March 4, 2011

An Assessment of the State of the Art for Measuring the Burden of Illness

Final Environmental Scan

Prepared for

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Washington, DC 20201

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1. INTRODUCTION

1.1 Background

Burden of illness measures are potentially useful to policy makers for establishing priorities for clinical and health services research, identifying opportunities for preventive and treatment interventions, budgeting for future health expenditures, enhancing surveillance of health conditions, and monitoring and evaluating the overall health of society and the performance of the health care system. Burden of illness measures provide information about the wide-ranging impacts of illness on society, government, and the individuals affected by disease and their families. Some burden of illness measures capture the number of people affected by a given disease or risk factor, whereas others capture the impact on longevity, costs, and quality of life.

The purpose of the environmental scan is to describe current efforts, innovative initiatives, and gaps in measures of the burden of illness or specific diseases in the United States. As a first step toward developing a description of burden of illness for policy makers, we prepared a background document that uses information from published, peer-reviewed manuscripts and textbooks to describe three types of burden of illness measures: epidemiologic, economic, and quality of life. The background document also used the published literature to identify concerns about burden of illness measures or measurement and approaches to improve burden of illness measurement. However, the methodologies surrounding burden of illness measurement are evolving rapidly, and the published literature may be several years behind the current state of knowledge in the field. It is therefore important to go beyond the published literature to ensure that we capture new approaches to burden of illness measurement in our description of the topic for policy makers.

For the past several months, we have been conducting an environmental scan to supplement the information on burden of illness measurement that we compiled through a literature search. One piece of the environmental scan has involved interviewing experts on epidemiologic, economic, and quality of life burden of illness measurement to obtain additional information about limitations of current burden of illness measurement approaches, new approaches or methods that may be under development, and gaps in burden of illness measurement that still need to be addressed. Another piece of the environmental scan has involved searching for new or recent grant awards or initiatives on federal health agency and private health-related foundation Web sites. In this document, we describe our approach for the environmental scan and then discuss our findings.

1.2   Environmental Scan Methodology

Our first step for the environmental scan task was to identify experts on burden of illness research to contact and request their participation in interviews. Because we had found it helpful in preparing the background document to break the burden of illness approaches into three areas of research—epidemiologic, economic, and quality of life—we focused on identifying 5 to 10 potential experts for each of the three burden of illness research areas. In preparation for speaking with burden of illness experts (Attachment 1), we developed a list of topics for the environmental scan interviews (Attachment 2). Nine of the potential experts were selected by the Office of the Assistant Secretary for Planning and Evaluation (ASPE) project management team for telephone interviews, and all but one of those agreed to participate. We first conducted interviews with 7 of those experts, and over the course of the project we interviewed a total of 13 experts. They are listed in the sections of the scan that most closely correspond to their area of expertise; some experts provided details that appear in more than one section. During the telephone interviews, we discussed each expert's current research interests, new and emerging research in their fields of expertise, and related topics they viewed as important to stress for policy makers. Over the course of these 30- to 60-minute telephone discussions, the experts have typically emphasized one or two key points that they view as especially important for health care policy. The information obtained from expert interviews is summarized in Section 2.

Our second step for the environmental scan task was to search federal agency and private foundation Web sites for information about new initiatives or newly awarded or recent grants/contracts related to burden of illness measurement. We conducted grant/contract searches and searched the full Web sites of the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), the Agency for Healthcare Research and Quality (AHRQ), the Centers for Medicare & Medicaid Services (CMS), and ASPE. Private foundations that we searched included the Robert Wood Johnson Foundation (RWJF), the Kaiser Family Foundation, and the Bill and Melinda Gates Foundation. For each of these agencies and organizations, we first went to the list of available or previously awarded grants and then searched for a variety of terms, such as "burden of illness," "quality of life," "epidemiology burden," and "economic methods," to identify potentially relevant projects out of the large number of grants. These searches produced references to thousands of grants from which we identified a handful that appeared to be closely related to burden of illness measurement. We briefly summarize these grants in Section 3. We also searched the overall Web sites of each of these agencies and organizations using the same set of search terms to identify initiatives or other project efforts related to burden of illness that are being supported by the agency/organization. Findings from these searches are also described in Section 2.

Our third step was to conduct a more general search for grants, works in progress, and government or agency initiatives using Google, Google Scholar, and the CVs of experts that contributed to the environmental scan. Through this search, we identified additional grants in progress, but the general Google searches yielded specific applications of burden of illness methods to particular diseases and subpopulations and did not lead to our identification of additional burden of illness measurement or data collection efforts.

Our final step for the environmental scan task was to supplement the findings from our interviews and Web site searches with information from the additional resources recommended by the experts we interviewed. As a result, we consulted with a few additional experts and reviewed the articles and other written materials recommended by experts. In Section 2, we briefly summarize information obtained from additional recommended resources. A summary of the resources recommended or provided by each interviewee is provided in Attachment 3.

2. TRENDS IN BURDEN OF ILLNESS MEASUREMENT

2.1 Epidemiology

2.1.1 Current Use of Epidemiology in Burden of Illness Studies

Epidemiologic measures are frequently used as health indicators, which are measures focused on one particular aspect of health in a population. Life expectancies, obesity prevalence, and vaccination rates are all epidemiologic measures used to assess the health of populations. Fryback (2010) explains that, although health indicators offer important details about a population's health, they cannot by themselves evaluate overall change in health status. If some indicators show better health, while some show worse health, it cannot be said whether the population as a whole is better off. Doing so requires aggregation and preference-based scoring. As such, many descriptive epidemiologic measures that serve as health indicators form the basis of population health measures with a higher level of aggregation, such as health status profiles and generic indexes (Fryback, 2010). They are also necessary for analytical epidemiologic studies, which quantify the association between health exposures and outcomes and test the hypotheses of causal relationships first developed through descriptive studies.

State of the USA

One major research effort to define key epidemiologic burden of illness measures has been the development of the State of the USA Health Indicators. As an Institute of Medicine (IOM) report notes,

> No single measure can possibly capture the health of a nation. A true measure would have to include indicators reflecting a broad range of factors that together, create a picture of the nation's population (IOM, 2006, p. 1).

State of the USA is a nonprofit recently commissioned by IOM to recommend a list of the most important 20 health indicators by which health in the United States can be tracked (IOM, 2009). The selected indicators fall into three categories: health outcomes, health-related behaviors, and health systems performance. All 20 indicators are listed below by category. Fifteen are epidemiologic, demonstrating the importance of epidemiology in government health planning. The other five indicators are better characterized as economic (*) or quality of life (†) burden measures.

Health Outcomes

- Life expectancy at birth

- Infant mortality

- Life expectancy at age 65

- Injury-related mortality

- Self-reported health status (†)

- Unhealthy days, physical and mental (†)

- Chronic disease prevalence

- Serious psychological distress

Health-Related Behaviors

- Smoking prevalence

- Physical activity prevalence

- Excessive drinking prevalence

- Nutrition prevalence as measured by conformance with federal dietary guidance

- Obesity prevalence

- Condom use prevalence among sexually active youth

Health Systems

- Health care expenditures (*)

- Insurance coverage (*)

- Unmet medical, dental, and prescription drug needs (*)

- Preventive services utilization prevalence for adults

- Childhood immunization prevalence

- Preventable hospitalizations rate measured as rate of hospitalizations for ambulatory care-sensitive conditions

Recent studies in the literature have also focused on comparing life expectancy across countries (Preston and Ho, 2009); on comparing life expectancy across geographically and ethnically defined populations within the United States (Murray et al., 2006); and on linking risk factors, such as obesity, to life expectancy over time within the United States (Olshansky et al., 2005).

2.1.2 Experts Interviewed

To learn more about current issues and trends in epidemiologic burden of illness measurement, we conducted interviews with two epidemiologic burden of illness experts: Katherine Flegal, PhD, and Ali Mokdad, PhD. Dr. Flegal is a senior epidemiologist at the

National Center for Health Statistics who has done a great deal of methodological work on estimating U.S. mortality that is potentially attributable to specific risk factors, such as obesity or smoking. Dr. Mokdad is a biostatistician who is currently Professor of Global Health at the University of Washington and a researcher with the University's Institute for Health Metrics and Evaluation. His recent research has focused on describing population health at a local level within the United States.

We also spoke with Elena Andresen, PhD, an epidemiologist at the University of Florida, but her expertise is better characterized as relating to quality of life burden measurement. We therefore describe the issues and resources she mentioned in the quality of life burden section (Section 2.3). Dr. Christopher Murray provided insights primarily on quality of life, but he also discussed epidemiological data needs in the United States; that portion of his interview is included in this section.

In talking with each of the experts, we learned that epidemiologic burden measures, such as prevalence, years of life lost, and number of deaths, tend to serve as the foundation for other burden measures, such as quality of life and economic measures of disease impacts. Current research efforts are focused on improving data collection approaches and methods for estimating epidemiologic burden measures.

