SEP Integration of Black Death Concepts and Data

As we maintained in Section A, the $\mathcal{G}$-formulated knowledge (conceptual, abstract, core, etc.) will be used to generate the pdf model $f_{\mathcal{G}}$ (Section B), whereas the $\mathcal{S}$-coded evidence (instrument- or survey-based etc.; Section C) will be used to update $f_{\mathcal{G}}$, thus leading to the final pdf model of the Black Death mortality, $f_{\mathcal{K}}$, across space and time ($\mathcal{K} = \mathcal{G} \cup \mathcal{S}$), see Chaper V. Although treated separately, from the SEP perspective the two major Black Death knowledge bases ($\mathcal{G}$ and $\mathcal{S}$) form an *integrated* whole[12]. In Section II.A we argued that the prime focus of scientific interdisciplinarity is to integrate concepts and not merely data—the latter being numbers that obtain meaning in the context of a sound theory. Staying close to the multi-sourced data, without at the same time having a clear theoretical picture of the situation, would give the impression that we try to be as *ad hoc* as possible[13]. Rather, our goal is to go as far beyond the Black Death evidential base as cognitively possible. In our view, an epidemiologist should be close to particulars, but not too close to miss seeing their overall importance. Furthermore, we are well aware of the fact that the observers have a significant role to play in the process of observation. This is called the "observer's effect" and its consequences are often recognized not only by the observers but by the observed, as well[14].

The paradigm choice can have significant consequences in the study of the Black Death epidemic. As Cipolla (1981: 9) in his study of the plague in Italy has warned us, "Actually, if the prevalent paradigm is totally alien to the reality under scrutiny, the investigator may not even notice what passes before his eyes; … if the investigator does take notice of the phenomenon, he may be induced to discard it as irrelevant." The SEP is a paradigm that seeks to prepare the public health modeller to *notice* and *appreciate* essential entities associated with the disease distribution (space-time disease variation, mortality dependence, general vs. specificatory data sources, etc.). Methodology is the core element of the paradigm that underlies all research efforts, whereas the various technical tools are ancillary and may vary, depending on the situation. E.g., while statistical tools are useful in a variety of technical ways (calculating the center and spread of data distributions,

[12] The integration of ideas and instruments plays a dominant role in creative music composition, as well. In the words of Peter Ilich Tchaikovsky: "So I conceive the musical idea and its orchestration simultaneously. Consequently, when I was writing the Scherzo of our symphony, I imagined it exactly as you heard it. It is unthinkable played any other way than pizzicato" (Garden and Gotteri, 1993: 200).

[13] At the additional risk of blurring the line between thought and routine.

[14] Remarkably, the observed have testified the sometimes dramatic feelings their experiencing of the "observer's effect" has generated. Merata Mita (1989: 30), e.g., maintained that, "We have a history of people putting Maori under a microscope in the same way a scientist looks at an insect. The ones doing the looking are giving themselves the power to define."

evaluating relationships between different datasets, assessing how closely the data conform to an ideal statistical law, etc.), they cannot generate scientific meaning (e.g., they cannot interpret the data physically and derive logical conclusions as to their substance). The latter is the task of the SEP methodology, which evaluates the various epidemic databases, arranges them in logical relationships, contrives an approach to manifest the meaning behind the databases, and generates results that improve our understanding of the epidemic.

The SEP theories and models should be judged by what they do, by the kind of further thinking they engender, not by their conformity to some excessively simple-minded version of common sense. Thus, the debate is not whether theorizing of this sort is philosophically legitimate, but whether it is useful, whether it can bring enlightenment to our thinking about Black Death rather than confusion.

Chapter V - Spatiotemporal Mapping of the Epidemic

"We had taken it for granted that maps were faithful reflections of reality; but we were somehow amazed when reality turned out to be true to the maps."
J.N. Wilford

A. Maps of the Epidemic, Their Interpretation and Findings

a. General Comments

Predicting the course and geographical spread of an infectious disease by means of space-time *mapping* is critical in any effort to understand some of the disease's main characteristics, to generate scientific hypotheses about the disease, and to control it. Indeed, a large part of "what can be known" about an epidemic distribution is precisely what can be seen on a map (topographical relations, disease correlations across space-time, propagation velocity, etc.), which is a kind of visual language for epidemic sciences. A general SEP was outlined in Chapter I that established a methodological framework of public health research and epidemic modelling in combined space-time domains. According to this framework, formal rules and tools can be used efficiently in map generation only when content is taken into consideration, a network of cross-checking techniques can be implemented that lead to collective reliability, map interpretation depends on the logical mind, reasoning skills, and objectivity of the public health researcher, etc.

Henry Poincare maintained that, "predictable facts can only be probable". In view of uncertainty, stochastic theory (Chapter II) suggests that one should give up the futile attempts to make exact (deterministic) predictions in favor of conditional (stochastic) predictions of epidemics. The predictions generated by stochastic theory are conditioned by a number of factors: the interdisciplinary knowledge bases available (Chapter III), the space-time heterogeneity characteristics of the disease distribution (Chapter IV), the conceptual and technical uncertainty associated with epidemic modelling, the prediction accuracy sought, and the objectives of the study. Thus, SEP provides public health scientists not only with informa-

tive spatiotemporal maps, but also with a sound theory and a mode of reasoning that are essential for scientific map-making and validation of contradictory data.

As we saw in previous chapters, our data search has revealed numerous contemporaneous sources of the Black Death epidemic, many of which are scattered and scarce. Also, these records are drawn from a variety of disciplines. Thus, a considerable amount of our effort was dedicated in the acquisition, evaluation, and taxonomy of these information sources, and the subsequent formulation of the corresponding BME functions of the TGIS technology. In the case of Black Death, the transformation of the multi-sourced databases into a quantitative form by the SEP techniques led to the creation of the following (see also Figure IV.1):

(*i*) Empirical laws of disease variables (e.g., the scaling law of Section IV.B.a), which can help us to assess the validity of hypotheses about the nature of the epidemic, especially in situations characterized by a considerable lack of information.
(*ii*) Epidemic models with properties that can be precisely mathematically analyzed (e.g., the ERF model of Section IV.B.b).
(*iii*) Correlation functions that express the structural patterns and dependencies of disease variables across space and time (e.g., the functions of Section IV.B.c).
(*iv*) Tabulations of multi-sourced information concerning essential parameters of the disease distribution (e.g., the Tables of Section III.D.c and Appendix B).
(*v*) Plots of probability functions that integrate interdisciplinary knowledge sources and offer a good fit to the site-specific database at each geographical region and time interval of interest (e.g., the mortality probability plots of Section IV.C.b).

In the SEP context, Fig. 1 below is a continuation of Fig. IV.1. As was pointed out in previous chapters, the procedure of Fig. 1 has many salient conceptual and operational layers that, when unmasked, tell a long and interesting story[1]. For epidemic-related theories to be most useful in the $\mathcal{G}$-KB context, they need not only to be evaluated but also to be updated and refined with site-specific information ($\mathcal{S}$-KB). In this sense, a distinction is made between appropriate theory refinement and *ad hoc* adjustments based on inadequate patchwork. Epidemic predictions are visualized by means of highly informative, science-based maps, $M_{s,t}$, in a composite space-time manifold. The generation of these maps relies on a powerful combination of sound theoretical support provided by stochastic theory (Section II.A-D) with modern technological facilities supplied by TGIS (Section II.E). The mathematical notation of the stochastic SEP theory allows us, while doing the practical calculations, to focus on the meaning of the theory. This brings out its conceptual poetry: the romance and fascination are preserved while one learns the formal mathematics of the subject.

[1] The reader may find it interesting to compare the procedure of Fig. 1 with that of Fig. II.6 used in environmental epidemiology applications.

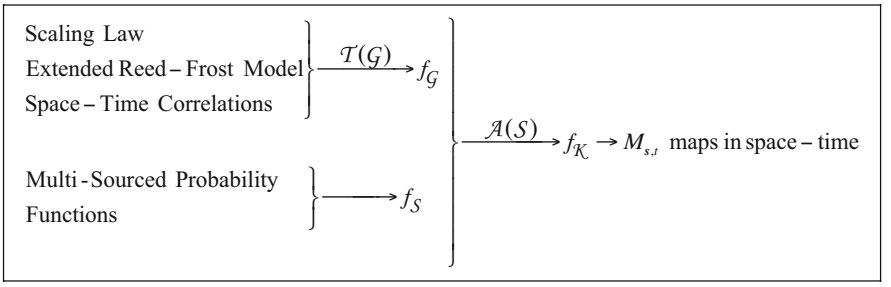


Figure 1. An outline of the procedure leading to space-time maps of Black Death mortality (see, also, Fig. IV.1).

Generally, space-time mapping is concerned with the geographical shape and extent of the epidemic, its temporal evolution, the possible origin of an infectious disease outbreak, the conditions that led to the epidemic, and suggesting ways to control the epidemic[2]. In such a context, epidemic maps should be seen as rigorous representations aiming at informing us as objectively as possible (convey scientific knowledge, discover patterns, offer clues, etc.), rather than as images aiming at affecting us sentimentally (inflicting terror, hatred, sorrow, etc.). The generated maps may also depend on the objectives of the study. E.g., some maps are designed to emphasize highly localized differences in the disease distribution, the goal of some others is to show only broad space-time patterns, whereas the motivation of yet another group of maps could be to offer information regarding disease etiology. In many cases, more information can be extracted from a map than is needed to construct it. Another significant practical advantage of space-time maps is that they bring the results of sophisticated modelling within easy reach of epidemiologists with little or no mathematical experience.

b. Mortality Maps

One way to assess a disease burden is through the number of deaths it causes across space-time, i.e., the *mortality* approach[3]. Mortality maps produced by BME can enable the determination of several useful characteristics of Black Death (e.g., direction and velocity of epidemic spread, prevailing trends and patterns, and relative significance of the different epidemic system components).

The BME technique of SEP (Section II.E.b) was employed to prepare the set of maps in Fig. 2, using the knowledge bases (KB) we constructed with the help of the methods discussed in Chapters III and IV. The BMElib software of TGIS scans these interdisciplinary KB seeking out patterns that can be projected into

[2] As we discuss in previous chapters, space-time mapping may not offer, generally, a definite proof of the actual cause of the epidemic. In certain circumstances, however, it could offer valuable clues in this respect.

[3] Other ways of assessing disease burden also exist, such as in terms of prevalence or in terms of disability caused by a disease, but are not considered here.

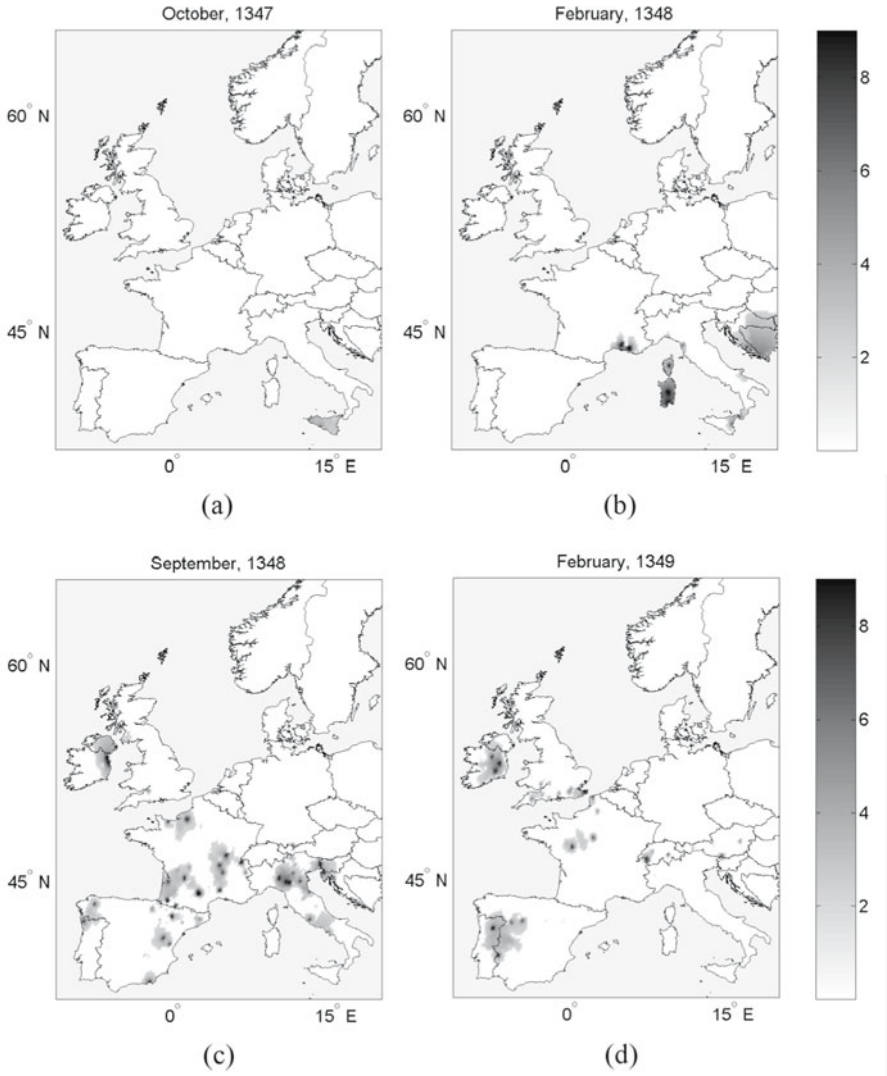


Figure 2. Selected space-time maps for Black Death percentage of monthly mortality (**continues**).

space-time in the most efficient manner possible. The complete set includes 40 monthly mortality maps from October 1347 to January of 1351. Due to space limitations, in Fig. 2 we show only a small subset of the available maps[4]. For details about a locality, the reader is referred to Appendix A.

[4] The reader is invited to visit the website http://www.unc.edu/depts/case/BlackDeath/ for a complete set of maps and color animations of Black Death distribution features.

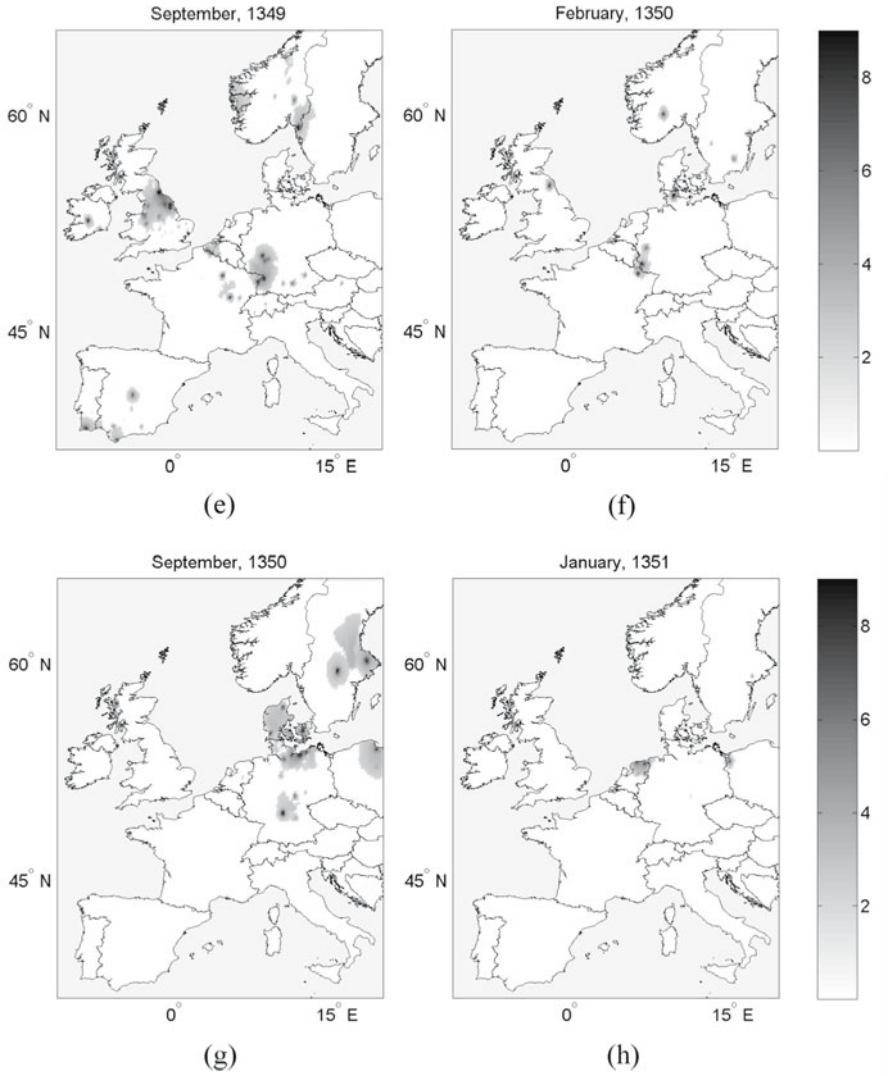


Figure 2. Selected space-time maps for Black Death percentage of monthly mortality (**concludes**).

To our knowledge, Fig. 2 presents the first systematic space-time maps of Black Death mortality during the 1347-51 epidemic. These maps make possible a deeper understanding of the role of space in the mortality of the epidemic and the fluctuation patterns over time. Note that BME can generate the pdf $f_{\mathcal{K}}^{bc}(\boldsymbol{m}_k)$ at each space-time point $\boldsymbol{p}_k$ across Europe, see Eq. (II.33), which provides a complete stochastic characterization of mortality. The mortality values (%) in the

maps of Fig. 2 are the BMEmean estimates, $\hat{\boldsymbol{m}}_{\boldsymbol{k},\text{mean}}(\boldsymbol{p}_k)$, see Eq. (II.35). An assessment of the accuracy of these estimates is provided by the associated estimation error standard deviation, $\sigma_{\mathcal{K}}(\boldsymbol{p}_k)$, defined in Section E.II.b. Given the $f_{\mathcal{K}}^{bc}(\boldsymbol{m}_k)$, other kinds of mortality estimates can be derived, as well; see, e.g., Table II.13. The specific set of maps in Fig. 2 shows the mortality distributions when the probability that mortality exceeds the 0.001% threshold is greater than 0.65. Several alternative sets of maps can be constructed by choosing different mortality and probability thresholds. These different choices allow one to study different space-time features of the Black Death epidemic and can have certain advantages in showing structure more clearly than previous methods of epidemic representation. In addition, the BME features above demonstrate the technical versatility of the general SEP approach.

There are interesting developments to analyze and observe at the national and regional levels of the epidemic distribution. The maps show that mortality moved throughout Europe in the form of a "wave" or "cloud" of varying intensity and size, depending on the geographical location. The disease visited almost the entire European continent with devastating results (note, e.g., the high mortality levels). Most of the regions of Europe that were not devastated by Black Death were uninhabited areas (due to topography, high mountains, etc.). The territories initially infected covered most of the warmer and drier climates in the south of Europe. Maps like those in Fig. 2 could enlighten certain issues, such as the differences in mortality from one region to another, the possible origins of the epidemic, its various fronts throughout Europe, its duration and strength, etc. Next, with the help of the maps of Fig. 2 we make some interesting observations regarding the Black Death evolution characteristics in specific regions of Europe.

In Italy the epidemic started in Sicily in October 1347 (the very first region in Europe). By the beginning of 1348 it had spread to several Italian ports. The epidemic reached its peak during the summer of 1348, moving to Austria and Switzerland. The Black Death epidemic disappeared in Italy early in April 1349.

From Austria the epidemic moved to Germany and the Czech Republic (Fall 1349). In Austria the epidemic ended in October 1349.

In Scandinavia, the epidemic started in April 1349 (port of Oslo), and then moved in all directions. The Black Death ended in Scandinavia in 1351.

In France the epidemic originated at the port of Marseille in December 1347. It then moved in all directions. Another front of the epidemic started independently in the northern part of France in June 1348 (at the same time the epidemic made its appearance at some southern English ports). By July 1348 the two well-established fronts in France were moving in opposite directions and they met each other in November 1348. After that the epidemic weakened considerably during the winter (it almost disappeared), only to reappear during the following summer along the borders with Belgium (May 1349) and with Switzerland (June 1349; at about the same time the epidemic entered Germany). In France the epidemic disappeared in April 1350.

In the Iberia Peninsula the first Black Death front appeared in April 1348 (Balearic Islands). An eastern front of the epidemic came from France in May

1348. At the same time a third front started in the northwestern part of Spain (Santiago de Compostela; presumably from pilgrims), which then moved south into Portugal. The three fronts eventually met in central Spain around October 1348. Then the epidemic almost disappeared during winter, but it gained considerable strength the following summer, starting in the Granada region. The epidemic ended early 1350.

Germany was hit from different directions. Black Death started at the border with Austria in July 1348 but then disappeared, so that Germany was essentially epidemic-free until June 1349. At this time the epidemic entered Germany from three points: the borders with France, Austria, and Switzerland. These fronts eventually were reinforced by a front that entered Germany via Luxemburg in early 1350. Then the epidemic moved east, north, and west (it entered the Netherlands in June 1350). In Germany, Black Death ended after January of 1351.

In the British Islands, Black Death first appeared in southern ports in June 1348, and then moved north. It disappeared in March 1350. In Ireland, the epidemic started in August 1348 in the eastern part of the country. It subsequently moved west and then disappeared in March 1350.

At this point it is worth re-emphasizing that the construction of the maps in Fig. 2 (as well as those that will follow) was made possible because of an important property of stochastic spatiotemporal theory that is not shared by "classical statistics": Stochastic theory rigorously accounts for the critical space-time dependence of mortality values--which classical statistics assumes to be independent--and it possesses powerful techniques that allow it to generate substantive mortality predictions across space and time. The fact that these realistic maps of mortality distribution could be generated by stochastic spatiotemporal theory but not by classical statistics amply demonstrates the superiority of the former over the latter in this kind of epidemic situations. Noticeably, during the last few decades, the main function of the so-called "spatial statistics" discipline has been to translate spatial dependence models developed in other fields (physics, engineering, forestry, meteorology, geostatistics, atmospheric sciences, etc.) into the language of classical statistics. Performed in relative isolation, this kind of translation had several rather restrictive consequences: focusing on purely statistical data processing and ignoring several important physical knowledge sources and reasoning modes; seeking to fit data to some ideal form of a statistical model; emphasizing form over substance; etc. Only recently there is some evidence that the spatial statistics discipline is realizing the drawbacks of this approach and is making an effort to walk "the well traveled road", to slightly paraphrase Robert Frost's well-known poem[5].

c. Epidemic Elasticity Maps

Among the types of maps that can be useful for epidemic risk analysis purposes are the epidemic elasticity maps. Elasticity ε_M is an indicator that measures the

[5] Frost (1967: 223).

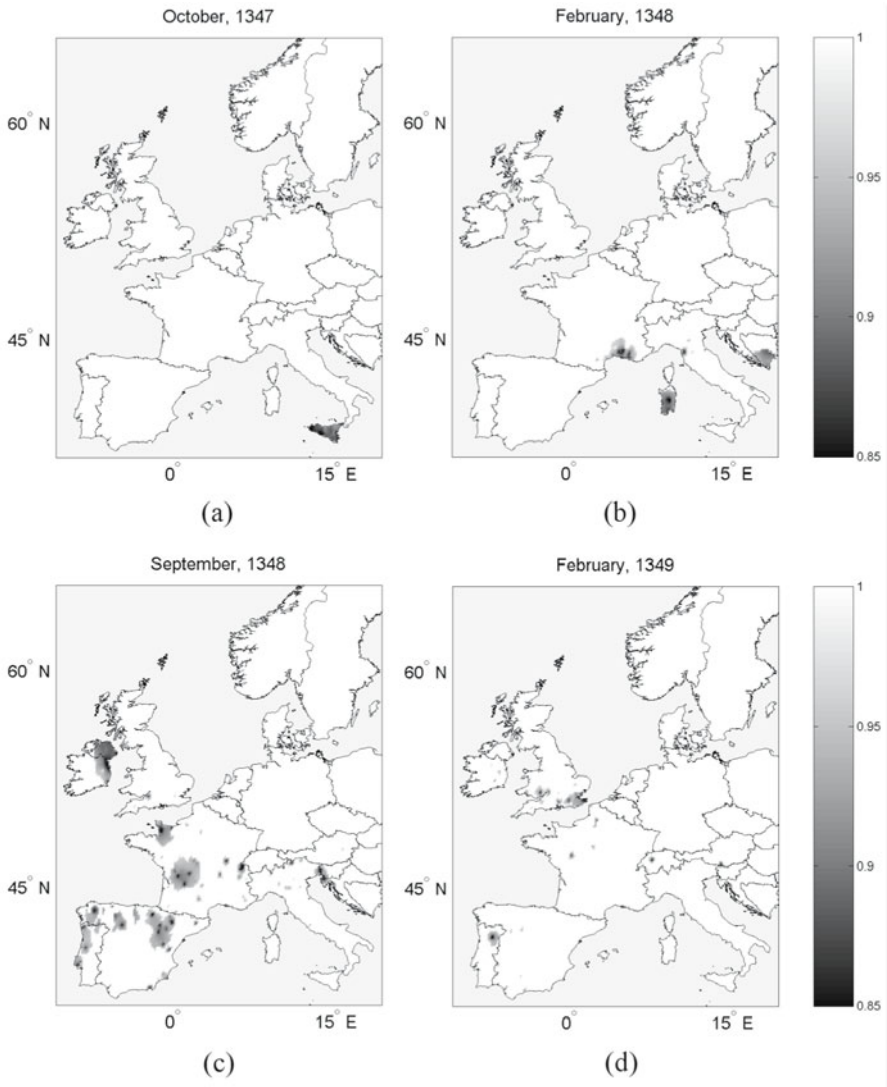


Figure 3. Spatiotemporal variation of the elasticity of the Black Death (**continues**).

ratio of the fractional increase in mortality, $M_{s,(k+1)\tau}$, over the fractional increase in the number of infecteds, $I_{s,k\tau}$; by definition, elasticity is a non-linear function of mortality and it also depends on the geographical factor f (see, Section IV.B.b).

For numerical illustration, direct implementation of Eq. (IV.12) led to the generation of some representative ε_M maps in Fig. 3 using the mortality values in the

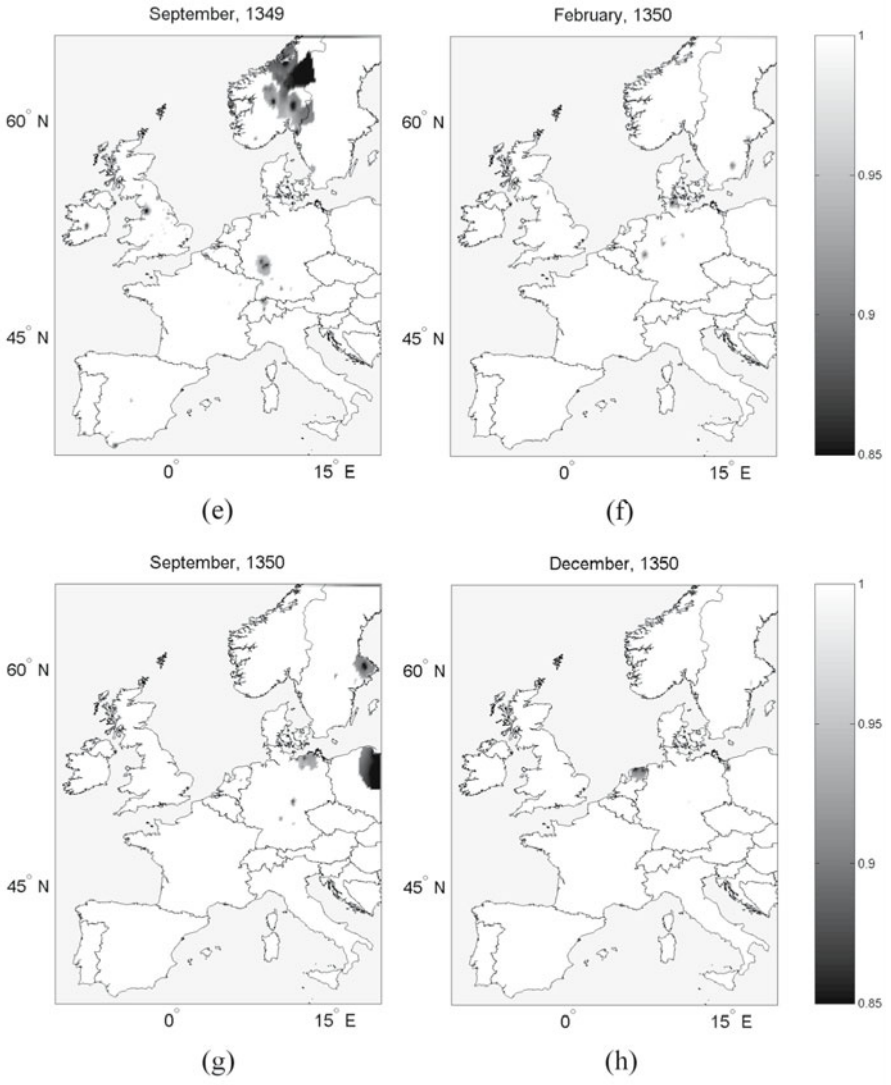


Figure 3. Spatiotemporal variation of the elasticity of the Black Death (**concludes**).

maps of Fig. 2 and the f values calculated in Appendix B (these values vary geographically throughout the 14th century Europe). These maps offer an additional description of the geography and temporal evolution of Black Death dynamics in a epidemic risk assessment context: the larger the ε_M, the smaller the fractional increase in infecteds required to yield a specified fractional increase in mortality; the same increase in the number of infecteds led to larger mortality increases in cer-

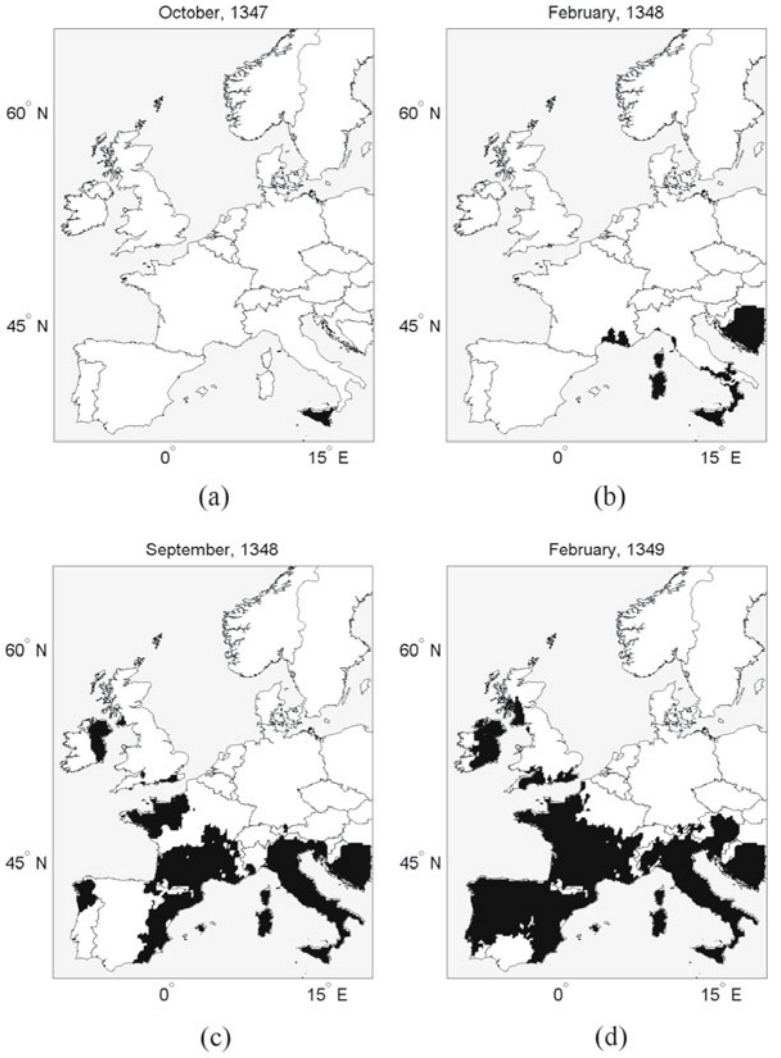


Figure 4. Total geographical area infected by Black Death at different times denoted in black. Blank areas denote no infection or insufficient data for estimation (**continues**).

tain areas than in some others (due to different f values, etc.). It is noteworthy that the applied results of Fig. 3 are in agreement with the theory of Section IV.B.b. Consider the following example. In Appendix B we find that in the vast majority of localities f is greater than 0.3 and in view of the mortality values in Fig. 2, the theoretical plots of Fig. IV.4b predict that the Black Death elasticity values should be between 0.85 and 1.0 across space-time, which is exactly the case with the elasticity estimates in the maps of Fig. 3.

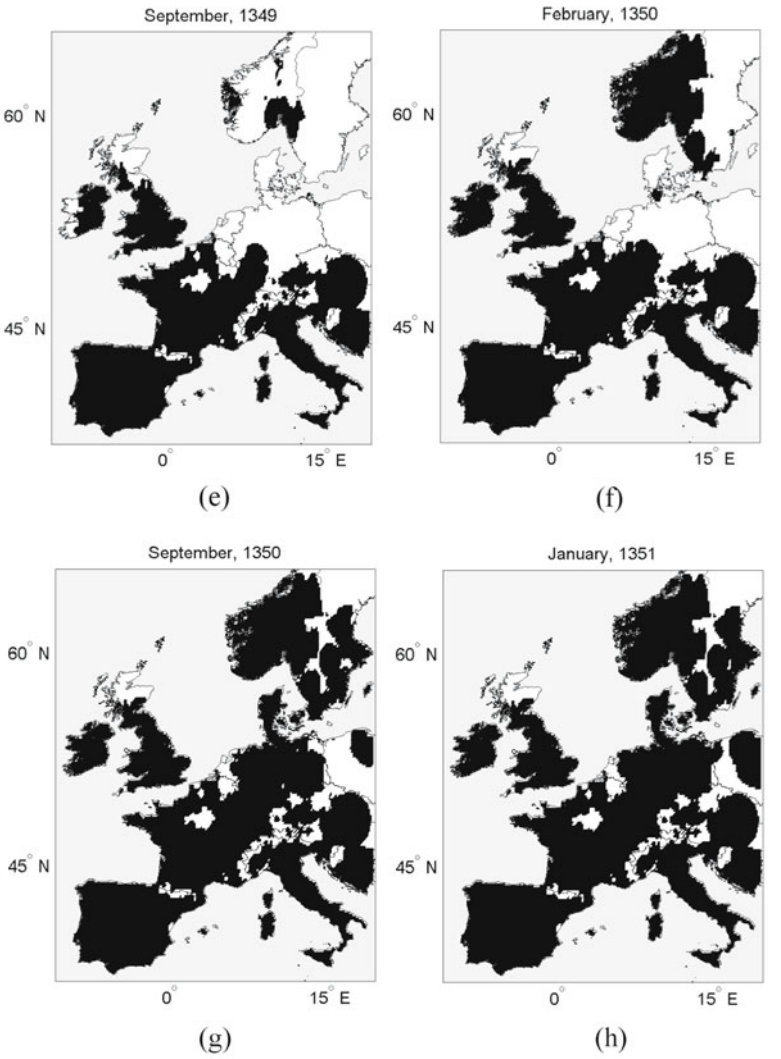


Figure 4. Total geographical area infected by Black Death at different times denoted in black. Blank areas denote no infection or insufficient data for estimation (**concludes**).

d. Maps of the Geographical Evolution of the Epidemic

In Fig. 4 we plot a series of representative maps of the epidemic spread across space and time. From a stochastic theory standpoint, the maps are maximally informative with respect to the general knowledge considered and accurate with respect to the total knowledge. With the exception of certain uninhabited areas,

Black Death moved throughout the entire continent at a rather fast pace (given the transportation means, etc., of the time). We notice certain differences between the epidemic spread maps of Fig. 4 and some related maps existing in the Black Death literature (Benedictow, 2004). The maps of Fig. 4, e.g., depict areas that had never been infected, which the previous maps did not detect. A more detailed discussion of Fig. 4 is presented in Section C below.

