

Methodological Approaches to Measuring the Burden of Disease due to the Ten Leading Health Indicators in Healthy People 2010.

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## BACKGROUND

Healthy People 2010<sup>1</sup> identifies 10 Leading Health Indicators (LHIs), which may be used to monitor the nation's progress in improving its public health efforts. These LHIs are listed in Table 1. Each of these indicators is a global behavioral risk factor, collection of diseases, or social factor that can be measured and tracked. Regardless of the nature of the indicator, each is associated with multiple illnesses or conditions. Presently, the nation's progress towards improving health outcomes related to these measures is tracked via changes in incidence rates, mortality rates, as well as other objective-specific outcomes via large national datasets.<sup>2,3</sup>

It is difficult for policymakers, health care professionals, and the general public to understand how progress made in reducing one indicator, such as injury and violence, compares with progress made toward reducing another, such as obesity. While injury and violence (indicator 7) often result in the loss of life, obesity (indicator 2) mostly results in morbidity. For example, while it is easy to understand that the incidence of injury and violence has decreased by 5 percent and the incidence of obesity has decreased by 2 percent over a given period, it is difficult to interpret the relevance of the changes in these incidence rates from an overarching perspective.

Table 1. LHIs to be used in Healthy People 2010.

- 
1. Physical Activity
  2. Overweight and Obesity
  3. Tobacco Use
  4. Substance Abuse
  5. Sexual Behavior
  6. Mental Health
  7. Injury and Violence
  8. Environmental Quality
  9. Immunization
  10. Access to care
- 

When presented as a summary measure, the burden of disease combines morbidity and mortality information within a single metric.<sup>4,5</sup> Burden of disease analyses can also summarize multiple conditions, such as those conditions attributable to a LHI.

Burden of disease measures tell consumers of Healthy People 2010 how many years of full health, or health-adjusted life years (HALYs), are lost to a particular condition or disease. (While other global outcome measures, such as disease-free life expectancy, fall under the rubric of burden of disease measures, we will not address these here.) Health-adjusted life years and healthy life expectancy (HALE) are standard measures of the burden of disease.<sup>4-6</sup> Both measures summarize: risk of various diseases or conditions that are attributable to a LHI, their prevalence, and their associated health-related quality of life (HRQL) and mortality.

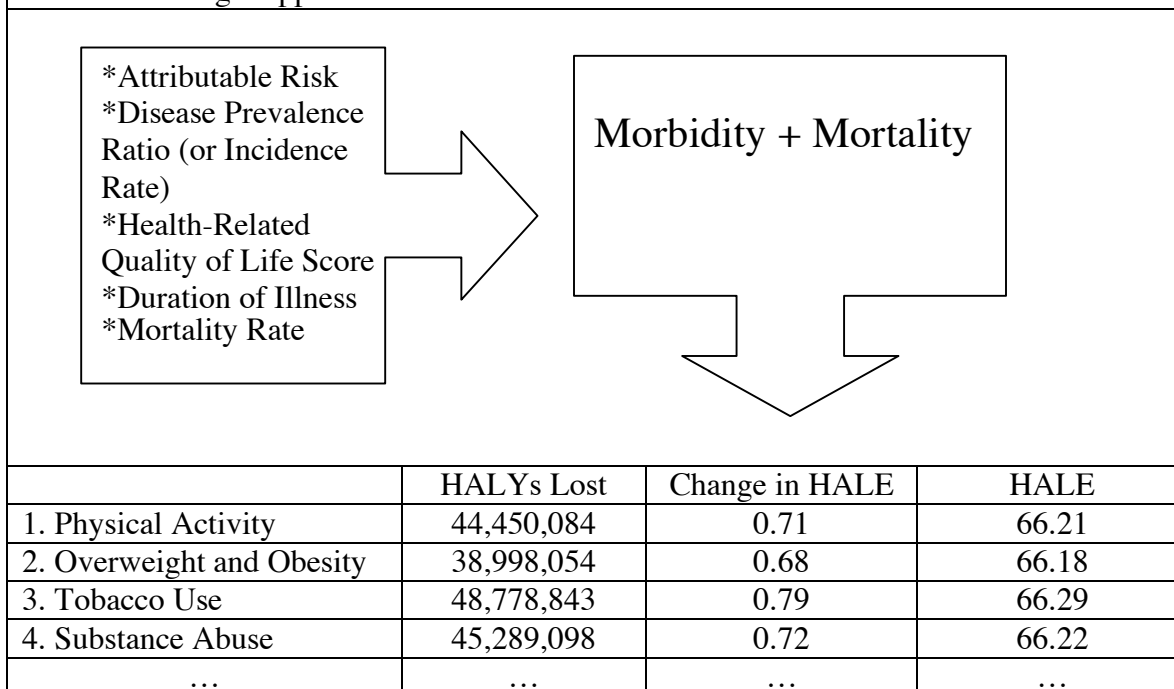
The HALY is an umbrella term that includes quality-adjusted life years (QALYs),<sup>7</sup> which were developed to evaluate economic outcomes from medical interventions, disability-adjusted life years (DALYs), which were designed to measure global burden of disease,<sup>8</sup> and years of healthy life (YHLs), which were designed to monitor the health of Americans for Healthy People 2000.<sup>9</sup> No summary measure of health is currently included in Healthy People 2010.

Health-adjusted life expectancy can be calculated using any of these measures and is equal to the life expectancy at birth in full health. There are various ways of presenting HALE. For instance, it would be possible to present the difference in HALE for persons who do and do not use tobacco (indicator 3)<sup>9</sup> or to present cause-deleted HALE, in which case the HALE for persons who do not use tobacco would be presented alongside the

average life expectancy.<sup>10</sup> Figure 1 demonstrates some ways in which burden of disease measures can be presented, using hypothetical values for the LHIs.

Using such burden of disease summary measures, it is theoretically possible to: 1) concisely communicate the nation's progress toward addressing each indicator, 2) provide information on the number of HALYs gained by improvements in the LHIs, and 3) prioritize one indicator relative to another in terms of its impact.

Figure 1. Various ways of presenting burden of disease summary measures for the LHIs should Healthy People 2010 objectives be met. The baseline HALE for the year 1999 was approximately 65.5 years.<sup>2</sup> Hypothetical values have been entered to illustrate how such a table might appear.



Burden of disease analyses simplify the presentation of health information. In addition to combining morbidity and mortality into a single number, as described earlier, they greatly simplify the presentation of information relating to multiple conditions. One problem encountered with Healthy People 2000 was that overall incidence and mortality rates of diseases with multiple etiologies were listed under multiple objectives (each with a document heading).<sup>1</sup> For instance, the overall rate of heart disease appeared under document headings for tobacco use, physical activity, nutrition, as well as others (including an overall heading for heart disease), causing redundancy and, potentially, confusion on the part of the reader.

To fix this problem, Healthy People 2010 presents the rate as a single objective and mentions the association between heart disease and multiple outcomes under each objective. Were burden of disease measures to be used, it would be theoretically possible to provide the number of HALYs lost to tobacco use as a single number that incorporates HALYs lost to heart disease, cancer, and other tobacco-associated conditions, as can be seen in Figure 1.

Burden of disease data can also help policymakers better understand which diseases should be prioritized for public health funding. For example, in the mid-1990s, the World Health Organization began reporting the burden of disease due to major health conditions using the disability-adjusted life year (DALY), a burden of disease measure.<sup>6</sup> Prevalent conditions that had previously been followed using mortality as an outcome but caused few deaths, such as depression, moved from the bottom of the rankings to near the top. The use of the DALY has allowed policymakers to better understand the impact of a range of mental and physical diseases and conditions within societies.

## **ISSUES AND APPROACHES**

The use of burden of disease measures is not without controversy, and the calculation of such measures is technically complex, especially when applied to a LHI. When estimating the burden of disease due to a LHI, researchers require information on attributable risk, prevalence ratios (or incidence rates), HRQL, and mortality rates associated with a disease or condition. Depending on the approach used and the disease under study, they may also require information on the duration of an illness, and whether or not the disease is episodic.

When applied to broad public health issues, such as the 10 LHIs, it becomes necessary to tease apart various risk factors for disease. For instance, the first three indicators—physical activity, tobacco use, and obesity—are each risk factors for heart disease. The burden of heart disease attributable to each of these indicators must be calculated separately. Moreover, exercise may reduce smoking and obesity simultaneously. Mathematical approaches to teasing risk factors apart are broadly known as attributable risk calculations.

The prevalence ratio of most conditions attributable to any given indicator may be estimated from large national datasets. However, large national datasets do not capture the incidence rate of diseases well. They also fail to capture the prevalence of rare conditions or conditions for which self-report data presents ethical problems (i.e., mental illness or HIV/AIDS).

One challenge is to obtain a reasonable estimate of HRQL. To combine lost health due to morbidity and mortality into a single metric, morbidity and mortality must be measured on the same scale. Some experts question whether the sacrifices that were necessary in creating a broad public health measure such as the DALY,<sup>6</sup> used for international comparisons, or the YHL,<sup>11</sup> used for tracking in Healthy People 2000, have succeeded in their attempts to correctly scale morbidity.<sup>4</sup>

Mortality due to a condition may be measured using death certificate data,<sup>12</sup> surveys linked to death certificate data,<sup>13,14</sup> prospective trials, or mathematical modeling. Each of these methods of measuring mortality presents trade-offs in terms of error, the extent to which rates can be tracked from year to year, and the ability to link risk factors with the number of deaths that occur. In sum, when estimating burden of disease, there are many different approaches, all with attendant issues, that must be considered when estimating the attributable risk, the measurement of morbidity, and the measurement of mortality.

