

PERSPECTIVE

Epidemiology: Quo vadis?

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Abstract. In our etiologic research, we epidemiologists need to leave behind the concepts of ‘cohort’ study and ‘case–control’ study and adopt that of *the* etiologic study as the singular substitute for these. We then need to realize that the etiologic study is well suited to be viewed as paradigmatic for intervention studies. We finally need to become serious about object design before methods design in both etiologic and intervention research. Once these developments have occurred, we’ll be ready for truly meaningful research to advance the knowledge base of both types of causality-oriented ‘gnosis’ in the practice of clinical medicine, etiognosis and intervention-prognosis; and

descriptive-prognostic study we’ll see as inherent in any intervention-prognostic study. As for diagnostic research, then, we need to come to see it as nothing but a special case of our familiar descriptive prevalence research. Because of this readily attainable theoretical readiness peculiar to us research epidemiologists, and for other reasons besides, only we can assume the central role in the production of the knowledge base for scientific medicine. We consequently have the obligation to assume this larger and higher, meta-epidemiologic mission – and some even higher ones besides.

Key words: Clinical epidemiology, Epidemiology, Evidence-based medicine, Medicine, Scientific medicine

Introduction

The nature of epidemiology as a line of endeavor is quite exceptional within medicine at large; and owing to its exceptional nature, epidemiology may in the future develop in one direction or another, depending on what vision of the ideal gets to be adopted.

Epidemiology naturally should be developed in the direction(s) in which it would best serve its genuine stakeholders’ legitimate interests. The genuine stakeholders do not include us epidemiologists, as epidemiologists. In practice and equally in research, we thus should not be serving ourselves but, only, people’s legitimate interests in maintenance and restoration of health. (I have never understood ‘health promotion.’)

In direction-setting for epidemiology, nothing is as consequential as a journal of epidemiology – through its editorial policies manifest in its contents, editorials first and foremost. Professor Hofman, as Editor-in-Chief of *European Journal of Epidemiology*, presumably felt the responsibility that accompanies this power when he asked me to produce an article on ‘Epidemiology: Quo vadis?’

This question is as daunting as it is important. The challenge of writing about it I accepted knowing that my answers will not mislead anyone: a number of eminent colleagues, through their respective

adjoining commentaries on this opinion piece, will ensure that epidemiology will indeed develop in the direction(s) in which it will best serve its genuine stakeholders’ legitimate interests.

Epidemiology’s dimensions at present

The concept of epidemiology now is a somewhat novel one; and there has come to be, even, some confusion about the meaning of the ever more widely used ‘epidemiology’ term. There obviously still is the duality constituted by epidemiological practice and epidemiological research, but the boundaries of these have become somewhat ill-understood.

Epidemiological practice now is of two fundamentally different types, both in the realm of public health. When the medical aspect of public health was a matter solely of community medicine, practice of community medicine, alone, constituted epidemiological practice. Quantification of morbidity (as a matter of ‘community diagnosis’) together with control of morbidity (by means of community-level intervention) constituted the sole mission in the practice of epidemiology. This work, still very important, now defines epidemiological practice in reference to a minor part of public health only.

National health insurance and its public-domain counterparts have brought *clinical* medicine into the

domain of public health; and with healthcare at large – as to its societal aspects – now the overall public-health concern, the modern mantras of public health have come to be ‘quality assurance’ and ‘cost containment’ in publicly provided healthcare. Epidemiology, in its continual subservience to public health, has come to have assessment of quality of healthcare practices as a new type of mission. Commonly mistaken to be research (‘health services research’), this actually is practice – ‘community diagnosis’ concerning professional behavior of healthcare providers, preparatory to intervention of an administrative sort, directed to those whose healthcare activities have been ‘diagnosed’ to be at variance with public policy.

Epidemiological research (genuine, scientific) naturally has been, and is, in the service of community medicine, aimed at advancement of community-level interventions – preventive – in morbidity control. As is very well known, it is etiologic research first and foremost, selectively supplemented by community-level preventive-intervention research. Screening – for a cancer, notably – is commonly mistaken to be prevention and a matter of community medicine; and it is, then, commonly studied as a matter of community-intervention research with a view to mortality, as distinct from research addressing clinical early-diagnosis and curability by early intervention.

