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Series: History of epidemiology

Evolution of epidemiologic methods and concepts in selected textbooks of the 20th century

Introductory note by Alfredo Morabia

This article closes the series of contributions on the history of epidemiologic methods and concepts. It traces, in *some* epidemiology textbooks published in the 20th century, the evolution of the way five main topics have been taught: study designs (cohort studies and case-control studies), confounding, bias, interaction, and causal inference. These correspond to the topics covered by the other papers in the series. The only exception is the concept of interaction, for which I had not been able to find an author. This final paper has been sent to review and/or comment to all the living authors of the textbooks. Three authors opted for commentaries which are also published in this issue of Social and Preventive Medicine and two for reviews.

Our publisher, Birkhäuser, has been kind enough to let us post the pdfs of all these papers on the website: www.epidemiology.ch (choose history). A revised version of these papers accompanied by a substantial introduction, pooled bibliography and index will appear in 2004 as a book entitled "The history of epidemiological methods and concepts" (Birkhäuser).

Summary

Textbooks are an expression of the state of development of a discipline at a given moment in time. By reviewing eight epidemiology textbooks published over the course of a century, we have attempted to trace the evolution of five epidemiologic concepts and methods: study design (cohort studies and case-control studies), confounding, bias, interaction and causal inference. Overall, these eight textbooks can be grouped into three generations. Greenwood (1935) and Hill (first edition 1937; version reviewed 1961)'s textbooks belong to the first generation, "early epidemiology", which comprise early definitions of bias and confounding. The second generation, "classic epidemiology", represented by the textbooks of Morris (first edition 1957; version reviewed 1964), MacMahon & Pugh (first edition 1960; version reviewed 1970), Susser (1973), and Lilienfeld & Lilienfeld (first edition 1976; version reviewed 1980), clarifies the properties of cohort and case-control study designs and the theory of disease causation. Miettinen (1985) and Rothman (1986)'s textbooks belong to a third generation, "modern epidemiology", presenting an integrated perspective on study designs and their measures of outcome, as well as distinguishing and formalizing the concepts of confounding and interaction. Our review demonstrates that epidemiology, as a scientific discipline, is in constant evolution and transformation. It is likely that new methodological tools, able to assess the complexity of the causes of human health, will be proposed in future generations of textbooks.

Keywords: **Epidemiology – History – Method – Bias – Confounding – Interaction – Causal inference.**

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Current courses of epidemiology teach students the tools to discover causal associations relevant to human health. These tools consist of: study designs (cohort studies and case-control studies) with their specific measures of outcomes and effects, and theories supporting the concepts of bias, confounding, interaction and causal inference. In this paper, we attempt to trace the origin of these five elements in selected textbooks published in the 20th century.

Comparing the content of textbooks of epidemiology published over the last century is therefore also a way of retracing the history of the discipline. Our objective here is to describe the evolution of the corpus of methods and concepts that are used by epidemiologists rather than reviewing the health issues that epidemiologists have been tackling over the years. This is the history of the methods and not of the scourges they helped to fight.

For this purpose, we have selected eight textbooks. The authors of the books are Greenwood (1935), Hill (1961), Morris (1964), MacMahon & Pugh (1970), Susser (1973), Lilienfeld & Lilienfeld (1980), Miettinen (1985), Rothman (1986). These books appeared in a given chronological order, but we did not necessarily review their first editions. For example, the first edition of Hill's textbook, *Principles of medical statistics*, was in 1937, compiled from a series of papers published in Lancet; Morris's first edition of *Uses of epidemiology* was published in 1957 (Morris 1957) building on ideas first introduced in a 1955 British Medical Journal paper (Morris 1955); MacMahon & Pugh's textbook, *Epidemiology: principles and methods*, was preceded by its 1960's version, *Epidemiologic methods*, by MacMahon, Pugh & Ipsen (MacMahon et al. 1960); and Lilienfeld & Lilienfeld's *Foundations of epidemiology* by Lilienfeld alone (1976). This set of textbooks is a selection which does not include influential texts such as Kleinbaum, Kupper & Morgenstern (1982), Gordis (2000), Mausner & Bahn (1974), Kelsey et al. (1996), Hennekens & Buring (1987), Rose (1994), Szklo & Nieto (2000), Rothman & Greenland (1998) or textbooks whose titles indicate that they specialize, for example, in clinical, occupational and genetic epidemiology. We do not include texts in languages other than English. This selection was guided by the objective of detecting how some concepts and methods have evolved. Therefore, some texts were deemed to belong to the same generation and therefore to reflect the same degree of achievement even if they differed by the way they explained the material. Having selected some texts and not others is therefore not a quality judgment but essentially an attempt to avoid redundancy. For example, the texts by Maussner & Bahn (1974), Gordis (2000) and Lilienfeld & Lilienfeld (1980) are considered to belong to the same generation of texts, influenced by the teaching at The Johns Hopkins School of Public Health of Abraham Lilienfeld. The selection may therefore be considered as arbitrary. We would be grateful to the readers familiar with these texts or their authors to express their disagreement if they feel that we missed some substantially innovative contribution of these other texts.

