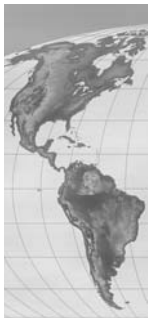
Part II

Sensitivity Analyses

Chapter **5**



Sensitivity and Uncertainty Analyses for Burden of Disease and Risk Factor Estimates

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Modern epidemiological studies generally report confidence or uncertainty intervals around their estimates, often based on the variation observed in sample data. Estimates of the burden of disease and of risk factors, which extrapolate from specific data sources and epidemiological studies to population-level measures, are subject to a broader range of uncertainty because of the combination of multiple data sources and value choices. Hence, the reported uncertainty intervals should ideally include all sources of uncertainty, including those arising from measurement error, systematic biases, and modeling and extrapolation to compensate for incomplete data. In contrast to uncertainty analysis, which attempts to formally quantify the limitations of available data, sensitivity analysis examines how key analytic outputs vary when input quantities are systematically varied. Following Murray and Lopez (1996b), this chapter uses sensitivity analysis to examine the specific effects of social values that have been incorporated in the design of the disability-adjusted life year (DALY).

Taking account of uncertainty in such value parameters as the rate of time preference used to discount future outcomes is not common. Even if there is empirical evidence on population preferences for discount rates and uncertainty in these estimates, investigators have argued that the choice of discount rate for use in analysis is essentially a social value judgment and should not include uncertainty (Morgan and Henrion 1990). Although there is uncertainty about the social value judgment and about its effects on decisions based on the analysis, varying the value deterministically in the analysis and performing a sensitivity analysis to examine the impact on the outcomes of interest is usually preferable to uncertainty analysis. Thus, the 1990 Global Burden of Disease (GBD) study (Murray and Lopez 1996b) examined the sensitivity of the ranking of causes of the burden of disease globally when discount rates and age weights were varied across a range of possible values.

Health state valuations, which link mortality information with information on nonfatal health outcomes in summary measures of population health, fit somewhat more ambiguously within the framework of uncertainty analysis. If we conceptualize a health state in terms of levels in multiple domains of health, health state valuation involves the weighting of these domains to arrive at an overall assessment of the health level associated with the state. These valuations, unlike

values such as time preference, do not have any clear normative basis; that is, while we might rely on philosophical arguments about intergenerational equity in choosing a discount rate, no obvious arguments pertain to the relative importance of mobility versus cognition in overall assessments of health levels. The choice of measurement strategies for eliciting health state valuations does sometimes introduce normative questions, but these pertain to additional considerations, such as concern for fair distribution, which are orthogonal to the assessment of the health state itself.

DISCOUNTING AND AGE WEIGHTING IN THE DALY MEASURE

This section briefly reviews the rationale and implementation of discounting and age weights in the standard DALY. To denote different choices for the discount rate and age weights, we use the notation DALYs(r,K), where r is the discount rate in percent (not a fraction as in the GBD 1990 study) and K is the age-weighting modulation factor, a parameter that allows uniform ($K = 0$) or the GBD nonuniform ($K = 1$) age weighting to be used. With this notation, DALYs(3,0) denotes the DALY with a 3 percent discount rate and uniform age weights as used in the Disease Control Priorities Project (DCPP) and DALYs(3,1) denotes the 3 percent discount rate and varying age weights as used in the GBD study. Similarly, we may refer to the DALY components of years of life lost due to premature mortality (YLL) and years of healthy life lost due to disability (YLD) as YLL(r,K) or YLD(r,K) using the same convention.

Discounting

Discounting future benefits is standard practice in economic analysis. Murray (1996) and Murray and Acharya (1997) review the theoretical and empirical arguments for and against discounting with a specific emphasis on health, including the possibility of negative discount rates. In addition to individual discounting and discount rates, policies dealing with risk must address the issue of benefits for different populations across time. As a result, these policies must address ethical and analytical dilemmas related to the valuation of current and future health and welfare in the form of social discount rates (Kneese 1999).

Some have argued that discounting should not be applied to future health gains or losses because health is not commensurable with money and cannot be reinvested elsewhere, but most criticisms of discounting in relation to the DALY have focused on the functional form and the level chosen (Fox-Rushby 2002). Epidemiologists and demographers, who tend to focus on measuring or estimating years of life or health without "valuing" either, rarely use discounting. Murray and Acharya (1997) conclude that the strongest argument for discounting is the disease eradication and health research paradox. According to this argument, not discounting future health would lead to the conclusion that all of society's health resources should be invested in research programs or programs for disease eradication, which produce an infinite stream of benefits, rather than any programs that improve the health of the current generation. Such an excessive intergenerational "sacrifice" is a particularly powerful argument for discounting future health (Parfit 1984). Note that this argument does not claim that future welfare or health is less valuable than current welfare or health, but rather uses discounting as a tool to avoid excessive sacrifice by the current generation to the point of investing all resources in future health.

Murray and Acharya argue that the social discount rate should be smaller than the return on capital investment, but note that the choice of a discount rate for health benefits, even if technically desirable, may result in morally unacceptable allocations between generations (see also Dasgupta, Mäler, and Barrett 1999). Because of the complexities in the choice of discount rate, the 1990 GBD study published discounted and undiscounted estimates of the global burden of disease (Murray and Lopez 1996a).

The U.S. Panel on Cost-Effectiveness in Health and Medicine has recommended that health economic analyses use a 3 percent real discount rate to adjust both costs and health outcomes (Gold and others 1996), but that analysts should examine the sensitivity of the results to the discount rate. The 1990 GBD study, the updated estimates published in recent World Health Organization (WHO) world health reports, and the DCPP have all used 3 percent discounting for DALYs.