As was mentioned in Section II.E.b, the SEP techniques used to generate the Black Death maps of the present chapter impose no restriction on the shape of the underlying probability densities or the form of the predictors employed (non-Gaussian distributions of any shape and non-linear predictors are automatically incorporated); these are powerful techniques that can produce substantive predictions by integrating many different kinds of knowledge (e.g., physical laws, biological equations, and epidemic relationships) and datasets that are not necessarily epidemic variables (hard, soft, and uncertain data that are relevant to the exposure chain or the transmission of an infectious agent, etc.); they can consider multiple-point moments across space-time; and they are very general, deriving previous techniques (spatial regression, kriging, etc.) as their limited cases. Also, due to its underlying epistemic features, SEP mapping is based not only on the knowledge bases themselves but on the understanding of what it means to gain knowledge as well. The above constitute considerable additional advantages of the SEP techniques over interpolation schemes (spatial statistics, neural networks, etc.) and statistical model-based methods (in terms of likelihood models involving Poisson processes, etc.), random effects, and mixture representations (for a review of these methods, see Arlinghaus, 1995; Lawson *et al.*, 1999; Haining, 2003).

e. Infected Area and its Temporal Change

A measure of the geographical propagation of the Black Death epidemic is the *total* area $T(t)$ [in km^2] of all geographic regions that were infected at least once prior to time t. The curve showing the total infected area $T(t)$ vs. time t is, by definition, strictly increasing with time t, as it represents the cumulative surface area of the monthly *newly* infected area $N(t)$, which is the surface area of all regions that are newly infected in month t. In Fig. 5 we plot both the square root of the total area $T(t)$, i.e. $T(t)^{1/2}$ [in km], as well as the square root of the monthly newly infected area, i.e. $N(t)^{1/2}$ [in km]. Conceptually, the plots of $T(t)^{1/2}$ and $N(t)^{1/2}$ are curves describing the propagation mechanism of the epidemic, which, as explained in Section II.E.a, may occur by relocation, expansion, and combined relocation-expansion diffusion. The contagious spread of the disease involved direct contact between infecteds and susceptibles. This was a process that was strongly influenced by certain rather anticipated factors. Nearby regions, e.g., had a much higher probability of infecteds-susceptibles contact than remote regions. On the basis of Fig. 5, it was calculated that the total infected area $T(t)$ initially increased as a function of t^4, and it started to slow down after the first 15 months. In Fig. 6 we plot the derivative $dT(t)/dt$ (in $km^2/month$) as a function of time t

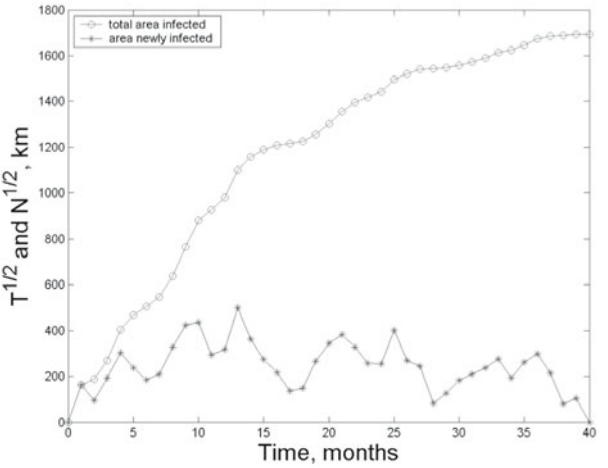


Figure 5. Plots of the square root of total infected area and newly infected area vs. time after the beginning of the epidemic in October 1347.

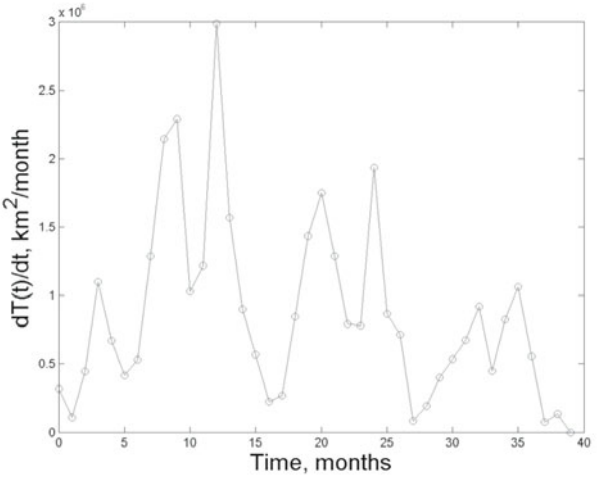


Figure 6. Plot of the derivative of the total infected area vs. time after the beginning of epidemic in October 1347.

(*month*), which offers information about the velocity of the epidemic propagation or spread over time (e.g., the largest increase in the infected area occurred during October 1348). Both Figs. 5 and 6 show that minimum values of the epidemic variables above occurred during winters.

f. Some Comparisons With Bubonic Plague

By contrast, the preliminary results we have obtained indicate that the bubonic plague in modern India moved at a slower pace than the 14th century Black Death (Fig. 7). For a more precise comparison of the space-time distributional character-

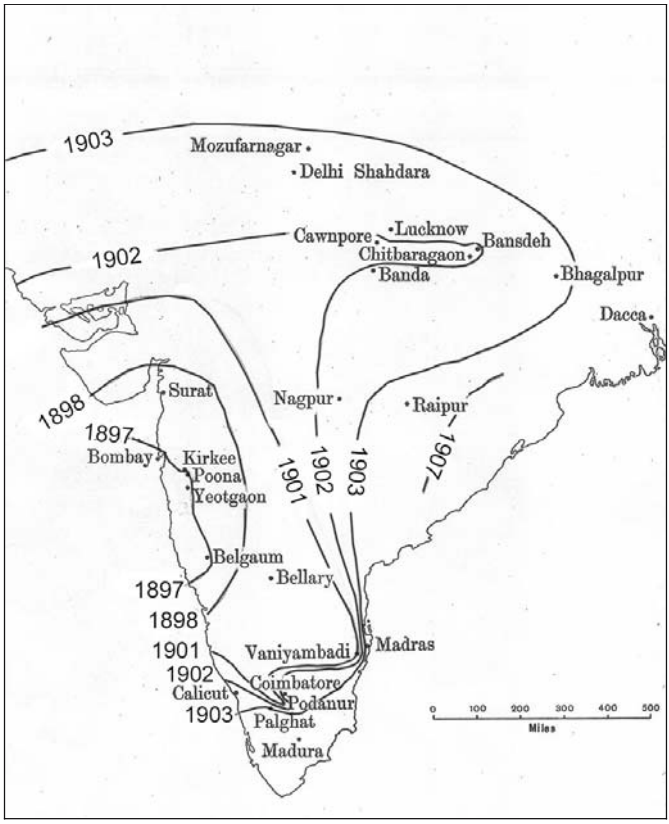


Figure 7. Propagation of the modern bubonic plague in India (adapted from Plague Research Commission, 1912).

istics of bubonic plague vs. Black Death, we prepared Fig. 8 that offers a visualization of the initial rate of variation of $T(t)^{1/2}$ [in km] in the case of the modern bubonic plague in India (essentially, the plot represents the peaks of the waves of increasing height in time). The discrepancy is significant, as the total infected area $T(t)$ in Fig. 8 increased only with t^2 instead of t^4, as was the case with Black Death (Fig. 5).

Another important space-time epidemic measure is the geographical *extent* of the Black Death disease, i.e. the area $A(t)$ [in km^2] infected by the epidemic on a given month t. Clearly $A(t) \geq N(t)$, because the area $A(t)$ includes both the newly infected area $N(t)$ as well as the area that remained infected from the prior months. In other words, while $N(t)$ describes only the *propagation* mechanism of an epidemic, $A(t)$ is a space-time measure describing the *combined* effect of both propagation and *re-infection* mechanisms (by *re*-infection we mean the continuation of the previous month's infection, or a re-emergence from a prior infection in the same area). By jointly displaying in Fig. 9 the geographical extent of the in-

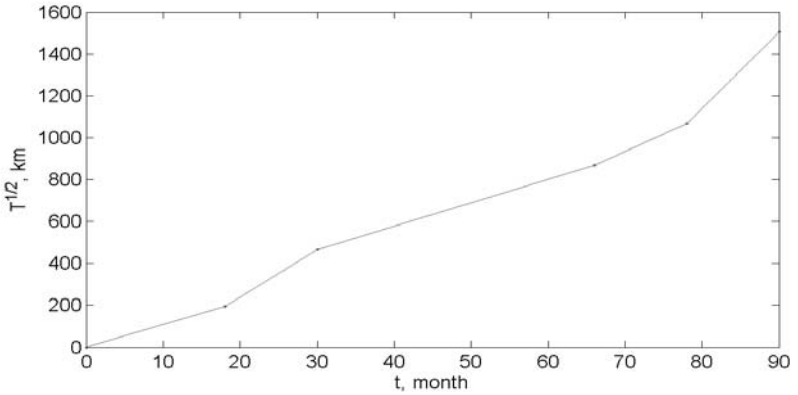


Figure 8. Plots of the square root of total infected area [$T(t)^{1/2}$ in km] versus time during the initial stages of the bubonic plague in India.

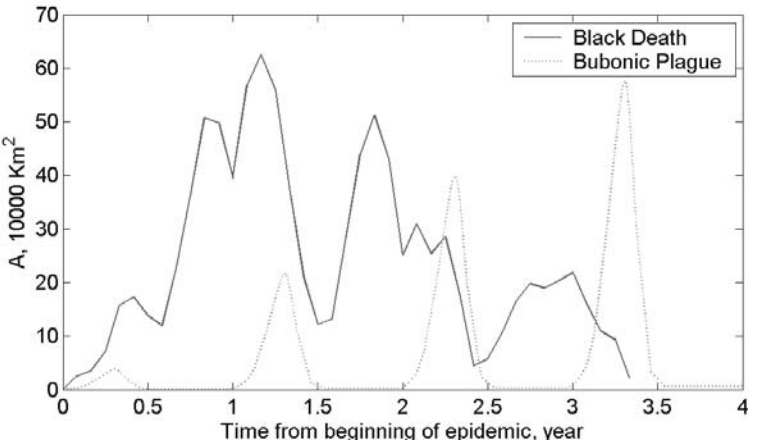


Figure 9. Geographical extent of infected area $A(t)$ (in km^2) at any given time for the Black Death (plain line) and for the bubonic plague in India (dotted line).

fected area $A(t)$ for the Black Death and the bubonic plague, we uncover two more important differences between the 14th century Black Death epidemic and the modern bubonic plague in India. Clearly, both diseases show strong seasonalities. However, while Black Death casualties slow down during the cold months of winter, bubonic plague fatalities in modern India were minimal to none during the dry and hot months of April-August (Hirst, 1953: 262-263). Bubonic plague started in Mumbai (Bombay) in August of 1896. Moreover, after the first summer Black Death reached a global maximum that was followed by maxima of decreasing levels, whereas bubonic plague kept reaching new heights during the initial years of the epidemic.

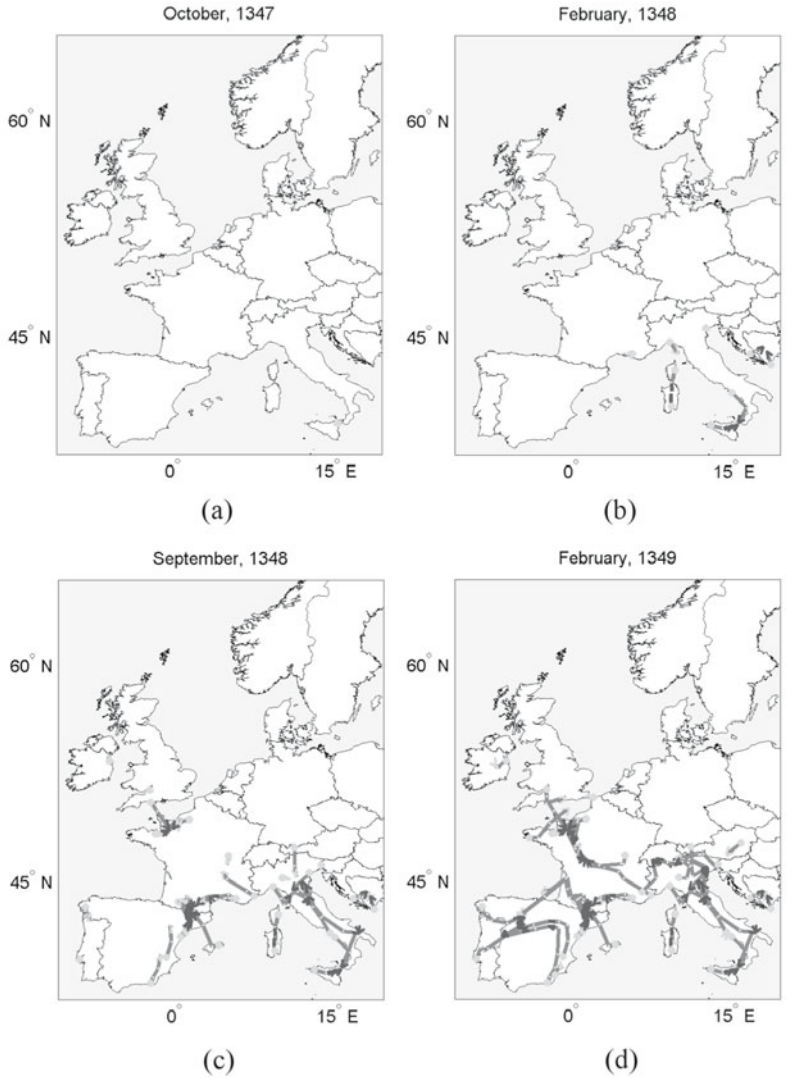


Figure 10. Time trajectory of the geographical centroid for various epidemic wave fronts (**continues**).

B. Wave Propagation

Space-time maps are important components of the scientific knowledge cycle that enable information to be moved, processed, and displayed. This procedure is particularly critical in the context of modern research where Internet networks

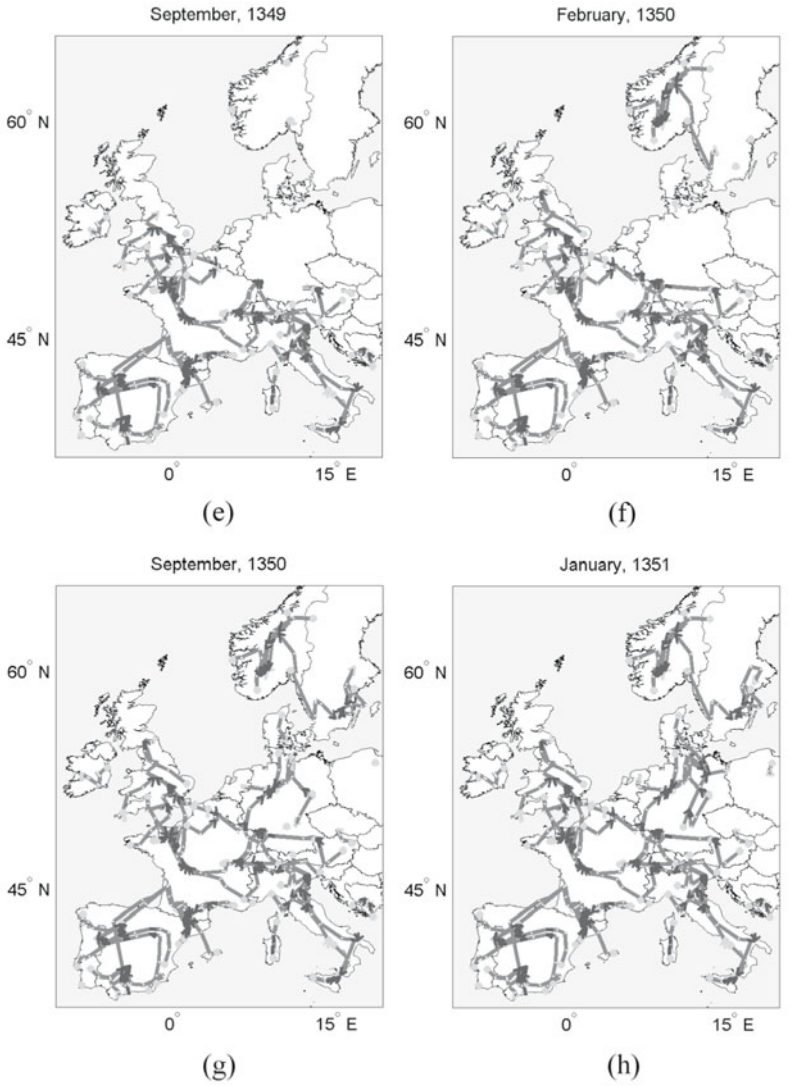


Figure 10. Time trajectory of the geographical centroid for various epidemic wave fronts (**concludes**).

provide powerful means for multi-disciplined information to be readily transferred and exposed to a vast audience worldwide.

a. Evolution of the Epidemic Centroid

The arrows in the maps of Fig. 10 depict the evolution of the *centroid* of the Black Death epidemic. Each centroid is defined as the centre of the geographical area covered by the epidemic at a given time (as shown in Fig. 4). Clearly there are several centroids of the infected areas corresponding to distinct wave fronts of the Black Death disease. By connecting the centroids of each area, one can follow the temporal changes in the geographical location of the epidemic wave-front and, thus, obtain an idea of the velocity of the epidemic (direction and speed). It is interesting to notice differences in the trajectories of the various disease centroids. Some trajectories move independently in time, whereas others come to life, as it were, only after two or more of the previous trajectories meet at some location in time. Certain trajectories have a simpler local structure (e.g., the one in Ireland), whereas others (e.g., the ones in France) have more complicated oscillating structures that extend into different countries.

Finally, in Fig. 11 we plot the *mean* centroid velocity (that is, the average of the velocities of the various centroids along all different directions throughout Europe) as a function of time. This plot clearly provides some insight concerning the mean velocity of the spread of the Black Death epidemic throughout Europe. This insight is also demonstrated by the fact that there is a general agreement between the temporal variation of the mean centroid velocity in Fig. 11 and that of the infected area expansion velocity of Fig. 6.

b. Visualization in Terms of Mortality Distributions

By means of space-time mapping the multi-sourced Black Death databases are interpreted, in the sense that they are transformed into units of insight and acumen. The maps in Fig. 12 present the evolution of the monthly mortality distribution along the direction of the wave propagation. Some interesting observations can be

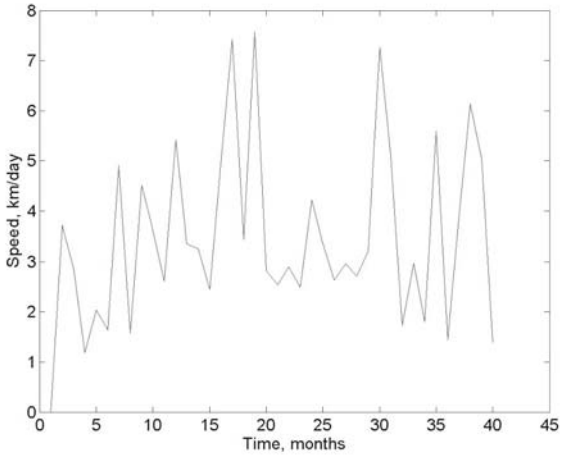
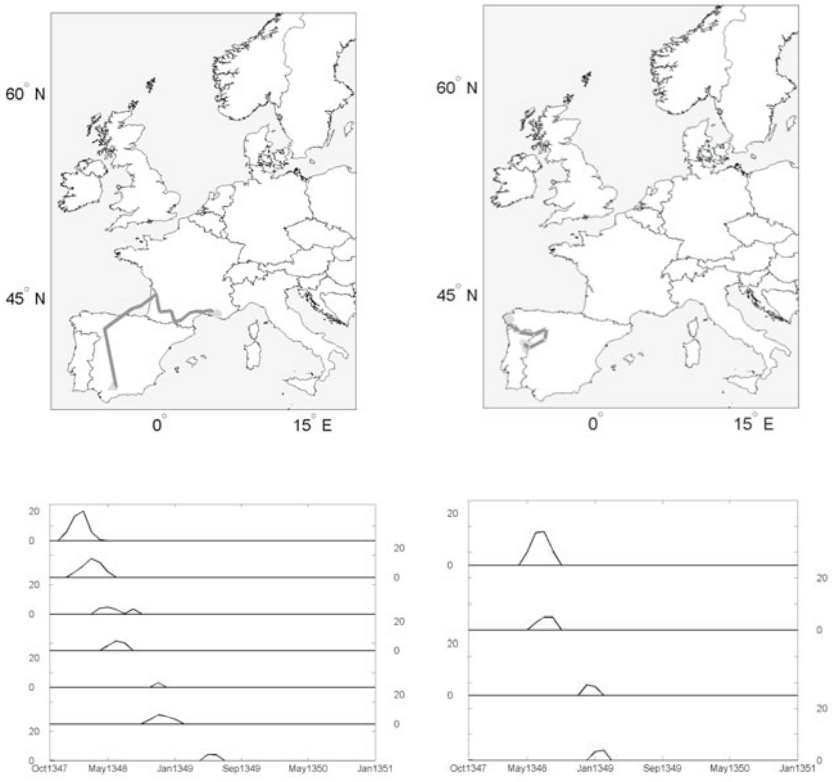


Figure 11. Mean centroid speed vs. time after the beginning of the epidemic in October 1347.

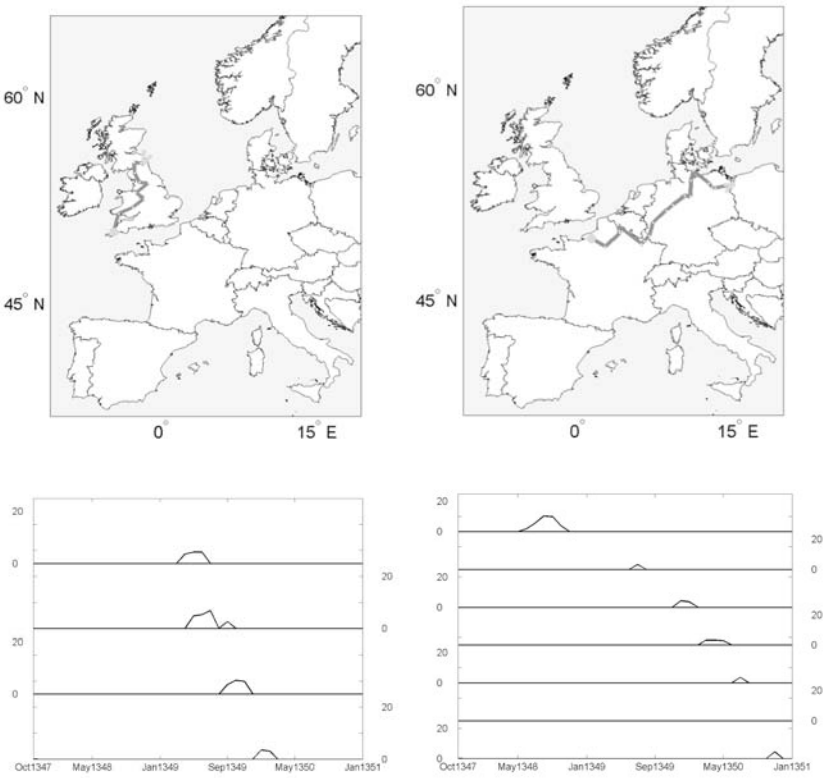


(a) (b)

Figure 12. Mortality distributions along the direction of wave front propagation, in percentage (**continues).**

readily made. The mortality distributions generated by the SPE models moved like "waves" or "clouds" with varying speeds throughout Europe. Also, the distributions have various sizes and shapes depending on the geographical locality, distance from the epidemic focal point, etc. Some of these distributions are multimodal, and their shape can be affected by the fact that they are associated with epidemic trajectories that come to life only after two or more of the previous trajectories have met at some location in time. In most cases the epidemic peaks tend to decrease with time. Also, notice that the shapes of the mortality distributions in Fig. 12 are, in general, similar to those obtained by means of ERF modelling (Section IV. C), an observation that further demonstrates the internal consistency of the SEP approach.

In Fig. 13 we plot the areal-averaged monthly mortality $\overline{M}_t$ vs. time t. The $\overline{M}_t$ values were obtained for every month t taking the numerical average of mortalities at all geographical locations throughout Europe for the same month. The $\overline{M}_t$ plot



(c) (d)

Figure 12. Mortality distributions along the direction of wave front propagation, in percentage (**concludes).**

shows an exponential kind of decrease as a function of time *t*, which is a novel but plausible result.

As was anticipated, the preceding maps and plots amply demonstrate that SEP's strength lies in its theoretically rigorous and technically sound approach toward understanding the space-time evolution of the disease in considerable detail and in a stochastic fashion. The approach is based mainly on uncertain city-level data (population, numbers of deaths, epidemic duration, etc.), which are properly generated from a variety of interdisciplinary Black Death sources.

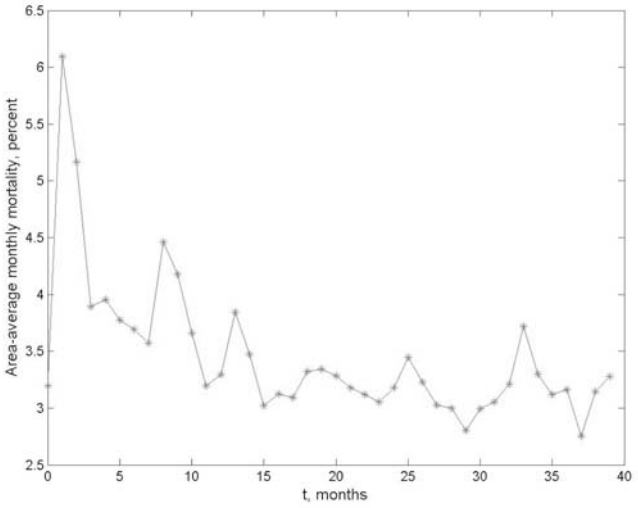


Figure 13. The areal-averaged monthly mortality (%) vs. time after the beginning of the epidemic in October 1347 (*months*).

C. Space-Time Inference

There are several forms of human communication--some as old as the cave paintings of Altamira. As already mentioned, mapping is an important form of communication. Remarkably, the way the maps are generated and interpreted can have a strong influence on the kind of ideas we can express, which then become the essential content of a space-time epidemic culture. SEP modelling includes sophisticated mapping techniques and technologies that allow public health scientists to convey valuable space-time information and exchange powerful messages. These substantive objectives cannot be achieved by epidemiologic statistics alone. The *form* of the latter excludes the *content* of the former[6].

a. Epidemic Maps From a Historical Evidence Perspective

What follows is a critical review of the main SEP modelling results of the previous sections in the light of historical evidence (uncertain contemporary interdisciplinary sources that lie far in the past). Public health reasoning modes, like the deductive syllogisms and inductive patterns of Section II.A, constitute the theoretical background of the space-time inferences attempted in this section. Infor-

[6] In the same way, e.g., that the smoke signals technology cannot be used to convey philosophical arguments.

mation can be made more informative by rearranging it in ways that facilitate its use in inference. The inductive patterns considered include both reasoning by analogy and by generalization, which also underlie hypothesis testing and evidence interpretation. In several cases the inferences are empirical rather than formal, i.e., they are not content-free but depend on taking into consideration multi-sourced databases. From an inferential standpoint, it is often expedient to reduce the main issue to a series of logical sub-issues that, when resolved, will resolve the main issue.

Italy

According to the notary Gabrielle de' Mussis and others, the port of Messina (Sicily, Italy) was the first European city to be visited by Black Death early in October of 1347 (see map in Fig. 2a). As recorded by de' Mussis, the appearance of the plague followed the docking of 12 galleys carrying merchants and sailors fleeing from the city of Caffa by the Black Sea[7]. While the incident of the galleys' arrival is indisputable at the moment, certain elements of de' Mussis' account have been questioned in recent years[8]. First, it has been discarded that de' Mussis was traveling in one of the galleys, thus stripping the story of an important eye-witnessing element. De' Mussis was a resident of Piacenza, where he apparently wrote what he heard about the case (Fig. 14). This must have happened shortly after the incident, because he died in 1356 (Wheelis, 2002: 972). Benedictow (2004: 70) disputes the reported number of galleys[9], whereas Scott and Duncan (2004: 230-231) do not discard the possibility of a merely coincidental timing of the outbreak with the arrival of the galleys. These scholars also maintain that Black Death may have come from another place in the Middle East. They even consider the possibility that the plague's origin was in Ethiopia (Fig. 15) rather than in Mongolia or China, as is usually claimed. Hence, our investigation of the matter led to the conclusion that so far the only one of de' Mussis' claims still remaining unchallenged is early October 1347 as the date of the beginning of Black Death in Europe--perhaps, give or take a few days. Remarkably, this is the only piece of information of any relevance to the SEP modelling and space-time mapping of the preceding sections. Legend has it that the galleys, after they were expelled from Messina, continued their deadly visitation in at least two more ports: Genoa and Marseille. At the

[7] The region was known to be suffering from an epidemic with symptoms similar to Black Death. Today Caffa is known as Feodosiya (Ukraine).

[8] This is not an unusual situation with eye-witnesses. As Aristotle remarked (Doody, 2002: 44): "But people notice different things, and much talking confuses the eyes".

[9] He maintains, "One should disregard the number of galleys that conform to the set of magical or mythological numbers of which medieval people were so fond and which they preferred over tedious and vulgar empirical observations".

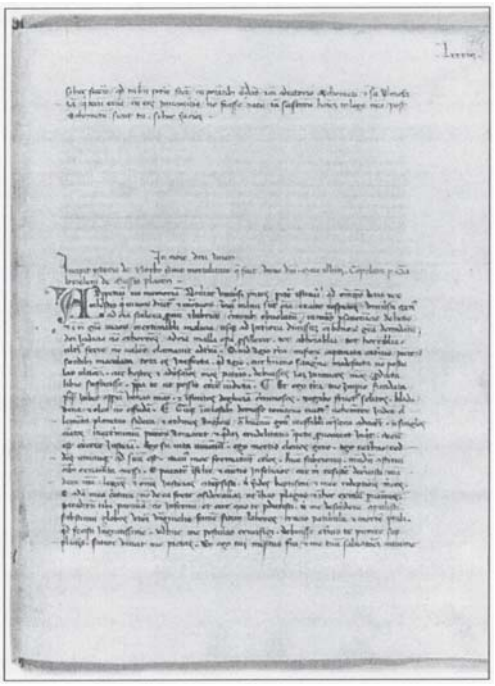


Figure 14. First page of de' Mussis' account included in a 1367 compilation of historical and geographical accounts. The original manuscript is lost (Wheelis, 2002: 972).

beginning of 1348, Pisa and Venice were also infected, the latter most likely from plague sources unrelated to Messina. Milan and Venice, both major cities with approximately 100,000 residents each, swiftly implemented sanitary practices to contain the epidemic, although with varying success. Milan was the first city to start isolating entire families once a member developed Black Death symptoms. Despite the cruelty of the measure, it proved rather effective (e.g., mortality was limited to about 15%) and, as a consequence, it served as a model for other places during subsequent outbreaks. Venice, despite its fragmented geographical distribution, completely failed to contain the impact of the disease, instead ending with one of the highest mortalities in the continent. Measures that were taken included delays in the admission of ships to the lagoon, and the designation of uninhabited islands as cemeteries in which the dead were buried at least 1.5 meters below the surface. Delaying the docking of ships coming from infected areas gave birth to a practice universally called *quarantine*, after the forty (*quaranta*) days that eventually were established as the minimum safety period to ensure that the ship was plague-free. It is noteworthy that proponents of the viral infection theory have used the quarantine length as evidence supporting the 37 days postulated as the average period between the infection point and the death of the victim (Scott and Duncan, 2004: 162). Figs. 2c and 4c support the view that the Black Death epidemic in Italy is believed to have reached its highest level during the summer months of 1348. Although in Europe, in general, and in Italy, in particular, there was no way to verify who infected whom, further spreading seems to have taken

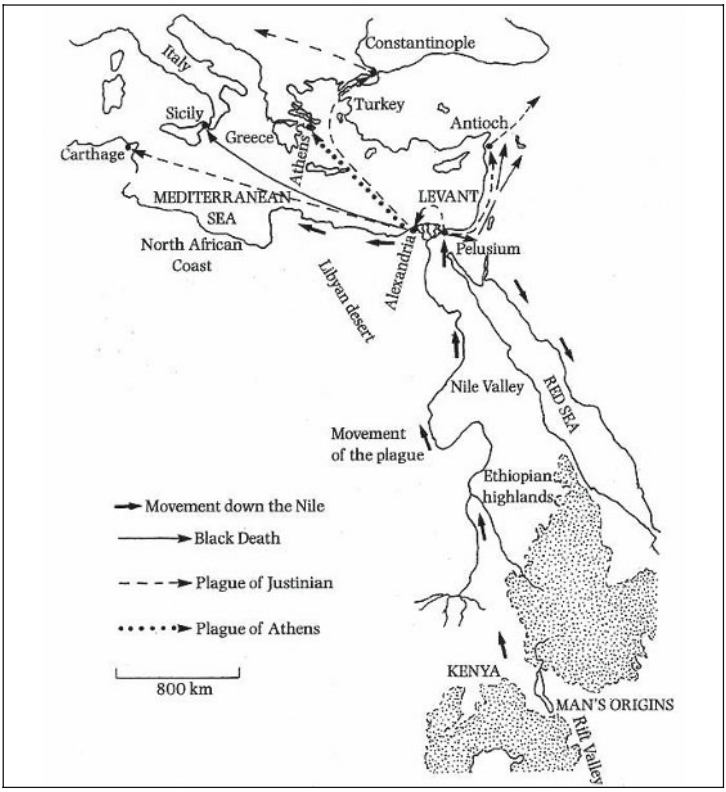


Figure 15. Black Death may share with the human race its origin in Great Rift Valley of Africa (Scott and Duncan, 2004: 231).

place primarily through overland traveling, starting at the main focal points of the epidemic and then propagating outward as a kind of a chain reaction. This was the case with most geographical regions of Europe.

From Genoa and Venice the plague propagated in all directions. As is shown in Fig. 10c, it moved southeast via Tuscany and northwest via Calabria. We consider the scarcity of data in southern Italy to be the result of poor chronicling and preservation rather than a result of the area being plague-free. Outside mainland Italy, the plague passed to Austria and Switzerland (Figs. 4d and 10d). Majorca and the islands of Corsica and Sardinia may have received the plague from mainland Italy too. All these paths of the plague are clearly displayed in the SEP maps derived in the previous sections.

Croatia

The ancient port of Ragusa (which today is known as the city of Dubrovnik in the young Republic of Croatia) was at the time controlled by the Republic of Venice. Ragusa most likely was another one of those places directly infected from sources

outside of the European continent. Not much is written in the literature about the place as regards the spatiotemporal propagation of Black Death. SEP modelling (e.g., Fig. 2b) shows that the plague spread inland.