We then considered five main topics of interest: study design (cohort studies and case-control studies), confounding, bias, interaction and causal inference. Here again, the choice may be considered arbitrary as we did not include the evolution of randomized trials or of ecologic studies, for example. The technique and analysis of randomized trials are not necessarily covered in depth in the current epidemiology core courses. "Ecological designs" should have been covered as they occupied an important place in classic epidemiology texts and have been the object of a renewed interest recently.

The work was divided as follows. Each of the authors, barring the first and last who were teaching the course (Epidemiology III: principles of epidemiology) in the Department of Epidemiology at Columbia University, were asked to prepare a 15 minute presentation on an assigned combination of books and topics, that is, either to review the way the five topics have been covered in a given textbook, or to follow the treatment of a given topic across all eight texts. A series of papers were available on www.epidemiology.ch/history and on the class website, including pre 1945 publications such as Snow (1936; Vandenbroucke et al. 1991), Baker (In Delta Omega Classics), Budd (In Delta Omega Classics), Louis (1836; Lilienfeld & Lilienfeld 1980; Morabia 1996), to which each one added the results of their own search.

The first and last authors then synthesized the information, drafted a manuscript that was then read and commented on by all the present authors. The journal Social and Preventive Medicine invited the authors of the reviewed texts who are still alive to review the paper and/or to write specific commentaries on it.

The main results of this research are presented in Table 1. We first perform a vertical reading of the table, that is, to track the evolutions of the topics across texts, and then a horizontal reading, which consist in comparing the relative coverage of the topics in each of the chronologically ordered texts.

1. Evolution of the specific concepts and methods (vertical reading of the table)

Bias and confounding

Bias and confounding are the only issues that we found systematically across all texts. It appears that early epidemiologists primarily concerned by the potential pitfalls of spurious

Soz.- Präventivmed. 49 (2004) 97 – 104

Box 1 Greenwood's formulation of Yule's "fallacy that may be caused by the mixing of distinct records", also known as Simpson's Paradox

"Sometimes the existence of a relevant difference is obvious; two fallacies which have vitiated many published reports are easily described. One has data of the experience of inoculated and uninoculated persons collected over a wide range in space or time, and brings them together in as single statistical summary, which tells us that upon *n* inoculated persons the attack-rate was *a* per cent and upon *m* uninoculated *b* per cent. If *n* and *m* are large numbers, the kind of statistical test I have described may lead to arithmetically overwhelming odds in favour of the inoculated, yet this *a priori* inference might be quite wrong. It might be that in some of the experiments *neither inoculated nor uninoculated ran any serious risk at all*; if in these groups there were *a great majority of inoculated*, the final summary would show a great advantage to them. Suppose in one experiment there were 1 000 uninoculated with a death-rate of 50 per cent and 100 inoculated also with a death-rate of 50 per cent, while in another experiment there were 1 000 inoculated with a death-rate of 5 per cent and 100 uninoculated also with a death-rate of 5 per cent. Summarizing, we should find 1 100 inoculated persons with 100 deaths, and 1 100 uninoculated with 505 deaths, an enormous "advantage" to the inoculated group. No confidence should be placed in odds computed from such summaries." ((Greenwood 1935) pp. 84–85).