2.1.3 Research Trends Highlighted by Experts

New Methods

Dr. Flegal and Dr. Mokdad both described that epidemiologic burden of illness measurement has largely focused on the accurate application of current methods, rather than the development of new methods for measuring burden of illness. However, sophisticated statistical methods are being applied in new ways to more accurately estimate epidemiologic burden measures for which limited data are available. For example, Rajaratnam et al. (2010a) and Obermeyer et al. (2010) have developed new methods for estimating adult mortality for countries without a central registry in place to track deaths (Mathers and Boerma, 2010). Rajaratnam et al. (2010a) analyzed worldwide mortality in adults aged 15 to 59 from 1970 to 2010 using Gaussian process regression to estimate the annual probability of death between 15 and 60 years.

Obermeyer et al. (2010) developed the Corrected Sibling Survival method for adjusting sibling reports of deaths to account for the fact that in families with high mortality, all siblings may have died and be unable to provide survey data on sibling deaths, and to account for lack of reporting due to forgetting some sibling deaths or being unsure of sibling status. In addition, Rajaratnam et al. (2010b) have developed new methods for estimating child mortality when incomplete birth history data are available (e.g., the researcher knows only how many live births a woman had and how many survived). Although all of these

approaches may prove useful for estimating child and adult mortality in developing countries, such methods are not needed to estimate mortality in the United States, where data on births and deaths are fairly complete at local, state, and national levels.

Other methodological advances that have implications for burden of disease measurement are efforts to improve approaches for detecting causal relationships between exposures to risk factors, such as smoking, or interventions to reduce the prevalence of risk factors, and disease outcomes. In particular, methods have focused on using observational data, such as data from health insurance claims or electronic medical records, to make causal inferences. James Robins and Miguel Hernan at the Harvard School of Public Health and Donald Berry from the MD Anderson Cancer Center have all been active in developing novel statistical approaches for estimating the impacts of risk factors or specific treatments on health outcomes. In an ideal world, policy and clinical decisions would be based on randomized experiments that compared the effectiveness of several randomly assigned interventions in large samples of people that adhered to the study parameters. Unfortunately, such ideal randomized experiments are uncommon due to concerns about ethics or practicality. Drs. Robins and Hernan's research is directed toward emulating these hypothetical experiments by combining observational data, assumptions, and statistical methods. They focus on using analytic approaches whose assumptions do not conflict with current subject-matter knowledge. Dr. Berry has used Bayesian statistics to develop innovative clinical trials, laboratory experiments, and observational studies with a focus on cancer. Dr. Flegal recommended these researchers as potential additional resources on new directions in epidemiologic burden of illness estimation.

Local versus National Burden

Another trend in epidemiologic burden of illness research is the development of burden estimates at the local or state level in addition to the national level. Dr. Mokdad described this as an important effort because disease burden for any particular disease may vary a great deal from one place to another, and decisions about public health priorities and how to allocate public health resources tend to be made at local and state levels in the United States. Local and state public health leaders need information about disease burden that is specific to their populations to make informed decisions.

Currently, few local areas consistently collect data on disease burden within the community, and data collection approaches are not uniform across communities that do collect data. The Behavioral Risk Factor Surveillance System (BRFSS) allows for uniform data collection at the state level and for some communities within the United States, but many of the BRFSS modules are optional and are therefore not collected across all states or communities.

Christopher Murray and his colleagues at the University of Washington have begun to focus on estimating burden of illness within the United States at local levels. For example, Ezzati

et al. (2008) estimated the mortality impacts of uncontrolled hypertension at the state level using BRFSS data and applying estimated relationships between self-reports of hypertension and clinical findings on hypertension prevalence from the National Health and Nutrition Examination Survey (NHANES). Dr. Mokdad and others at the Institute for Health Metrics and Evaluation are conducting several studies to estimate disease burden at local or state levels.

Disease Modeling Efforts

Efforts are underway to improve models of the impact of preventive and treatment interventions on disease incidence and mortality. For example, the Cancer Intervention and Surveillance Modeling Network (CISNET), a consortium of National Cancer Institute (NCI)-sponsored investigators, is using a common population and set of outputs to help understand similarities and differences across various cancer microsimulation models (http://cisnet.cancer.gov/modeling). The Archimedes model is a simulation model that contains pathways related to multiple diseases, including diabetes, heart disease, obesity, and some cancers (http://archimedesmodel.com), to help ensure that health care systems are more accurately simulated.

2.1.4 Research Needs

Data Needs

The primary research need identified through our interviews and review of additional resources was the need for more complete and uniform burden data at local and state levels. Because disease and risk factor incidence and prevalence vary widely across regions within the United States, local-level estimates of the burden of specific diseases are needed to guide communities' public health decision making about how to allocate prevention funds across diseases and risk factors.

Dr. Mokdad reported that he is currently working with New York City to generate local area burden of illness estimates. In general, New York has good data on mortality associated with specific diseases, but the city's data on risk factors and their prevalences are limited. For example, he has been able to obtain local-level data on the prevalence of fruit consumption, but not on smoking prevalence.

Dr. Murray stated that being able to explain the relative magnitude of different health problems to policy makers is a fundamental goal in constructing summary measures of population health. Such summary measures of health combine information on mortality and non-fatal health outcomes at the population level into a single measure that can be easily compared across diseases, across populations, and across time. Such summary measures are used more widely in the rest of the world than they are in the United States. In the United States, comparisons of population burden across risk factors or diseases are limited

because of the lack of widespread use of a uniform measure of population burden. In contrast, much of the rest of the world uses the World Health Organization (WHO) burden of disease metrics that have been in use since the original Global Burden of Disease project launched in 1990. Because these WHO burden measures incorporate experts' valuation of whether it is worse to live with one disease versus another, they represent a quality of life burden measure and are described further in Section 2.3.

Two dominant traditions exist for attributing health outcomes to particular diseases or risk factors: categorical attribution and counterfactual analysis. Categorical attribution assignments follow a set of rules whereby each death or other health outcome is assigned to a unique cause. As an example, deaths from tuberculosis in HIV-positive individuals are all assigned to HIV. This approach is the standard method used in the Global Burden of Disease 1990 effort. Counterfactual analysis, by contrast, estimates the contribution of specific diseases, injuries, and risk factors by comparing the current and future levels of a summary measure of population health with the levels that would be expected under an alternative hypothetical scenario (Murray et al., 2002). Counterfactual analysis is the norm in most epidemiological studies.

Dr. Murray explained that categorical attribution is often more useful for policy makers than counterfactual analysis because it is easier to understand conceptually. In particular, it ensures that when counts of deaths or other outcomes are summed across all diseases or risk factors, the total does not exceed the actual number of deaths or outcomes that occurred within the population. It also allows for straightforward disaggregation of the burden by population subgroups. Dr. Murray expressed that from a policy standpoint, it is more important to implement an easily understood and standardized approach for measuring population health than to debate about the appropriate methodology for measuring population health.

Experts in other areas of burden of illness measurement (e.g., quality of life, economics), such as Dr. Cella and Dr. Russell, also discussed the lack of local data on the burden of specific diseases and the lack of uniformity across communities in the data that are being collected as problems. Although methods are being developed to deal with missing or limited data, the collection of quality and uniform data across communities would contribute to a better understanding of how disease burden differs across communities within the United States and to the development of policies to reduce disparities in the impact of disease across subpopulations.

Other Challenges

Experts interviewed identified two other challenges in estimating the burden of illness. The first is that publication bias may affect the quality of burden of illness estimates in the published literature. The concern is that journals may not wish to publish even sound

methodological articles that show little to no impact of disease on health or related outcomes. Moreover, because the largest estimates are viewed by researchers as more publishable than smaller estimates, researchers may choose to describe findings from the methodological approach that yields the highest burden estimates.

A second significant challenge when estimating the epidemiological burden of illness is the difficulty of attributing health outcomes to any single disease because of the high degree of comorbidities among people with chronic illnesses. Some of the resulting estimates end up double counting utilization, death, costs, or other outcomes (e.g., attributing an outcome to both diabetes and kidney disease when an individual had both). In the cases where individuals have multiple illnesses or risk factors, it is very difficult to predict what the health outcomes would have been in the absence of the disease or risk factor because of competing risks. For these studies, the burden of illness experts recommended that researchers clearly state their assumptions; show the attributable risk formula used in the calculations; show the values of all key variables used in the calculations, such as relative risks; and clearly indicate the degree to which uncertainty in the parameters affects estimates by providing confidence intervals.

2.2 Economics

2.2.1 Current Use of Economics in Burden of Illness Studies

Economic burden of illness is sometimes described in terms of health care spending and trends over time in spending. Health care spending represents a large and growing share of the full economic burden of illness. However, other important components of the economic burden of illness include nonmedical spending, work-loss resulting from increased morbidity or early mortality, and the impact on family members' employment or patients' psychological well-being. Estimates of the economic burden of illness attempt to capture the full economic costs of a disease, where the economic costs reflect the "opportunity costs" of having a disease (i.e., the value of health and non-health outcomes that patients and their families and friends are unable to enjoy as a result of the disease).

Approaches to valuing the economic burden of disease often describe burden using five broad economic burden of illness categories: direct medical spending, direct nonmedical spending, indirect costs resulting from excess morbidity, indirect costs resulting from early mortality, and broader disease burden estimates (i.e., willingness-to-pay) that capture the psychosocial costs of illness in addition to direct costs and productivity losses. The literature review prepared for this project provides detailed information about the need for guidance on a consistent set of methods for economic burden of illness estimation.

