Measuring the Risks and Causes of Premature Death: Summary of a Workshop

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Summary of Workshops

Holly G. Rhodes, *Rapporteur*

Committee on Population
Division of Behavioral and Social Sciences and Education

Board on Health Care Services
Institute of Medicine

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This report summarizes the proceedings of two workshops convened in September 2013 and September 2014 to consider issues in the measurement of the risks and causes of premature death. The workshops were sponsored by the National Institute on Aging (NIA) and convened by the Committee on Population (CPOP) in the Division of Behavioral and Social Sciences and Education (DBASSE) of the National Research Council (NRC) in cooperation with the Institute of Medicine (IOM).

The workshops were organized by a seven-member steering committee composed of experts in the fields of demography, population health, epidemiology, and health measurement. The committee was cochaired by Linda Waite of the University of Chicago in 2013 and Eileen Crimmins of University of Southern California in 2014. The committee included Christine Bachrach, University of Maryland; Lisa Berkman, Harvard University; Majid Ezzati, Imperial College London; Christopher Murray, University of Washington; and Samuel Preston, University of Pennsylvania. The committee provided guidance in developing the workshop agendas, securing expert presentations, and facilitating the conduct of the workshops. The committee also benefited from the input of Richard Suzman, National Institute on Aging, prior to and during the two workshops. Although the steering committee members played a central role throughout, they did not actively participate in writing this summary.

The presentations during the workshops provided the basis for lively and informative discussions. In addition to presentations by several steering committee members, we greatly appreciate the contributions of Robert Anderson, Centers for Disease Control and Prevention; Mark Cullen, Stanford University; Jessica Ho, Duke University; Michael McGinnis, Institute of Medicine; Ali Mokdad, University of Washington; Haidong Wang, University of Washington; and Theo Vos, University of Washington.

The steering committee acknowledges the work of the staff of the NRC in organizing the workshops and this report. Thomas Plewes, CPOP director, provided overall direction and guidance for the project. Holly Rhodes of the Board on Science Education of DBASSE served as rapporteur for this summary. Kevin Kinsella and Danielle Johnson of CPOP provided assistance with logistical details and various aspects of report preparation. Paula Whitacre edited the report, and Kirsten Sampson Snyder orchestrated the review process. The steering committee also is grateful to Linda Ettinger and other staff of the Institute for Health Metrics and Evaluation in Seattle, Washington, for arranging meeting space and logistical support for the 2014 workshop.

This workshop summary was reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the Report Review Committee of the NRC. The purpose of this independent review is to provide candid and critical comments that assist the institution in making its report as sound as possible, and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process.

The panel thanks the following individuals for their review of this report: Jessica Y. Ho, Population Research Institute and Department of Sociology, Duke University; Richard G. Rogers, Institute of Behavioral Sciences, University of Colorado Boulder; and Michael A. Stoto, Health Systems Administration and Population Health, School of Nursing and Health Studies, Georgetown University.

Although the reviewers listed above provided many constructive comments and suggestions, they were not asked to endorse the conclusions or recommendations, nor did they see the final draft of the report before its release. The review of this report was overseen by Mark D. Hayward, Population Research Center, Department of Sociology, University of Texas at Austin. Appointed by the NRC, he was responsible for making certain that

the independent examination of this report was carried out in accordance with institutional procedures and that all review comments were carefully considered. Responsibility for the final content of the report rests entirely with the author and the NRC.

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Steering Committee for the Workshops
on Measuring the Risks and Causes of
Premature Death

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1

Introduction

BACKGROUND

In 1993, Michael McGinnis and William Foege published work in the *Journal of the American Medical Association* on the actual causes of death in the United States (McGinnis and Foege, 1993). A key finding showed that about 40 percent, or nearly half of all deaths, could be explained by factors that were preventable given current knowledge, many of which were behavioral in nature. These preventable factors included tobacco, diet and activity patterns, alcohol, microbial agents, firearms, sexual behaviors, motor vehicles, and illicit drug use. McGinnis and Foege gathered these data from the literature and other sources using conservative rounded estimates or actual counts of factors when they existed. This seminal work garnered a great deal of attention and highlighted the significant proportion of deaths due to preventable factors. Although this work focused on all deaths, McGinnis explained at the 2013 workshop the importance of paying particular attention to deaths that are "clearly early," both from an analytical as well as a societal perspective. Ultimately, McGinnis argued, understanding these early deaths, as well the causes of morbidity and loss of quality of life, are important to public health and policy. He stated, "Unfortunately, we are not spending our resources in a very effective or efficient manner if we want to improve the health of the population."

Since that initial work in the early 1990s, Steven Schroeder published a provocative review paper (Schroeder, 2007) that focused on document-

ing and explaining the factors that explain the poor health of people in the United States, using international rankings of health status to assess the impact of five domains—genetics, social circumstances, environmental exposures, behavioral patterns, and health care shortfalls. Using the data assembled by McGinnis and Foege (1993), Schroeder found that "medical care played a relatively minor role" (p. 1222) in reducing early deaths, accounting for only 10 percent of premature deaths (p. 1225) and suggesting that "if the entire U.S. population had access to excellent medical care—which it does not—only a fraction of these deaths could be prevented" (p. 1222). The review concluded that "the greatest opportunity to improve health and reduce premature deaths lies in personal behavior" (p. 1222). The prevalence of causes of death associated with personal behaviors has been variously estimated. One study concluded that approximately 40 percent of all deaths in the United States are associated with four health behaviors: tobacco use, unhealthy diet, physical inactivity, and problem drinking (Mokdad et al., 2004, 2005).

More recent work employing a broad perspective that considered both downstream, proximate determinants of health and more upstream distal ones has informed several other major health studies, including the World Health Organization's Commission on the Social Determinants of Health (2008), the "Marmot Review" of health in the United Kingdom (Marmot, 2010), and the Robert Wood Johnson Foundation's Commission to Build a Healthier America in the United States (Braveman and Egerter, 2008).

Two recent National Research Council (NRC) and Institute of Medicine (IOM) reports have put these findings into sharp relief, reporting that the United States spends more on health care than any other country, but its health outcomes are "no better" than those of other rich nations. In fact, the situation is far worse: Americans are in poorer health and die earlier than people in other high-income countries (National Research Council, 2011; National Research Council and Institute of Medicine, 2013).

The 2011 NRC report *International Differences in Mortality at Older Ages: Dimensions and Sources* presented a descriptive analysis of causes of death but also moved from "description to identifying the underlying determinants of the observed differences, a necessary first step toward ultimately developing an integrated model of causal processes" (National Research Council, 2011, p. 143). The NRC Panel on Understanding Divergent Trends in Longevity in High-Income Countries, the group that conducted the analysis, examined a number of possible risk factors and considered how differences among countries in exposure to these risk factors might

account for observed disparities in improvement in life expectancy. For some factors, comparable cross-country data exist on the current levels of risk; for others, surprisingly little direct evidence can be brought to bear. The report concluded that few countries are conducting systematic surveillance of health risk factors, so directly comparable data even for the present often are not available for a large number of countries, and for a substantial number of countries, data are available for almost no risk factors for the 50-year period examined for this study. For example, much is known about current international differences in smoking patterns and levels of obesity, but far less about international differences in stress, physical exercise, or social networks. Moreover, very little is known about changes over time and across countries in lifetime exposures and behaviors for most risk factors. The dynamic nature of the relationship between mortality and some of the major risk factors is another important consideration.

The panel adopted the strategy of establishing the strength of the evidence for a number of the most commonly proffered explanations for differences in life expectancy between the United States and other high-income countries—for example, that these differences are the result of a particularly inefficient U.S. health care system or that they are a function of poor health behaviors in the United States, particularly with respect to smoking, overeating, and failing to exercise sufficiently. The panel also considered differences among countries in levels of social integration and in socioeconomic inequality. Ultimately, all of these potential risk factors will need to be examined in an integrated framework across the entire life course, taking account of the effects of differences in socioeconomic status, behavioral risk factors, and social policy, as well as effects across particular cohorts and periods.

The 2013 NRC/IOM report cited above, *U.S. Health in International Perspective: Shorter Lives, Poorer Health*, considered these issues over the entire life course, concluding that even U.S. newborns have a shorter life expectancy than those in other high-income countries and that premature death is not just associated with the diseases of aging. In attempting to account for this pervasive pattern, the NRC/IOM Panel on Understanding Cross-National Differences Among High-Income Countries found clues in almost every class of health determinants it considered, beginning with the obvious difference between health care in the United States and other countries—the lack of universal health insurance coverage. But the U.S. health care system has many other differences, such as a weaker foundation in primary care and greater barriers to access and affordable care.

The report narrowed in on individual behaviors and found that although Americans are currently less likely to smoke (due to successful tobacco control efforts) and may drink alcohol less heavily than adults in peer countries, they have a greater propensity for a variety of other unhealthy behaviors. As summarized in the report, Americans consume more calories per capita, abuse more drugs, are less likely to fasten seat belts, have more traffic accidents involving alcohol, and own more firearms than do people in other high-income countries.

The report also concluded that socioeconomic conditions matter greatly to health. Such factors as income inequality and high rates of relative poverty, relative lack of social mobility, and failure to keep pace with improving educational outcomes in peer countries and emerging economies were seen to play a role in producing less favorable health outcomes in the United States than in other countries (OECD, 2011). The NRC/IOM panel recognized that relevant scientific evidence was at once vast (e.g., for understanding the determinants of health) and scant (e.g., for establishing causality for the U.S. health disadvantage). It called for an international collaboration to collect prospective data and devise innovative study designs to pursue new lines of scientific inquiry that get at the roots of the U.S. health disadvantage.

One way to approach these issues is to examine recent data on the risks and causes of premature mortality, including the important scientific and technological advances affecting the prevalence of particular causes of premature mortality over the past two decades. At the workshop, Richard Suzman of the National Institute on Aging argued that despite the mounting research findings and the high-profile reports summarized above, public health and particularly the substantial contributions of social and behavioral factors to premature mortality have not received the attention they deserve.

THE WORKSHOPS AND THIS REPORT

The Committee on Population of the National Research Council at the National Academies conducted two workshops to address the data sources, science, and future research needs to understand the causes of premature mortality in the United States on behalf of the National Institute on Aging of the National Institutes of Health. The first workshop was held in September 2013, with a follow-up workshop held in September 2014. The purpose of the workshops, organized in cooperation with the Institute of Medicine, was to examine previous work in the field in light of newly

emerging data sources, particularly data generated as part of the work of the NRC Panel on Understanding Divergent Trends in Longevity in High-Income Countries (National Research Council, 2011) and the NRC/IOM Panel on Understanding Cross-National Differences Among High-Income Countries (National Research Council and Institute of Medicine, 2013).

Workshop participants considered the state of the science of measuring the determinants of the causes of premature death and, to a limited extent, the related constructs of disability and health loss. They discussed the availability and quality of data sources and identified future courses of action to improve the understanding of the causes of premature death. Presenters shared their approaches to and results of measuring premature mortality and specific risk factors, with a particular focus on those factors most amenable to improvement through public health policy.

The agendas were developed in accordance with the statement of task (see Box 1-1) and are included in Appendix A. Because a workshop is not a consensus activity, no recommendations or other consensus findings are

BOX 1-1
Statement of Task

An ad hoc steering committee will organize a public workshop on updating the classification of the determinants of the real causes of premature death in the United States. The purpose of the workshop, which will be organized in cooperation with the Institute of Medicine, will be to review previous work in the field in light of new data generated as part of the work of the NRC Panel on Understanding Divergent Trends in Longevity in High-Income Countries (National Research Council, 2011) and the NRC/IOM Panel on Understanding Cross-National Differences Among High-Income Countries (National Research Council and Institute of Medicine, 2013). The committee will develop an agenda, select and invite speakers and discussants, and moderate the discussions. The workshop will feature presentations that will consider the state of the science of measuring the determinants of the causes of premature death, assess the availability and quality of data sources, and chart future courses of action to improve the understanding of the causes of premature death. The products of the workshop will be a verbatim transcript in 508-compliant format and a published individually authored workshop summary prepared by a designated rapporteur.

offered in this report. This report offers a summary of the views expressed during the workshop meetings; therefore, all views expressed are those of the workshop presenters or other workshop attendees.