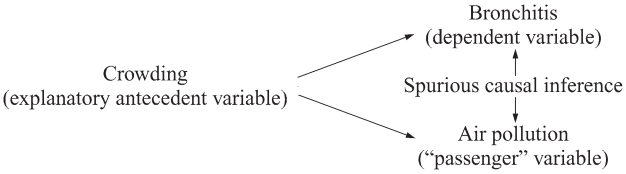

Figure 1 Diagram popularized by Susser to represent the potential connections between variables that may lead to confounding. Source: Susser (1973). Causal thinking in the health science, New York: Oxford University Press

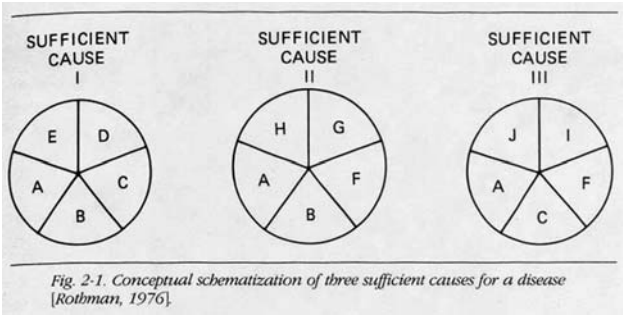

Figure 2 The causal pies popularized by Rothman to describe sufficient and component causes. Source: Rothman (1986). Modern epidemiology, Boston: Little, Brown and Company

associations. Greenwood and Hill refer to biases as sources of "fallacy". Bias and confounding are not really distinguished in the early textbooks, so that their history needs to be considered simultaneously.

Greenwood identifies several types of fallacies (pp. 84–86), one of which was first stated by a British statistician and friend of Greenwood, G. Udny Yule (Yule 1903). This fallacy (quoted in Box 1) is referred to today as the Simpson's paradox (Simpson 1951). It actually described the mechanism of confounding. The Yule's fallacy is also described by Hill in addition to several others.

The consequences of misclassification of exposure or disease are given increasing importance from McMahon and Pugh's texts on, and a full theory of misclassification appears in Rothman's text.

Susser's text popularizes the three-point diagram (confounding, exposure and disease) that became a classic way of depicting confounding (see Fig. 1).

Cohort and case-control design

Greenwood gives the example of a study comparing "incidence" in two cohorts but does not describe or mention the case-control design. Hill mentions the existence of prospective and retrospective designs, but does not explain their properties. In contrast, Morris does. MacMahon & Pugh and Lilienfeld & Lilienfeld dedicate separate chapters to cohort and case-control studies, describing their methodological aspects in detail. Case-control studies and cohort studies are essentially considered as distinct designs until Miettinen proposes the concept of "study base". From then on, the case-control study becomes conceptualized as a specific sampling technique within cohorts or "dynamic populations". Rothman explains this with most clarity.

Causal inference

The necessary and sufficient conditions for disease occurrence are recognized in Greenwood's early textbook whereas the theory of multiple causation is first presented by Morris. The description of a specific method for causal inference in epidemiology appears in McMahon & Pugh's text. In the books of McMahon & Pugh, Susser, and Lilienfeld & Lilienfeld, we essentially find different versions of Hill's causal criteria (Hill 1965). Susser mentions the concept of sufficient and necessary causes, and Miettinen alludes to a new approach to causality. Rothman's text has the most thorough discussion of causality. Using the now classic causal pies (Fig. 2), he relates interaction and strength of association to relation between component causes.