France

Black Death visited almost every single corner of the country (Figs. 4f-h). The highest virulence occurred in the warmer and drier southern part of the country. Evidential sources seem to indicate that the plague spared a few more places in addition to the uninhabited mountainous areas in the Pyrenees and the Alps. Documented evidence indicates normal mortality during the entire year of 1348 at Carpentras in Provence (Dubled, 1969: 20), the Béarn districts (Tucoo-Chala, 1951: 84), and an area east of Calais (Scott and Duncan, 2001: 87). This kind of evidence has convinced these scholars that Black Death spared the above areas during 1347-51. Identifying areas that escaped Black Death is more difficult than it may seem at first glance, because it was a common practice in those times to destroy evidence of the effects of the plague (Higounet-Nadal, 1978: 146). Therefore, we came to the conclusion that one cannot infer with certainty that the epidemic spared a geographical region on the basis of the fact that the plague was not mentioned in that region during the period 1347-51. Instead, the documentation of normal levels of labor demand and prices constitutes more conclusive inductive evidence for drawing any inferences concerning a region escaping the plague.

France was the most populous and one of the most prosperous territories of Europe at the time. Its population, within its present borders, must have been approximately 25 million people (Ziegler, 1969: 63). The position of the king within the societal system was supreme. Both the feudal lords and the clergy had been shorn of much of their power, and a real sense of national unity was developing. By 1309 the Pope had moved to Avignon, to the delight of the French people (Deaux, 1969: 96-98), although Avignon was not part of France until 1791. All scholars agree that Marseille was the first place to be visited by the plague, within the geographical region of what is today's France (this is shown in the map of Fig. 2b). Marseille was by far the most lethal infection focal point in the entire continent. Noticeably, it was from Marseille that the epidemic moved to the rest of the country and eventually throughout the rest of Europe--with the exception of most of Spain, Italy, and certain regions directly north of Italy. This is a conclusion that can be derived directly from the maps of Figs. 2, 4, and 10.

Not taking into account areas around the English Channel, evidence supports the view that the plague was spread by means of overland traveling. During the first semester of 1348, starting from Marseille the Black Death epidemic propagated in all directions. To make things worst, during the summer a second front opened in the north (this event is clearly detected by the map of Fig. 4c). Our analysis demonstrated that at the beginning of the summer the plague made its appearance in Saint Marie Laumont in Calvados, in Rouen, and most likely at the Channel Islands. However, according to our modelling calculations, it was too early for the plague to have come overland from the south. Other than these three places, nothing else points to further leapfrogging of the plague due to rapid

propagation by sea. Most likely, the initial infection in places on both sides of the English Channel must have come from ships traveling from ports already infected during the spring, such as those along the Mediterranean coast or Galicia (northwest Spain).

Space-time SEP mapping shows that both epidemic fronts eventually collided at the Loire Valley during the fall of 1348 and continued toward Germany and Belgium to the east and northeast, respectively (see the epidemic paths in the map of Fig. 10d). Remarkably, the front that moved northeast from Paris toward Belgium showed a systematically low virulence (Figs. 2f and 4f). It eventually died out completely when it reached Belgium, which explains why territories further northeast (in what is today The Netherlands) escaped the ravage of plague temporarily.

Our inferential analysis of minor inconsistencies concerning the beginnings of the epidemic in the five locations studied by Biraben (1987) consistently supported the choice of the earlier of his two dates (see, also, Table III.2). In order to confirm our findings beyond any doubt, it would be necessary to obtain additional plague-related information at places like Centre (southwest of Paris) and Bourgogne (southeast of Paris). The latter was simply too uncertain to be used in mortality estimation, thus resulting in a blank area (see Fig. 4f).

Iberia Peninsula

Like Italy, the Iberian peninsula had the characteristic of Black Death originating at several focal points. At the time, the country was divided into four kingdoms: Castile, Aragon, Navarra, and Granada (Kagay and Vann, 1998: 1). As is shown in Fig. 10d there were at least three points of entry (the map representation is in remarkable agreement with the discussion in Gottfried, 1983: 51). Firstly, and probably most importantly in our view, merchant ships from Italy may have brought Black Death to the Balearic Islands and then to the major ports of the west coast, Barcelona and Valencia. Secondly, just as Mecca was visited early on by Muslim pilgrims coming from areas ravaged by Black Death, the plague seems to have moved to the northwestern corner of Spain by Christian pilgrims who wished to temper the Lord's wrath by visiting St. Jacob's shrine in Santiago de Compostela (Phillips, 1998: 49). Thirdly, the plague must have come from the north, across the Pyrenees, to the Basque-speaking villages. Finally, it is likely that the south (particularly Almeria and the Muslin Kingdom of Granada) was infected from North Africa (Gottfried, 1983: 51).

The occurrence of plague in Santiago de Compostela is a controversial claim supported by a limited amount of evidence. The claim is based primarily on the abnormal mortality of bishops during 1348-49, which Ubieto (1975) attributes to the plague. From an inferential viewpoint, the central role of Santiago de Compostela derives from the combination of timing, the importance of the city, and the need to explain the indisputable fact of plague making its appearance in Coimbra (Portugal) on September 29, 1348. Geographically, Coimbra is located inland hundreds of kilometers west of the two closest infected areas, Aragon and Valencia. Logically, the plague's presence in Coimbra requires a source of infection

from some port along the east cost of the peninsula. Our SEP modeling is in agreement with the times proposed by Ubieto at several places in the northwest. The modeling is also consistent with the plague ravaging the Spanish province of Zamora in October of 1348. Vaca Lorenzo (1990), fifteen years after the publication of Ubieto's seminal work, found plague evidence in the village of Villalobos. Note that this evidence has nothing to do with deaths of benefited clergy.

It seems plausible to assume that the plague spread in several different directions in Spain because of the multiplicity of its focal points. This is easily seen from a visual inspection of the maps in Figs. 2 and 10. While the 1347-51 Black Death is characterized by a general propagation direction from south to north, Portugal has the peculiarity of being the only present-day country that had the plague moving primarily from north to south (Figs. 2c, d, and e).

The Valencia and Barcelona fronts merged early (June of 1348; Fig. 4c). Four months later they merged with the waves from Almeria and Santiago to form a single U-shape front extending all the way from Lisbon to Navarra to Almeria (Fig. 4d). By then, the central plains and Andalusia were doomed. The devastation of the peninsula was completed during 1349. Most of the cities and villages in Spain suffered more or less severely.

Austria

In Austria the plague came from Italy (Figs. 2, 4, and 10), most likely through the Brenner Pass, late in the summer of 1348, according to records found in Marienberg (western Austria). It took a year for the plague to reach the eastern section of the country and infect the capital city of Vienna, where it raged out of control. With a population of about 20,000 residents, the chroniclers have mentioned that 900 people were dying daily during the worse days of the plague (Ziegler, 1969: 84). Yet, nothing compares to the situation at Neuberg in the southwest part of the country, where the local population was assaulted simultaneously by the plague and by wolves coming from the mountains (Deux, 1969: 112).

As is depicted in Fig. 4e, the plague front passed from Austria to Bavaria and Bohemia, where the severity of the pestilence was rather mild. Eventually, the German front merged with another front coming from France and continued north, along the Rhine valley (Fig. 10f). Most likely, the forests served as a barrier that prevented the front from traveling into northern Bavaria and Thuringia. Unfortunately, the plague's sparing of the territories north of Regensburg was only temporary--Black Death eventually arrived in these territories from a different direction. Not much is known beyond Bohemia. As was mentioned above, however, lack of documentation cannot be used as a proof that the plague did not propagate beyond Bohemia.

Switzerland

At the time of the Black Death epidemic, most of present-day Switzerland was under the rule of the Holy Roman Empire. Switzerland had the Black Death first coming from France (Fig. 2c). Geneva was the point of entry in August of 1348.

From there, it propagated along two directions. Moving up the Rhone River, the plague was at Sion in March of 1349 (Sion is the highest locality along the valley with documented evidence). In its propagation parallel to the Jura Mountains, the epidemic reached Zurich in October of 1349 (Fig. 2e). Shortly after, the French wave merged with the wave moving down the Rhine river and the combined front passed to Germany (Fig. 10g).

Bellinzona in Ticino had the plague starting in the fall of 1348 (Fig. 4d). If one agrees with Sticker (1908:56), the disease reached Dissentis (Grisons), on the other side of the Lepontine Alps, by December of the same year. Dissentis is on the upper valley of the Rhine river, thus once there, it was not difficult for the plague to travel downstream all the way to Lake Constance, where it arrived in the fall of 1349. On its way to Lake Constance, the plague infected cities such as Pfäffers and St. Gallen, for which we have found well-documented evidence.

The cities of Engelberg and Dissentis offer a good example of how effectively natural barriers could sometimes restrain the propagation of the plague. These cities are on opposite sides of the Glarner Alps. In Dissentis the plague started in December of 1348, coming from Italy to the south. Interestingly, although they are only 40 km apart, Engelberg was never infected by Dissentis. Indeed, our analysis shows that Engelberg did not have problems with the plague until September of 1349, when it came from France through Lucerne (Figs. 4e and 10e).

Apparently, despite Switzerland having the most rugged terrain in Europe, the Black Death reached almost every inhabited region of the country, resulting in an average mortality of about 40%. This mortality level lies in the middle range of death rates reported for the rest of Europe.

United Kingdom

The UK does not have insurmountable natural barriers to serve as obstacles to the propagation of Black Death, which reached every corner of the UK. Not surprisingly, the epidemic was initiated in the south of the country and progressed inexorably northward through the British island.

Curiously, in the case of the UK most of the Black Death timing controversy concerns the early stages of the epidemic. The maps (Figs. 2, 4, and 10) were prepared assuming an initial outbreak at Weymouth (June 23, 1348), and that the epidemic arrived in London on September 29, 1348. These assumptions have a direct effect on subsequent inferences concerning the geographical source of infection, spread distribution, etc. Contrary to the opinion of several scholars, we decided to discard the most popular explanation that the plague initially reached the UK from the northern and northwestern French territories controlled by the English, as part of their initial success during the Hundred Years War. With the exception of the Channel Islands, all other places had the plague later: Calais (December, 1348), Bordeaux (August, 1348). We inferred that both sides of the English Channel must have received the plague from Mediterranean ports or from Galicia in northwest Spain, the only places along the European coast to have plague in the spring of 1348. Once the epidemic had started in the UK, our modelling shows further infection from France (Fig. 10e). Aside from this issue concerning the origin of

the infection, the UK has one of the best regional databases that prove that the plague first reached the entire south coast of England and then moved north steadily (Fig. 4d, e, and f). As far as Wales is concerned, the information is minimal and goes back to the research of Rees (1920).

Nothing is known about the effects of the plague in Northern Ireland, and little is known about what happened in Scotland, other than that the plague was introduced by soldiers returning from combat in England. Our modelling of the mortality space-time distribution in Northern Ireland is rather a theoretical extrapolation, which is not supported by local databases.

Republic of Ireland

Not much was known about Black Death in the Republic of Ireland, until the recent research work by Maria Kelly (2001 and 2003). Her work is an encouraging example of how much a dedicated research effort can achieve in advancing epidemic knowledge, proving once more that data sources are far from exhausted. Using Kelly's findings, SEP modelling generated plots showing a clear plague front sweeping from east to west (see Fig. 10f).

Scandinavia

Knowledge about the effects of Black Death in northern Europe is fairly sketchy and contradictory. As a matter of fact, there is not a single piece of information about mortality for any locality in Sweden or Denmark. The only data for the entire region is a mortality of 50% for the port of Oslo that we found on the Internet[10]. Similar is the case with the duration of the epidemic. We only found dates for the end of the epidemic in two Norwegian villages: Hamar (Benedictow, 2004: 150) and Sandsvær (Benedictow, 1992: 99).

Despite such fragmentary information, we were able to model the evolution of the epidemic across space-time. More specifically, after discarding an assumed start in January of 1349 in Copenhagen, we followed the suggestion of Benedictow (2004: 153) to declare the port of Oslo as the first infection point (April 1349), relegating to second place the rather more conventional choice of Bergen (Benedictow, 2004: 220-221). The accounts about the spreading of the plague have the ingredients of a legend rather than a historical fact. Legend has it that Black Death started in Bergen, following the discovery that all sailors on board a ship that drifted into the harbour were dead. Some scholars date the event in June of 1348 (e.g., Biraben, 1975: 80), but Benedictow shifted it to August of the same year. In any case, there is not enough information to support one view over the other. In Norway, the general progression of the Black Death epidemic was from south to north, with most of the country been visited by the plague before the end of 1349 (see the map in Fig. 4f).

From Norway, Black Death passed to Sweden (Fig. 4f and 10f). Based primarily on church donations, Benedictow has collected data showing that the southern

[10] See http://www.lonelyplanet.com.

part of the country was swept from northwest to southeast, mostly during the year 1350. There is absolutely no data in the geographical area north of Uppsala.

The limited data available indicate that in Denmark the plague began in the summer of 1350. In view of this timing, the SEP modelling indicated that the plague came, once more, from the south, in this case from Germany. It should be noticed that we discarded the view that the epidemic in Copenhagen started in early 1349. We found it rather peculiar that there is no evidence of plague in any other place in the region shortly thereafter, thus implying that the Black Death plague was contained completely to Copenhagen. In the end, a decision was made not to enter Copenhagen in the BME database. Instead, following the view of Biraben (1975: 80), we coded information sources that assign the beginning of plague to Zealand Island in July of 1350. This is an indirect way to infer that the pestilence was in Copenhagen during the summer of 1350, since Copenhagen is in the Zealand Island.

Germany

In Germany the plague arrived overland from an area that today includes three different countries--Austria, Switzerland, and France. At the time, Germany and most of Switzerland and Austria were part of the Holy Roman Empire. In the summer of 1349, Black Death entered southern Germany by means of two fronts that arrived almost simultaneously. One came into Baden-Würtemberg from France to the west and the other entered Bavaria from Austria to the east (see Fig. 4e). Both fronts merged and the combined wave proceeded down the Rhine river (Fig. 10g).

SEP modelling revealed that in November of 1349 a wave from Switzerland reached Konstance in Baden-Würtemberg. This third front went nowhere, which is in agreement with the "no re-infection rule": given that the rest of the territory already had Black Death, there was no "virgin" population to suffer from the plague.

With further reinforcements from France, the Rhine front of Black Death left the valley at the beginning of 1350 and went on to infect northern Germany, eventually passing also into The Netherlands and Denmark. Within Germany, the wave moved east along the Baltic coast, and after making a clockwise move it went back toward the south to reach the Thuringia and northern Bavaria regions, which had escaped the plague the previous year (see Fig. 10g).

Low Countries

The history of Black Death's spread through Belgium and The Netherlands has some interesting peculiarities. At the time, Belgium was a prosperous region having several of the characteristics of Tuscany, such as flourishing trade and large cities. Yet, unlike northern Italy, mortality in Belgium was the lowest among the present-day countries, with about 20% mortality at most. Another peculiarity is that the plague did not proceed into the virgin regions of The Netherlands.

There are two possible scenarios concerning the plague in The Netherlands. Biraben (1975: 77) has a plague focal point in Friesland, starting in December of 1349. Nobody has reported plague passing to another nearby city, whereas Deventer was the next outbreak, six months later. For this reason, we agreed with Blockmans (1980:843) that the plague in Friesland did not start until the end of 1350. Under this assumption, the SEP model predicted that the plague came to The Netherlands from Germany (see map in Fig. 10h).

b. More Detective Work

Because of the historical nature and multi-sourced features of much of the information about Black Death (it involves a variety of human activities, historical events, and time periods), it is not uncommon for epidemic modellers to perform extensive *detective* work using the methods of logic and the mathematical modelling tools to their avail (Sections II.A and III.C). The detective work involves conditional thoughts, i.e. thoughts that we assert to be true on the condition that some premises are true or will turn out to be true. In many circumstances, the content and context can affect the mode of thinking employed by the detective process (a thinking mode can be contextualized considerably by one's prior information and belief, the multi-sourced evidence may permit several empirical inferences to be drawn that can be used to assess an explanation based on hypothetical thinking, etc.). Let us consider a few representative examples of detective work in the fashion described above.

Example C.1. From a logical viewpoint, the duration of the epidemic in a region consisting of several villages should be longer than the duration of the epidemic in a large city with the same population as the region. Since the population is dispersed in several places, it seems logical that it takes extra time for the disease to move from place to place. The calculated ground speed of Black Death was in the range of 0.7-5.0 km/day (Biraben, 1975: 90; Andenmatten and Morerod, 1987: 31). For a given ground speed, the Black Death duration in a large region also depended on the urban mixture, topography, size, shape, and orientation of the region relative to the direction of the plague propagation. E.g., this was the case of Saint Maurice, in the Valais canton of Switzerland. On the eve of the plague, the parish had a population estimated at approximately 1300 residents. If the population had been concentrated at the village, the Black Death outbreak should have lasted no more than 5 months. But only 40% of the people lived at the larger village of Saint Maurice. About 45% of the population was dispersed in other smaller villages, 37% in the mountains and 8% in the valley, while there is no information for the remaining 15%. Pasche (1998: 127-129) has carefully documented the plague lasting 8 months in the parish, with the second month of the epidemic (February of 1349) being the worst month, accounting for 27% of all fatalities. Our analysis came to the conclusion that the case of Saint Maurice is in clear agreement with observations by Woods *et al*. (2003: 437) concerning the aggregation at the English archdioceses of Coventry and Lichfield.

Example C.2. If one is certain about the duration of the epidemic in a geographical region, the SEP scaling law introduced by Eq. (IV.1) can be used in a reverse manner to determine town populations. Let us investigate the case of three of the largest European cities on the eve of the Black Death plague: Paris, London, and Florence:

- Medievalists have never been able to come to agreement in deciding the population size of Paris right before the Black Death epidemic. Estimates range from 80,000 to 200,000 residents (Bardet and Dupâquier, 1997: 176). There is, nonetheless, better agreement in assessing the duration of the Black Death epidemic to be close to a year and a half (Deaux, 1969: 105; Mollat, 1977: 505). Under those circumstances, the scaling law predicts that the population of Paris should have been closer to 80,000 residents than to 200,000 residents.
- Florence is another interesting case. There is not much disagreement about the duration of the epidemic, which is said to have lasted 8 months at most (Biraben, 1975: 77 and 103; Cohn, 2002: 167-168). This duration was typical of cities between 40,000-50,000 residents, such as the neighboring cities of Bologna and Pisa. The city size, though, is in contradiction with this prediction, with estimates of at least 90,000 residents coming from none other than the reputable Giovanni Villani. Our detective work led to the conclusion that Villani was misled by his sources, which were primarily based on the number of bread tickets issued during the famine of April 1347 (Ziegler, 1969:51-52)[11]. The scaling law gives Florence a pre-plague population of about 45,000 residents, a finding that is in agreement with the view that Florence reached a maximum population of 60,000 in 1300 (Chandler *et al.*, 1987: 16-18), which during the next 47 years dropped by 25-50% (Gottfried, 1983:46). In an effort to have an independent assessment of the population of Florence, we compared its *topography* with that of Bologna. In 1333, the city of Florence completed construction of its sixth and last city wall, which had a perimeter of 8.5 km enclosing an area of 430 hectares[12]. On the other hand, the wall of the city of Bologna, the third and most recent, had a perimeter of 7.8 km and an enclosed area of 410 hectares[13]. It was started and completed at about the same time as that of Florence and, as is shown in Fig. 16, neither city had dwellings outside the newly finished walls. We regard as highly unlikely that two cities with similar characteristics, in the same part of the country, with the same duration of the Black Death epidemic and almost identical urban areas, would have had greatly different populations. In our opinion, the value of the population for Florence derived from the scaling law is correct: on the verge of the plague, Florence had about the same population as Bologna (i.e., 40,000 residents or 10% more at most).

---

[11] Apparently, corruption was rampant during the distribution of bread tickets, giving the impression that Florence was a larger city than it actually was, an impression that is reinforced by the 100,000 casualties reported by Boccaccio (Deaux, 1969: 85).

[12] See website: http//www.aboutflorence.com.

[13] The calculations were made using the map available at the website: http//urp.comune.bologna.it

(a)

(b)

Figure 16. The 14th century walls of the city of (a) Florence and (b) Bologna. None of the maps show any population outside the newly constructed walls.

- The opposite is the case of London. The Black Death plague is repeatedly and fairly consistently reported to have lasted in London at least as long as it did in Venice and Paris (Ziegler, 1969: 156-157; Cohn, 2002b: 142). Yet, the dominant view is that the population of London was 50,000 residents (Gottfried, 1983: 64), in which case the 50,000 fatalities claimed by the chroniclers (Britnell, 1994: 199) is a gross exaggeration. Our investigation seems to support the dissenting view of the London historian Derek Keene (1984: 20) that the population of London in 1300 was 100,000 or more residents, thus making the 50,000 casualties more likely[14].

In general, the scaling law is a convenient and rigorous way to bring consistency to reported values for population size and epidemic duration. Note that in all three cases discussed above (Paris, London, and Florence), our results coincided with existing opinions of other scholars; our findings did not produce unexpected new figures. I.e., the detective work in these Black Death cases involves the diligent following up of clues aiming at confirming and filling in the details of a picture whose broad outline is suspected or anticipated.

[14] Keene based his conclusion on irregularities he discovered in subleasing and occupancy that created a ghost population.

Example C.3. Another interesting case was that of Bordeaux (France), for it allows a number of inferences to be drawn about the epidemic distribution. Castile became a coveted ally of England after the outbreak of the Hundred Years War between England and France in 1337. In 1348, a marriage was in the making as part of an Anglo-Castilian alliance (Russell, 1955: Chapter 1). It was the marriage of Princess Joan de la Tour to Prince Pedro. The event is described in detail in Cantor (2001: Chapter 3). Joan was the 15-year-old daughter of King Edward III of England and her fiancée was the heir to the Castilian throne[15]. Three important events mentioned by Cantor and others are relevant to the study of Black Death:

- The Princess Joan arrived at Bordeaux with a numerous entourage in early August of 1348.
- The Princess's advisor and former royal chancellor Robert Bourchier died on August 20, 1348.
- The Princess herself died on September 2 of the same year.

These events lead to some rather interesting inferences motivated by some systematic historical detective work.

The first inference has to do with the *beginning* of the plague in Bordeaux. By early 1348, European authorities had started to follow closely the plague's progress to try to cope with it. It is safe to assume that the royal court in London was not aware of the plague in Bordeaux when the Princess left home by mid-July, otherwise they would have made alternative plans for the trip. At that time, a trip from London should have taken about 20-25 days, depending on conditions such as the average sailing speed (which was 40-50 km/day). Thus, knowledge about the Bordeaux situation in England was essentially reduced to what happened in Bordeaux 20-25 days earlier. Considering such speed for communications, we can draw a first conclusion: Bordeaux was free of plague by the end of June 1348. This finding is in agreement with the majority of scholars who claim that the epidemic started there in July or August (Renouard, 1965: 363; Deaux, 1969: 104; Ziegler, 1969: 64; Biraben, 1975: 74; Gottfried, 1983: 49).

The second inference has to do with the *source* of the UK infection. A start of the epidemic in Bordeaux no earlier than July would have been simultaneous or slightly later than the outbreak in the UK (see Table 1), thus making Bordeaux an unlikely source of infection for the UK.

The third inference has to do with the *nature* of the plague. Within days of Princess Joan's arrival at Bordeaux, members of her traveling party fell sick and died. Advisor Bourchier was one of the first to pass away. If we assume that these people were infected in Bordeaux, an approximate period of two weeks is

[15] Less than two years after the engagement, Pedro started to reign as Peter I of Castile--The Cruel. He succeeded his father King Alfonso XI, who was a plague victim at Gibraltar in March 26, 1350.

Table 1: Start of Black Death in UK according to various sources (Horrox, 1995: 62-64).

Date	Place	Source
23 June 1348	Weymouth	Gray Friars of Lynn Chronicle
24 June 1348	Bristol	Monk Ranulphus Higden
7 July 1348	Weymouth	Eulogioun Historiarum
1 August 1348	Dorset Co.	Robert de Avesbury
1 August 1348	Bristol	Anominalle Chronicle

too short a time to die of the hemorrhagic plague, which according to Scott and Duncan (2004: 162) had a 37-day period from infection to death. About the only possibility in favor of the hemorrhagic theory, in this case, would be that infection occurred before the Princess departed the UK. This possibility would require that at least some members of the Princess's royal delegation spent time at an infected port in the southern UK at the beginning of July, because London did not have the plague at that time. However, we have found no further historical information about the beginning of Joan's fateful trip.

As the above examples show, Black Death inference involves both the logical structure of the epidemic system and various other factors (problem context and content, etc.) as well.

c. Topography and Modelling Parameters

Another important element of the $\mathcal{S}$-KB is the topography of the geographical region within which the epidemic propagated. As the Black Death infected areas expand at a certain rate, the associated mortality may increase as a function of the area size. This relationship between area-mortality can be interrupted by the regional topography; e.g., the epidemic front can run into a topographic barrier, which can then change its direction or terminate its spread. One of the most remarkable examples comes from Engelberg and Dissentis in central Switzerland. The villages are only 40 km apart, but because those are 40 km of tall mountains, Black Death came first to Dissentis from Italy to the south in December of 1348 (Sticker, 1908: 56) and moved northeast, downstream along the Rhine, reaching as far as Germany within the next ten months, but not to Engelberg. On a map, Engelberg seems close to Dissentis, but the two cities do not connect by roads. Engelberg was not ravaged by the pestilence until September of 1349 (Fossel, 1987: 9), when the epidemic came from France to the west. A different example was considered in the previous section, in which we used a description of the cities of Florence and Bologna to obtain evidential support for our population estimates.

d. Fowl or Fish?

Marcel Proust once commented: "The real voyage of discovery often consists not in seeking new landscapes, but in having new eyes". In the case of Black Death, using the "eyes" of SEP modelling and space-time mapping, convincing evidence is obtained that the Great Pestilence and the bubonic plague exhibit certain significant differences in their spatiotemporal structure.

An initial interesting result was obtained during the preparation of the data. It refers to the good agreement between fatalities predicted by the extended Reed-Frost (ERF) model and the actual mortality data. Previously, Scott and Duncan (2001) had employed the original Reed-Frost model in their analysis of the different visitations of the plague in the UK. Fig. 17 presents mortality distributions for the city of Givry in Bourgogne (France) obtained by the present approach. As was shown in Table III.2, this city has the extraordinary feature of having preserved daily records of fatalities during the Black Death period. The good agreement between the actual fatalities and the predictions of the mathematical ERF model offers some indication that the plague presumably satisfied the assumptions of the model (e.g., the disease propagates at a fixed contagion rate, people are responsible for the transmission, and the disease ends with the exhaustion of susceptibles). Note that in contrast to Fig. IV.23a the mortality period in Fig. 17 was reduced to τ =20 days intervals, same as the serial generation number, which is the minimum interval possible. The reduction of the interval from a month to 20 days was done in order to have as many mortality values as possible, in an effort to strain the ERF fitting to the limit. One cannot escape noticing that this mechanism is much simpler than the elaborate cycle of bubonic plague involving resistant rodents, rats, blocked fleas, and people. In the view of Scott and Duncan (2001: 29) the Reed-Frost model can only explain simple infectious diseases and cannot represent infections with multiple hosts, such as the bubonic plague.

According to the evidence gained in India, modern bubonic plague is a rural disease hitting harder the small villages in the countryside (Fig. III.18a). On the

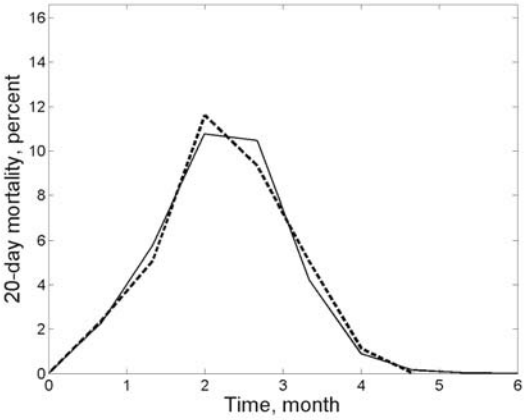


Figure 17. Progression of Black Death at Givry (France) from July 28 to November 15, 1348. Actual fatalities (solid line); ERF model prediction ($P_{s,0} = 2000$, $\tau = 20$, $K_s = 3$, $I_{s,\tau} = 140$, and $f = 0.32$; dashed line).

other hand, our findings related to city size and mortality during the Black Death epidemic (Fig. III.18b) reveal no correlation between city size and mortality, thus supporting the view of a majority of scholars that Black Death was a devastating epidemic that indiscriminately attacked large urban centers and the countryside (Creighton, 1891: 135; Baratier, 1961: 111-112; Naphy and Spicer, 2000: 41). We did find, however, a considerable positive correlation between city size and duration (Fig. IV.2). For any given size, there is a margin of error of plus or minus two months, but cities with markedly different sizes definitely had different duration: 3-5 months for the smallest villages, 5-9 months for medium cities, and longer than a year for the few large cities with more than 70,000 residents. This difference in duration has an interesting effect on monthly mortality. Let us consider two different cities with about the same mortality, say 60%. Venice (Italy) and the manor of Cuxham (UK) had this level of overall mortality rate, but while Venice had a population of over 100,000 residents and the plague lasted for 18 months, Cuxham had a population of 200 residents and the epidemic lasted only 3 months. This means that 60% of the population in Venice died during a time period that was 6 times longer than in Cuxham. As a result, Venice never reached the high monthly mortality levels of Cuxham: the epidemic modelling indicates that the worst monthly mortality at Cuxhan was 35% vs. only 12% in Venice. Obviously, these values are percentages of the surviving population and do not mean that more people died during Cuxhan's worst month than during any time period in Venice. E.g., 35% of 200 residents (=70 fatalities per month) is a much smaller number in absolute terms than 12% of 100,000 residents (=12,000 fatalities), but it is far more pervasive, most likely affecting every single family in Cuxham during the same month.

According to the SEP maps, Black Death moved swiftly across space and time. The systematic advance of the epidemic front indicates that the epidemic passed from one location to the next without skipping intermediate territory. Only occasionally a new focus appeared away from infected areas, suggesting potential leapfrogging of the epidemic mostly by sea. This was, e.g., the case of the start of the epidemic in the English Channel area, in which case the closest infected region was 400 km away in central France. Similar is the case of the beginning of Black Death outbreak in Oslo, where the next closest outbreak occurred in the UK, on the other side of the North Sea. Yet, for the majority of Europe, most of the spread took place because of overland traveling (occasionally assisted by river navigation, not necessarily downstream). Previous studies have calculated epidemic propagation velocities of 0.66-5 km/day based on the distance between the infected city and the infecting city[16] (Biraben, 1975: 90; Andenmatten and Morerod, 1987: 31). The above range is in agreement with the global propagation velocities we derived from the SEP mortality maps, which showed velocity fluctuations mainly around 1.5-6 km/day (Figs. 11 and 13). Remarkably, this range of values for the propagation velocity is an order of magnitude faster than the propagation velocity of modern bubonic plague overland. E.g., it took 28 years for the bubonic plague to cover the distance from Kunming, Yunnan, to Hong Kong

[16] I.e., the city that was the source of infection for the infected city.

(Scott and Duncan, 2001: 49-50), which implies a propagation velocity of 2 km/month. In India it took bubonic plague the entire time period 1897-1902 to cover the 500 miles from Bombay to Nagpur, that is, it traveled with a speed of 10 km/month. Also, while in the case of Black Death initially the square root of newly infected area increased proportionally to the 4th power of time, the bubonic plague increased only proportionally to the 2nd power of time.

Previous mapping was limited to depicting the location of the leading edge of the epidemic front (Fig. III.1). By displaying the geographical propagation of the epidemic at one-month intervals, the SEP maps allow one to observe its duration at any geographical region. This reveals another marked difference between Black Death and bubonic plague: with the exception of the largest cities, Black Death stayed at any given place for less than a year. A characteristic of the bubonic plague, on the other hand, is that it often stayed in the same locality for several years with pauses during wintertime.

The maps of Fig. 2 offer yet another way of portraying the extraordinary virulence of Black Death. During the first year, with an entire virgin continent ahead of it, the plague advanced at an accelerated pace that peaked in October of 1348, when it infected a quarter of a million km^2 in one month (Fig. 6). This initial expansion is higher than the known rate for any other infection. From then on, with less than half of western Europe remaining to be infected, the epidemic expanded at a decreasing pace, eventually dying out by the beginning of 1351 with the exhaustion of new places to infect. Europe did not have an appearance of a new plague with Black Death characteristics until 1361-62. Not re-infecting the same place for years after the end of an outbreak is another special characteristic of Black Death (Scott and Duncan, 2004: 45), one that was implicitly taken into account in the preparation of the SEP maps. By contrast, the modern bubonic plague of India reappeared at the same locality every year for several decades.

There is also a seasonal variation superimposed over the long-term trends in the mortality variation of infected areas. The fact that Black Death was more widespread during the summer has been acknowledged early on by the chroniclers, but some scholars seem to have exaggerated its effect by declaring a complete halt in the course of the plague during the winters (e.g., Benedictow, 1992: 94; Herlihy, 1997: 25). This possibility would make more sense if the bubonic plague theory is adopted, in which case the winter situation is explained in terms of the decreasing activity of fleas during this period. Moreover, the complete disappearance of the plague for a season is not possible if a person-to-person transmission is taking place, simply because such a long pause would result in the disappearance of the infecteds that are needed to continue the transmission of the disease. Figs. 2 and 4 show clear seasonality, particularly starting after the first winter, but without the epidemic coming to a complete halt (Fig. 6). The number of places experiencing the epidemic was reduced, but in some of the places still having it, the most severe mortality sometimes took place in the middle of winter; see, e.g., Avignon (Ziegler, 1969: 66), Bath and Wells diocese (De Hahn, 2002: 83), Marseille (Michaud, 1998: 408), Murcia (Torres, 1981: 10-14), and Saint Maurice (Pasche, 1998: 127-129).

The global mortality calculated on the basis of the systematic space-time mapping of Fig. 2 generates monthly mortality rates mostly in the range of 3-6% per month. Notice that in India the bubonic plague during the period 1900-1950 did not exceed 0.4% per year (Scott and Duncan, 2001: 75), which is another significant difference between Black Death and bubonic plague.

Based on their own findings, Scott and Duncan (2004) have postulated a viral nature of the Black Death epidemic that they have called *hemorrhagic* plague. The significance of the matter was discussed in Section III.B.c. A critical temporal aspect of hemorrhagic plague as postulated by Scott and Duncan (2004: 162) is that the period from infection to death was on average 37 days. Without explanations, this long incubation period does not fit well with certain accounts alleging fatalities occurring shortly after healthy people came in contact with infected individuals. The most classic of these accounts is chronologically related to the beginning of the epidemic in Messina. In particular, the account of chronicler de' Mussis states that: "As it happened, among those who escaped from Caffa by boat were a few sailors who had been infected with the poisonous disease. Some boats were bound to Genoa, others went to Venice and to other Christian areas. When the sailors reached these places and mixed with the people there, it was as if they had brought evil spirits with them: every city, every settlement, every place was poisoned by the contagious pestilence, and their inhabitants, both men and women, died within a few days." Scott and Duncan (2004: 229-230) have addressed the issue by declaring that the plague had arrived in Messina before the arrival of the galleys, early enough to incubate and to go into full swing by the time the galleys arrived. The population, partly ignorant of the situation and partly in need of a scapegoat, blamed the sailors for the outbreak of the epidemic. The timing was a mere coincidence; the sailors had nothing to do with the outbreak.

