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Dicing with Death
Living by Data

As a result of the COVID-19 pandemic, medical statistics and public health data have become staples of newsfeeds worldwide, with infection rates, deaths, case fatalities and the mysterious *R* figure featuring regularly. However, we don't all have the statistical background needed to translate this information into knowledge. In this lively account, Stephen Senn explains these statistical phenomena and demonstrates how statistics is essential to making rational decisions about medical care.

The second edition has been thoroughly updated to cover the developments of the last two decades and includes a new chapter on the medical statistical challenges of COVID-19, along with additional material on infectious disease modelling and the representation of women in clinical trials. Senn entertains with anecdotes, puzzles and paradoxes while tackling big themes, including: clinical trials and the development of medicines, life-tables, vaccines and their risks or lack of them, smoking and lung cancer, and even the power of prayer.

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Living by Data

SECOND EDITION

STEPHEN SENN
Statistical Consultant

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For Victoria, Helen and Mark

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. . . the twain were casting dice
'The game is done! I've won! I've won!'
Quoth she and whistles thrice.

Samuel Taylor Coleridge, *The Rime of the Ancient Mariner*

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Preface to the Second Edition

I wrote *Dicing with Death* as an attempt to explain to a lay audience what it was that statisticians, and in particular medical statisticians, *did*. At the time I felt that non-statisticians could, perhaps, be divided into two classes: those who had never encountered statistics (as a subject) and could not imagine any circumstance in which they would want to, and those who had encountered statistics already and could not imagine any circumstance in which they would wish to do so again. This was, I felt, an unsatisfactory state of affairs, and the book was my small attempt to remedy the matter.

Little did I imagine to what extent medical statistics, as a result of the COVID-19 pandemic, would become the staple of newsfeeds, with infection rates, deaths, case fatalities, the mysterious *R* figure, vaccine efficacy and clinical trials figuring regularly. I can reassure the reader, however, that if this is the cost of making the public familiar with medical statistics, it is too high. I too prefer the old arrangement.

However, the old arrangement of our lives is not available, and when David Tranah at Cambridge contacted me asking if I would be prepared to consider a second edition I very quickly said 'yes'. The result is before you and includes an extra chapter on the statistics of COVID-19, but also new material in Chapter 5 covering, in particular, the representation of women in clinical trials and also new material on infectious disease modelling in Chapter 9, with various other discussions and figures (for example, on life expectancy) brought up to date.

With the first edition, I always felt that the last chapter (Chapter 11) was a good one to start with and that Chapter 9 was the most demanding. Now I shall suggest some different strategies for reading. If you are interested primarily in COVID you might start with the new chapter

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(Chapter 12). However, Chapter 11, which covers the story of measles, mumps and rubella, will form a much gentler introduction. Chapter 9, followed by 11 and then 12, is another logical path through the material but, as I have already said, Chapter 9 is not easy. Yet another one is to start with Chapter 7, which covers the history of life-tables and then follow with ... Never mind. To cut a long story short, here are some possible journeys through the book (Table 0.1).

Table 0.1 *Possible journeys through the book.*

Descriptor	Chapters	What's covered
COVID lite	12	Various aspects of COVID stats
From measles to COVID	11, 12	Plus, the MMR story
Infectious epidemiology	9, 11, 12	Plus, some theory of disease modelling
Life, death and disease	7, 9, 11, 12	Plus, life-tables and survival analysis
From trials to tribulations	3, 7, 9, 11, 12	Plus, clinical trials
Getting granular	3, 5, 7, 9, 11, 12	Plus, studying the sexes
The full med stats medley	3, 5, 6, 7, 8, 9, 11, 12	Plus, observational studies and meta-analysis
From soup to nuts	2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12	Plus, philosophy of stats x 2 & the law

The attentive reader will have noted that I have not got around to mentioning Chapter 1. That is because I think everybody *should* read it but also because everybody should feel entitled *not* to.

As with the first edition, I have many people to thank. A big thank you in particular goes to Robert Bakula, who translated the first edition into Slovenian and spotted various typos and who also made some excellent suggestions for improving clarity; to Nick Holford, who gave extensive advice on pharmacometrics; to Walter Kremers, who provided me with very useful data that he had prepared on deaths in Minnesota; to George Davey Smith, who made very helpful comments on a first draft; and to Klaus Rose, who took the lead in writing a paper together on the ethics of trials in children that is now discussed in Chapter 5. Others who made helpful comments or provided me with useful information are Sheila Bird, Adrian Bowman, David Brunnen, Ged Dean, Nicholas Erskine, Nigel Marriott, John Skilling, David Spiegelhalter and Michel Vaillant.

Special thanks are also due to David Tranah, who has now twice acted as midwife to this twice-born child of mine. I also thank Vidya Ashwin,

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Anna Scriven, Helen Cooper, Clare Dennison and all at Cambridge and Integra Software for help in producing the book.

It just remains for the reader to choose their route and proceed. Good luck!