Interaction

The last concept to appear in this set of texts is interaction. The possibility of observing synergy and antagonism between several causes is mentioned in all texts from

Table 1 Summary of the content of eight epidemiology textbooks with respect to the concepts of confounding, bias, cohort studies, case-control studies, causal inference and interaction. Grey background indicates that the concept is covered in the textbook

Textbook (publ. year)	Confounding	Bias	Cohort	Case-control	Causal inference	Interaction
Greenwood (1935)	• Greenwood's Fallacy • (see Box 1)	• No specific mention of bias, but discusses comparability among groups and how certain differences arise	• Has an example which compares case incidence of typhoid in two cohorts of soldiers, one of which had been inoculated	• Absent	• Mentions necessary and sufficient conditions; the concept of causal inference is absent	• Mention of the interaction among innate qualities of the body, personal habits and constitutions of the atmosphere, but no theory of interaction is absent
Hill (1961)	• Emphasis on comparison groups should be the same in all relevant aspects; presents the third variable and mixing of non-comparable records but does not used the word confounding	• Has an entire chapter of selection, refers to non-representativity of the universe, self-selection and loss to follow-up as common forms of bias	• Proposes two observational forms of inquiry, one of which is prospective inquiry; however, no extensive discussion on cohort designs	• Proposes two observational forms of inquiry, one of which is the retrospective inquiry; compares the pros and cons of these two approaches; no mention on odds ratio	• Distinguishes association from causation; the concept of causal inference is absent	• Absent
Morris (1964)	• The concept is embedded in the presentation of selection problem; provides the first suggestion of stratification	• No terms of selection bias, recall bias and interviewer bias, but provides examples on all; concepts on reproducibility, validity, false positives and false negatives are developed	• Provides the first formal description of a cohort study design termed as longitudinal and forward looking	• The first mention of the term case-control studies, comparing it with prospective studies, no mention of odds ratio	• Elaborates multiple causes model	• Absent; interaction is used as meaning interrelation, not synergy or antagonism
MacMahon & Pugh (1970)	• Presented as non causal statistical associations or secondary associations; develops the criteria for potential confounders; suggests two possible solutions: matching and stratification	• No formal or systematic definition of bias, but selection bias, recall bias and interviewer bias are all described. The first theory of misclassification bias, sensitivity, specificity and predictive value are defined	• Gives a systematic treatment of cohort studies and coins the name cohort study	• Entire chapter devoted to case-control study, including control selection; case-control study is presented as inferior to the cohort study; theory of relative odds as an estimate of relative risk	• Illustrates web of causation mechanism, distinguishes causal and non-causal association, direct and indirect causal association; five criteria to evaluate causal association	• Interaction is presented as synergistic effect, corresponding to current additive interaction but proposed mode of evaluation is in the multiple scale

Table 1 (continued)

Textbook (publ. year)	Confounding	Bias	Cohort	Case-control	Causal inference	Interactio
Susser (1973)	• Original contribution to confounding, introduces the now widely-used three arrows diagram; confounding can be handled in both study design and analysis	• States that randomization removes two kinds of bias: bias inherent in selecting subjects and bias inherent in foreknowledge of the outcome	• No conceptual refinements	• Indicates relative odds or cross-products ratio could stand on its own as a measure of association	• Defines necessary and sufficient cause; entire chapter on causal inference; introduces Mil's canons to identify causes	• Defines moderator variables
Lilienfeld & Lilienfeld (1980)	• Refers to artificial association or indirect association	• Contains a more elaborated theory of selection bias; introduces Berkson's bias	• Distinguishes concurrent prospective and non-concurrent prospective studies	• Dedicates one entire chapter to retrospective and cross-sectional studies; states odds ratio	• Criteria for causal inference modified from Evans's criteria	• Calls interaction as interrelationship between risk factors, and the theory is still not fully developed
Miettinen (1985)	• Indicates that confounding belongs to conditional relations; first formalizes distinction between confounding and effect modification; introduces the method of controlling confounding in regression analysis	• Definition of bias, a classification of biases into three categories: comparability of effects, comparability of populations and comparability of information	• Introduces the concepts of study base: the population experience manifesting the occurrence under study	• Introduces the concepts of study base and case-referent study; provides a detailed mathematical discussion on odds ratio and confidence intervals	• No mention of causal inference	• Refers to interaction as interdependence in coaction, defines synergism and antagonism
Rothman (1986)	• Defines confounding as a mixing of effect; first entire chapter on matching; both weak and strong criteria for confounding	• Definition of validity as lack of systematic error; distinguishes between internal and external validity; internal validity relates to selection bias, information bias and confounding	• Clarifies measures of disease occurrence in cohort studies	• Relates sampling of cases and controls independently of exposure status to removal of the sampling fractions in the odds ratio.	• Improved definition of cause; develop causal pies' and sufficient-component causes model • Elaborates on Hill's criteria as well as caveats when using these criteria as a hard and fast rule posed for causal inference	• Distinction between additive and multiplicative interaction; concepts of statistical, biological and public health interactions, applies sufficient component causes model to interpret interaction