Compounding these issues, no unified source of data exists that can be used to develop a mathematical model of the independent and correlated effects of all 10 LHIs on

morbidity and mortality. Instead, it is necessary to estimate the burden of disease from many different sources of information. Some data can be linked via a process called mapping, in which data from two or more sources are linked together. This process introduces unique sources of error and will not likely provide enough information to adequately model the burden of disease due to all 10 LHIs.

While it is not possible to provide a coherent framework for tabulating the burden of disease due to the 10 LHIs, we will outline possible methodological approaches for measuring incremental annual changes in HALYs or HALE and flag some of the issues that have arisen in past efforts. We also discuss how the burden of disease might be tabulated for special populations, such as persons of low income. We summarize the opinions of experts in tackling these critical issues, present standard and theoretical approaches to calculating risk, morbidity, and mortality from the public health literature, and synthesize this information where possible. The objective of this report is to draw on the strengths of different schools of thought to formulate a menu of methodological options for calculating the burden of disease due to the 10 LHIs.

## **METHODS**

We began the project with an extensive review of the burden of disease literature. This was conducted using a Medline search between the years of 1980 and 2001, a ProQuest search for publications beyond the scope of the medical literature, and an Internet search for relevant government documents and publications. We also obtained relevant books and publications using library searches.

Though most approaches to the estimation of burden of disease have been published, many of the issues that have arisen in applying these measures have not. Therefore, we interviewed experts in the field of burden of disease analysis to obtain their ideas and perspectives on how the 10 LHIs might be approached (see Appendix A for a list of participants). These consultants were selected based on 1) their familiarity with attributable risk, morbidity measures, and/or mortality estimations, 2) their history of working with disparate approaches (to avoid bias toward a particular approach), and 3) their experience with working in teams or with government agencies charged with calculating the burden of disease.

We sent each participant a letter of introduction describing the project as well as a technical document describing the issues, major datasets that might be used, and some of the approaches currently in use. We then conducted informal telephone interviews using open-ended questions to learn how each participant might approach the particular aspect of burden of disease measurement for which the expert is familiar. We also obtained information on issues the expert encountered in applying these methods in previous research efforts. Finally, we conducted a more structured interview asking the expert to assist us with data issues or methodological approaches specific to each indicator. Those persons with broad expertise in burden of disease analysis were asked to comment on draft copies of the synthesized document so that a cohesive framework could be created that would link each of the methodological approaches together.

To present the issues and approaches in a coherent way, we have divided the remainder of this document into sections describing major nationally representative health datasets, the estimation of attributable risk, measures used for estimating

morbidity, and methods for estimating mortality. The final section describes issues and approaches specific to each of the 10 LHIs.

## **NATIONAL DATASETS**

Healthy People 2000 used a wide variety of nationally representative datasets to track the nation's progress toward meeting the objectives outlined in that project. Foremost among these were the National Health Interview Survey (NHIS), the Medical Expenditure Panel Survey (MEPS), the National Health and Nutrition Examination Survey (NHANES), the Multiple Cause of Death Datafile, and the Behavioral Risk Factor Surveillance System (BRFSS).

For any particular datafile, it is desirable to have a set of core variables for which the assessment changes little from year to year so that burden of disease calculations can be reliably obtained and tracked on a regular basis. While no single survey likely contains enough information to calculate the burden of disease due to an indicator, it may be possible to combine survey data. The data sources listed below are not all comparable and differences may occur when a specific outcome measure is obtained from two different sources.<sup>15</sup>

### **THE NATIONAL HEALTH INTERVIEW SURVEY (NHIS)**

The NHIS is an annual nationally representative survey of the civilian non-institutionalized population that was first conducted in 1957. The annual survey consists of a core file that varies little from year to year (though major changes are made to the core file once every 10 years). The entire sampling frame consists of 110,000 persons in 40,000 households. Income, race and ethnicity data are collected, and black and Hispanic households are oversampled. Adults in the household serve as respondents; proxy responses are allowed for absent adults and are required for children or persons unable to respond themselves.

Due to the relatively large sample size and large number of prevalent conditions examined, this survey is useful for burden of disease estimation for most common conditions. The survey is limited by recall bias, inclusion of proxy responses, and a lack of a validation mechanism for conditions (e.g., gastroenteritis may be reported as "the flu").

### **THE MEDICAL EXPENDITURE PANEL SURVEY (MEPS)**

The survey consists of a household component, an insurance component, a nursing home component and a medical provider component. The medical component is useful for supplementing and/or validating information provided in the household component.

The MEPS household component utilizes the same sampling frame as the NHIS but the total sample size is smaller. It includes additional information, including survey questions from 2 health status instruments, the EuroQol and the SF-12. It also includes information that, when linked with other ongoing surveys, could be used for economic studies of the 10 LHIs, should such information be desired in future research endeavors.

Moreover, these data are linked to other components of the MEPS, such as data from the respondents' medical and insurance providers.

Data for comprehensive socio-demographic variables, including income, education, race, and ethnicity, are collected. The MEPS has recently been increased to encompass 15,000 households and approximately 40,000 persons (Steve Cohen, personal communication).

### **THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES)**

The NHANES is a survey of the civilian non-institutionalized population of the United States that contains detailed dietary, laboratory, and medical examination data. Beginning in 1999, the survey will be conducted annually and will be linked to the NHIS and the Continuing Survey of Food Intakes by Individuals, a dietary survey conducted by the United States Department of Agriculture. The survey is linked to the NHIS at the Primary Sampling Unit level, rather than at the individual level. Furthermore, 5000 individuals are added to the sample each year. Non-Hispanic blacks, Mexican-Americans, the young, and the elderly were oversampled. Complete socio-demographic information is available for tabulations by race, ethnicity and socioeconomic status.

These data are subject to little non-random error since the parameters are measured by health professionals and are not subject to recall bias. For instance, correlates of smoking status can be measured via cotinine levels in the blood rather than reports of the number of cigarettes smoked.

The NHANES cohort is linked to death certificate data, allowing risk factors to be associated with causes of death. These data may serve to validate mortality data obtained from death certificates or to apportion the risk of death for certain conditions using attributable risk models. For instance, in calculating the burden of disease due to substance abuse (indicator 4), it may be possible to use the NHANES-linked mortality data to determine the proportion of cirrhosis cases attributable to alcoholism.

### **BEHAVIORAL RISK FACTOR SURVEILLANCE SYSTEM (BRFSS)**

The Behavioral Risk Factor Surveillance System (BRFSS) is a telephone-based survey of over 150,000 persons that is conducted at the state level.<sup>16</sup> Core questions are conducted on a rotating basis and are available once every two years. Included in the sample are variables specific to tobacco use, alcohol consumption, immunization status, health care access, weight control, exercise, diabetes, cardiovascular disease and socio-demographic composition. Socio-demographic variables include race, ethnicity, education, and income. This survey also incorporates an accounting of "healthy days." These are not suitable for calculating HALYs, however.

Using this survey, it is possible to apportion the risk of various leading diseases by risk factor. The survey is conducted annually. Since states conduct the survey, combining these data is methodologically challenging. Moreover, while each state asks the same set of core conditions, many variables are state-specific.



### **NATIONAL HOUSEHOLD SURVEY ON DRUG ABUSE (NHSDA)**

The NHSDA is conducted annually and is a representative sample of persons aged 12 and older residing in the US. It contains both incidence and prevalence data of non-medical drug use, all relevant socio-demographic variables, and some conditions associated with drug use.

### **COMMUNITY TRACKING SURVEY (CTS)**

The CTS is a sample of 36,200 families in 60 communities. In this survey, subjects are representative of the community in which they live; however, they are not weighted to the United States population as a whole. The survey includes the Short Form 12 (SF-12), which is a health status measure, and relevant socio-demographic variables.

### **ANNUAL SURVEY OF OCCUPATIONAL INJURIES AND ILLNESSES (ASOII).**

The ASOII is an annual survey conducted by the Bureau of Labor Statistics of approximately 250,000 private establishments. This survey excludes the self-employed, small farmers, and government workers, but it contains variables pertinent to most workplace injuries. The survey is subject to underreporting.

### **DEATH CERTIFICATE DATAFILES**

Death certificate datafiles, which include the multiple cause of death datafile, are useful for calculating the years of life lost in burden of disease analyses. They contain information on the decedents' age, education level, and the cause of death; however, they do not contain information on decedents' income, limiting analyses by socio-economic status.

The multiple cause of death datafile and other death certificate datasets are not obtained from a sample. Rather, these datasets contain information on all reported deaths in the United States each year, so they are not subject to random error. However, since the precise cause of death is sometimes difficult to determine, and since the person filling out the form may misclassify the cause of death, some causes of death are subject to non-random sources of error, and the data do not contain information on individual risk factors. Therefore, attributable risk estimates cannot be obtained using these data. These data are useful for tracking annual changes in mortality rates once attributable risk has been determined via other sources.

### **NATIONAL MORTALITY FOLLOWBACK SURVEY (NMFS)**

This survey enhances death certificate information with a sample of responses from next of kin who were familiar with the decedent's life history. The latest survey was conducted in 1993 and sampled the next of kin of persons who died in 1993 aged 15 or older. It is based on 22,957 death certificates and contains comprehensive socio-demographic information, risk factors for disease, and health utilization. Blacks, persons under 35, and women are oversampled. These data are limited by respondent bias and

are considerably older than other sources of mortality data. However, they may be useful in creating a model that calculates the risk of death attributable to a particular risk factor.