Age Weighting

The 1990 GBD study weighted a year of healthy life lived at young ages and older ages lower than years lived at other ages. This choice was based on a number of studies that indicated a broad social preference to value a year lived by a young adult more highly than a year lived by a young child or an older adult (Murray 1996). Not all such studies agree that the youngest and oldest ages should be given less weight; nor do they agree on the relative magnitude of the differences.

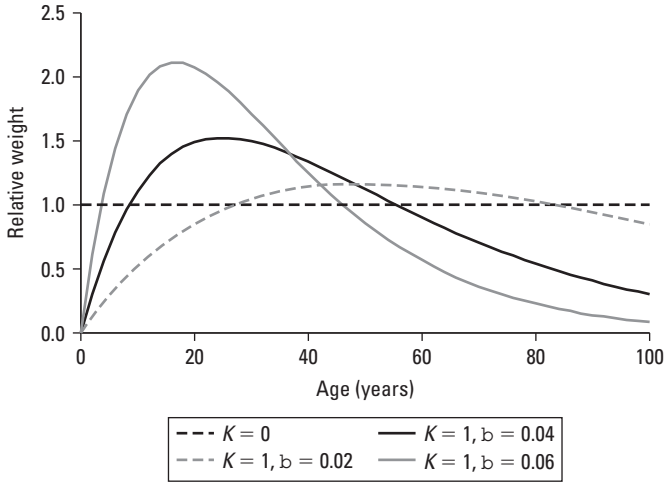
Age weights are perhaps the most controversial value choice built into the DALY. Criticisms of age weights have fallen into five categories:

- Age weighting is unacceptable on equity grounds and every year of life is of equal value (Anand and Hanson 1997).
- Age weights are not empirically based and have not been validated for large populations.
- Age weights do not reflect social values; for example, the DALY values the life of a newborn about equally to that of a 20-year-old, whereas the empirical data suggest a fourfold difference (Bobadilla 1996; see also chapter 6 in this book).
- Age weights result in more YLL for deaths at all ages from birth to 39 compared with discounted YLL not weighted by age (Barendregt, Bonneux, and van der Maas 1996).
- Age weights add an extra level of complexity to burden of disease analysis that obscures the method and makes little overall difference to the rankings of diseases and injuries.

Murray and Acharya (1997) argue that age weights are not in themselves inequitable, because everyone potentially lives through every age, and that they do reflect legitimate societal priorities. As discussed in chapter 3, the DCPP uses uniform age weights and thus values a year of healthy life equally at all ages. Chapter 6 presents an analysis in which a more extreme form of age weighting is applied to the deaths of young children.

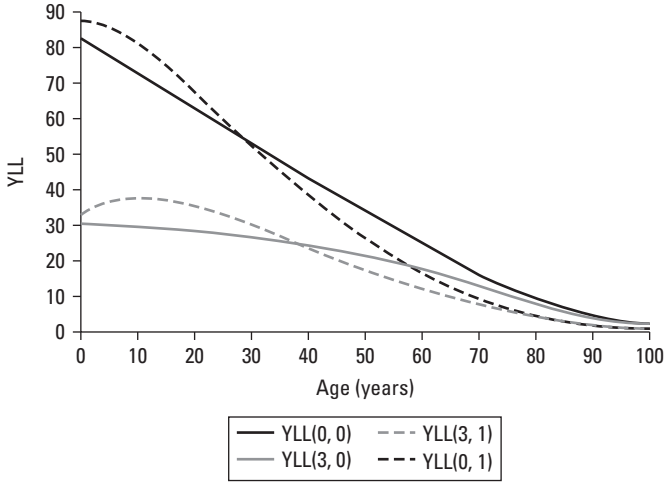
Discounting, Age Weights, and the YLL Loss Function

DALYs are calculated as the sum of YLL from a cause and the YLD for incident cases of the health condition (see chapter 3 for more details). Murray (1996) provides general formulas for YLL and YLD that allow the annual discount rate r and the age-weighting parameters (K, C, β) to be varied. When K is set equal to 1, then the DALY includes an age-weighting function of the form $Cxe^{-\beta x}$, where x is the age in years and β and C are constants. For the 1990 GBD study, Murray and Lopez chose $\beta = 0.04$. The value of $\beta = 0.04$ was chosen to give an age pattern similar to that seen in available empirical data. C is a parameter chosen to ensure that the total global DALYs are the same with and without age weighting, estimated at $C = 0.1658$ for the 1990 GBD study. Figure 5.1 illustrates the form of the age-weighting function for $\beta = 0.02$, 0.04, and 0.06. For the other two



Source: Authors' calculations.

Figure 5.1 Age-Weighting Function Incorporated into the DALY



Source: Authors' calculations.

Note: YLL(r, K) denotes YLL calculated with discount rate r (percent) and standard age weighting ($K = 1$) or uniform age weighting ($K = 0$).

Figure 5.2 Effect of Age Weighting and Discounting on the YLL per Death at Various Ages for Females

choices of β (0.02 or 0.06), the value of C was varied to ensure the same area under the curve from age 0 to 100 years.

