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# **Clinical Epidemiology**

**A Basic Science  
for Clinical Medicine**

**Second Edition**



**Clinical Epidemiology:  
A Basic Science  
for Clinical Medicine**



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Gordon H. Guyatt, and Peter Tugwell

Second Edition

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# Clinical Epidemiology

## A Basic Science for Clinical Medicine

### Second Edition

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**Little, Brown and Company  
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This book is dedicated to  
Kilgore Trout, J.G.L., Francois Marie Arouet, and  
the Emperor's new clothes

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# Preface

## Origins

*Clinical Epidemiology* had its origins in clinical practice, as we struggled with the diagnosis and management of our patients and fell slowly behind in our clinical reading. All of us had been trained in internal medicine, and all of us believed that we were practicing the Art (derived from the beliefs, judgments, and intuitions we could not explain), as well as the Science (derived from the knowledge, logic, and prior experience we could explain), of clinical medicine.

At different times, and in different situations, it dawned on each of us that there was, in fact, a science to the art of medicine. For D.L.S., this realization came when the Cuban missile crisis transformed him, a tenderfoot nephrologist and renal tubular physiologist, into a reluctant field epidemiologist in the U.S. Public Health Service. Although obligated to learn epidemiology (most of it for the first time), he remained a clinician at heart and was repeatedly surprised by the extent to which his growing knowledge of epidemiologic principles could shed light both on the illnesses of patients and on the diagnostic and management behavior of their clinicians. Moreover, it dawned on him that applying these epidemiologic principles (plus a few more from biostatistics) to the beliefs, judgments, and intuitions that comprise the art of medicine might substantially improve the accuracy and efficiency of diagnosis and prognosis, the effectiveness of management, the efficiency of trying to keep up to date, and, of special importance, the ability to teach others how to do these things. The opportunity to explore this science of the art of medicine burgeoned with the creation of a new medical school at McMaster University, which D.L.S. joined in 1967 and where he later teamed up with the other authors to write the first edition of this book.

For R.B.H., the need for an additional basic science for clinical medicine entered his consciousness during a preclerkship lecture on Freudian concepts of psychiatric illness. When he meekly requested the evidence for one of these concepts, the speaker expostulated that the purpose of the lecture was to transmit content, not defend it (and then admitted that he didn't believe it himself). This need for a more systematic approach to gathering and interpreting clinical evidence was reinforced repeatedly during R.B.H.'s early postgraduate training in eastern Canada, most noisily in a running battle between two of his senior attendings as to how he was to measure blood pressures of their patients. These experiences impelled R.B.H. to combine his postgraduate training in internal medicine with graduate work in clinical epidemiology so that he could apply this latter, additional basic science to the interpretation of clinical phenomena. The resulting combined career in clinical epidemiology and clinical practice has led to many things, including the collaboration that produced the first edition.

As a medical student in England, P.T. was attracted to clinical epidemiology by the challenges of trying to apply the principles of population epidemiology

to the care of individual patients. However, when he sought career guidance from a world-renowned London epidemiologist, he was informed that it was "amoral" to combine epidemiology with clinical practice! Discouraged from his initial career plan, he entered traditional postgraduate training in internal medicine, spent an exciting three years in Africa, and wound up as Chief Resident in Medicine at McMaster. Encouraged by the attempts to combine clinically oriented epidemiology and clinical medicine that were underway there, P.T. satisfied his rekindled interest by completing training in both clinical epidemiology and rheumatology. He then chaired the Department of Clinical Epidemiology and Biostatistics at McMaster. P.T. practices as an academic rheumatologist, and collaborates with D.L.S. and R.B.H. in projects such as the first edition.

Our common conviction was stated as follows: The important acts we carry out as clinicians require the particularization, to the individual patient, of our prior experiences (both as individual clinicians and collectively) with groups of similar patients. Thus, the rational evaluation of a symptom, sign, or laboratory test result in today's patient demands our critical appraisal of how this clinical finding has behaved previously among groups of patients with the same differential diagnosis. Similarly, the rational selection of a treatment for today's patient requires our appraisal of how similar patients have fared with various treatments in the past. If, on average, they enjoyed better clinical outcomes and fewer side effects on one treatment rather than on others, we will likely prescribe that regimen to today's patient.