### **CENSUS OF FATAL OCCUPATIONAL INJURY (CFOI)**

The CFOI, conducted by the Bureau of Labor Statistics' Occupational Safety and Health Statistics Program, is a collection of disparate state and federal data sources rather than a survey per se. It identifies, verifies, and profiles fatal work injuries by cross-referencing source documents, such as death certificates, workers' compensation records, making it a good source of data on work-related fatalities.

### **ATTRIBUTABLE RISK**

The attributable risk refers to the amount of additional risk of disease conferred by having a risk factor for the disease. For instance, the risk of heart disease is increased for people with a sedentary lifestyle, smokers, and overweight people, among many other factors (e.g., diet and genetics).

Some indicators will not require attributable risk calculations. For instance, under-immunization refers to society's failure to administer measles, mumps, rubella, tetanus, and other vaccines on an appropriate schedule to appropriate groups. With notable exceptions, such as influenza virus and pneumococcal vaccines, most vaccine preventable illnesses are entirely attributable to under-immunization. When performing calculations for vaccine preventable illnesses, the burden of disease calculations will require inputs for vaccine efficacy and herd immunity effects but not the attributable risk of illness. Most LHIs, however, will require attributable risk calculations.

Attributable risk can be applied in various ways. First, a simple estimation of the burden of disease for various diseases or conditions attributable to a risk factor can be obtained. The burden of disease attributable to a risk factor can then be determined by summing across conditions. We will refer to this approach as the "simple approach." Second, logistic regression models can be developed that include the risk factor in question and all or most of the diseases and conditions attributable to that risk factor as variables.<sup>17</sup> In this approach, a separate model is developed for a relevant morbidity dataset and a relevant mortality dataset. The burden of disease is then estimated using resulting odds ratios (which can then be converted to risk ratios).<sup>18</sup> Finally, it is possible to use a combination of datasets and, in some instances, parameters from the medical literature, to create a mathematical model that can be repopulated with disease prevalence or mortality data on a yearly basis. We will refer to the latter approach as the "indirect approach."

### **SIMPLE ATTRIBUTION OF RISK**

The overall proportion of disease in the population attributable to the risk factor may be obtained using the formula:

$$AR = \frac{I_t - I_o}{I_t}$$

## Equation 1

where,  $I_t$  is the total risk in the population and  $I_o$  is the incidence among persons without the risk factor. This is sometimes referred to as the population attributable risk.

However, it is not always possible to obtain the incidence of a disease with and without a particular risk factor. Therefore, the prevalence of exposure to a risk factor and the relative risk of disease may be used to obtain the population attributable risk using the formula:

$$AR = \frac{P \cdot (RR - 1)}{1 + P \cdot (RR - 1)}$$

## Equation 2

where  $P$  is the prevalence of exposure and  $RR$  is the relative risk of the disease.

For the purposes of burden of disease measurement, it is sometimes convenient to calculate the proportion of cases attributable to a risk factor *among persons exposed to the risk factor*. For instance, for the purpose of calculating burden of disease estimates associated with the LHIs, investigators may need to estimate how many tobacco users developed heart disease as a result of having smoked, rather than the overall risk of heart disease attributable to smoking. This is sometimes referred to as the attributable fraction among the exposed, and it is accomplished using the formula:

$$AR = \frac{RR - 1}{RR}$$

## Equation 3

While each risk factor may be associated with multiple diseases (and even other risk factors), these formulas allow for the calculation of the risk attributable to each disease when independence across risk factors and conditions is assumed.<sup>19</sup> The burden of disease due to each risk factor can then be summed across diseases.

To increase the specificity of this approach, it is possible to calculate a risk schedule for various levels of exposure to a risk factor. For instance, if  $n$  is a particular level of exposure (e.g., a cholesterol level of 200 to 240), then Equation 2 becomes:

$$AR = \frac{\sum_{n=1}^x P \cdot (RR - 1)}{1 + \sum_{n=1}^x P \cdot (RR - 1)}$$

## Equation 4

If multiple risk factors are present, counting burden of illness from each one separately may overestimate the total burden of illness since independence is a tenuous assumption. To apply equation 4 to LHIs for which exposures overlap (i.e. exercise and tobacco use), information on joint exposures is needed. Where this is not available, a

more conservative approach may be to simply exclude overlapping exposures.<sup>19</sup> Age-stratification will pose additional challenges, and appropriate age intervals must be determined by estimating the sample size in various age intervals across datasets.

The advantage of this approach is that it is relatively transparent. The disadvantage is that it is difficult to determine the extent to which multiple diseases, conditions, and risk factors overlap. It may also be more resource intensive than deriving risk using regression analyses.

## USING REGRESSION ANALYSIS

The proportion of prevalent cases of a disease attributable to any given indicator may be calculated using nationally representative datasets, controlling for covariates via logistic regression analysis. For instance, Must et al calculated prevalence odds ratios (POR) for multiple conditions associated with obesity, for persons with varying body mass indices, relative to persons of normal weight using data obtained from the NHANES III.<sup>17</sup> (A POR is an odds ratio constructed from prevalence rates rather than incidence rates.) Outcomes were then adjusted to prevalence ratios using methods forwarded by Zhang and Yu.<sup>18</sup>

They examined the prevalence of type II diabetes, gallbladder disease, coronary heart disease, and osteoarthritis among persons falling into various National Heart, Lung, and Blood Institutes' weight classifications. This model controlled for age, smoking status, race, and ethnicity. The advantage of using logistic regression models is that it is possible to control for such socio-demographic covariates as well as comorbid conditions in calculating prevalence ratios. This method has been employed to test the effect of health insurance status on both morbidity<sup>20</sup> and mortality<sup>21</sup> and will be referred to in this report as the "regression method." This method may be appropriate when analyzing a single risk factor for multiple conditions (e.g., smoking).

One issue that arises when looking at multiple conditions or risk factors is whether the risk factors are independent and additive in conferring risk of disease. For instance, it is important to determine whether the risk of a coronary death for someone who is both obese and a smoker can safely assume that these variables are independent. When definitive information regarding risk factor independence is absent, expert opinion may serve as a useful starting point for estimating the contributions of different risk factors to disease.

This approach may be best employed when 1) a dataset is available that contains the relevant risk factor and all relevant conditions, 2) the sample size of the dataset is adequate, and 3) the model can be validated using standard distributional and probabilistic tests used in logistic regression analyses. Most federal datasets require the use of software packages that can analyze complex sample schemes, such as SUDAAN or STATA.

Advantages of this approach include its relative simplicity and the ability to delineate interactions and error more objectively relative to other approaches. Disadvantages include the inability to apply the approach to all indicators, the inability to account for error in burden of estimates across datasets (i.e., the extent to which the use of one dataset might differentially favor some effects a risk factor has on disease

estimates when one dataset is used relative to another dataset), and the inability to estimate all effects when the sample size is small or the model is imperfect.

One issue that arises in applying the regression approach to national datasets is the compromise between trackability and non-random error of various datasets. For instance, while few experts dispute that the NHANES is the best dataset for calculating the attributable risk of overweight and obesity (since health professionals measure height and weight in this study), it may not be as useful for tracking disease on an annual basis as surveys that are broadly applied to the population on an annual basis. The NHIS requires subjects to self-report their height and weight, but it is conducted on an annual basis, allowing data to be easily tracked. One modestly resource intensive method of circumventing this problem would be to use the NHANES to validate models generated from the NHIS or the MEPS, an area in which work has already been done.<sup>22</sup> Were we to extend this approach by including multiple datasets to increase the breadth of variables and to cross-validate the results, we would obtain the indirect approach to deriving attributable risk, which is much more resource intensive.

### **USING THE INDIRECT APPROACH**

It can be argued that the attributable risk of disease may not vary a good deal over the relatively short ten-year period for which Healthy People 2010 is conducted, and that the use of a single, well-designed indirectly derived (or static) model can provide a sturdy skeletal framework for capturing the burden of disease. In the indirect approach, a static attributable risk model is built using multiple sources of data. This model can then be populated with annual disease prevalence and mortality data, so that the burden of disease can be tracked from year-to-year.

When attributable risk models are built using the best combination of data sources available, the specificity of the analysis may be enhanced. It is also possible to use multiple datasets to cross-validate uncertain parameters, such as HRQL values or self-reported rates. Year-to-year changes in the burden of disease may then be measured by tracking changes in the disease prevalence ratio (or incidence rates) and mortality rates.

Cross-validation can be achieved by comparing values generated using different datasets. For instance, the HRQL of tobacco users can be obtained by generating values from the YHL measure, which is linked to the NHIS, and the EuroQol (another HRQL measure that is described in detail below), which is linked to the MEPS. Under the guidance of experts, these scores can be used to obtain a range of error and a best-estimate of the HRQL and attributable risk.

It may also be possible to utilize variables that have been mapped across datasets or to obtain estimates from the medical literature<sup>23,24</sup> when more information is needed than is available from a solitary source. However, the type of error inherent to a data varies greatly across datasets and not all authors present results of analyses with and without sociodemographic covariates that may be relevant for Healthy People 2010, such as race and income, limiting the usefulness of such an approach.

The advantage of the indirect approach is that it adds flexibility by increasing the variables available to researchers and may improve validity by providing a rough range of error. Disadvantages include the intensive nature of the analysis and the inability to measure main effects in any model with certainty. It can also be argued that a dynamic

relationship exists between risk factors for disease that cannot be accounted for in a single snapshot of disease prevalence attributable to a particular risk factor. For example, more African-Americans appear to be exercising while simultaneous, and paradoxical, increases in obesity and smoking have been reported for this group.<sup>2</sup> Reliance upon attributable risk models derived using the indirect approach may therefore belie the objective of tracking the nation's progress toward improving the LHIs. Nonetheless, such models are likely to be needed when the simple or regression approaches cannot be employed.