2.2.2 Experts Interviewed

To learn about current issues and trends in economic burden of illness measurement, we conducted interviews with three experts: Dr. Martin Brown, Dr. David Cutler, and Dr. Louise Russell. Dr. Brown is Chief of NCI's Health Services and Economics Branch. His research focuses on estimating the economic burden of cancer to individuals and society. Dr. Cutler is Professor of Economics at Harvard University. His research focuses on health care spending and, in particular, the development of national health expenditure accounts. Dr. Russell is Professor of Economics at Rutgers. Much of her research has focused on estimating the value of preventive services. She also co-chaired the U.S. Public Health Service's Panel on Cost-Effectiveness in Health and Medicine. All participated in a workshop on health care costing issues and contributed to the July 2009 *Medical Care* supplement on health care costing.

2.2.3 Research Trends Highlighted by Experts

Health Indicators

Because the States of the USA Health Indicators (IOM, 2009) project described that no single burden estimate captures all of the important factors affecting the health of a nation, their recommended indicators include a few economic measures:

- health care expenditures (per capita),

- insurance coverage (percentage of adults with health coverage), and

- unmet medical, dental, and prescription drug needs (percentage of the noninstitutionalized population who did not receive or delayed receiving these).

Attributing Medical Spending to Specific Diseases

One important issue emphasized by experts we interviewed is the importance of attributing health care spending and costs to the appropriate underlying diseases or risk factors. Two related efforts are addressing this issue: disease-specific National Health Expenditure Accounts (NHEAs) and a satellite account for medical care spending (Rosen and Cutler, 2009; Aizcorbe et al., 2008).

With respect to the first, current annual NHEAs show health care spending only by types of medical care purchased (such as doctor visits or drug purchases) and how those purchases are financed (Heffler, Nuccio, and Freeland, 2009). Although these data contribute to our understanding of where the dollars spent on medical care are going and the distribution of spending across payers, they do not provide information about spending on particular diseases. A more productivity-oriented view of health care spending would provide estimates of spending by disease and by payer or service for a set of predefined diseases or risk factors. The steps needed to generate such disease-specific NHEAs are to link

microlevel spending data to national-level total health spending, determine the diseases and risk factors for which costs will be estimated, and allocate spending to each of these diseases (Lipscomb et al., 2009a).

To infer the value of medical care at the disease level, Rosen and Cutler (2007) conducted a study comparing how existing approaches allocate spending across diseases. These approaches might provide a consistent linkage between the micro-cost estimates for specific diseases and the macro-cost estimates for aggregate national health care. They would also help to eliminate "adding up" problems of disease-specific cost estimates by ensuring that the sum of disease-specific health care spending does not exceed total annual health expenditures. Similar work by Trogdon et al. (2008) has developed an algorithm for attributing medical costs to specific diseases when the population under study has multiple diseases. This algorithm is used in CDC's Chronic Disease Cost Calculator to ensure that specific costs are allocated to no more than one disease category (http://www.cdc.gov/chronicdisease/resources/calculator/index.htm).

Although attributing costs to any particular disease is challenging, Dr. Cutler recommends starting with total health care costs to ensure that the cost attributed to any particular disease is attributed only once. However, creating the algorithms to implement this type of top-down approach is challenging. For example, it may be difficult to determine whether a given expenditure is to treat a patient's obesity or the diabetes that was caused by obesity.

Aizcorbe et al. (2008) describe an initiative by the U.S. Bureau of Economic Analysis (BEA) to construct a health care satellite account that would allow analysts to more effectively assess the returns to disease treatments and the underlying causes of changes in health care costs. This multistep initiative seeks to develop disease-based estimates of health care spending much like disease-specific NHEAs (see Rosen and Cutler, 2009). However, the BEA approach differs from the NHEA allocation to diseases. For example, Aizcorbe and Nestoriak (2007) used computer algorithms to analyze health claims data and allocate spending to hundreds of types of disease episodes. Unfortunately, the "episode grouper" software programs they used are novel, and their properties are not well understood. Aizcorbe et al. (2008) explain that, depending on how sensitive disease-based measures are to the method of allocation, the BEA satellite account may provide different measures of spending by disease.

The satellite account also aims to improve the measures of real health care services, such that changes in spending can be split into changes in price versus changes in quantity of services. For example, an increase in the cost of diabetes treatment could be caused either by more patients receiving treatment, a price increase of existing treatment, or an improvement in treatment quality. Changes in "real services" delivered are normally derived by deflating nominal expenditure with a related price index, much like nominal gross

domestic product (GDP) is deflated to produce real GDP. Based on a recent National Academies Panel recommendation, BEA has decided to construct price deflators that assume constant quality of care over time, such that changes in health care costs can be attributed to changes in either quantity consumed or price (Aizcorbe et al., 2008).

In addition to the academic approaches for measuring health care costs, measures and cost prediction tools have been developed and used primarily by insurance companies to generate predictions of patient health care utilization and medical costs, given health conditions and past episodes of care. Thompson's Medstat Episode Grouper (MEG) and Ingenix's Symmetry Episode Treatment Groups (ETGs) are two episode-based approaches to measuring health care costs and efficiency. These tools use insurance claims data to construct discrete episodes of care, organized around treatment of a specific acute illness or a set time period for management of a chronic disease. Efficiency is measured by comparing the resources used to produce an episode of care (Hussey et al., 2009). They also allow for estimation of health care costs using different assumptions about the case-mix of patients treated by a provider and across several thousand health states. Because they are used almost exclusively by commercial clients, it is not clear how the costing approaches and estimates from MEG or ETGs compare with medical cost approaches and estimates generated by academic researchers. MedPAC has tested the feasibility of using episode-based efficiency measures in the Medicare Program, testing MEG and ETG-based measures using Medicare claims files for six geographic areas. They found that most Medicare claims could be assigned to individual episodes and that most episodes could be assigned to physicians (Hussey et al., 2009).

Dr. Cutler recommended that we review Michael Chernew's work on value-based insurance, an application of health care efficiency measurements. Generally, value-based insurance programs reduce patient co-payments for services that provide high clinical benefits relative to costs; they commonly focus on prescription drugs. Value-based insurance design recognizes that even modest co-payments for drugs and services that greatly improve health outcomes may discourage their use, resulting in suboptimal outcomes. Chernew et al. (2010) examined a value-based insurance program in which a large employer reduced co-payments for five classes of drugs commonly used to treat chronic conditions. This initiative rests on the reasoning that high-value services aimed at reducing the probability of adverse events are much less costly than treating the events themselves. Chernew et al. found that the change in co-payment broke even from a broader employer and employee cost perspective, although a more targeted intervention, focusing on high-risk patients, would have had a more favorable financial impact. They suggest other possibilities for cost neutrality, including co-pay increases for other less valuable clinical services.

Data Limitations and the Estimation of Medical Spending Attributable to Disease

The estimation of medical costs attributable to a disease often relies on administrative data, such as health insurance claims and encounter data from private insurers, Medicare, Medicaid, the Veterans Health Administration, and other public programs. However, because administrative data are collected for purposes other than research, the results from using these data may not be generalizable to broader populations and generally lack additional information that may be needed to estimate burden of disease. For example, it is not feasible to use administrative data to estimate the costs of the early stages of chronic kidney disease because those stages are rarely reported as diagnoses on patients' health care claims.

In estimating the costs of cancer, Dr. Brown and his colleagues have been able to supplement administrative data with cancer registry data to estimate incidence- or prevalence-based costs of cancer (Yabroff et al., 2009a, 2009b). They have used these data to estimate costs for people with cancer compared with controls who were matched by age group, sex, and geographic location. Their estimates show that using the linked Medicare expenditure and cancer registry data leads to different cost estimates from analyses that use Medicare expenditure data only. Their approach may have implications for the estimation of other cancer costs. The approach may also be of use for estimating disease costs using population-based survey data linked to Medicare expenditure data, such as using NHANES linked to Medicare expenditure data.

Non-Medical Costs

Although Lipscomb et al. (2009b) focus on methods for estimating the health care costs of disease or the costs of interventions, they also argue for the need to conduct studies to compare human capital and willingness-to-pay (WTP) approaches for valuing morbidity- and mortality-related losses. These approaches are described in more detail in the literature review for this project. Human capital approaches value mortality attributable to any disease or risk factor using earnings profiles across the years of life lost. WTP approaches capture the monetary value of the direct and indirect impacts of an illness, often through direct elicitation of how much survey respondents would be willing to pay to avoid an increase in the risk of having a disease. Of particular interest is the extent to which both human capital and WTP estimates differ across population subgroups, such as individuals with lower labor market participation rates. Because human capital estimates are based on labor market and household productivity estimates, individuals who do not work outside the home are necessarily assigned lower values. Similarly, WTP estimates are bounded by income because individuals cannot report that they would be willing to pay more than they are actually able to pay for a small reduction in risk.

Murphy and Topel (2006) have developed a framework for valuing health improvements that is based on individuals' WTP. This approach differs from cost-of-illness (COI) methods

that value the resources used to diagnose and treat health conditions in a population. They estimate the economic gains resulting from increased life expectancy in the United States and find that gains in life expectancy over the 20th century were worth over $1.2 million per person to the current population. Murphy and Topel (2006) also estimated gains in life expectancy from 1970 through 2000 to have added $3.2 trillion per year to national wealth.