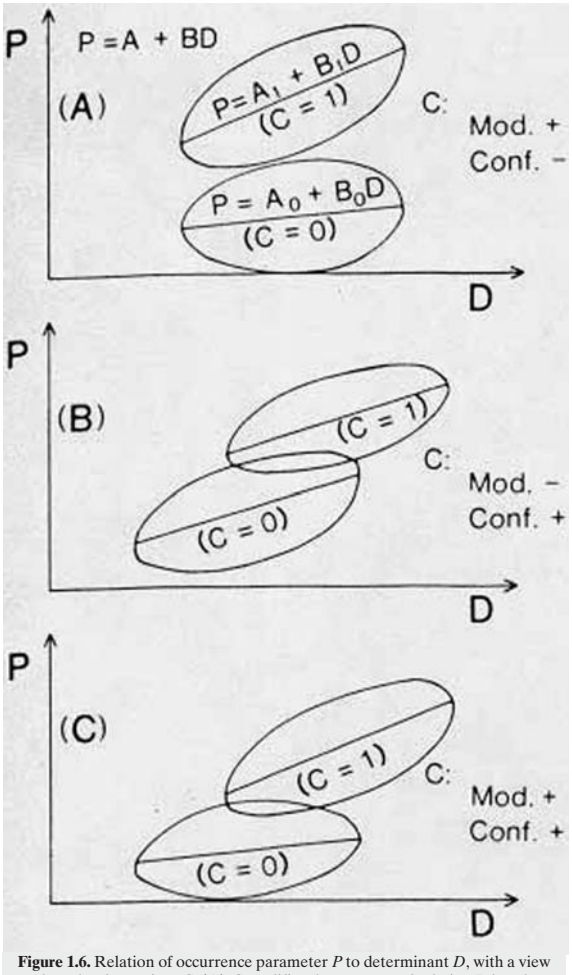

Figure 1.6. Relation of occurrence parameter *P* to determinant *D*, with a view to the role of covariate *C*. (A) *C* modifies the measure of relation B but does not confound it. If *C* is ignored, the average (in a sense) of the conditional slopes is obtained. (B) No modification, but confounding. (C) Modification and confounding.

Figure 3 Schematic distinction between confounding and interaction (i.e., effect modification) by Miettinen. Source: Miettinen (1985). Theoretical epidemiology, New York: John Wiley & Sons

Greenwood to Lilienfeld & Lilienfeld, but the concept is not rigorously approached before Miettinen neatly distinguishes it from confounding (see Fig. 3) and Rothman describes it systematically. It is of note that both McMahon & Pugh and Rothman use the now classic example of the interaction between asbestos exposure, cigarette smoking and mortality from lung cancer (Hammond et al. 1979).

In summary, bias and confounding are the first modern concepts to be systematically present in the eight texts. The issue of study design has been a central concern only since Morris. The concept of causal inference appears somewhat later and interaction is the latest concept to be formalized.

2. Evolution of the specific texts (horizontal reading of the table)

The evolution of the texts themselves, suggests that they can be grouped into three generations: the generation of early epidemiology, of classic epidemiology and of modern epidemiology.

Early epidemiology

Greenwood and Hill belong to the first generation. From the standpoint that we have chosen, they can be considered as statisticians or as epidemiologists. Their texts really insist on the issue of bias or fallacy, and for Hill on analytical methods. Interestingly, the differences between study designs do not appear to be a major concern. These designs were only starting to appear at the time of Greenwood. But even though Hill has been viewed as a pioneer of case-control studies and cohort studies, he never included specific chapters in his most reprinted text.

