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Opinion

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Epidemiology at a time for unity

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Introduction

The mission and methods in the field of epidemiology are currently being debated. Discourse is healthy for the field, as it fosters understanding of other viewpoints and it may allow for the correction of misconceptions. Some argue to move away from 'risk factor' epidemiology to 'consequentialism'.[1–3] The importance of complex systems,[4–7] the equivalence of the parametric g-formula and agent-based models,[8–10] and causal inference frameworks[11–20] have been discussed. These important deliberations have, however, not been united in place or mind. On one side there are methodological discussions on the causal inference framework[11–20] and on the other there are more big-picture debates on whether epidemiology has become too focused on methods rather than impact, with some recent pleas for complex systems to return to the consequential nature of epidemiology.[1,4–7,21,22]

How should we as epidemiologists integrate these ideas, viewpoints and topics? We aim to begin a constructive conversation to bring epidemiology back to the 'big picture', without ignoring important and necessary methodological advances in the field. We do not aim to be exhaustive, but try to integrate prominent viewpoints put forth to date.

Axioms of Epidemiology

There are three principal axioms in our discourse.

The first axiom of epidemiology: the big picture—improving public health

We may disagree on how to improve the health of the population as a whole, but likely not with this mission statement. Galea recently argued that epidemiology is too concerned with causes and distributions of disease and far less with improving population health.[1] He further argues that causal methods have been emphasized in a way that hinders epidemiologists in pursuing their critical public health mission. This would re-focus our training of young epidemiologists around this goal, rather than on complex methods and aetiological research.[1]

One can hardly disagree with the argument that epidemiology should be driven by public health impact. However, what constitutes consequential epidemiology may depend on the context of the disease being studied. Sometimes our knowledge of a condition is so limited that even a little information has great public health impact. For example, in emerging infectious diseases, describing the geographical distribution and the population at greatest risk may influence how public health agencies respond. However, for non-transmissible diseases, we may know the action targets and risk factors, but struggle in reaching solutions despite gains in understanding and modest improvements in public health.

One aspect of epidemiology that might determine public health impact is the translation into public health action. The translation of findings from studies that maximize internal validity can be challenging. Study populations can be very restricted, in particular in clinical trials that are expected to provide the highest level of evidence. There is a trade-off between internal and external validity, and there can be no doubt that internal validity is a prerequisite to answering any scientific question. But with unclear external validity, it is difficult to translate our findings into action. Technological advances, like electronic health records (EHR) and the collection and analysis of 'big data', might enable us to leave the realm of narrowly defined cohorts and groups and move into the general population for questions of public health impact. The 'general population', however, is a place filled with heterogeneity, competing risks, confounding, measurement issues and effect modification. Yet we would expect findings in the general population, or a population mimicking the general population, to be easily translatable into public health action. It is a methodological challenge to produce research with clear external validity, and this challenge might be met by new methods for generalizability and transportability of estimates from studies across various populations.[23–30]

Is academic epidemiology removed from public health impact?

Developing methods and validating them is not of public health impact per se, but it does empower the field. There are few places outside academia with interest, creativity and band-width to tackle fundamental methodological challenges. Of course, academic epidemiology is not regulated to solely developing methodology. Therefore, addressing relevant public health questions is necessary to retain public health impact. This may range in addressing descriptive, inferential or policy-relevant epidemiological questions, depending on the context of the disease being studied. Ultimately, epidemiology is a 'team sport' and not everyone needs to be or should be focused on tackling the big picture public health challenges, as long as the interdisciplinary team(s) will keep their eyes on the ball.

There may also be structural issues in academic epidemiology that hinder progress in our science. We should continue to beat the drum to call for innovations such as funding individuals rather than projects,[31] promoting creativity among our trainees instead of purely absorbing knowledge, and engaging with the complexity of populations.