Recently, ‘clinical epidemiology’ has emerged, though more as a term than as a concept. The tenable concept of clinical epidemiology, insofar as it would be needed at all, would involve epidemiology in the meanings just outlined but with the concept of community or population of its practice concern one of patients and other clients of clinical healthcare. Its practice would involve control of (morbidity from) nosocomial infections and iatrogenic illnesses; and it would involve quality assessment of specifically clinical care (of which work in diagnostic laboratories, for example, is not part). Its research, correspondingly, would focus on iatrogenesis of illness, intrainstitutional iatrogenesis above all, possibly supplemented by intervention research directed to control of iatrogenic morbidity.

As it is, however, ‘clinical epidemiology’ has its roots in Feinsteinian ‘clinimetrics’ (‘clinical biostatistics’) rather than in the traditions and current realities of epidemiology [1]. The concept remains a seriously malformed one, insofar as it has become formed at all. Sackett et al. expressly left it undefined in their textbook on the subject [2]. They did, however, present it as a “science” (which epidemiology in none of its genuine meanings is) and, even more astoundingly, as a “basic” science (of clinical medicine)! *Journal of Clinical Epidemiology*, by contrast, has defined clinical epidemiology in each one of its issues – as “the interplay of clinical medicine, epidemiology and biostatistics”!

Epidemiology’s uniqueness in medicine

Any line of activity in medicine *per se*, and in medical research also, is unique by its very definition; but there are some notably unique qualities in the uniqueness of epidemiological practice and research.

Epidemiological practice, uniquely in medicine, embodies the big-picture outlook of both community medicine and modern public health, the latter now subsuming the societal aspects of clinical care also (cf. above).

Epidemiological research, again uniquely in medical research, has all illnesses within its purview even as the epidemiologic research community remains cohesive, with its own journals, for example. We epidemiologic researchers thus form an interspecialty agency for medical research – so long as we continue to cohere instead of becoming scattered among medical specialties.

Unique about epidemiological practice also is its interface with extramedical scholarly fields, demography for one and statistics for another. At issue here is statistics in the original meaning of the term (which entered the English language, from German, two centuries ago): collection of social facts for the state (hence the term) on a large scale (with the first set of facts downright gargantuan, published as a 21-volume compilation of survey-based facts concerning rural Scotland).

Epidemiological research, in turn, has come to interface with statistics in a new meaning of this: the branch of mathematics that complements probability theory (deductive) by theory of statistical inference (inductive). Unique about this interface is that we epidemiologic researchers have become quite self-sufficient in the statistical aspects of our research. And this is the way it should be: statistics is to epidemiological research as mathematics is to physics, research in physics without the physicist mastering the requisite mathematics being unimaginable. An epidemiologic researcher is a statistician just as a physicist – or an engineer for that matter – is a mathematician (to the extent necessary for self-sufficiency with most problems). Epidemiological research is statistical research (in form, while medical in substance). But, as epidemiologic researchers, we need to shun hypertrophy of statistics in our work and, by the same token, in the education of our students (cf. below). We need to bear in mind, as a paradigm, that astronomy is about the cosmos and not about the telescope.

Particularly unique about us epidemiologists as medical researchers is our devotion to and cultivation of methodology of our etiologic research. This methodology, commonly held as definitional to epidemiological research, is what makes our epidemiologic research community cohere despite the diversity of subject matter in epidemiological research. Methodology is what a student preparing for

epidemiological research studies; and upon graduation (s)he is a methodologist first and foremost, commonly without devotion to any particular substantive area of epidemiological research.

The larger applicability of etiologic research methodology

Etiologic research methodology has been developed, by our predecessor research epidemiologists, for etiologic research specifically. We have been accustomed to think of epidemiological intervention research in methodologically different terms; and in this we have been prone to defer to biostatisticians as presumedly possessing a higher level of expertise.

What we now, much belatedly, need to do first is to put our methodologic house in order in respect to etiologic research; and having done this we need to adopt the view that intervention research is an obvious extension of application for our endogenous approach to the etiologic genre of causal research for medicine.

Our house of etiologic research methodology will be in basic order once 'cohort' and 'case-control' studies have been demolished and *the* etiologic study has been constructed as the replacement for them [3]. This construct will rest firmly on an expressly defined *study base*, the referent of the study's result. The result will concern, as before, a rate ratio of the outcome's occurrence, subject to causal interpretation by virtue of presumedly being conditional on all confounders; but confounding will be understood always to be a feature of the study base first and foremost – and, ideally, of it only.