Classic epidemiology

The senior authors of the second generation of textbooks are mostly physicians (Jerry Morris, Brian McMahon, Abraham Lilienfeld and Mervyn Susser) interested in public health. They put great emphasis on clarifying the qualities and properties of study designs, and in particular what distinguishes case-control studies from cohort studies. The texts also deal much more seriously with the issue of causal inference. This emphasis on study designs and causal inference may reflect the context in which these papers were written. These were the times when the scientific and political community met with a lot of skepticism on the epidemiological results showing that tobacco smoking had deleterious health effects. The interpretation of studies having different designs and the rationale for synthesizing the evidence demonstrating causality played a central role in the preparation of the US Surgeon General's Report on the health risk associated with smoking.

Modern epidemiology

Miettinen appears as the founder of this last generation. His innovative concepts, such as study-base, dynamic population, etc., revolutionize the way study designs and measures of effect are conceived. The theory of epidemiologic methods and concepts becomes one level more complex. Actually, Miettinen acknowledged this in the preface of his text by saying that epidemiology was previously "widely regarded as common sense activity, a line of research that any physician – even one without statistical education – is prepared to engage in" (pp. VIII). We speculate that because of

a convoluted style, which aggravates the complexity of the new material, the novelty of the approach was first only understood by a small circle of students, who re-expressed the new concepts and made them accessible to a wider audience. One of them is Rothman, whose text title can characterize the new generation: "modern epidemiology". In contrast to the previous generation, Miettinen and Rothman are much more inclined towards mathematics. Where classic epidemiology expressed concepts which have no necessary mathematical translations, almost all concepts, be it related to bias, confounding, interaction, etc., from Miettinen's and Rothman's texts can be written indifferently in words or in equations.

Conclusion

As a conclusion, we would like to stress some limitations, pitfalls and potential fallacious interpretations that may result from our work.

We insist that this review of eight texts be considered as an initial attempt to describe the evolution of epidemiologic concepts and methods in the material used for teaching the discipline. Much remains to be done. Within each generation there are many more texts. They may not only give different perspectives of the same concepts. Some may have been really innovative, in particular when they focus on specific issues (e.g., case-control study, randomized trial) or fields (e.g., occupational epidemiology, genetic epidemiology). They are certainly useful as their diversity matches the diversity of students of epidemiology.

Also, our starting points (i.e., currently taught epidemiological concepts) confer an advantage to the most recent texts, which of course cover more of the topics and discuss them more in depth. Textbooks are an expression of the state of development of a discipline at a given moment in time. They usually do not incorporate the latest methodological and conceptual developments, but tend to present material that has been around long enough to reach some level of consensus among scholars in the field. Texts therefore rarely reflect the innovative thinking of their authors but rather the author's ability to incorporate and synthesize other people's work. We found that the texts reviewed are not all as fair in acknowledging their theoretical debt.

Our review of specific topics could not capture the real historical impact of the texts. For example, Morris's text may well have been a model for the other classic epidemiology texts. Some books have genuine qualities that are not necessarily historically relevant. The texts could be reviewed for their literary quality. We are, for example, all seduced by the beautiful style and coherence of MacMahon & Pugh's text.

Textbooks are not simply a neutral compilation of material. The way the material is selected, assembled and presented reflects the global vision of the discipline of the author(s). As a whole the content of a textbook is not only of a scientific but also of a philosophical nature. This could be another way of revisiting epidemiology textbooks.

Finally, there is a time lag between the state of the literature and the content of textbooks. The content of the texts does not always reflect the full breadth of the contribution of their authors to the evolution of the discipline. This is most striking for Austin Bradford Hill whose text does not cover cohort and case-control studies in detail even though Doll and Hill designed and performed case-control and cohort studies that are considered as historical landmarks. Nor do we find a discussion of causal inference reflecting Hill's landmark paper (Hill 1965). Similar considerations can be made about Jerry Morris, Brian MacMahon, Mervyn Susser and Abraham Lilienfeld.