If rational clinical practice requires the projection of diagnostic findings, prognoses, and therapeutic responses from groups of patients to the individual patient, then the strategies and tactics used to understand groups of patients (that is, the strategies and tactics of epidemiology and biostatistics) ought to be useful to the clinician. Moreover, it should be possible to take a set of epidemiologic and biostatistical strategies developed to study the distribution and determinants of disease in groups and populations, recast them in a clinical perspective, and use them to improve our clinical performance. The first edition summarized our initial attempts to do so.

In it, we addressed the three challenges that face every clinician every day: reaching the correct diagnosis, selecting the management that does more good than harm, and keeping up to date with useful advances in medicine. In each case, we proposed some practical applications of clinically oriented epidemiology and biostatistics that might help readers improve the accuracy, efficiency, and enjoyment of their clinical efforts.

We begged the readers of the first edition to recognize that it was not a book for the "doers" of research. It contained no discussions on how to pose scientific hypotheses, draw random samples, conduct blind outcome measurements, or perform actuarial analyses. Rather, it was presented as a book for the "users" of research done by others. Moreover, it was organized in terms of clinical actions (diagnosis, management, keeping up to date), not epidemiologic topics. As a result, issues such as statistical significance arose only when they could help in reaching a better clinical decision, and then only within the context of the clinical problem to be solved.

Clinical examples appeared abundantly in those pages, and usually represented actual patients whom we were trying to help when we discovered the usefulness of the particular application of a general strategy of epidemiology or biostatistics. Given the heterogeneity of our intended audience, we anticipated that our readers would be bound to find some of our examples arcane and others oversimplified (and still others managed with approaches unique to southern Ontario) and would risk learning more than they really wanted to know about some of our favorite patients.

Moreover, we emphasized that we all were still pretty new at this game of trying to link group approaches used in epidemiology and biostatistics to individual patients and clinicians and predicted that history (as well as book reviewers) would reveal some spectacular errors in our initial attempts. We hoped, *nonetheless*, that our mistakes would not prevent our readers from enjoying as well as mastering the lessons to be learned.

### Why a Second Edition?

The response to the first edition surprised and delighted us. We made thousands of new friends, received hundreds of letters from students and practitioners who enjoyed both the content and style of the book, and were gratified by the numbers of both young and mid-career clinicians who wrote to tell us how their careers and attitudes toward medicine changed from reading it.

A lot has happened both to us and to the field since we wrote the first edition. D.L.S. decided to put his career where his mouth was and repeated his residency in internal medicine; in addition to being highly educational, this two-year "re-treading" in acute, in-patient referral practice was edifying, terrifying, and hilarious. He then became a full-time clinician on the Chedoke-McMaster medical service, where, surrounded by colleagues whose opinion of his competence was higher than his own, he was made Chief of Medicine. Thus, he has had plenty of recent opportunities to apply the ideas in this book to patient care, to teaching, and to running an ever-busier medical service with ever-fewer resources. Bedside discussions and debates with brilliant clinical clerks, conscientious house staff, and imaginative colleagues have led to the development of some new ways of thinking about and making diagnostic and management decisions, and the ones that have appeared useful are in this edition.

Since the first edition, R.B.H. has become preoccupied with understanding and tightening the connection between the evidence obtained from sound health-care research and what actually happens to patients. Among his activities has been a series of studies on how to find and organize the best clinical evidence right in the emergency room, ICU, ward, or clinic, an effort that has been enriched by always interesting and often productive liaisons with scientists, professional societies, librarians, and colleagues. One of these liaisons found him wearing a penguin suit as he joined several editors of clinical journals in the shadow of Big Ben to celebrate the history of past and present clinical journals. Another has led to his appointment as editor of a new clinical journal, sponsored



by the American College of Physicians, the *ACP Journal Club*, which uses the principles of critical appraisal of medical evidence described in this book to identify and present important new findings in internal medicine soon after their primary publication.

