The Future of Epidemiology


Abstract

In this article, the authors discuss current challenges and opportunities in epidemiology that will affect the field’s future. Epidemiology is commonly considered the methodologic backbone for the fields of public health and outcomes research because its practitioners describe patterns of disease occurrence, identify risk factors and etiologic determinants, and demonstrate the usefulness of interventions. Like most aspects of science, epidemiology is in rapid flux. Several factors that are influencing and will continue to influence epidemiology and the health of the public include factors fundamental to framing the discipline of epidemiology (i.e., its means of communication, its methodologies, its access to data, its values, its population perspective), factors relating to scientific advances (e.g., genomics, comparative effectiveness in therapeutics), and factors shaping human health (e.g., increasing globalization, the environment, disease and lifestyle, demographics, infectious disease).

A cover article in the New York Times Magazine in 2007 proclaimed, "Much of what we're told about diet, lifestyle, and disease is based on epidemiologic studies. What if it is just bad science?""2 In particular, the lack of replication of results from observational studies within randomized clinical trials has raised public doubt about the research and the science.3 However, that concern stems from a misconception about the process of science, as well as a public desire for more clear-cut and immediate answers. Science progresses through a slow-growing compilation of evidence that develops by nonlinear, contested, and often controversial steps.

In the future, epidemiologists and other scientists must find ways to expedite and better communicate the translational process; that is, they must establish mechanisms for rapid-fire hypothesis generating and testing, agreeing on basic principles for how to reach consensus among themselves and how to live (more harmoniously) with uncertainty; and they must train themselves to express publicly where they are in the process of scientific progress. Once epidemiologists and other scientists reach a consensus, they must advocate for policy based on research, survey for population-based effects of the policy, and move on to other important public health challenges.

Factors Fundamental to Epidemiology

Communication and advocacy

Despite the advances that epidemiology has contributed to public health, the media has recently attacked the field.2

Epidemiology is commonly considered the methodologic backbone for the fields of public health and outcomes research because its practitioners describe patterns of disease occurrence, identify risk factors and etiologic determinants, and demonstrate the usefulness of interventions. Historically, epidemiologists have used inductive approaches that relate a single
risk factor to a single health outcome. Using this method, epidemiologists have discovered many, if not most, simple biologic and sociologic relationships. What remains to be discovered are more complex etiologic links between risk factors and outcomes. Techniques such as factor analysis, multilevel modeling, and causal diagrams provide tools to help make sense out of these complex relationships. However, all of these techniques derive from inductive reasoning and, as such, have limitations in their ability to uncover previously unimagined interrelationships between etiologic factors. 

Epidemiologists use dynamic systems models, a deductive approach to understanding etiology, in infectious disease and environmental epidemiology, but less so in chronic disease epidemiology. An infectious disease example would be a model predicting the effectiveness of social isolation during a pan-influenza epidemic. One of the most attractive features of dynamic systems models is that they have the potential to predict empiric observations. In the best cases, these models can predict the outcomes of clinical trials. Thus, this approach can preclude costly trials, serving as a surrogate and limiting the number of trials that scientists need to actually conduct for validation. Dynamic systems models, which evolve based on observations of the impact of interactions among systems elements (e.g., feedback), also provide a framework for identifying what scientists know and what they do not know, and they allow for complex interactions at levels from the subcellular to the community.

System modelers start from a theory or theories about hypothesized relationships and build mathematical models, embedding available data to elaborate these. Mathematical models are used to gain insights about system behavior and about the need for additional or confirmatory data. A highly predictive, complex model may expedite hypothesis generation and early hypothesis testing, thereby allowing epidemiologists to more efficiently describe a complex world.