The second axiom of epidemiology: it is about the scientific and public health questions, and the methods are a means to those ends

The second axiom suggests that the scientific or public health question drives the methods. The rise of the causal inference framework, counterfactuals, directed acyclic graphs (DAGs) and newer analytical methods (propensity scores, g-methods, etc.) grew naturally as we aimed to define and explain cause. However, are we so dedicated to perfecting the method that the scientific question gets lost?

Causal inference and the development of methods per se are not problematic. The adoption of the potential outcomes framework has allowed us to formulate better questions and outline the assumptions.[17,32] For instance, analysing observational data using trial methodology suggested that the protective effects of statins on cancer outcomes may be due to bias.[33] Furthermore, causal inference is not tied to any particular method, but rather the assumptions (some of which are untestable) that one is willing to adopt to move from statistical association to causal interpretation.[32]

The rapid 'elevation of causal thinking'[1] has resulted in a sentiment among some that 'there is little room for working across disciplines—anthropology, biology, demography, economics, genetics, medicine, politics, public health, psychology, sociology etc.—and working on problems of importance—ageing, climate change, conflict, development, emergent infections and pandemics, equity, health, and social care, global health etc'.[21]

Perhaps the emphasis on methods has had unintended consequences. First, the quick adoption and advancement in methods may have left applied epidemiologists feeling out of touch instead of empowered to better answer pressing questions. In essence, it may appear that causal inference methodology has taken over epidemiology at the cost of applied, 'shoe-leather epidemiology'[34,35] that led to measurable public health impact. Second, trainees (students, post-doctoral fellows) may internalize that epidemiology is all about complicated methods. Anecdotally, many of our students' first draft of their thesis proposals focus on using an 'advanced method' to understand an exposure-outcome relationship, and shy away from addressing the underlying scientific question. The significance and impact of the work is often eclipsed by wanting to use a method. Finally, although some concepts defining our field are inherently causal, like confounding, selection, information bias and effect modification, others are not—including the distribution of variables across a population. Causal concepts emerge as critical when we interpret the data, and epidemiologists should communicate clearly when description turns to inference.

The third axiom of epidemiology: the occurrence, distribution, determinants and control of health states are important cornerstones to the study of both descriptive and inferential epidemiology

In many of the ongoing discussions, descriptive epidemiology has not been at the forefront, but its importance remains a cornerstone to epidemiology that should not be forgotten. Indeed, doctoral students may be entering a career at a public health agency such as the Centers for Disease Control and Prevention (CDC) with a feeling that their training in descriptive epidemiology is suboptimal.[36] The value of descriptive epidemiology is especially apparent as we address emerging diseases. Describing the distribution of disease in a population is a key step towards public health impact. The surveillance of Zika virus in Florida is a recent example, in which travel advisories and mosquito control in the two areas of Miami-Dade County may have prevented Zika from becoming a broader issue.[37] Another example is the use of antiretroviral therapy for pregnant women with HIV as a powerful intervention in substantially reducing the risk of mother-to-child transmission.[38] Good estimates of HIV prevalence across communities are critical to understand where to deploy resources.[39] The intersection of descriptive, causal and implementation research using epidemiological methods needs to be emphasized in order to achieve and sustain public health impact.

Descriptive epidemiology, if granular, is also a key component of precision public health. Indeed, a recent commentary stated that 'the value of precise disease tracking was baked into epidemiology from the start' and argued for more precise disease surveillance.[37] In addition, descriptive epidemiology may lead to questions that require development of causal scientific methods. We stand with others in calling for an increased focus on monitoring and surveillance using epidemiological data.[21]

Paradigm and framework

Epidemiology has employed different paradigms over its history.[40] In 1996, Susser and Susser coined the term eco-epidemiology for the future era of epidemiology and used an analogy of Chinese boxes. The authors recognized the multi-level causation within a causal network.[41,42] Along the same lines, Pearce argued that there has been a shift in the analysis from the population level to that of the individual, with a focus on the randomized clinical trial for investigating individual risk factors while paying less attention to the contextual setting and the need to address social constructs.[43] He outlined that we were using more technology to study trivial issues at the expense of the population causes of disease, and that we needed to reintegrate into public health.