Beyond these limitations, this survey of eight textbooks and five concepts/methods demonstrates that epidemiology, as a scientific discipline, is in constant evolution and transformation. Epidemiology students received a qualitatively different training across the 20th century and used texts that did not always cover the same material. All indicates that the process will continue and that epidemiology tomorrow will be taught differently from today. We are probably at the eve of a new qualitative change in epidemiology. Many have expressed the need to have new methodological tools able to assess the complexity of the causes of human health. The next generation of textbooks will have to address this issue and propose solutions.

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References

Delta Omega Classics (2003). www.deltaomega.org/classics.htm.

Gordis L (2000). Epidemiology. Philadelphia: W.B. Saunders.

Greenwood M (1935). Epidemics and crowd diseases: an introduction to the study of epidemiology. New York: The Macmillan Company.

Hammond EC, Selikoff IJ, *Seidman H* (1979). Asbestos exposure, cigarette smoking and death rates. Ann NY Acad Sci *330*: 473–90.

Hennekens CH, Buring JE (1987). Epidemiology in medicine. Boston: Little Brown.

Hill AB (1937). Principles of medical statistics. New York: Oxford University Press.

Hill AB (1961). Principles of medical statistics. New York: Oxford University Press.

Hill AB (1965). Environment and disease: association or causation? Proc R Soc Med *58*: 295–300.

Kelsey JL, Whittemore AS, et al. (1996). Methods in observational epidemiology. New York: Oxford University Press.

Kleinbaum DG, Kupper LL, *Morgenstern H* (1982). Epidemiologic research: principles and quantitative methods. Belmont: Lifetime Learning Publications.

Lilienfeld AM, Lilienfeld DE (1976). Foundations of epidemiology. New York: Oxford University Press.

Lilienfeld AM, Lilienfeld DE (1980). The French influence on the development of epidemiology. Henry E Sigerist Suppl Bull Hist Med *4*: 28–42.

Louis PCA (1836). Researches on the effects of bloodletting in some inflammatory diseases. Boston: Hilliard, Gray & Company.

MacMahon B, Pugh TF, *Ipsen J* (1960). Epidemiologic methods. Boston: Little, Brown and Company.

MacMahon B, Pugh TF (1970). Epidemiology: principles and methods. Boston: Little, Brown and Company.

Mausner JS, Bahn AK (1974). Epidemiology: an introductory text. Philadelphia: Saunders.

Miettinen OS (1985). Theoretical epidemiology: principles of occurrence research in medicine. New York: John Wiley & Sons.

Morabia A (1996). P. C. A. Louis and the birth of clinical epidemiology. J Clin Epidemiol *49* (12): 1327–33.

Morris JN (1955). Uses of epidemiology. Br Med J: 395–401.

Morris JN (1957). Uses of epidemiology. Edinburgh: E. & D. Livingstone.

Morris JN (1964). Uses of epidemiology. Edinburgh: E. & S. Livingstone.

Rose G (1994). The strategy of preventive medicine. New York: Oxford University Press.

Rothman KJ (1976). Causes. Am J Epidemiol *104*: 587–92.

Rothman KJ (1986). Modern epidemiology. Boston: Little, Brown and Company.

Rothman KJ, Greenland S (1998). Modern epidemiology. Philadelphia: Lippincott Williams & Wilkins.

Simpson SH (1951). The interpretation of interaction in contingency tables. J Royal Stat Soc Ser. B (*13*): 238–41.

Snow J (1936). Snow on cholera. New York: The Commonwealth Fund. In Delta Omega Classics www.deltaomega.org/ classics.htm. delta omega classics.

Susser M (1973). Causal thinking in the health sciences: concepts and strategies of epidemiology. New York: Oxford University Press.

Szklo M, Nieto FJ (2000). Epidemiology: beyond the basics. Gaithersburg: Aspen Publishers.

Vandenbroucke JP, Eelkman Rooda HM, *Beukers H* (1991). Who made John Snow a hero? Am J Epidemiol *133*: 967–73.

Yule UG (1903). Notes on the theory of association of attributes in statistics. Biometrika *2*: 121–34.

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