Data access

Human subjects research cannot advance without access to data—that is, without persons willing to share some very personal, including medical, information. Unfortunately, policy and public opinion in the United States are conflicted and inconsistent when it comes to privacy. Americans accept the fact that advances in technology have eroded confidentiality, and they contribute to that erosion by posting self-revealing information on My Space or by conducting public conversations about private issues on cell phones. Yet, many Americans are concerned about sharing health information. In several European countries, hospitalizations, outpatient visits, national pharmaceutical databases, and birth and death registries are coupled with individual identification numbers to provide powerful record linkages. Record linkage studies are often the only way to discover uncommon risk factors (such as in drug safety) and to study uncommon diseases. Increasingly sophisticated computer software streamlines the capability for examining massive amounts of data. The fragmented nature of the U.S. health care system, the independence of local institutional review boards (IRBs) from one another and from federal regulators, and the lack of a universally accessible national identification number slow or impede data availability in the United States.

Another challenge to population-based research is legislation in the form of the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule, which permits health care provider organizations to disclose individually identifiable health information for research only if the researcher has obtained from each patient written authorization or, if that is impractical, a waiver of the authorization requirement from an IRB. Protecting health information privacy is a long-standing and widely held goal of the public, legislators, and the research community. However, the HIPAA Privacy Rule, as currently written and implemented, adds uncertainty, cost, and delay to research on humans, without adding additional privacy protections. If Americans want to continue to benefit from rapid-paced biologic discoveries of public health import, they must work with scientists and legislators to find the right balance between autonomy and the public good. Similarly, the Family Educational Rights and Privacy Act (FERPA, 20 U.S.C. § 1232 g; 34 CFR Part 99) poses limitations that sometimes obstruct the conduct of critically important public health research. By coming together, the advocates for data access and the advocates for data privacy can each achieve a greater appreciation for the concerns of the other. Mutual understanding of the real tension between the two positions is needed if the public health interest is to be served.

Values and ethics

Ethical guidelines for epidemiologists, first proposed in 1985 and adopted by many professional societies in the late 1990s, reflect normative values including obligations to people who participate as research subjects, obligations to society, obligations to funders and employers, and obligations to colleagues. Biomedical research is governed by four basic bioethics principles that require professionals (i.e., researchers and practitioners) in public health: (1) to respect the personal autonomy of people, (2) to do no harm (nonmalefiance), (3) to do good (beneficence), and (4) to uphold equity in the distribution of the benefits and risks of research and policy (i.e., to uphold the principle of distributive/social justice). In addition, as professionals we are duty-bound to exercise both moral and scientific integrity. Finally, in public health we note that by researching and developing policies designed to protect the most vulnerable in society, we thereby protect all members of society.

The challenge presented by the uneven uptake of these guidelines likely reflects tensions between the values articulated in the guidelines and the local contexts of their application. As an example, consider that the United States was founded on libertarian values, within which individual rights are paramount. Many European countries, on the other hand, were founded on egalitarian (or communitarian) values, in which the common good is enshrined in policy. This, put briefly, is why disparities in the social determinants of health are relatively greater in the United States and also why data accessibility for health and social research is embraced in other countries more so than in the United States.

Ethics review by independent IRBs of proposed studies has become the standard in epidemiologic research in many countries. Ethics review is based on an evaluation of benefit versus
harm to research subjects. The utilitarian thinking so common to epidemiology must be carefully weighed against any violation of individual rights, particularly given that such studies rarely impart individual benefit. Thus, for example, the need for access to medical records must be balanced against the individual’s right to privacy. Epidemiologists should become actively involved in continuously developing and revising ethics guidelines. IRBs need to include epidemiologists as part of their standard constitution.

Although epidemiology takes a population perspective, this does not necessarily translate into a public health perspective. Examples of epidemiology without a public health perspective include market research and some market-driven clinical trials for therapeutics that may have beneficial effects at the patient level but not at the population level.

Factors Related to Scientific Advances

Molecular and genetic epidemiology

Population genetics is rapidly evolving. High-throughput genotyping has recently been applied to stored DNA samples, providing an unprecedented opportunity for gene discovery. These studies have demonstrated that very large sample sizes that use multicohort consortia are needed to identify typically small genetic variant effects. From a public health perspective, findings to date have been largely disappointing because they contribute little to explaining disease variation in populations. However, from a biologic perspective, candidate polymorphism—and, more so, genome-wide association studies—have provided invaluable insights. This discrepancy highlights the need for multidisciplinary teams involving basic scientists, epidemiologists, and clinicians to undertake this work.