Nobody seems to have addressed, however, the case of Princess Joan de la Tour of England, which refers to the opposite situation: healthy people coming to an infected area. She arrived at Bordeaux from the UK on her way to Spain in order to marry the heir to the throne of Castile. This important Black Death event was reported in Cantor (2001: 45-47). He also mentioned hundreds of dead people with plague symptoms lying on the docks and streets by the time the healthy Princess Joan and her escorts arrived. Against the warnings of the mayor of Bordeaux, the party decided to have a break and went to stay at a castle, where very soon many of them started to feel sick. Being ignorant of the severity of the situation, they did not flee. Joan saw the party becoming decimated within two weeks of arrival, until eventually she died as well. The infection of members of Joan's entourage before departing the UK is the only way to explain her death as a result of the hemorrhagic plague scenario advocated by Scott and Duncan (2004: 161-163). If this is the case, she would not have been the only royal to catch the plague in one place and die in another. Aragon's Queen Leonor felt sick while traveling from Zaragoza to Valencia. The entourage had to stop in Jérica because of her deteriorating condition, where she died within a few days. Although Jérica had the pestilence at the time, chronicles make clear that she already arrived sick, thus eliminating the possibility that Jérica played any part in the death of the queen.

Over the years, a number of scholars have come up with serious objections against the bubonic plague theory (see Section III.B.c). Their proposals are radically different than the bubonic plague etiology, which has been the prevailing view during the last century. In recent years these "heretic" (so to speak) proposals have been supported by new evidence. One of the most damaging pieces of evidence against the bubonic plague theory was recently announced: tests made on teeth from skeletons found in 14th century mass graves showed no genetic trace of the *Y. pestis* associated with bubonic plague (see, also, Section III.B.c). In light of the aforementioned considerations, this chapter's contribution to the debate may be summarized as follows:

- The findings of advanced stochastic modelling and spatiotemporal mapping support the view that Black Death was a different kind of epidemic than bubonic plague.
- No damaging hard evidence has been found against the new proposals concerning the Black Death etiology.

In the context of the Black Death project, we saw ourselves as scientists working *on* problems rather than *in* disciplines. This implied various types of boundary crossing as well as moving between theory, computation, and implementation. We processed the rather scant evidence and uncertain information sources available in an efficient manner using state of the art technology, and we focused on the substantive modelling of the space-time distribution and propagation characteristics of the Great Pestilence, without delving into its biological etiology. Nevertheless, the results we obtained do not support the theory that Black Death was, in fact, bubonic plague--a conclusive proof of this theory has not yet been offered.

Chapter VI - Epea Pteroenta

"S'il peut y avoir la moindre chance d'atteindre l'oreille de l'autre, ce n'est qu'en donnant le plus de tranchant possible à son propos. Voilà pourquoi le trait est ici accentué. Les temps heureux ou l'on pourrait s'en dispenser, où l'on pourrait éviter l'outrance et faire dans la sobriété, ne sont pas encore venus."[1]

G. Anders

A. What to do With the Philistines?

As the title of this last chapter we have chosen the Homeric phrase *Epea Pteroenta*[2]. Indeed, in this chapter certain thoughts are shared and comments are made that are discussed among many public health researchers, but are not always expressed in writing (see discussion in Christakos, 2004). As a matter of fact, some of these thoughts and comments have already appeared in an explicit or implicit form in the arguments and methods presented in the previous chapters, in which case the present chapter may serve as a kind of poetic summary in the Homeric tradition.

There is an influential "elite" in public health education and institutionalized research nowadays, that regards the *content* of scientific culture with indifference. Rather, the focus of this *philistine*[3] elite is to use scientific culture to achieve objectives quite separate from that culture's inner content. Aspiration for *knowledge* and the pursuit of the *truth* are not high on the priority list of such elites. Knowledge is increasingly viewed as the product of a technical process, rather than as the product of human *intellectual* effort. In many public health fields, the philistine agenda promoted unconscious research that has rarely lead to more than simply confirming what was already known. Phillips *et al*. (2004) maintain: "Given the resources expended by the health science research enterprise, epidemiology

---

[1] "If there can be the slightest chance to reach the ear of the other, it is only by giving the most abrasive edge in one's discourse. For this reason the issue is pronounced here. Happy times when we could exempt ourselves from doing so, when we could avoid excess and make things in sobriety, did not come yet."

[2] "Winged words" (meaningful words spoken, uttered, or flying from one person to another); a favorite, immortal Homeric phrase (*Homer-Iliad*: 1-201).

[3] Here, we expand upon the term "philistine"--as used in Frank Furedi's recent work (Furedi, 2004)--to denote a person guided by materialism, who is disdainful of intellectual or artistic values.

(which we define broadly, including both population health and clinical research, and covering biological, behavioral, and economic dimensions) is characterized by remarkably little innovation, let alone critical review of existing dogma. The outputs of the science have increased to a torrent; research to improve the quality of the science is a trickle"; and "It is troubling that we plow ahead with billions of dollars worth of research every year while making minimal effort to answer fundamental questions about what that research is really telling us. Epidemiology is far too important to our society to be treated as an exercise in uncritically following existing formulae." After many years of research, several areas of epidemiology are still in a state characterized by the following: (a) the scientific issues are very subtle and complex, (b) the necessary observations and measurements are difficult to acquire and share[4] and they are often misinterpreted, and (c) there is no substantial theoretical content within which to work. Public health philistines may be the last to realize the importance of theoretical modelling. Remarkably, even researchers in the business world have emphasized that "our society, to a greater degree than before, will require people who have the skills and the competency to develop theories/models" (Arbnor and Bjerke, 1997: xxi).

Philistines despise intelligence, because they cannot bear their doubts. Thus, the struggle for research support is in its essence a struggle of vested interests and forces, not of arguments. Matters of friendship, politics, and power (which should be irrelevant) enter into the decision-making process concerning research priorities and financial support. Afraid that it may have to share influence and resources, the philistine elite strongly opposes an interdisciplinary approach to epidemic research. Under the philistine influence, mainstream public health research appears as an expensive fraud in the eyes of its critics. In the view of these critics, some of the most important public health research issues today are not related so much to the availability of research funds as to their improper handling by the elite. The same critics increasingly argue that in certain public health areas, there is a shortage of people in a position to generate innovative approaches to important research problems, rather than there being shortage of funds. If the criticism is valid, then one wonders whether it is the heavy price we have to pay for the systematic persecution of scientific excellence over the years, and its subsequent replacement with political or professional correctness in their various forms. Given the circumstances, Lewis Thomas' suggestion is particularly relevant (Thomas, 1995: 151): "It is time to develop a new group of professional thinkers, perhaps a somewhat larger group than the working scientists, who can create a discipline of *scientific criticism*. Science needs critics of this sort, but the public at large needs them more urgently."

The situation is no brighter in higher public health *education*. What is often offered in our public health schools today is training rather than education. The difference is obvious--training is learning how to perform a job, whereas education is learning how to learn. Education traditionally promotes critical thinking skills, whereas training focuses upon learning how to perform a job and obtain uniform predictable behavior from trainees, without the necessity of their understanding

[4] Due to a variety of scientific, social, political, etc. reasons.

why they should act in the prescribed manner[5]. In reality the latter is of limited value because it may lead to jobs in the near future, but it cheats the student out of long-term benefits. In a dynamic culture, where technical knowledge and fashionable views are raised up and overthrown many times in the course of one's career, the ability to think critically is of far greater importance than the ability to regurgitate fashionable tools that are of value today but obsolete tomorrow[6]. Furthermore, most public health textbooks and courses do not address salient interdisciplinary, multicultural, and multiparadigmatic trends at all. As a result, students are not adequately prepared to fit their work into an intellectual discourse that would allow them to appreciate the essence of these trends and act accordingly. Education should be a living reality in a conscious attempt to improve their ability to comprehend the process of learning, produce and develop knowledge, and understand what the knowledge they have acquired really is knowledge about. Lacking this critical element of education, public health students will tend to bear the brunt of change rather than anticipate and participate in how change happens.

In today's chaotic world, indeed public health scientists have certain important *tasks*: to obtain an improved understanding of the environment and its health effects in order to improve the chances of protecting people's health, avoiding epidemic disasters, and aiding decision makers in producing sustainable policies. The fact that an understanding of the environment may require a *synthetic* view of the nature of things is not a new idea in scientific inquiry. Ruelle (1991: 4) has commented, "The great Isaac Newton characteristically shared his efforts among mathematics, physics, alchemy, theology, and the study of history in relation to the prophesies". Knowledge integration requires understanding the relevant context and content, and an ability to look across different scientific fields to see what matters most, rather than merely borrowing specifics from these fields. Remarkably, in every new tool we create, an idea is embedded that may go beyond the function of the tool itself[7]. In the end, it is all a matter of conscientious choice--to operate in a creative way, synthesizing, analyzing, and transforming knowledge--or to surrender to the philistine way by moving through life in a routine fashion, content merely to gather information and apply it mechanically.

For their views to retain credibility, it is critical that public health scientists consistently employ the *epistemic* method to study the nature of their intellectual

---

[5] For those among our readers who would prefer a more picturesque representation of the matter, the following quote by Jay Cross (1994: 62) may be appropriate: "If your 16 year-old daughter told you that she was going to take a sex education course at high school, you may be pleased. What if she announced she was going to take part in some sex training at school? Would that elicit the same response?"

[6] This problematic situation is not limited to public health education. As Steven J. Bartlett remarks in his essay *Barbarians at the Door* (Bartlett, 1993: 296): "The international emphasis on vocational education is a regressive change that marks the reestablishment of a primitive view of man and of a fundamentally barbaric attitude concerning the purposes of living."

[7] E.g., the invention of eyeglasses not only improved defective vision but also promoted the idea that humans do not need to accept as final the restrictions imposed on them by nature.

frame, assess the reliability of the generated knowledge, and offer norms for scientific behavior. The production of high quality public health research and education depends on the scientist's ability to manage the issues that reach deeper into the methodological roots of knowledge. The richer one's conceptual knowledge, relative to the health system at hand, the greater the chance of performing creatively. The "just look and see" approach of traditional epidemiology should be rejected in favor of one that assigns deeper meaning to the close interaction between observation and theory. Alternative modes of thinking about public health issues can lead to unique blends of perspective and innovative solutions. Often the path to problem solving is manifold and variable rather than fixed and singular. The situation described in the above lines constitutes a vital element of interdisciplinary public health research and development in the emerging Conceptual Age.

Furthermore, the study of epidemics is characterized by considerable uncertainty in various interdisciplinary forms, which present serious conceptual and empirical challenges, and the particular area of mathematics most useful for dealing with these challenges is *stochastics*. Indeed, stochastics possesses the strong epistemic underpinnings and conceptual context that make it able to integrate interdisciplinary laws of change in a mathematically rigorous and epidemiologically meaningful manner; account for space-time dependencies of epidemic systems; and interpret and transform interdisciplinary information sources. These crucial issues are usually neglected by classical statistics, which is why substantive maps of epidemic systems can be generated by stochastics but not by classical *statistics*. In a similar vein, the role of conventional statistics in epidemiology is sometimes undermined by the fact that it merely focuses on formal techniques (pattern fitting, etc.) and does not pay sufficient attention to substantive issues. The manipulation of form in terms of statistical techniques has become such a powerful dogma in epidemiology that research is often viewed as merely a matter of doing such manipulations. But form is not substance, in the same way Achilles' armor was not Achilles himself, thus leading to the well-known tragic outcome (*Iliad*, Book XVI): "Standing over his fallen foe, Hector mockingly tells the dying Patroclos that the armor of Achilles has not protected him and that he will never again assail Troy's walls".

Yet another very special task of public health scientists is that of occasionally swimming against the tide, i.e., supporting new ideas even if doing so is *unfashionable* and *professionally incorrect*. New ideas may indicate an intellectual need that the ruling ideology cannot satisfy, often associated with the fact that established dogmas are outdated and do not serve any purpose other than to prolong the *status quo*. Despite the efforts of the philistines, the ultimate goal of scientific reasoning will always be the search for truth and knowledge, and this often involves the creation of *new* ideas and paradigms. Of course, one should not uncritically accept any idea that is presented as new. Some views have the glamour and allure of novelty, but when it comes time to tell the sober truth, they seem merely quixotic--long on flash and panache, but short on good sense. Thus, any new idea must go through a critical evaluation stage, and the same should be the case with the old ideas that have become dogmas. Indeed, for intellectuals--who live *for* ideas rather than off ideas (Coser, 1965: viii)--what distinguishes science

from most other intellectual activities is the critical attitude towards its most cherished ideas. The *criticism* of ideas is an essential ingredient of public health reasoning, perhaps second in importance only to the generation of new ideas. It would be encouraging if an increasing number of public health scientists decided to openly criticize many of the existing dogmas and to fight the widespread tendency to follow the lead of some ruling fashion, whether the current epidemiologic paradigm, a public health tradition, or an influential *science a la mode*[8]. The intellectual pressure that constructive criticism could exert would force the established elites to examine their ideas and positions for their weaknesses and complacencies, which could open the way to new and fruitful definitions, creative conjectures and postulates, and innovative tools and methods, and it may even lead to a much needed paradigm change. This is especially true in light of the considerable changes in the intellectual and social background underway nowadays.

B. The Oedipus State and Epidemic Warning Systems

In real world situations, every kind of prediction is conditioned, to a larger or a smaller degree, by interactions and decisions that can affect the prediction. This is true in public health research, as well. Depending on the adequate assessment of the situation, and the timely action taken, the hazardous consequences of epidemic predictions could be limited or even eliminated. Unfortunately, this is not always the case. Occasionally, public health scientists predicting future epidemics find themselves in a so-called "Oedipus state"--named after the ancient Greek king who, despite becoming aware of his tragic future, was unable to change it[9]. Of course, like most major issues in life, public awareness about the dangers of diseases may be represented metaphorically as the familiar double-faced Janus. Increasing public awareness about the dangers of diseases is an appropriate approach, but there are also situations in which public awareness campaigns about potential epidemic outbreaks have led to an irrational framework for dealing with the disease, rather than a rational one.

It is in such Janusian circumstances that this book's primary suggestion should be considered: Rather than serving a philistine agenda, developing the background context of intellectual work and creativity would provide a fair assessment of potentially serious future epidemics--and would help public health scientists make a stronger case to authorities and to the public, when doing so is justifiable.

---

[8] On occasion, one may have to go against his own followers. "Moi, je ne suis pas Marxist," Karl Marx once claimed in an effort to emphasize that he was not restricted by the boundaries of his own theory (in fact, some of the boundaries were developed by his followers and not Marx himself). Undoubtedly, it takes a lot of courage and intellectual depth to make such a statement, not to be a slave of one's own construct, not to be dedicated "soul-and-body" to a paradigm--in brief, not to take oneself too seriously. Philistines have a lot to learn from Marx, indeed.

[9] The "Oedipus state" should not to be confused with the "Oedipus syndrome," to which Sigmund Freud assigned a certain sexual interpretation.

By focusing on methodological issues and how they can affect decision-making, epidemic risk analysis possesses a strong cultural element as well.

In the case of the infamous Black Death epidemic discussed in the book, the *synthetic epidemic paradigm* (SEP) managed to produce useable maps of the ways the epidemic propagated through geographical space and time. These maps can help one discover an underlying coherence in disease distribution that was buried within reams of contemporary evidence that had so far defied quantitative understanding. We studied important epidemic aspects by adapting our methods of scientific inquiry to the breadth and complexity of contemporary evidence. We developed well-constructed scientific arguments on the basis of reliable knowledge and sound logical reasoning. We used stochastic methods that allowed us to exhibit considerable receptivity to different kinds of historical data and make judgments under conditions of uncertainty rather than giving up due to incomplete knowledge about an epidemic issue. Since Black Death had grave societal, public health, and financial effects, the study of these maps can offer valuable insight into these effects, as well as into similar effects that could result from potential contemporary epidemics.

Just as this book demonstrated to be the case with Black Death, we now have the opportunity to study infectious and other onset diseases as well, in a more informative manner. This leaves plenty still required with regards to the intellectual background of public health discourse. There is, e.g., a need for sufficiently precise hypotheses concerning the spread of disease suitable for expression in mathematical terms. Team members will need to grasp the overall public health situation and strive for conceptual synthesis, which means that interdisciplinary work requires broadly educated researchers. These researchers should consider a wider perspective in their work that would allow them to change working modes depending on the epidemic aspect they are studying. Moreover, a lot of what is going on in public health studies today has to do with *ad hoc* explanations. If an epidemic explanation is going to be meaningful, however, the theory that does the explaining must be richer in *content* than the situation to be explained. This is yet another point that seems to escape the Philistines. Instead, their focus is mainly on the kind of uninspiring research vividly described in Lakatosian terms: give someone $ 2 million to set sail from the UK to follow in Darwin's path, and then find out he vomited somewhere in the Indian Ocean.

SEP models can study large-scale population phenomena related to social and public health measures, which may then be proposed or applied, and, together with TGIS technology, they could build an *Epidemic Warning System* (EWS) offering powerful visual simulations of the expected effects of potential epidemics, at local or global space-time scales. The EWS can enable boundary crossing and knowledge integration across sciences, it can improve communication and the distribution of information units within institutions, and by using sophisticated computational tools it can bring to life multi-sourced databases and interdisciplinary theories. In this manner, EWS-generated spatiotemporal simulations can adequately represent the various possible scenarios of epidemic effects, assess the significance of the relevant disease variables and parameters, and allow adequate planning and preparation to deal efficiently with the consequences of the epidemic

on the population and the infrastructure. Furthermore, a properly developed EWS has the power to go beyond its original context into new ones, where it can find unexpected uses. The visualization power of spatiotemporal maps and the embedded epistemology can help people organize their minds and integrate their experiences of the world, and in doing so, they can influence public health decision making in myriad forms.

C. There is no Rest for the Wicked

One thing is certain nowadays: a rapidly changing world is both challenging old paradigms and generating new ones to meet the emerging realities. In this book we made an attempt to articulate as clearly as possible some critical standards concerning a synthetic epidemic paradigm for public health research purposes. We cannot imagine a fairer destiny than that this effort should simply point the way toward an improved and more comprehensive paradigm. With regards to institutionalized research administration, one can always hope that someday a decision will be made to become more objective and to extend its "inner circle" beyond members of the philistine elite[10]. Listening to the opening theme of Beethoven's Fifth Symphony might be helpful in this respect[11].

Although our discussion of interdisciplinary matters was made in a constructive spirit and with the best of intentions, some of the views expressed in the book may become the targets of attack by some. Interdisciplinary work is likely to upset everyone. Indeed, this is the fate of those who, not recognizing themselves in any of the most widespread disciplinary solutions to a public health problem, seek to synthesize elements deriving from the various proposals and end up drawing the wrath of all. What makes, however, the interdisciplinary quest so inviting is precisely this attempt to find a balance between divergent or even opposing proposals, to draw out and combine that which is plausible in each one of them.

On the other hand, we have no problem with such attacks, as long as they are carried out by the right people. Even vilification when done by the right people

[10] Sad as it is, the "elite" phenomenon is not limited to public health affairs. As is emphasized in a recent article in *The Economist* (2005: 23-24): "Everywhere you look in modern America--in the Hollywood Hills or the canyons of Wall Street, in the Nashville recording studios or the clapboard houses of Cambridge, Massachusetts--you see elites mastering the art of perpetuating themselves. America is increasingly looking like imperial Britain, with dynastic ties proliferating, social circles interlocking, mechanisms of social exclusion strengthening and a gap widening between the people who make the decisions and shape the culture and the vast majority of ordinary working stiffs… The students in America's places of higher education are increasingly becoming an oligarchy tempered by racial preferences. This is sad in itself, but even sadder when you consider the extraordinary role that the same universities--particularly Conant's Harvard--played in promoting meritocracy in the first half of the 20th century."

[11] Thus Fate knocks on the door" are the noticeable words applied by Beethoven to the opening theme of the Fifth Symphony.

can make one's reputation rise[12]. Not to mention that we possess a capacity for detached amusement, which in most cases enables us to ignore unfair critics' harangues and complaints and to see that their arguments are bound to fail in the end. We have a certain robustness of spirit and do not take criticism personally. More to the point, we can distinguish between knife wounds and fleabites that are harmless[13]. If we have confidence in our own hearts that certain of our proposals are right, we do not need public affirmation of their rightness. On the other hand, there are Black Death issues about which we had doubts before our decision to study the epidemic was made and about which we continue to have doubts afterwards. In this case, the criticism can be particularly enlightening. Of course, there is always the possibility that we will be treated like the *kabbalists*, who despite their startling and even provoking ideas aroused relatively little opposition[14].

Have we been emotional? Perhaps. Even so, though, we can still hope that in the end the present book may serve to demonstrate that scientific reasoning and emotion can work together to deliver a studious product. After all, life is an effort that deserves a better cause.

[12] This comment should be read in the spirit of Samuel Taylor Coleridge's remark: "No mind is thoroughly well organized that is deficient in a sense of humor."

[13] Unless, of course, these are Black Death fleas.

[14] See *De Arte Cabalistica* by Johannes Reuchlin (1517).

Appendices

"You have to start somewhere. You make an assumption and explore the consequences."
Democritus

Appendix A. Annotated Black Death Data Summary

Tables in this appendix summarize relevant information about the Black Death of 1347-51 in Europe. Places in italics denote a geographical area larger than a city, e.g. *Bohemia* or *Catalonia*. Those locations marked with an asterisk (*) were not used in the preparations of the maps in Chapter V, such as Braunau* (Austria). If the date is omitted in the pre-plague population column, the number of residents relates to a date no more than ten years before the outbreak of the pestilence.

We have limited to include in the tables only the information that according to our studies is the most accurate. In case of multiple authors supporting a value or date, mostly we have limited to one reference for the sake of conciseness in an effort to avoid cluttering the tables. The following is a list of references that directly or indirectly helped us to shape the information in the tables despite not being referenced directly: Barron (1995); Brothen (1996); Bur (1987); Courtenay (1980); Desportes (1983); Dobson (2000); Falsini (1971-72); Favreau (1985); Fournée (1978); Fryde (1978); Giblin (1995); Gyug (1994); Herlihy (1965); Higounet-Nadal (1965); Hubscher (1986); Jenks (1977); Keene (1995); Kent (1985); Le Moigne (1986); Livet and Rapp (1987); López (1965); Macary (1972); Nohl (1999); Parentin (1974); Prevenier (1983); Russell (1966); Ruiz (1998); Simpson (1905); Sivéry (1965); Trenchs (1972); Trenchs (1980); Ubieto (1967); Valdeón (1981); Vasold (2003); Verlinden (1971); Wetzstein (1996); Williamson (1957).

a. Austria

Austria received the epidemic wave that started in Venice (http://encarta). From Austria the epidemic continue its spreading into neighboring territories with decreased intensity.

Place	Pre-plague Population	Start	End	Mortality
Braunau*				High[Hoeniger 1882:15-16]
Eggenburg		Summer 1349[Biraben 1975:83]		
Marienberg		Priest died September 13, 1348[Klein 1960:95]		
Neuberg		September 29, 1348[Benedictow 2004:182]	April 12, 1349[Benedictow 2004:182]	Especially ferocious[Ziegler 1969:84]
Pongau		November 11, 1348[Klein 1960:114]		
Upper Inntal		Late Fall 1348[Benedictow 2004:182]		
Vienna	22,000[Chandler 1987:16-18]	April 12, 1349[Gasquet 1908:74]	Sept. 29, 1349[Gasquet 1908:74]	33-66%[Ziegler 1969:84]
Villach		January, 1349[Biraben 1975:77]		

b. Belgium

The Black Death came to Belgium from France. The epidemic reached a dead end in Belgium and had a mild intensity despite advanced urban development similar to northern Italy, where the pestilence had devastating consequences.

Place	Pre-plague population	Start	End	Mortality
Antwerp*	15,000-22,000[http://scholar]			20-25%[Naphy and Spicer 2000:38-39]
Ath		Summer of 1349[Benedictow 2004:113]		16%[Blockmans 1980:837]
*Brabant**				Low[Despy 1977:209]
Bruges	42,000[Bardet and Dupâquier 1997:412]	May, 1349[Blockmans 1980:838]	December, 1349 Nicholas 1992:266	20-25%[Gottfried 1983:57]
Brussels*				20-25%[Gottfried 1983:57]
*Flanders**				16-25%[Nicholas 1992:266]
Ghent	64,000[Bardet and Dupâquier 1997:412]	July, 1349[Kowalewsky 1911:261]		20-25%[Gottfried 1983:57]

Place	Pre-plague population	Start	End	Mortality
Liège	22,000 Chandler 1987:16-18			Escaped the disease Scott and Duncan 2001:87
Lovain				Spared Kelly 2001:17
Maubeuge*				24% Blockmans 1980:837
Mons		July, 1349 Biraben 1975:77		
Tournai	19,000 in 1400 Chandler 1987:18	July, 1349 Biraben 1975:77		
Ypres	30,000 Bardet and Dupâquier 1997:412	July, 1349 Kowalewsky 1911:261		20-25% Gottfried 1983:57

c. Croatia

The disease either came from outside Europe or from the Republic of Venice, which controlled the area at the time.

Place	Pre-plague population	Start	End	Mortality
Dubrovnic		January 13, 1348 Deaux 1969:85		
Istria		August, 1348 Benedictow 2004:182		
Split		December, 1347 Benedictow 2004:72		

d. Czech Republic

The epidemic came to current Czech Republic from Austria.

Place	Pre-plague population	Start	End	Mortality
Bohemia		Late in Fall of 1349 Gasquet 1908:75		10% Gottfried 1983:68
*Moravia**		1350 Biraben 1975:77		

e. Denmark

There is great uncertainty about the beginning of the plague in Denmark. The *Chronicle of Zealand* mentions that "a pestilence ravaged the country" in 1348, and that, in 1349, "there was a great mortality in Denmark" Benedictow (2004:159). Some scholars have shifted the outbreaks by one year and others have even discarded the first one.

Place	Pre-plague population	Start	End	Mortality
Aalborg		July, 1350[Biraben 1975:80]		
Bornholm	7,000[http://home3]	1349[http://home3]	1350[http://home3]	50%[http://home3]
Copenhagen*		Jan., 1349[Biraben 1975:80] Early 1349[Fössel 1987:6] Sept., 1350[Benedictow 2004:164]		
Ribe		Late summer or early autumn, 1350[http:www.hum]		Donations to cathedral starting June 1350 [0 3 6 1 1 0]; background: 1.7 per year[Benedictow 2004:161:163]
Roskilde*		Late summer or early autumn, 1350[http:www.hum]		Donations to cathedral starting Oct. 1350 [1 5]; background: 1.4 per year[Benedictow 2004:163]
Zealand Island		July, 1350[Biraben 1975:80]		

f. France

Marseille was by far the most lethal focus of infection among all places where the Black Death was first started. From Marseille the epidemic moved to the rest of the country and eventually through the rest of the continent, with the exception of Italy, areas directly north of Italy and most of Spain (Smail 1996:11).

France and Italy are supposed to have the highest mortality in the whole Europe (http://ragz-international), which may be a real fact or just the result of better documentation than the rest of continental Europe.

Place	Pre-plague population	Start	End	Mortality
Abbeville		April, 1349[Biraben 1987:1980]		
Agen		May, 1348[Biraben 1987:178]		
Aix-en-Provence	6,000 Baratier 1961:128	December, 1347 Biraben 1987:178		45%[Baratier 1961:128-129]

Place	Pre-plague population	Start	End	Mortality
Albi		July 8, 1348[Biget 1983:92]		55%[Prat 1952:17]
Alès		July-September 1348[Biraben 1987:179]		
Amiens		January, 1349[Biraben 1987:179]	After winter 1348-1349[De Calonne 1976:273]	High[Ziegler 1969:80]
Angers	22,000 in 1300[Chandler 1987:17]	November 30, 1348[Biraben 1987:179]		25%[Lebrun 1975:35]
Angoumois		September, 1348[Biraben 1987:179]		
Anjou		November 30, 1348[Biraben 1987:179]	End of 1349[Landais 1997:123]	
Arbois		April, 1349[Biraben 1987:180]		
Arles	17,000 in 1300[Chandler 1987:16-17]	January, 1348[Biraben 1987:178]		High[Deaux 1969:96]
Arras	20,000 in 1300[Chandler 1987:17]			Spared[Cohn 2002b:180]
*Artois**				Low[http:// www.artehistoria
Auch		May, 1348[Biraben 1987:178]		
Aurillac		October-December 1348[Biraben 1987:179]		
*Auvergne**	500,000 in 1328[Audisio 1968b:344]	April, 1348[Biraben 1987:178]		
Auxerre*		1348[http://perso		
Avignon	30,000-38,000[Gagnière *et al*. 1979:212-213]	January, 1348[Biraben 1975:91]	July, 1348[Vasold 1991:43]	At least 50%[Scott and Duncan 2004:24]
Bayeux		October, 1348[Désert 1981:76]		
Bayonne*		1348[Biraben 1975:74]		
Béarn				Partially spared[Tucoo-Chala 1951:84]
Beaune		April, 1349[Biraben 1987:180]		
Beauvais		1348[Ganiage 1987:60]		

Place	Pre-plague population	Start	End	Mortality
Besançon		May, 1349[Biraben 1975:76]	After September, 1348[Cohn 2002b:181]	
Béziers	20,000 in 1200[Chandler 1987:16]	February, 1348[Biraben 1987:178]	Not before August 1348 Biraben 1974:506	High mortality[Sagnes 1986:137]
*Bigorre**	50,000 in 1328[Berthe 1976:39]	June 29, 1348[Berthe 1976:51]	April 12, 1349 Berthe 1976:51	50-67%[Berthe 1976:51]
Blois*	5,000[Denis 1988:55]	1348[http://www.ac-orleans-tours]		
Bordeaux	30,000[Chandler 1987:16-18]	August, 1348[Prosperi 2000:45]		40%[Gottfried 1983:49]
Bourg-en-Bresse		April, 1349[Biraben 1987:180]		
Bourges*		1348[Meslé 1983:147]		
Buis-les-Baronnies		April-June 1348[Biraben 1987:179]		
*Burgundy**		July, 1348[Ziegler 1969:65]		
Cadenet		January-March 1348[Biraben 1987-179]		
Caen	20,000[Chandler 1987:17-18]	October 1348[Jouet 1972:272]	January 1349[Jouet 1972:272]	40-50%[Gottfried 1983:55] Choices of burial place, starting in Sept., 1348 [0 4 9 2 1 0][Jouet 1972:272]
Cajarc*				50%[Clavaud 1995:62]
Calais		December, 1348[Biraben 1987:179]		
Carcassonne		March, 1348[Biraben 1987:178]	May, 1348[Guilaine and Fabre 1984:96]	40%[Gottfried 1983:49]
Carpentras				Spared[Dubled 1969:20]
Castellane		October-December 1348 Biraben 1987:179		
Castres*	10,000[Wolff 1967:239]			57% between 1347 and 1373 Wolff 1967:239

Place	Pre-plague population	Start	End	Mortality
Châlons-en-Champagne		July-September 1349 Biraben 1987:179		
Chambéry		October-December 1348 Biraben 1987:179		
Chartres*		1348 Chédeville 1983:131		
Châteauroux		October-December 1348 Biraben 1987:179		
Colmar		June, 1349 Biraben 1987:180		
Corsica		December, 1347 Biraben 1987:178		67% http:// ragz-international
Coutances		Peaked in November and lingered through the winter. Cohn 2002b:180-181		
Die		May 1348 Biraben 1987:178		
Digne	2,000 Baratier 1961:128	October-December 1348 Biraben 1987:179		41% Baratier 1961:128-129
Dijon	18,000 Chandler 1987:17	July-September, 1349 Biraben 1987:180		
Douai				Spared Cohn 2002b:179-180
Draguignan	2,000 in 1316 Baratier 1961:150	May, 1348 Biraben 1987:178		
Forez		August 1348 Audisio 1968a:261	April, 1349 Dupâquier *et al.* 1988:319	
Fresnois-la-Montagne		October, 1349 Noël 1995:741		10-25% Noël 1995:748
*Ganges**				53% Gottfried 1983:51
Givry	2,000-2,200 Biraben 1987:188	28 July 1348 Biraben 1975:161	19 November 1348 Biraben 1975:161	30% Biraben 1975:157-160 Fatalities, starting in July, 1348 [11 110 302 168 35] with background of 2.5 Biraben 1975:157-160
Grasse	4,000 Baratier 1961:65	May, 1348 Biraben 1987:178		46% Baratier 1961:65

Place	Pre-plague population	Start	End	Mortality
La Châtre		October-December 1348[Biraben 1987:179]	1349[http://www.chez]	
*Languedoc**				50-70%[Gottfried 1983:51]
Laon*				High[http://www.hyw.com/books/history/Plague.htm]
Lexy		October, 1349[Noël 1995:741]		10-25%[Noël 1995:748]
Lille	16,000-18,000[Trenand 1970:200]	August 1349[Aubry 1983:338]	Beginning of 1350[Aubry 1983:338]	Minimal[Trenand 1970:368-369]
Limoges*		October-December 1348[Biraben 1987:179]		Moderate mortality[Pérouas 1989:105]
Limousin		September, 1348[Biraben 1987:179]		
Limoux*		1348[Biraben 1975:74]		
Luz-Saint-Sauveur		June 29, 1348[Berthe 1976:51]		
Lyon	35,000[Chandler 1987:17-18]	April 1348[Biraben 1987:178]	October 1348[Biraben 1975:103]	30-40%[Latreille 1975:112-113]
Malaucène		April-June 1348[Biraben 1987-179]		
Manosque*		1348[http//:www.geocities.com/jmdesbois]		
Marseilles	20,000-25000 by 1300[Baratier 1961:66]	November 1, 1947[Biraben1975:91]; January 1348[Smail 1996:13]	May, 1348[Michaud 1998:408]	50-60%[Gottfried 1983:49] Wills, starting January 1348 [3 13 23 5 5 0][Michaud 1998:408]
Marsillargues*	1,000[Gottfried 1983:51]			50%[Gottfried 1983:51]
Maubeuge		April-June 1349[Biraben 1987:179]		
Maurienne		May 1348[Gelting 1991:21-23]		45%[Gelting 1991:38]
Metz	25,000[Trenand 1970:200]	December, 1349[Biraben 1987:180]		
Millau	4,000 after the plague[Cohn 2002b:155]	May 1348[Cohn 2002b:149]	Sept. 1348[Cohn 2002b:149]	40%[Lucenet 1985:91] Wills, starting in April, 1348 [0 2 23 86 32 3 0][Cohn 2002b:149]

Place	Pre-plague population	Start	End	Mortality
Montauban		April, 1348 Biraben 1987:178		40% Gottfried 1983:49
Montbéliard		May, 1349 Biraben 1975:76		
Montpellier		February, 1348 Biraben 1987:178	After May, 1348 Reyerson 1978:261	At least 50% Deaux 1969:95
Moustiers*	2,500 Baratier 1961:128	1348 Biraben 1975:74		67% Baratier 1961:128-129
Nancy		October-December 1349 Biraben 1987:179		
Narbonne	25,000-30,000 Gottfried 1983:49	March, 1348 Biraben 1975:74		40% Gottfried 1983:49
Navarrenx		July-September 1348 Biraben 1987:179		50% Tucoo-Chala 1951:83
Nîmes		January-March 1348 Biraben 1987:179		
Nyons		April-June 1348 Biraben 1987:179		
Orleans	35,000 Chandler 1987:17	October-December 1348 Biraben 1987:179		
Paray-le-Monial		April, 1349 Biraben 1987:180		
Paris	80,000-200,000 Bardet and Dupâquier 1997:176	End of August, 1348 Mollat 1971:151	Winter 1349-1350 Mollat 1977:505	
Périgord		August, 1348 Biraben 1987:179		
Pernes*		1348 Biraben 1975:74		
Perpignan	12,000-15,000 Gottfried 1983:49	12 April 1348 Ziegler 1969:65	12 August 1348 Ziegler 1969:65	50-70% Emery 1967:616-619
Pia		May, 1348 Cohn 2002b:159	July, 1348 Cohn 2002b:159	
Poitou		October 1348 Biraben 1987:179		50 % Lucenet 1985:91
Poligny		April, 1349 Biraben 1987:180		
Prades*				100% of the officials Shirk 1984:34
Puget-Théniers*		1348 Biraben 1975:74		
Quimper		November, 1348 http://membres.lycos.fr	January, 1349 http://membres.lycos.fr	

Place	Pre-plague population	Start	End	Mortality
Reims	15,000 Chandler 1987:17	April 1349 Desportes 1979:545	Oct. 1349 Desportes 1979:547	25% Desportes 1979:549
Revel		April-June 1348 Biraben 1987-179		
Roanne		July-September 1348 Biraben 1987-179		
Rodez	5,000 in 1328 Dupâquier *et al.* 1988:322	May, 1348 Biraben 1987:178		
Rouen	30,000-40,000 Mollat 1979:79	Beginning of summer 1348 Bois 1984:289	Dec. 1348 Bois 1984:289	40-50% Gottfried 1983:55
Saint-Bertin*		1349 Delmaire 1981:48		
Saint Denis		August, 1348 Biraben 1975:74		30% Bourderon and Peretti 1988:125
Saint-Etienne		July-September 1348 Biraben 1987-179		
Saint-Flour		April, 1348 Biraben 1987:178		34% Lucent 1985:91
Saint-Pierre-de-Soucy*				50% Ziegler 1969:81
Sainte Marie Laumont	800 Ziegler 1969:80	July, 1348 Ziegler 1969:80	September, 1348 Ziegler 1969:80	50% Corzine 1997:43
Saintes-Maries-de-la-Mer*				55–58% Benedictow 2004:314
Salins		May, 1349 Biraben 1975:76		
Savoy*		1348 Guichonnet 1973:468		50% Guichonnet 1973:468
Strasbourg	16,000 Chandler 1987:17-18	8 July 1349 Fössel 1987:9	October 1349 Fössel 1987:10	
Tarbes	3,500 Berthe 1976:55	May, 1348 Biraben 1987:178		50% Berthe 1976:51
Toulon	2,000 Baratier 1961:65	April 1348 Biraben 1987:178		High mortality Agulhon 1980:32
Toulouse	30,000-40,000 Bardet and Dupâquier 1997:176	April 1348 Wolff 1974:184	After July and August, 1348, which were the worse months Lavigne 1971:415	High mortality Henneman 1968:414
Tulle		October-December 1348 Biraben 1987:179		High http://membres

Place	Pre-plague population	Start	End	Mortality
Ugine*	1,300 Benedictow 2004:318			53% Benedictow 2004:318
Uzerche*		1348 Biraben 1975:74		
Valenciennes		June, 1349 Biraben 1975:76		
Verdun		October-December 1349 Biraben 1987:179		

g. Germany

By the time the Black Death began penetrating into the present German boundaries, the country was surrounded by infested territories. Germany received the epidemic from all direction except from the East.