## **MORBIDITY**

To begin a discussion of the morbidity component of a burden of disease analysis, it is necessary to describe how morbidity is combined with years of life lost in estimating the burden of disease. Health-adjusted life years are calculated by combining the amount of time lived with disease or a health condition with years of full health lost when a person dies of a condition. Each year of life lived with disease is assigned a HRQL weight that assumes a value between 0 and 1. Depending on how the measure is calculated, 1 is either equal to full health (as in the QALY) or death (as in the DALY), and 0 is assigned to the converse state. For instance, in the QALY, 1 is assigned a state of full health and the HRQL score 0.75 is equivalent to 0.75 years of full health.<sup>4,6</sup>

The details of HRQL weight assignment have been described in detail elsewhere,<sup>4,5</sup> but it is important to note that there are two steps in this process. One is the description of a health state, either by the person experiencing it or by researchers. In describing the health state, scenarios or health state descriptions are used to describe domains or dimensions that are commonly viewed as central to health. These might include physical and psychological function, role function, and pain or other symptoms.

After a health state is described, it needs to be valued. Valuation is accomplished in a number of ways. For instance, in the standard gamble, a subject is asked to choose between an undesirable state of health (e.g., living with diabetes) and a gamble between full health and death. The chance of death is varied until the subject is ambivalent towards choosing the treatment over the undesirable health state. The probability of death that is acceptable to the subject is equal to the HRQL score.

We will demonstrate the principle of weighting using an example. People living with diabetes might be assigned a QALY-compatible HRQL value of 0.75 for every year lived with the disease. Thus, if 1000 people aged 60 are living with diabetes and their life expectancy with diabetes at age 60 is 10 years, they would be assigned  $1000 \cdot 0.75 \cdot 10 \text{ years} = 750 \text{ years of full health}$ . Conversely, if the DALY were employed, it can be said that  $1000 \cdot 0.25 = 250 \text{ years of full health are lost to diabetes}$ .

To improve the specificity of the HRQL score, it may be desirable to capture changes in HRQL associated with multiple conditions, such as people who have diabetes as a result of being overweight or obese (indicator 2). Obese persons may plausibly have a lower than average HRQL score. Were it possible to capture both of these effects simultaneously, a person with both diabetes and obesity may have an HRQL of less than 0.75. Some measures and techniques are better suited to capturing multiple conditions. This will be discussed after reviewing potential sources of HRQL scores.

## SOURCES OF HEALTH-RELATED QUALITY OF LIFE SCORES

Here, we will discuss three common sources of HRQL scores that have been used to calculate HALYs or HALE in burden of disease analyses. First, HRQL scores may be obtained by linking nationally-representative surveys to generic preference-weighted HRQL instruments.<sup>11</sup> This approach was used to generate HALE in Healthy People 2000.<sup>2,3</sup> Second, it is possible to utilize a community sample of weights as a primary source of HRQL weights. For instance, Health Canada presently uses values obtained from the Health Utilities Index (HUI), a QALY-compatible measure based on a sample of community preferences, to calculate cause-deleted HALE.<sup>10</sup> Finally, the DALY utilizes lists of values generated by professionals to calculate HALYs.<sup>8</sup>

Generic preference-weighted HRQL instruments are essentially survey tools that are linked to a sample of community-derived preference weights. These instruments typically ask respondents questions concerning various health states, which are grouped into a number of different dimensions of health; different instruments capture different dimensions of illness. (For an example of such an instrument, see the EuroQol in Appendix 3.) The values entered into the instrument are then assigned a numerical score that is mathematically combined with responses to other questions on the instrument to derive an HRQL score.

The different instruments, which include the HUI and the Quality of Well-Being Scale (QWB), and the domains they capture are described elsewhere.<sup>5,6</sup> To maximize the specificity of HRQL scores, the match between the dimensions of the illness under study and the dimensions captured by the preference-weighted instrument should overlap. Since different instruments capture different dimensions of an illness, health economists have advocated careful selection of instruments in analyses of particular diseases when they are applied to cost-effectiveness analyses.<sup>4-6</sup> However, in burden of disease analyses that focus on many different diseases and conditions, the use of different methods for eliciting HRQL scores may affect the comparability of each analysis.<sup>25</sup> Therefore, it may be preferable to use a single measure.

The Short Form-36 (SF-36)<sup>26</sup> is a commonly used health measure that consists of a series of questions that capture functioning, feelings, abilities, and attitudes. This measure, which is available in abbreviated forms including the SF-12, is based on a 0 to 100 non-interval scale that cannot be directly used as a summary measure. Instead, this measure has been used to graphically represent both morbidity and mortality by presenting survival curves coupled with curves representing mild, moderate, and severe levels of morbidity.<sup>27</sup> More promisingly, the SF family of measures has been modified to include death as an anchor point and has been combined into a unitary measure of morbidity in an instrument called the SF-6D, which can utilize data from health surveys containing SF measures.<sup>28</sup> The SF family of measures has also been extrapolated onto the QWB scale, a QALY-compatible measure.<sup>29</sup>

The DALY utilizes weights obtained from person trade-off exercises administered to health professionals. Here, informants are asked how many people would need to be cured of a particular disease to equal the saving of a life. These weights were then used to devise scores for a large list of conditions. The Centers for Disease Control and Prevention (CDC) recently developed DALY weights for diseases and conditions

associated with the following risk factors: tobacco use, alcohol use, unsafe sex, obesity, and physical activity (McKenna—personal communication).

Lists of scores have also been extracted from the medical literature in an effort to compile a complete catalog of HRQL weights at Harvard University.<sup>30</sup> This catalog contains weights derived from a variety of different instruments and methods, so the scores contained therein are not comparable. We will therefore focus on dataset-linked measures and the DALY measure in this report.

#### **DATASET-LINKED MEASURES**

As of 2001, the MEPS began including the EuroQol instrument among its survey items. This initial step permits a description of the health states experienced by persons sampled therein. Coons et al will begin collecting U.S. preference weights for the EuroQol in early 2002, and results are expected to be available in 2003 (Coons—personal communication). Once preferences are available, it will also be possible to link them to the EuroQol health states described within the MEPS sample. This will provide information about weights or values, on a scale of 0-1, that are associated with the diseases and/or conditions contained within the MEPS survey. Using this measure, it will be possible to calculate and track the HALE of the non-institutionalized civilian population in the United States as well as the contribution of particular diseases to the overall disease burden.

In Healthy People 2000, the HALE of the population in general was calculated using the YHL measure, which was based on the Health and Activity Limitation Index (HALex).<sup>11</sup> Health-related quality of life scores were obtained using a technique called correspondence analysis, which extrapolated responses on health status and role function from the NHIS onto a preference-weighted instrument. By linking responses obtained from the NHIS to the HUI using correspondence analysis, it is possible to capture comorbid conditions. Still, correspondence analysis has yet to be validated, it is only community preference weighted via its association with the HUI, and relatively few health dimensions are captured by this measure.

The MEPS and the CTS contain questions specific to the SF-12, a subset of the SF-36 questions. The SF family of measures is widely used in the clinical and research settings, and it may also play an important role in mapping data from one data set to another. Methods forwarded by Fryback et al,<sup>4</sup> which allow for linkage between the SF questions and QWB scores, or, alternatively, the SF-6D, may be used to generate HRQL scores from datasets containing the SF-36 or subsets of SF questions.

In some instances, the EuroQol/MEPS linked data, YHL/NHIS data, or SF-based HRQL instruments may permit the calculation of HRQL for each LHI either using regression models or using the indirect approach. As with calculation of prevalence ratios using nationally-representative datasets, the sample size of the MEPS and the selected number of conditions available from the NHIS limit analyses of multiple conditions and the generation of age-specific scores for less prevalent conditions.



## ISSUES AND APPROACHES TO CAPTURING HRQL

Two issues that arise when considering HRQL scores are whether the measure captures co-morbidity and whether existing dataset-linked measures are adequate for capturing both disease prevalence and HRQL. In the example above, we saw that it would be desirable to capture changes in HRQL due to both diabetes and obesity. When preference-weighted generic instruments are used, both of these effects may be captured when entering values for various health domains. For instance, a severely obese person may have more mobility limitations than the average diabetic.

Murray and Lopez<sup>31</sup> recommend capturing co-morbidity by summing DALY scores under the assumption that co-morbidity is additive; however, this assumption has not been tested, and it is unlikely to be accurate since many conditions are likely to overlap.<sup>32</sup>

The use of a preference-weighted generic instrument that has been linked to variables in nationally representative surveys, such as that planned for the EuroQol, would circumvent many of the problems associated with comorbid conditions. Measures linked to nationally-representative datasets add specificity to the analysis by accounting for most co-morbid conditions subjects might have, regardless of exposure. Thus, in addition to accounting for changes in HRQL for most conditions associated with a particular exposure, it would be possible to compare the HRQL of persons with a sedentary lifestyle with the HRQL of the average person in the US (i.e., with a score less than 1) rather than a person in full health.

While the prevalence of illness may vary from year to year, the overall health-related quality of life of individuals afflicted with a particular condition can be expected to vary little, since this measure is based on an individual's perception of illness. Though the severity of most conditions may vary slightly, this may not have a large impact on HRQL from one year to the next. Therefore, it may be acceptable to apply scores that are not tracked from year-to-year, such as DALY weights. The use of such scores, however, may limit the ability to capture changes in health beliefs or disease severity over time.