The age-weighting function specifies the relative value of a year of life lived at different ages either for YLD or YLL estimates. To estimate the total years of life lost due to death at age x, the age-weighting function is integrated over all ages above x. Table 5.1 shows the resulting loss function for selected exact ages, also plotted in figure 5.2 for females. The male-female gap in YLL(0,0), 2.5 years at birth, is reduced to 0.1 years for YLL(3,1) (figure 5.3). Figure 5.4 shows the effect on YLL of varying the parameter β in the age-weighting

Table 5.1 Standard Life Expectancies at Selected Exact Ages and Discounted YLL Due to a Death at Selected Ages

	YLL (0,0) per death–standard life expectancy (years)		YLL (3,0) per death–3% discounting, uniform age weights (years)		YLL (3,1) per death–3% discounting, standard age weights (years)	
Age	**Males**	**Females**	**Males**	**Females**	**Males**	**Females**
0	80.00	82.50	30.31	30.53	33.01	33.13
5	75.38	77.95	29.86	30.12	36.46	36.59
15	65.41	68.02	28.65	29.00	36.80	36.99
30	50.51	53.27	26.01	26.59	29.62	29.92
45	35.77	38.72	21.93	22.90	20.17	20.66
60	21.81	24.83	16.01	17.51	11.48	12.22
70	13.58	16.20	11.15	12.83	6.69	7.48
80	7.45	8.90	6.67	7.81	3.27	3.76
90	3.54	4.25	3.36	3.99	1.30	1.53
100	1.46	2.00	1.43	1.94	0.42	0.57

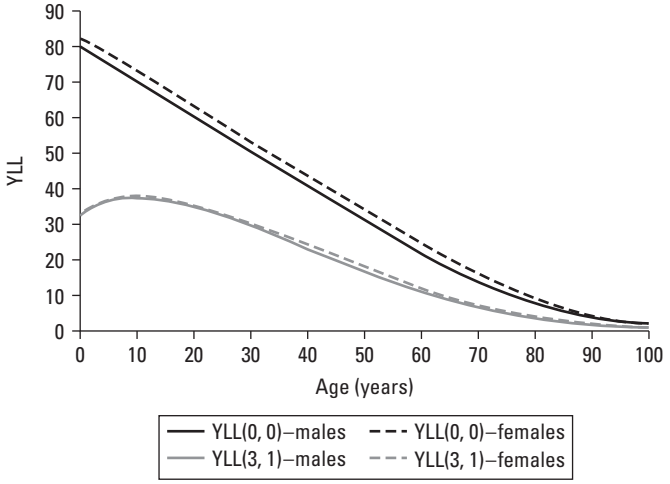
Source: Authors' calculations.

function. Values of β higher than 0.04 give relatively greater weight to younger ages and less to older ages; values of β lower than 0.04 give relatively lower weight to younger ages and more to older ages.

Table 5.2 further examines the effects of varying the parameter β in the age-weighting function on the weights applicable at different ages. For the standard DALY, $\beta = 0.04$ implies a maximum age weight of 1.52 at age 25, and the age weight is greater than 1 over the range 8.4 to 54.2 years. Compare this with $\beta = 0.03$, which gives a maximum age weight of 1.29 at age 33.3 years with a prime age range (weight greater than 1) of 14.9 to 63.0 years. Note that the choice of $\beta = 0.03$ gives a prime age range that matches fairly typical ages for formal entry and exit from work in many societies (Mahapatra 2001). We do not consider variations in β further here. Sensitivity analyses for GBD 2001 that follow compare standard age weights ($\beta = 0.4$) with uniform age weights.

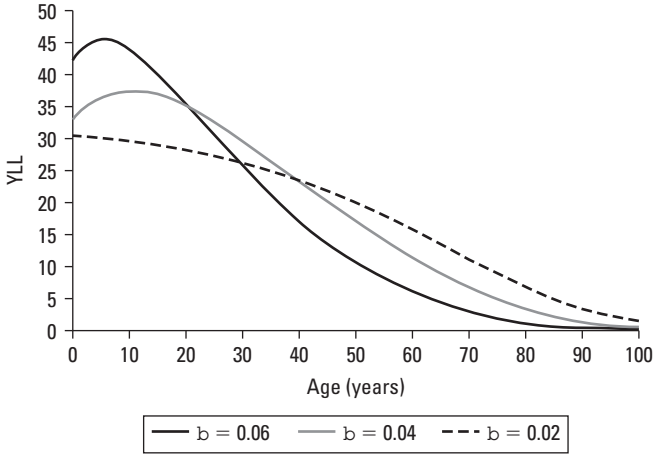
SENSITIVITY OF BURDEN OF DISEASE AND INJURY RESULTS TO VARIATIONS IN KEY PARAMETER VALUES

This section examines the sensitivity of the DALY estimates for the global burden of disease in 2001 to alternative assumptions about the discount rate and age weighting. As discussed in chapter 3, the DALY measures the future stream



Source: Authors' calculations.

Figure 5.3 Effect of Age Weighting and Discounting on the Male-Female Gap in YLL per Death



Source: Authors' calculations.
Note: The discount rate is held constant at 3 percent for the examples shown.

Figure 5.4 Effect on YLL per Death of Varying the Parameter β in the DALY Age-Weighting Function

Table 5.2 Implications of Variation in Choice of Age-Weight Parameter β on the Age-Weighting Function

Age-weight parameter β	Age-weight[a] constant C	Maximum age weight	Age of maximum age weight	Age range for which age weight is > 1
0.02	0.0634	1.17	50.0	27.2–83.1
0.03	0.1051	1.29	33.3	14.9–63.0
0.04	0.1658	1.52	25.0	8.4–54.2
0.05	0.2487	1.83	20.0	5.2–50.7
0.06	0.3560	2.18	16.7	3.5–46.9

Source: Authors' calculations.
Note: This form of presentation was suggested by Mahapatra 2001.
a. For values of β other than 0.04, the age-weight constant C was chosen so that total global DALYs(3,1) for 2001 were the same as for $\beta = 0.04$.

of healthy years of life lost due to each incident case of disease or injury. It is thus an incidence-based measure rather than a prevalence-based measure. The GBD study applied a 3 percent time discount rate to years of life lost in the future to estimate the net present value of years of life lost. With this discount rate, a year of healthy life gained in 10 years' time is valued at 24 percent less than one gained now (note that the standard DALY uses an instantaneous 3 percent discount rate, which results in an annual discount factor that is slightly higher).