This report summarizes the presentations and discussions at both the 2013 and 2014 workshops. Chapter 2 presents a summary of the data sources and a description of the methodological approaches and issues that presenters described in their work on premature mortality. Chapter 3 summarizes presenters' current data from large international studies of premature mortality or sources of variation in mortality and risk within the United States. Finally, Chapter 4 offers a look toward the future with a summary of suggested improvements offered by some participants for data sources and methodology and for next steps for research.

2

Data Sources and Methodology in the Study of Premature Mortality

Certain behaviors, exposures, and predispositions place people at risk for early death or poor health outcomes. The impetus for the workshops was to better understand the risk factors most amenable to prevention and health policy efforts, primarily behavioral risk factors. The definition of "early" can vary. Michael McGinnis' initial work focused on deaths prior to age 75, but later work has focused on deaths before age 80. The World Health Organization's Global Burden of Disease compares years of life lost against a reference age of 86, or the highest average lifespan of a country with a population over 5 million. Other studies have focused on survival to age 70. The implications of these definitions, sources of data, and other methodological considerations are the focus of this chapter.

REVIEW OF THE METHODOLOGY FOR THE 1993 ESTIMATES OF THE ACTUAL CAUSES OF MORTALITY

As described in Chapter 1, McGinnis and Foege (1993) and later Schroeder (2007) published work on the causes of premature mortality. At the 2013 workshop, McGinnis revisited this work, stating that the five domain determinants—genetic predisposition, social circumstances, environmental exposures, behavioral choices, and health care shortfalls—"represent, from my perspective at least, essentially the domains that work independently and collectively to shape our health prospects." The relative

contribution of these domains naturally varies with changing circumstances, he noted. Data used to produce these estimates come from various sources, including research published in the *Journal of the American Medical Association*[1] and by the Centers for Disease Control and Prevention,[2] with genetic predisposition estimated from the residual. McGinnis stressed that these estimates are not only very approximate but also are quite dynamic and in need of updating and further study. Although risk factors are most often studied in isolation, tracking these factors and their interactions in a societal context might yield a better understanding about the real sources of problems. McGinnis indicated a need "to move our sense of what the vital statistics for the nation are away from the autopsy table and into society, as a whole, so that we have a much better means and reason for tracking the real sources of problems and opportunities that confront Americans."

The following sections describe various approaches to measuring premature mortality and associated risk factors presented at the workshops.

APPROACHES TO MEASURING PREMATURE MORTALITY AND RISK FACTORS

Samuel Preston, University of Pennsylvania, described two basic approaches to identifying deaths attributable to a particular type of behavior. The first is categorical based on the use of cause-of-death assignments. For causes such as homicide or alcohol poisoning, the proximate cause-of-death attribution is straightforward and easy to interpret. In these cases, researchers can compare the differences in mortality between countries by particular causes. The second approach involves causes that are multifactorial, such as cardiovascular disease. These multifactorial causes of death become increasingly important the older the population. For these causes, cause-of-death data often do not help to identify behavioral risk factors. Therefore, researchers use risk factor exposure data to combine a set of relative risks associated with a given behavior, such as smoking, with the population distribution of that behavior, in order to estimate the percentage of deaths that would be averted if everyone were a nonsmoker. This "what-if" approach to identifying amount of risk is also called the counterfactual or cause-deleted approach.

[1]See U.S. Burden of Disease Collaborators (2013).

[2]See http://www.cdc.gov/nchs/fastats/alcohol.htm [November 2013].

During his presentation in 2014, Theo Vos, Institute for Health Metrics and Evaluation, shared his views on these two approaches. A benefit of the categorical approach is that a single underlying cause of death is assigned. All causes total 100 percent and proportions are easily assigned. This approach avoids a criticism of disease-specific estimations where numbers of deaths attributed to the disease of interest are often overly inclusive. However, the disadvantage of the categorical approach is that it is not always easy to assign an underlying cause of death. Variations in medical coding practices pose an additional methodological challenge to making estimates comparable over time and between geographies, according to Vos. Similar challenges of ascertainment of cause of death apply in a counterfactual approach to estimating causes of death, he argued.

Researchers have used these two broad approaches to understand and compare the risks of premature mortality. However, they have also conceptualized and measured premature mortality in various ways within these approaches. Presenters described these approaches, as summarized below.

Categorical Approaches

The assigned cause of death is key information used in the categorical approach to measuring premature mortality. Robert Anderson, National Center for Health Statistics (NCHS), described the vital statistics data available to researchers, the data's applications and limitations, and his suggestions for improvement. The responsibility for death registration in the United States lies with the states. In some cases, cities such as New York City have their own systems. Funeral directors generally provide demographic and personal information, and physicians, medical examiners, and coroners provide the cause-of-death information. These records from various states are compiled into the National Vital Statistics System, which then generates national statistics. In return for the records, the states receive standards, training, and some funding.

A standard death certificate was provided to states in 2003. By 2010, a subset of 36 states or other areas was using it, which has implications for comparability and completeness of the national data, Anderson noted. One item on the standard form relates to whether the death was tobacco related. The physician who certifies the death can enter "yes," "no," "probably," or "unknown." As the number of adopting states increased, so did the numbers of tobacco-related deaths. Although the form is now better at detecting tobacco-related deaths, it probably still underestimates these deaths because

nearly 50 percent of the time, respondents check "unknown." In some cases, this is because the certifying physician does not know, but in other cases there may be insurance-related ramifications from checking "yes" that may make some physicians reluctant to provide this information on the death certificate.

Anderson indicated that data from death certificates tend to underestimate obesity-related deaths, primarily because physicians do not see that condition as the proximal cause. Education, consisting of highest degree attained, is currently the only indicator of socioeconomic status available in the vital statistics system. Education was previously measured in years, so comparability between versions of the certificate is an issue. Occupation/industry was provided until 1999 when it was dropped as a reporting requirement from the items collected by NCHS. Data on income are not available. The National Vital Statistics System contains accurate and reliable counts of deaths due to firearms, drugs, and alcohol. The system does not capture alcohol-related motor vehicle fatalities.

Electronic health and death records and the potential for linkages between them and other sources of data have the potential to increase the timeliness, amount, and quality of data on the risk factors for premature mortality, Anderson said. Currently, only a portion of the states and jurisdictions using the standard form are registering them electronically. In many cases, the funeral director uses an electronic system but the certifying physician does not. As use of electronic systems increases, however, Anderson argued that the potential exists that certifying physicians could have access to a decedent's medical history through the electronic medical record that could enable improved information about cause of death. It may also be possible to populate certain fields on the death certificate with information from electronic health records, reducing the burden on respondents. These possibilities are being examined in an NCHS pilot study in Utah.

The National Death Index[3] and the National Longitudinal Mortality Study[4] also afford opportunities for linkage with other datasets like the Current Population Survey. Indian Health Service (IHS) records and the Census Bureau are also potential sources of data on the American Indian population. Anderson stated that "the reporting of American Indian race is very poor on the death certificate. It is about 30 percent underreported. So our death rates are way, way too low based on vital records data." Linkages between mortality data and both IHS and census data are being created

[3]See http://www.cdc.gov/nchs/ndi.htm for more information [November 2014].

[4]See https://www.census.gov/did/www/nlms/ for more information [November 2014].

to improve the assessment of American Indian mortality, according to Anderson.

Counterfactual/Cause-Deleted Approaches

Presenters described various ways to conceptualize premature mortality using counterfactual methodology: years of life lost (YLL), life expectancy/longevity, health loss, years lived with disability (YLD), and disability adjusted life years (DALY). One of the largest efforts using these methods is the World Health Organization's Global Burden of Disease (GBD) Study, which applies this methodology to collaborative efforts to systematically understand the risks associated with premature death and health loss around the world.

Years of Life Lost

Christopher Murray, University of Washington, and Vos described YLL as a method of conceptualizing premature mortality.[5] The reference life table chosen for GBD 2010 and beyond defines the ideal life expectancy at each age. The life table is based on the lowest mortality rates at each age observed in any country with a population over 5 million. The life expectancy at birth in this standard life table is 86 years. Vos noted that at any age, even above 100 years, some YLL accrue. This standard life expectancy was updated from a previous standard with life expectancy at birth of 80 for men and 82.5 for women.

Murray explained the counterfactuals examined using the GBD. For certain factors, like smoking or intimate partner violence, zero exposure is the ideal. However, for other factors, like blood pressure or body mass index (BMI), Murray and his colleagues identified the theoretical minimum risk distribution using population-based means. For example, they assumed a mean systolic blood pressure of 115 mmHg and a BMI of 21 kg/m^2. Overall, for each risk factor, GBD researchers defined these "theoretical minimum risk exposure distributions" and used them in subsequent counterfactual analyses to determine the YLL attributable to each risk factor.

Jessica Ho, Duke University, described the use of cause-deleted methods as applied by the Panel on Understanding Cross-National Differences

[5]Further information on YLL can be found at http://www.who.int/whosis/whostat2006YearsOfLifeLost.pdf [November 2013].

(National Research Council and Institute of Medicine, 2013). According to Ho, this approach allows researchers to estimate the contribution of specific causes of death to the U.S. disadvantage in YLL relative to comparison countries. Each analysis is performed separately by sex and for each country. The contribution of a specific cause (e.g., cardiovascular disease) to the U.S. disadvantage in YLL is based on the difference between the death rate for all causes and the counterfactual death rate without cardiovascular disease. This approach assumes that there are no interactions between causes, an assumption that is more applicable to causes at younger ages, according to Ho. An older person who dies of a particular cause, such as heart attack, may have died of another related cause (e.g., stroke) had they lived.

Other participants discussed some of the implications of using this approach to measure premature mortality. Steven Martin, Urban Institute, indicated that for people under age 50, YLL produces large numbers, which can make certain types of causes look like a greater proportion of the total relative to the overall number of deaths from that cause. In other words, the proportions of premature mortality attributed to different risk categories look different at different ages and limit the coherence of the overall picture. Preston noted that this is a disadvantage to considering premature mortality separately below and above age 50 as the two NRC studies had done. According to Preston, a key implication of the NRC report on divergent trends in longevity is the need to factor in the role of premature mortality before age 50 in the United States in any future analyses. He added that the present workshop offered a step toward blending the view of the two age groups.

Life Expectancy/Longevity

A similar method of conceptualizing premature mortality is longevity, or "the upside-down version of death," according to Preston. Vos defined life expectancy as a "measure synthesizing mortality rates in a population by age into what a hypothetical birth cohort would live to on average if the same mortality rates would continue indefinitely into the future." Health expectancy is a related concept, calculated as life expectancy minus the prevalence of all types of disability weighted by severity, as illustrated in Figure 2-1. Figure 2-1 also shows how DALY, described in a later section, relate to both life expectancy and health expectancy.

Haidong Wang, University of Washington, has also examined life expectancy in his work on geographic differences in life expectancy across

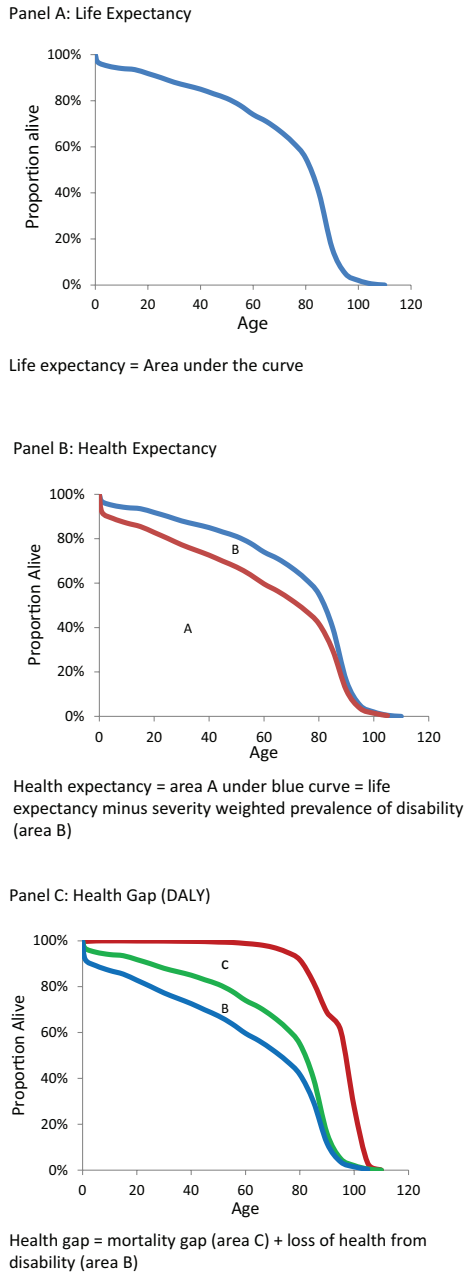

FIGURE 2-1 Life expectancy, health expectancy, and health gap.
SOURCE: Vos (2014).

the United States. He noted, "Life expectancy is . . . a good indicator because it summarizes all the age-specific mortality rates we observed in a given year. It is also not that good because it is a summary index, where we were not able to look at the age-specific change."