Obtaining HRQL information for all of the LHIs presents a special challenge, since few datasets are linked to HRQL measures. One way of approaching HRQL estimates would be to utilize multiple datasets containing the SF family of scores. For instance, if the CTS were to be used to assess morbidity associated with poor environmental quality, it would be possible to generate both disease prevalence estimates and changes in HRQL using this dataset.

## MORTALITY

The calculation of unadjusted years of life lost due to each condition is less controversial than approaches to the calculation of attributable risk or HRQL. Life tables produce reliable estimates of life expectancy and may be employed to calculate the HALE for persons with a particular condition or risk factor.<sup>9,11,33</sup> Formulaic approaches include mathematically-derived curves that estimate life expectancy as well as those anchored on a ideal life expectancy, used to calculate DALYs.<sup>31</sup> Rosenberg et al review various techniques, including the use of Bayesian analysis.<sup>34</sup>

The estimation of the aggregate risk of mortality due to a particular indicator is not possible using death certificate data alone, since such data do not contain data on exposure to risk factors. Therefore, there is no reliable way of tracking changes in the risk of death attributable to a particular risk factor on a year-to-year basis. Sources of risk factor-associated deaths, such as the National Mortality Followback Survey or the NHANES I and II, may be used to attribute risk of mortality in aggregate to some of the indicators.

### USING LIFE TABLES TO CALCULATE HALYS

Erickson et al describe the use of the YHL measure for calculating HALE in the United States.<sup>11</sup> It is also possible to utilize the HRQL scores from the EuroQol, to use SF-12/36 data linked to the QWB or the SF-6D, or to utilize community samples to capture the overall health of the United States population.<sup>9,29,34</sup> Disease-specific HRQL scores may be used to estimate cause-deleted HALE using any measure, including the DALY.<sup>31</sup> For a worked description of calculating HALE due to a specific condition or cause-deleted life expectancy, Muennig and Gold.<sup>11</sup> Wolfson also provides an excellent overview of HALE.<sup>10</sup>

To health-adjust life table values, the total number of person-years in any given age interval in an abridged life table is simply multiplied by the HRQL score of interest. HALE is then calculated for persons with and without the condition(s) of interest as follows:

$$\text{HALE}_{\text{Population}} - \text{HALE}_{\text{Disease}}$$

Equation 5

where “disease” refers to the condition of interest. For a complete description of standard life table methods, see Anderson.<sup>35</sup>

### USING DALYS

The number of DALYs lost to a particular condition is calculated using the formula:

$$\text{The Years of Life Lost (YLL)} + \text{The Years Lost to Disability (YLD)}$$

Equation 6

where YLL is the total years lost to the disease, and YLD is equal to the product of the time spent in a health state and the disability weight.<sup>31</sup>

In the DALY, the disability weight utilizes 0 as full health and 1 as death, such that the product of the DALY HRQL score and the time in the health state yields the years of life lost to disease. When a HRQL score associated with QALYs is used, the score may be subtracted from 1 and then substituted into Equation 6. A detailed description of the use and theory of the DALY measure may be found in Murray and Lopez.<sup>31</sup>

The CDC is nearing completion of a DALY-based US-specific burden of disease analysis for various risk factors and conditions that overlap with those discussed here. Risk factor analyses include tobacco use, alcohol use, unsafe sex, obesity, and physical activity (McKenna—personal communication). Conditions that underlie some of the indicators of Healthy People 2010 or are themselves indicators include ischemic heart disease, stroke, neuropsychiatric disorders, diabetes mellitus, cancer, HIV/AIDS, and injuries. In all, the CDC analysis includes all indicators but environmental quality (indicator 8), immunization (indicator 9), and health care access (indicator 10).

## **INDICATOR-SPECIFIC ISSUES AND APPROACHES**

In this section, we suggest ways of synthesizing disease prevalence, HRQL, and mortality data and addressing issues and approaches specific to each of the 10 LHIs. We draw heavily from the lessons learned, data sources, and other information provided in Healthy People 2000.

The optimal methodological approach and data sources will vary from indicator to indicator; no uniform method is currently available for estimating the burden of disease associated with all indicators. Moreover, we do not suggest which approach is optimal, but we do highlight relevant methodological considerations and data issues. Table 2 lists possible sources of data by indicator. Consultation with experts in each of these areas was beyond the scope of this paper, but it may be important to include such consultation when tabulating the burden of disease due to the LHIs.

In some instances, it may not be necessary to include all of the conditions associated with the risk factor in the analysis, since some conditions contribute little to the overall burden of disease associated with a particular risk factor. When using regression models to attribute risk, inclusion of minor conditions may not be possible due to sample size limitations. Since the duration of acute conditions limits their contribution to societal morbidity, acute conditions may only be relevant in instances in which the prevalence ratio or mortality rate associated with them is high. Throughout this section, we also attempt to highlight those conditions which may be less relevant based on their prevalence, severity, or duration.

### **PHYSICAL ACTIVITY**

Between 14 and 23 percent of all premature deaths in the United States may be associated with physical inactivity.<sup>23,36</sup> Physical activity has been shown to reduce the risk of heart disease, diabetes, and high blood pressure. It may reduce the risk of other diseases or condition other risk factors as well.<sup>37-40</sup>

Physical activity is currently regularly monitored in the NHIS, which asks respondents about different levels of exercise performed and is also included in the NHANES. These data may be used to obtain prevalence ratios and attributable risk data for heart disease, overweight and obesity, diabetes, colon cancer, and high blood pressure. By linking NHIS and MEPS data, it may be possible to generate overall HRQL scores for persons who do and do not participate in exercise, after controlling for covariates using any of the methods described in the Morbidity section above.

Since many of the conditions associated with physical activity and obesity are similar, a single multivariate model could be used to determine attributable risk and HRQL scores for each indicator. Relevant dependent and independent variables could then be substituted. It is also possible to calculate the risk attributable to each condition, or to combine multiple datasets with the medical literature via the indirect approach mentioned in the Morbidity section above.<sup>41</sup>

### **OVERWEIGHT AND OBESITY**

Overweight and obesity increase the risk of heart disease, stroke, diabetes, gallbladder disease, hypertensive disease, and possibly other illnesses and conditions.<sup>42</sup> The burden of disease and the attributable risk of these conditions may be examined one by one, cumulatively using a single regression model, or via the indirect approach.

The calculation of the prevalence of overweight and obesity may be obtained from the NHIS and/or the NHANES. Health-related quality of life information for specific conditions is available from MEPS/EuroQol data, the YHL, or SF-36 extrapolated measures. Mortality risk may be estimated using the NHANES or the Mortality Followback survey.

The prevalence of overweight and obesity obtained from the NHIS underestimates prevalence values for this condition obtained from the NHANES.<sup>2</sup> Therefore, it may be useful to obtain the initial attributable risk calculations and burden of disease estimates from the NHANES, and then track adjusted values from the NHIS. Alternatively, this information may be calculated using the NHIS or MEPS for annual monitoring purposes with the caveat that the self-report data may bias the results of the analysis.

### **TOBACCO USE**

Tobacco use is associated with cancer, heart disease, chronic obstructive pulmonary disease, and stroke, and it may account for as many as one in five deaths in the United States.<sup>23,43</sup> The prevalence of tobacco use may be obtained from the NHIS, MEPS, or the NHANES, and the attributable risk of the leading conditions associated with its use may also be obtained and tracked using any of these datasets. In an earlier cost-effectiveness analysis, QALYs were calculated for smokers, non-smokers, and former smokers using the YHL measure;<sup>44</sup> it will also be possible to perform these calculations using the MEPS.

As with other broad indicators, conditions may be examined individually, a best baseline estimate may be obtained using the indirect approach, or the overall risk may be assessed using a single model. Whether to capture less prevalent conditions associated with tobacco use (e.g. bladder cancer) depends on the extent to which capturing these conditions would impact sufficiently upon the overall burden of disease estimate to justify the additional effort, or requirements for other data sources.

### **SUBSTANCE ABUSE**

Healthy People 2010 includes alcohol and other illegal drugs under the rubric of substance abuse, but it separates tobacco use into a separate header. The leading

conditions associated with morbidity and mortality due to substance abuse include HIV/AIDS, motor vehicle accidents, cirrhosis, and other less prevalent or acute conditions.<sup>2</sup> The calculation of the burden of disease due to substance abuse presents unique challenges given that the incidence, prevalence, and mortality rates of these conditions are not tracked in the most common national datasets.

The NHSDA, which contains both incidence and prevalence data of non-medical drug use, all relevant socio-demographic variables, and some conditions associated with drug use, may be the best source of prevalence data. It may be also be necessary to estimate morbidity and mortality due to substance abuse via the medical literature and expert estimations of the risk of conditions such as HIV, AIDS, endocarditis, automobile accidents, workplace accidents, and cirrhosis attributable to substance abuse. Therefore, the indirect method of estimation is perhaps the most useful approach to burden of disease estimations for this indicator.

Importantly, substance use itself is likely to result in decrements in HRQL. While we were not able to find a source of HRQL scores specific to substance abuse, it may be possible to estimate this HRQL value using preference-weighted generic instruments that capture role functioning and mental illness using expert opinion.