Inclusion of Non-Monetary Costs in Burden Analyses

Another issue that economic burden of illness research is beginning to address is the need to include non-monetary costs, such as time costs, when estimating the full burden of a disease or evaluating interventions to treat or prevent a disease. These non-monetary costs may represent large components of a disease's overall burden, but they are frequently overlooked in cost analyses or economic evaluations of treatment interventions (Russell, 2009; Freeman and Loewe, 2000). Dr. Russell emphasized the need to collect and report on non-monetary costs, such as the value of a patient's time spent obtaining care or managing a disease. She also stressed that time costs may extend to others involved in the patient's care, such as a family member who accompanies a patient for doctor visits.

One example is the cost of diabetes treatment, where management costs appear much higher if the time that patients spend monitoring their glucose levels is valued and included in burden estimates (Russell, Suh, and Safford, 2005). A similar example is colonoscopy screening, where the inclusion of patient time costs greatly increases the overall intervention costs (Jonas et al., 2007). In fact, interventions that appear to be clearly cost-effective without the inclusion of time and other non-monetary cost values may not be cost-effective when such costs are included.

2.2.4 Research Needs

Attributing Medical Spending to Specific Diseases

One of the key research needs identified by Drs. Cutler and Russell is the need to create disease-specific NHEA accounts for the United States. Such accounts could be useful for tracking spending by disease and to assess the success of current prevention efforts. Although efforts are underway to develop these accounts, researchers face many challenges in identifying which diseases and risk factors to include and determining how to allocate costs to those diseases and risk factors, ensuring that no cost gets allocated to more than one disease or risk factor. Additionally, although a great deal of recent work has focused on developing statistical approaches for estimating the health care costs attributable to a disease or risk factor, particularly the estimation of generalized linear models, Basu and Manning (2009) recommend several additional areas of research on health care cost modeling and the development of cost predictions.

Data Needs

Research into the costs attributable to specific diseases or risk factors could also benefit from additional data from population-based surveys or disease registries that can be linked to administrative data to provide more complete information about a patient's background for estimating costs. Administrative data alone may not be representative of broader populations of interest. Furthermore, administrative data are limited in the amount and nature of data available for controlling for differences in costs between patients. For example, little demographic information beyond age and sex is available to use as controls in analyses that use administrative data.

Inclusion of Non-Medical Costs in Burden Analyses

Other research needs are in the area of non-medical costs, especially in generating productivity cost estimates or broader estimates of WTP for improvements in health. For example, the extent to which income affects WTP estimates has not been fully explored (Lipscomb et al., 2009b). Lipscomb et al. (2009b) also advocate for the inclusion of time cost for patients and informal caregivers in estimates of disease burden and in economic evaluations of treatment and prevention interventions.

2.3 Quality of Life

2.3.1 Current Use of Quality of Life in Burden of Illness Studies

Measures of the quality of life impacts of disease are generally reported as health-related quality of life (HRQoL) impacts or as health-adjusted life years (HALYs). HRQoL represents a person's perceived physical and/or mental health over a period of time, where perceptions of changes in HRQoL due to a particular disease or to illness are of interest for burden of disease analyses. HALYs are a composite measure that reflects the impact of disease on life expectancy and HRQoL in remaining life-years. HALYs integrate the quality of life and longevity impacts of disease into a single measure to allow for ease of comparing HALY impacts for policy decisions or for use in additional analyses, such as cost-effectiveness analysis. The quality-adjusted life year (QALY) measure provides a health-weighted measure of life expectancy that has been widely used in economic evaluations of clinical interventions (e.g., to assess the cost per QALY gained of a treatment or prevention intervention).

2.3.2 Experts Interviewed

To learn more about current issues and trends in quality of life-related burden of illness measurement, we conducted interviews with seven experts in the field of HRQoL measurement: Elena Andresen, David Cella, David Feeny, Theodore Ganiats, Robert Kaplan, Rosemarie Kobau, and Christopher Murray. Dr. Andresen is Chair of the Department of Epidemiology and Biostatistics at the University of Florida. Her research focuses on testing

and refinement of HRQoL and disability instruments. Dr. Cella is Chairman of the Department of Medical Social Sciences at Northwestern University School of Medicine. He is an expert on quality of life measurement and currently serves as principal investigator for NIH's Patient-Reported Outcome Measurement Information System (PROMIS) Initiative. Dr. Feeny is an expert on measuring HRQoL who is currently a senior investigator at Kaiser Permanente Northwest's Center for Health Research. Dr. Ganiats is Chair of the Family and Preventive Medicine Department at the University of California at San Diego's Medical School. He has extensive experience with the measurement of HRQoL for use in cost-effectiveness analysis. Dr. Kaplan is Distinguished Professor in the Department of Health Services at the UCLA School of Public Health and an expert on quality of life measurement. Rosemarie Kobau, MPH, MAPP, is a Public Health Advisor in the Division of Adult and Community Health at CDC's National Center for Chronic Disease Prevention and Health Promotion. Christopher Murray, MD, DPhil, is Professor of Global Health at the University of Washington and the director of the Institute for Health Metrics and Evaluation.

2.3.3 Research Trends Highlighted by Experts

Selecting Measures for Health-Related Quality of Life

The seven experts provided us with in-depth descriptions of the primary strengths and weaknesses of HRQoL and HALY measures. Drs. Cella, Feeny, Ganiats, and Kaplan described the importance of considering the nature of the disease or group of diseases under study to select the most appropriate measures of HRQoL, a recommendation that was also made in the IOM (2006) report, "Valuing Health for Regulatory Cost-Effectiveness Analysis." Below we describe the main issues concerning generic HRQoL indexes that users should take into account when selecting an index for a given analysis. No single generic HRQoL index is best in all situations. Researchers should therefore select the HRQoL measure that most closely matches the illness and population being studied.

- **Domains measured**. The domains included in the index should correspond to the functional domains or health states affected by the disease or intervention. For example, if a disease has impacts on cognition, the researcher should select a generic index that captures cognitive impacts, such as the Health Utilities Index (HUI), or the appropriate disease-specific index.

- **Population surveyed for preference elicitation**. The generic HRQoL indexes have used various populations for preference elicitation. Researchers should consider the extent to which the population under study (e.g., institutionalized versus community-dwelling adults) is represented in the HRQoL measurements in selecting a given index. For example, the HUI-2 collected preference information for children from parents. Consequently, the HUI-2 may be the best generic index for valuing the burden of a disease in children. The EQ-5D is the only index that has recently collected preferences from a sample of American adults. Asakawa et al. (2009) found that the determinants of health differ between people living in institutions and those residing in the community.

- **Nature of the disease or intervention—healthy versus sick people**. Some of the most widely used HRQoL indexes exhibit floor effects (i.e., cannot fully capture the impacts of disease for people with poor quality of life), whereas others exhibit ceiling effects (i.e., do not adequately distinguish between health states for people who are generally healthy). Therefore, it is important to select an index that will best capture the full range of HRQoL impacts of a disease or intervention. For example, if the disease or illness of interest tends to affect people in overall good health, such as injury among runners, then the SF-36 or SF-6D should be selected over the EQ-5D or HUI, because the latter two exhibit ceiling effects for relatively healthy populations.

- **Nature of the disease or intervention—single domain versus multiple domains affected.** The approaches used to combine the preference-weighted HRQoL scores into a single measure differ across the widely used generic indexes. The QWB uses a straight linear additive model, and the EQ-5D, SF-6D, and SF-36 use linear additive models with additional terms. The HUI-2 and HUI-3 use multiplicative models that allow for interactions between preferences across domains. If a disease or intervention affects multiple domains, these interactions across domains may be important to capture. For example, individuals with diabetes experience physical impairment that may be causally related to mental health effects of diabetes, such as depression. This issue is unlikely to be important for illnesses that affect only one health state or domain. The literature review provides links to the questionnaires that form the basis of each of the generic health indexes.

Dr. Andresen pointed out that despite much discussion about the differences in generic HRQoL domains, preference elicitation, and scoring, the way we collect and analyze data on HRQoL has changed little since the 1970s, when the earliest versions of the indexes were used.

Adaptation to Disease and Quality of Life

Drs. Andresen, Feeny, and Kaplan told us that people with an illness adapt to having the disease and, in fact, often report HRQoL values close to 1, whereas people in the general population are likely to report a much lower HRQoL value for the same disease. The implications of this difference in HRQoL valuation between people with an illness and the general population are not fully understood. Valuation of disease and intervention impacts using HRQoL values from the affected population may lead policy makers to conclude that the disease impact is minimal or that limited research or intervention is needed as a result of this adaptation in the patient's perceived health status. On the other hand, HRQoL measures and the resulting HALY measures are often criticized on the grounds that they discriminate against people with preexisting disabilities or illness because their conditions constrain possible improvements in physical or mental health functioning (Harris, 1988).

Limitations of QALYs

Dr. Feeny described that an important limitation of QALYs is that the measure assumes independence between health status and life expectancy. Despite this limitation, in addition to the limitations of HRQoL measures used in generating QALY measures, he and Drs.