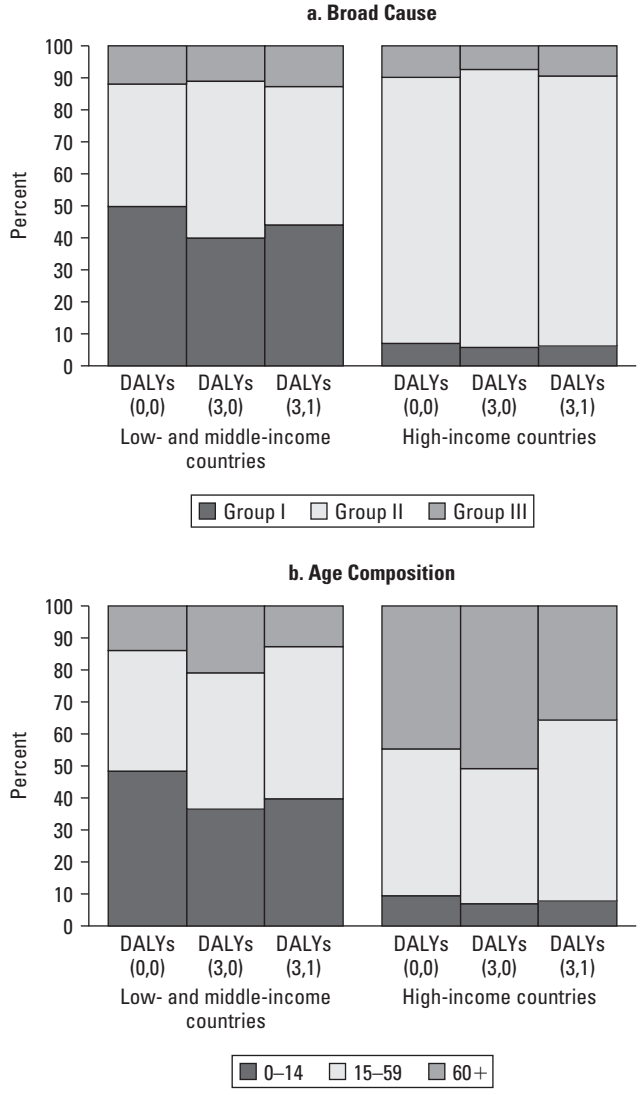
Table 5.3 summarizes the effects of varying the discount rate and age weights. Changes in the discount rate and age weights have little effect on the proportion of the burden in males and females. However, changes in the discount rate have an important effect on the proportion of the burden due to nonfatal outcomes (YLD), on the age distribution of the burden, and on the distribution of the burden by broad cause group. When the discount rate is set to zero, the proportion of burden due to YLD is just over a quarter of the total burden. When the discount rate is set to 3 percent, then 36 to 38 percent of the burden is due to YLD, depending on whether age weights are also applied.

Similarly, a nonzero discount rate significantly reduces the importance of the burden of disease or injury in children. This effect is more pronounced in low- and middle-income countries, where children bear a disproportionately large share of the total burden (figure 5.5). Because of the differences in the cause structure of the disease burden by age, these effects also influence the overall distribution of DALYs by broad cause group for low- and middle-income countries. In contrast, for high-income countries, while some changes in the age distribution of the burden are apparent, the choice

Table 5.3 Comparison of the Effects of Changing the Discount Rate (r) and the Age-Weighting Factor (K) on the Composition of DALYs(r,K), 2001

	World			Low- and middle-income countries		
	DALYs(0,0)	DALYs(3,0)	DALYs(3,1)	DALYs(0,0)	DALYs(3,0)	DALYs(3,1)
Total DALYs (millions)	2,645	1,536	1,476	2,447	1,387	1,357
By outcome (%)						
Total YLD	27	36	38	26	34	36
Total YLL	73	64	62	74	66	64
By cause (%)						
Group I	47	37	41	50	40	44
Group II	42	53	47	38	49	43
Group III	12	11	12	12	11	13
By sex (%)						
Male	51	52	52	51	52	52
Female	49	48	48	49	48	48
By age group (%)						
0–4	39	28	30	41	31	32
5–14	6	6	8	7	6	8
15–44	26	27	35	26	28	35
45–59	12	15	14	12	15	13
60+	16	24	15	14	21	13

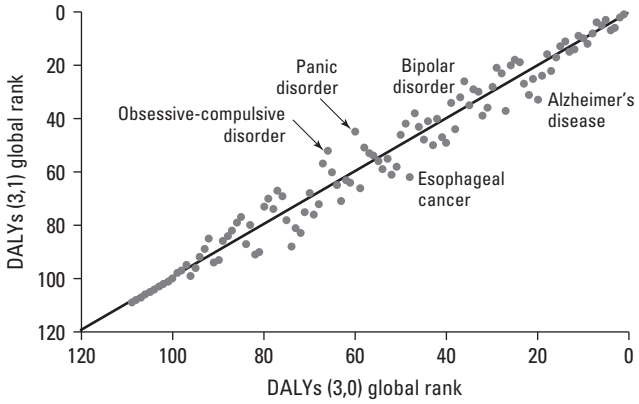
Source: Authors' calculations.