Other things, too, will be understood from the study-base vantage, and from this vantage only: If the rate-ratio at issue concerns incidence density of an outcome event, as indeed it usually does, then the study base is an aggregate of population-time. In this situation the rate ratio's documentation always involves two series: the case series, consisting, in principle, of all cases of the outcome event (as defined *ad hoc*, and not necessarily inclusively) occurring in the study base; and a base series, drawn as a fair sample of the study base. And it involves documentation of both series, as to etiologic histories in particular, as of the person-moments involved. If at issue is a proportion-type rate (of incidence or prevalence), then the study base is a finite series of person-moments, all of them documented in a single series, again as of the person-moments involved.

Having come to these understandings of our etiologic study, we need to turn to intervention studies and ask, What, if anything, relative to our etiologic research, is fundamentally different about this genre of causality-oriented medical research? The study population is a cohort, its follow-up forming an aggregate of population-time for the study. Nothing is new

about this. If the proximal concern is with prospective incidence density of an outcome event (in causal relation to its intervention determinant), our etiologic-research background leads us to aim at securing the series of all cases of the event occurring in this study base, and to draw a sample (finite) of the infinite number of person-moments constituting the study base. In both series, causal histories obviously address intervention as to its generic type and its temporal aspect – attained duration or time since it was carried out, as of the person-moments at issue. Having fitted a version of our familiar logistic-regression function ('model') to the data, we have empirical incidence-density ratio as a joint function of the type of intervention and prospective/prognostic time (as well as of the prognostic indicators documented as of cohort/prognostic T_0). The logistic function we readily translate into its corresponding function for incidence density itself, by multiplying its exponential by the ratio of the base series' size to the amount of population-time in the study base. And from this we, with utter simplicity, proceed to intervention-specific, descriptive, risk functions. These functions naturally are prognostically more meaningful than mere incidence-density ('hazard') ratios from Cox regression, or Kaplan–Meier survival curves for that matter.

Our next obvious step in intervention research is to go beyond the events-oriented 'survival analysis' topic and to address possibly affected or otherwise prognostically relevant outcome *states*, their prospective prevalences, in somewhat analogous terms. To this end we will be ready to use that base series involved in addressing outcome events. In this, though, some subtlety will arise in respect to the precision of the parameters' empirical values, to avoid overstating the amount of information in an arbitrarily large series.

None of this will be fundamentally novel to us as etiologic researchers; but it will be novel as an approach to intervention research. In our etiologic research we have tended to think of intervention research as the paradigm. I am here proposing reversal of paradigms between these two lines of causality-oriented medical research.

The larger-than-methodologic outlook in theory of epidemiological research

Apart from having been in the rut of 'cohort' and 'case-control' studies in our etiologic-research methodology, we've had another equally bad habit. We've been producing carefully quantified empirical rate ('odds') ratios ('relative risks') in reference to altogether carelessly – simplistically – defined etiologic-history contrasts, failing to appreciate that quantification of the ill-defined is meaningless. This meaninglessness is a built-in feature of the 'cohort' study as we are accustomed to define it: a consequence

of the involvement of etiologic histories as of cohort T_0 as opposed to etiologic T_0 , the time of outcome (of case occurring, in the case series, or not occurring, in the base series from the prospective population-time). Apart from this definitional flaw in ‘cohort’ studies, in both ‘cohort’ and ‘case-control’ studies the epitome of this carelessness has been the nondefinitional but nevertheless common ever-never contrast in histories of ‘exposure’ (which commonly is not actual exposure).

Implicit in this criticism of our etiologic research is a much larger point. A method is a means of pursuing/achieving a preset end, the (*sic*) etiologic study being the (*sic*) means to obtain empirical content of the form of the etiologic research-object at issue. Method of study is directed to the object of study; and therefore, method(s) design for a study, we need to come to understand, is subordinate to its antecedent and principles-guided *object design* for the study. Medical journal editors also are subject to criticism about this, as for the imposed structures of study reports’ abstracts in particular [4].

It is, I believe, useful to make this very important point also in linguistically different and more philosophical terms. In our cherished self-image we have been methodologists of etiologic research. Rephrased, we have been *epistemologists* with this focus. Now we, of logical and philosophical necessity, need to adopt a larger view and think of ourselves, as to etiologic research, as *ontologists* first and as epistemologists only secondary to this. (‘Objectologist’ doesn’t quite cut it as a synonym for ‘ontologist,’ even as ‘methodologist’ and ‘epistemologist’ work comfortably as synonyms.)

As we become serious about object design for each epidemiological study, we go all the way in this: the end result of object design is a regression function (logistic) that defines the object set of parameters – and, thereby, also the form of the study’s ultimate result (while the study proper will produce empirical content of that form).