Ganiats and Kaplan maintained that QALYs provide a very important and useful summary measure of the quality of life and life expectancy impacts of disease.

QALYs and DALYs—Two Widely Used HALY Measures

Dr. Murray described a distinction between the two primary measures of health-adjusted life expectancy in terms of whether disease incidence and prevalence rates are aggregated into a summary measure that reflects health, such as DALYs, or that captures well-being related to health, such as QALYs. DALYs focus on the impact of a disease or condition on the performance of an individual as rated by health professionals (Gold et al., 2002). QALYs use assessments of preferences for different levels of health functioning that are often established by sample subpopulations rather than professionals. However, because DALY measures incorporate the health professionals' opinions about the disutility of one disease as compared to another, they also capture a measure of health-related well-being (based on doctors' opinions). As a result, QALYs and DALYs capture essentially the same information about quality of life over remaining life expectancy. In practice, however, the two measures have tended to be used differently: QALYS are often used as a common unit of measurement to compare specific interventions or treatment programs. DALYS, specifically formulated to quantify the global burden of disease and comparative health of populations, have been used by WHO as the international standard summary measure of population health.

A great deal of research in the past 10 years, both within the United States and internationally, has addressed how to measure and report on HRQoL and HALYs. Systematically tracking HRQoL and HALYs can help policy makers identify trends in the population or in specific subpopulations. It can also provide the inputs needed to evaluate the impact of clinical or preventive research strategies on an individual's quality and length of life. Most of the experts with whom we spoke conduct research on the measurement of HRQoL. A key theme from our interviews is that the selection of health status measurement questionnaires and scoring algorithms should consider the nature of the disease, set of diseases, or interventions under study. Some of the generic indexes may be better for capturing the impact of an intervention on people with severe illness or disability, whereas others may be best for evaluating health status in a relatively healthy population.

Wide Use of the EQ-5D for Valuing Health-Related Quality of Life

Despite the number of competing HRQoL indexes, the EQ-5D has become widely adopted across the European Community, enabling policy makers to compare health outcomes across countries. With only 243 possible health states and a large ceiling effect among fairly healthy respondents, the EQ-5D is not without practical limitations, but its ease of use and range of languages and weighting algorithms enabled its broad use.

Health Indicators

Although the United States lacks a commonly used measure of HRQoL in its national data sets, progress has been made in tracking quality of life at the state and substate levels. One of the State of the USA criteria submitted to IOM was that data can be broken down to the community level. Two of the resulting IOM indicators are directly related to HRQoL:

- self-reported health status (percentage of adults reporting fair or poor health) and

- unhealthy days, physical and mental (mean number of physically or mentally unhealthy days in the past 30 days).

CDC Measurement of Health-Related Quality of Life

The latter health indicator measure recommended by the State of the USA is based on CDC's approach to measuring HRQoL. CDC's telephone survey-based BRFSS uses a set of four questions known as the "Healthy Days Measures" to assess population health and health disparities (www.cdc.gov/hrqol). Healthy Days data have been routinely collected on BRFSS at the state and substate levels since 1993. The four Healthy Days questions ask respondents to rate their general health and the number of days out of the past 30 in which their physical and mental health were poor or kept them from engaging in usual activities.

Although the Healthy Days Measures of HRQoL are gaining acceptance for use as a measure of population health status and trends, the data cannot be used in cost-effectiveness analyses because the various health state outcomes have not been valued based on individuals' preferences. However, Jia and Lubetkin (2008) obtained indirect estimates of EQ-5D scores from the Healthy Days Measures by matching BRFSS data on Healthy Days with data from the Medical Expenditure Panel Survey, which directly measured HRQoL using the EQ-5D.

Ms. Kobau emphasized the advantages for policy makers of using Healthy Days measures of HRQoL. They have been used since 1993 as key indicators for tracking quality of life in the United States, and they are easily understood and calculated, making them especially useful for tracking population health. One drawback is that the CDC measures are not especially sensitive to change with respect to a clinical intervention.

Ms. Kobau directed us to two current projects that support the use of the CDC HRQoL measures. The first is Mobilizing Action Towards Community Health (MATCH), initiated at the University of Wisconsin Population Health Institute and funded by the Robert Wood Johnson Foundation. The most relevant MATCH activity is producing county health rankings in all 50 states (countyhealthrankings.org). These rankings were highly publicized when they were released on February 17, 2010. The project integrated data for population health outcomes (mortality and morbidity) and health factors (access to care, tobacco use, socioeconomic factors, and others) from a number of national sources, including BRFSS, the

National Vital Statistics System, and the National Center for Education Statistics. To produce the rankings, summary composite scores were created for health outcomes and health factors, shown in Table 2-1.

Table 2-1.   Measures Captured in MATCH County Health Rankings

Health Outcomes	Focus Area	Measure
Mortality (50%)	Premature death	Years of potential life lost before age 75 (50%)
Morbidity (50%)	Quality of life	Percent reporting poor or fair health (10%) Physically unhealthy days (10%) Mentally unhealthy days (10%)
Health factors	Focus area	Measure
Health behaviors (30%)	Smoking (10%)	Adult smoking rate (10%)
	Diet and exercise (10%)	Adult obesity rate (10%)
	Alcohol use (5%)	Binge drinking (2.5%) Motor vehicle crash death rate (2.5%)
	Unsafe sex (5%)	Chlamydia rate (2.5%) Teen birth rate (2.5%)
Clinical care (20%)	Access to care (10%)	Adult uninsured rate (5%) Primary care provider rate (5%)
	Quality of care (10%)	Hospitalization rates for ambulatory-sensitive conditions (5%) Diabetic screening rate (2.5%) Hospice use rate (2.5%)
Social and economic factors (40%)	Education (10%)	High school graduation rate (5%) Adults with college degrees (5%)
	Employment (10%)	Unemployment rate (10%)
	Income (10%)	Children in poverty (7.5%) Income inequality (2.5%)
	Family and social support (5%)	Social and emotional support (2.5%) Single-parent households (2.5%)
	Community safety (5%)	Violent crime or homicide rate (5%)
Physical environment (10%)	Environmental quality (5%)	Unhealthy air quality due to particulate matter (2.5%) Unhealthy air quality due to ozone (2.5%)
	Built environment (5%)	Access to healthy foods (2.5%) Liquor store density (2.5%)

The second project that employs CDC HRQoL data is the Selected Metropolitan/Micropolitan Area Risk Trends (SMART) Project, an extension of BRFSS. Although BRFSS was designed to produce state-level estimates, the large number of available respondents now makes it

possible to produce prevalence estimates for smaller areas. SMART is a state-based system of health surveys that captures information about risk behaviors, preventive practices, and health care access in metropolitan and micropolitan statistical areas (MMSAs) with 500 or more respondents. By providing health officials with local surveillance data, SMART helps them to implement and evaluate community-specific prevention efforts.

Factors that Drive Differences in Health-Related Quality of Life Index Values

The state of the art in measuring utilities and health preferences continues to evolve. As more head-to-head comparisons are reported in the literature, it is becoming increasingly apparent that different generic HRQoL indexes (e.g., EQ-5D, SF-6D, QWB, HUI-3) yield different estimates of QALYs and QALY changes (e.g., in response to an intervention) for the same respondents. This poses a major problem because it means that cost-utility ratios for the same treatment will differ depending on which HRQoL index is used in the analysis (McDonough and Tosteson, 2007). HRQoL scores can differ across indexes because of differences in (1) the questionnaires used (e.g., EQ-5D or QWB), (2) the preference elicitation methods used to value health states, or (3) the scoring algorithm used to combine preference-weighted health states into a single utility, or HRQoL, measure. Each of these sources of potential differences in HRQoL impacts has been addressed through a considerable amount of research in the past decade.

Many of these issues and the ensuing research to address inconsistencies across measures of HRQoL are described in IOM's 2006 report, "Valuing Health for Regulatory Cost-Effectiveness Analysis." This report provides guidance for measuring the health and safety improvements of federal regulations using cost-effectiveness analysis (CEA). Such guidance was needed because the U.S. Office of Management and Budget (OMB) required in 2003 that agencies supplement benefit-cost analysis (BCA) with CEA for "economically significant health and safety regulations" (IOM, 2006, p. 2). The IOM report provides several recommendations regarding how to present the net health effects of a regulation on population health and data and research needs. Of most relevance for burden of illness measurement is the committee's recommendation that CEAs "that integrate combined morbidity and mortality impacts in a single effectiveness measure should use the quality-adjusted life-year (QALY)" to represent health impacts (IOM, 2006, p. 11).

However, many of the concerns about QALY measures relate to the underlying HRQoL values used to quantify the morbidity-related impacts of disease. To address the differences in the domains and specific questions used to assess health status across the HRQoL indexes, a great deal of research has focused on developing a comprehensive set of questionnaires to measure health-related patient-reported outcomes (PROs). PROMIS is an NIH Roadmap Initiative research program to "standardize and promote a common measurement system for PROs across clinical research" (Cella et al., 2007, p. 9). PROMIS specifically seeks to develop, validate, and standardize groups of questions (i.e., "item

banks") to measure PROs that are relevant across multiple medical conditions (Cella et al., 2007). Dr. Cella, one of the experts who participated in our environmental scan, is the principal investigator (PI) for the PROMIS statistical coordinating center site.