Source: Authors' calculations.

Note: The notation DALY(r, K) denotes DALYs calculated with discount rate r (percent) or standard or uniform age weighting ($K = 1$ or 0, respectively).

Figure 5.5 Effects of Changing the Discount Rate and Age Weighting on DALYs' Broad Cause and Age Composition, 2001



Source: Authors' calculations.

Note: Rank 1 is the largest cause.

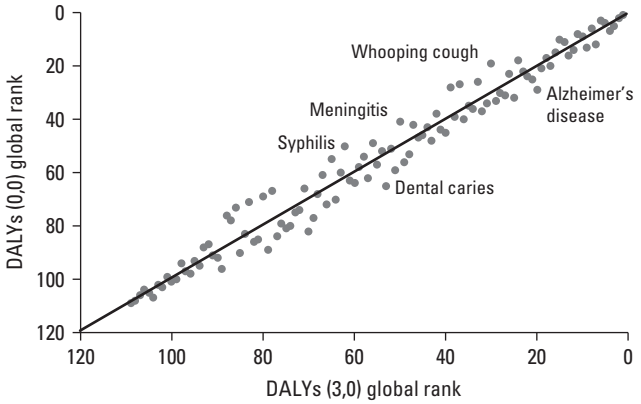
Figure 5.6 Relationship between the Rank Order of Causes of the Global Burden Using DALYs(3,1) and DALYs(3,0) in 2001

of discounting (and age weights) has relatively little influence on the broad cause group breakdown of the total burden of disease (figure 5.5).

The effects of introducing nonuniform age weights are generally much smaller than the effects of introducing nonzero discounting. A comparison of the discounted DALYs with and without age weighting in table 5.3 shows that the main effect is on the age distribution of the disease burden. For both high-income and low- and middle-income countries, age weights reduce the importance of the share of the burden borne by older people. In low- and middle-income countries, people aged 60 years and older suffer 21 percent of the total burden of disease and injury. This declines to 13 percent when nonuniform age weights are used. As shown in the second part of figure 5.5, the effects of discounting and age weighting on the age structure of the burden of disease largely offset each other for older ages, so that for DALYs(0,0) and DALYs(3,1) the share of the burden for those aged 60 years and older is quite similar. Overall, the importance of Group I conditions (communicable diseases, maternal and perinatal conditions, and nutritional deficiencies) is also slightly enhanced by age weighting and that of Group II conditions (noncommunicable diseases) is reduced. The effects on Group III (injuries) are relatively minor.

Figure 5.6 compares the rank order of causes contributing to the global burden of disease measured using DALYs(3,1) and DALYs(3,0). The introduction of nonuniform age weights has the most impact on neuropsychiatric disorders, such as bipolar disorder, panic disorder, and obsessive-compulsive disorder, whose prevalence is greatest in younger and middle-aged people. Age-weighted DALYs give less importance to causes whose burden falls predominantly on older ages.

Figure 5.7 compares ranks for causes measured using undiscounted DALYs(0,0) and discounted DALYs(3,0), both with uniform age weights ($K = 0$). A zero discount rate gives greater importance to causes with a larger burden at younger ages, such as whooping cough (pertussis) and meningitis, and lower importance to causes predominantly affecting older ages. However, the different choices of discount rates and age weights do not cause any large changes in the rank ordering of diseases and injuries, which is to a large degree anchored in absolute differences in the burden arising from large differences in prevalence and mortality levels across causes.



Source: Authors' calculations.
Note: Rank 1 is the largest cause.

Figure 5.7 Relationship between the Rank Order of Causes of the Global Burden of Disease in 2001, Using Uniform Age Weights and 3 Percent Discounting and No Discounting