As we thus get to be masters of both of the two stages of etiologic study design, its preparatory object design and the study-design proper, we become masters of this larger domain of scholarship in etiologic research, whatever be the term for it. The term actually is quite an obvious one: at issue is theory (ontal as well as epistemic) of etiologic research. In this theory, I might add, ‘data analysis’ (misnomer) has become essentially a nontopic, given that object design has come to subsume design of the regression function (its form), and given also the modern, ready availability of software for fitting the function to the data.

The ready extension of epidemiological research to all quintessentially ‘applied’ medical research

All of medical research, to the extent that it indeed deserves to be characterized as medical, involves the

vision that the resulting knowledge will be, potentially at least, useful in advancing (the art of) medicine. It thus is ‘applied’ – application-oriented, instrumentalist – rather than theoretical or ‘pure’ research, which quite possibly is empirical. (The original concept of pure research was that of rationalist, nonempirical research.)

Medical research is quintessentially ‘applied’ when it is aimed at advancing the knowledge base of (the art of) scientific medicine. A doctor’s first concern is to get to know about the client’s (individual’s or community’s) health, as this knowing is the necessary basis for actual ‘doctoring’ – teaching the client about their own health (cf. etymology of ‘doctor’). This *ad-hoc* knowing results from bringing general (abstract) knowledge to bear on interpretation of the health implications of such *ad-hoc* facts as the doctor has ascertained on the client. That practice-relevant general knowledge derives, in scientific medicine, from quintessentially ‘applied’ medical research.

Most natural for us epidemiologists is to aim at serving the clinical practitioner in his/her need to know whether a potentially etiologic antecedent, which was there, actually was causal to the adverse outcome that has occurred. The answer to this etiognostic question is, of course, unknowable in categorical, yes–no terms. But in the usual case in which the antecedent can only be causal, never preventive, we know very well how the correct etiognostic probability can, in principle, be set on the basis of the relevant etiologic rate-ratio. But, to serve these etiognostic purposes – most notably in respect to iatrogenesis and ergogenesis of illness – we need to have this type of application in mind when designing the object of an etiologic study. In particular, the regression function needs to be designed in reference to the practice-characterizing detail in the etiologic history and the rate-ratio’s modifiers – the latter being etiognostic indicators that define subdomains of the designed domain for the study’s object function [3, 4].

As we come to view medical intervention studies from the etiologic vantage – as providing for causal understanding of outcome occurrence, retrospectively, as of the time of outcome (cf. above) – we are ready to pursue mastery of intervention-prognostic research for clinical prognosis. Object design is, again, critical for the study’s relevance for the knowledge base of this intervention-prognostic aspect of clinical practice. Not only must the object function address whatever possibly affected outcome entity as to its occurrence with specificity to prognostic time; also necessary is specificity to the effect-measure’s modifiers as of prognostic T_0 – to intervention-prognostic indicators in the meaning of them defining subdomains of the domain of prognostication. The descriptive-prognostic study is, as I indicated above, an extremely simple extension inherent in this type of intervention-prognostic study.

With these the ready extensions of the prevention-oriented etiologic study, the diagnosis-serving study for clinical medicine is, as I noted, a special case of descriptive epidemiologic studies – on prevalence, specifically. The correct diagnostic probability is the prevalence of the illness at issue in instances such as the case at hand – in terms of the diagnostic profile formed by the realizations of a set of diagnostic indicators (risk-related and manifestational). Study of prevalence as a joint descriptive function of its determinants, in whatever defined domain, is well within our ken as research epidemiologists. But once again, we need to concern ourselves with the particulars of object design – of the diagnostic prevalence function for a particular domain of diagnostic challenge – for the research to be truly practice-serving.

Epidemiologists' obligation to assume larger – and higher – missions

You see things; and you say “Why?”
But I dream things that never were;
and I say “Why not?”

– George Bernard Shaw

Having described what my colleagues, like I, might see epidemiology to be and why, I have gone on to describe the potential that we research epidemiologists uniquely have to advance the knowledge base of scientific medicine at large. I consequently dream us actually assuming this larger mission. For it is an obligation that flows from our unique readiness to assume this mission, not only larger but altogether critical in the advancement of the unquestioned ideal of scientific medicine. Recognizing this potential and its consequent obligation, we need not – and must not – be held back by what has been our definition of epidemiological research. Let us simply call the realm extension meta-epidemiologic.