Health Loss

Murray defined health loss as measured in DALY as the comparison of a population in a particular period against an ideal life expectancy in full health. Vos added that the focus is on health loss due to factors such as diseases and injuries and, therefore, does not include loss of general welfare outside the domain of health. DALY combine health loss due to death and due to nonfatal causes. Amount of health loss varies based on age (i.e., newborn, young adult, elderly), and data are examined by age, sex, geography, and timepoint. The GBD also enables researchers to compare health loss from a particular disability to health lost from death at any age.

Years Lived with Disability and Disability Adjusted Life Years

YLD are calculated by multiplying the prevalence of a given clinical health state by the health state weights estimated from public responses in various country surveys and an open-access Internet survey. These surveys present pairings of conditions with anchoring vignettes to respondents and ask them to indicate which of the pair they consider "the healthier." Currently, the weights are calculated based on data from 60,000 respondents and more than 600,000 pair-wise comparisons. DALY are the simple addition of YLL and YLD.

Murray and others noted that the proportions of various risk factors associated with DALY are different than those associated with premature mortality. In particular, behavioral risk factors account for a smaller proportion of DALY than YLL. Murray explained that some of the differences are due to shifting from counting deaths to measuring years of life lost. Adding disability to that picture adds a number of conditions such as mental disorders, substance abuse, and musculoskeletal disorders, which are major causes of disabilities rather than deaths.

Vos described DALY in more detail. Currently, 220 health states have disability weights between zero and one assigned, where zero is optimal health and one is death. He noted that the same health state can be used for a number of diseases that lead to the same type of disability, such as hear-

ing loss. Eileen Crimmins, University of Southern California, said DALY present conceptual challenges and indicated her preference for YLD because this metric is easier for others to understand and is expressed in whole years. However, Vos noted YLD alone draw no distinction between disability and death, both of which are important for health policy decision making. Vos indicated that the DALY metric allows GBD researchers to be "comprehensive in the amount of health loss that we measure."

Discussions among members of the workshop panel addressed the impact of using a unisex reference life table for the counterfactual analyses. According to Vos, the reference life tables for men and women in the earlier GBD version showed women having a life expectancy 2.5 years longer than men. However, Murray stated, "it is pretty hard to sustain the argument that in an optimized environment, there is much of a difference between men and women in potential life expectancy." After controlling for risk taking by men in terms of exposing themselves to injuries and substance abuse, the difference is almost gone, according to Murray. The risks become increasingly equalized, others suggested.

METHODOLOGY USED IN MAJOR STUDIES OF PREMATURE MORTALITY

NRC Panel on Understanding Divergent Trends in Longevity in High-Income Countries

The NRC Panel on Understanding Divergent Trends in Longevity in High-Income Countries was charged with identifying trends in longevity and seeking to understand why the trends differ between the United States and other countries for individuals above age 50 (National Research Council, 2011). According to Preston, cochair of the study panel, "the U.S. started to fall short of other countries for men in the 1950s, for women in the 1980s," adding that "at this point, the shortfall is very, very considerable."

Preston described the methods used by the panel to determine why the United States had high mortality rates relative to nine other countries.[6] The panel primarily used the counterfactual approach, which he described as "estimates of relative risk associated with a particular risk factor combined with a comparative distribution of exposures across populations." Preston

[6]Australia, Canada, Denmark, France, Italy, Japan, the Netherlands, Spain, and United Kingdom.

noted that this approach can involve either comparing U.S. exposure to a risk factor to zero exposure or to another country's actual exposure. The NRC panel used the first option. In total, the NRC panel examined the following risks: health care system inequality, social integration and social interaction, smoking, obesity, physical activity, and hormone replacement therapy. However, Preston focused his workshop remarks primarily on the two most significant factors, smoking and obesity, and noted the limitations in focusing on physical activity.

Smoking

The NRC Panel on Understanding Divergent Trends in Longevity in High-Income Countries used lung cancer mortality as an indicator of smoking. According to Preston, 90 percent of male deaths and 85 percent of female deaths from lung cancer are attributable to smoking. Data on lung cancer deaths are readily available across countries over time and are well diagnosed and coded, whereas detailed and comparable data on smoking history (cigarettes smoked, years smoked, years since quit, age started smoking, etc.) over individuals' lifetimes are generally not available. "You have available to you in lung cancer mortality an index that comprehends all of those different features of smoking," Preston stated. Others have used a similar approach with virtually identical results (e.g., Peto et al., 1994), according to Preston.

The NRC study used the model to estimate deaths from smoking in 20 countries from 1950 to 2006, using data from the Human Mortality Database and the World Health Organization Mortality Database consisting of 10 billion person years of exposure and 300 million deaths. The model included death rates due to lung cancer and death from all other causes in 5-year age intervals by sex. This approach assumes that the lung cancer death rates in the absence of smoking are the same as those for nonsmokers in the American Cancer Society longitudinal study.

Obesity

Obesity is another single risk factor that has received a great deal of attention, although the populations of people who smoke and who are obese are largely independent of one another. The NRC study defined obesity as a BMI of 30 or above. Although there is significant controversy about the risk associated with BMIs between 30 and 35, a BMI over 35 is very dangerous, according to Preston. The United States compares unfavorably

to other nations in obesity, particularly at the higher BMIs. Preston cited several studies used to estimate the relative risk of premature mortality due to obesity (e.g., Mehta and Chang, 2009; Prospective Studies Collaborative, 2009). The NRC panel applied the same methodological approach to these data as those used in the Global Burden of Disease Study.

Preston noted that the findings about relative risk of premature death due to obesity vary based on the source of the data. The datasets are often biased toward underestimating the effect of obesity on mortality. One of the more significant biases occurs because people who are sick lose weight and move out of the high-risk BMI category, reducing the relative risk of those in the high BMI group. Based on his recent work, Preston said he believes that estimates showing higher risks due to obesity are more likely to be accurate. Despite the uncertainty of the risk estimate, obesity remains an important risk factor implicated in explaining a sizeable amount of the differences in life expectancy between the United States and other countries, he said.

Physical Activity

Preston noted the existing epidemiology on physical activity is inconclusive in part because of the challenges of accurately measuring how much people do. At the time of the NRC study, no reliable datasets were available to estimate the impact of physical activity on premature mortality. However, overall, the U.S. population appears to be highly variable with more almost completely sedentary individuals as well as more highly active adults than in other countries.

NRC/IOM Panel on Understanding Cross-National Differences

Ho described the data sources and approaches used in the NRC/IOM Panel on Understanding Cross-National Differences. This study made use of three primary datasets: the Human Mortality Database, World Health Organization (WHO) Mortality Database, and data from Statistics Canada. The panel used the Human Mortality Database for all-cause death rates and other life table information by age, sex, and country. The WHO database provided international data for 16 of the countries on cause of death by age and sex, and Statistics Canada provided similar but the most up-to-date data for Canada.

Ho described the two primary methods used in the Cross-National Differences study. The first, age decomposition, focused on the contribution of specific age groups to the gap in life expectancy at birth between

the United States and other countries. The study sought to identify how much of the gap in life expectancy was attributable to mortality differences below age 50 and how much was attributable to differences above age 50. The second method they applied was the use of cause-deleted life tables.

Global Burden of Disease

Christopher Murray described the risk factors included in the GBD. Overall, the GBD examines risk-outcome pairs, risks that are associated with a particular cause of death or disability.[7] The GBD 2013 annual update covered 188 countries between 1990 and 2013, 323 diseases and injuries, 1,134 sequelae, and 72 risk factors. Relative risks vary from country to country based on differences in the underlying causes, according to Murray, which helps to explain the GBD approach. The most recent risks examined by the GBD emerged from the debate of a 28-member internal scientific council about which risk pairings are most important for health policy, have sufficient data to estimate exposure at the country level, and have sufficient evidence for "convincing or probable evidence"[8] of causality and generalizability. The risks are identified through meta-analyses of published research on the topic, taking into account the certainty of the data. The GBD researchers identify effect sizes to estimate exposure, synthesize the data, and examine trends over time by age and sex. Murray and his colleagues also work to correct selection and other known systematic biases. "A classic example is if you think about the bias in self-reported exposure, weights and heights is an example. We don't actually use self-report. We only use measured weights and heights. But that would be an example of a systematic bias that we would try to correct for," stated Murray. Social risk factors, such as income, education inequality, or employment, were not included because they did not meet the criteria for inclusion at the specific risk-outcome pairing level, and they are often measured in variable ways across studies. These social risk factors are more often associated with all-cause mortality and disability rather than specific causes, explained Murray.

[7]For more detailed information about the data sources and methods of the Global Burden of Disease Study, see http://www.healthdata.org/gbd and http://www.who.int/topics/global_burden_of_disease/en/ [December 2014].

[8]Based on the World Cancer Research Funds' criteria for what risk factors it included, the GBD used their criteria for convincing or probable evidence, which means evidence from trials or consistent evidence from cohort studies.

The most recent work on the GBD builds on previously published 2010 analyses (e.g., U.S. Burden of Disease Collaborators, 2013). This recent work will update the time series through 2013. The GBD includes over 1,080 collaborators from 106 countries, all of whom are governed by an extensive protocol that specifies methodology to be used and the inclusion of new diseases or risk-outcome pairs. This extensive standardization helps to maintain the quality of the data and analyses over time as individual investigators change. Geographic sensors and satellite imagery are also being added to generate exposure estimates. Overall, "the goal is for somebody to be able to trace each source of data through to the final result," Murray explained.

Among the changes that affected the most recent GBD work are changes to international medical coding, new research, and expansion of subnational data collection. The International Classification of Diseases (ICD) used around the world shifted from ICD-9 to ICD-10, affecting certain ill-defined categories, such as injury, heart failure, and sepsis. Although WHO adopted the ICD-10 in 1990, the United States began using it to classify mortality data in the United States beginning in 1999 with implementation for clinical purposes occurring more recently (Centers for Disease Control and Prevention, 2014). Some problems with poorly defined codes have been addressed through estimation techniques. New analysis of epidemiological studies has also produced changes in risk estimates around Alzheimer's disease. New work is beginning in selected countries, including China, Mexico, and the United Kingdom, to conduct assessments at the subnational level. Future work will include other countries as well, aided by improvements in computational power. Finally, between the 2013 and 2014 workshops on premature mortality, Murray and his colleagues examined change in life expectancy by groups of causes and shared findings from other member countries of the OECD.

For analyses conducted for the 2014 meeting, Murray and his colleagues examined all behavioral risk factors combined at their theoretical minimums. This analysis was designed to address the question, "what would the premature mortality in the U.S. look like if everybody was thin, nobody smoked . . . nobody used excess alcohol, had optimized their diet, were physically active, et cetera," Murray explained. These theoretical minimums are the subject of debate as the science around them advances and what is seen as biologically possible changes, according to Murray. Crimmins noted that separating the aging process from the behavioral risk factors is a challenge for conditions like cardiovascular disease.

Three new risk factors included in the present GBD work are the effect of intimate partner violence on HIV, a new metabolic risk factor called low glomular filtration rates,[9] and unsafe sexual practice. In addition, Murray and his colleagues made a change to the risk contribution of water and sanitation, which has the greatest impact on results from developing countries.

Considering the current set of risk factors, including the recent changes, they created a hierarchical model of risks shown in Box 2-1. They developed this model to estimate the joint distribution of behavioral, metabolic, environmental, and occupational risk factors. This work was prompted by discussion at the 2013 workshop. In addition, the modeling was an effort to address the overlap between these domains of risk that a typical ad hoc approach examining single risk factors at a time does not.