The mortality rates vary widely, 10% in some areas, 70% in others. Overall mortality was lower than in northern Europe or the Mediterranean Sea (http://cternus). Firm statistics are few and far between and, where they do exist, are often hard to reconcile with each other (Ziegler 1969:86). In the scarcity of mortality data, we have used as proxy the rate of desertion of rural villages and cultivated land during the Later Middle Ages.

Place	Pre-plague population	Start	End	Mortality
Ausburg		Summer, 1349 Biraben 1975:83		25% desertion Abel 1965:520
Baden-Baden		July-August, 1349 Biraben 1975:75		40% desertion Abel 1965:520
Bielefeld		Early 1350 Fössel 1987:11		10% desertion Abel 1965:520
Borau		June 3, 1350 Biraben 1975:77		At least 40% desertion Abel 1965:520
Braunschweig		Early 1350 Fössel 1987:11		At least 40% desertion Abel 1965:520
Bremen	12,000-15,000 Gottfried 1983:68	May, 1350 Biraben 1975:77		50-67% mortality Gottfried 1983:68 20% desertion Abel 1965:520

Place	Pre-plague population	Start	End	Mortality
Cologne	50,000 Kelly 2003:28	December 18, 1349 Biraben 1975:77		35% desertion Abel 1965:520
Erfurt	30,000 Chandler 1987:16-18	25 July 1350 Fössel 1987:11	2 February, 1351 Fössel 1987:11	At least 40% desertion Abel 1965:520
Frankfurt-am-Main	11,616 in 1387 Bardet and Dupâquier 1997:196	22 July 1349 Gasquet 1908:75	2 February 1349 Gasquet 908:75	20% desertion Abel 1965:520
Frankfurt-an-der-Oder*		1351 Benedictow 2004:219		20% desertion Abel 1965:520
Güstrow	About 8,000 Boll 1855:Ch. 1	Fall, 1350 Boll 1855:Ch. 1	1351 Boll 1855:Ch. 1	At most 30% mortality Boll 1855:Ch.1 30% desertion Abel 1965:520
Halberstadt		May, 1350 Biraben 1975:77		53% desertion Bardet and Dupâquier 1997:195
Hamburg	10,000 Vasold 1991:57	May, 1350 Biraben 1975:77		50-66% mortality Vasold 1991:57
Hanover		May, 1350 Biraben 1975:77		30% desertion Abel 1965:520
Harz*				53% desertion Bardet and Dupâquier 1999:195
*Hesse**		July-August, 1349 Biraben 1975:75		44% desertion Bardet and Dupâquier 1997:195
Holstein*		July-August, 1349 or January-March, 1350 Biraben 1975:75		66% mortality Deaux 1969:113
Kiel		Authorization for new cemetery on June 24, 1350 Benedictow 2004:198		30% desertion Abel 1965:520
Kontanz		November, 1349 Biraben 1975:77		15% desertion Abel 1965:520
Landshut*				High mortality- Hoeniger 1882:15-16

Place	Pre-plague population	Start	End	Mortality
Limburg-am-Lahn		Summer, 1349[Benedictow 2004:194]		44% desertion[Bardet and Dupâquier 1997:195]
Lübeck	22,000 Chandler 1987:17-18	May 1350 Cohn 2002b:182	October 1350[Cohn 2002b:182]	27% mortality among property owners[Gottfried 1983:68] Number of wills, starting in April, 1350 [2 10 2 27 35 15 8 0] Cohn 2002b:182 30% desertion[Abel 1965:520]
Lüneburg*		Early 1350[Fössel 1987:11]		36% mortality[Bulst 1979:53] 20% desertion[Abel 1965:520]
Magdeburg	15,000[Chandler 1987:17-18]	16 May 1350[Fössel 1987:11]	29 Sept. 1350[Fössel 1987:11]	50% mortality[Carpentier 1962:1065] 53% desertion[Bardet and Dupâquier 1997:195]
Mainz	24,000[Chandler 1987:16-17]	July-August, 1349[Biraben 1975:75]		20% desertion[Abel 1965:520]
Minden		January-March, 1350[Biraben 1975:77]		10% desertion[Abel 1965:520]
Mühldorf		June 29, 1349[Benedictow 2004:189]		15% desertion[Abel 1965:520]
Munich*				High mortality[Hoeniger 1882:15-16]
Münster		May, 1350[Biraben 1975:77]		High mortality-Gottfried 1983:68 5% desertion[Abel 1965:520]
Nuremberg	15,000-20,000[Gottfried 1983:68]	July-September, 1350[Biraben 1975:77]		10% mortality-Gottfried 1983:68 30% desertion[Abel 1965:520]
Osnabrück		January-March, 1350[Biraben 1975:77]		5% desertion Abel 1965:520
Paderborn		January-March, 1350[Biraben 1975:77]		At least 40% desertion[Abel 1965:520]

Place	Pre-plague population	Start	End	Mortality
Parchim	About 8,000 Boll 1855:Ch. 1	Fall, 1350[Boll 1855:Ch. 1]	1351[Boll 1855:Ch. 1]	At most 40%[Boll 1855:Ch. 1] 30% desertion[Abel 1965:520]
Passau		Summer, 1349[Biraben 1975:83]		20% desertion[Abel 1965:520]
*Pomerania**				67% mortality [Deaux 1969:113]
Regensburg		July 25, 1349[Fössel 1987:8]		20% desertion[Abel 1965:520]
Rostock		July-September, 1350[Biraben 1975:77]		30% desertion[Abel 1965:520]
Schleswig		January, 1350[Fössel 1987:6]		30% desertion[Abel 1965:520]
Stralsund		July-September, 1350[Biraben 1975:77]		30% desertion Abel 1965:520
Trier		December 18, 1349[Biraben 1975:77]		30% desertion[Abel 1965:520]
Ulm		Late summer, 1349[Benedictow 2004:190]		40% desertion[Abel 1965:520]
Wismar		July-September, 1350[Biraben 1975:77]		42% mortality[Biraben 1975:175] 30% desertion[Abel 1965:520]
Würtzburg		July-September, 1350[Biraben 1975:77]		30% desertion[Abel 1965:520]

h. Gibraltar

Place	Pre-plague population	Start	End	Mortality
Gibraltar		July, 1349[Ubieto 1997:85]	Not before king Alfonso XI death, March 26, 1350[Amasuno 1996:64-65]	

i. Ireland

There is still much that is obscure about the course of the Black Death in Ireland. We cannot even be sure where it came from. The most likely source is England, but it could well have come directly from Gascogny or one of the ports of Brittany (Ziegler 1969:195-196).

The most commonly accepted general guide for the mortality in the larger towns and ports of the east and south controlled by the English settlers is 40-50% (Kelly 2001:97), while the native Irish, living in the mountains and uplands, suffered less severely (Kelly 2001:37).

Place	Pre-plague population	Start	End	Mortality
Cashel*		Infected at an undetermined time[Kelly 2001:35]		
Clonmel*		Infected at an undetermined time[Kelly 2001:35]		
Cork*		Infected at an undetermined time[Kelly 2001:35]		40-50%[Kelly 2001:97]
Dalkey*		August, 1348[Biraben 1975:78]		
Drogheda		August, 1348[Biraben 1975:78]		40-50%[Kelly 2001:97]
Dublin	25,000[Chandler 1987:16-17]	August, 1348[Kelly 2001:34]	January, 1349[Kelly 2003:62]	50%[Kelly 2001:95]
Dundalk		September of 1348[Biraben 1975:78]		
Ennis		November 1, 1349[Kelly 2001:35-36]		
Ferns		The Bishop of Ferns died in October 1348[Kelly 2001:112]		
Kildare		Late in 1348[Kelly 2001:34]		
Kilkeny		Dec. 25, 1348[Kelly 2001:35]		50%[http://library.thinkquest]
Limerick		Nov. 1, 1349[Kelly 2001:35]		
Louth*		Late in 1348[Kelly 2001:34]		High[Kelly 2001:69]

Place	Pre-plague population	Start	End	Mortality
Mayo*			1350[Kelly 2001:37]	
Meath		December, 1348[Kelly 2001:34]	After the bishop died in July, 1349 Kelly 2001:35	High[Kelly 2001:69]
Moylurg		December, 1349[Kelly 2001:36]		
Nenagh		August, 1349[Biraben 1975:80]		
New Rose*		Infested at an undetermined time[Kelly 2001:35]		40-50%[Kelly 2001:97]
Waterford		Prior of the monastery of St Catherine's died of plague in June, 1349.[Kelly 2001:35]		40-50%[Kelly 2001:97]
Youghal*				40%[http://tyntescastle]

j. Italy

The prevailing view is that the Italians brought the Black Death to their country in their merchant boats trading with areas in the Middle East and Ukraine, thus starting the epidemic in Europe (Wheelis 2002). On average, at the time, Italy and Belgium were the two countries with the most extensive urban development (Gottfried 1983:57; Turner 1988:25). Along with France, Italy seems to have had the highest mortality rates (Scott and Duncan 2004:24). Apparently, fatalities were at least 3 million people (http://www.hyw.com/books/history/Black_De.htm).

Place	Pre-plague population	Start	End	Mortality
Agrigento	10,000-11,000 [Gi-natempo and Sandri 1990:192]	October, 1347[Biraben 1975:74]		
Ancona	20,000-30,000 [Gi-natempo and Sandri 1990:148]	May, 1348[Biraben 1975:74]		
Arezzo	17,000-18,000 [Gi-natempo and Sandri 1990:148]	April, 1348[Cohn 2002b:156]	September, 1348[Cohn 2002b:156]	Testaments, starting March 1348 [0 2 5 25 11 7 3 0] [Cohn 2002b:156]
Bari	12,000-14,000 [Gi-natempo and Sandri 1990:190]	March 1348[http:// historymedren]		
Bobbio*				High[Scott and Duncan 2004:18]

Place	Pre-plague population	Start	End	Mortality
Bologna	40,000 Ginatempo and Sandri 1990:85	March, 1348 Biraben 1975:74	Nov. 1348 Cohn 2002b:149	35 to 40% Wray 1993:55 Testaments, starting March, 1348 [25 30 80 330 455 185 70 46 30 7] Cohn 2002b:149
Cagliari	10,000-13,000 Ginatempo and Sandri 1990:192		May, 1348 Biraben 1975:103	
Catania		October, 1347 Marks1971:54	April, 1348 Marks1971:54	100% McGowen 1995:19
Cesena	6,640 in 1371 Ginatempo and Sandri 1990:87	June 1, 1348 http://www.shsu		
Elba Island		December, 1347 Biraben 1975:74		
Faenza	7,704 in 1371 Ginatempo and Sandri 1990:87	June, 1348 Del Panta 1980:112		
Ferrara	12,000-15,000 in 1310 Ginatempo and Sandri 1990:86	July, 1348 Biraben 1975:74		
Florence	100,000 Carmichael 1997:62 45,000 Chandler 1987:16-18; Gottfried 1983:46	March, 1348 http://ides0100	October, 1348 http://ides0100	45-75% Kohn 1995:252
Friuli		August, 1348 Del Panta 1980:112		
Genoa	60,000-65,000 Epstein 1996:213	December 1347 Vasold 1991:41		30% to 40% Gottfried 1983:43
Lucca	20,000-30,000 Ginatempo and Sandri 1990:148	February, 1348 Biraben 1975:74		39% Biraben 1975:175
Messina	15,000-22,000 http://scholar	Oct., 1347 Wheelis 2002:971		Nearly 50% Biel 1989:27
Milan*	100,000 Bardet and Dupâquier 1997:176	1348 Cantú 1999:120		15% Kelly 2001:18
Modena	18,000-20,000 in 1306 Ginatempo and Sandri 1990:86	March, 1348 Biraben 1975:74		
Naples	40,000 Chandler 1987:16-18	May, 1348 Biraben 1975:74	December, 1348 Cohn 2002b:141	

Place	Pre-plague population	Start	End	Mortality
Orvieto	14,000-17,000 Ginatempo and Sandri 1990:148	May 1, 1348 Biraben 1975:74	September 7, 1348 Carpentier 1993:145	50% Ziegler 1969:52
Padua	27,000-30,000 in 1281 Ginatempo and Sandri 1990:82	April, 1348 Biraben 1975:74	September, 1348 Biraben 1975:103	67% Scott and Duncan 2004:17
Parma	20,000 Chandler 1987:18; http://scholar	June 20, 1348 Biraben 1975:74	December, 1348 Biraben 1975:103	Low Ziegler 1969:62
Perugia	23,000-28,000 Ginatempo and Sandri 1990:148	April 8, 1348 Cohn 2002b:141	August, 1348 Cohn 2002b:141	Testaments, starting in March, 1348 [0 2 1 40 24 9 0] Cohn 2002b:141
Piacenza	15,000-22,000 http://scholar; Chandler 1987:16-18	July, 1348 Biraben 1975:74		33% Nasalli 1973:18
Piombino		April, 1348 Biraben 1975:74		
Pisa	40,000 Gottfried 1983:43	January, 1348 Carpentier 1993:116	September, 1348 Biraben 1975:103	30-40% Gottfried 1983:43
Pistoia	24,000 Gottfried 1983:44	May, 1348 Ziegler 1969:55	October 1348 Chiappelli 1887:4	40% Gottfried 1983:44
Prato	10,559 Herlihy and Klapisch-Zuber 1978:168	Peacked in June-July, 1348 Fiumi 1968:85		40% Gottfried 1983:43
Pusteria		October, 1348 Benedictow 2004:182		
Reggio d'Emilia	12,000 in 1315 Ginatempo and Sandri 1990:86	June 20, 1348 Biraben 1975:74	December, 1348 Biraben 1975:103	
Reggio di Calabria	At most 4,000-5,000 Ginatempo and Sandri 1990:191	December, 1347 Del Panta 1980:111		
Rimini	8,960 in 1371 Ginatempo and Sandri 1990:87	June, 1348 Cohn 2002b:141	November 1, 1348 Cohn 2002b:141	67% Sticker 1908:55
Rome	15,000-22,000 http://scholar	August, 1348 Biraben 1975:74		
San Gimignano*	7,600-8,500 in 1332 Day 2002:126			58% Ziegler 1969:52
San Giorio*	700 Comba 1977a:75			46% Comba 1977a:75

Place	Pre-plague population	Start	End	Mortality
Sardinia		December, 1347[Biraben 1975:74]		
*Sicily**		October, 1347[Davis 1986:460]	April 1348[Davis 1986:460]	75%[http://www.mrkland]
Siena	25,000[Bowsky 1964:5]	April, 1348[Biraben 1975:74]	Oct., 1348[Biraben 1975:103]	51%[Bowsky 1964:18]
Syracuse	10,000-12,000 Ginatempo and Sandri 1990:192	October, 1347[Biraben 1975:74]		High[Scott and Duncan 2004:14]
Trapani	15,000-16,000[Ginatempo and Sandri 1990:192]	October, 1347[Biraben 1975:74]		Completely depopulated[Scott and Duncan 2004:14]
Trent	5,000 in 1335[Ginatempo and Sandri 1990:92]	June 2, 1348[Biraben 1975:92]		83%[Ginatempo and Sandri 1990:91]
Turin	3,500-4,500[Ginatempo and Sandri 1990:65]	November 11, 1348[Comba 1977b:55]		33%[Ginatempo and Sandri 1990:65]
*Tuscany**	2,000,000[Herlihy 1997:31]			Very hard hit[http://4thmoon]
Varese		October or November 1348[Del Panta 1980:112]		
Venice	110,000-120,000[Mueller 1980:94]	December, 1347[Naphy and Spicer 2000:25]	May, 1349 [Naphy and Spicer 2000:25]	60% [Gottfried 1983:48]
Ventimiglia		April, 1348[Del Panta 1980:112]		
Verona	40,000[Del Panta *et al.* 1996:55]	End May, 1348[Biraben 1975:74]		45%[Del Panta *et al.* 1996:55]
Vintschgau		September 1348[Benedictow 2004:181]		

k. Norway

Possibly there were at least two independent introductions of the pestilence in Norway, one in the East county, with Oslo as the likely point of entrance, and another in Bergen on the western coast (Benedictow 1992:100). From Norway the disease moved toward the remainder of Scandinavia.

Norway's high mortality, cold weather and low population density has been a focal point of contention against the possibility that the Black Death was an earlier case of the modern bubonic plague (Scott and Duncan 2001:357).

Place	Pre-plague population	Start	End	Mortality
Agder		October, 1349[Benedictow1992:97]		
Bergen		August, 1349[Benedictow 2004:156]		
Hamar		September 8, 1349[Benedictow 2004:150]	November 1, 1349[Benedictow 2004:150]	
Idd		August, 1349[Benedictow1992:90]		
Lom		November, 1349[Benedictow1992:96]		
Oslo		April, 1349[Benedictow 2004:153]		50%[http://www.lonelyplanet]
Sandsvær			December 16, 1349[Benedictow1992:99]	99% Benedictow1992:99
Stavanger		January, 1350[Benedictow1992:90]		
*Telemark**		December, 1349[Biraben 1975:80]		
Tinn		December, 1349[Benedictow1992:97]		
Tønsberg		November 2, 1349[Benedictow 1992:99]		
Toten		September, 1349[Benedictow 2004:152]		
Trondheim		Archbishop died from plague by middle of October 1349[Benedictow1992:101]		
Upper Eiker		May-June, 1349[Benedictow 2004:150]		
Vågå		October, 1349[Benedictow1992:97]		
Valdres		October, 1349[Benedictow1992:97]		

I. Poland

The disease started at the Hansiatic League cities trading with other ports to the west.

Place	Pre-plague population	Start	End	Mortality
Elblag*		Summer of 1350[Biraben 1975:80]		
Gdansk		Summer of 1350[Sticker 1908:67]		
Malbork*		Summer of 1350[Biraben 1975:80]		
Torun		End summer of 1350[Fössel 1987:6]		

m. Portugal

Unfortunately there is little information about Portugal, particularly in the south, as well as the neighbouring region of Spanish Extremadura.

Place	Pre-plague population	Start	End	Mortality
Beira*		Fall 1348[http://pwp.netcabo.pt]		33-50% http://pwp.netcabo.pt
Braga		Archbishop died on Dec. 22, 1348[Ubieto 1975: 48]		High mortality[Mattoso 1997:284]
Bragança*				High mortality[Martín *et al.* 1991:595]
Buarcos*				Decimated http://figueira
Caminha*				High mortality[Serrão 1981b:75]
Coimbra	25,000 in 1200[Chandler 1987:16]	Sept. 29, 1348[Rau 1967:331]		High mortality[Mattoso 1997:284]
Evora		1349[Biraben 1975:77]	Lasted more than a year Verlinden 1838:110. Ended before March, 1350[Phillips 1998:50]	
Figueira da Foz*				Decimated http://figueira
Lamego		Bishop died in 1349 and replacement started on July 27, 1349 [Ubieto 1975:64]		
Lisbon	35,000 in 1300 [Chandler 1987:16-18]	Sept. 1348[Martín *et al.* 1991:595]		High mortality-Martín *et al.* 1991:595
Porto*		1348[http://www.cedofeita]		
Santarém*				Highly depopulated[Serrão 1981b:75]
Silves		Fray Álvaro Peláez died in December 1349[Serrão 1981a:515; http://www.coaat-se]		Close to being depopulated[Serrão 1981b:75]
Valença*		End of 1348[Amasuno 1996:66]		

n. Spain

Like Italy, Iberia suffered the misfortune of receiving the Black Death from disparate sources. At the time, the country was divided in four kingdoms: Castille, Aragon, Navarra, and Granada (Kagay and Vann, 1998:1) There were at least three avenues of entry (Gottfried 1983:51). First, and probably most important, merchant ships from Italy brought the Black Death to the Balearic Islands and then to the major ports of the west coast, Barcelona and Valencia. Second, in the same way as Mecca attracted pilgrims from areas ravaged by the Black Death in the Muslim world and was visited early, the Black Death undoubtedly performed the remarkable feat of leaping to the north-western corner of Spain helped by pilgrims who were shocked by the Lord's awesome epidemic punishment and wished to temper his wrath by performing a pilgrimage to the shrine of St Jacob in Santiago de Compostela (Phillips, 1998:49). Third, it came from the north, across the Pyrenees to the Basque-speaking villages. Finally, it is likely that the south, particularly the Muslin Kingdom of Granada, was infected from North Africa (Gottfried 1983:51).

Most of the cities and villages in Spain suffered more or less severely, and the sickness appears to have lingered longer here than in most other countries (Gasquet 1908:67). The mortality seems to have been less in Spain though than in Italy, and about as considerable as in France (http://ragz-international).

Place	Pre-plague population	Start	End	Mortality
Almería	25,000 Chandler 1987:17-18	May 30, 1348 Ubieto 1975:54	Shortly after beginning of February, 1349 Ubieto 1975:55	50% http://www.agpa
Almudévar		Before Sept. 27, 1348 Ubieto 1975: 57		
*Aragón**				30% Gottfried 1983:52
Arjona*				High mortality Rodríguez 1978:139
Asturias		October, 1348 Amasuno 1996:64		
Badajoz		1348 http:// enciclopedia	New bishop on May 25, 1349 Ubieto 1975:64	
Baeza*				High mortality Rodríguez 1978:139
*Balearic Islands**		End of March or beginning of April, 1348 López 1959:336	August, 1348 López 1959:342-344	Deaths and appointments, starting March, 1348 [1 1 1 11 4 5] López 1959:342-344

Place	Pre-plague population	Start	End	Mortality
Barcelona	50,000[Gottfried 1983:44] 42,000[Biraben 1975:216]	May 2, 1348[Biraben 1975:216]	February, 1349[Gyug 1983:388]	Benefited clergy mortality: 62%[Benedictow 2004:278] Population mortality: 36%[Biraben 1975:216] Clergy appointments, benefices minus devolutions, starting March, 1348 [1 0 10 15 65 42 8 9 15 12 7 4 8 1][Utterback 1988:428] Testaments starting in April, 1348 [6 39 55 7 1 3 1 2][Gunzberg 1989:24]
Bayona*		End of 1348[Amasuno 1996:66]		
Berga		Sept., 1348[Biraben 1975:75]		High mortality[Cabrillana 1965:493]
Borja		Raging on Oct. 6, 1348[Ubieto 1975:58]		
Cádiz		New bishop on May 25, 1349[Ubieto 1975:64]		
Calatayud		September, 1348[Biraben 1975:75] Before October 25, 1348[Ubieto 1975:59]		
Camprodón		Mid June, 1348[Guilleré 1984:106]	End August, 1348[Guilleré 1984:106]	
Cardona*		1348[Galera 1994:72]		
Cartagena		New bishop on July 24, 1349[Ubieto 1975:64]		
Castellón	2,000[Doñate 1969:29]			0%[Doñate 1969:31]

Place	Pre-plague population	Start	End	Mortality
*Castile**				20-25%[Gottfried 1983:52]
*Catalonia**	365,000 in 1359[Smith 1944:497]			30%[Gottfried 1983:52]
Cerdanya		April, 1348[Ubieto 1975: 50]		
Córdoba	40,000 Chandler 1987:17	March 21, 1349[Amasuno 1996:65]	August, 1349-July, 1350[Amasuno 1996:65]	High mortality[Ballesteros 1982:103]
Duero Valley		October, 1348[Amasuno 1996:64]		High mortality[Valdeón and Martin 1996:85]
Estella		Sept., 1348[Ubieto 1997:85]		Population declined by 63% between 1330-66[Zavalo 1968:83]
Girona	4,000 in 1378[Wolff 1985:60]	Mid May, 1348[Guilleré 1984:106]	End of August, 1348[Guilleré 1984:106]	2/3 died[Veny 1971:30] 50% among notaries and 40% among merchants[Guilleré 1984:118-119]
Granada	90,000[Chandler 1987:17] 23,000-49,000 http://scholar	The poet Kathemat Alansaraeus passed away on May 22, 1349[Ubieto 1975:65]		30%[Gottfried 1983:52]
Huesca		Raging in Sept., 1348[Ubieto 1975:56]	Subsided in November, 1348[Ubieto 1975:57]	
Igualada*		1348[Biraben 1975:75]		
Inca*	5,750[Santamaría 1969:122]			20%[Santamaría 1969:122]
Jérica		Oct., 1348[Ubieto 1997:85]		
León	25,000 in 1300 Chandler 1987:17	October, 1348 Amasuno 1996:64		
Lérida	10,000[Veny 1971:30]	Shortly after April 24, 1348[Arrizabalaga 1991:75]		At least 23%[Veny 1971:30]

Place	Pre-plague population	Start	End	Mortality
Lugo		July, 1348 Ubieto 1975:63	Dec., 1348 Ubieto 1975:63	65% González 1989:110
Málaga	15,000 Calero 1991:66	March, 1349 Calero 1991:63	After poet Alkailuzi died on July 11, 1349 Ubieto 1975:65 Before March, 1350 Calero 1991:63	
Mallorca		March 28, 1348 Santamaría 1969:120	August, 1348 López 1959:342-344	23% Santamaría 1969:120
Manresa*		1348 Biraben 1975:75		High mortality Cabrillana 1965:493
Medina del Campo*		1348 Vasold 1991:47		
Minorca		April, 1348 Biraben 1975:75		
Montblanc		1348 Biraben 1975:75		
Morella		End June, 1348 Grau 1970:150	End August, 1348 Grau 1970:150	Monthly testaments, starting in June 1348 [2 17 13 1 1] Grau 1970:150
Murcia	25,000 in 1300 Chandler 1987:17	October, 1348 Torres 1981:12	March, 1349 Torres 1981:14	High mortality Torres 1981:11
*Navarra**		October, 1348 Ubieto 1997:85		Hardly hit Ubieto 1997:85
Oviedo*		October, 1348 Ubieto 1975:48		
*Palencia**				19% villages disappeared, more than 50% died in many others Cabrillana 1968:255-6
*Pamplona**				54%, partly due to famine Berthe 1983:306
Plana de Vic	16,500 Pladevall 1963:365	June, 1348 Ubieto 1975:53		66-74% drop in hearths Shirk 1981:365

Place	Pre-plague population	Start	End	Mortality
Puertollano	1,000 http://www.puertollanovirtual			93% http://www.puertollanovirtual
Salamanca*		1348 http://www.exitmedia		
Salvatierra*				90% Gasquet 1908:68
San Joan*	500 Santamaría 1969:122			13% Santamaría 1969:122
San Juan de la Peña		D. de Arresal died on December 17, 1348 Ubieto 1975: 57		
*Sangüesa**				47%, partly due to famine Berthe 1983:306
Santesteban		June, 1348 Benedictow 2004:88		
Santiago de Compostela		June, 1348 Phillips 1998:49		
Sarrión		June 21, 1348 Martínez 1969:16		
Segorbe			Long before Oct. 30, 1348 Suárez y Reglá 1966:XXVIII	
Seu d'Urgell*	1,300 Villaró 1986-7:281	June 12, 1348 Villaró 1986-7:278	August 12, 1348 Villaró 1986-7:278	23-38% mortality Villaró 1988-9:343 Wills, starting June 1348 [50 250 20] Villaró 1986-7:279
Seville	65,000 to 80,000 in 1284 Bardet and Dupâquier 1997:177	1349 Ladero 1976:208; Collantes 1977:154	1350 Ladero 1976:208; Collantes 1977:154	
Soria		End of 1348 Benedictow 2004:86		
Tarazona		October, 1348 Trenchs 1981:201	Plague related institution on 10 Dec., 1348 Trenchs 1981:201	
Tarragona	11,000 Virgili 1979:33	May 1, 1348 Ubieto 1975:51	After Aug.1, 1348 Trenchs 1969:55	50% Virgili 1979:38

Place	Pre-plague population	Start	End	Mortality
Teruel	5,300 Sobrequés 1970-1:75	End of July, 1348 Ubieto 1975:56	No later than November 6, 1348 Gautier-Dalché 1962:67	Bankrupt economy in 1349 Cabrillana 1965:502
Toledo	33,000 Chandler 1987:17	Summer of 1349 León 1977:334		
Tortosa	6,000 in 1366 Wolff 1985:60	Bishop Oliver died July 14, 1348 Ubieto 1975: 52		
Tudela*		1348 http://www.conelarte		
Tuy		March-July, 1348 Ubieto 1975:61 Aug.-Oct., 1348 Valdeón and Martin 1996:84		
Urgell		New bishop June 13, 1348 Ubieto 1975:60		
Valencia	15,000 to 22,000 http://scholar	May 1348 Ubieto 1975:53	August, 1348 Rubio 1979:28	30-40% Gottfried 1983:52 Wills, starting in May 1348: [0 31 11 5 1] Rubio 1979:26
Vic*	3,000-3,500 in 1365 Bautier 1988:438	End of June 1348 Guilleré 1984:106	End of Aug.1348 Guilleré 1984:106	
Villafranca del Penedés*		1348 Biraben 1975:75		
Villalobos	200 to 300 Vaca 1990:163	October 1348 Vaca 1990:164	December 1348 Vaca 1990:164	
Viseo		New bishop on July 8, 1349 Ubieto 1975:64		
Zaragoza	22,000 Chandler 1987:17	Sept., 1348 Pueyo 1993:724	April, 1349 Pueyo 1993:715	Up to 300 deaths daily Suárez and Reglá 1966:XXVIII Institutions, starting in Sept. 1348 [12 58 48 33 20 13 7 6 10 4 5 3 1 1 0] Pueyo 1993:724-733

o. Sweden

Moving northwards and north-eastwards in Europe, the historical evidence which can be used in the study of the Black Death becomes increasingly poor. The Black Death's history in Sweden reflects the continuation of this unfortunate development, which means that the attainable insights into this momentous event in its history are severely limited. The sources also tend to take on the character of pieces of epidemic structures that have been atomized by history in the sense that the outcome of dedicated endeavours to collect sources for the history of the Black Death in Sweden consists of a number of dispersed pieces of information that can only with great difficulty be correlated in a meaningful way to produce a rough outline of the temporal and spatial dimensions of the event, especially church donations (Benedictow 2004:176).

The Black plague devastated Sweden. Evidences point toward mortality levels close to 50% (http://www.genealogi).

Place	Pre-plague population	Start	End	Mortality
East Gotland		February, 1350 Benedictow 2004:175-176	November, 1350 Benedictow 2004:175-176	
*Gotland**		May, 1350 Biraben 1975:80		
Halmstad		End of August, 1349 Benedictow 2004:172		
Lund		Summer 1350 http://www.hum		
Örebo		Church donation in August, 1350 Benedictow 2004:175-176		
Smalandia		February, 1350 Benedictow 2004:175-176	December, 1350 Benedictow 2004:175-176	
Söderman-land		Church donation in December, 1350 Benedictow 2004:175-176		
Stockholm				High Gasquet 1908:79
Uplandia		September, 1350 Benedictow 2004:175-176	November, 1350 Benedictow 2004:175-176	
Visby		March 28, 1350 Benedictow 2004:173		
Westrogothia		December, 1349 Benedictow 2004:175-176	March, 1350 Benedictow 2004:175-176	

p. Switzerland

Switzerland received the Black Death from two original focus of infection. The western cantons were raged by the wave that starting from Marseilles moved up the Rhone valley. The wave originated at Genoa ravaged the rest of the country.

On average, mortality seems to have been in the middle range by comparison to the rest of the continent.

Place	Pre-plague population	Start	End	Mortality
Aargau		Sept. 8, 1349[Biraben 1975:77]		
Basel		May, 1349[Fössel 1987:9]		
Bellinzona		October-November 1348 [Biraben 1975:75]		
Bern		February, 1349[Fössel 1987:9]		
Chillon		December, 1348[Fössel 1987:9]		
Dissentis		December 1348[Sticker 1908:56]		
Engelberg		Sept. 8, 1349[Fössel 1987:9]	January 6, 1350[Fössel 1987:9]	
*Entremont**	4,500[Benedictow 2004:328]			41%[Benedictow 2004:328]
Geneva		August 10, 1348[Andenmatten and Morerod 1987:26]	October 11, 1348[Andenmatten and Morerod 1987:26]	
Lausanne		Nov. 10, 1348[Andenmatten and Morerod 1987:24-25]	August 18, 1349[Andenmatten and Morerod 1987:24-25]	Wills, starting in October 1348 [0 3 6 2 7 5 8 9 5 4 2 0] [Pasche 1998:126-129]
Lucerne		March, 1349[Fössel 1987:9]		
Monthey*	1,200 in 1329[Benedictow 2004:329-330]			43%[Benedictow 2004:329-330]
Nyon		Sept. 20, 1348[Andenmatten and Morerod 1987:26]		
Pfäfers		May, 1349[Biraben 1975:77]	November 1349[Hoeniger 1882:17]	
Rutwil		March, 1349[Biraben 1975:77]		
Saint Gallen		April, 1349[Fössel 1987:9]		

Place	Pre-plague population	Start	End	Mortality
Saint Maurice	1,500 Pasche 1998:129	January, 1349 Pasche 1998:127-129	August, 1349 Pasche 1998:127-129	30-40% Dubuis 1980:10 Fatalities, starting in January 1349 [45 120 45 90 60 45 30 15] Pasche 1998:127-129
Sion		March, 1349 Andenmatten and Morerod 1987:27	September, 1349 Andenmatten and Morerod 1987:27	Wills, starting in February, 1349 [0 3 13 14 20 24 3 8 0] Andenmatten and Morerod 1987:27
Vevey		Nov. 20, 1348 Andenmatten and Morerod 1987:26	May 17, 1349 Andenmatten and Morerod 1987:26	
Zurich		October 11, 1349 Biraben 1975:75		60% http://www.memo

q. The Netherlands

The Black Death most likely came from neighboring Germany. It raged more generally than until now accepted, but the losses never seem to have been so dramatic as in the North-Italian towns or in England (Blockmans 1980:845).