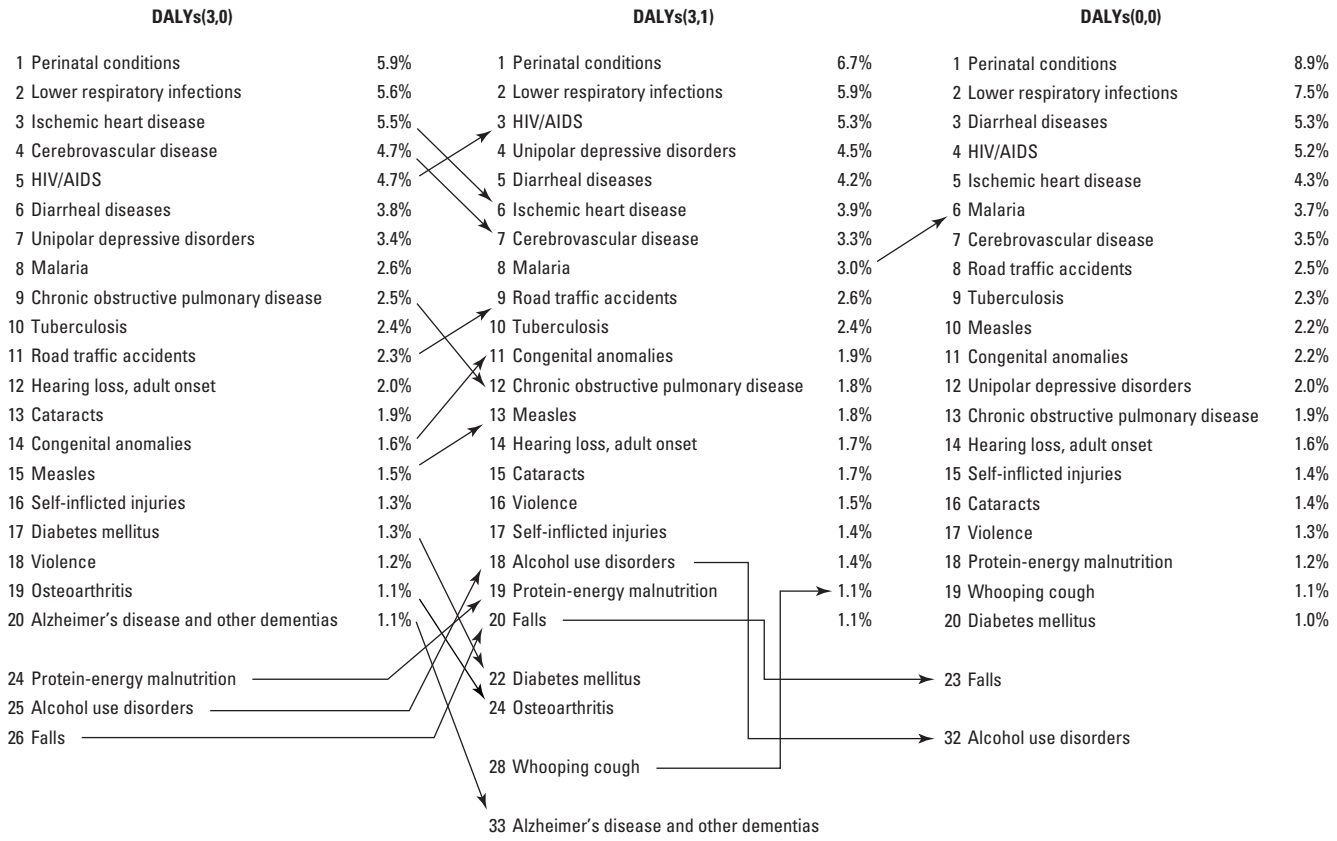
Table 5.4 compares DALYs(3,0) with DALYs(3,1) and DALYs(0,0) in more detail according to the second level of cause disaggregation within a group. These more detailed results confirm the major conclusions outlined earlier on the impacts of discounting and age weighting. DALYs(0,0) give greater weight to perinatal conditions (the International Classification of Diseases [ICD] category of conditions arising in the perinatal period) and respiratory infections, which primarily affect young children, than either of the discounted forms of DALYs. In contrast, the age-weighted DALYs(3,1) give more weight than DALYs(3,0) to causes that predominantly affect younger adult ages, such as neuropsychiatric conditions and injuries. DALYs(3,0) give greater weight than either DALYs(3,1) or DALYs(0,0) to causes that predominantly affect older people, such as cardiovascular diseases and cancers.

Figure 5.8 summarizes the effects of changing the discount rate and age weighting on the global rankings for the

Table 5.4 Effects of Changing the Discount Rate (r) and the Age-Weighting Factor (K) on the Second-Level Cause Group Composition of DALYs(r,K), 2001
(percentages of total DALYs)

	Low- and middle-income countries			High-income countries		
Group/cause	**DALYs(0,0)**	**DALYs(3,0)**	**DALYs(3,1)**	**DALYs(0,0)**	**DALYs(3,0)**	**DALYs(3,1)**
All causes	100.0	100.0	100.0	100.0	100.0	100.0
I. Communicable, maternal, perinatal, and nutritional conditions	49.8	39.8	43.9	6.9	5.7	6.1
A. Infectious and parasitic diseases	28.0	23.1	25.5	2.5	2.3	2.3
B. Respiratory infections	8.2	6.3	6.6	1.6	1.7	1.3
C. Maternal conditions	1.8	1.9	2.2	0.3	0.3	0.4
D. Perinatal conditions	9.4	6.4	7.2	1.9	0.9	1.3
E. Nutritional deficiencies	2.2	2.1	2.3	0.6	0.6	0.8
II. Noncommunicable diseases	38.4	48.9	43.4	83.1	86.6	84.7
A. Malignant neoplasms	4.5	5.4	4.2	17.4	17.3	14.8
B. Other neoplasms	0.1	0.1	0.1	0.4	0.4	0.3
C. Diabetes mellitus	0.9	1.1	0.9	2.7	2.8	2.6
D. Endocrine disorders	0.6	0.8	0.5	1.5	1.6	1.4
E. Neuropsychiatric conditions	7.1	9.9	11.7	18.8	20.9	27.0
F. Sense organ diseases	3.9	5.2	4.6	5.3	5.1	4.8
G. Cardiovascular diseases	10.0	12.9	9.4	18.8	20.0	15.6
H. Respiratory diseases	3.2	4.2	3.4	6.3	6.6	6.5
I. Digestive diseases	3.0	3.8	3.0	4.1	4.4	4.1
J. Genitourinary diseases	1.0	1.2	1.0	1.2	1.4	1.2
K. Skin diseases	0.2	0.3	0.3	0.2	0.2	0.2
L. Musculoskeletal diseases	1.4	1.9	1.8	4.2	4.3	4.1
M. Congenital anomalies	2.2	1.7	2.0	1.7	1.0	1.3
N. Oral conditions	0.3	0.5	0.5	0.6	0.6	0.7
III. Injuries	11.9	11.2	12.7	9.9	7.5	9.3
A. Unintentional injuries	8.7	8.2	9.3	6.9	5.3	6.5
B. Intentional injuries	3.2	3.1	3.5	3.0	2.3	2.8

Source: Authors' calculations.



Source: Authors' calculations.