At the first level of the model, Murray explained that they estimated the joint distribution of all risk factors. The second level of the model addressed the joint distributions of all behavioral, all environmental and occupational together, and all metabolic risk factors. Statistical analyses at this level addressed the pathways of risk to outcome, including correlations between individuals and corrections to the pathway estimates based on the mediation of different risks through each other. This involves quantifying how much of one risk factor is mediated through another. For example, obesity is a risk factor that is mediated through other factors like blood pressure, cholesterol, and metabolic glucose levels. In this case, Murray explained, BMI, unadjusted, has a relative risk of 1.27, but correcting for cholesterol yields a relative risk of 1.24. Similar methods were applied to diet. Murray and his colleagues used empirical data for their estimates of these pathways whenever possible (e.g., Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration (BMI Mediated Effects), 2014).

The third level of this model estimates how much of the variance in years of life lost can be explained by 12 groupings of risk factors, followed by the fourth level, which includes each of 70 different risk factors. Murray stated, "We want to actually complete a Venn Diagram [illustrating the amount of overlap between behavioral, metabolic, environmental, and occupational risk factors] because a tremendous amount of metabolic risks are actually explained by the behavioral risks [with] less overlap on the environmental and occupational risks."

[9]Low glomular filtration rates have been linked to gout, heart disease, kidney disease, and stroke.

BOX 2-1
Hierarchical Models of Risk in the Global Burden of Disease Study

- Level 1: All risk factors joint TMRED adjusted for mediation of behavioral risks through metabolic risks.
- Level 2: Behavioral, environmental/occupational, and metabolic risks clusters.
- Level 3: 12 clusters of risk factors: Dietary risks, tobacco, air pollution, physical inactivity and low physical activity, other environmental risks, water and sanitation, occupational risks, unsafe sex, alcohol and drug use, child and maternal undernutrition, sexual abuse and violence, and physiological risks.
- Level 4: Full detail with all 70 risk factors (e.g., 15 components of diet).

NOTE: For each risk factor examined in the GBD project, the distribution of exposure was compared with an alternative (counterfactual) distribution termed TMRED, the theoretical-minimum-risk exposure distribution (see Lim et al., 2012).
SOURCE: Murray (2014).

Geographic Disparity and Life Expectancy in the United States

Haidong Wang described a study examining geographic disparities in life expectancies across the United States. He noted that although the country has seen improvement in life expectancy and healthy life expectancy for both men and women during the period 1990 to 2010, it has dropped significantly in international rankings of these measures. Wang noted understanding variation in life expectancy at birth within the United States itself is an important step in addition to understanding why it compares unfavorably with other developed nations. His study focused on U.S. disparities by county.

Wang used vital registration data and population estimates from the National Center for Health Statistics and the Census Bureau. Data from the more than 3,100 U.S. counties were grouped into 2,356 county clusters, which helped address statistical issues associated with small numbers of deaths in some areas. The study used time pooling, structured relationships

among socioeconomic covariates, and regression techniques to estimate county-level age-specific mortality rates.

Wang described additional and ongoing research that focuses on understanding the reasons for geographic heterogeneity in health and premature mortality. In particular, research has examined the impact of socioeconomic factors on these outcomes, as well as the ways in which outcomes vary by ethnicity and gender across the country. Current work focuses on determining the impact of a range of behavioral, metabolic, and physical and mental health risk factors on county variation. Wang and colleagues use risk factor data collected at various timepoints to identify risk factor trends by county and gender. The relative infrequency of vital events, small sample sizes at the county level, and cause-of-death coding errors all pose challenges to this research, according to Wang. Discussion centered on the extent to which examining these trends over time provides insight about potential underlying causes, historical patterns, and the extent to which exposures early in life affect later risk and mortality.

Sex, Race, and Geographic Differences in Mortality

Mark Cullen, Stanford University, described methodology and measures used to estimate survival to age 70 by county. Cullen and his colleagues selected survival to age 70 because "disparities are more apparent before the age of 70, and . . . when you look at economic disparities in the aging population, they begin to diminish." The more than 3,000 counties in the United States were grouped to form 950 units to address data problems, including very small counties. Within each unit, data for whites and blacks were disaggregated and other ethnicities excluded. Overall, 22 predictor variables were examined, including 10 personal socioeconomic status (SES) factors and 12 environmental factors.[10] Census data served as the major source for these factors. Cullen said the Behavioral Risk Factor Surveillance System of the Centers for Disease Control and Prevention was only a useful source of data for counties with a primarily white population.

[10]Personal SES factors included low educational attainment, high educational attainment, high occupational attainment, income, poverty, wealth (property), homeownership, wealth (property) distribution, immigrant status, and living without a partner. Environmental factors included between race disparity in wealth, urban county, part urban, in the South, population growth rate, proportion of county that is black, black population in surrounding area, availability of fast food, quality of acute hospital care, cold climate, warm climate, and air pollution.

ISSUES IN THE MEASUREMENT OF PREMATURE MORTALITY AND RISK FACTORS

Individual participants at both workshops identified issues to consider regarding the measurement of premature mortality and associated risk factors, including (1) taking into account the interactions, factors, and clusters of risk; (2) acknowledging the dynamic nature of risk factor distributions; (3) taking into account the independence of risks; (4) determining whose behavior is being measured; (5) considering the impact of adherence to medication and health care; (6) framing analyses by birth cohort versus age linked; and (7) addressing coding inconsistencies. These issues are highlighted below.

Interactions, Factors, and Clusters of Risk

"Ultimately, the most important issue is clearly not the contribution of any one domain on our health prospects, but the way these domains intersect to affect each other and to affect the impact on individuals and society," stated McGinnis. This means that health research and policy must address not only genetic and biomedical determinants of health, but also the behavioral, the social, and the environmental determinants, he argued, due in part to the fact that the biomedical aspects of health are inextricably intertwined with the other domain determinants.

Preston shared findings from a study that examined the underlying factors that lead to variation in population mortality (Tencza, Stokes, and Preston, 2014). This work used correlations among causes of death and revealed among other findings that behavioral factors are particularly important causes of early death among males. This factor analysis yielded three coherent behavioral factors, especially for males: smoking/obesity, drugs, and injury. In these analyses, the causes of death associated with smoking were found to be highly correlated with and in many cases not readily distinguished from causes of death associated with obesity (e.g., cerebrovascular disease and ischemic heart disease), yielding a single behavioral factor. The correlations of cause of death within those categories can help to elucidate the underlying factors behind causes of early death, Preston and others noted. Analyses also indicate that these clusters are not highly correlated with per capita income or poverty. Ho suggested that some of the intercorrelations might vary by age. For example, risky behaviors appear to cluster together more at younger ages. Miron Straf, NRC Divi-

sion of Behavioral and Social Sciences and Education (DBASSE), suggested examining various combinations of risk factors to determine how they might differ between the United States and other countries and help to explain underlying causes behind the proximal risk factors.

Dynamic Nature of Risk Factor Distributions

Participants discussed a number of other issues that affect the measurement of premature mortality. John Haaga, National Institute on Aging, noted that risk factor distributions are dynamic rather than constant, citing the decline in deaths from heart disease and stroke occurring at a faster rate than the decline in associated risk factors. Murray said these relationships can be due to treatment but also to factors and relationships that have yet to be identified. For example, research may continue to reveal a greater relationship between infectious diseases and chronic diseases, he explained.

Further, changing risk exposures in childhood may not yet have revealed their impact in a population. Murray added that he and his colleagues are developing 25-year forecasts of premature mortality and disability, with a focus on removing all possible risk factors, and then separately modeling various scenarios or trends with each risk, and examining potential trends for various conditions. Haaga and Crimmins noted that work to determine the nature of risk factors associated with trends in Alzheimer's disease is also focused on identifying underlying and modifiable risks that affect outcomes.

Independence of Risks

Another methodological issue in the measurement of joint distribution of risks is that the modeling assumes independence of the individual risks out of necessity. The models do not take into account the correlations between various risk factors; however, the models do include steps to avoid double-counting. Despite these methodological limitations, Preston shared his views that the assumptions of the model and statistical methodology employed were common in the literature and very defensible. Majid Ezzati, Imperial College, indicated that certain conditions, such as cirrhosis, are not subject to multiple interrelated risk factors, eliminating concerns around independence. For cardiovascular causes of death, joint distributions of risk attributable to behaviors such as smoking, diet, and physical activity at times explain a large proportion of the difference between populations with

high versus low cardiovascular disease rates. Ezzati reached the conclusion that when this happens, the techniques Murray was employing were robust. Murray and Ezzati indicated adding risk factors to the models' approaches explaining up to 100 percent of the occurrence of a given cause of death, with the marginal error becoming smaller and smaller.

Determining Whose Behavior Is Being Measured

Participants considered key behavioral risk factors for causes of premature death; however in some cases, determining whose behavior constitutes a risk is an issue. For example, for causes of death, such as homicide, medical errors, and auto fatalities, other people's behaviors besides the decedent's are responsible for the risk. Robert Hauser, DBASSE, suggested the group be specific when referring to behavioral risk factors.

Impact of Adherence to Medication and Health Care

Another behavioral risk factor receiving recent attention, according to Richard Suzman, is adherence to medication regimens. This behavior is not currently quantified or included in any GBD models. However, Murray and others noted that measuring this would be challenging for several reasons. First, identifying people who are receiving treatment but not reaching treatment goals could either reveal a nonadherence issue or an inappropriate prescription. Alternatively, Crimmins said even those with an appropriate prescription and adherence could result in varying distributions, much of which would be based on behaviors including education and quality of communication by health care providers. Several participants indicated there may be health outcomes that appear to be explained by metabolic factors, but which in fact are explained to a greater extent than previously thought by behaviors.

Cullen indicated that health care itself is an important factor to examine, and that a number of natural experiments exist to help determine the impact of access and quality on life expectancy. He and others stated this is a major policy question that may help explain previously unattributed portions of outcomes. However, Crimmins cautioned that misattribution is a significant potential problem because "we don't know whether it's really education or it's early childhood physicians or a whole set of things. Everything changes together over time."

Birth Cohort Versus Age Linked

Haaga noted recent NRC studies showed the age group at which Americans' mortality rates compare favorably to those of other developed nations has been rising over time. Currently, that age is 75. However, he argued an alternative way to frame this issue is to indicate the birth cohort before which Americans compared favorably, after which they increasingly compare unfavorably. This may be more explanatory than indicating an age at which Americans "suddenly start to look good." Ho shared research indicating U.S. mortality rates by birth cohort going back as far as 1850 compare favorably between the ages of 65 and 80; however, the most recent cohorts fare far worse at young ages with the exception of those born at the end of and shortly after World War II, which may be indicative of conditions in Europe at the time.

Coding Inconsistencies

Murray highlighted two important issues in working with cause-of-death data: (1) variation in the use of ICD codes across countries, and (2) the use of codes for certain health care encounters that do not constitute a cause of death but end up being assigned as such. Murray and colleagues address these coding challenges using various probabilistic and statistical techniques. Issues with coding have the potential to have a significant impact on analyses. Wang noted that within the United States, inconsistent coding across states or counties can be a particular problem. He shared data indicating that correcting the cause-of-death assignment is necessary in 15 to 32 percent of cases depending upon the state.

SUMMARY

Various sources of data and approaches to studying premature mortality exist. Presenters described the ways in which premature mortality has been conceptualized, and the data sources that they have used to gather data on causes of death and risk factors. They also described the methodology used in major studies of this topic, highlighting the implications of their approaches, as well as key methodological issues to be addressed in future efforts. Ultimately, understanding these approaches is critical for making sense of the results of the major studies presented in Chapter 3.

3

Data from Major Studies of Premature Mortality

Understanding the determinants of premature mortality has important implications for public health policy. Research over the last 20 years has shown that preventable factors—factors amenable to change—could account for 40 percent or more of premature deaths (McGinnis and Foege, 1993; Mokdad et al., 2004; Schroeder, 2007). However, new research studies can add to this body of work to reflect more recent mortality and risk factor data. Providing further impetus for examining current studies in this area are recent international comparisons showing that the United States compares poorly with other developed nations in longevity and years of life lost (YLL). Presenters described current data and analyses of the determinants of premature mortality.