P.T. finished his ten years as Chairman of the Department of Clinical Epidemiology and Biostatistics at McMaster, took on a combination of clinical, academic, and administrative responsibilities as director of a new Centre for Arthritic Diseases and Chief of Medicine for the Chedoke Division of Chedoke-McMaster Hospitals, and helped form a collaborative group of colleagues at Rheumatic Diseases Units across the country who are combining methodological and clinical questions in their studies. His career as a clinical epidemiologist has been enormously enriched and broadened through involvement in the International Clinical Epidemiology Network (INCLEN) program [4]. Watching and helping the INCLEN fellows and alumni (56 so far at McMaster and more than 150 worldwide) successfully implement locally relevant studies of high quality under extraordinarily difficult circumstances has been a source of inspiration and wonder. As this second edition was going to press, he was named Chairman of the Department of Medicine at the University of Ottawa.

A fourth author has joined us. When G.H.G. was in his final year of post-graduate training and aiming toward a career as a general internist and clinical teacher at a university-affiliated community hospital, he stumbled into the McMaster clinical epidemiology graduate program and decided that it might make that year more interesting. Exhortations from senior colleagues led to an exploratory foray into clinical research. One of the sparks caught and has led to a career at the boundary between research methods and clinical practice. Thus, G.H.G.'s areas of interest are best defined in terms of methods for understanding and solving clinical problems: the measurement of the health-related quality of life, the assessment of health technologies, the application of single-subject (N-of-1) designs to research and clinical practice, the performance and interpretation of scientific overviews, and the practice and teaching of evidence-based medicine.

But, of course, ours has been a small contribution to the total development of the field of clinical epidemiology. Departments and divisions of clinical epidemiology have been created in health science faculties all over the world, and the fastest growing specialty sections of several research societies are devoted to this area. Under the leadership of Alvan Feinstein and Walter Spitzer, a revitalized *Journal of Chronic Disease* has been renamed the *Journal of Clinical Epidemiology*. Clinical epidemiologists have been selected for chairs and chairmanships of departments of medicine and for senior editorships of major clinical journals. Moreover, there has been a salutary critical appraisal of critical appraisal, and we are learning more about when and where it works and doesn't work [1, 3, 5, 6, 7]. A plenitude of new ideas and approaches have come from these developments, and we decided that it was time for us to develop a second edition that would incorporate them.

To our surprise, when we solicited suggestions for how to revise the first

edition from about a hundred colleagues here and there, the most common advice we received was "don't fix it if it ain't broke." We were strongly cautioned not to turt up the book or change examples that were already effective in getting our points across. Accordingly, the rules that we applied in revising the book follow.

1. *New examples of the ways of thinking, executing, or learning already presented in the first edition would replace the originals only if they had been shown to be more effective in getting the related principles, strategies, and tactics across to readers.* Thus, the creatine kinase example (based on data from the Edinburgh Royal Infirmary in the 1960s) has yet to be bettered as a means of learning how to interpret diagnostic data, as have the old-fashioned approaches to evaluating exertional chest pain. Our resolve not to bow to calendar time in this matter was strengthened by a reviewer of the first edition who opined: "Less topical examples would have been preferable" [2].

On the other hand, newer or otherwise better examples do appear at several spots in the second edition, especially in Chapters 4, 7, and 9-14.

2. *New ways of thinking about, executing, or learning about diagnosis, management, and keeping up to date would be included if we had been using them for at least a year and their evaluation to date had led us to conclude that they were useful.* This led to the inclusion of 15 new elements or major changes in this edition. Thus, in the section on diagnosis, we've added discussions on the utility of diagnostic tests (page 62), their use in defining the severity of disease (page 54), how to select them when no gold standard is available (page 53), and how to become a faster (as well as more accurate) diagnostician through the application of SpPin and SnNout (page 83).

In the part on management, Chapters 6 (on making a prognosis) and 7 (on deciding on the best therapy) now include sections on how to interpret confidence limits (pages 174 and 217), and the latter has new sections on how to understand utilities (page 209) when they appear in clinical articles about the efficacy of therapy and how to use the number-needed-to-treat as a measure of clinical significance (page 204), and a major, new section on how to conduct your own N-of-1 trials of therapy in your own patients (page 223).

In Part III, Keeping Up to Date, Chapter 10 drops an occasional approach to assessing your own performance that we never faithfully carried out and documents some additional ones that have been shown to improve performance. Breakthroughs in our ability to track down, retrieve, and catalog clinically useful information have led us to rewrite virtually all of Chapter 11 on tracking down the solutions to clinical problems and Chapter 12 on surveying the medical literature in order to keep up to date.