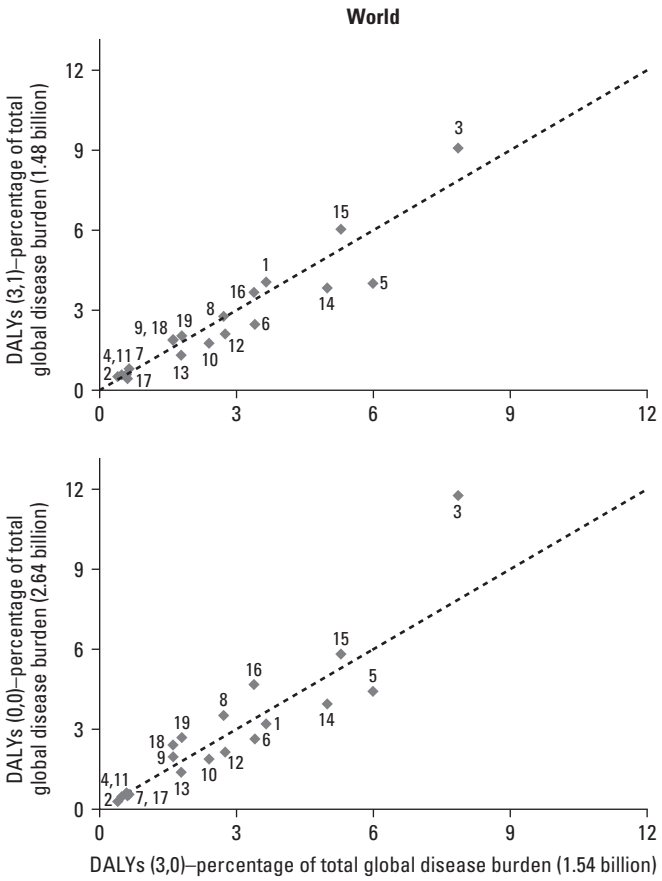
Figure 5.8 Effects of Changing the Discount Rate and Age Weighting on Global Rankings for the Top 20 Causes of the Burden of Disease, 2001

top 20 causes of the burden of disease in 2001. The left-hand column shows the rankings for causes measured using DALYs(3,0) as used for the DCPP. The middle column is for DALYs(3,1), as used by WHO to present the GBD analysis. The principal difference is that the use of DALYs(3,0) results in relatively greater importance being placed on chronic diseases of middle and older ages, such as ischemic heart disease and stroke, and somewhat lesser on HIV/AIDS, road traffic accidents, congenital anomalies, and other disorders affecting children and younger adults. Undiscounted DALYs, shown in the right-hand column, give proportionately greater importance to conditions affecting children, such as malaria and measles.

SENSITIVITY OF RISK FACTOR ESTIMATES TO VARIATIONS IN KEY PARAMETER VALUES

Figures 5.9 to 5.11 examine the sensitivity of the burden of disease attributable to each of the 19 risk factors discussed in chapter 4 to key DALY discounting and age-weighting parameters for the world, for low-and-middle-income countries, and for high-income countries. The figures plot the attributable disease burden estimated by altering one key parameter against the baseline of DALYs(3,0) used in chapter 4. To allow comparability, all burdens attributable to risk factors are shown as a proportion of the total global or regional disease burden, which is itself estimated with the corresponding parameters.

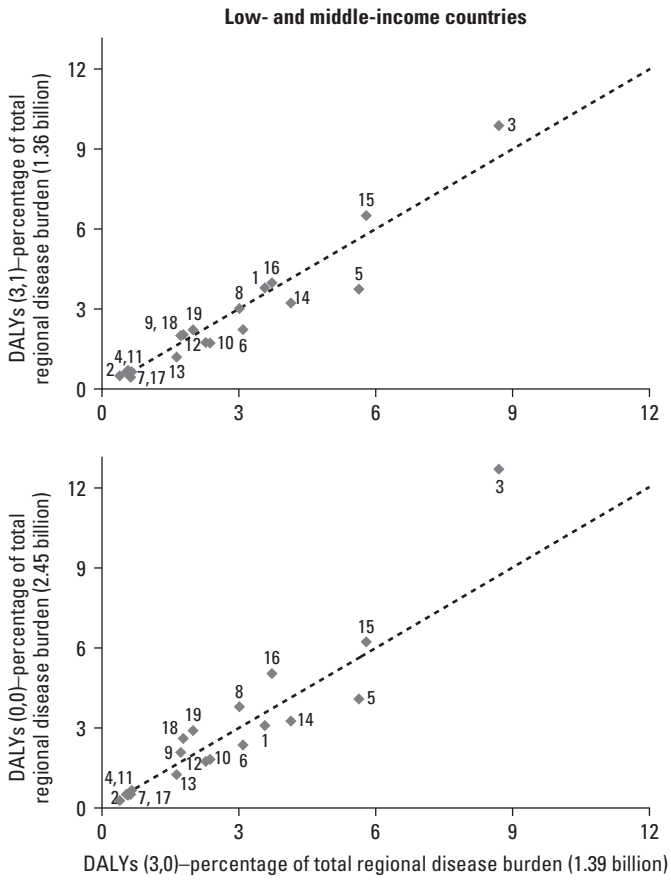
Including age weighting, DALYs(3,1), increases the relative health consequences of risks that affect people in young and middle ages (alcohol use, illicit drug use, and unsafe sex) and lowers the relative contribution of those risks that result in death in older ages (high blood pressure, high cholesterol, low fruit and vegetable intake, overweight and obesity, physical inactivity, and smoking). In addition, the burden of disease attributable to childhood and maternal underweight increases as a proportion of the total global or regional burden of disease. This increase probably reflects a relative reduction in the total burden of those diseases that affect older adults, and hence a relative increase in the total burden of those diseases that affect young children. Because childhood and maternal underweight is a risk factor for this



Source: Authors' calculations.