We present a modified framework that outlines three broad domains of epidemiology: descriptive, causal and implementation investigations (Figure 1). We include implementation because we view this domain to include questions such as: (i) cost-effectiveness analysis; (ii) investigating 'policy-relevant estimates' obtained through population-attributable fractions and, more recently, parametric g-formula focused on the so-called intervention effects rather than the contrast of 'exposed' versus 'unexposed';[44–47] (iii) comparing specific implementation strategies through mathematical models and complex systems science,[48] resembling Marshall's reasoning;[5] (iv) and, finally, implementation science.[49] We also show diversity of our focus today, due to improved methodology and data from multiple sources. Our framework intentionally envelops both 'traditional' and 'modern' epidemiology (Table 1).

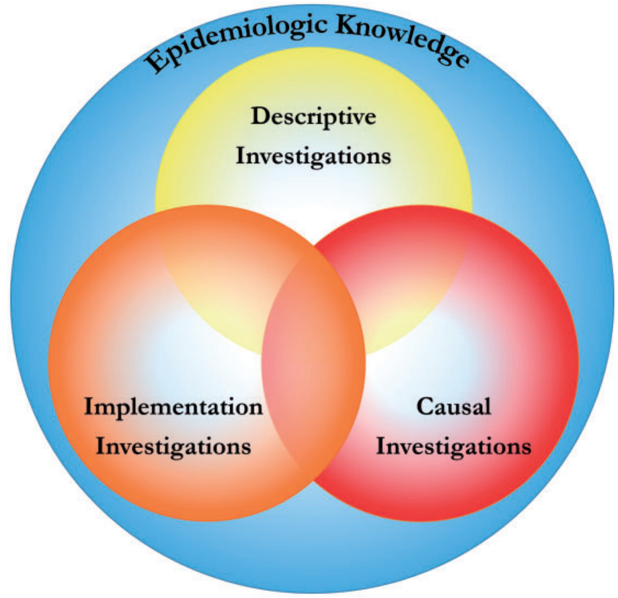

Figure 1. The three domains encompassing epidemiological research. The three domains inform each other and information from these domains are synthesized into our epidemiological knowledge about the public health challenge. Each of the three domains displays a gradient which reflects that these domains can be conducted at various levels of investigation, whether focusing on population, acknowledging the multi-level of individuals nested within groups, or focusing on individual characteristics.

For each of these domains, each axiom is relevant. The methodological advancement of causal inference arose out of a gap in our approach to asking causal questions[52] and has led to clearer questions[17,32,53] as well as 'deconstructing' some of the previously observed paradoxes.[54] Descriptive research investigates how the health states are distributed across a population (i.e. person, place and time). Causal investigations determine how a set of characteristics relate to drive this distribution of disease. Implementation investigations assess how the potential manipulation of the distribution of a set of factors may impact on the distribution of disease and the cost associated with such implementation.

The intersecting nature of the framework calls for the reassessment of public health problems after one full cycle across description, causal investigation and implementation to describe how the state of health has been changed. Each of the domains can, interestingly, be evaluated from the broadest population (all humans) to smaller populations (e.g. countries, states, counties, cities, towns etc.) to the individual level. This framework has room for risk factor epidemiology as well as complex systems, individual- to population-level of analysis and contextual to context-free views. Thus, this framework allows for bridging the dichotomy that Pearce outlined (Table 1)[43] and stimulates impact on all levels and domains.