Place	Pre-plague population	Start	End	Mortality
Deventer		June, 1350 Blockmans 1980:843	August, 1350 Blockmans 1980:843	Deaths starting May, 1350 [1 10 25 13 3]; background: 4 Blockmans 1980:843
Foswert*		December, 1349 Biraben 1975:77		
Friesland		1350 Blockmans 1980:843	1351 Blockmans 1980:843	
Groningen		1350 Blockmans 1980:843	1351 Blockmans 1980:843	
Zwolle		Late 1350 Benedictow 2004:204-205	First months of 1351 Benedictow 2004:204-205	

r. United Kingdom

The English part of the country has the best documented regional account of the disease because of numerous ecclesiastical and manorial records. For the rest of the kingdom, particularly Northern Ireland and Scotland, the information is close to none.

Chronicles and scholars disagree about the place and time of the outbreak and the exact source of the infection. Lately the distinction for place of first outbreak in the UK tends to go the southern port of Weymouth, which may have happened as early as June 24, 1348 or as late as August 1 of the same year (Horrox 1995:63-64).

Also there is disagreement about the intensity of the epidemic. J.F.D. Shrewsbury is the leading proponent of a low national mortality of no more than 5% (Shrewsbury 1970:123), but increasingly the opinion is that the mortality was high, close to 50%, especially in the south of England (Ziegler 1969:Chapter 14; Britnell 1994; Dohar 1995:40).

Like in most other countries, particularly France, once the Black Death started in Great Britain and Ireland, the timing of the spreading suggests the infection moved by land as no credible cases of leapfrogging are reported along the numerous ports along the coast.

Place	Pre-plague population	Start	End	Mortality
Aberdeen*		1350 http://www.geocities.com/localhistories/aberdeen.html		50% population mortality http://www.geocities
Abergavenny		March, 1349 Rees1920:117		At least 65% population mortality Rees1920:117
Alnwick*		Plague death reported on March 25, 1350 Gasquet 1893:160		
*Anglesey Isle**				High population mortality Benedictow 2004:143
Bath and Wells diocese	84,111 in 1377 Shrewsbury 1970:27	October, 1348 de Hahn 2002:83	May, 1349 de Hahn 2002:83	48% clergy mortality http://www.geocities.com/Athens Ecclesiastical appointments, starting November, 1348 [9 32 47 43 36 40 36 7] de Hahn 2002:83; background: 3 Gasquet 1908:192

Place	Pre-plague population	Start	End	Mortality
Bedford archdeaconry	30,508 in 1377[Shrewsbury 1970:27]	March, 1349[Thompson 1911:346-347]	September, 1349[Thompson 1911:346-347]	39% clergy mortality[Thompson 1911:324] Ecclesiastical appointments, starting April, 1349 [1 2 8 15 16 2 3 0][Thompson 1911:346-347] Background: 6 a year[Thompson 1911:335]
*Berkshire**	34,084 in 1377[Shrewsbury 1970:27]	1348[James 1999:11]		
Billingham*				40%-49% population mortality[Lomas 1989:130]
Bishops Lynn*				50% population mortality[http://www.geocities.com/localhistories]
Blandford*		A few weeks before Nov. 20, 1348[Watts 1998:23]		
Bodmin*	4,000[Creighton 1891:126]	December 25, 1348[Cartwright and Biddiss 2000:25]		37%[Creighton 1891:116 and 126]
Brightwell*	200[Ballard 1916:208]	1349[Ballard 1916:208]		30% population mortality[Ballard 1916:208]
Bristol	20,000[Dyer 2000:758; Titow 1969:67-68]	August 15, 1348[Boucher 1938:34]	Mid March 1349[Horrox 1995:62]	35%-40% population mortality[http://cternus] 50% clergy mortality[Boucher 1938:36]
Buckingham archdeaconry	37,008 in 1377[Shrewsbury 1970:27]	March, 1349[Thompson 1911:347-348]	October, 1349[Thompson 1911:347-348]	37% clergy mortality[Thompson 1911:322] Ecclesiastical appointments, starting April, 1349 [1 8 17 24 13 5 5 1 0][Thompson 1911:347-348] Background: 1 a year[Thompson 1911:336]
Bury Saint Edmunds*	7,000[Gottfried 1989:344]			50% clergy mortality[Gottfried 1983:66]
Cadland*	300 in 1377[James 1999:6]	Before May 6, 1349[Watts 1998:26]	Around July 25, 1349[Watts 1998:26]	100% population mortality[Watts 1998:27]

Place	Pre-plague population	Start	End	Mortality
Caernarvon*				High population mortality[Twigg 1984:62]
Calstock*			Before September, 1349[Hatcher 1970:105]	62% population mortality[Hatcher 1970:105]
Cambridge*	4,403[Russell 1948:292]	May 9, 1349[Biraben 1975:80]	August, 1349[Gottfried 1989:344]	40% population mortality[Gottfried 1989:344]
Canterbury	10,000[http://www.kessler-web]	Late December 1348[Gasquet 1908:118]	End May 1349[Gasquet 1908:118]	50% population mortality[http//www.kessler-web]
Cardigan		Summer of 1349[Twigg 1984:61]		High population mortality[Twigg 1984:61]
Carmarthen		End of March, 1349[Rees 1920:121]		High population mortality[Twigg 1984:61]
Channel Islands		Summer 1348[http://www.dudleyfamilypages]		
Chartham*	900[Langridge 1984:229]			50%[Langridge 1984:229]
Chester archdeaconry	15,503 in 1377[Shrewsbury 1970:27]	June, 1349[Wood *et al.* 2003:443]	September, 1349[Wood *et al.* 2003:443]	37% clergy mortality[Wood *et al.* 2003:441] Ecclesiastical deaths, starting April, 1349 [0 1 8 4 8 9 0][Wood *et al.* 2003:443]
Chesterfield*		Lord Thomas Wake died of plague on 30 May 1349[Bestall 1974:72]		51%[Bestall 1974:117]
Cleverland archdeaconry		July, 1349[Thompson 1914:137]	November, 1349[Thompson 1914:137]	30% clergy mortality[Thompson 1914:137] Ecclesiastical appointments, starting June, 1349 [0 1 7 10 6 1 1 0][Thompson 1914:137] Background: 1 a year[Thompson 1914:129]
Climsland*			Before Sept., 1349[Hatcher 1970:105]	42% population mortality[Hatcher 1970:105]
Coltishall*	600[Campbell 1984:96]			56% population mortality[Campbell 1984:96]

Place	Pre-plague population	Start	End	Mortality
Cornard Parva*	180[http://www.harvestfields]	Before March 31, 1349[Gasquet 1908:150]	After May 1, 1349[http://www.harvestfields]	At least 42% population mortality[Gasquet 1908:150]
Cornwall archdeaconry	51,411 in 1377[Shrewsbury 1970:27]	December, 1348[Hatcher 1970:103]	October, 1349[Hatcher 1970:103]	56% clergy mortality[Biraben 1975:174] Ecclesiastical appointments, starting December, 1348 [0 3 3 5 13 12 14 13 6 9 5 4 1][Hatcher 1970:103]; background: 0.3[Gottfried 1983:60]
Coventry*	15,000[Dyer 2000:758; Titow 1969:67-68]	March 1349[Gooder 1998:39]	After peacking in May, 1349[Gooder 1998:39]	25-35% population mortality[Gooder 1998:41-43]
Coventry archdeaconry		April, 1349[Davies 1989:87]	October, 1349[Wood *et al.* 2003:443]	56% clergy mortality[Wood *et al.* 2003:441] Ecclesiastical deaths, starting March, 1349 [0 9 12 10 10 5 2 2 0][Wood *et al.* 2003:443]
*Crowland**	450[Page 1934:84-88]	May, 1349[Page 1934:121]	Before November, 1349[Page 1934:121]	50%[Page 1934:84-88, 121]
Cuxham*	200[Harvey 1965:135; Russell 1948:131]	Shortly before March 20, 1349[Harvey 1965:136]	Before June 23, 1349[Harvey 1965:136]	67% population mortality[Gottfried 1989:340]
Deganwy*				High population mortality[Twigg 1984:62]
Derby archdeaconry	36,433 in 1377[Shrewsbury 1970:27]	June, 1349[Woods *et al.* 2003:443]	September, 1349[Woods *et al.* 2003:443]	66% clergy mortality[Wood *et al.* 2003:441] Ecclesiastical deaths, starting April, 1349 [0 1 10 23 21 10 0][Wood *et al.* 2003:443]
Devon archdeaconry	78,707 in 1377[Shrewsbury 1970:27]	November, 1348[Benedictow 2004:131]		51%[Biraben 1975:174]
Doncaster*	2,000[Dyer 2000:759; Russell 1948:131, 246]			Ecclesiastical appointments, starting July, 1349[2 3 7 7 3 4][Gasquet 1908:176-177]
Dorchester*		A few weeks before Oct. 19, 1348[Watts 1998:23]		

Place	Pre-plague population	Start	End	Mortality
Dorset archdeaconry	51,361 in 1377[Shrewsbury 1970:27]	June, 1348[Horrox 1995:63]	July, 1349[Twigg 1984:60]	Ecclesiastical appointments, starting October, 1348 [4 17 28 21 12 12 6 9 3 11 5][Fletcher 1922:7]
Downton*	600[Ballard 1916:213]	1349[Ballard 1916:213]		66% population mortality[James 1998:14]
Durham	13,091 in 1377[Shrewsbury 1970:27]	Second semester, 1349[Benedictow 2004:141-142]		50% population mortality[Lomas 1989:131]
*East Anglia**		March, 1349[Ziegler 1969:167]	Fall, 1349 Ziegler 1969:167	High population mortality[Gottfried 1983:65]
East Lulworth*		A few weeks before Nov. 18, 1348[Watts 1998:23]		
East Reading archdeaconry		May, 1349[Thompson 1914:138-139]	January, 1350[Thompson 1914:138-139]	48% clergy mortality[Thompson 1914:111] Ecclesiastical appointments, starting May, 1349 [0 3 3 5 17 17 3 3 2 2 1][Thompson 1914:138-139] Background: 5 a year[Thompson 1914:129]
Edinburgh*		1349[http://www.portfolio		33% population mortality[http://www.portfolio
Ely diocese	46,461 in 1377[Shrewsbury 1970:27]	March, 1349[Aberth 1995:280]	December, 1349[Aberth 1995:280]	47% clergy mortality[Aberth 1995:279] Ecclesiastical appointments, starting March, 1349 [0 6 6 17 22 10 7 6 4 4 3 1][Aberth 1995:279]
*Essex**		1349[Poos 1991: 107]		45% population mortality[Poos 1991: 107]
Exeter*	4,000[Shrewsbury 1970:24; Russell 1948:246]			Almost 50% population mortality[Sloan 1981:648]
*Exeter diocese**	130,118 in 1377[Shrewsbury 1970:27]	November, 1348[Gasquet 1908:100-102]		49% clergy mortality[Coulton 1943:496]
Fingreth	600[Fisher 1943:13-20]	Shortly before March 23, 1349[Fisher 1943:14]	Between June 1 and June 30, 1349[Fisher 1943:14-19]	50% population mortality[Fisher 1943:20]

Place	Pre-plague population	Start	End	Mortality
Frodsham*	181 Dodd 1981-2:28			20-40% population mortality Dodd 1981-2:30
Funtley*	60 in 1377 James 1999:6	Before April 23, 1349 Watts 1998:26	Before July 25, 1349 Watts 1998:26	100% population mortality Watts 1998:27
Glastonbury*				57% Ecclestone 1999:25
Gloucester*	7,500 Holt 1985:149; Russell 1948:246	End of August, 1348 Biraben 1975:78		At least 33% Holt 1985:149
Gloucester archdeaconry	68,016 in 1377 Shrewsbury 1970:27	February, 1349 Ziegler 1969:138	August, 1349 Ziegler 1969:138	47% clergy mortality Biraben 1975:174
*Halesowen**	1974 Razi 1980:25 and 75	March 1349 Razi 1980:102	August 1349 Razi 1980:102	42% population mortality Razi 1980:103 Deaths of males, staring March, 1349 [2 3 21 25 22 3] Razi 1980:102
Hampshire archdeaconry	60,849 in 1377 Shrewsbury 1970:27	November, 1348 Gasquet 1908:130	August, 1349 Gasquet 1908:130	49% clergy mortality Biraben 1975:174 Ecclesiastical appointments, starting December, 1348 [7 12 19 33 46 29 24 18 11 12] Gasquet 1908:130
Hereford diocese	25,831 in 1377 Shrewsbury 1970:27	January, 1349 Dohar 1995:46-47	October, 1349 Dohar 1995:46-47	48% clergy mortality Biraben 1975:174 Ecclesiastical appointments, excluding exchanges and resignations, starting January, 1349 [1 3 7 9 11 13 30 30 18 11 9 1] Dohar 1995:46-47; background: 1 Gasquet 1908:165
Hertfordshire archdeaconry	29,962 in 1377 Shrewsbury 1970:27	May, 1349 Gasquet 1908:114	November, 1349 Gasquet 1908:114	35% clergy mortality Biraben 1975:174 Ecclesiastical appointments, starting June, 1349 [6 8 4 4 0 2 1] Gasquet 1908:114
Higham Ferrers*		Early May, 1349 Groome 1982-3:310		At least 37% population mortality Groome 1982-3:310

Place	Pre-plague population	Start	End	Mortality
Holywell		Spring, 1349 Gottfried 1983:87	Fall, 1349 Gottfried 1983:87	High population mortality Gottfried 1983:87
Huntingdon archdeaconry	21,243 in 1377 Shrewsbury 1970:27	March, 1349 Thompson 1911:348-350	October, 1349 Thompson 1911:348-350	37% clergy mortality Thompson 1911:322 Ecclesiastical appointments, starting April, 1349 [2 7 12 22 15 1 3 2 1 1 0] Thompson 1911:348-350 Background: 3 a year Thompson 1911:336
*Isle of Wight**				High population mortality Ziegler 1969:146
Kibworth Harcourt*	200 Howell 1983:16-17	Peacked before the end of April, 1349 Howell 1983:42		70% Lomas 1989:131
Kingston Russel*		A few weeks before Nov. 13, 1348 Watts 1998:23		
Lancashire	35,820 in 1377 Shrewsbury 1970:27	September 8, 1349 Little 1890:525	January 11, 1350 Little 1890:525	
Leicester*	4,800 in 1327 Russell 1948:293			50% Bitnell 1994:200
Leicester archdeaconry	50,748 in 1377 Shrewsbury 1970:27	March, 1349 Thompson 1911:350-351	November, 1349 Thompson 1911:350-351	37% clergy mortality Thompson 1911:324 Ecclesiastical appointments, starting April, 1349 [2 7 16 16 13 12 6 4 6 0] Thompson 1911:350-351 Background: 9 a year Thompson 1911:337
*Lichfield diocese**		March, 1349 Wood *et al.* 2003:443	October, 1349 Wood *et al.* 2003:443	40% clergy mortality http://www.geocities Ecclesiastical appointments, starting January, 1349 [2 3 0 13 21 35 50 48 30 10 2 0] Shrewsbury 1970:70
Lincoln*	9,000 Shrewsbury 1970:24; Russell 1948:246	April 5, 1349 Benedictow 2004:138		60% population mortality Benedictow 2004:359

Place	Pre-plague population	Start	End	Mortality
Lincoln archdeaconry		April, 1349[Thompson 1911:339-344]	January, 1350[Thompson 1911:339-344]	45% clergy mortality[Thompson 1911:325] Ecclesiastical appointments, starting April, 1349 [1 5 23 72 80 38 21 17 8 5 7 3][Thompson 1911:339-344] Background: 7 a year[Thompson 1911:334]
London	50,000[Gottfried 1983:64] At least 100,000 in 1300[Keene 1984:20]	September 29, 1348[Cohn 2002b:142]	Spring 1350[Gottfried 1983:65]	35-50% population mortality[Gottfried 1983:65]
Lulworth*		A few weeks before Nov. 18, 1348[Watts 1998:23]		
Mells*	300[McGarvie 2000:409]	Peak before May 3, 1349[McGarvie 2000:409]		67% population mortality[McGarvie 2000:409]
Newark*	3,000[Dyer 2000:758; Russell 1948:131, 246]	New cemetery on May 15, 1349[Benedictow 2004:139]		
Norfolk	146,726 in 1377[Shrewsbury 1970:27]	January, 1349[Bolton 1996:22]		
Northampton archdeaconry	62,553 in 1377[Shrewsbury 1970:27]	March, 1349[Thompson 1911:351-354]	December, 1349[Thompson 1911:351-354]	33% population mortality[Groome 1982-3:309] 37% clergy mortality[Thompson 1911:323] Ecclesiastical appointments, starting April, 1349 [2 9 17 38 28 11 3 10 2 5 4 1][Thompson 1911:351-354] Background: 9 a year[Thompson 1911:337]
Northumberland	25,210 in 1377[Shrewsbury 1970:27]	December 1349[http://www.hindmarsh		
Norwich*	13,000 in 1311[Russell 1948:293]	January, 1349[Bolton 1996:22]		40-45% population mortality[Bolton 1996:22]

Place	Pre-plague population	Start	End	Mortality
*Norwich diocese**	240,569 in 1377[Shrewsbury 1970:27]	January, 1349[Shrewsbury 1970:99]	November, 1349[Shrewsbury 1970:99]	49% clergy mortality[Coulton 1943:496] Ecclesiastical appointments, starting January, 1349 [3 8 12 17 65 110 194 135 70 65 46 19][Shrewsbury 1970:99]
Nottingham archdeaconry	43,328 in 1377[Shrewsbury 1970:27]	June 1349[Thompson 1914:139-140]	December 1349[Thompson 1914:139-140]	36% clergy mortality[Biraben 1975:174] Ecclesiastical appointments, starting May, 1349 [1 15 12 15 8 4 2 2 0][Thompson 1914:139-140]; background: 6 a year Thompson 1914:129
Oxford*	6,000[Shrewsbury 1970:24; Russell 1948:246]			43% population mortality[Ziegler 1969:139]
Oxford archdeaconry	41,008 in 1377[Shrewsbury 1970:27]	March, 1349[Thompson 1911:354-356]	November, 1349[Thompson 1911:354-356]	39% clergy mortality[Thompson 1911:338 & 354-356] Ecclesiastical appointments, starting April, 1349 [4 7 12 27 9 7 3 2 2 2 1 0][Thompson 1911:354-356] Background: 3 per year [Thompson 1911:338]
Portchester*		Before March 12, 1349[Watts 1998:25]	Between May 3 and July 25, 1349[Watts 1998:25]	
Quob*				100% population mortality[James 1999:6]
Rochester*	1,400[Dyer 2000:759; Russell 1948:131, 246]			50% population mortality[Britnell 1994:199]
*Rochester diocese**		December, 1349[Shrewsbury 1970:93]		
Ruthin	200[Gottfried 1989:340]	June, 1349[Ziegler 1969:191]	August, 1349[Ziegler 1969:191]	
Saint Albans*		April 3, 1349[Biel 1989:38-39]		47% population mortality[Russell 1948:223]

Place	Pre-plague population	Start	End	Mortality
*Salisbury diocese**	154,187 in 1377[Shrewsbury 1970:27]	June, 1348[Horrox 1995:63]		
Salop archdeaconry	40,242 in 1377[Shrewsbury 1970:27]	June, 1349[Woods *et al.* 2003:443]	October, 1349 Woods *et al.* 2003:443	63% clergy mortality[Wood *et al.* 2003:433] Ecclesiastical deaths, starting May, 1349 [0 2 8 10 5 1 0][Wood *et al.* 2003:443]
Selkirk		Fall of 1349[Biraben 1975:80]		
*Snowdonia**				High population mortality[Benedictow 2004:143]
Southampton*		July 1348[Biraben 1975:80]		
Stafford archdeaconry	33,734 in 1377[Shrewsbury 1970:27]	April, 1349[Woods *et al.* 2003:443]	September, 1349[Woods *et al.* 2003:443]	39% clergy mortality[Wood *et al.* 2003:433] Ecclesiastical deaths, starting March, 1349 [0 2 6 6 10 9 3 0][Wood *et al.* 2003:443]
Stow archdeaconry		May, 1349[Thompson 1911:344-345]	December, 1349[Thompson 1911:344-345]	57% clergy mortality[Thompson 1911:325] Ecclesiastical appointments, starting April, 1349 [0 1 6 18 11 13 4 4 3 5 1][Thompson 1911:344-345] Background: 5 a year[Thompson 1911:335]
Surrey archdeaconry	27,058 in 1377[Shrewsbury 1970:27]	December, 1348[Gasquet 1908:130]	August, 1349[Gasquet 1908:130]	56% clergy mortality[Biraben 1975:174] Ecclesiastical appointments, starting January, 1349 [5 8 12 22 23 6 7 2 5][Gasquet 1908:130]; background: 0.8[Gasquet 1908:209]
Swanwick*	150 in 1377[James 1999:6]	Before March 12, 1349[Watts 1998:25]	Between May 6 and July 25, 1349[Watts 1998:25]	64% population mortality[Watts 1998:27]
Tilgarsley*				100% population mortality[James 1999:6]

Place	Pre-plague population	Start	End	Mortality
Tillingdown*		Before September 29, 1349[Saaler 1992:38]	Before end of 1349[Saaler 1992:38]	
*Titchfield**	600 in 1377[James 1999:6]	Shortly before October 31, 1348[Watts 1998:24]	Between March 11 and May 8, 1349[Watts 1998:24]	72% population mortality[Watts 1998:27]
Toller Porcorum*		A few weeks before Nov. 19, 1348[Watts 1998:23]		
Ulster*		1349[Kelly 2001:35-36]		
Walsham-le-Willows*	1,250-1,500[Lock 1992:321]	May 1349 [Lock 1992:316]	July 1349 [Lock 1992:316]	45-55%[Lock 1992: 321]
Warmwell*		A few weeks before Oct. 9, 1348[Watts 1998:23]		
Warwickshire archdeaconry	45,396 in 1377[Shrewsbury 1970:27]	March, 1349[Gasquet 1908:145]	September, 1349[Gasquet 1908:145]	36% clergy mortality Biraben 1975:174 Ecclesiastical appointments, starting April, 1349 [4 13 17 20 15 7 10] [Gasquet 1908:145]
West Chickerell*		A few weeks before Sept. 30, 1348[Watts 1998:23]		
Westminster*		December, 1348 http://www.harvestfields		
Weymouth		June 23, 1348-August 1, 1348[Horrox 1995:63-64]		
*Wiltshire**	68,742 in 1377[Shrewsbury 1970:27]	1348[James 1999:11]	1349[James 1999:11]	
Winchester*	5,000-8,000[Gottfried 1983:63]	Late in 1348[Gottfried 1983:63]		At least 50% population mortality Sloan 1981:648
*Winchester diocese**	87,907 in 1377[Shrewsbury 1970:27]			65% population mortality[Titow 1969:70] 49% clergy mortality Ziegler 1969:145 Ecclesiastical appointments, starting November, 1348 [0 3 3 11 40 64 56 35 25 13 15 16][Watts 1998:22]

Place	Pre-plague population	Start	End	Mortality
Winter-bourne Zelton*		A few weeks before Nov. 19, 1348[Watts 1998:23]		
Witney*	400[Turner 1988:21]	1349[Turner 1988:21]		66% population mortality[Turner 1988:21]
Wool*		A few weeks before Oct. 19, 1348[Watts 1998:23]		
Worcester*	2,336 in 1377[Shrews-bury 1970:24]	April, 1349[Gasquet 1908:142]		
Worcetser diocese	137,560 Shrewsbury 1970:27	February, 1349[Ziegler 1969:138]	September, 1349[Gasquet 1908:145]	42% population mortality[Dyer 1980:238] 48% clergy mortality[Biraben 1975:174]
Wycombe*		May, 1349[Ziegler 1969:141]	September, 1349[Ziegler 1969:141]	50% population mortality[Ziegler 1969:141] 60% clergy mortality[Ziegler 1969:141]
Yarmouth*	More than 10,000[Ziegler 1969:167]			Up to 70% population mortality[http://www.godecookery]
York*	12,000[Shrews-bury 1970:109]	May 9, 1349[Biraben 1975:80]		High clergy mortality[Sloan 1981:648] Ecclesiastical appointments, starting May, 1349 [1 4 4 3 6] [Thompson 1914:105]
*York diocese**		May, 1349[Twigg 1984:66]	February, 1350[Twigg 1984:66]	40-45% population mortality[Kermode 2000:676] 40% clergy mortality[Hatcher1977:26] Ecclesiastical apointments, starting May, 1349 [1 7 24 37 63 51 15 18 6 9 4][Twigg 1984:66]
York archdeaconry		May, 1349[Thompson 1914:135-137]	January, 1350[Thompson 1914:135-137]	45% clergy mortality[Thompson 1914:135-137] Ecclesiastical appointments, starting April, 1349 [1 0 4 5 13 21 20 7 12 1 4 2][Thompson 1914:135-137] Background: 5 a year[Thompson 1914:129]

Appendix B. Parameters for the Non-linear Extended Reed and Frost (ERF) Model

a. Austria

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Eggenburg	100	20	3	5	0.369
Marienberg	100	20	4	5	0.4
Neuberg	100	20	4	5	0.356
Pongau	100	20	4	5	0.356
Upper Inntal	100	20	2.3	3	0.524
Vienna	100	20	2.3	7	0.51
Villach	100	20	3	5	0.369

b. Belgium

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Ath	100	20	4	5	0.356
Bruges	100	20	1.7	7.5	0.336
Ghent	100	20	1.4	5.5	0.505
Mons	100	20	4	5	0.152
Tournai	100	20	3	7	0.263
Ypres	100	20	2.2	3	0.233

c. Croatia

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Dubrovnic	100	20	3	3.5	0.467
Istria	100	20	4	4	0.356
Split	100	20	3.3	5	0.467

d. Czech Republic

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Bohemia	100	20	4	5	0.102

e. Denmark

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Aalborg	100	20	4	5	0.305
Bornholm	100	20	4	5	0.407
Ribe	100	20	4	5	0.305
Zealand Island	100	20	3	6.5	0.421

f. France

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Abbeville	100	20	4	5	0.203
Agen	100	20	4	4	0.350
Aix-en-Provence	100	20	3.5	5	0.467
Albi	100	20	3	6	0.579
Alès	100	20	4	6	0.457
Amiens	100	20	2.7	7	0.215
	100	20	4	4	0.254
Angers	100	20	2.5	6.5	0.275
Angoumois	100	20	2.7	6.5	0.377
Anjou	100	20	2	3	0.49
Arles	100	20	3	6	0.527
Auch	100	20	4	5	0.407
Aurillac	100	20	4	5	0.407
Avignon	100	20	2.3	3	0.628
Bayeux	100	20	3	6.5	0.421
Beaune	100	20	4	5	0.356
Beauvais	100	20	2	6	0.182
	100	20	2.5	6.5	0.275
Besarçon	100	20	3	5	0.369
Béziers	100	20	2.5	6.5	0.44
Bordeaux	100	20	3	6.5	0.421

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Bourg-en-Bresse	100	20	4	5	0.356
Buis-les-Baronnies	100	20	4	5	0.457
Burgundy	100	20	2.2	3	0.466
Cadenet	100	20	4	5	0.457
Calais	100	20	3	7	0.316
Carcassonne	100	20	4	6	0.407
Castellane	100	20	4	5	0.407
Châlons-en-Champaigne	100	20	4	5	0.356
Chambéry	100	20	4	5	0.457
Châteauroux	100	20	4	5	0.457
Colmar	100	20	4	4	0.356
Corsica	100	20	4	6	0.407
Die	100	20	3	5	0.369
Digne	100	20	4	5	0.407
Dijon	100	20	4	5	0.356
Draguignan	100	20	4	6	0.457
Forez	100	20	2	3	0.421
Fresnois-la-Montagne	100	20	4	4	0.153
Grasse	100	20	4	6	0.457
La Châtre	100	20	3	6.5	0.421
Lexy	100	20	4	4	0.153
Lille	100	20	2.2	6	0.173
Limousin	100	20	3.3	5	0.467
Luz	100	20	3	6	0.527
Lyon	100	20	2.7	6.5	0.366
Malaucène	100	20	4	5	0.457
Marseille	100	20	2.3	3	0.685
Maubege	100	20	4	4	0.153
Maurienne	100	20	2	3	0.49
Metz	100	20	4	6	0.305
Montauban	100	20	4	5	0.407
Montbéliard	100	20	4	5	0.356
Montpellier	100	20	2.3	3	0.628
Nancy	100	20	4	5	0.305
Narbonne	100	20	2.2	3	0.466
Navarrenx	100	20	4	5	0.508
Nîmes	100	20	4	5	0.508
Nyons	100	20	4	5	0.457
Orleans	100	20	1.6	5	0.506
Paray-le-Monial	100	20	4	5	0.356
Paris	100	20	1.32	5	0.279
	100	20	1.5	5	0.233
Périgord	100	20	4	5	0.407

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Perpignan	100	20	3	6	0.579
Pia	100	20	6	10	0.301
Poitou	100	20	3	6	0.527
Poligny	100	20	4	5	0.457
Quimper	100	20	6	10	0.351
Reims	100	20	2.2	3	0.291
Revel	100	20	4	5	0.407
Roanne	100	20	4	5	0.356
Rodez	100	20	4	5	0.407
Rouen	100	20	2.3	3	0.524
Saint Denis	100	20	1.32	5	0.279
	100	20	1.5	5	0.233
Saint-Etienne	100	20	4	5	0.356
Saint-Flour	100	20	3.5	5	0.467
Saint Marie Laumont	100	20	6	10	0.501
Salins	100	20	4	5	0.457
Strasbourg	100	20	3	5	0.369
Tarbes	100	20	4	5	0.508
Toulon	100	20	4	5	0.508
Toulouse	100	20	2.3	2.4	0.4
Tulle	100	20	4	5	0.407
Valenciennes	100	20	4	5	0.305
Verdun	100	20	4	5	0.305

g. Germany

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Ausburg	100	20	3	7	0.263
Baden-Baden	100	20	3	6.5	0.421
Bielefeld	100	20	4	5	0.407
Borau	100	20	4	5	0.407
Braunschweig	100	20	4	5	0.457
Bremen	100	20	2.3	7	0.51
Cologne	100	20	1.8	3	0.659
Erfurt	100	20	2.2	3	0.466
Frankfurt-am-Main	100	20	2.3	2.4	0.4
Güstrow	100	20	4	5	0.305
Halberstadt	100	20	3	6.5	0.421
Hamburg	100	20	3	6	0.579
Hanover	100	20	4	5	0.254
Kontanz	100	20	3	7	0.158

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Limburg	100	20	3	7	0.316
Magdeburg	100	20	3	6	0.527
Mainz	100	20	2.2	3	0.233
Minden	100	20	4	5	0.1
Mühldorf	100	20	4	5	0.152
Münster	100	20	3	6.5	0.421
Nuremberg	100	20	4	5	0.102
Osnabrück	100	20	4	5	0.051
Paderborn	100	20	3.3	5	0.436
Parchim	100	20	4	6	0.407
Passau	100	20	4	5	0.203
Regensburg	100	20	4	5	0.203
Rostock	100	20	4	5	0.305
Schleswig	100	20	3	6.5	0.421
Trier	100	20	4	5	0.305
Ulm	100	20	4	5	0.407
Wismar	100	20	3	6.5	0.421
Würtzburg	100	20	3	7	0.316

h. Gibraltar

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Gibraltar	100	20	1.6	5	0.578

i. Ireland

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Drogheda	100	20	3.5	5	0.457
Dublin	100	20	2.3	7	0.51
Dundalk	100	20	4	5	0.407
Ennis	100	20	4	5	0.356
Ferns	100	20	3	5	0.369
Kildare	100	20	3.3	5	0.467
Kilkenny	100	20	3.3	5	0.467
Limerick	100	20	4	5	0.356
Meath	100	20	4	5	0.407
Moylurg	100	20	4	5	0.407
Nenagh	100	20	4	5	0.356
Waterford	100	20	3.3	5	0.467

j. Italy

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Agrigento	100	20	3	6	0.579
Ancona	100	20	4	5	0.457
Bari	100	20	3.3	5	0.467
Cagliari	100	20	2.3	7	0.566
Catania	100	20	2.3	3	0.685
Cesena	100	20	3.3	5	0.457
Elba Island	100	20	4	5	0.407
Faenza	100	20	3.3	5	0.467
Ferrara	100	20	3	6.5	0.421
Florence	100	20	2	3	0.601
Friuli	100	20	3	5	0.369
Genoa	100	20	1.3	5.3	0.663
Lucca	100	20	3	6.5	0.421
Messina	100	20	2.3	7	0.51
Modena	100	20	3	6.5	0.421
Naples	100	20	2	3	0.551
Orvieto	100	20	3.3	5	0.467
Padua	100	20	2.3	7	0.51
Parma	100	20	2.2	3	0.466
Piacenza	100	20	2.7	6.5	0.377
Piombino	100	20	4	5	0.407
Pisa	100	20	1.6	5	0.506
Pistoia	100	20	2.5	6.5	0.44
Prato	100	20	4	6	0.407
Pusteria	100	20	4	5	0.356
Reggio d'Emilia	100	20	2.2	3	0.466
Reggio di Calabria	100	20	4	5	0.457
Rimini	100	20	3	6	0.527
Rome	100	20	2.3	2.4	0.4
Sardinia	100	20	2.3	3	0.571
Siena	100	20	2.3	3	0.524
Syracuse	100	20	3	6	0.527
Trapani	100	20	3	6	0.632
Trent	100	20	3	6.5	0.421
Turin	100	20	4	4	0.356
Varesse	100	20	4	5	0.407
Venice	100	20	2	3	0.184
	100	20	2	3	0.429
	100	20	2.2	3	0.116
Ventimiglia	100	20	4	5	0.356

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Verona	100	20	2.3	3	0.628
Vintschgau	100	20	4	5	0.407

k. Norway

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Agden	100	20	4	4	0.356
Bergen	100	20	3	6.5	0.421
Hamar	100	20	6	10	0.251
Idd	100	20	4	5	0.356
Lom	100	20	4	5	0.356
Oslo	100	20	3	6	0.527
Stavenger	100	20	4	5	0.356
Tinn	100	20	4	5	0.356
Tønsberg	100	20	4	5	0.356
Toten	100	20	4	5	0.305
Trondheim	100	20	3	6	0.527
Upper Eiker	100	20	3	5	0.305
Vågå	100	20	4	5	0.356
Valdres	100	20	4	5	0.356

l. Poland

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Gdansk	100	20	4	5	0.305
Torun	100	20	4	5	0.305

m. Portugal

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Braga	100	20	3.3	5	0.467
Coimbra	100	20	6	10	0.491
Evora	100	20	2.3	2.4	0.4

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Lamego	100	20	2.9	6	0.424
Lisbon	100	20	3	7	0.453
Silves	100	20	2.3	7	0.453

n. Spain

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Almería	100	20	1.6	6	0.774
Almudevar	100	20	4	4	0.356
Asturias	100	20	3	5	0.369
Badajoz	100	20	3	5	0.369
Berga	100	20	3	5	0.369
Borja	100	20	4	4	0.356
Cádiz	100	20	2.2	3	0.466
Calatayud	100	20	4	4	0.356
Camprodrón	100	20	6	10	0.301
Cartagena	100	20	2.3	7	0.51
Cerdanya	100	20	4	4	0.356
Cordoba	100	20	2	3	0.49
Duero Valley	100	20	2	3	0.551
Estella	100	20	2.5	6	0.661
Girona	100	20	3.3	5	0.467
Granada	100	20	1.45	5	0.7281
Huesca	100	20	2.9	6	0.424
Jérica	100	20	4	4	0.356
León	100	20	2.7	6.5	0.377
Lérida	100	20	3	5	0.369
Lugo	100	20	2.7	7	0.323
Málaga	100	20	2.3	7	0.51
Mallorca	100	20	3	5	0.358
Minorca	100	20	6	10	0.351
Morella	100	20	4	5	0.305
Murcia	100	20	2.3	7	0.51
Plana de Vic	100	20	3.3	5	0.519
Puerto Llano	100	20	6	10	0.451
San Juan de la Peña	100	20	6	10	0.351
Santesteban	100	20	4	6	0.407
Santiago de Compostela	100	20	2.9	6	0.424
Sarrión	100	20	4	5	0.254
Segorbe	100	20	4	4	0.356

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Seville	100	20	1.4	5.5	0.673
Soria	100	20	4	4	0.356
Tarazona	100	20	4	4	0.356
Tarragona	100	20	3.3	5	0.467
Teruel	100	20	4	4	0.305
Toledo	100	20	1.6	5	0.578
Tortosa	100	20	2.9	6	0.424
Tuy	100	20	4	5	0.407
Urgell	100	20	4	5	0.356
Valencia	100	20	3	5	0.369
Villalobos	100	20	6	10	0.401
Viseo	100	20	4	4	0.356

o. Sweden

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
East Gotland	100	20	1.4	5.5	0.728
Halmstad	100	20	3	5	0.369
Lund	100	20	1.6	5	0.65
Örebo	100	20	3	5	0.369
Smalandia	100	20	1.3	5.5	0.847
Södermanland	100	20	3	5	0.369
Uplandia	100	20	3	6.5	0.421
Visby	100	20	2.2	3	0.466
Westrogothia	100	20	2.7	6.5	0.377

p. Switzerland

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Aargau	100	20	4	5	0.356
Basel	100	20	3	6.5	0.421
Bellinzona	100	20	3	5	0.369
Bern	100	20	4	5	0.356
Chillon	100	20	4	5	0.305
Dissentis	100	20	4	5	0.356
Engelberg	100	20	3	6.5	0.421
Geneva	100	20	3	5	0.369

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Lucerne	100	20	4	5	0.407
Nyon	100	20	4	5	0.407
Pfäffers	100	20	4	5	0.356
Rutwil	100	20	4	5	0.356
Saint Gallen	100	20	3	7	0.316
Vevey	100	20	4	5	0.305
Zurich	100	20	3	6.5	0.421

q. The Netherlands

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Friesland	100	20	3	7	0.316
Groningen	100	20	3	7	0.316
Zwolle	100	20	3	6.5	0.421

r. United Kingdom

Place	Population $P_{s,0}$	Serial Time τ	Contacts K_s	Initial Cases $I_{s,\tau}$	Factor f
Abergavenny	100	20	4	5	0.508
Bristol	100	20	2.2	3	0.466
Canterbury	100	20	3.3	5	0.508
Cardigan	100	20	3	6.5	0.421
Carmarthen	100	20	3	6.5	0.421
Channel Islands	100	20	4	5	0.407
Devon	100	20	1.8	3	0.672
Durham	100	20	3	6	0.527
Fingreth	100	20	4	5	0.508
Gloucestershire	100	20	2	5	0.571
Holywell	100	20	3.3	5	0.467
Lancashire	100	20	3	6	0.527
London	100	20	1.3	3	0.673
	100	20	2	3	0.184
Northumberland	100	20	3	5	0.369
Ruthin	100	20	4	5	0.356
Selkirk	100	20	3	5	0.369
Weymouth	100	20	3	6.5	0.421

References

"The originator of a new idea is not the most
suitable person to develop it, because his fears
of something going wrong are really too strong."
P. Dirac

A. Printed References

Abel W (1965) Désertions rurales: bilan de la recherche allemande. In: Villages Desertes et Histoire Économique, XI^{e} – XVIII^{e} Siècle. SEVPEN, Paris, pp 515-531.