NIH Initiatives—PROMIS and Toolbox

Dr. Cella provided an overview of the PROMIS Initiative efforts that include developing reliable, self-reported questionnaires for capturing multiple dimensions of health status and quality of life impacts, including modules on pain, fatigue, and depression. The PROMIS researchers are attempting to extract the best components of all existing frameworks to create a standardized set of questionnaires that more accurately captures the nature of self-reported disease (www.nihpromis.org).

PROMIS uses the WHO framework for health status assessment, which captures physical, mental, and social functioning. PROMIS has also selected five subdomains and a measure of overall health and quality of life as the starting point for developing questions for inclusion in item banks. These are physical functioning, fatigue, pain, emotional distress, and social role participation (Cella et al., 2007). The researchers first compiled a database of more than 10,000 questions from existing HRQoL indexes and have narrowed the list by eliminating redundant and irrelevant questions. PROMIS also plans to administer the item banks to a large sample of individuals in the United States to obtain valuations of different health states for use in clinical research or to assess population health. According to Dr. Cella, PROMIS researchers are also using item response theory to calibrate items for each subdomain so that subdomain scores can be measured on the same metric even when different sets of items are administered in studies.

We asked Dr. Ron Hays, leader of the psychometric workgroup of PROMIS, about how PROMIS relates to existing preference-based HRQoL indexes, such as the EQ-5D. Dr. Hays explained that while item response theory is different from the econometric models that underlie generic indexes, there have been some intersections between the two. The EQ-5D questionnaire was included in PROMIS Wave 1 (the initial domain validation efforts), and Hays and colleagues derived regression equations to predict an EQ-5D score from PROMIS domain scores. There was also a proposal in PROMIS Wave 1 to derive a multi-attribute utility-based preference score from PROMIS items; this was put on hold, but Dr. Hays said that his team may try to create a preference-based score from PROMIS items in the future.

Cherepanov and Hays (in press) indicate that the future importance of patient-reported outcome measures, such as those provided by PROMIS, is enhanced with the recent passage of HR 3590, the Patient Protection and Affordable Care Act, which established a nonprofit corporation, the Patient-Centered Outcomes Research Institute, to advance the quality and relevance of evidence concerning the manner in which diseases and health conditions can be prevented, diagnosed, monitored, and treated through research. Patient-

reported outcome measures greatly enhance health researchers' ability to track wellness among the U.S. population. As such, Cherepanov and Hays expect patient-reported outcomes to gain particular significance in coming years, as the focus of health care delivery shifts from diagnosis and treatment of health problems to wellness and disease prevention.

Another related NIH Roadmap Initiative that Dr. Cella mentioned is the Toolbox effort (www.nihtoolbox.org). The Toolbox Initiative is focused on developing instruments for measuring neurological function. Toolbox researchers are compiling and developing sets of questions to measure cognition, emotion, motor functioning, and sensation.

Other Initiatives to Standardize Health Status Measurement

The Consensus-based Standards for the selection of health status Measurement Instruments (COSMIN) study is an international effort to create a checklist of measurement properties to evaluate health status instruments (Mokkink et al., 2010). Some of the measurement properties that COSMIN participants agreed should be included are internal consistency, reliability, content validity, construct validity, responsiveness, and interpretability (Mokkink et al., 2010). This checklist can be used by researchers when selecting an instrument for assessing health outcomes or to evaluate the quality of other published or unpublished analyses. Dr. Andresen participated as a member of the COSMIN study team. The use of checklists, such as those provided by the Panel on Cost-Effectiveness in Health and Medicine (1996), to guide research and evaluate the quality of published or unpublished studies was also recommended by Dr. Feeny.

Research into How Measurement and Valuation Methods Affect Health-Related Quality of Life Measures

Concerns about differing estimates of HRQoL across the most widely used generic indexes have also spurred research on the influence of preference elicitation methods (time trade-off, standard gamble, or visual analog rating scale) and other study design features on the derivation of preference weights. These approaches are described in detail in the literature review for this project and represent different ways of asking people whether they would prefer being in one health state to another. For example, Krabbe et al. (1997) compared a sample's valuation using four preference elicitation approaches for 13 health states in the EQ-5D and showed good correspondence in the valuations for three of the approaches.

Some analyses have examined the extent to which the preference-based algorithms used to value health status measures from generic surveys affect HRQoL outcomes. For example, Pickard et al. (2005) calculated cost-effectiveness ratios using estimated QALYs calculated using 10 different published algorithms for valuing health states in the SF-12 and SF-36. They found that the choice of preference-based algorithm led to widely differing cost-effectiveness ratios and that the varying ratios could affect policy decisions about whether a given intervention is cost-effective.

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Another line of research has been examining the extent to which utility values can be estimated or "mapped" from existing function measures like the SF-36 or PROMIS. For example, Revicki et al. (2009) predicted EQ-5D scores from PROMIS global items (e.g., physical health, mental health, pain, social satisfaction) and found good correspondence between the predicted and actual EQ-5D scores in a sample of more than 2,700 U.S. adults. Similarly, Bosch, Halpern, and Gazelle (2002) compared estimated SF-36 utilities and HUI scores from the same sample of patients and found relatively good correspondence between measures. Feeny, Wu, and Eng (2004) contributed to this research by comparing SF-6D and HUI-2 and HUI-3 for a sample of hip arthroplasty patients. They found low agreement between estimates of changes in utility following total hip replacement. Sullivan and Ghushchyan (2006) mapped the EQ-5D from the SF-12 questionnaire responses collected in the Medical Expenditure Panel Survey in 2000 and 2002.

All of the quality of life burden experts, and some of those with expertise in economic and epidemiologic burden of illness measurement, suggested that we review the work of Dennis Fryback and the Health Measurement Group, especially their analysis of how HRQoL values differ across generic health status measurement surveys for the same sample of individuals. Fryback et al. (2010) compared HRQoL scores from the EQ-5D, HUI2, HUI-3, QWB, and the SF-6D using data from the National Health Measurement Survey of more than 3,800 U.S. adults. They compared the index scores from each of these five HRQoL indexes and the Health and Activities Limitation Index (HALex) to a measure of underlying summary health for all of the survey respondents and found that some of the indexes are best when underlying health status falls at the bottom end of the distribution, whereas others do better when health status is at the top of the distribution. For example, the HUI-3 may be best when underlying health is below the population mean, whereas the QWB or SF-6D may work best when population health is above the population mean. Several of the measures are unable to differentiate between relatively good health states (e.g., EQ-5D, HUI-2, HUI-3, and HALex). Fryback et al. (2010) conclude that it may be possible to develop linear crosswalks between the five HRQoL indexes for groups of individuals with health states below the mean, but it may not be possible to do so for healthier groups.

Other researchers are focusing on how HRQoL or HALY varies across the lifetime or across income levels and for community-dwelling versus institutionalized adults. For example, Asakawa et al. (2009) used the HUI-3 to compare determinants of health for people living in institutions versus those in the community. McIntosh et al. (2009) examined differences in HALE by income decile, and Orpana et al. (2009) assessed HRQoL following a cohort of Canadians from mid- to late-life.

IOM Recommendation to Use Quality of Life Measures to Compensate Veterans

Although HRQoL measures are primarily used to assess population health status or to evaluate the cost-effectiveness of treatment and prevention interventions for specific

diseases, IOM (2007) has recently recommended that the Department of Veterans Affairs (VA) use quality of life measures to compensate veterans for quality of life losses that go beyond losses in earnings or limitations in daily life. Currently the VA compensates for loss of earning capacity only (IOM, 2007).

2.3.4 Research Needs

Collection of Quality of Life Impacts on U.S. Population Health Surveys

Although many efforts are underway to improve the measurement of HRQoL in the United States, the experts with whom we spoke also identified several research needs. First, many of the experts and the IOM (2006) report describe the need for a measure of population health status on U.S. population-wide health surveys. Such a measure would allow for the tracking of health status in a uniform manner over time and could help policy makers identify trends in health status for the population as a whole or for subgroups and to identify and create policies to narrow disparities in health across population subgroups. Canada uses the HUI and Western Europe has uniformly adopted the EuroQol (EQ-5D) to monitor population health status, but in the United States, only limited efforts have attempted to track population health status, such as the use of the SF-12 on some years of the Medical Expenditure Panel Survey and the creation of the HALex as a HRQoL measure. HALex is a controversial measure of HRQoL, as described by Fryback (2010), because it includes self-rated health as a domain, instead of using population-based preferences for different health states, and because it captures only a limited set of health domains.

Quality of Life Valuation among Special Populations

In addition to the need to select and include a general index of HRQoL on a national health survey, experts also described several other research and data needs. Dr. Andresen discussed the need for additional research to better understand the implications of using preference valuations from the general population in studies that deal specifically with the health status or impact of interventions in a population with illness or disability. She has done a great deal of research on HRQoL in people with disabilities, and because of people's ability to adapt, has found that individuals with a given disability often report higher valuations for the health states they experience (e.g., blind or unable to walk) than do individuals without the disability. Additional research is needed to better understand the implications of this finding for HRQoL estimates, changes in HRQoL, QALYs/QALY changes, and cost-effectiveness study results.