Epigenetic changes in histone proteins and DNA methylation, which control gene expression; proteomics; and gene–environment interactions are important new horizons that epidemiologists hope will better explain disease variation in population studies. The control of DNA transcription—rather than DNA itself—may ultimately prove to be the most appropriate target for population risk stratification and preventive interventions. These research avenues are challenging to fully incorporate into epidemiologic studies because they require tissue samples, the methods change rapidly, the studies require massive sample sizes, or the data are difficult to analyze and interpret, particularly over the course of a lifetime. Clearly, collaborative and multidisciplinary research that includes epidemiologists is critical to moving genetics research forward.

Another challenge is phenotype definition and control group identification. Definition and harmonization of phenotypes across existing studies is cumbersome compared with the rapid pace with which genetic assays can be done. Lack of specificity in phenotype definition may partly explain the limited ability to find associations with common chronic diseases. Control groups should be equally as well characterized as case groups.

Epidemiologists need to be actively involved alongside geneticists in designing these studies, incorporating the rich collection of environmental data and biological samples. Epidemiologists of the future will need to be trained to understand key genetic principles and the functional significance of genetic alterations. Collaborative research across disciplines, institutions, and countries will reign. Collaborative work will need to be rewarded, necessitating new paradigms for professional advancement.

As this work progresses, it is critical that the confidentiality of study participants is protected. Whole genome scanning provides a level of detail that can uniquely identify an individual. Ongoing efforts to educate the public and improve the consenting process are needed, as are more secure systems for handling genetic information.

Pharmacoepidemiology and comparative effectiveness

Medications, vaccines, and medical devices are the mainstay of modern health care. Pharmacoepidemiology applies epidemiologic thinking and reasoning to the evaluation of such therapeutics. Contributions in the past have documented safety risks of drugs (e.g., vaginal adenocarcinoma in young women following diethylstilbestrol exposure in utero, Reye syndrome and aspirin), have refuted safety signals (e.g., no association between bendectine exposure and birth defects), have shown beneficial effects of medications in preventing disease or disability (e.g., folic acid supplementation in early pregnancy to reduce spina bifida in the offspring), and have contributed to knowledge about treatment patterns and appropriateness of treatment (e.g., underuse of beta-blocking drugs after acute myocardial infarction resulting in increased mortality). U.S. and European governmental agencies have recognized the need for more research on the use, safety, and comparative effectiveness of therapeutics, especially given both the cost burden of therapeutics to large government payers and the aging of the population. Following highly publicized withdrawals of drugs from the market, including Propulsid, Rezulin, and Vioxx, the Institute of Medicine called on the U.S. Food and Drug Administration to tighten safety provisions, including requiring manufacturers to conduct postmarketing surveillance for rare, adverse effects. In 2007, legislation mandated many of their recommendations. As the federal government begins to consider health care financing reform, head-to-head comparisons of the benefit-to-harm ratio (comparative effectiveness) and of the cost of various medication options will be of increasing import.

There is now an unprecedented amount of interest by government and industry organizations in supporting pharmacoepidemiologic research. However, the ability to implement the number and quality of evaluations needed in the coming years requires many more formally trained pharmacoepidemiologists than currently exist. The complexity of the research, particularly to distinguish the effect of the therapies from the effects of the underlying disease being treated, requires pharmacoepidemiologists with knowledge of treatments, diseases, the health care setting, and advanced quantitative methods. With only a handful of pharmacoepidemiology academic training programs in the United States and fewer than 30...
worldwide, pharmacoepidemiology faces a capacity crisis.