## **SEXUAL BEHAVIOR**

The burden of disease contributed by acute infectious conditions may be small relative to HIV/AIDS, since they are either of short duration or are asymptomatic and lead to little mortality. With the exception of pelvic inflammatory disease and an increased risk of ectopic pregnancy, acute STDs are also associated with few complications. Syphilis and associated conditions may lead to severe long-term illness, but the prevalence of this disease is less than 0.004 percent.<sup>45</sup>

HIV/AIDS is prevalent, affects young persons, and is increasingly transmitted sexually to women of reproductive age. The extent to which HIV/AIDS or protease inhibitors increase risk for other chronic conditions may merit inclusion in a burden of disease analysis, as might highly prevalent acute conditions such as Chlamydia.

It will not be possible to generate HRQL or prevalence estimates for sexually transmitted diseases using national datasets, such as the NHIS or the MEPS. The prevalence of HIV/AIDS and other sexually transmitted diseases may be estimated from the medical literature, however, and surveillance data may be used to track changes from year to year. The BRFSS contains a set of questions pertaining to the risk of contracting the disease and whether or not subjects had received counseling. Death certificate data may be used to calculate mortality rates.

## **MENTAL HEALTH**

Mental disorders are common and varied, the most prevalent being major depressive episodes, panic disorder, manic episodes, agoraphobia, social phobia, simple phobia, post-traumatic stress, generalized anxiety disorder, schizophrenia and other nonaffective psychoses. Capturing the burden of disease due to the large array of disorders poses special data challenges as well as design challenges. Moreover, there is growing evidence that mental illness, especially mood disorders, may increase the overall

risk of comorbid conditions, such as heart disease.<sup>46</sup> There is also evidence that these conditions are linked to substance abuse, including tobacco use.<sup>47</sup>

The wide variety of mental illnesses coupled with few national survey data also presents a challenge.<sup>48</sup> While surveys such as the MEPS and NHANES contain some information on psychological functioning, these surveys are not adequately comprehensive to capture either the prevalence or the HRQL associated with the breadth of mental illnesses specific to this indicator. The EuroQol collects information on anxiety, depression, self-care, and usual activities—dimensions that may capture some aspects of mental illness. Data from the SF-12 contained within the MEPS may be useful for augmenting information on mental health. Data linked to other surveys, including community samples, may be mapped to larger datasets or useful on their own (see discussion of the indirect method above). It may also be useful to analyze variables specific to depression contained within the NHANES to obtain the risk of non-mental illness attributable to depression, as well as depression itself. The NHSDA contains data relevant to substance abuse and mental health. The extent to which mortality from suicide can be ascertained using death certificate data is unknown, but it is likely to be underreported.

One bright point in terms of data availability is the National Co-morbidity Survey (NCS), which collects data using DSM IIR and DSM IV criteria as well as the Composite International Diagnostic Interview. This survey was last conducted in the year 2000 and may be used to estimate the prevalence of these conditions. However, this survey is only conducted periodically, presenting monitoring challenges. In addition, there is significant morbidity associated with subsyndromal mental illness.<sup>49</sup> These data may be analyzed alongside, or mapped to, other datasets, such as Beaver Dam and local mental health studies if the indirect method is employed.

## **INJURY AND VIOLENCE**

The NHIS collects data on episodes of injury. The Bureau of Labor Statistics (BLS) maintains the ASOII, which is useful for obtaining prevalence estimates and the CFOI, which is useful for tabulating fatalities. The CFOI may contain less misclassification bias than death certificate data. Preference weights may be obtained in aggregate from the MEPS or the NHIS. The BLS data include variables pertaining to workplace violence. It may be necessary to estimate the episodes of violence outside of the workplace from the literature. The input of experts will be needed to estimate the extent to which such episodes can be tracked using Department of Justice datasets and/or the extent to which reports of injury capture episodes of violence.

The heterogeneity of injuries presents problems with respect to tabulating HRQL, unless injury is measured in aggregate using regression models. However, an episode-by-episode approach may still be possible if only prevalent conditions are examined. Since injury and violence are episodic, cross-sectional surveys will not capture changes in HRQL unless the injury is of long duration or the acts of violence are ongoing.

## **ENVIRONMENTAL QUALITY**

One way of estimating the burden of disease due to environmental illnesses is to build a multivariable or multivariate regression model that utilizes geographic regions as the unit of analysis, pollution indices and other environmentally-related variables as one of the dependent variables, and environmentally-related illnesses (in aggregate) as an independent variable. This type of analysis, referred to as a small area analysis, is susceptible to ecological bias. The advantage of a small area analysis is that variables from two or more unrelated datasets may be more readily used in the analysis.

It is also possible to conduct individual level analyses utilizing environmental variables as covariates. SUDAAN or STATA may be used to adjust for differentials in aggregation. While this approach offers the advantage of increasing the specificity of the analysis, it may be difficult to link individual-level data with multiple pollution indices from different datasets. One way of managing this problem is to assign a severity score to geographic identifiers in datasets.

While some national datasets, such as the MEPS, contain information on subjects' Metropolitan Statistical Area (MSA), small area analyses may be limited by sample size unless variables common to many datasets are used in the analysis. The CTS may prove to be useful for analyses of environmental factors. The survey includes the SF-12 and relevant socio-demographic variables.<sup>50</sup> Death certificate data may be employed for either small area or individual level analyses of mortality. Death certificate data, which are not associated with information on individual risk factors, may be employed in environmental analyses because the risk factors in these analyses must be obtained from secondary data sources.

## **IMMUNIZATION**

The calculation of the burden of disease due to under-immunization is limited by underreporting in the National Electronic Surveillance System (NESS), which is the primary source of surveillance data. Though the NHIS, MEPS, and BRFSS are limited by recall bias (for which acute diseases are especially susceptible), it is possible to obtain reasonable estimates of common vaccine-associated conditions, such as influenza virus infections, using these data. Rough estimates of uncommon conditions may be obtained using NESS data coupled with literature on underreporting in passive surveillance systems; however, these conditions may be too rare to merit inclusion in an analysis.

The majority of fatal vaccine preventable illnesses are due to under-immunization of chronically ill or elderly persons, who should receive the influenza and pneumococcal vaccines. Cost-effectiveness analyses have been conducted on both of these conditions which include an estimate of the overall burden of disease due to these conditions.<sup>51,52</sup> In these analyses, the duration of illness was a critical variable and was obtained from the medical literature.

Duration of illness estimates are complicated by the availability of treatment options, herd immunity (which affects the susceptibility of the overall population to illness), and varying time intervals separating the onset of illness and the onset of treatment. For example, the duration of pneumococcal infections must be estimated

among a cohort of persons receiving antibiotics at different intervals, and these intervals may vary by socio-demographic predictors.

Because the majority of vaccine-preventable diseases are short-lived, cross-sectional surveys cannot be used to estimate the HRQL scores. Therefore, it will most likely be necessary to obtain these scores using preference-weighted generic instruments, or to utilize DALY weights.

It may not be possible to measure the HRQL or incidence of these conditions in aggregate, so it may be necessary to tabulate the burden of disease due to these conditions on a disease-by-disease basis. The mortality rate attributable to under-immunization for conditions that are associated with secondary illness (e.g., influenza) may require estimations of excess deaths. Excess deaths are calculated by subtracting the number of deaths due to the condition at hand and conditions associated with the illness during seasons of low incidence from those that occur during from deaths that occur during the season of peak incidence. For instance, excess deaths due to influenza-associated conditions are calculated by subtracting the total deaths due to influenza during the peri-influenza season from those occurring during influenza season.<sup>53</sup>

#### **ACCESS TO CARE**

The CTS, NHIS, MEPS, and the CPS contain information on insurance status as well as other variables specific to access to care. The MEPS and/or the CTS may prove to be especially useful for constructing a multivariable regression analysis that tabulates the overall prevalence of illness and HRQL among persons with access to care and who lack access to care after controlling for socioeconomic and other demographic covariates. The NHANES and National Mortality Followback Survey may be utilized to obtain the relative risk of mortality due to lack of access to care after controlling for covariates.

The foreign-born population presents a methodological challenge in such an analysis since it consists of over 10 percent of the population, is healthier than the native-born population, and 40 percent of the population lacks insurance.<sup>54-56</sup> Though birth outside of the United States can be measured using death certificate data, only the NHANES contains country of origin data. Therefore, it may be useful to conduct a multivariable regression analysis using NHANES data alongside an analysis using MEPS data. This would provide information on the extent to which the foreign-born population biases the estimates.



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 Table 2. Potential sources of data and HRQL measures for calculating the burden of disease for each of the 10 Leading Indicators of Health.
 

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Indicator	Prevalence	HRQL (conditions)	HRQL (overall)	Mortality
Physical Activity	NHIS, NHANES	MEPS, DALY, YHL	MEPS, YHL, SF-Measures	Death Datafile, NHANES, NMFS
Overweight/Obesity	NHIS, NHANES	MEPS, DALY, YHL	MEPS, YHL, SF-Measures	Death Datafile, NHANES, NMFS
Tobacco	NHIS, MEPS, NHANES	MEPS, DALY, YHL	MEPS, YHL, SF-Measures	Death Datafile, NHANES, NMFS
Substance Abuse	NHSDA	Preference-weighted generic instruments or mapped data.		Death Datafile (For some conditions.)
Sexual Behavior	Literature, BRFSS	MEPS, DALY, YHL	None	Death Datafile
Mental Health	NCS, NHANES	DALY	SF-Measures	Death Datafile, NHANES
Injury and Violence	NHIS, MEPS	MEPS, DALY, YHL	MEPS, YHL, SF-Measures	Death Datafile, NHANES, NMFS, BLS
Environmental Quality	CTS, NHIS, MEPS, NHANES	MEPS, DALY, YHL	MEPS, YHL, SF-Measures	Death Datafile, NHANES
Immunization	NHIS, BRFSS, Surveillance data	DALY, Generic preference-weighted instruments	Not applicable	Death Datafile, NHANES, NMFS
Access to Care	MEPS, NHIS, BRFSS, CTS	Not applicable	SF-Measures via CTS, MEPS, YHL	Death Datafile, NHANES, NMFS

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### SUMMARY

Burden of disease analyses provide information that is easy to present and understand. They also provide sufficient information to rank conditions by their overall societal impact. While burden of disease analyses greatly improve the presentation and usefulness of health information, the difficulties associated with attributing risk, finding adequate data sources, and estimating burden of disease in a methodologically consistent fashion across indicators is not trivial.