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Preface to the First Edition

> *'What's the most frequent word?' asks Jessica. 'Your number one. The same as it's always been at these affairs,' replies the statistician, as if everyone knew: 'death'.*
>
> Thomas Pynchon, *Gravity's Rainbow*[1]

Statistics is dull but disreputable, prosaic but misleading. Statisticians are the auditors of research: negative and uncreative book-keepers. If mathematics is the handmaiden of science, statistics is its whore: all that scientists are looking for is a quick fix without the encumbrance of a meaningful relationship. Statisticians are second-class mathematicians, third-rate scientists and fourth-rate thinkers. They are the hyenas, jackals and vultures of the scientific ecology: picking over the bones and carcasses of the game that the big cats, the biologists, the physicists and the chemists, have brought down.

Statistics is a wonderful discipline. It has it all: mathematics and philosophy, analysis and empiricism, as well as applicability, relevance and the fascination of data. It demands clear thinking, good judgement and flair. Statisticians are engaged in an exhausting but exhilarating struggle with the biggest challenge that philosophy makes to science: how do we translate information into knowledge? Statistics tells us how to evaluate evidence, how to design experiments, how to turn data into decisions, how much credence should be given to whom to what and why, how to reckon chances and when to take them. Statistics deals with the very essence of the universe: chance and contingency are its discourse and statisticians know the vocabulary. If you think that statistics has nothing to say about what you do or how you could do it better, then you are either wrong or in need of a more interesting job.

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If you tend to the first of these views, this book is written to persuade you of the truth of the second and if you already accept the second it is here to confirm your faith. Statistics is all-pervading in science but it is also misunderstood. The non-scientist in the street probably has a clearer notion of physics, chemistry and biology than of statistics, regarding statisticians as numerical philatelists, mere collectors of numbers. The truth must out, and I am determined to out it and this book is how I have chosen to reveal it, but in a book like this it would be impossible to tell it all. Even within my own field of application, medical statistics, I cannot do that. There are many matters I should like to have covered but have not: the logic, or otherwise, of screening for disease, the use of statistics in health care planning, statistical approaches to the creation of expert systems for diagnosis, the wonderful science of decision analysis and its application to selecting which drugs to develop, the world of sample surveys, the mathematics of genetics, the statistical approach to quality control and its application to monitoring surgery, the interpretation of hospital league tables, sequential analysis and the design of experiments.

Nevertheless, we shall cover some important matters: paradoxes in probability, significance tests, clinical trials, the Bayesian and frequentist schools of inference, the generalisability of results, the safety, or otherwise, of medicines and tobacco, life-tables and survival analysis, the summarising of evidence, the mathematics of measles, and even the application of statistics to the law. (If the relevance of the last of these to medical statistics is not clear, all will be revealed in Chapter 10.) Naturally I am convinced that this is all good stuff but some of it, I know, is strong medicine. I have tried to sugar the pill by coating the numerical with the biographical. We shall discuss not just statistics the subject but also the statisticians who created it and a curious lot they turn out to be. We shall also, occasionally, take some strange diversions and the medically qualified reader may detect the symptoms of *knight's-move thought* (kmt) and conclude that the author is schizophrenic. (It must surely have been someone with kmt who first called it kmt.) But despite these diversions, whether biographical or otherwise, the numerical cannot be entirely avoided. I have helped the reader to spot it by spotting it myself, or at least starring it. There are two starred chapters, and these are more demanding than the rest. They can safely be omitted by those who find the mathematics off-putting, although, of course, I would not have included them if I had not felt that they were worth the struggle. A star attached to a section within a chapter also indicates more difficult

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material that can be skipped. A starred section within a starred chapter is for the top of the class.

I make no claims to omniscience. Statistics is the science of inference, the science of inference *for* science, and the defining characteristic of science is not its infallibility but its self-correcting ability. Some of what I say will need correcting. Although I have done some original historical research myself, this is limited to the first half of the last century and even there it is limited to a small part of the story. Elsewhere I have relied extensively on secondary sources, in particular the magnificent books by Anders Hald and Stephen Stigler.[1] Other sources are indicated in the endnotes to the chapters. I have also strayed into areas in which I have no particular expertise, the modelling of infectious diseases and statistics applied to the Law, for example. The subject is so vast that nobody can be expert in all aspects of it. My own personal research is mainly in the design and analysis of clinical trials but the book needed more than just that to give it wings.

I have many debts to acknowledge. Doris Altmann, Klaus Dietz, Paddy Farrington, Joe Gani, John Hayward and Jonathan Koehler provided me with copies of their papers. Abelard, Tom Boyd, Damien Defawe, Douglas Fleming, Marta Gacic-Dobo, Richard Greenway, Gerard Michon, Kenneth Milslead, Jane Oakley, Heikki Peltola, Belinda Thornton and Isabel Trevenna helped me obtain papers of others or provided me with data or information. David Brunnen, Iain Chalmers, Giovanni Della Cioppa, Paul Greenwood, Valerie Isham, Martin Jarvis, Geoff Paddle, Mervyn Stone and my daughter, Helen, provided helpful comments on various chapters. The book was submitted for the Wellcome Prize and was a runner up in 2002 and I am grateful to Sarah Bronsdon of the Wellcome Foundation for her encouragement. I am also most grateful to David Tranah of Cambridge University Press for welcoming the completed book with enthusiasm and to Sarah Price for her expert help in editing. Finally, I should like to thank my wife Victoria for persuading me to write it.

So, on with the book. I am going to try and convince you that when it comes to making decisions and scientific inferences, if you can't count you don't count. Let us roll the first die.

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