UPDATING MCGINNIS' ACTUAL CAUSES OF DEATH

At the 2013 workshop, Michael McGinnis presented analyses of the determinants of premature mortality, comparing the contribution of known preventable factors from 1990, 2000, and 2010. He applied the same methodology to derive estimates in each of those years using available mortality data and, as previously, used a rounding rule to avoid false precision. He underscored that the updated assessments were provisional pending further work. Table 3-1 shows the comparison of these preventable factors at the three timepoints.

TABLE 3-1 Rounded Estimates of Preventable Factors Causing U.S. Premature Mortality in 1990, 2000, and 2010

Cause	1990 Number of Deaths	2000 Number of Deaths	2010 Number of Deaths
Tobacco	375,000	375,000	(350,000)
Diet/activity patterns	300,000	350,000	(400,000)
Alcohol	90,000	80,000	(70,000)
Microbial agents	90,000	80,000	(80,000)
Medical errors	NA	70,000	(70,000)
Toxic agents	60,000	60,000	(60,000)
Firearms	35,000	30,000	30,000+
Sexual behavior	30,000	20,000	(15,000)
Motor vehicles	25,000	25,000	(20,000)
Illicit use of drugs	20,000	15,000	(20,000)
Total of premature mortality	1,095,000	1,105,000	(1,115,000)
All causes of mortality	2,150,000	2,400,000	2,470,000

NOTES: Provisional estimates are shown in parentheses. Medical errors were not calculated in 1990.
SOURCE: McGinnis (2013).

McGinnis explained that his most recent analyses of tobacco and alcohol were computed from the model, rather than using the Centers for Disease Control and Prevention (CDC) estimates as was done for the 1990 figures. In addition, the number of deaths due to medical errors was not originally available in 1990 but was estimated using the report *To Err Is Human* (Institute of Medicine, 2000). He added that data from 2010 continue to require analysis and further adjustment to refine the estimates.

McGinnis explained that Table 3-1 shows that the number of deaths from tobacco is decreasing, but the contribution of diet and exercise patterns to early and preventable deaths has increased over the past 20 years, erasing gains from reductions in other factors like tobacco and alcohol. He pointed out that deaths attributed to sexual behavior decreased as deaths from HIV decreased. Table 3-2 compares the estimated percentages of deaths attributed to preventable causes between 1990 and 2010. These data show that as of 2010, approximately 48 percent of all early deaths are due to preventable factors, as was the case with his earlier findings. McGinnis

TABLE 3-2 Adjusted Percentages of Proximate Preventable Factors Causing Premature Mortality in 1990 and 2010

Cause	1990 % of Total Deaths	2010 % of Total Deaths
Tobacco	17	15
Diet/activity patterns	14	18
Alcohol	4	3
Microbial agents	4	2
Medical errors	N/A	3
Toxic agents	3	2.5
Firearms	2	1.5
Sexual behavior	2	1
Motor vehicles	1	1
Illicit use of drugs	1	1
Total	48	48
All causes	100.0	100.0

NOTE: Medical errors were not calculated in 1990.
SOURCE: McGinnis (2013).

concluded this update by noting that better assessments of socioeconomic factors, including social engagement, are important for future analyses.

FINDINGS FROM INTERNATIONAL COMPARISONS

Several presentations at the 2013 workshop and the follow-up meeting in 2014 addressed comparisons between the United States and other countries on causes of premature mortality and associated risk factors.

Explaining Divergent Levels of Longevity in High-Income Countries

Samuel Preston presented the major findings from the National Research Council (NRC) study on *Explaining Divergent Levels of Longevity in High-Income Countries* (National Research Council, 2011), which focused on identifying trends in longevity and sought to understand why the trends differ between the United States and other countries for

individuals above age 50. (See also the discussion about this study in Chapters 1 and 2.) This study examined seven risk factors for shorter lifespans across 10 countries, including the United States. Of the seven factors—health care system, inequality, social integration and social interaction, smoking, obesity, physical activity, and hormone replacement therapy—smoking and obesity emerged as the most important factors explaining the differences in longevity. As shown in Figure 3-1, the United States had the lowest average life expectancy at age 50 in 2006 of all the comparison countries. Japan had the highest life expectancy on average, and particularly so for women.

Smoking explains a high proportion of the differences in longevity between the United States and other countries, according to Preston. Between 1945 and 1985, the United States consumed the most tobacco

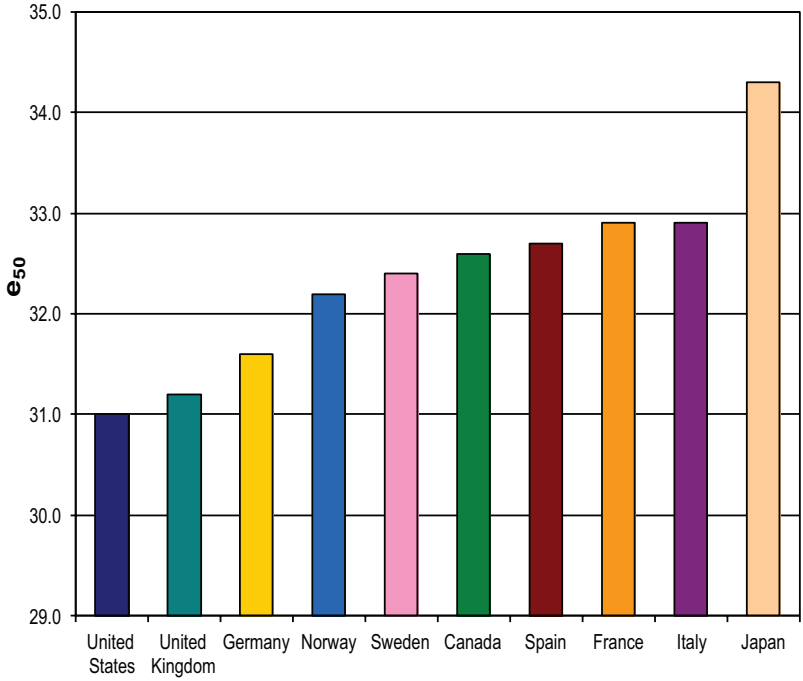

FIGURE 3-1 Average life expectancy in 2006 at age 50 in the United States and comparison countries.
NOTE: e50 is life expectancy at age 50.
SOURCE: Preston (2013).

per capita in the Western world, replaced in more recent decades by Japan. Prevalence of smoking was also high in the United States, but the patterns were quite different for males and females. The difference between U.S. men and women widened for 40 years until the mid-1980s when it began to contract. Since that time, the sex difference in mortality has contracted substantially because smoking prevalence peaked for women born during World War II. The heavy smoking history in the United States manifests itself in lung cancer mortality. Denmark and the Netherlands also have high lung cancer mortality. Canada has high rates of lung cancer mortality, but less of a shortfall in overall life expectancy than the United States.

Trends in the number of U.S. deaths over age 50 due to smoking indicate that between 1955 and 1980, attributable deaths for men increased from 9 percent to 24 percent, then remained steady until 2003. For women, only 1 percent of deaths over age 50 were attributable to smoking in 1955. This rose to 7 percent in 1980, and, by 2003, the percentage increased substantially to 23 percent. Canada has a similar pattern and percentages; however, many other developed nations, including France, Italy, and Spain, have a much lower percentage of deaths due to smoking, in part because women did not smoke in these countries until much more recently, did not smoke very heavily, and are not dying from smoking-related causes, according to Preston.

Overall, Preston reported that smoking explains approximately 80 percent of the difference in longevity for women at age 50 between the United States and the nine other nations. Further, U.S. women lose an estimated 2.33 years of life due to smoking compared to a mean of 1.07 across all other countries. U.S. men lose more years of life due to smoking than do women, but the difference between the United States and other countries for men is not as great. Smoking explains about 41 percent of the difference in longevity for U.S. men compared to men in other countries.

The United States compares unfavorably to other nations in the prevalence of obesity as well, particularly at the highest and most dangerous levels of obesity, and for women more than men. According to Preston, "Our conclusion on obesity was that it is important. Even if you took the lower set of risks, it looks like about a fifth of the difference in life expectancy between the United States and these other nine countries would be attributable to obesity. If you took the PSC [Prospective Studies Collaboration] estimates, it is more in the neighborhood of 40 percent." Moreover, he added that existing biases in the data, as described in Chapter 2, tend to result in underestimating the effect of obesity on mortality.

U.S. Health in International Perspective Study

Jessica Ho shared findings from *U.S. Health in International Perspective: Shorter Lives, Poorer Health* (National Research Council and Institute of Medicine, 2013). This study focused on mortality under age 50, comparing the United States to 16 other high-income countries on life expectancy at birth, probability of survival to age 50, age-specific death rates, age-standardized mortality rates for specific causes, and YLL from particular causes under 50. (See also Chapters 1 and 2 for discussion of this study.) Overall, as of 2007, the United States ranks last among 17 countries for men at 75.6 years and second to last for women at 80.8 years in life expectancy at birth. The highest ranking Swiss males could expect to live 3.7 years longer than American males. The highest ranking Japanese women could expect to live 5.2 years longer than American women. According to Ho, "on average, the people in the other countries could expect to live over two years longer than Americans."

Between 1997 and 2007, life expectancy in the United States increased by 1.5 years, but the rate of increase is much slower than in other countries. Even freezing life expectancy of other countries at their current levels, it would take the United States 20 to 40 years to catch up to the world leaders in life expectancy at the current rate, according to Ho. At each age, U.S. death rates rank at or near the bottom of this list of countries for both men and women until age 75, after which it moves toward the top of the rankings.

As Ho explained, this study examined how different age groups contribute to the shortfall in life expectancy between the United States and other countries. In total, based on 2007 data, mortality under age 50 explains 67 percent of the shortfall for men and 41 percent of the shortfall for women. Infant mortality accounts for just over 12 percent of the total shortfall for males and 10 percent of the shortfall for females. Mortality at younger ages is a particular issue for U.S. men. For example, these data show that the 20–24 age group for males contributes 9.1 percent toward the shortfall, compared with 2.9 percent for females in this same age group. For nearly all comparison countries, more than half of the difference in life expectancy compared to the United States is due to mortality under age 50 for men, because U.S. men have higher mortality rates at younger ages. For women, mortality before age 50 accounts for 20 percent or more of the difference in life expectancy between the United States and other countries.

According to Ho, the United States is losing more years of life below age 50 than are other countries, with men faring worse than women. American men lose 1.36 years of life below 50 compared to less than 1 year for the next nearest country. American women also rank last in YLL, losing 0.8 years before age 50. For both men and women, English-speaking countries cluster near the bottom in YLL. As shown in Figure 3-2, homicides account for the biggest proportion (19 percent) of the difference in YLL for men between the United States and other countries, the majority of which are due to firearms. According to Ho, over 70 percent of all homicides under age 50 in the United States are due to firearms, compared with an average of 26 percent among comparison countries.

Transport fatalities account for 18 percent of the difference in YLL for men, most of which are motor vehicle accidents. Ho explained that although the United States had lower fatality rates per kilometer driven than other countries until 2004, Americans have more fatalities because they have much more exposure to this risk, driving many more total miles per year than people in other countries. Nontransport injuries explain 16 percent of the difference in YLL for men, the majority of which are accidental drug overdoses due primarily to prescription drugs like opioid painkillers, which have overtaken heroin and cocaine in causing overdose deaths.

Homicide explains a much smaller proportion of the differences in YLL for women at 7 percent, with similar percentages to men for transport and nontransport injuries (see Figure 3-2), Ho stated. Accidental drug overdoses constitute a greater proportion of nontransport injuries among women, however. Cardiovascular disease makes very similar contributions for men and women, accounting for about 8 to 9 percent of U.S. excess YLL below age 50. For women, other noncommunicable diseases and perinatal conditions account for 20 and 19 percent, respectively, of differences in YLL between the United States and other countries.

Global Burden of Disease Study

Christopher Murray shared the latest data from the Global Burden of Disease (GBD) Study at both the 2013 workshop and the follow-up meeting held in 2014.

In 2013, Murray presented data on the leading causes of death in the United States for 1990 through 2010. Using age-standardized rates, deaths attributed to Alzheimer's disease, chronic kidney disease, and drug-use disorders increased during this period, while deaths from cirrhosis were stable.