Since our own libraries continue their rapid change, and because we didn't much like the first edition's chapter on creating and running your own library, we dropped it. Moreover, since our earlier chapter on how to read a clinical journal was highly repetitious of information provided elsewhere in the book, we dropped that one, too.

The growing interest in meta-analysis as a means of deciding how to manage

patients led us to write a new chapter, which combines guides for reading reviews, overviews, and meta-analyses with our earlier guides for reading economic analyses. Finally, new strategies and tactics for teaching and learning clinical epidemiology at the bedside continue to emerge, and we have revised Chapter 14 accordingly.

## On Definitions and Traditions

The first edition lacked a formal definition of clinical epidemiology. So does this one. The reasons are two. First, those readers who don't already know us will soon discover that we are pretty short on formality. Second, we agree with Peter Medawar that: "The innocent belief that words have an essential or inward meaning can lead to appalling confusion and waste of time" [8]. It seems to us that the "essentialist" approach (which invokes ontology and insists that every word has a single, formally correct definition) is simply not up to the tasks that must be carried out in clinical and health care.

Rather, we are forced by both logic and necessity to behave as "nominalists" if we are to cope successfully with the multiple definitions for real-world situations like coronary heart disease (which can be defined in terms of signs and symptoms, or electrocardiograms, or serum enzymes, or gross and microscopic anatomy, or ventricular wall motion, or radioisotopic perfusion, or even symptomless predictors). Again, of course, Medawar said it better: "Let us take it that our business is to attach words to ideas and definitions, not to attach definitions to words." Thus, in order to be helpful to our patients and each other we have lived by the conviction that "clinical epidemiology is what clinical epidemiologists do."\* Those who really want to ponder the definition of clinical epidemiology can do it on their own time.†

We also won't attempt to chronicle the development of clinical epidemiology as a basic science for ancient and modern medicine and will leave to others debates about whether Thomas Sydenham, John Snow, or Eve was the first clinical epidemiologist. One thing is clear in 1990, however, and that is that all of us currently working in this field are indebted to Alvan Feinstein for his success in making it scientifically rigorous, academically legitimate, and rollicking fun.

## And Finally

If, in the final analysis, the practice of this "science of the art of medicine" is to do more good than harm to patients and clinicians, five additional ingredients must be added to the study of this book. First, its elements must be integrated with those of the other basic sciences, such as morphology, physiology, and biochemistry, as they are applied; were the approaches presented here to consti-

\*Actually, we lifted this flagrantly nominalist definition from a "big-E" epidemiologist named Reuel Stallones who, in turn, attributed it to Sandy Gilliam [10].

†The best current starting point is probably the paper from C. David Naylor and his colleagues in the *Journal of Clinical Epidemiology* [9].

tute the sole scientific basis for clinical action, we would simply be substituting a new tyranny of unachievable methodologic rigor for the old tyranny of unteachable clinical art. Second, this approach to diagnosis, management, and keeping up to date must be fed by an increasing body of valid and clinically useful new knowledge, generated from sound, relevant clinical research; without this new knowledge, the approach described in this book could rapidly degenerate into nihilism and therapeutic paralysis. Third, clinical epidemiology must continue to generate new strategies and tactics for identifying and solving problems in diagnosis, management, and keeping up to date; otherwise, this basic science will risk subservience to clinical and information technology. Fourth, this additional basic science for clinical medicine must be applied with abundant humility, recognizing that much of its justification stems from its ability to explain and to teach, not replace, the art of medicine.

Finally, we hope that as you use the strategies and tactics of clinical epidemiology we present in this book, you will add sufficient enthusiasm, irreverence, and merriment to have as much fun in their application as we have had in their development!

D.L.S.  
R.B.H.  
G.H.G.  
P.T.

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## **Notice**

The indications and dosages of all drugs in this book have been recommended in the medical literature and conform to the practices of the general medical community. The medications described do not necessarily have specific approval by the Food and Drug Administration for use in the diseases and dosages for which they are recommended. The package insert for each drug should be consulted for use and dosage as approved by the FDA. Because standards for usage change, it is advisable to keep abreast of revised recommendations, particularly those concerning new drugs.

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