First, flexibility may be required in estimating burden of disease inputs. While no one approach is likely to be sufficient for estimating the burden of disease due to all 10

LHIs, regression models may be useful for many of them. Likewise, it may be possible to calculate the overall burden of disease due to the conditions underlying each indicator and then apportion these estimates among indicators using attributable risk formulas.

Second, some indicators present unusual methodological challenges. For instance, tabulation of the burden of disease due to sexually transmitted disease may require the use of non-annual datasets, expert opinion, limits on the number of conditions examined, and/or broad assumptions on the part of the researchers. Other indicators may require the input of experts in the design of the burden of disease analysis, into the nuances of the characteristics of disease within society, and in estimation of unknown parameters.

Third, differences in how HALYs are calculated remains a fractious area of discussion in the literature.<sup>32</sup> The decision surrounding whether to use DALYs or QALYs (and if QALYs, what HRQL score scheme to use) in tracing the LHIs has implications for the comparability of efforts across US agencies and across nations.

For example, the World Health Organization primarily relies upon the DALY for burden of disease estimates.<sup>31</sup> The advantages of the DALY are that it is easy to use and allows for international comparisons. Disadvantages include the use of professionally derived HRQL scores, the unavailability of HRQL scores for various conditions, the inability to fully capture comorbid illness, and the lack of a dynamic mechanism for tracking changes in HRQL.

Approaches that utilize QALYs afford more specificity with respect to HRQL, offer the ability to capture comorbid illness, and may be used to dynamically track the HRQL of a population. The use of the EuroQol within the MEPS will allow a better understanding of the health status of Americans in comparison with a number of other nations, where this information is already available.

It is also possible to combine these various approaches to deriving HRQL scores and calculating the burden of disease. However, amalgamated methods shed some of the advantages of traditional approaches. For instance, it is possible to apply the DALY formula for combining morbidity and mortality using QALY-based weights. This approach may improve researchers' ability to dynamically track HRQL, permit comorbidities to be accounted for, and would allow for community-based preferences rather than scores derived from health professionals, while affording the simplicity of DALY formulas. However, it would render burden of disease estimates in the US and other nations based on DALY scores incomparable to those produced using a combined approach.

The use of various HRQL values would broaden the range of HRQL scores available, providing flexibility in approaching burden of disease estimates for each of the 10 LHIs. On the other hand, mixing and matching HRQL scores from published lists of QALY and DALY scores with those obtained from MEPS-linked EuroQol scores will reduce the validity, and thus credibility, of burden of disease estimates across indicators. It is also likely to affect the rank order of conditions.<sup>9</sup>

In this document, we did not describe issues and approaches related to evaluating the economic impact of each indicator or ethical dimensions of different approaches to tabulating the burden of disease. Economic data would assist policymakers in further prioritizing the 10 LHIs and may broaden the impact of Healthy People 2010. For instance, it may provide useful information for public health law; economic data would

allow current revenues from tobacco taxation and employment to be contrasted against the health costs of tobacco. Moreover, it is possible that some conditions that lead to a relatively small loss of healthy life have a large economic impact on the healthcare system and therefore deserve more attention. An economic component to a burden of disease analysis can, in part, be achieved with electronic datasets and should be considered in future Healthy People 2010 endeavors.

Moreover, there are ethical issues that should be addressed before a specific approach is decided upon. One issue that arises is the question of distributive justice. While society may prefer to invest resources in curing rare fatal conditions over investments in curing the common cold, burden of disease analyses would likely estimate that more HALYs are lost to the cold than to acute neurodegenerative syndromes. As the Panel on Cost-Effectiveness in Health and Medicine points out,<sup>5</sup> and as experience with purely empiric approaches demonstrates,<sup>57</sup> it is not wise to make policy decisions on burden of disease estimates alone.

Although burden of disease quantification with respect to the LHIs contained in Healthy People 2010 appears possible using some of the techniques and approaches described within this document, the challenges remain extensive in creating an account that is comprehensible and scientifically rigorous. The thorny issues of attributing risk and avoiding double or undercounting will require the input of a broad array of experts who can provide a more in-depth examination of the specific of the content areas. The decision regarding which metric to use in generating HALYs is one that should have vetting and buy-in from other parts of Health and Human Services, who are developing parallel studies of burden of disease. For example, the Inter-Agency Group on Summary Measures provides a forum for these types of discussions.<sup>58</sup> It would be useful for the ODPHP to present this project within that group to provide preliminary discussion and guidance in this area.

## OTHER RESOURCES

Gold MR, Siegel JE, Russell LB and Weinstein MC, ed. Cost-Effectiveness in Health and Medicine. New York: Oxford University Press, 1996.

Drummond MF, O'Brien BO, Stoddart GL, Torrance GW. Methods for the Economic Evaluation of Health Care Programmes, 2<sup>nd</sup> edition, London: Oxford University Press, 1997.

Field MJ, Gold MR, Eds. Summarizing Population Health: Directions for the Development and Application of Population Metrics. Washington: National Academy Press, 1998.

Haddix AC, Teutsch SM, Shaffer PA, Dunet DO. Prevention Effectiveness. A Guide to Decision Analysis and Economic Evaluation. New York, Oxford University Press, 1996.

Muennig PA. Designing and Conducting Cost-Effectiveness Analyses in Medicine and Healthcare. San Francisco: Jossey-Bass, 2002.

Murray CLJ, Lopez AD. The global burden of disease: a comprehensive assessment of mortality and disability from disease, injury and risk factors in 1990 and projected to 2020. Vol. 1. Boston: Harvard University Press, 1996

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## APPENDIX 2: EUROQOL

(English Version for the United Kingdom)

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

### **Mobility**

- I have no problems in walking about
- I have some problems in walking about
- I am confined to bed

### **Self-Care**

- I have no problems with self-care
- I have some problems washing or dressing myself
- I am unable to wash or dress myself

### **Usual Activities** (*e.g. work, study, housework, family or leisure activities*)

- I have no problems with performing my usual activities
- I have some problems with performing my usual activities
- I am unable to perform my usual activities

### **Pain/Discomfort**

- I have no pain or discomfort
- I have moderate pain or discomfort
- I have extreme pain or discomfort

### **Anxiety/Depression**

- I am not anxious or depressed
- I am moderately anxious or depressed
- I am extremely anxious or depressed

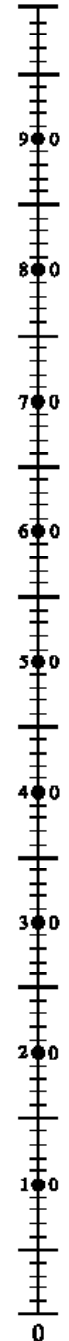
To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

**Your own  
health state  
today**

Best  
imaginable  
health state

100



Worst  
imaginable  
health state

Because all replies are anonymous, it will help us to understand your answers better if we have a little background data from everyone, as covered in the following questions.

1. Have you experienced serious illness?

	Yes	No
<i>in you yourself</i>	<input type="checkbox"/>	<input type="checkbox"/>
<i>in your family</i>	<input type="checkbox"/>	<input type="checkbox"/>
<i>in caring for others</i>	<input type="checkbox"/>	<input type="checkbox"/>

PLEASE TICK  
APPROPRIATE  
BOXES

2. What is your age in years?

3. Are you:

	Male	Female
	<input type="checkbox"/>	<input type="checkbox"/>

PLEASE TICK  
APPROPRIATE  
BOX

4. Are you:

- a current smoker*
- an ex-smoker*
- a never smoker*

PLEASE TICK  
APPROPRIATE  
BOX

5. Do you now, or did you ever, work in health or social services?

	Yes	No
	<input type="checkbox"/>	<input type="checkbox"/>

PLEASE TICK  
APPROPRIATE  
BOX

If so, in what capacity? .....