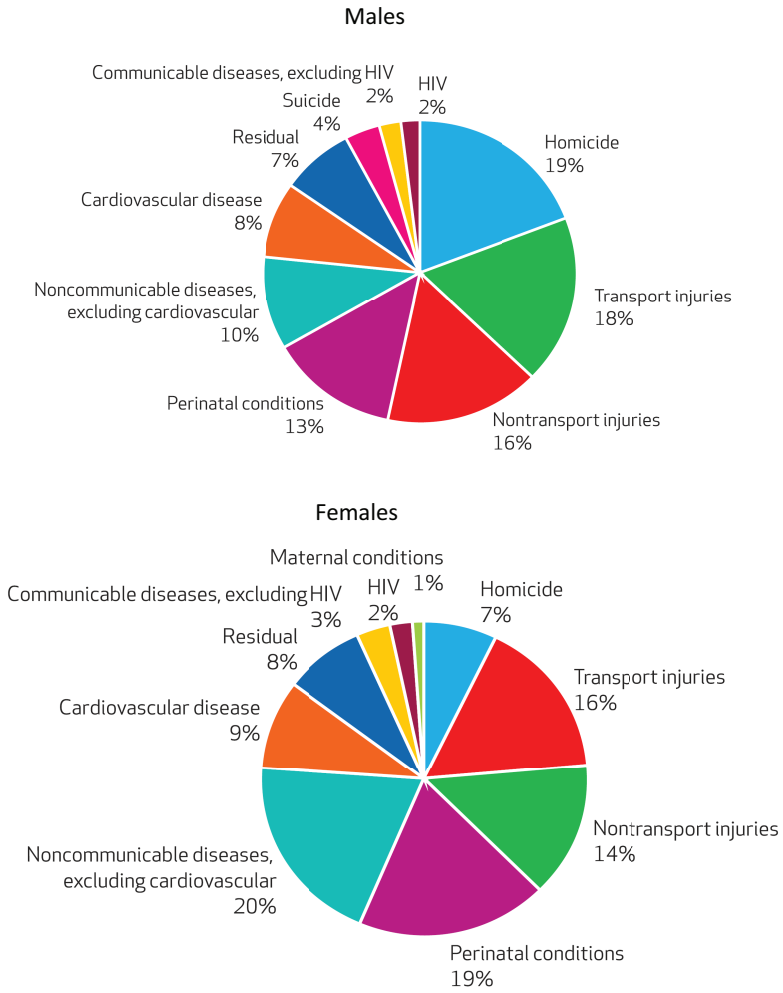

FIGURE 3-2 Cause-specific contribution to the U.S. disadvantage in years of life lost below age 50, 2006–2008.
SOURCE: Ho (2013). Copyrighted and published by Project HOPE/*Health Affairs* as Ho (2013). Mortality under age 50 accounts for much of the fact that U.S. life expectancy lags that of other high-income countries. *Health Affairs 32*(3), 459–467. The published article is archived and available online at http://www.healthaffairs.org.

A different picture emerges when examining YLL. Ischemic heart disease, lung cancer, and road injury top the list of causes of death that result in the highest YLL, even though age-standardized rates of these causes have decreased in recent decades. Suicide and interpersonal violence are also among the top 10 causes associated with YLL in the United States.

Trends in life expectancy across countries in the OECD reveal the greatest improvements for males in South Korea and for females in Turkey. The United States had some of the smallest increases. Across countries, cardiovascular disease is the leading cause of death. Cancer is an important factor in particular countries, such as Belgium. Other countries have seen decreases in factors such as road transport injuries.

The conditions associated with the most disability adjusted life years (DALY) are entirely different from those associated with YLL in the United States. Depression, lower back pain, and other musculoskeletal conditions rank highest because of their prevalence and because they generally do not cause premature mortality. Murray noted that although the United States fares poorly against other nations in terms of the age-standardized YLL burden, it ranks near the top on DALY. More research is needed to understand these phenomena, he stated.

Risk Factors for Premature Mortality

The top risk factors for premature mortality are diet, high blood pressure, obesity, and tobacco use, he reported. Tobacco remains the second leading risk factor, despite the 37 percent decrease over two decades in age-standardized rates in current smoking prevalence.

Murray noted that analyses of GBD data generally involve comparing a single risk factor to the counterfactual. In some cases, clusters of risk factors are analyzed. However, these analyses have not included correction for double-counting. As a result, conditions such as ischemic heart disease and cancer may both be making claims on deaths related to poor diet, smoking, high blood pressure, obesity, low physical activity, and high fasting plasma glucose. Murray stated, "If you rescaled them to 'avoid double-counting,' you would have a huge effect on the number. [There] has been an enormous controversy, at least in the comparative risk field, about the desirability of doing that."

Murray discussed U.S. deaths attributable to poor diet, a cluster of 14 risk factors comprised of low fruit, nuts, and seeds; high sodium; low vegetables; high processed meat; and other elements. Diet accounts for

14 percent of overall premature mortality and disability, or over 650,000 deaths in 2010. Tobacco accounts for 12 percent of premature mortality and disability, obesity just under 12 percent, followed by high blood pressure. Obesity (high body mass index [BMI]) has risen to be the third leading cause of YLL to early death in the United States in 2010, up from fourth place in 1990.[1]

At the 2013 meeting, Murray reported that the combined behavioral risk factors of diet, physical activity, alcohol and drugs, tobacco, and high BMI accounted for 50 percent of early deaths in the United States in 2010. A significant portion of those deaths were due to heart disease. However, behavioral risks accounted for only 35 percent of DALY in the United States when disabilities were added to the analysis, according to Murray.

At the 2014 meeting, Murray presented updated analyses of premature mortality attributed to risk factors. He described the portions of various causes of early deaths in the United States in 2013 explained by all risk factors combined. Eighty-three percent of cardiovascular disease and 72 percent of chronic respiratory disease can be explained by behavioral, environmental, and metabolic risk factors, he noted, but only 38 percent of cancer deaths can be explained by these same types of factors. Injuries have been a rising source of YLL in the United States over the past two decades. Overall, approximately 50 percent of premature U.S. deaths can be accounted for by one of the quantified risks.

Behavioral risks top metabolic and environmental risk factors in terms of explaining premature mortality in the United States, Murray explained, noting that about 35 percent of U.S. premature mortality is related to behavioral risks. Metabolic risks account for 29 percent and environmental risks account for 7 percent of early deaths.[2] Behavioral risk factors account for more early deaths among men than among women. High BMI, high blood pressure, and smoking account for the greatest percentages of YLL in the United States, followed by air pollution, alcohol, cholesterol, drug

[1]The varying estimates of obesity-related deaths presented at the two workshops underscore the difficulty of making precise attributions of the mortality impact for certain risk factors and changes in impact over time (see, e.g., Mark, 2005; Greenberg, 2013; Masters et al., 2013).

[2]The figures included in this workshop summary represent the latest figures provided by Murray and his colleagues after the workshop. During the workshop, Murray indicated that 42 percent of premature mortality was attributable to behavioral risk factors, 24 percent attributable to metabolic risk factors, and 14 percent attributable to environmental risk factors.

use, high fasting plasma glucose, intimate partner violence, low glomular filtration rate, and poor diet.

Disability Adjusted Life Years

Theo Vos presented analyses of risk factors associated with DALY at the meeting in 2014. The top causes of years lived with disability (YLD), such as low back pain, have low mortality rates. He and Murray explained that health care expenditures are more highly correlated with the causes of YLD than with YLL. For example, musculoskeletal disorders account for 15 percent of health care spending in the United States.

Murray noted risks for YLD are less well known than for YLL. Such risks include neurological disorders, mental health disorders, and musculoskeletal conditions. By contrast, far more is known about the determinants of cardiovascular disease and cancer, he explained.

VARIATION WITHIN THE UNITED STATES

Geographic and Socioeconomic/Race/Ethnicity Disparities in the Causes of Premature Death

Haidong Wang presented findings from two studies of the geographic disparities in life expectancy in the United States based on work he published in July 2013 and ongoing work on the socioeconomic status (SES) determinants of life expectancy at the county level (Wang et al., 2013). (See also Chapter 2.) He noted that while life expectancy and healthy life expectancy for both men and women in the United States increased between 1990 and 2010, other developed nations have outperformed this nation on these measures during the same time period. Understanding the patterns at the U.S. county level can help to shed light on why the United States is lagging behind other nations despite the fact that the United States spends more than any other country on health care, he argued.

Life expectancy at birth varies widely across the United States. For men, life expectancy in the highest counties is 82 years, higher than the top countries, including Japanese and Swiss men, and the lowest slightly less than 65, lower than men in Bangladesh in the year 2010. Wang explained that counties that currently rank highly have seen significant and steady improvement in life expectancy, while those that lag behind have barely changed over the past 25-year period. For women, life expectancy ranged

from below 73 years to 85 years in 2010, the most recent year for which they provided estimates; however, 42 percent of the counties in the United States stayed the same or declined in female life expectancy. In fact, while 72 counties had significant decreases in life expectancy for women, only one U.S. county had a significant decrease for men.

Wang also showed that heterogeneity in life expectancy between counties is increasing for both males and females. For women, inequalities have grown steadily, while inequalities for men have occurred in several phases. During the period 2002 to 2010, the number of counties with significant decreases in both sexes life expectancy declined. Great variation between males and females is also observed within counties as well. Wang explained, "In the worst-performing counties, the difference between the life expectancy of men and women could be over 11 to 13 years, and in the best-performing counties, the difference is only around two to four years." Overall, men's average life expectancy is lower than women's but improving at a faster rate.

The lowest life expectancies across time are seen in the South, the Mississippi basin, West Virginia, Kentucky, and counties with large Native American populations. Some of the regions with the lowest life expectancies including Kentucky and West Virginia are also the places where smoking prevalence is highest in the United States, Wang pointed out. Some of the lowest life expectancies are found where proportions of Native American populations are highest.

Wang suggested four possible explanations for the disparities in life expectancy he observed: domestic and international migration; SES factors like education and poverty; lack of access to or poor quality of health care; and behavioral, environmental, or metabolic risk factors. He and his colleagues are conducting analyses to determine the relationship between mortality at the county level and socioeconomic factors, including gross domestic product (GDP), education, percentage of the population that is African American, and percentage of the population that is Hispanic, Asian, or Native American. Since 1985, the areas of the country with the lowest life expectancies generally have been those areas with lower levels of education; however, the proportion of the adult population with at least a high school diploma has increased significantly. During the same time period, the proportion of the population that is Asian, Hispanic, or Native American has increased.

Using a within and between estimator model, Wang and his colleagues examined differences between counties and variation within counties.

Counties with historically higher income levels and counties with lower proportions of minority populations tend to have higher life expectancies. Within counties, when migration to a county increases, life expectancy at birth also increases. Preston suggested that Wang could consider disaggregating Native Americans from the group with the Hispanic and Asian populations because the mortality rates and patterns between the groups are quite different. Somewhat counterintuitively, Wang noted, when a county gains new income or wealth, life expectancies decrease. Follow-up analyses support the theory that new income may be spent on more risky behavior, including drinking and smoking. Preston added other research has supported this theory as well, and automobile accidents may increase as a result of increased income, which tends to increase the amount of driving that people do. He suggested the impacts of smoking as a result of new income would likely not explain increased mortality rates because the detrimental effects of smoking are more often long term. Longer-term changes in mean levels of income at the county level, however, are protective, Wang stated.

At the 2014 meeting, Wang presented new analyses aimed at determining patterns of risk factors that would explain disparities in longevity and mortality rates at the county level. He and his colleagues examined outliers, those counties whose life expectancies decreased despite improving per capita income and vice versa. Analyses were done separately for men and women considering a wide range of risk factors.

Examining a range of risk factors, Wang shared results that indicate that over the period 1996 to 2012, 40 percent of the counties have seen significant decrease in smoking prevalence for men, compared to only 16 percent for women (see Figure 3-3). Analyses of the prevalence of obesity in 2011 also show that women have fared worse than men at the county level (see Figure 3-4). During this time period, no counties saw a significant decrease in the prevalence of obesity, Wang pointed out. Murray and Mark Cullen also noted that patterns among the Hispanic population add complexity to interpreting the results because this population has relatively high rates of obesity and often has less than a high school education, but appears to have lower mortality rates than other populations.