But there also is a more proximal, and higher, obligation that we academic epidemiologists in particular should feel and also assume. Just as object design for quintessentially ‘applied’ medical research is a predicate for its methods design, so understanding of the generic nature of the knowledge base of scientific medicine is a prerequisite for meaningful object design for such research. We thus have the obligation to move ‘upstream’ and concern ourselves with pursuit of this understanding. Only we have the readiness for this, and no other discipline is concerned with this.

This aspect of theory of scientific medicine, even, is predicated on something more proximal, on a yet higher level. Theory is a matter of normative statements, concerning correct thinking. These are predicated on the existence of the requisite concepts, and theoretically tenable concepts at that. As it is, even

the most elementary concepts of medicine, such as those of illness and disease, and even that of medicine itself, remain poorly developed [5]. We epidemiologists, therefore, need to assume the obligation of developing tenable general (generic) concepts of medicine. Again, who else?

These things I dream; and most notably, I have no answer to the why-not question in respect to them. (That why-not question cited above was put to Eve in Paradise; and it was put to her by the Serpent. Through Aesculapius, serpent has come to be with us in modern medicine, even, but only symbolically and without diabolic implications.)

Beginning to assume the larger-and-higher – meta-epidemiologic – missions

Given the absence of any answer, on my part at least, to the why-not question above, a succedaneous question arises for me to answer: What do I expect my epidemiology colleagues to increasingly do? My answer is pluritiered:

For a start, I strongly urge my colleagues active in the research dimension of epidemiology to consider adopting the outlook of quintessentially ‘applied,’ gnosis-oriented research, not only etiognostic but also diagnostic and prognostic, the latter typically both intervention-prognostic and descriptive-prognostic. A bit more specifically, I urge consideration to adopt this outlook – or that of ‘basic’ medical research (by epidemiologic means) – and to thereby shun medical occurrence research that does not qualify as either quintessentially ‘applied’ or exquisitely basic.

Second, I urge colleagues who do adopt this outlook to appreciate that much of etiologic and intervention research has remained rather inconsequential on account of deficient, if any, attention to object design for the research. This needs to come to an end. In fact, all of us really need to become ontologists first and epistemologists second only.

Third, it is my wish that at least some of my fellow epidemiologic researchers not only change themselves in the directions just outlined but become agents of change in their respective nonepidemiologic environments, academic ones in particular. The beginning in this is cultivation of understanding, by colleagues outside epidemiology, of what scientific medicine really is all about, so different from what they likely presume it to be (whether from the Flexnerian or the Sackettian perspective). To us academic epidemiologists, I presume, it is generally obvious that scientific medicine is to be defined by two qualities: by its theoretical framework being logical (e.g., one of prevalence functions rather than Bayes’ theorem in diagnosis), and by its knowledge base for application in such a framework deriving from science. Once this elementary understanding takes root around us,

medical education might change quite dramatically, and medical practice secondary to this.

Finally, the beginning should be guided by a vision of the end: a world of genuine education for and practice of ever more advanced scientific medicine. Basic medical science – the source of precious innovations in medicine – will have flourished and will continue to flourish, but in association with biology more than medicine; and it will have come to be understood not to be a concern in the education of doctors just as it is not in their practice of scientific medicine. Education of practitioners will be front-loaded with theory of (the art of) scientific medicine, with the specialties of medicine – rationally defined – introduced in this. The subsequent, principal segment of medical education will be specialty-oriented from the outset (cf. engineering studies), with general practice among the specialties. Future professionals in quintessentially ‘applied,’ gnosis-oriented medical research typically will receive the general-practice education, followed by postgraduate education in theory of such research. And practitioners, then, will practice the way true professionals do: not as creative problem-solvers but as humdrum gnosticians and doctors, with up-to-date gnostic probability functions readily accessible through their computers or extensions of these – courtesy of meta-epidemiologic ‘applied’ research having been made subject to actually being applied through technologic development.

I may be in error in some particulars of this sketch of my vision of the future, but the main thing I am certain about: direction-setting in the advancement of scientific medicine is principally the province of the academic epidemiologist, for the reasons I’ve outlined in the foregoing.

Pursuit of progress will be frustrating, however, as strong forces not only of tradition but also of sheer self-interest will be hindering the realization of the dream of reason – yes, even in medicine, in principle the most noble subset of all science-based professions. Writing about the past of ‘scientific’ medicine (only recent), Paul Starr, lamentfully and with lapidary concision, noted, ‘The dream of reason did not take power into account’ [6].

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