Aberth J (1995) The Black Death in the diocese of Ely: the evidence of the bishop's register. J of Medieval History 21(3):275-287.

Aczel J, Daroczy Z (1975) On Measures of Information and Their Characterization. Academic Press, New York.

Agulhon M (ed) (1980) Histoire de Toulon. Privat, Toulouse.

Aickin M (2002) Causal Analysis in Biomedicine and Epidemiology. Marcel Dekker Inc, New York.

Allen C, Bekoff M, Lauder G (eds) (1998) Nature's Purpose: Analyses of Function and Design in Biology. MIT Press, Cambridge.

Allinson AR (1930) The Satyricon–Petronius. The Panurge Press, New York.

Amasuno Sárrega MV (1996) La Peste en la Corona de Castilla durante la Segunda Mitad del Siglo XIV. Junta de Castilla y León, Salamanca, Spain.

Andenmatten B, Morerod JD (1987) La peste à Lausanne au XIV siècle (1348/1349, 1360). Etudes de Lettres 2-3:19-49.

Anderson RM, May RM (1995) Infectious Diseases of Humans. Oxford University Press, New York.

Arbnor I, B Bjerke (1997) Methodology for Creating Business Knowledge. Sage Publications, Thousand Oaks.

Arlinghaus SL (ed) (1995) Practical Handbook of Spatial Statistics. CRC Press, Boca Raton.

Arriazabalaga J (1991) La Peste Negra de 1348. Dynamis 11:73-117.

Aubry M (1983) Les mortalités lilloises (1328-1369). Revue du Nord LXV(257):327-342.

Audisio G (1968a) La peste en Auvergne au XIV^{e} siècle. Revue d'Auvergne 82:257-265.

Audisio G (1968b) La crise démographique en Auvergne au XIVe siècle. Revue de la Haute-Auvergne 70(41):343-353.

Ayliffe GAJ, English MP (2003) Hospital Infection: From Miasmas to MRSA. Cambridge Univ Press, Cambridge.

Bailey NTJ (1957) The Mathematical Theory of Epidemics. Hafner Publishing Co, New York.

Ballard A (1916) The manors of Witney, Brightwell, and Downton. In: P. Vinogradoff (ed) Oxford Studies in Social and Legal History, Vol 5. Oxford at the Clarendon Press, London; also reprinted in 1974 by Octagon Books, New York, pp 181-220.
Ballesteros Rodríguez J (1982) La peste en Córdoba. Estudios Cordobeses, Estudios de la Excelentísima Diputación Provincial. Imprenta San Pablo.
Baratier E (1961) La Démographie Provençale du XIIIe au XVIe Siècle. SEVPEN, Paris.
Bardet JP, Dupâquier J (eds) (1997) Histoire des Populations de l'Europe. I Des origenes aux prémices de la revolution démographique. Fayard, Paris.
Barron CM (1995) London in the later Middle Ages 1300-1550. The London J 20(2):22-33.
Bartlett SJ (1993) Barbarians at the Door. Modern Age 35(4):296-310.
Bautier RH (1988) Un nouvelle ensemble documentaire pour l'histoire des pestes du XIV^{e} siècle, l'example de la ville de Vich en Catalogne. Académie des Inscriptions & Belles-Lettres, Comptes Rendus des Séances 1988(2):432-456.
Bean JMW (1982) The Black Death: The crisis and its social and economic consequences. In: Williman D (ed) The Black Death—The Impact of the Fourteenth-Century Plague. Center for Medieval & Early Renaissance Studies, Binghamton, New York, pp 23-38.
Bechtel W (ed) (1986) Integrating Scientific Disciplines. Martinus Nijhoff Publ, Dordrecht.
Bender EA (2000) Mathematical Methods in Artificial Intelligence. IEEE Computer Society Press, Los Alamitos.
Benedictow OJ (1992) Plague in the Late Medieval Nordic Countries. Middelalderforlaget, Oslo.
Benedictow OJ (2004) The Black Death 1346–1353: The complete History. The Boydell Press, Woodbridge, Suffolk.
BenMap (Benefits Mapping and Analysis Program) (2003) Environmental Benefits Mapping and Analysis Program. Abt Associates Inc, Prepared for US-EPA, Research Triangle Park.
Beran MJ (1968) Statistical Continuum Theories. Interscience Publishers. J Wiley & Sons, New York.
Bernardo JM, Smith AFM (1994) Bayesian Theory. J Wiley & Sons, New York.
Berthe M (1976) Le Comté de Bigorre—un Milieu Rural au Bas Moyen Âge. SEVPEN, Paris.
Berthe M (1983) Famines et pestes en Navarre au Bas Mogen Âge. Académie des Inscriptions & Belles-Lettres Comptes Rendus des Séances 1983(2):299-314.
Bestall JM (1974) History of Chesterfield, vol 1. Borough of Chesterfield.
Biel TL (1989) The Black Death. Lucent Books Inc., San Diego.
Biget JL (ed) (1983) Histoire d'Albi. Editions Privat, Toulouse.
Biraben JN (1975) Les Hommes et la Peste en France et dans les Pays Européens et Méditerranéens—Tome I, La Peste dans l'Histoire. Mouton, Paris.
Biraben JN (1987) L'inexorable marche de la Peste noire. In: Delumeau J, Lequin Y (eds) Les Malheurs des Temps—Histoire de Fléaux et des Calamités en France. Larousse, Paris, pp 178-192.
Bleukx K (1995) Was the Black Death (1348-49) a real plague epidemic? England as a case study. In: Verbeke W, Haverals M, De Keyser R, Goosens J (eds) Serta Devota in Memoriam Guillelmi Lourdaux. Leuven University Press, Louvain, pp 65-113.
Blockmans WP (1980) Effects of plague in the Low Countries. Revue Belge de Philologie et d'Histoire LVIII(4):833-863.
Bogaert P, D'Or D (2002) Estimating Soil Properties from Thematic Soil Maps—The Bayesian Maximum Entropy Approach. J Soil Sc Soc of Am 66:1492-1500.
Bois G (1984) The Crisis of Feudalism—Economy and Society in Eastern Normandy c. 1300–1550. Cambridge University Press, Cambridge.

Boll E (1855) Geschischte Mecklenburgs mit besonderer Besichtigung der Kulturgeschichte. Selbstverlag, Neubrandenburg. 1995 reprint by Federchen-Verlag.
Bolton J (1996) 'The world upsidedown'. Plague as an agent of economic and social change. In: Ormrod WM, Lindley PG (eds) The Black Death in England. Paul Watkins, Stamford, pp 17-78.
Boucher CE (1938) The Black Death in Bristol. Trans of the Bristol and Gloucestershire Archaeol Soc LX:31-46.
Bourderon R, Peretti P (eds) (1988) Histoire de Saint-Denis. Privat, Toulouse.
Bowsky WM (1964) The impact of the Black Death upon Sienese government and society. Speculum XXXIX(1):1-34.
Britnell R (1994) The Black Death in English Towns. Urban Hist 21(2):195-210.
Brooks, JM, Chrischilles E, Scott S, Ritho S, Chen-Hardee S (2000). Information gained from linking SEER Cancer Registry Data to state-level hospital discharge abstracts. Surveillance, Epidemiology, and End Results. Medical Care 38(11): 1131-1140.
Brothen JA (1996) Population decline and plague in late medieval Norway. Annales de Démographie Historique, pp 137-149.
Bulst N (1979) Der Schwarze Tod—Demographische, wirtschafts- und kulturgeschichtliche Aspekte der Pestkatastrophe von 1347-1352. Bilanz der neueren Forschung. Saeculum 30(1):45-67.
Bur M (ed) (1987) Histoire de Laon et du Laonnois. Privat, Toulouse.
Buringh E (2002) Health Risk Assessment of Factors in the Local Environment. Unpublished Internal Report, MNP-LOK 500029 001, RIVM, The Netherlands.
Bury KV (1975) Statistical Models in Applied Science. J Wiley, New York.
Cabrillana N (1965) Villages désertés en Espagne. In: Villages Desertes et Histoire Économique, XIe – XVIIIe Siècle. SEVPEN, Paris, pp 461-512.
Cabrillana N (1968) La crisis del siglo XIV en Castilla: La Peste Negra en el Obispado de Palencia. Hispania, Revista Española de Historia XXVIII(109):245-258.
Calero Secall MI (1991) La peste en Málaga, según el malagueño al-Nub_h_. Homenaje al Profesor Jacinto Bosh Vilá, vol I. Universidad de Granada, Granada, pp 57-71.
Campbell BMS (1984) Population pressure, inheritance and the land market in a fourteenth-century peasant community. In: Smith RM (ed) Land, Kinship and Life-Cycle. Cambridge University Press, Cambridge, pp 87-134.
Camus A (1970) Lyrical and Critical Essays. A Vintage Book, New York.
Cantor NF (2001) In the Wake of the Plague. The Black Death and the World it Made. The Free Press, New York.
Cantú C (1999) Storia di Milano. Atesa Editrice, Bologna.
Carmichael AG (1997) Bubonic plague: the Black Death. In Kiple FF (ed) Plague, Pox & Pestilence. Weidenfeld & Nicolson, London, pp 60-67.
Carpentier É (1962) Autour de la Peste Noire: famines et épidémies dans l'histoire de XIVe siècle. Annales E.S.C. – Economies, Sociétés, Civilisations 17(6):1062-1092.
Carpentier É (1993) Une Ville devant la Peste – Orvieto et la Peste Noir 1348. 2nd edition, De Boeck, Brussels.
Cartwright FF, Biddiss M (2000) Disease and History. Second edition. Sutton Publishing, Phoenix Mill, Glocestershire.
Caselton WF, Luo WB (1992) Decision making with imprecise probabilities: Dempster-Shafer theory and application. Wat Resour Res 28(12):3071-3083.
Chandler T (1987) Four Thousand Years of Urban Growths – A Historical Census. St David's University Press, Lewiston, New York.
Chédeville A (ed) (1983) Histoire de Chartres et du Pays Chartrain. Privat, Toulouse.
Chen CJ (2005) Personal communication. Chapel Hill.

Cheney CR (1956) The Records of Medieval England, an Inaugural Lecture. Cambridge University Press, Cambridge.
Cheney CR (ed) (1996) Handbook of dates for students of English History. Reprinted with corrections from the original 1945 edition. Cambridge Univ Press, Cambridge.
Cherfas J (1986) Exploding the myth of the melanic moth. New Scientist 112(1540/41): 25
Cherkassky V, Mulier F (1998) Learning from Data: Concepts, Theory, and Methods. J Wiley & Sons, New York.
Chiappelli A (1887) Gli ordinamenti sanitari del Comune di Pistoia contro la pestilenza del 1348. Archivo Storico Italiano, Serie 4 XX:3-24.
Choi KM, Serre ML, Christakos G (2003) Efficient mapping of California mortality fields at different spatial scales. J Expos Anal & Env Epid 13(2):120-133.
Christakos G (1992) Random Field Models in Earth Sciences. Academic Press, San Diego (Out of Print) New edition, 2005, Dover Publ Inc, Mineola.
Christakos G (2000) Modern Spatiotemporal Geostatistics. Oxford Univ Press, New York.
Christakos G (2001) Stochastic modelling of human exposure. In: El-Shaarawi AH, Piegorsch WW (eds) Encyclopedia of Environmentrics. J Wiley & Sons, Ltd, Chichester 3:1290-1296.
Christakos G (2002a) On a deductive logic-based spatiotemporal random field theory. Prob Theory & Math Statistics 66:54-65.
Christakos G (2002b) On the assimilation of uncertain physical knowledge bases: Bayesian and non-Bayesian techniques. Adv Wat Resour 25(8-12), 1257-1274.
Christakos G (2003a) Critical conceptualism in environmental modelling and prediction. Envir Sci & Tech 37:4685-4693.
Christakos G (2003b) The role of conceptual frameworks in hydrologic research and development. Kovar K, Hrkal Z (eds). IAHS Publ 277, Oxfordshire, pp 277-285.
Christakos G (2004) The influence of philistinism upon public health. The Risk & Biomedical Debate on Plagues of the Future. On-line Spiked-Risk Debates (http://www.spiked-online.com/Articles/0000000CA83F.htm).
Christakos G, Bogaert P, Serre ML (2002) Temporal GIS. Springer-Verlag (with CD-Rom), New York.
Christakos G, Hristopulos DT (1998) Spatiotemporal Environmental Health Modelling. Kluwer Academic Publ, Boston.
Christakos G, Kolovos A (1999) A study of the spatiotemporal health impacts of ozone exposure. J of Expos Anal & Env Epid 9(4):322-335.
Christakos G, Kolovos A, Serre ML, Vukovich F (2004) Total ozone mapping by integrating data bases from remote sensing instruments and empirical models. IEEE Trans Geosc and Remote Sens 42(5):991-1008.
Christakos G, Lai J (1997) A study of the breast cancer dynamics in North Carolina. Soc Sc & Medicine 45(10):1503-1517.
Christakos G, Serre ML (2000) A spatiotemporal study of exposure-health effect associations. J of Expos Anal & Env Epid 10(2):168-187.
Christakos G, Vyas V (1998) A novel method for studying population health impacts of spatiotemporal ozone distribution. Soc Scien & Medicine 47(8):1051-1066.
Christodoulou D (1999) The Action Principle and Partial Differential Equations. Princeton Univ Press, Princeton.
Cipolla CM (1981) Fighting the Plague in Seventeen-Century Italy. The Univ of Wisconsin Press, Madison.
Clavaud F (1995) Évolution et structures de la population à Cajarc, consulat du Haut-Quercy, au XIVe siècle: un example du cas des petites villes. In: Guyotjeannin O (ed),

Population et Démographie au Moyen Âge, Actes du 118e Congrès National des Sociétés Historiques et Scientifiques. Éditions du CTHS, Paris, pp 51-83.
Clayton D, Hills M (1993) Statistical Models in Epidemiology. Oxford Univ Press, New York.
Cliff A (1995) Incorporating spatial components into models of epidemic spread. In: Mollison D (ed), Epidemic Models. Cambridge Univ Press, Cambridge, pp 119-149.
Cohn Jr SK (1992) The Cult of Remembrance and the Black Death. The John Hopkins University Press, Baltimore.
Cohn Jr SK (2002a) The Black Death: end of a paradigm. The American Historical Review 107(3):703-738.
Cohn Jr SK (2002b) The Black Death Transformed: Disease and Culture in Early Renaissance Europe. Arnold, London.
Coleman HW, Steele WG (1999) Experimentation and Uncertainty Analysis for Engineers. 2nd Edition, J Wiley & Sons Inc, New York.
Collantes de Terán A (1977) Sevilla en la Baja Edad Media, la Ciudad y sus Hombres. Sección de Publicaciones del Excelentísimo Ayuntamiento de Sevilla, Seville.
Comba R (1977a) Vicende demografiche in Piemonte nell'ultimo medioevo. Bolletino Storico-Bibliografico Subalpino LXXV:39-125.
Comba R (1977b) La popolazione in Piemonte sul finire del medioevo. Deputazione Subalpina di Storia Patria, Turin.
Coser LA (1965) Men of Ideas. The Free Press, New York.
Corzine P (1997) The Black Death. Lucent Books, San Diego.
Coulton GG (1929) The Black Death. Ernest Benn Limited, London.
Coulton GG (1943) Medieval Panorama. Cambridge at the University Press, Cambridge.
Courtenay WJ (1980) The effect of the Black Death on English higher education. Speculum 55(4):696-714.
Creighton C (1891) A History of Epidemics in Britain from A.D. 664 to the Extinction of the Plague. Cambridge at the University Press, Cambridge.
Cross J (1994) Education vs. training—A distinction that makes a difference. Bank Securities Journal 3(6):62-63.
Daley DJ, Gani J (2001) Epidemic Modelling: An Introduction. Cambridge Univ Press, Cambridge.
Dalton L (2003) Chemical analysis of disaster: Scientists struggle to understand the complex mixture of aerosols released during and after the destruction of the World Trade Center. Chemical and Engineering News, CENEAR 81(42):26-30.
Daniels H (1995) A perturbation approach to nonlinear deterministic epidemic waves". In: Mollison D (ed) Epidemic Models. Cambridge Univ Press, Cambridge, pp 202-214.
Davies RA (1989) The effect of the Black Death on the parish priests of the medieval diocese of Coventry and Lichfield. Historical Research XXII(147):85-90.
Davies RT (1924) A Sketch of the History of Civilization in Medieval England 1066-1500. MacMilland and Co, London.
Davis DE (1986) The scarcity of rats and the Black Death: an ecological history. J of Interdiscipl Hist XVI(3):455-470.
Day Jr WR (2002) The population of Florence before the Black Death: survey and synthesis. J of Medieval Hist 28:93-129.
De Calonne A (1976) Histoire de la Ville d'Amiens. Laffitte Reprints, Marseille.
De Hahn T (2002) The Black Death. Chelsea House Publishers, Philadelphia.
Deaux G (1969) The Black Death. Hamish Hamilton, London.
Del Panta L (1980) Le Epidemie nella Storia Demografica Italiana (secoli XIV-XIX). Loescher Editore, Turin.

Del Panta L, Livi Bacci M, Pinto G, Sonio E (1996) La Popolazione Italiana dal Medioevo a Oggi. Editori Laterza, Roma.
Delmaire B (1981) Contribution à l'étude de la peste au bas moyen âge. Un fragment de compte inédit de l'abbaye de Saint-Bertin pour Bas-Warneton. Mémoires de la Societé d'Histoire de Comines-Warneton et de la Région 11:36-50.
Denis Y (ed) (1988) Histoire de Blois et de sa Région. Privat, Toulouse.
Denissenko MF, Pao A, Tang M, Pfeifer GP (1996) Preferential formation of benzo[a]pyrene adducts at lung cancer mutational hotspots in p53. Science 274:430-432.
Désert G (ed) (1981) Histoire de Caen. Privat, Toulouse.
D'Espagnat B (1995) Veiled Reality. Addison-Wesley, Reading.
Desportes P (1979) Rheims et les Rémois. Éditions A & J Picard, Paris.
Desportes P (ed) (1983) Histoire de Rheims. Privat, Toulouse.
Despy G (1977) La Grande Peste Noire de 1348 "A-t-elle touché le Roman pays de Bravant?" In: Centenaire du Séminaire d'Histoire Médiévale de l'Université Libre de Bruxelles, 1876-1976. La Renaissance de Livre, Bruxelles, pp 195-217.
DHHS (Department of Health and Human Services) (2003) Superfund Basic Research and Training Program, RFA Number: ES-04-001. National Institutes of Health, Bethesda.
Dickey JM, Chen C (1985) Direct subjective-probability modeling using ellipsoidal distributions. In: Bernardo JM, De Groot MH, Lindley DV, Smith AFM (eds) Bayesian Statistics II. North-Holland, Amsterdam, pp 157-182.
Diekmann O, Heesterbeek JAP (2000) Mathematical Epidemiology of Infectious Diseases: Model Building, Analysis and Interpretation. J Wiley, New York.
Dobson B (2000) General survey 1300-1540. In: Palliser DM (ed) The Cambridge Urban History of Britain. Cambridge University Press, Cambridge, pp 273-290.
Dodd JP (1981-1982) The population of Frodsham manor, 1349-50. Transac of the Historic Society of Lancashire and Cheshire 131:21-33.
Dodds B (2002) Durham priory tithes and the Black Death between Tyne and Tees. Northern History XXXIX(1):5-24.
Dohar WJ (1995) The Black Death and Pastoral Leadership—The diocese of Hereford in the Fourteenth Century. University of Pennsylvania Press, Philadelphia.
Doñate Sebastia JM (1969) Datos negativos, referidos a la Plana de Castellón, en relación con la peste negra de 1348. VIII Congreso de la Corona de Aragón, La Corona de Aragón en el Siglo XIV, Valencia II(1):27-43.
Doody M (2002) Aristotle Detective—Murder and Mystery in Ancient Athens. Arrow Books, The Random House Group Ltd, London.
D'Or D, Bogaert P (2003) Continuous-valued map reconstruction with the Bayesian Maximum Entropy. Geoderma 112(3):169-178.
Dostoevsky, F (2003) The Grand Inquisitor. Continuum, New York.
Douaik A, Van Meirvenne M, Toth T, Serre ML (2004) Space-time mapping of soil salinity using probabilistic Bayesian maximum entropy. Stoch Envir Res and Risk Assessment 18:219-227.
Dubled H (1969) Les épidémies de peste à Carpentras et dans le Comtat Venaissin. Provence Historique 19(75):17-48.
Dubuis P (1980) L'épidémie de peste de 1349 a Saint-Maurice d'Agaune. Etudes de Lettres, series 4 3(1):4-20.
Dupâquier J, Biraben JN, Étienne R, Pietro C, Pietro L, Bautier H, Dubois H, Higounet-Nadal A, Klapisch-Zuber C (1988) Histoire de la Population Française vol. 1, Des Origenes à la Renaissance. Presses Universitaires de France, Paris.
Dupre J (1993) The Disorder of Things. Harvard Univ Press, Cambridge.

Dyer A (2000) Ranking list of English medieval towns. In: Palliser DM (ed) The Cambridge Urban History of Britain. Cambridge Univ Press, Cambridge, pp 747-770.
Dyer C (1980) Lords and Peasants in a Changing Society—the Estates of the Bishopric of Worcester, 680-1540. Cambridge Univ Press, Cambridge.
Eamon W (1997) The Black Death and the Transformation of the West. Harvard Univ Press, Cambridge.
Ecclestone M (1999) Mortality of rural landless men before the Black Death: the Glastonbury head-tax lists. Local Population Studies 63:6-29.
The Economist (2005) Ever higher society, ever harder to ascend. Special Report: Meritocracy in America, January 1, 2005, pp 22-24.
Eddington A Sir (1958) The Philosophy of Physical Science. Ann Arbor Paperbacks. The Univ of Michigan Press, Ann Arbor.
Edwards AWF (1972) Likelihood. Cambridge Univ Press, Cambridge.
Emery RW (1967) The Black Death of 1348 in Perpignan. Speculum XLII(4):611-623.
Epstein SA (1996) Genoa and the Genoese. The University of North Carolina Press, Chapel Hill.
Falsini AB (1971-1972) Firenze dopo il 1348. Le conseguenze della peste nera. Archivo Storico Italiano CXXIX(4):425-503.
Favreau R (1985) Histoire de Poitiers. Privat, Tolouse.
Feldman J (2000) Minimization of Boolean complexity in human concept learning. Nature 407:630-633.
Fisher JL (1943) The Black Death in Essex. Essex Review 52:13-20.
Fiumi E (1968) Demografia, Movimento Urbanistico e Classi Sociali in Prato dall'età Comunale ai Tempi Moderni. Leo S Olschki, Florence.
Fletcher JMJ (1922) The Black Death in Dorset (1348-1349). In: Proceedings of the Dorset Natural History and Antiquarian Field Club 43:1-14.
Fournée P (1978) Les Normands Face a la Peste—Trois siècles et demi de Peste en Normandie. Le Pays bas-Normand, Flers, Orne.
Fössel A (1987) Der "Schwarze Tod" in Franken 1348-1350. In: Mitteilungen des Vereins für Geschichte der Stadt Nürnberg 74:1-75.
Frost R (1967) Robert Frost's Poems. Washington Square Press, Pocket Books, New York.
Fryde E (ed) (1978) The tenants of the bishops of Coventry and Lichfield and Worcester after the plague of 1348-9. In: Hunnisett RF, Post JB (eds) Medieval Legal Records, edited in memory of Mekings CAF. Her Majesty Stationery Office, London, pp 223-266.
Furedi F (2004) Where Have All the Intellectuals Gone? Continuum, London.
Gagnière S, Granier J, Poly JP, Guillemain B, Chiffoleau J, Venard M, Feuillas M, Moulines R, Lapied M, Maureau A, Grosso R (1979) Histoire d'Avignon. Édisud, Aix-en-Provence.
Galavotti MC, Suppes P, Constantini D (eds) (2001) Stochastic Causality. CSLI Publ, Stanford.
Galera i Pedrosa A (1994) Les salines de Cardona i la pesta negra de 1348: la disminució de les rendes de la sal. Miscellània d'Estudis Bagencs 9:69-98.
Galison P, Stump DJ (eds) (1993) The Disunity of Science. Stanford Univ Press, Stanford.
Ganiage J (ed) (1987) Histoire de Beauvais et du Beauvaisis. Privat, Toulouse.
Garden E, Gotteri N (eds) (1993) To My Best Friend: Correspondence Between Tchaikovsky and Nadezhda von Meck, 1876-1878. Translated by Galina von Meck with an introduction by E Garden. Oxford Univ Press, New York.
Gardenfors P (2000) Conceptual Spaces: The Geometry of Thought. Bradford Books MIT Press, Cambridge.

Gardiner CW (1990) Handbook of Stochastic Methods. Springer-Verlag, New York.
Gasquet FA (1893) The Great Pestilence. Simkin Marshall, Hamilton, Kent & Co, London.
Gasquet FA (1908) The Black Death of 1348 and 1349. George Bell and Sons, London; 1977 reprint, AMS Inc, New York.
Gauch HG Jr (1993) Prediction, parsimony and noise. American Scientist 81:468-478.
Gautier-Dalché J (1962) La peste noire dans les etats de la Couronna d'Aragon. Bulletin Hispanique, vol 64 bis Mélanges offerts à Marcel Bataillon, pp 65-80.
Gelting MH (1991) The mountain and the plague: Maurienne, 1348. Collegium Medievale 4(1):7-45.
Giblin JC (1995) When plagues strike—the Black Death, Smallpox, AIDS. HarperCollins Publishers, New York.
Gilbert MTP, Cuccui J, White W, Lynnerup N, Titball RW, Cooper A, Prentice MB (2004) Absence of Yersinia pestis-specific DNA in human teeth from five European excavations of putative plague victims. Microbiology 150:341-354.
Gillot-Voisin J (1982) 1348: La peste noire à Givry. Nos Ancêtres et Nous 16:17-18.
Ginatempo M, Sandri L (1990) L'Italia delle Città: Il Popolamento Urbano tra Medioevo e Rinascimento (Secoli XIII-XVI). Le Lettere, Firenze.
Glimcher PW (2004) Decisions, Uncertainty, and the Brain. MIT Press, Cambridge.
Glymour C (1981) Theory and Evidence. Princeton Univ Press, Princeton.
Goldman AI (1986) Epistemology and Cognition. Harvard Univ Press, Cambridge.
González Balash MT (1989) Un nuevo documento sobre la peste negra en Galicia. Cuadernos de Estudios Gallegos 38(103):107-112.
Gooder A (1998) Coventry at the time of the Black Death. The Coventry Branch of the Historical Association, Coventry and County Heritage Series Booklet No. 23.
Gordis L (1996) Epidemiology. WB Saunders Co, Philadelphia.
Gottfried RS (1983) The Black Death—Natural and Human Disaster in Medieval Europe. The Free Press, New York.
Gottfried RS (1989) Plague, Public Heath and Medicine in Late Medieval England. In: Bulst N, Delort R (eds) Maladies et Societé. Éditions du Centre National de la Recherche Scientifique, Paris, pp 337-365.
Gras P (1939) Le register paroissial de Givry (1334-1357) et la Peste Noire en Bourgogne. Bibliothèque de l'Ecole des Chartes 100:295-308.
Grau Monserrat M (1970) La peste negra en Morella. Boletín de la Sociedad Castellonense de Cultura. 46:148-160.
Grenfell BT, Pybus OG, Gog JR, Word JLN, Daly JM, Mumford JA, Holmes EC (2004) Unifying the epidemiological and evolutionary dynamics of pathogens. Science 303:327-332.
Groome N (1982-1983) The Black Death in the hundred of Higham Ferrers. Northamptonshire Past and Present 6(6):309-311.
Guichonnet P (ed) (1973) Histoire de la Savoie. Privat, Toulouse.
Guilaine J, Fabre D (eds) (1984) Histoire de Carcassonne. Privat, Toulouse.
Guilleré C (1984) La Peste Noire à Gérone (1348). Annals de l'Institut d'Estudis Gironins 27:87-161.
Gunzberg J (1989) Las crisis de mortalidad en la Barcelona de siglo XIV. Boletín de la Asociación de Demografía Histórica 7(2):9-35.
Gyug RF (1983) The effects and extent of the Black Death of 1348: New evidence for clerical mortality in Barcelona. Medieval Studies 45:385-398.
Gyug RF (1994) The Diocese of Barcelona during the Black Death. Pontificail Institute of Medieval Studies, Toronto.
Haggett P (2000) The Geographical Structure of Epidemics. Clarendon Press, Oxford.

Haining R (2003) Spatial Data Analysis. Cambridge Univ Press, Cambridge.
Hankin EH (1905) On the epidemiology of plague. J of Hygiene 5:48-83.
Harman G (1999) Reasoning, Meaning and Mind. Oxford Univ Press, Oxford.
Harre R (2002) Cognitive Science. Sage Publ, London.
Harvey PDA (1965) A Medieval Oxfordshire Village—Cuxham 1240 to 1400. Oxford Univ Press, London.
Hatcher J (1970) Rural Economy and Society in the Duchy of Cornwall—1300-1500. Cambridge Univ Press, Cambridge.
Hatcher J (1977) Plague, population, and English economy, 1348-1530. In: Anderson M (ed) (1996) British Population History. Cambridge Univ Press, Cambridge, pp 10-93.
Hawkins J (2004) On Intelligence. Times Books. Henry Holt and Company, New York.
Hempel CG, Oppenheim P (1948) Studies in the logic of explanation. Philosophy of Science 18:135-175.
Henneman JB Jr (1968) The Black Death and Royal Taxation in France: 1347-1351. Speculum XLIII(3):405-428.
Herlihy D (1965) Population, plague and social change in rural Pistoia, 1201-1430. The Economic History Review, second series XVIII(2):225-244.
Herlihy D (1997) The Black Death and the Transformation of the West. Harvard Univ Press, Cambridge.
Herlihy D, Klapisch-Zuber C (1978) Les Toscans el leurs Familles. Editions de l'École des Hautes Etudes en Sciences Sociales, Paris.
Higounet-Nadal A (1965) Les Comptes de la Taille et les Sources de l'Histoire Démographique de Périgueux au Siècle XIV^{e}. SEVPEN, Paris.
Higounet-Nadal A (1978) Périgueux aux XIV^{e} et XV^{e} Siècles – Étude de démographie historique. Société Nouvelle des Imprimeries Delmar, Bordeaux.
Hill AB (1965) The environment and disease: association or causation? Proc R Soc Med 58: 295-300.
Hirshleifer J (1996) Disaster and Recovery: The Black Death in Western Europe. Memorandum RM-4700-TAB prepared for the United States Atomic Energy Commission. The Rand Corporation, Santa Monica.
Hirst LF (1953) The conquest of plague—A Study of the Evolution of Epidemiology. Oxford at the Clarendon Press, London.
Hoeniger R (1882) Der Schwarze Tod in Deutchland. Sändig, Walluf bei Wiesbaden, 1973 edition.
Hofstadter DR (1986) Metamagical Themas: Questing for the Essence of Mind and Pattern. Bantam Books, New York.
Holmes EE (1997) Basic epidemiological concepts in a spatial context. In: Tilman D, Kareiva P (eds) Spatial Ecology. Princeton Univ Press, Princeton.
Holt R (1985) Gloucester in the century after the Black Death. Trans Bristol Gloucestershire Archaeological Society 103:149-161.
Horrox R (1995) The Black Death. Manchester Univ Press, Manchester.
Howell C (1983) Land, Family, and Inheritance in Transition—Kibworth Harcourt 1280-1700. Cambridge Univ Press, Cambridge.
Hubscher R (ed) (1986) Histoire d'Amiens. Privat, Toulouse.
James TB (1998) The Black Death in Berkshire and Wiltshire. The Hatcher Review 5:11-20.
James TB (1999) The Black Death in Hampshire. Hampshire Papers 18(1):26.
Jaynes ET (1989) Clearing up mysteries – The original goal. In: Skilling J (ed) Maximum Entropy and Bayesian Methods,1-27. Kluwer Acad Publ, Dordrecht.
Jaynes ET (2003) Probability Theory. Cambridge Univ Press, Cambridge.