Data Needs

Dr. Kaplan described the need for better local and state data on health status to contribute to the tracking of population health status trends at local levels and to guide public health policy decisions. This recommendation echoes the recommendation from epidemiologic

burden of illness experts that uniform data be collected on disease prevalence, incidence, and mortality at local and state levels.

Including Non-Patient Quality of Life Impacts

Dr. Feeny pointed out that HRQoL measures almost exclusively capture the burden of illness impacts on patients and ignore the quality of life (health-related and non-health) impacts on family members or friends. He described that these impacts are rarely captured in HRQoL indexes, although some economic measures of burden attempt to capture the impacts of disease from a societal perspective—including all economic impacts, regardless of who bears them.

IOM Recommendations

The IOM (2006) report, "Valuing Health for Regulatory Cost-Effectiveness Analysis," made several recommendations for additional research to improve health outcome valuation in regulatory analyses. Key recommendations of most relevance to the measurement of quality of life and burden of illness are as follows:

- the need for improved data on the types of health risks addressed by regulatory actions are needed;

- the need to collect HRQoL information through routinely administered U.S. population health surveys; and

- the need for a research agenda to improve the quality, breadth, and applicability of HRQoL measures for use in cost-effectiveness analysis.

The specific research priorities identified by the IOM committee are

- methods for eliciting preference values for investments in health,

- methods for measuring children's HRQoL, and

- methods to correlate QALY values based on different generic HRQoL indexes so that estimates from different valuation surveys can be used in the same regulatory analysis.

The recent study by Fryback et al. (2010) is an effort to compare HRQoL indexes and explore the feasibility of developing crosswalks from one HRQoL index to another.

3. GRANT INFORMATION

Grants are sources of funding for studies that have measurable impact and advance the mission of the grant issuer, which for the purposes of this study is either the federal government or private foundations devoted to improving health care. Knowledge of current calls for proposals and newly awarded grants is a way to track trends in research and new approaches that are being pursued. To further gauge the state of the art in burden of illness measurement, we searched federal agency and private foundation Web sites, in addition to conducting broader Google searches and reviewing experts' CVs for information about new initiatives that have been supported or newly awarded grants. In the subsections that follow, we briefly describe the relevant grant announcements or ongoing efforts that we identified.

3.1 Epidemiology

The National Institutes of Health (NIH) has an open grant announcement titled *Small Grants Program for Cancer Epidemiology* (grant number PAR-08-237, maximum $100,000 over 2 years). The request for applications began on August 14, 2008, and will end November 19, 2011. Topics included in this small grants program are new epidemiology techniques related to cancer, particularly support for pilot projects; testing of new techniques; secondary analyses of existing data; and development of innovative projects for more comprehensive cancer research. Advances in epidemiology methods supported by these grants could contribute to improved disease burden measurement.

The Robert Wood Johnson Foundation funded a project from December 1, 2006, to November 30, 2009, titled *Common Ground: Transforming Public Health Information Systems* (grant number 59674, $563,674). The grantee was the State of South Carolina Department of Health and Environmental Control. Common Ground was designed as a collaboration between local and state health departments to advance the use of information systems in treating chronic disease. Although South Carolina has high mortality rates from chronic diseases, the project is charged with redesigning prevention and treatment methods and refocusing the state public health agency's resources. Although this research study is less relevant to our project than some of the others we describe, understanding of trends and development of data systems to capture the epidemiologic burden of illness at local and state levels may have been important for this study.

3.2 Economics

David Cutler and Allison Rosen's work on expanding the National Health Expenditure Accounts is funded by an NIH grant (project number 1P01AG031098-01A1, $9,739,727). They are adding a measure of population health to be tracked alongside expenditures in

order to track the value of health spending over time. They are also looking in more detail at spending within specific diseases.

The Robert Wood Johnson Foundation has awarded grants to the Engelberg Center for Health Care Reform at the Brookings Institution and America's Health Insurance Plans Foundation as part of the National Effort to Measure and Report on Quality and Cost-Effectiveness of Health Care. This work aims to improve the quality of U.S. health care by determining the most cost-effective methods of treatment that are found when methods of costing and quality determination methods are standardized. Specific study goals relating to this project are patient data aggregation and identification of key cost measures to address health disparities. This project supports the vision of the Quality Alliance Steering Committee, which was established in 2006, to make consistent and useful information about the quality and cost of health care widely available. The grant title is *Developing a Data Aggregation Method to Construct Performance Measures Assessing Quality and Cost-Effectiveness and Differences in Quality Measures* (grant number 61926, $3,557,740), and it ran from August 1, 2007, to July 31, 2010.

The Robert Wood Johnson Foundation has also awarded a grant to Archimedes Inc., titled *Building the Archimedes Health Care Simulator (ARCHeS)* (grant number 57707, $15,600,000), which runs from June 1, 2007, to May 31, 2012. The project extends an existing simulation model of health care, called Archimedes, to make it directly available to health care decision makers. The simulator addresses the effects of clinical and administrative interventions on health, logistic, and economic outcomes in defined populations. It will explore problems related to delivery of health care, including effects of various clinical management activities, setting priorities, conducting cost-effectiveness analyses, and adapting programs to changes in clinical knowledge and technology. The completed system, called ARCHeS, will be sold to decision makers in a variety of organizations, such that it can be applied to the formulation and evaluation of public health policy. This project may be relevant for economic burden of illness approaches because the simulation relies on up-to-date data on the cost of illness and cost-effectiveness of potential interventions.

3.3   Quality of Life

The Bill and Melinda Gates Foundation recently awarded a grant of $8,226,870 to the University of Washington to update the Global Burden of Disease (GBD) study. Running from April 2008 to December 2010, the grant funds the first major effort since the original GBD 1990 study to systematically assess data on all diseases and injuries worldwide. It also seeks to produce comparable estimates of global burden of disease for two time periods, 1990 and 2005. The original GBD study created a common metric—the disability-adjusted life year (DALY)—to estimate the health loss associated with morbidity and mortality. Until

the current update, there had not been a comprehensive revision, and estimates of disease and disability prevalence were outdated and inconsistent. [1]

NIH is funding a research grant (R01) titled *Incorporating Cost-Effectiveness Analysis Into Factors Affecting Quality-of-Life Health Related Research* (grant number RFA-NR-09-005, $2,000,000 for three to four projects). Although cost-effectiveness analysis is a useful tool for comparing the costs and outcomes of similar health interventions, there are lingering inconsistencies in use of terminology, variations in methodologies, and differences in the reporting of data across healthcare disciplines. NIH seeks research focused on the refinement and integration of cost-effectiveness evaluation into clinical and patient outcomes research, particularly health-related quality of life (HRQoL). In the context of burden of illness research, this is an important grant because it may result in improved and consistent methods for estimating the "effectiveness" of an intervention using QALYs or other health-adjusted life year (HALY) measures.

The Robert Wood Johnson Foundation is funding an ongoing project by the University of Wisconsin Population Health Institute titled *Mobilizing Action Toward Community Health (MATCH)* (grant number 65017, $4,934,201), which runs from January 1, 2009, to December 31, 2011. MATCH is described in Section 2.3 of the environmental scan. Its initial goal, completed February 2010, was to produce county health rankings in all 50 states. Although the rankings incorporated numerous metrics encompassing mortality and morbidity, and health factors such as health behaviors and clinical care, HRQoL as measured in the Behavioral Risk Factor Surveillance System (BRFSS) was one of the two major components of measured morbidity. This research highlights the increased importance of nationally based measures of quality of life.

We identified another potentially relevant grant effort that is ongoing through 2013. This grant was awarded in 2008 to the University of Michigan by the Robert Wood Johnson Foundation and is entitled *Emotional Adaptation and the Goals of Health Care Policy* (grant number 63913, $334,995). The grant runs from July 1, 2008, to June 30, 2013, and funds research that examines quality of life in severely injured people, such as quadriplegics, and their ability to adapt to their situation. Through this adaptation, the self-reported utilities of these patients typically exceed the utilities that healthy people would report for similar types of limitations. This study is exploring the differences in utilities between the affected population and the general population and their possible implications in terms of funding allocations and determining health care priorities. This study is important in its potential to introduce insights from well-being research into debates about cost-effectiveness of medical care.

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[1] Previously, the Gates Foundation provided a grant of $1,580,124 to Harvard College with the same goal.

A final grant that may be relevant to this project was awarded by the Robert Wood Johnson Foundation to the University of Pennsylvania. *Exploring the Concept of Positive Health* (grant number 63597, $2,771,990) runs from August 15, 2008, to December 14, 2011, and will lay the foundations for a new approach called Positive Health, which focuses on health strengths instead of the usual emphasis on diagnosis, treatment, and prevention of disease. Principal Investigator Martin Seligman, PhD, writes in *Applied Psychology* that a scientific discipline of health—beyond the mere absence of disease—barely exists. He outlines the rationale for positive health and his prediction that significant health improvements will result from such a change in focus (Seligman, 2008). This is an important trend in quality of life research, because it seeks to broaden policy makers' vision of ways to measure and value health beyond measuring and valuing disease states and absence of disease.