6. Which of the following best describes your main activity?

<i>in employment or self employment</i>	<input type="checkbox"/>
<i>retired</i>	<input type="checkbox"/>
<i>housework</i>	<input type="checkbox"/>
<i>student</i>	<input type="checkbox"/>
<i>seeking work</i>	<input type="checkbox"/>
<i>other (please specify)</i>	<input type="checkbox"/>

PLEASE TICK  
APPROPRIATE  
BOX

7. Did your education continue after the minimum school leaving age?

	Yes	No
	<input type="checkbox"/>	<input type="checkbox"/>

PLEASE TICK  
APPROPRIATE  
BOX

8. Do you have a Degree or equivalent professional qualification?

	Yes	No
	<input type="checkbox"/>	<input type="checkbox"/>

PLEASE TICK  
APPROPRIATE  
BOX

9. If you know your postcode, would you please write it here:



## REFERENCES

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1. Department of Health and Human Services. Healthy people 2010. 2d ed. With understanding and improving health and objectives for improving health. 2 vols. Washington: U.S. Government Printing Office, 2000.
2. National Center for Health Statistics. Healthy People 2000 Final Review. Hyattsville, Maryland: Public Health Service, 2001.
3. Office of Disease Prevention and Health Promotion. Healthy People. <http://www.health.gov/healthypeople>. Accessed 11/04/01.
4. Fryback DG. Methodological issues in measuring health status and health-related quality of life for population health measures: A brief overview of the "HALY" family of measures. In Summarizing Population Health, Washington DC. Institute of Medicine. National Academy Press, 1998.
5. Gold MR, Siegel JE, Russell LB and Weinstein MC, ed. Cost-Effectiveness in Health and Medicine. New York: Oxford University Press, 1996.
6. Field MJ, Gold MR, Eds. Summarizing Population Health: Directions for the Development and Application of Population Metrics. Washington: National Academy Press, 1998.
7. Weinstein MC and Stason, WB. Foundations of cost-effectiveness analysis for health and medical practices. *New Engl J Med* 1977;296:716-721.
8. Murray CJL, Lopez AD, Jamison DT. Global burden of disease in 1990: summary results, sensitivity analysis and future directions. *Bull World Health Organization* 1994;72:429-445.
9. Muennig P, Gold MR. Using the Years Of Healthy Life measure to calculate quality adjusted life years. *Am J of Prev Med* 2001;20: 12-17
10. Wolfson M. Health-adjusted life expectancy. *Health Rep.* 1996;8:41-46.
11. Erickson P, Wilson R, Shannon I. Years of Healthy Life. *Statistical Notes.* 1995;7:1-14.
12. Hoyart DL, Kochanek KD, Murphy SL. Deaths: final data for 1997. *National Vital Statistics Report.* 1999;47:1-146.
13. National Mortality Followback Survey. Available online at: <http://www.cdc.gov/nchs/about/major/nmfs/desc.htm>. Accessed 11/18/01.
14. National Health Examination and Nutrition Survey. [www.cdc.gov/nchs](http://www.cdc.gov/nchs). Accessed 12/01/01.
15. Wilson R, Freedman MA, Klein RJ. Issues related to monitoring the healthy people 2000 objectives. Healthy people statistical notes; no 4. Hyattsville, Maryland: National Center for Health Statistics. 1993.
16. Centers for Disease Control and Prevention. Behavioral Risk Factor Surveillance System. Available online at: <http://www.cdc.gov/nccdphp/brfss/ti-surveydata2000.htm>. Accessed 11/17/01.
17. Must A, Spandano J, Coakley EH, et al. The disease burden associated with overweight and obesity. *JAMA.* 1999;282:1523-29.
18. Zhang J, Yu KF. What's the relative risk? A method for correcting the odds ratio in cohort studies of common outcomes. *JAMA.* 1998;280:1690-91.

19. Haddix AC, Teutsch SM, Shaffer PA, Dunet DO. Prevention Effectiveness. A Guide to Decision Analysis and Economic Evaluation. New York, Oxford University Press, 1996.
20. Franks P, Clancy CM, Gold MR, Nutting PA. Health insurance and subjective health status: data from the 1987 National Medical Expenditure Survey. *Am J Public Health* 1993; 83:1295-1299.
21. Franks P, Clancy CM, Gold MR. Health insurance and mortality. Evidence from a national cohort. *JAMA* 1993; 270:737-741.
22. U.S. Public Health Service. Healthy People 2000. National Health Promotion and Disease Prevention Objectives. Washington D.C: U.S. Dept of Health and Human Services; 1991. Publication PHS 91-50212.
23. McGinnis JM, Foege WH. Actual causes of death in the United States. *JAMA* 1993;270:207-12.
24. Centers for Disease Control and Prevention. Smoking-attributable mortality and years of potential life lost—United States, 1990. *MMWR* 1993;42(33):645-9.
25. Gold MR, Franks P, McCoy KI, Fryback DG. Toward consistency in cost-utility analyses: Using national measures to create condition-specific values. *Med Care* 1998;36:778-792.
26. Ware J, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Medical Care* 30(6):473-483, 1992.
27. Gunnig-Schepers L. Presentation for the Institute of Medicine Workshop on Summary Measures of Population Health Status, Washington, DC, December 12, 1997. In *Summarizing Population Health*, Washington DC. Institute of Medicine. National Academy Press, 1998.
28. Brazier J, Usherwood T, Harper R, Thomas K. Deriving a preference-based single index from the UK SF-36 Health Survey. *J Clin Epidemiol.* 1998;51:1115-28.
29. Fryback, DG, Lawrence WG, Martin PA, Klein R, Klein BEK. Predicting Quality of Well-Being scores from the SF-36: results from the Beaver Dam Health Outcomes Study. *Med Decision Making* 1997;17:1-9.
30. Harvard School of Public Health. Cost Utility Database. [www.hsph.harvard.edu/organizations/hcra/cuadatabase/intro.html](http://www.hsph.harvard.edu/organizations/hcra/cuadatabase/intro.html). Accessed 11/10/01.
31. Murray CLJ, Lopez AD. The global burden of disease: a comprehensive assessment of mortality and disability from disease, injury and risk factors in 1990 and projected to 2020. Vol. 1. Boston: Harvard University Press, 1996
32. Gold MR, Stevenson D, Fryback DG. HALYs and QALYs and DALYs, oh my: Similarities and differences in summary measures of population health. *Annu Rev Public Health* 2002;115:23-34.
33. Anderson RN. Life tables, 1996. *National Vital Statistics Reports.* 1998;47:1-20.
34. Rosenberg MA, Fryback DG, Lawrence WF. Computing population-based estimates of health-adjusted life expectancy. *Med Decis Making* 1999;19:90-7
35. Anderson RN. Method for constructing complete annual U.S. life tables. *National Center for Health Statistics. Vital Health Stat* 2. 1999;129:1-30.
36. Kujala UM, Kaprio J, Sarna S, et al. Relationship of leisure-time physical activity and mortality: The Finnish twin cohort. *JAMA* 1998;279:440-4.
37. Department of Health and Human Services. Physical activity and health: A report of

---

the Surgeon General. Atlanta, GA: Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion. 1996.

38. Paffenbarger RS, Hyde RT, Wing AL, et al. The association of changes in physical-activity level and other lifestyle characteristics with mortality among men. *N Engl J Med* 1993;328:538–45.

39. Kushi LH, Fee RM, Folsom AR, et al. Physical activity and mortality in postmenopausal women. *JAMA* 1997;277:1287–92.

40. Sherman SE, D’Agostino RB, Cobb JL, et al. Physical activity and mortality in women in the Framingham Heart Study. *Am Heart J* 1994;128(5):879–84.

41. Macera CA, Powell KE. Population attributable risk: implications of physical activity dose. *Med Sci Sports Exerc* 2001;33:S635-9.

42. Flegal KM, Carroll MD, Kuczmarski RJ, et al. Overweight and obesity in the United States: Prevalence and trends, 1960–1994. *International J Obesity* 1998;22:39–47.

43. Department of Health and Human Services. Reducing tobacco use: A report of the Surgeon General. Atlanta, Georgia: Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health. 2000.

44. Fiscella, K., Franks, P. 1996 Cost-Effectiveness of the Transdermal Nicotine Patch as an Adjunct to Physicians' Smoking Cessation Counseling. *JAMA* ;275:1247-1251.

45. Primary and secondary syphilis—United States, 1997. *Morb Mortal Wkly Rep.*1998;47:493-497.

46. Connerney I, Shapiro PA, McLaughlin JS, Bagiella E, Sloan RP. Relation between depression after coronary artery bypass surgery and 12-month outcome: a prospective study. *Lancet.* 2001;358:1766-1771.

47. Anda RF, Croft JB, Felitti VJ, Nordenberg D, Giles WH, Williamson DF, Giovino GA. Adverse childhood experiences and smoking during adolescence and adulthood. *JAMA.* 1999 Nov 3;282(17):1652-8.

48. Sherbourne CD, Unutzer J, Schoenbaum M, et al. Can utility-weighted health-related quality of life estimates capture health effects of quality of life improvement for depression? *Med Care* 2001;39:1246-59.

49. Kroenke K, Spitzer RL, deGruy FV, III, Hahn SR, Linzer M, Williams JB et al. Multisomatoform disorder. An alternative to undifferentiated somatoform disorder for the somatizing patient in primary care. *Arch Gen Psychiatry* 1997; 54(4):352-358.

50. Center for Studying Health System Change. [www.hschange.org](http://www.hschange.org). Accessed 12/3/01.

51. Sisk JE, Moskowitz AJ, Whang W, et al. Cost-effectiveness of vaccination against pneumococcal bacteremia among elderly people. *JAMA* 1997;278:1333-9.

52. Muennig P, Khann K. Cost-effectiveness of strategies to prevent or treat influenza in healthy adults: *Clinical Infectious Disease* 2001;33.

53. Centers for Disease Control and Prevention. Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1998;47:1-25.

54. U.S. Bureau of the Census. Place of Birth, Citizenship and Year of Entry. 1990; U.S. Bureau of the Census : Washington. Census Questionnaire Content, CQC-12.

55. Rubia M, Marcos I, Muennig P. Increased risk of heart disease and stroke among foreign-born females residing in the United States. *Am J Prev Med.* 2002; 22(1):15-20.

56. Chen J, Wilkins R, Ng E. Health expectancy by immigrant status, 1986 and 1991. *Health Rep* 1996 Winter;8(3):29-38.
57. Eddy D. Oregon's methods: did cost-effectiveness analysis fail? *JAMA* 1991;265:2218-2225.
58. Ottawa Conference. [www.unece.org/stats/documents/2000.10.health.htm](http://www.unece.org/stats/documents/2000.10.health.htm). Accessed 12/22/01.