Jeffrey R (1965) The Logic of Decision. McGraw-Hill, New York.
Jenks S (1977) The Black Death and Würzburg: Michael de Leone's Reaction in Context. Dissertation Abstracts International Series A. 37(7):4524-4525.
Jorgenson JL (2001). Aldrin and dieldrin: a review of research on their production, environmental deposition and fate, bioaccumulation, toxicology, and epidemiology in the United States. Environmental Health Perspectives 109 Suppl 1: 113-39.
Jouet R (1972) Autour de la Peste Noire en Basse-Normandie au XIV^{e} siècle. Annales de Normandie 22(4):265-276.
Kagay DJ, Vann TM (eds) (1998) On the Social Origins of Medieval Institutions. Brill, Leiden.
Kanehisa M (2000) Post-Genome Informatics. Oxford Univ Press, Oxford.
Kawachi I, Kennedy BP (2002). The Health of Nations : Why Inequality is Harmful to your Health. New Press, New York.
Keene D (1984) A new study of London before the Great Fire. In: Reeder D (ed) Urban History Yearbook 1984. Leicester Univ Press, pp 11-21.
Keene D (1995) London in the early Middle Ages 1300-1550. The London J 20(2):9-20.
Keller EF (2002) Making Sense of Life. Harvard Univ Press, Harvard.
Kelly M (2001) A History of the Black Death in Ireland. Tempus, Stroud, Gloucestershire.
Kelly M (2003) The Great Dying – The Black Death in Dublin. Tempus, Stroud, Gloucestershire.
Kent FW (1985) The Black Death of 1348 in Florence: a new contemporary account? In: Morrogh A, Gioffredi FS, Morselli P, Borsook E, (eds), Renaissance Studies in Honor of Craig Hugh Smyth. Giunti Barbèra, Florence, pp 117-128.
Kermode J (2000) Northeatern towns. In: Palliser DM (ed) The Cambridge Urban History of Britain. Cambridge Univ Press, Cambridge, pp 657-679.
Klein H (1960) Das Grosse Stern von 1348/49 und seine Auswirkund aus die Besiedlung der Ostalpenländer. Mitteilungen der Gessellschaft für Salzburger Landeskunde 100:91-100.
Knight J (2002) Statistical error leaves pollution data up in the air. Nature 417:667.
Kohn GC (ed) (1995) Encyclopedia of Plague and Pestilence. Facts on File, Inc, New York.
Kolovos A, Christakos G, Serre ML, Miller CT (2002) Computational BME solution of a stochastic advection-reaction equation in the light of site-specific information. Water Resour Res 38:1318-1334.
Kolovos A, Christakos G, Hristopulos DT, Serre ML (2004) Methods for generating non-separable spatiotemporal covariance models with potential environmental applications. Adv in Water Resour 27:815-830.
Kovitz J, Christakos G (2004a) Assimilation of fuzzy data by the BME method. Stoch Envir Research & Risk Assess 18(2):79-90.
Kovitz J, Christakos G (2004b) Spatial statistics of clustered data. Stoch Envir Research & Risk Assess 18(3):147-166.
Kowalewsky M (1911) Die ökonomische Entwicklung Europas bis zum Beginn der kapitalistischen Wirtschaftsform 5. Verlag R L Prager, Berlin.
Krebs JR, Davies NB (eds) (1991) Behavioural Ecology. 3rd edition. Blackwell Scientific Publ, Cambridge.
Krewski D, Wigle D, Clayson DB, Howe GR (1989) Role of epidemiology in health risk assessment. Recent Results in Cancer Research 120:1-24.
Ladero Quesada MA (1976) La ciudad medieval (1248-1492), Historia de Sevilla, tomo II. Publicaciones de la Universidad de Sevilla, Seville.
Lafayette MD (1980) La Princesse De Clèves. Lettres Françaises. Collection de l'Imprimerie Nationale, Paris.

Landais H (ed) (1997) Histoire de Saumur. Privat, Toulouse.
Langer WL (1964) The Black Death. Scientific American 210(2):114-121.
Langridge AM (1984) The population of Chartham from 1086 to 1600. Archaeologia Cantiana 101:217-244.
Last JM (1995) A Dictionary of Epidemiology. Oxford Univ Press, New York.
Lathem EC (ed) (1979) The Poetry of Robert Frost. Henry Holt & Co, New York.
Latour B (1988) Science in Action: How to Follow Scientists and Engineers Through Society. Harvard Univ Press, Cambridge.
Latreille A (ed) (1975) Histoire de Lyon et du Lyonnais. Privat, Toulouse.
Lavigne RL (1971) La peste noire et la commune de Toulouse. Le Temoignage du livre de matricules de notaries. Annales du midi 83(4):413-417.
Law DG, Serre ML, Christakos G, Leone PA, Miller WC (2004) Spatial analysis and mapping of sexually transmitted diseases to optimize intervention and prevention strategies. J. of Sexually Transmitted Infection 80:294-299.
Lawson A, Biggeri A, Böhning D, Lesaffre E, Viel JF, Bertollini R (eds) (1999) Disease mapping and risk Assessment for Public Health. J. Wiley & Sons Ltd, Chichester.
Le Moigne FY (ed) (1986) Histoire de Metz. Editions Privat, Toulouse.
Lebrun F (ed) (1975) Histoire d'Angers. Privat, Toulouse.
León Tello P (1977) Judíos toledanos víctima de la peste negra. Sefarad XXXVII:333-337.
Lewis D (1976) Probabilities of conditionals and conditionals of probabilities. Philosophical Rev 85:297-315.
Little AG (1890) The Black Death in Lancashire. The English Historical Rev XIX:524-530.
Livet G, Rapp F (eds) (1987) Histoire de Strasbourg. Privat, Toulouse.
Lock R (1992) The Black Death in Walsham-le-Willows. Proceedings of the Suffolk Institute of Archaeology and History 37(4):316-337.
Lomas R (1989) The Black Death in the County Durham. J of Medieval History 15(2)127-140.
López de Meneses A (1956) Documentos acerca de la Peste Negra en los dominios de la corona de Aragón. In: Estudios de Edad Media de la Corona de Aragón, vol 6. Consejo Superior de Investigaciones Científicas, Zaragoza, pp 291-447.
López de Meneses A (1959) La peste negra en las Islas Baleares. VI Congreso de Historia de la Corona de Aragón, pp 331-344.
López de Meneses A (1965) La Peste Negra en Cerdeña. In: Maluquer de Motes D (ed) Homenaje a Jaime Vicens Vives. Universidad de Barcelona, Barcelona, pp 533-541.
Lucenet M (1985) Les Grandes Pestes en France. Éditions Aubier Montaigne, Paris.
Macary MM (1972) La peste et saint Roch en Bas-Limousin. Bulletin de la Société Scientifique, Historique, et Archéologique de la Corrèze 94:81-93.
Mach E (1905) Erkenntnis und Irrtum: Skizzen zur Psychologie der Forschung. Leipzig. McGuiness B (ed) (1975) English translation for the Vienna Circle Collection, Knowledge and Error: Sketches on the Psychology of Enquiry. D Reidel Pub Co, Dordrecht.
Macintyre S, Ellaway A, Cummins S (2002) Place effects on health: how can we conceptualise, operationalise and measure them? Social Science & Medicine 55:125-139.
Mackie JL (1974) The Cement of the Universe. Clarendon Press, Oxford.
Maia J de OC (1952) Some mathematical developments on the epidemic theory formulated by Reed and Frost. Human Biology 24:167-200.
Mahner M, Bunge M (1997) Foundations of Biophilosophy. Springer, New York.
Marks G (1971) The Medieval Plague—The Black Death of the Middle Ages. Doubleday & Company Inc., Garden City, New York.

Martín Duque MA, Ramírez Vaquero E, Lacarra y de Miguel JM, González Antón L, Lalinde Abadía J, Ubieto Arteta A, Suárez Fernández L (1991) La Expansión Peninsular y Mediterránea (c. 1212-c. 1350). Historia de España Menéndez Pidal series, XIII(II). Espasa-Calpe, Madrid.

Martínez Ortiz J (1969) Una víctima de la peste, la reina doña Leonor. VIII Congreso de la Corona de Aragón, II(1), La Corona de Aragón en el Siglo XIV, Valencia, pp 9-25.

Mattoso J (ed) (1997) História de Portugal. Editorial Estampa 2.

McGarvie M (2000) Mells during the Black Death. Notes and Queries for Somerset and Dorset 34:409-413.

McGowen T (1995) The Black Death. Franklin Watts, New York.

McPherson K (2002) Epidemiology on trial—confessions of an expert witness. The Lancet 360:889-890.

Mellor DH (1995) The Facts of Causation. Routledge, London.

Meslé E (1983) Histoire de Bourges. Édition Horvath, Le Coteau, Loire.

Michaud M (1998) La peste, la peur et l'espoir. Le pèlerinage jubilaire de romeaux marseillais en 1350. Le Moyen Age, series 5, col. 12 104(3-4):400-434.

Miller AI (1996) Insights of Genius: Imagery and Creativity in Science and Art. Springer-Verlag, New York.

Millikan R (2004) Personal Communication.

Mita M (1989) Merata Mita On… In: The New Zealand Listener, Oct. 14, p 30.

Moeller DW (1997) Environmental Health. Harvard Univ Press, Cambridge.

Mollat M (ed) (1971) Histoire de l'Ile-de-France et de Paris. Privat, Toulouse.

Mollat M (1977) Notes sur la mortalité à Paris au temps de la Peste Noite d'après les comptes de l'oeuvre de Saint-Germain-l'Auxerrois. In: Etudes sur l'Économie et la Societé de Occident Médiéval XII^{e}-XV^{e} Siècles. Variorum Reprints, London, pp 505-527.

Mollat M (1979) Histoire de Rouen. Privat, Toulouse.

Mollison D (1995) The structure of epidemic models. In: Mollison D (ed) Epidemic Models. Cambridge Univ Press, Cambridge, pp 17-23.

Morales KH, Ryan L, Kuo TL, Wu MM, Chen CJ (2000) Risk of Internal Cancers from Arsenic in Drinking Water. Envir Health Perspectives 108(7):655-661.

Morgan MG, Henrion M (1990) Uncertainty. Cambridge Univ Press, New York.

Moolgavkar S, Cross F, Luebeck G, Dagle G (1990) A Two-Mutation Model for Radon-Induced Lung Tumors in Rats. Radiation Research 121:118.

Morris C (1971) Book review of A History of Bubonic Plague in the British Isles, by JFD Shrewsbury. The Historical J XIV(1):205-215.

Mueller RC (1980) Peste e demografía. In: Comune di Venezia (ed) Venezia e la Peste 1348/1797. Marsilio Editori, 2nd edition, Venice, pp 93-96.

Naphy W, Spicer A (2000) The Black Death and the history of plagues 1345-1730. Tempus, Stroud, Gloucestershire.

Nasalli Rocca E (1973) Le epidemie in Piacenza nel Secolo XIV. Bollettino Storico Piacentino 68(1):12-22.

Nicholas D (1992) Medieval Flanders. Longman, New York.

Noël R (1995) Première attaque de la peste en Lorraine du Nord, de la ville à la campagne? In: Paesants & Townsmen in Medieval Europe, Studia in Honorem Adriaan Verhulst. Snoeck-Ducaju & Zoon, Ghent, pp 739-751.

Nohl J (1999) The Black Death's grim death toll. In: Nardo D (ed) The Black Death. Greenhaven Press, San Diego, pp 48-56.

Nuckols JR, Ward MH, Jarup L (2004) Using geographic information systems for exposure assessment in environmental epidemiology studies. Environmental Health Perspectives 112(9): 1007-15.

Ohlin G (1966) No safety in numbers: some pitfalls of historical statistics. In: Rosovsky H (ed) Industralization in Two Systems. Essays in Honor of Alexander Gerschenkron. John Wiley & Sons, Inc, New York, pp 68-90; also reprinted in 1974 in Essays in Quantitative Economic History. Clarendon Press, Oxford, pp 59-78.

Olea RA, Christakos G (2005) Duration assessment of urban mortality for the 14th century Black Death epidemic. Human Biology. In press.

Orent W (2004) Plague—The Mysterious Past and Terrifying Future of the World's most Dangerous Disease. Free Press, New York.

Page FM (1934) The Estates of Crowland Abbey—a Study of Manorial Organization. Cambridge at the University Press, London.

Parentin L (1974) Cenni sulla peste in Istria e sulla difensa sanitaria. Archeografo Triestino, series 4 34(83):7-18.

Pavlin JA, Mostashari F, Kortepeter MG, Hynes NA, Chotani RA, Mikol YB, Ryan MA, Neville JS, Gantz DT, Writer JV, Florance JE, Culpepper RC, Henretig FM, Kelly PW (2003). Innovative surveillance methods for rapid detection of disease outbreaks and bioterrorism: results of an interagency workshop on health indicator surveillance. American Journal of Public Health 93(8): 1230-5.

Pasche V (1998) Les épidémies de peste en Suisse Romande. Vers de nouvaux comportements? In: Paravicini Bagliani A, Santi F (eds) The Regulation of Evil. Sismel, Florence, pp 125-136.

Pearce, N (1996). Traditional epidemiology, modern epidemiology, and public health. American Journal of Public Health 86(5): 678-83.

Pearl J (2000) Causality. Cambridge Univ Press, Cambridge.

Pennington DW, Norris G, Hoagland T, Bare JC (2001) Metrics for Environmental Comparison of Process Alternatives in a Holistic Framework. In: Sikdar SK, El-Halwagi MM (eds) Process Design Tools for the Environment. Taylor and Francis, London, pp 65-104.

Pérouas L (ed) (1989) Histoire de Limoges. Privat, Toulouse.

Phillips CV, Goodman KJ, Poole C (eds) (2004) Lead editorial: The need for greater perspective and innovation in epidemiology. Epidemiologic Perspectives & Innovations 1(1).

Phillips WD Jr (1998) Peste Negra: The Fourteenth-century plague epidemics in Iberia. In: Kagay DJ, Vann TM (eds) On the Social Origins of Medieval Institutions. Brill, Leiden, pp 47-62.

Picard P, Lefevre C (1990) A unified analysis of the final size and severity distribution in collective Reed-Frost epidemic processes. Adv Appl Prob 22:269-294.

Pladevall A (1963) La dismunicio de poblament a la Plana de Vich a Mitjans del segle XIV. AUSA XLIV:361-373.

Plague Research Commission (1912) Seventh Report on Plague Investigations in India. Plague Supplement II. J Hyg, 12:207-242.

Platt C (1996) King Death—The Black Death and its aftermath in late-medieval England. Univ of Toronto Press, Toronto.

Plotkin H (1997) Darwin Machines and the Nature of Knowledge. Harvard Univ Press, Cambridge.

Poos LR (1991) A rural Society after the Black Death: Essex 1350-1525. Cambridge Univ Press, Cambridge.

Postan MM (1972) The Medieval Economy and Society—an Economic History of Britain in the Middle Ages. Weidenfeld and Nicolson, London.
Prat G (1952) Albi et la Peste Noir. Annals du Midi 64(17):15-25.
Prevenier W (1983) La démographie des villes du comté de Flandre aux XIII^{e} et XIV^{e} siécles. Revue du Nord 65:257-275.
Prosperi A (2000) Storia Moderna e Contemporanea, I. Della Peste Nera alla Guerra dei Trent'anni. Piccola Biblioteca Einaudi, Turin
Pueyo Colomina P (1993). La peste negra en la diócesis de Zaragoza: el registro de actos comunes del Arzobispo Guillermo de Agrifolio (1348-1350). In: Aragón en la Edad Media, homenaje a la profesora emérita María Luisa Ledesma Rubio, Universidad de Zaragoza, pp 705-735.
Pybus OG, Charleston MA, Gupta S, Rambaut A, Holmes EC, Harvey PH (2001) The epidemic behavior of the hepatitis C virus. Science 292:2323-2325.
Radnitzky G, Bartley WW III (eds) (1993) Evolutionary Epistemology, Rationality, and the Sociology of Knowledge. Open Court, La Salle, Illinois.
Rau V (1967) Un document portugais sur la peste noire de 1348. In: Hommages à Yves Renouard (1908-1965). Privat, Toulouse, pp 331-334.
Razi Z (1980) Life, Marriage and Death in a Medieval Parish—Economy, Society and Demography in Halesowen 1270-1400. Cambridge Univ Press, Cambridge.
Rees W (1920) The Black Death in Wales. Transactions of the Royal Historical Society (London), series 4 3:117-135.
Reichborn-Kjennerud I (1948) Black Death. J of the History of Medicine III(2):359-360.
Renouard Y (1948) Consequences and intérèt démographiques de la Peste noire de 1348. Population 3(1):459-466.
Renouard Y (ed) 1965 Bordeaux sous les Rois d'Angleterre. Fédération Historique du Sud-Ouest, Bordeaux.
Reuchlin J (1517) De Arte Cabalistica Libri Tres. Thomas Anselm, Haguenau, France.
Revkin A (2002) Data revised on soot in air and deaths. New York Times, June 5, p A23.
Reyerson KL (1978) Changes in testamentary practice at Montpellier on the eve of the Black Death. Church History 47(2):253-269.
Ricketts, TC (2003). Geographic information systems and public health. Annual Review of Public Health 24: 1-6.
Robert-Jones P, Robert-Jones F (2002) Peter Bruegel. Harry N Abrams, Inc, Publ, New York.
Rodríguez Molina J (1978) El Reino de Jaén en la Baja Edad Media—Aspectos Demográficos y Económicos. Universidad de Granada, Granada.
Rosenberg A (2000) Philosophy of Science. Routledge, New York.
Rosenkrantz RD (1977) Inference Method and Decision. D. Reidel Co., Boston.
Rothman KJ (2002) Epidemiology—An Introduction. Oxford Univ. Press, Oxford.
Rothman KJ, Greenland S (1998) Modern Epidemiology. Lippincott-Raven Publ, Philadelphia.
Rubio A (1979) Peste Negra, Crisis y Comportamientos Sociales en la España del Siglo XIV. La ciudad de Valencia (1348–1401). Universidad de Granada, Granada.
Ruelle D (1991) Chance and Chaos. Princeton Univ Press, Princeton.
Ruiz de Loizaga S(1998) Documentos sobre la peste negra (1348) en Navarra, según algunos datos del Archivo Vaticano. Scriptorium Victoriense 45(1-2):177-193.
Russell JC (1948) British Medieval Population. The University of New Mexico Press, Albuquerque.
Russell PE (1955) The English Intervention in Spain & Portugal in the Time of Edward III and Richard II. Oxford at the Clarendom Press, London.

Russell RC (1966) Effects of pestilence and plague, 1315-1385. Comparatives Studies in Society and History 8(4):464-473.
Saaler M (1992) The manor of Tillingdown: the changing economy of the demesne 1325-71. Surrey Archaeological Collections 81:19-40.
Sagnes P (ed) (1986) Histoire de Béziers. Privat, Toulouse.
Salmon WC (1998) Causality and Explanation. Oxford Univ Press, New York.
Sancha S (1982). The Luttrell Village. W Collins Sons & Co Ltd, Glasgow.
Santamaría Arandez Á (1969) La peste negra em Mallorca. VIII Congreso de la Corona de Aragón, La Corona de Aragón en el Siglo XIV, Valencia II(1):103-130.
Savitz D (2004) Personal communication. Chapel Hill.
Schmidt-Nielsen K (1999) Scaling. Cambridge Univ Press, Cambridge.
Schulte PA, Perera FP (eds) (1993) Molecular Epidemiology. Academic Press, San Diego.
Scott S, Duncan CJ (2001) Biology of Plagues: Evidence from Historical Populations. Cambridge Univ Press, Cambridge.
Scott S, Duncan C (2004) Return of the Black Death—The World's Greatest Serial Killer. John Wiley & Sons Ltd, Chichester.
Scriven M (1975) Causation as explanation. Nous 9:3-16.
Serrão J (1981a) Dicionário de História de Portugal. Livraria Figueirinhas, Porto, 4
Serrão J (1981b) Dicionário de História de Portugal. Livraria Figueirinhas, Porto, 5.
Serre ML, Christakos G (1999) BME studies of stochastic differential equations representing physical laws-Part II. 5th Annual Confer, Intern Assoc for Math Geology, Trodheim 1:93-98.
Serre ML, Kolovos A, Christakos G, Modis K (2003) An application of the holistochastic human exposure methodology to naturally occurring Arsenic in Bangladesh drinking water. Risk Analysis 23(3):515-528.
Shand J (2000) Arguing Well. Routledge, New York.
Shipley B (2000) Cause and Correlation in Biology. Cambridge Univ Press, Cambridge.
Shrewsbury JFD (1970). A history of Bubonic Plague in the British Isles. Cambridge at the Univ Press, Cambridge.
Shirk M (1981) The Black Death in Aragon—1348–1351. J of Medieval History 7(4):357-367.
Shirk MV (1984) Violence and the plague in Aragón, 1348—1351. J of the Rocky Mountain Medieval Assoc 5:31-39.
Simpson WJ (1905) A Treatise on Plague. Cambridge at the Univ Press, London.
Sivéry G (1965) Le Hainaut et la peste noire. Mémoires et publications de la Societé des Sciences, des Arts et des Lettres du Hainaut 79:431-447.
Skilling J (ed) (1989) Maximum Entropy and Bayesian Methods. Proceed of the 8th Maximum Entropy Workshop, Cambridge, UK, Aug 1988. Kluwer Acad Publ, Dordrecht.
Sklar L (1993) Physics and Chance. Cambridge Univ Press, Cambridge.
Sloan AW (1981) The Black Death in England. South African Medical J 59(18):646-650.
Smail DL (1996) Accomodating plague in medieval Marseille. Continuity and Change 13(1):11-41.
Smith RS (1944) Fourteenth century population records of Catalonia. Speculum 19:494-501.
Sobrequés Callicó J (1970-1971) La Peste Negra en la península Ibérica. Anuario de Estudios Medievales 7:67-102.
Starck JL, Murtagh F, Bijaoui A (1998) Image Processing and Data Analysis. Cambridge Univ Press, Cambridge.

Sticker G (1908) Abhandlungen aus der Seuchengeschichte und Seuchenlehre. I Band. Die Pest Verlag von Alfred Töpelmann, Giessen.
Stover L (2004) Bohemian Manifesto. Bulfinch Press, New York.
Suárez Fernández J, Reglá Campistrol J (1966) España Cristiana, Crisis de la Reconquista, Luchas Civiles. Historia de España Menéndez Pidal series, XIV, Espasa-Calpe, Madrid.
Suppes P (1970) A Probabilistic Theory of Causality. North Holland, Amsterdam.
Susser M (1985) Epidemiology in the United States after World War II: the evolution of technique. Epidemiological Review 7: 147-77
Taubes G (1995) Epidemiology faces its limits. Science 269:164-169.
Taylor JR (1982) An Introduction to Error Analysis. University Science Books, Suasalito.
Terracini B (1992) Environmental epidemiology: A historical perspective. In: Elliott P, Cuzick J, English D, Stern R (eds) Geographical and Environmental Epidemiology: Methods for Small-Area Studies, World Health Organization Regional Office for Europe. Oxford Univ Press, New York, 253-263.
Thagard P (1999) Conceptual Revolutions. Princeton Univ Press, Princeton.
Thomas L (1995) Late Night Thoughts on Listening to Mahler's Ninth Symphony. Penguin Books, New York.
Thompson AH (1911) Registers of John Gynewell, bishop of Lincoln, for the years 1347-1350. The Archaeological J LXVIII(4):300-360.
Thompson AH (1914) The pestilence of the fourteenth century in the diocese of York. The Archaeological J LXXI(4):97-154.
Titow JZ (1969) English Rural Society. George Allen and Unwin Ltd, London.
Tomassi P (1999) Logic. Routledge, New York.
Tomkinson JL (1999) The Enterprise of Knowledge. Leader Books SA Publ, Athens, Greece.
Torres Fontes J (1981) Tres epidemias de peste en Murcia en el siglo XIV: 1348-49, 1379-80, 1395-96. In: Torres J, Casal F, Mula A, Ayala J, Marset P (eds) De Historia Medica Murciana, T II, Las Epidemias. Ediciones de la Academia Alfonso X el Sabio, Murcia, pp 9-25.
Trenand L (ed) (1970) Histoire de Lille. Libraire Giard, Lille.
Trenchs Odena J (1969) La archidiócesis de Tarragona y la peste negra: los cargos de la catedral. VIII Congreso de la Corona de Aragón, La Corona de Aragón en el Siglo XIV, Valencia II(1):45-64.
Trenchs Odena J (1972) La diócesis de Zaragoza y la peste de 1348. Cuadernos de Historia Jerónimo Zurita 25-26:119-140.
Trenchs Odena J (1980) Documentos pontificios sobre al peste negra en la diócesis de Gerona. Cuadernos de Trabajo de la Escuela Española de Historia y Arqueología en Roma 14:183-230.
Trenchs Odena J (1981) La epidemia de peste de 1348 y las diócesis de Huesca y Tarazona. Cuadernos de Historia Jerónimo Zurita 39-40:197-204.
Tucoo-Chala M (1951) La peste de 1348 en Verán. Revue Régionaliste des Pyrénées 111-112:80-85.
Tuchman BW (1978) A Distant Mirror—the Calamitous 14th Century. Alfred A Knopf, New York.
Turner D (1988) The Black Death. Longman, 2nd ed, London.
Twigg G (1984) The Black Death: a Biological Reappraisal. Batsford Academic and Educational, London.

Ubieto Arteta A (1975) Cronología del desarrollo de la Peste Negra en la península Ibérica. In: Estudios sobre el Reino de Valencia, cuadernos de historia anexos de la revista Hispania 5:47-66.
Ubieto Arteta A (1997) Historia Ilustrada de España, Volume 3, Siglos XII-XV. Editorial Debate, Spain.
Ubieto Arteta A (1967) Documentos para el estudio de la historia aragonesa de los siglos XIII y XIV: monasterio de Santa Clara, de Huesca. In: Estudios de Edad Media de la Corona de Aragón, Consejo Superior de Investigaciones Científicas, Zaragoza, pp 547-701.
Utterback KT (1988) The date of composition of bishops' registers from the plague years in the diocese of Barcelona. J of Eclessiastical History 39(3):412-432.
Vaca Lorenzo A (1990) La Peste Negra en Castilla. Nuevos testimonios. Studia Historica VIII:159-171.
Valdeón J (1981) La Baja Edad Media – Crisis y Renovación de los Siglos XIV-XV. Historia de España, 5, Historia 16, Madrid.
Valdeón J, Martín JL (1996) La Baja Edad Media Peninsular, Siglos XIII y XIV—La Población, la Economía, la Sociedad. Historia de España Menéndez Pidal series, XII. Espasa-Calpe, Madrid.
Vapnik VN (2000) The Nature of Statistical Learning Theory. Springer, New York.
Vasold M (1991) Pet, Not und schwere Plagen. Seuchen und Epidemien vom Mittelalter bis heute. Beck, Munich.
Vasol M (2003) Die Ausbreitung des Schwarzen Todes in Deutschland nach 1348. Historische Zeitschrift 277(2):282-308.
Veny i Clar J (1971) 'Regiment de Preservació de pestilèncis' de Jacme d'Agramont (S. XIV). Publicaciones de la Excelentísima Diputación Provincial, Tarragona.
Verlinden C (1938) La grande peste de 1348 en Espagne. Revue Belge de Philologie et d'Histoire XVII(1-2):103-146.
Verlinden C (1971) Spain: a temporary setback. In: Bowsky WM (ed) The Black Death, a Turning Point in History? Holt, Rinehart and Winston, New York, 89-90.
Villaró A (1986-1987) La pesta negra, el 1348, a la Seu d'Urgell. Urgellia 8:271-302.
Villaró A (1988-1989) Noves dades sobre la pesta negra a la Seu (1348). Disposicions pietoses l'any de la pesta. Urgellia 9:343-364.
Virgili i Colet A (1979) El papel de la Peste Negra de 1348 sobre la demografia de Tarragona: problemes de mètode i intent de construcció. In: Ier Col-loqui d'Història del Camp de Tarragona Conca de Barberà i Priorat. Excma. Diputació Provincial de Tarragona, Tarragona, pp 25-39.
Walters C (1986) Adaptive Management of Renewable Resources. MacMillan Publ Co, New York.
Wang C (1993) Sense and Nonsense of Statistical Inference. Marcel Dekker Inc., New York, NY.
Watts DG (1998) The Black Death in Dorset and Hampshire. The Hatcher Review 5:21-28.
Webster M (2003) Communicating climate change uncertainty to policy-makers and the public. An Editorial Comment. Climatic Change 61:1-8.
Weil S (1978) Lectures on Philosophy. Cambridge Univ Press, Cambridge.
West M (1988) Modeling expert opinion. In: Bernardo DM, De Groot MH, Lindley DV, Smith AFM (eds) Bayesian Statistics III. Clarendon Press, Oxford, pp 493-508.
Wetzstein T (1996) Die Pest in Freiburg des 14. und 15. Jahrhunderts – eine kritische Revision. Zeitschrift des Breisgau-Geschichtsvereins 115:11-17.
Weyl N (1975) The Black Death and the intellect of Europe. Mankind Quarterly XV(4):243-254.

Wheelis M (2002) Biological Warfare at the 1346 siege of Caffa. Emerging Infectious Diseases 8(9):971-975.
White PD, Van Leeuwen P, Davis BD, Maddaloni M, Hogan KA, Marcus AH, Elias RW (1998) The conceptual structure of the integrated exposure uptake biokinetic model for lead in children. Envir Health Perspectives 106(S6):1513-1530.
Williamson R (1957) The plague in Cambridge. Medical History 1:51-64.
Wills C (1997) Plagues—their Origins, History, and Future. Flamingo, London.
Wilson J (1963) Thinking with Concepts. Cambridge Univ Press, Cambridge.
Wilson EO (1975) Sociobiology. Harvard Univ Press, Cambridge.
Wimsatt WC (1976) Reductionism, levels of organization, and the mind-body problem. In: Globus G, Maxwell G, Savodnik I (eds) Conciousness and the Brain: A Scientific and Philosophical Inquiry. Plenum Press, New York.
Wolff P (ed) (1967) Histoire de Languedoc. Privat, Toulouse.
Wolff P (ed) (1974) Histoire de Toulouse. Privat, Toulouse.
Wolff P (ed) (1985) Histoire de Perpignan. Privat, Toulouse.
Wood JW, Ferrel RJ, Dewitte-Aviña SN (2003) The temporal dynamics of the fourteenth-century Black Death: New evidence from English ecclesiastical records. Human Biology 75(4):427-448.
Wray SK (1993) The experience of the Black Death in Bologna as revealed by the notarial registers. J of the Rocky Mountain Medieval and Renaissance Assoc 14:45-64.
Yersin A (1894) La peste bubonic a la Hong Kong. Ann Inst Pasteur (Paris) 8:662-667.
Zavalo Zabalegui FJ (1968) Algunos datos sobre la regresión demográfica causada por la peste en la Navarra del siglo XIV. Miscelanea José María Lacarra 5:81-87.
Ziegler P (1969) The Black Death. Collins, London. Illustrated 2nd edition, 1995, Allan Sutton, Phoenix Mill, Gloucestershire.
Ziman J (1991) Reliable Knowledge. Cambridge Univ Press, Cambridge.

B. Electronic References[1]

http://4thmoon.com/styx/blackdeath.htm
http://cternus.home.texas.net/research/plague/
http://encarta.msn.com/encyclopedia_761588279/Black_Death.html
http://enciclopedia.us.es/index.php/Badajoz_(Badajoz)
http://figueira.net/datas/
http://historymedren.about.com/library/weekly/aapmaps6.htm
http://home3.inet.tele.dk/oz4cg/hist-gb.htm
http://idcs0100.lib.iup.edu/WestCivI/the8.htm
http://library.thinkquest.org/C005417/1210.htm
http://membres.lycos.fr/eedfliban99/tulle.htm
http://perso.wanadoo.fr/mahistaux/Ahistoire3.htm
http://pwp.netcabo.pt/epidemiologia/aaahuman_134801.htm
http://ragz-international.com/black_death.htm
http://scholar.chem.nyu.edu/tekpages/urbanpop.html
http://tyntescastle.com/medieval.html
http://urp.comune.bologna.it/WebCity/WebCity.nsf/0/
f86a318f0d79dde9412569b90039898d/$FILE/mappa_parcheggi.jpg

[1] Accessed during February-June, 2004

http://www.aboutflorence.com/history-of-Florence.html
http://www.ac-orleans-tours.fr/rdv-histoire/archives/2001/peste-sida.htm
http://www.agpa.arrakis.es/geo/bole/bole8/NTEGRACIoN.htm
http://www.artehistoria.com/frames.htm?http://www.artehistoria.com/historia/contextos/1128.htm
http://www.cedofeita.j-f.org/historia1.htm
http://www.chez.com/lcb/htm/origines.html
http://www.coaat-se.es/revistaApa/lectura/numero_65/65_monumentos.html
http://www.conelarte.com/EstebanOrta/Esteban%20Orta%20en%20internet/Murchante_Medieval_Esteban_Orta.htm
http://www.dudleyfamilypages.20m.com/photo6.html
http://www.exitmedia.tv/lossantos/introduccion.htm
http://www.genealogi.se/roots/year.htm
http://www.geocities.com/Athens/Styx/5709/chaptertwo.html
http://www.geocities.com/jmdesbois/fichemanosque.htm
http://www.geocities.com/localhistories/aberdeen.html
http://www.geocities.com/localhistories/Kingslynn.html
http://www.godecookery.com/plague/plague05.htm
http://www.harvestfields.netfirms.com/etexts/34/04.htm
http://www.hindmarsh.org.uk/page4.htm
http://www.hum.ou.dk/projects/histtid/summary/91_43.html
http://www.hyw.com/books/history/Black_De.htm
http://www.hyw.com/books/history/Plague.htm
http://www.kessler-web.co.uk/History/FeaturesBritain/BritishCanterbury.htm
http://www.lonelyplanet.com/destinations/europe/oslo/history.htm
http://www.memo.fr/article.asp?ID=MOY_TAR_004
http://www.mrkland.com/hist/sicily.htm
http://www.portfolio.mvm.ed.ac.uk/studentwebs/session5/16/Edinburgh%20Black%20Deathbrill.htm
http://www.puertollanovirtual.com/puertollano/fiestas.htm

Index

Printing and Binding: Stürtz GmbH, Würzburg