Subsequent discussion focused on the impact of migration patterns within the United States on life expectancy. John Haaga suggested that migration of young and/or healthy individuals away from unhealthy communities might explain why certain counties have stagnated or decreased in longevity. In his view, such migration patterns could be an underlying

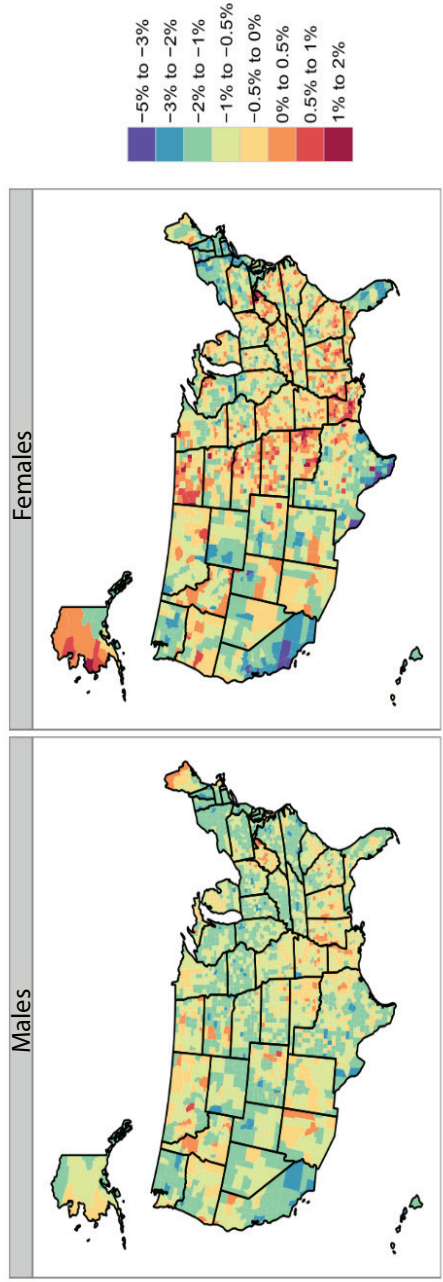

FIGURE 3-3 Annualized rate of change in U.S. smoking prevalence, by county, 1996–2012.
SOURCE: Institute for Health Metrics and Evaluation (2014).

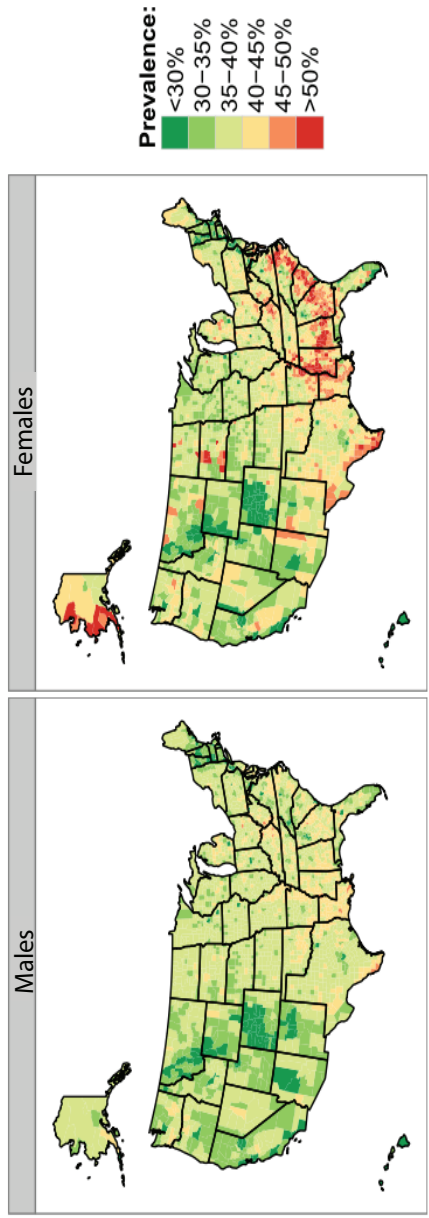

FIGURE 3-4 Obesity prevalence in U.S. counties, 2011.
SOURCE: Institute for Health Metrics and Evaluation (2014).

explanation for patterns in risk factor and health distributions. However, Murray said his analyses of Internal Revenue Service tax return data at the county level indicate that there is a net migration from healthy communities to unhealthy communities, although exceptions exist. Ali Mokdad also described recent research that found that being from an area with higher risk factors earlier in life was an important risk factor in explaining mortality rates. Cullen and Haaga affirmed these findings in their own work. Haaga stated, "If you were born in the 'stroke belt' and grew up there, you carry your stroke risk with you wherever you go." Mokdad indicated that migration patterns only account for a small portion of patterns in risk factors. For example, historical, economic, and social patterns are also helpful to consider in understanding trends in smoking prevalence at the county level, he and Wang suggested. Finally, Haaga noted that county-level data offer a picture of heterogeneity across regions that would not be captured at the state level.

Sex, Race, and Geographic Differences in Mortality

Mark Cullen examined the factors that predict survival to age 70 for men and women, and for white and black populations. Using county-level data, the 22 predictors he examined had high explanatory power for predicting survival to age 70; however, the patterns were quite distinct between white males, white females, black males, and black females. The indicator of medical care was an important positive predictor for all four populations. Having a managerial or professional occupation was also a positive predictor. Although low education was a stronger negative for whites than for blacks, the strongest negative predictors were poverty and living singly. However, he said, the prevalence of immigrants is also a huge factor because immigrants, particularly those from Mexico, tend to have low educational levels but high survival rates. When prevalence of immigrants is removed from the analysis, education and income are eliminated as significant predictors of survival to age 70.

Considering behavioral data from the Behavioral Risk Factor Surveillance System for the white population did not add a great deal of explanatory power to the model, he said. Cullen and his colleagues also worked to determine the factors that explain the racial differences in survival to 70 using county-level data, and concluded that most of the differences between races can be explained by differences in upstream determinants such as socioeconomic factors.

Cullen highlighted key differences in the life expectancy patterns of men and women, using both U.S. and international data. He stated, "I think there is an extraordinary potential value in recognizing that the population who is losing the most life….is men." These differences are socially driven, he argued. Women tend to have higher survival rates than men, but these differences narrow as household income increases. In models considering gender differences and predictive factors in the United States, high school graduation, income, poverty, and obesity are significant, but smoking adds little predictive power to the model. According to Cullen, "upstream determinants are probably pretty strong predictors of such things as smoking, dietary factors, activity, and the like."

Similar patterns can be observed between countries and within other countries. Cullen indicated that there is a strong positive linear relationship between GDP per capita and the ratio of male-to-female life expectancy. In other words, more gender disparity in life expectancy is associated with lower GDP. The higher the GDP, the more women's and men's life expectancies are the same; however, Cullen has not identified any instances worldwide where men's life expectancy across a population matches or exceeds women's life expectancy. This pattern is maintained within other countries as well.

At the state level within the United States, the relationship between the ratio of men's and women's survival to age 70 and the log of percentage of high school graduation is "stunningly linear," according to Cullen, and only slightly less so for log low income per capita. Women benefit from increased rates of high school graduation and higher income, but these factors have a greater impact on men's survival to 70. Cullen concluded that future health interventions should take into account the findings that show that "women are clearly more resistant to taking up the bad habits that cause chronic disease, and to the extent that they do take them up, appear less likely to die from them."

Subsequent discussion focused on the differences between men and women. Cullen indicated that more research is needed to identify underlying and/or currently unmeasured social or biological factors that explain these different outcomes. Other studies are also identifying gender differences in mortality, he pointed out. For example, a recent study examining disease prevalence found that men and women appeared similar with regard to disease severity for conditions such as coronary disease, chronic obstructive pulmonary disease, or cirrhosis, but had different mortality outcomes (Case and Paxson, 2005). The convergence of lifestyles between men and women has been to the benefit of men, Cullen summarized.

Cullen noted that his analyses did not consider risk-taking behavior, injuries, or other causes of death. Although others have seen changes in the patterns of cohort smoking as a potential reason for the closing of the gap between men and women, Cullen's cross-sectional analyses do not support smoking as a significant explanatory variable, after taking socioeconomic status into account. Cullen suggested research on the determinants of premature mortality consider the "upstream/downstream" issues, but also indicated his findings do not diminish the importance of the behavioral determinants of premature mortality, which, as he noted, "at the individual level [are] probably everything."

Cullen's ongoing longitudinal work following the incidence rates of diabetes, hypertension, and heart disease and other conditions among different manufacturing workforces in 24 states showed remarkably different incidence patterns among groups who seemed similar on factors, such as education, obesity, and smoking. He explained these differences prompted his work on identifying underlying factors through an ecological approach. He suggested that behavior is quite heterogeneous and may also be representative of other upstream determinants, such as early life experiences and environments. Nevertheless, he argued that it is important to understand the direct effects of behavior.

SUMMARY

McGinnis and Murray both provided recent analyses of the behavioral determinants of premature mortality, indicating that the risk factors amenable to change account for between 35 and 50 percent of early deaths in the United States. Other presenters helped to place these findings in context, both from an international perspective and by demonstrating how patterns of risk and mortality vary across the United States by region, age group, sex, and socioeconomic factors.

At the 2014 meeting, individual participants summarized additional key points from each presentation as follows:

1. Behavioral risks account for a smaller proportion of DALY than of various measures of premature mortality, including YLL, but this finding appears likely to change with further study (Vos, Murray).
2. Risks vary by geographic area and gender within the United States, with behavior as a more important determinant in some places

than in others, particularly with regard to tobacco use and obesity (Mokdad, Wang, Murray, Vos).

3. Risky behavior is an important determinant of premature death, particularly for men over time (Cullen, Crimmins).
4. These behaviors may have their roots in upstream social causes, and these linkages are in need of further study (Cullen).

4

Ideas for Improving Data Sources, Methodology, and Research

Individual presenters and participants at the 2013 and 2014 workshops offered their views on (1) principles for work on premature mortality and risk factors, (2) ways to improve existing data sources, (3) suggestions for improving methodology, and (4) future research needed to further understanding on these topics.

PRINCIPLES FOR FUTURE WORK

During his presentation, Michael McGinnis suggested a list of principles that, in his view, could guide future policy and research on premature mortality and risk:

- Clarify the analytic agenda—the present workshop is a beginning.
- Keep the focus on the most important elements.
- Avoid "risk factor envy" whereby researchers focused on one topic compete against those studying another topic—the whole picture is more important than any single element.
- Avoid the inadvertent double standard with a higher burden of proof for prevention over treatment.
- Don't let the perfect be the enemy of the good but know what the imperfections are.

- Consider the determinants of lifetime health and not just early death.

IMPROVING DATA SOURCES

Throughout both workshops, many participants recognized the need to improve consistency, measurement, and comparability of data on mortality and risk factors (especially cause-specific mortality data, social network measures, and physical activity measures) across countries, states, and counties. In addition, participants discussed two key ways that data sources used to understand premature mortality and risk factors could be improved—incorporation of social and economic factors among the risk factors for premature mortality, and more precise measurements of behavior at the county level. First, more work to incorporate social risk factors both at the individual and aggregate level into research on the determinants of premature mortality is needed, according to a number of participants. Christopher Murray noted that he and his colleagues working on the Global Burden of Disease (GBD) Study plan to broaden the set of risk factors they analyze to incorporate social risk factors, a process that will take at least 2 years. Researchers will discuss how to develop comparable ways to quantify social risk factors and their effects on population health outcomes. Christine Bachrach added that more data and research are needed to strengthen the basis for communicating about the importance of social factors because they are deeply intertwined with and shape behaviors that are important to health outcomes. Therefore, a focus only on behaviors as health determinants is seriously misleading, according to Bachrach. More work is needed to determine which social and economic elements, ranging from community social engagement to prevalence of crime in an area, should be incorporated, others noted. Eileen Crimmins observed that measuring social determinants of premature mortality is particularly challenging in an international context. Murray noted Norway is beginning to create a national dataset incorporating educational attainment among other social factors, but that country is an exception.

Samuel Preston also indicated social and economic factors are important to study, but noted an interstate factor analysis of causes of death points to the importance of behavior more than poverty or medical care factors. Further, Preston shared that research on the impact of educational change on health and mortality indicates compulsory school laws can have an effect. However, current frameworks used to examine the

proximate determinants may not be suitable for examining socioeconomic differences.

