

Time for a Creative Transformation of Epidemiology in the United States

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THE LATE US SENATOR (D, KY) AND VICE PRESIDENT Alben Barkley enjoyed telling the story of his encounter with a disgruntled constituent. “I recalled how I had helped get an access road built to his farm, how I had visited him in a military hospital . . . , how I had assisted in securing him veteran benefits, . . . how I had got him a disaster loan. . . . Surely you remember all these things I have done for you?’ ‘Yeah,’ the fellow said, ‘I remember. But what have you done for me lately?’”^{1(pp84,85)}

In 1948, when Barkley was elected vice president (under President Harry S Truman), the National Heart Institute launched the Framingham Heart Study, an innovative and now internationally recognized population-based epidemiological project that brought together prominent scientists with members of the community of Framingham, Massachusetts. Thirteen years later, in 1961, the Framingham investigators introduced the term *risk factor* into the medical lexicon.² They described the links between incident coronary heart disease and hypertension, hypercholesterolemia, and electrocardiographic left ventricular hypertrophy. Later reports described other risk factors, including smoking and diabetes. These early discoveries led to further research in risk factor elucidation and management, management that has contributed to the remarkable 50-year decline in cardiovascular mortality in the United States.³

Yet today, despite these extraordinary contributions, the value of epidemiology is questioned. Critics cite excess expense,⁴ repudiated findings, studies that offer small incremental knowledge, inability to innovate at reasonable cost, and failure to identify research questions with the greatest merit.⁵ At a time of unprecedented budgetary constraints, these critics wonder what epidemiology has done for medical science lately. A survey of the field suggests 2 answers: much and not enough.

That epidemiology continues to provide important knowledge is evident in 2 reports published in this issue of JAMA. In one report, Safford and colleagues⁶ analyzed the course of more than 24 000 participants in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study. Compared with white men and women, black men and women, who comprised more than 40% of the cohort, were more likely to smoke; be obese; and have diabetes, hypertension, and renal dysfunction. During 4 years of follow-up, black men and women had substantially higher rates of fatal coronary heart

disease; in regression models, these higher rates were largely accounted for by the risk factors. The REGARDS findings are consistent with other reports of persistent health disparities⁷ and highlight the likely important role of risk factors, some of which are reversible, among some racial/ethnic groups.

In another report in this issue of JAMA, Daviglus and colleagues⁸ describe the prevalence of cardiovascular risk factors in a large, diverse population-based cohort of US Hispanic and Latino individuals, including more than 15 000 participants of Cuban, Dominican, Mexican, Puerto Rican, Central American, and South American origin. The burden of risk factors was high: 80% of men and 71% of women had at least 1 risk factor. Persons of Puerto Rican origin carried an especially high burden, with 25% having at least 3 risk factors. Risk factor burden was also associated with levels of education, immigration history, and preferred language.

The reports by Safford et al⁶ and by Daviglus et al⁸ send a powerful and sobering message: despite 50 years of epidemiological knowledge and despite numerous therapeutic advances, risk factor burdens among minority populations are unacceptably high and consequential. Both reports offer, with appropriately cautious language, how their findings might translate into clinical and public health interventions that could reduce disparities. Still, critics of the US biomedical research enterprise suggest that not enough is being done. More specifically, they wonder why researchers are not working more closely with patients, clinicians, and policy makers to improve public health in a more direct way.⁹ Some authorities note that clinical and population research takes place within separate spheres from clinical care and public health and that long-standing US models for governing and executing epidemiological studies are being eclipsed by non-US studies that are much larger, yet considerably less expensive.¹⁰

How then can researchers more effectively work across the boundaries prescribed by traditional stakeholder roles—epidemiologists, clinicians, patients, policy makers, funders, regulators, food and drug manufacturers, urban planners, and others—where such boundaries might be impediments to scientific discoveries and the translations and uses of such discoveries that will best improve public health?

One approach to strategic decision making, results-based accountability, offers a transformative principle for working across boundaries.¹¹ First, define the conditions of well-being for which no single stakeholder can be solely accountable and then work

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backward, together, to determine the best means for achieving those conditions of well-being. In this case, start with racial/ethnic disparities in cardiovascular health and work backward together analyzing the factors driving disparities and together hypothesizing and testing the best comprehensive strategies to reduce the disparities. An important consideration involves leveraging ongoing technological, social, economic, and political trends. This kind of collaborative ends-to-means strategic decision making allows stakeholders to transcend their individual roles and, in so doing, fosters greater innovation, including redefining roles and boundaries among stakeholders. By engaging all stakeholders, including researchers in cardiovascular epidemiology, in this kind of strategic approach, creative, substantial, and timely transformations will follow. Such transformations will likely include refocused scientific questions, centralized and integrated governance, different types of exposure and outcome measures, and embedded clinical and policy trials.

Refocused Scientific Questions. Simple canonical pathways do not adequately explain disease incidence and burden; the few such pathways, such as the link between low-density lipoprotein cholesterol and coronary heart disease, that do reflect “low-hanging fruit” were “picked” long ago. Determinants of most chronic diseases act within complex, often scale-free networks made up of a relatively small number of “hubs” that are extensively linked to many more relatively isolated determinants and that are remarkably similar in structure and function at genetic, molecular, cellular, clinical, environmental, and societal levels.¹² Determining how these complex networks contribute to disease and how best to mitigate these effects will require studies with enormous sample sizes.

Centralized and Integrated Governance. The UK Biobank investigators successfully enrolled and assessed in-depth phenotypes of more than 500 000 people at a cost of \$100 million (or \$200 per study participant).¹³ In lieu of distributed governance among multiple field sites, the UK Biobank used a centralized unit that oversaw the activities of mobile, flexible assessment centers. The project also was integrated within the UK National Health Service, enabling low-cost, reliable follow-up for incident clinical events. One concern is whether such a structure would work in the United States given its highly fragmented health care system, but the development of large integrated systems that have robust electronic health record infrastructures provide hope that such efficient research is possible in the United States.

Exposure and Outcome Measures. According to some, the digital revolution is being largely missed by US medicine.¹⁴ As increasing numbers of persons become digitally connected, such as via the web or smartphones, and as increasing numbers of health systems adopt electronic health records, epidemiological researchers will need to determine how best to leverage these technologies. It is easy to dismiss these technologies as yielding data that are of inferior quality to data now obtained by in-person “research-grade” examinations. But it is important to recall the histories of previous “disruptive technologies,” like the personal computer and digital camera, that initially were dismissed as inferior but later largely eclipsed older methods.

Embedded Clinical and Policy Trials. The US clinical trial enterprise is facing challenges in part due to the excessive expense and complexity of trials. Some investigators, particularly in Europe, are conducting “clinical registry trials,” embedded within preexisting observational registries. These trials can relatively easily enroll large numbers of patients at low cost. In the United States, some clinical and policy trials have already been successfully embedded in preexisting clinical registries or administrative databases.¹⁵

The reports by Safford et al⁶ and Daviglius et al⁸ demonstrate the ongoing power of epidemiology. These reports should stimulate results-based transformations of epidemiological science that, in consonance with digital revolution, are better, faster, cheaper, and more responsive to current needs. These transformations will occur if epidemiologists and their supporters join forces with many other stakeholders. This is already happening to some degree with the Million Hearts Initiative and the National Program to Reduce Cardiovascular Risk.¹⁶ These transformations will also ensure that epidemiology will have much to give, whether lately or later.

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