4. CONCLUSIONS

An overall theme that emerged from speaking with our experts and reviewing the reference materials they suggested and provided is the need to look at multiple burden of illness measures when considering a disease's impact. Relying on a single measure may not reflect the full breadth of a disease's impact or may overstate or understate the impacts of a disease that has a large burden when measured one way, but a smaller impact when measured another way. Although within each burden of illness measurement area (epidemiology, economic, and quality of life), researchers may disagree about the best measurement approaches, the implications of the findings tend to be similar across the measurement approaches and have very real practical value for contributing to policy decisions about research priorities for disease treatment, prevention, or health promotion.

Another important point that was made by the experts is that burden of illness measures are most likely to be valid if the results are reproduced using multiple methods. Additionally, reporting the range of uncertainty in burden of illness estimates enhances transparency and validity.

Each burden of illness measure tends to have its own set of advantages and disadvantages and taken alone may not provide a complete picture of the impact of disease or any particular disease on individuals or the population as a whole. For example, mortality, life expectancy, or years of life lost may be preferred as measures of disease burden because, within the United States, they are accurately and objectively measured. But not all diseases have large impacts on life expectancy. Arthritis or multiple sclerosis tend to have extensive negative impacts on an individual's quality of life, but may have little to no effect on life expectancy. Burden measures, such as HALYs, represent disease impacts on both life expectancy and quality of life; however, they are limited in that HRQoL values are often typically based on individual perceptions of health status, which may differ a great deal across demographic and socioeconomic groups, and because HALY values and HALY changes depend at least to some extent on which HRQoL indexes and preference valuation approaches are used. Economic measures of burden of illness, such as productivity losses plus health care spending or willingness to pay (WTP) for improvements in health have the advantage of capturing broader impacts of illness than the monetary impacts most often captured in estimates of health care spending. However, these studies require specific information about how the disease affects employment or individuals' perceptions of what they would be willing to pay to avoid an illness, and collecting such detailed information on disease impacts is time and resource-intensive.

Although approaches are constantly evolving to improve upon the measurement and reporting of burden of illness to provide information needed to inform health policy

decisions, environmental scan interviewees identified several areas where additional research or information is needed:

- Local data for measuring all types of disease burden

- Valuing quality of life impacts of disease in a U.S. population

- Consistent measurement and tracking of preference-weighted HRQoL in the U.S. population

- Disease-specific national health spending data

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ATTACHMENT 1:
ENVIRONMENTAL SCAN EXPERTS AND THEIR AREAS OF EXPERTISE

Name	Affiliation	Area of Expertise and Contributions
Epidemiology		
Katherine Flegal	CDC	Senior epidemiologist who has done much work on disease research, primarily obesity. She has analyzed the deaths attributable to obesity. Good understanding of attributable fraction methods for disease risk factors.
Ali Mokdad	University of Washington	Prominent biostatistician who focuses on epidemiological research relating to chronic diseases, most notably obesity. Has also done considerable research in health survey implementation and methodology. Has also analyzed the deaths attributable to obesity.
Quality of Life		
David Cella	Center of Outcomes, Research, & Education	Principal Investigator of PROMIS initiative. Focusing primarily on quality of life research he is working to standardize the measurement of several major conditions that are important to people such as fatigue, pain, physical functioning, distress, depression, anxiety, and social functions.
Christopher Murray	Harvard University	One of the leading researchers behind the Global Burden of Disease Project. Helped to create the DALY. Has published a lot of work on all facets of disease burden.
Elena Andresen	University of Florida	Research measures and methods, psychometrics and refinements of health related quality of life and disability instruments.
David Feeny	Kaiser Permanente Northwest's Center for Health Research	One of the developers of the HUI; expert on HRQoL issues use of QALY measures in cost-effectiveness analysis
Dennis Fryback	University of Wisconsin	PI for Health Measurement Research Group, which has the goal to evaluate the use of widely used health measures, understand the strengths and limitations of each, and create a versatile "toolbox" of summary measures of health that can be used to track changes in the public's health over time. Also publishes on patient reported outcomes.
Ted Ganiats	UCSD	Has extensive experience with measuring HRQoL for use in cost-effectiveness analysis.

Name	Affiliation	Area of Expertise and Contributions
Robert Kaplan	UCLA	Has researched and published works relating to a wide range of health topics, including QALYs, epidemiology, outcome measurement, and data analysis. Has recently worked with quality of life measurements and their effectiveness.
Rosemarie Kobau	CDC	Public health advisor in the Division of Adult and Community Health at CDC's National Center for Chronic Disease Prevention and Health Promotion. Also works with the CDC's health-related quality of life program.
Economic Cost		
Martin Brown	National Cancer Institute	Chief of NCI's Health Services and Economics Branch. His research focuses on the economic burden of cancer to individuals and society and the financial structure of research support in the context of the changing system of healthcare delivery organization and financing.
Louise Russell	Rutgers University	Research focuses on the methods and application of cost-effectiveness analysis. Recent work focuses on preventative care and the possible economic benefits.
David Cutler	Harvard University	Has worked on National Health Expenditure Accounts. Very involved with current health care reform and the high costs associated with preventable disease.

ATTACHMENT 2:
LIST OF DISCUSSION TOPICS FOR ENVIRONMENTAL SCAN INTERVIEWS

February 17, 2010

All:

- Purpose of the project and the environmental scan
- Why we have selected you to interview for the environmental scan
    - focusing on your expertise in [epidemiologic, economic, or quality of life] burden of illness measurement

Epidemiology experts:

- How current epidemiologic burden measures are being used
- Current epidemiological research
    - New definitions, classifications, or initiatives
- Potential efforts to standardize existing methodologies
- Problems and limitations relating to obtaining reliable data
    - Initiatives to standardize and improve data collection
- Directions for future research
    - What areas need to be addressed?
        - Potential hurdles and setbacks
- Other potential epidemiological experts
    - Focus on experts conducting groundbreaking research or attempting to use new methods
- General comments relating to burden of illness
    - Epidemiology related
    - Economic cost or quality of life

Economic Burden of Illness experts:

- Issues in cost-of-illness (COI) estimation that we have identified
    - Health care costing
        - Differences in methodologies, disease definitions, and data sources lead to wide differences in COI estimates
        - Double counting of costs from studies that use a bottom-up approach
    - Human capital approaches
        - Appropriateness of friction cost methods
        - Lack of valuation of morbidity-related losses for children or older adults
    - Willingness-to-pay (WTP) approaches
        - Estimates differ widely depending on approach used for WTP estimation
        - Limited data availability
        - WTP estimates are bounded by income
    - Are there other issues about which we should be aware?
- New research on economic burden of illness
    - Disease-specific National Health Accounts
    - BEA allocations of disease spending across diseases

- – Comparisons of WTP and human capital estimates of morbidity- and mortality-related losses from disease
- – Other new research about which we should be aware?
- Other areas for future research?
- Names of other potential economic burden of illness experts with whom we should speak
- General comments relating to burden of illness
    - – Epidemiologic measures
    - – quality of life measures

Quality of Life experts:

- Use of current quality of life measures
- Functional status research
    - – Improvements to existing measures
    - – Disease specific measures
    - – Future research and improvement
        - • Existing problems that need to be addressed
- New research concerning utility and its measurement
    - – Work relating to Standard Gamble and Time-Trade-Off approaches
- Research involving QALYs, DALYs and HALYs
    - – Discussion of life valuation thresholds
- Status of specific U.S. burden of disease projects
- Updates on PROMIS initiative (from experts involved with PROMIS)
    - – Additional standardization efforts
    - – Future areas of focus
    - – Methodologies and lessons learned
    - – Additional government initiatives?
- Direction of future research
    - – What areas need to be addressed?
        - • Potential hurdles and setbacks
- Names of other potential quality of life experts with whom we should speak
- General comments relating to burden of illness
    - – Quality of life related
    - – Economic cost or epidemiology

Attachment 2-2

ATTACHMENT 3:
ADDITIONAL RESOURCES PROVIDED BY ENVIRONMENTAL SCAN INTERVIEWEES

Interviewee	Additional experts recommended	Additional materials recommended for review
Elena Andresen	Ron Hays	2006 IOM Report; COSMIN study; Fryback et al., 2010
Martin Brown	Steve Krower, Ron Hays, Cam Donaldson	
David Cella	Bill Riley, Rosemarie Kobau	NIH "PROMIS" and "Toolbox"
David Cutler	Ana Aizcorbe, Emmett Keeler, Kevin Murphy, Bob Topel, Michael Chernew	
David Feeny	Jane Sisk	HUI documentation, McIntosh et al. (2009)
Katherine Flegal	Miguel Hernan, James Robbins, Donald Berry	CISNET, Archimedes Model
Ted Ganiats		
Ron Hays		ISOQOL, Cherapanov and Hays (2010)
Robert Kaplan	Marthe Gold	
Rosemarie Kobau		MATCH, SMART (extension of BRFSS)
Ali Mokdad	Majid Ezzati, Christopher Murray, Goodarz Danaei	Murray et al. (2006)
Christopher Murray	Colin Mathers	Murray et al. (2002)
Louise Russell	Robin Yabroff	Fryback et al. (2010)