Factors Shaping Human Health
Global health, multinationalism, and the Millennium Development Goals

In 2000, 190 countries within the United Nations adopted the Millennium Development Goals (MDGs; List 1) as a rallying point for action to achieve a sustainable approach to improving worldwide well-being, particularly by reducing the gap between the world’s “have more” and “have less” countries. Eight years later, some but not enough progress has been made. Although a minority of the goals directly target health, there is growing understanding that poverty and lack of education are inexorably linked to global health and vice versa. Epidemiology is at the core of surveillance that identifies health risks that impede MDG progress (e.g., the entrenchment of poverty in sub-Saharan Africa is in part a result of AIDS and other infectious diseases). Observational studies and community trials test the usefulness of intervention strategies.

A first step toward improving global health must be to recognize the impact of inequalities on sustainability and, consequently, on health and well-being. These limits apply not only to the scope of epidemiology, captured in the 10/90 gap, where 90% of research funding is channeled into diseases affecting only 10% of the world’s population; they also derive from the problems in sustaining genuinely multidisciplinary research, globally.

In a multinational world, in which infectious disease spreads at the rate of air travel and environmental impacts are universal, the health of affluent populations cannot be sustained if inequalities increase. Sustainable development must include effective provision to less economically developed and underserved populations of the tools needed to advance their own health.

Environmental issues

Developments in exposure science, including improvements in detection and quantification technology, have enabled scientists to describe the distribution of chemical, biological, and radiological agents in the environment with increasing rapidity, ease, and precision. New monitoring technologies and biomarker measures better characterize individuals’ exposures. Coupled with the evolving ability to characterize individual differences in genetic makeup, these tools are revolutionizing the study of risk and predisposition to disease.

Improved analytic technology has facilitated differentiation and speciation of chemical compounds, such as characterizing differences between organic and inorganic arsenic (i.e., the latter but not the former is believed to cause cancer). One application has led to the recognition of environmental sources (e.g., sulfur dioxide and nitric oxide in auto emissions) for adverse health effects. Indeed, population-based studies demonstrated the substantial impact of air pollution on cardiovascular disease, whereas laboratory studies initially missed air pollution’s impact on the respiratory system.

Improved methods for studying environmental impacts on human populations have become available. These include the following:

- spatial analytic techniques (e.g., geographical information systems);
- temporal analytic techniques (e.g., analyzed with techniques such as Poisson regression);
- case-crossover study designs; and
- exposure analysis at levels from the individual to the community (using hierarchical Bayesian models).

More broadly, the global environment is in critical decline. Despite increasing rhetoric to the contrary, the pace and intensity of human affairs will likely adversely impact environmental sustainability and the health and well-being of future generations.

Epidemiology is responding to this challenge with a relatively new subspecialty called eco-epidemiology, which focuses on the relationship between human health and the dynamics of global ecological change. The goal is to predict the likelihood of future scenarios under various assumptions about ongoing trends. Predictive systems models (described above) are used and include dynamic environmental data, geospatial techniques, scenario analysis, and participatory methods. Eco-epidemiology will help scientists to identify key elements of complex systems and in particular systemic (“upstream”) drivers and proximate (“downstream”) exposures that may be targeted for intervention.

Disease and lifestyle—The epidemics of obesity and diabetes mellitus

Obesity and one of its major consequences, diabetes, are enormous threats to human health. Current surveillance estimates suggest that about 1.6 billion people worldwide (one fifth of the population) are overweight and 400 million are obese. In the United States, the rise of obesity is depicted by maps showing that in 1985, no states reported having obesity rates of over 15%, whereas in 2005, no states reported that their rate of obesity was less than 15%. Diabetes has been increasing worldwide in parallel with increases in obesity. With greater levels of obesity and diabetes come higher rates of the most common causes of mortality: cardiovascular disease and cancer.

To say that an ounce of prevention is worth a pound of cure is an adage particularly appropriate to obesity. Once individuals develop diabetes, weight loss is particularly difficult because many of the medications used to maintain glucose control can increase weight. Lifestyle interventions prior to the development of diabetes, including dietary modification and physical activity, as well as medications such as orlistat, metformin, acarbose, and rosiglitazone, all reduce weight and reduce the risk for developing diabetes.