Table 1. Epidemiological paradigms over time adapted from Pearce[42]

	Traditional epidemiology	Modern epidemiology	Epidemiology today
Motivation	Public health	Science	Public health and science
Level of study	Population	Individual/organ/tissues/cell/molecule	From molecule to human to population
Context of study	Historical/cultural	Context free	Context matters
Paradigms	Demography/social science	Clinical trial	Multidisciplinary
Epistemological approach[a]	Realist	Positivist	[b]
Epistemological strategy	Top down (structural)	Bottom up (reductionist)	Many directions
Level of intervention	Population (upstream)	Individual (downstream)	All levels(individual to population)

[a]Epistemological approach is the theory of nature and knowledge acknowledging limits and validity. Realism asserts that the world exists independent of our knowledge, that all knowledge is fallible, knowledge is theory laden and current knowledge is subject to review, change, and correction.[50] Positivism asserts that development of knowledge is from general statement via based upon sense, experience and positive verification. It is concerned with developing laws of general understanding through explanatory and predictive models, and that scientific knowledge is testable and there is one single truth.[50,51]

[b]We leave the epistemological approach for 21st century epidemiology to the future as epidemiology continues to evolve rather than presuppose. However, with a wide range of views and a variety of evidence to be collected, to develop knowledge perhaps a post-positivism approach, which asserts that there is one single reality but this is never fully perceived (therefore requiring triangulation of views), would be appropriate.[51]

To contextualize this framework, recall the important work of voluntary medical male circumcision (VMMC) and HIV prevention. In 1986, it was hypothesized that VMMC protected against HIV transmission due to the foreskin being easily abraded.[55] This was followed by ecological studies correlating HIV prevalence with lower circumcision prevalence.[56,57] Cross-sectional, cohort and case-control designs of varying methodological quality followed and suggested that VMMC had a protective effect.[58] Further, causal investigations were conducted using randomized clinical trials. The first trial was stopped at an interim analysis with a rate ratio of 0.40 [95% confidence interval (CI): 0.24–0.68] comparing circumcised with uncircumcised men for HIV infection.[59,60] Two additional trials were reported in 2007: one was stopped early with a risk ratio of 0.47 (95% CI: 0.28–0.78) and the other reported a rate ratio of 0.51 (95% CI: 0.16–0.72).[61,62] With the accepted causal effect of VMMC on HIV transmission, investigation into the implementation of VMMC began, exploring mathematical models to address the question of public health impact and cost, and also examining contextual factors and health service delivery.[63–67] The implementation science of using HIV prevention tools continues.[68] The combination of both scaling-up of antiretroviral therapy and VMMC has reduced HIV infection by about 42% in Uganda, from an unadjusted 1.17 infections to 0.66 infections per 100 person-years.[69]

Looking towards the future: implication of a holistic paradigm

Given this framework, how should the field of epidemiology look to the future?

The paradigm takes the eco-epidemiology model[41,42] of nested boxes and transforms it into a multidimensional framework. This holistic, multidimensional framework addresses challenges from different directions (the three domains) and various levels from social determinants of health to individuals factors, with a variety of methods.

Not every epidemiologist must work in each domain or with each population level, or be restricted to a single research area. The diversity between research areas and the levels of focus suggests that we need an epidemiological community to reach across these boundaries, to help inform each other's work. A team of intellectually diverse individuals across the domains is critical not only to synthesize the information but to address the science. However, the scope of this framework does create challenges for the training of epidemiologists. Training must allow for individuals to focus on some subset of these domains but must provide exposure to all. The concept of group trainee advising may be a solution that leads us towards team science within epidemiology, and not just across other disciplines. Furthermore, having three domains and a multilevel framework suggests that there is a need for methodology in all domains, and that methodology cannot be restricted to statistical methodology. For example, both the development of new sampling schemes to engage hard-to-reach populations (e.g. respondent-driven sampling) and the usage of programmatic data to inform interventions should be recognized as epidemiological methods.

We believe that epidemiology by its nature has public health impact. As a field, we currently face major public health challenges, such as the opioid epidemic, climate change and firearm injury and mortality. A diverse community of multidisciplinary scholars like ours fosters teamwork that will propel epidemiology forward as a discipline with continued impact on public health. With these clear goals for the field of epidemiology, we outline a set of axioms and a framework that allows for diversity of skills and viewpoints to show a path forward.

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