Second, many participants at the 2014 meeting noted the importance of more precise measurements of behavior at the county level. Specifically, Ali Mokdad indicated that he would like to see improvements made to the Behavioral Risk Factor Surveillance System. He explained that a national sample with physical measurements in every state would be an efficient way to accomplish "integrated surveillance." In addition, more county-level data with pooled cohorts might improve imputation, as John Haaga, Murray, and others discussed.

IMPROVING METHODOLOGY

One of the primary methodological issues the group addressed for future efforts was the significance of measuring disability adjusted life years (DALY) versus years of life lost (YLL) and other measures of premature death. As noted during the presentations, behavior explains a smaller percentage of DALY than deaths. Some suggested that the array of risk factors that explain disability outcomes might differ in important ways from those that explain early deaths, requiring an expansion of risk factors considered or a separate effort. Preston noted the two concepts of DALY and YLL are related in that the combination of these two indices equals the years lost to a particular condition, and that the GBD currently captures both. He suggested the choice of examining DALY versus YLL is more of a conceptual choice to be made. Crimmins and others discussed whether considering the determinants of disability requires weighting disability life years, a particularly difficult policy issue, and how closely related they are to YLL.

Majid Ezzati raised a second methodological issue that he and his colleagues will be addressing in the future. He stated that over the coming year, they will examine issues around ranges of key values of risk factors related to premature mortality, including obesity, as well as changes in effect sizes and mediation using a worldwide cohort of over 10 million participants.[1] He noted biases will continue to exist at some level because the data are observational. However, he added this and other large studies will help to address uncertainty in findings about particular risks such as obesity and diabetes.

[1]Some of this work has been published since the workshop: Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration (BMI Mediated Effects) (2014).

INDIVIDUAL IDEAS FOR FUTURE RESEARCH

Several presenters were asked to share their ideas about future research needed in this topic area. Suggestions, and the people who offered them, included the following:

- application of the complete GBD framework to measure risk at the local level especially for the United States (Murray, Haidong Wang);
- more intense study of geographic differences by urban, suburban, rural, or other units of geographic analysis beyond the county (Connie Citro);
- greater study to identify determinants of musculoskeletal disorder, mental health outcomes, and other disability conditions (Murray);
- quantification of distal socioeconomic determinants of specific diseases related to premature mortality and addressing the problems of limited generalizability for all-cause mortality findings (Murray);
- research on causes of early mortality that include lack of vaccination, lack of access to care, and other factors related to medical care (Theo Vos);
- quantification and development of a stronger evidence base about severity distributions for diseases and long-term disabilities and measure how these are affected by treatments (Vos).

References

Braveman, P.A., and Egerter, S. (2008). *Overcoming Obstacles to Health*. Report from the Robert Wood Johnson Foundation to the Commission to Build a Healthier America. Princeton, NJ: Robert Wood Johnson Foundation. Available: http://www.commissiononhealth.org/PDF/ObstaclesToHealth-Report.pdf [March 2013].

Case, A., and Paxson, C. (2005). Sex differences in morbidity and mortality. *Demography, 42*(2), 189–214. doi:10.1353/dem.2005.0011.

Centers for Disease Control and Prevention. (2014). *International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM).* Available: http://www.cdc.gov/nchs/icd/icd10cm.htm [December 2014].

Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration (BMI Mediated Effects). (2014). Metabolic mediators of the effects of body-mass index, overweight, and obesity on coronary heart disease and stroke: A pooled analysis of 97 prospective cohorts with 1.8 million participants. *Lancet, 383*(9921), 970–983.

Greenberg, J.A. (2013). Obesity and early mortality in the United States. *Obesity, 21*(2), 405–412.

Ho, J.Y. (2013). Mortality under age 50 accounts for much of the fact that U.S. life expectancy lags that of other high-income countries. *Health Affairs 32*(3), 459–467.

Institute for Health Metrics and Evaluation. (2014). *U.S. Health Map*. Seattle: University of Washington. Available: http://vizhub.healthdata.org/us-health-map/ [December 2014].

Institute of Medicine. (2000). *To Err Is Human: Building a Safer Health System*. Committee on Quality of Health Care in America. Washington, DC: National Academy Press.

Lim, S.S., Vos, T., Flaxman, A.D., Danaei, G., Shibaya, K., et al. (2012). A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: A systematic analysis for the Global Burden of Disease Study 2010. *Lancet*, *380*(9859), 2224–2260.

Mark, D.H. (2005). Deaths attributable to obesity. *Journal of the American Medical Association*, *293*(15), 1918–1919.

Marmot, M.G. (2010). *Fair Society, Healthy Lives: The Marmot Review*. Available: http://www.instituteofhealthequity.org/projects/fair-society-healthy-lives-the-marmot-review [November 2014].

Masters, R.K., Reither, E.N., Powers, D.A., Yang, Y.C., Burger, A.E., and Link, B.G. (2013). The impact of obesity on U.S. mortality levels: The importance of age and cohort factors in population estimates. *American Journal of Public Health*, *103*(10), 1895–1901.

McGinnis, J.M. (2013). *Actual causes of death, 1990–2010*. Presentation at the Workshop on Determinants of Premature Mortality, September 18, National Research Council, Washington, DC.

McGinnis, J.M., and Foege, W.H. (1993). Actual causes of death in the United States. *Journal of the American Medical Association, 270*(18), 2207–2212.

Mehta, N.K., and Chang, V.W. (2009). Mortality attributable to obesity among middle-aged adults in the United States. *Demography, 46*(4), 851–872.

Mokdad, A.H., Marks, J.S., Stroup, D.F., and Gerberding, J.L. (2004). Actual causes of death in the United States, 2000. *Journal of the American Medical Association, 291*(10), 1238–1245.

Mokdad, A.H., Marks, J.S., Stroup, D.F., and Gerberding, J.L. (2005). Correction: Actual causes of death in the United States, 2000. *Journal of the American Medical Association, 293*(3), 293–294.

Murray, C.J. (2014). *Expert meeting on determinants of premature death*. Presentation at the Second Workshop on Determinants of Premature Mortality, September 4, Institute for Health Metrics and Evaluation, Seattle, WA.

National Research Council. (2011). *International Differences in Mortality at Older Ages: Dimensions and Sources.* Panel on Understanding Divergent Trends in Longevity in High-Income Countries. Washington, DC: The National Academies Press.

National Research Council and Institute of Medicine. (2013). *U.S. Health in International Perspective: Shorter Lives, Poorer Health.* Panel on Understanding Cross-National Differences Among High-Income Countries. Washington, DC: The National Academies Press.

OECD. (2011). *Education at a Glance: OECD Indicators 2011*. Paris: Author.

Peto, R., Lopez, A.D., Boreham, J., Thun, M., and Heath, C., Jr. (1994). *Mortality from Smoking in Developed Countries 1950–2000: Indirect Estimates from National Vital Statistics*. Oxford, England: Oxford University Press.

Preston, S. (2013). *Measures Used in the NRC Study "Explaining Divergent Levels of Longevity in High-Income Countries."* Presentation at the Workshop on Determinants of Premature Mortality, September 18, National Research Council, Washington, DC.

Prospective Studies Collaboration. (2009). Body-mass index and cause-specific mortality in 900,000 adults: Collaborative analyses of 57 prospective studies. *Lancet, 373*(9669), 1083–1096. doi:10.1016/S0140-6736(09)60318-4.

Schroeder, S.A. (2007). We can do better—Improving the health of the American people. *New England Journal of Medicine*, *357*, 1221–1228. doi:10.1056/NEJMsa073350.

Tencza, C., Stokes, A., and Preston, S. (2014). Factors responsible for mortality variation in the United States: A latent variable analysis. *Demographic Research*, *31*(2), 27–70.

U.S. Burden of Disease Collaborators. (2013). The state of U.S. health, 1990–2010: Burden of diseases, injuries, and risk factors. *Journal of the American Medical Association, 310*(6), 591–608. doi:10.1001/jama.2013.13805.

Vos, T. (2014). *Population Health Metrics*. Presentation at the Second Workshop on Determinants of Premature Mortality, September 4, Institute for Health Metrics and Evaluation, Seattle, WA.

Wang, H., Schumacher, A.E., Levitz, C.E., Mokdad, A.H., and Murray, C.J. (2013). Left behind: Widening disparities for males and females in US county life expectancy, 1985–2010. *Population Health Metrics*, *11*, 8. doi:10.1186/1478-7954-11-8PMCID: PMC3717281.

World Health Organization. (2008). *The Global Burden of Disease: 2004 Update*. Geneva, Switzerland: Author.

Appendix A

Workshop Agendas

Workshop on Determinants of Premature Mortality
Keck Center of the National Academies
500 Fifth Street, NW, Washington, DC 20001
September 18, 2013

AGENDA

1:00 p.m. **Welcome and Introductions**
Christine Bachrach, University of Maryland, *Chair*

1:05 p.m. **Need for an Understanding of the Causes of Premature Mortality**
Richard Suzman, National Institute on Aging

1:15 p.m. **Review of the Methodology for the 1993 Estimates of the Actual Causes of Mortality**
Michael McGinnis, Institute of Medicine

1:45 p.m. **Measures Used in the NRC Study "Explaining Divergent Levels of Longevity in High-Income Countries"**
Samuel Preston, University of Pennsylvania

2:15 p.m. **Mortality Under Age 50: Findings from the U.S. Health in International Perspective Study**
Jessica Ho, Duke University

2:45 p.m. **Estimates of the Causes of Premature Mortality Using Risk-Factor Exposure Data Based on the Global Burden of Disease 2010 Study**
Christopher Murray, University of Washington (via video conference)

3:15 p.m. ***Break***

3:30 p.m. **Geographic and SES/Race/Ethnicity Disparities in the Causes of Premature Mortality**
Haidong Wang, University of Washington

4:00 p.m. **National Vital Statistics System Data on Causes of Premature Mortality**
Robert Anderson, National Center for Health Statistics, Centers for Disease Control and Prevention, U.S. Department of Health and Human Services

4:30 p.m. **Discussion of Future Directions in Determining the Causes of Premature Mortality**
Christine Bachrach

5:00 pm **Adjourn**

Second Workshop on Determinants of Premature Mortality
Institute for Health Metrics and Evaluation
University of Washington
September 4, 2014

AGENDA

9:00 a.m. **Welcome and Goals for the Second Meeting**
Eileen Crimmins, University of Southern California, *Chair*

9:05 a.m. **Updated Estimates of the Causes of Premature Death Using Risk-Factor Exposure Data**
Christopher Murray, University of Washington

10:15 a.m. **Population Health Metrics: Comparing the Optional Indicators for Depicting Determinants of Premature Death—Years of Life Lost, Years Lived with Disability, Disability Adjusted Life Years, Quality Adjusted Life Years, and Healthy Life Expectancy**
Theo Vos, University of Washington
Ali Mokdad, University of Washington

10:45 a.m. **Geographic and SES/Race/Ethnicity Disparities in the Causes of Premature Mortality**
Haidong Wang, University of Washington
Mark Cullen, Stanford University

11:45 a.m. **Summary and Adjourn**
Eileen Crimmins

Appendix B

Workshop Steering Committee and Presenters

STEERING COMMITTEE

Eileen M. Crimmins, *Cochair,* Davis School of Gerontology, University of Southern California
Linda J. Waite, *Cochair*, Department of Sociology, University of Chicago
Christine Bachrach, Maryland Population Research Center, University of Maryland
Lisa F. Berkman, Harvard Center for Population and Development, Harvard University
Majid Ezzati, School of Public Health, Imperial College London
Christopher J.L. Murray, Institute for Health Metrics and Evaluation, University of Washington
Samuel H. Preston, Department of Sociology, University of Pennsylvania

PRESENTERS

Robert Anderson, National Center for Health Statistics, Centers for Disease Control and Prevention
Mark Cullen, Division of General Medical Disciplines, Stanford University School of Medicine
Jessica Ho, Department of Sociology, Duke University
Michael McGinnis, Institute of Medicine, National Academy of Sciences

Ali Mokdad, Institute for Health Metrics and Evaluation, University of Washington
Theo Vos, Institute for Health Metrics and Evaluation, University of Washington
Haidong Wang, Institute for Health Metrics and Evaluation, University of Washington