Unfortunately, only a fraction of those who attempt to maintain weight loss are successful. The best strategy is never to become obese. Scientists and physicians know remarkably little about the antecedents to childhood overweight and

List 1

Millennium Development Goals

1. Eradicate extreme poverty and hunger
2. Achieve universal primary education
3. Promote gender equality and empower women
4. Reduce child mortality
5. Improve maternal health
6. Combat HIV and AIDS, malaria, and other diseases
7. Ensure environmental sustainability
8. Develop a global partnership for development
obesity. Is it access to high-calorie foods (e.g., soft drinks, fast foods, trans fats, large portion sizes), lack of physical education in the schools, paucity of safe outdoor play places, too much time spent watching TV and playing computer games, exposure to toxic substances? Future epidemiologic studies will need to examine obesity-causing factors in the environment. Intervention studies using multiple lifestyle modalities and innovative approaches to engineering healthier environments must be tested.

Demographics—The epidemiology of aging
The successes of epidemiology and public health are perhaps most apparent in the rapid increase in the number of people who now survive to old age. At the same time, the aging of the population is increasing health care needs, health care expenses and other costs, and stresses on families and communities. The only way to offset this societal burden is to improve active life expectancy by reducing disability and dementia. The incidence of disability at any given age in the United States has decreased, but the sheer number of adults reaching old age has resulted in an increase in the number of people needing care. Disability in old age is heterogeneous, is often due to the co-occurrence of chronic conditions (e.g., arthritis or dementia), can be catastrophic or gradual, and can be progressive or fluctuating. Recent work shows that disability can be detected years in advance by observing subtle impairments. For example, grip strength in midlife, endurance for walking 400 meters, cognitive speed, and ability to sustain attention can identify high-risk individuals who should be targeted for prevention efforts.

Large, community-based studies of older adults are ideal for assessing the multiple co-occurring conditions that contribute to functional decline. Methods that assess the joint impact of multiple risk factors, account for changes over time, and incorporate assessments of competing risk are developing. These include multilevel modeling and predictive modeling, which both attempt to describe complexity and interactions of systems at the basic, organ, personal, and social levels.

Chronic inflammation, oxidative stress, and hormonal factors can explain part of the strong association of age itself with disease risk. A better understanding of senescence may lead to new risk factors, therapeutic targets, and treatment strategies. These studies should be conducted in cohorts of contemporaries so that the tremendous changes in the environment of successive birth cohorts can be better understood.

Clinical trials have included very few adults over age 70. With the rapid growth in the oldest old, clinical trials may need to be repeated in this cohort. The potential for treatments focused on underlying aging processes has increased and will require new clinical trials that consider physical and cognitive function as primary outcomes. Future research will require a careful balance of resources across generations, as well as across traditionally marginalized groups among whom disease and premature mortality rates remain elevated.

Infectious diseases epidemiology
Among the great successes of public health and epidemiology are major reductions in infectious and communicable diseases. Yet, the emergence of microbial resistance and pandemics from heretofore unknown agents such as HIV present great new challenges.

Rapid advances in genetic, molecular, and cellular biologic methods have allowed scientists to discover and refine knowledge about disease agents, disease agent-host interactions, and host susceptibility. Methods such as DNA amplification and sequence identification play a role in new conceptions of causality, replacing Koch’s postulates (from the early ages of bacterial research) in a world wherein for many agents we have neither culture nor nonhuman models. For instance, the discovery of a novel agent as the cause of Kaposi sarcoma by P.S. Moore and Y. Chang was at first “merely” a report of a conserved nucleic acid sequence found by subtraction analysis. Implementation by clinical laboratories of heretofore advanced research methods allows direct characterization of organism strains and thus identifies particularly pathogenic agents (e.g., methicillin-resistant Staphylococcus aureus), improves disease surveillance (e.g., fingerprinting of E. coli O157:H7 to identify multistate outbreaks), and identifies infectious agents as causes of diseases previously thought to be noninfectious (e.g., H. pylori and gastric cancer, human papillomavirus, cervical cancer). In the future, the distance between academic and practice-based epidemiologists needs to be substantially narrowed.

Several trends will influence future control of infectious diseases. First, our growing global economic interdependence, with exchanges of goods, services, and persons, allows infectious diseases to rapidly “hitchhike” across the globe. Complex systems models (described above) allow prediction of disease spread as well as evaluation of prevention interventions (such as social isolation during an influenza outbreak). Such models incorporate

- agent characteristics;
- geospacial, economic, genetic, and population dynamics of hosts (both animal and human);
- host susceptibilities; and
- multiple environmental influences.

International and intergovernmental agreements related to disease surveillance, prevention, and control measures are few and vary among nations and regions, limiting surveillance and safety enforcement. Thus, for example, foodborne outbreaks in the United States—those related to new “global” food distribution practices such as the importation of raw foodstuffs, those related to the wide dissemination of single-sourced or improperly handled contaminated raw foodstuffs, or those related to multiple food products—are ongoing problems. Ultimately, international and intergovernmental public health agreements, increased sharing of information, and greater enforcement across jurisdictional lines will need to be strengthened to protect the health of the public.

Secondly, related to the spread and control of infectious disease, is the fact that the world faces the threat of bioterrorism. Initiated by the events of September 11, 2001, and the weapons-grade anthrax powder sent in letters to
Epidemiologists have quite a world of discovery ahead, including bacterial-human symbiosis. Work using polymerase-chain-reaction-based analyses of 18S ribosomal DNA suggest a massive “microbiome” within humans—perhaps more than 100 times the number of genes as our own genome of 2.85 billion base pairs. This complex flora, particularly in the human gut, appears involved in many functions, including modulation of host energy metabolism, immune response, developmental programs, vitamin production, and xenobiotic (drug) metabolism.

**Conclusions**

Epidemiologists are poised to serve the public interest on the basis of ever-improving, methodologically sound science. They face a series of unfolding population-based health challenges, such as aging, emerging infections, obesity, poverty, and environmental degradation. To develop an evidence base to overcome the health effects from these challenges and take full advantage of the opportunities, epidemiologists must have access to data, public support, integration with other scientific disciplines, and enhanced opportunities for training.

**Dr. Ness** is a representative of the Joint Policy Committee, Societies of Epidemiology and Dean, The University of Texas School of Public Health, Houston, Texas.

**Dr. Andres** is a representative of the Joint Policy Committee, Societies of Epidemiology and Vice President, Pharmaceutical Epidemiology and Risk Management, RTI Health Solutions, RTI International, Research Triangle Park, North Carolina.

**Dr. Gaudio** is a representative of the Joint Policy Committee, Societies of Epidemiology and senior immunization and Maternal and Child Health Medical Epidemiologist, Public Health Division, Public Health Division, Department of Human Services, State of Oregon and Department of Public Health and Preventive Medicine, Oregon Health and Sciences University, Portland, Oregon.

**Dr. Newman** is a representative of the Joint Policy Committee, Societies of Epidemiology and Professor of Epidemiology and Medicine, Department of Epidemiology, University of Pittsburgh School of Public Health, Pittsburgh, Pennsylvania.

**Dr. Soskolne** is a representative of the Joint Policy Committee, Societies of Epidemiology and Professor of Epidemiology, Department of Public Health Sciences, School of Public Health, University of Alberta, Edmonton, Canada.

**Dr. Stürmer** is a representative of the Joint Policy Committee, Societies of Epidemiology and Associate Professor of Epidemiology, Department of Epidemiology, University of North Carolina Gillings School of Global Public Health, Chapel Hill, North Carolina.

**Dr. Wartenberg** is a representative of the Joint Policy Committee, Societies of Epidemiology and Professor, Environmental Epidemiology and Statistics, Department of Environmental and Occupational Medicine, University of Medicine and Dentistry of New Jersey—Robert Wood Johnson Medical School, Piscataway, New Jersey.

**Dr. Weiss** is a representative of the Joint Policy Committee, Societies of Epidemiology and Professor in the Department of Preventive Medicine and Community Health, University of Medicine and Dentistry of New Jersey—New Jersey Medical School, Newark, New Jersey.

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