Note: Each point corresponds to the proportion of total GBD attributable to one risk factor. (1) alcohol use; (2) child sexual abuse; (3) childhood underweight; (4) contaminated injections in health care setting; (5) high blood pressure; (6) high cholesterol; (7) illicit drug use; (8) indoor smoke from household use of solid fuels; (9) iron deficiency anemia; (10) low fruit and vegetable intake; (11) non-use and use of ineffective methods of contraception; (12) overweight and obesity (high body mass index); (13) physical inactivity; (14) smoking; (15) unsafe sex; (16) unsafe water, sanitation, and hygiene; (17) urban air pollution; (18) vitamin A deficiency; (19) zinc deficiency.

Figure 5.9 Effects of Changes in Key DALY Parameters on Proportion of the Global Disease Burden Attributable to Risk Factors.



Source: Authors' calculations.

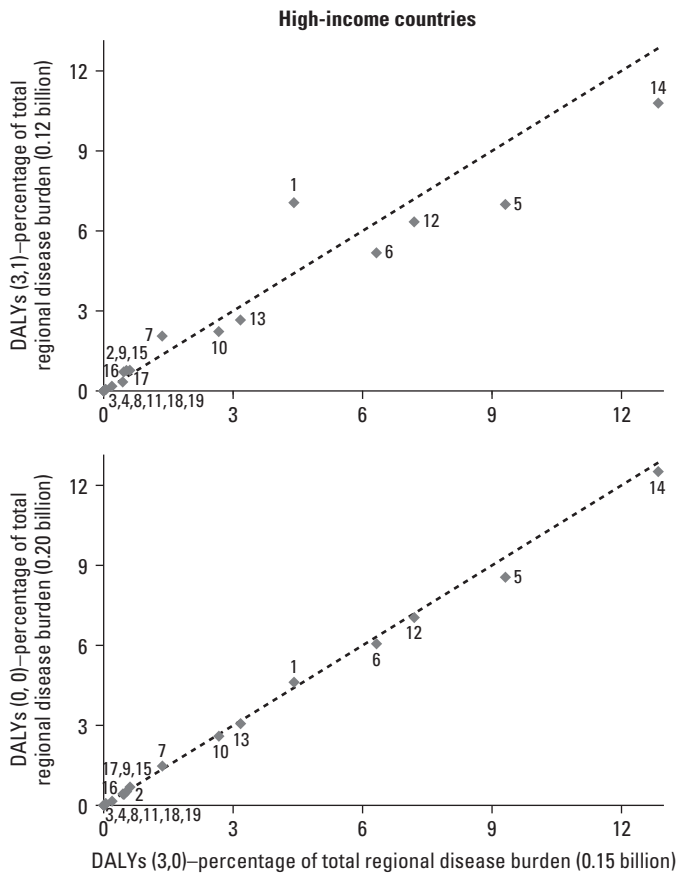
Note: Each point corresponds to the proportion of total GBD attributable to one risk factor. (1) alcohol use; (2) child sexual abuse; (3) childhood underweight; (4) contaminated injections in health care setting; (5) high blood pressure; (6) high cholesterol; (7) illicit drug use; (8) indoor smoke from household use of solid fuels; (9) iron deficiency anemia; (10) low fruit and vegetable intake; (11) non-use and use of ineffective methods of contraception; (12) overweight and obesity (high body mass index); (13) physical inactivity; (14) smoking; (15) unsafe sex; (16) unsafe water, sanitation, and hygiene; (17) urban air pollution; (18) vitamin A deficiency; (19) zinc deficiency.

Figure 5.10 Effects of Changes in Key DALY Parameters on Proportion of the Regional Disease Burden Attributable to Risk Factors for Low- and Middle-Income Countries

latter group of diseases, its attributable burden as a share of the total global or regional disease burden increases.

Removing discounting, DALYs(0,0), results in a large relative increase in the disease burden attributable to risk factors that affect young children, including childhood underweight; indoor smoke from household use of solid fuels; unsafe water, sanitation, and hygiene; vitamin A deficiency; and zinc deficiency. This is mirrored by a decrease in the disease burden attributable to the risk factors for diseases that affect adults, because the total burden of the chronic diseases affected by these risks is reduced. This effect is more noticeable in the low- and middle-income countries than in the high-income countries, where childhood mortality is low and the overall share of the disease burden is less sensitive to discounting.

Sensitivity to key DALY parameters differed in the low- and middle-income countries and the high-income countries. The burden of disease attributable to risk factors for chronic diseases in adults (high blood pressure, high cholesterol, low fruit and vegetable intake, overweight and obesity, physical inactivity, and smoking) was more sensitive to these parameters in low- and middle-income countries than in high-income countries because deaths attributable to these risks occurred at younger ages in the former. By contrast, the burden of disease attributable to alcohol was much more sensitive to age-weighting in the high-income countries because many of the hazards of this risk, especially those related to injuries and neuropsychiatric conditions, occur among younger adults in this group of countries.



Source: Authors' calculations.

Note: Each point corresponds to the proportion of total GBD attributable to one risk factor. (1) alcohol use; (2) child sexual abuse; (3) childhood underweight; (4) contaminated injections in health care setting; (5) high blood pressure; (6) high cholesterol; (7) illicit drug use; (8) indoor smoke from household use of solid fuels; (9) iron deficiency anemia; (10) low fruit and vegetable intake; (11) non-use and use of ineffective methods of contraception; (12) overweight and obesity (high body mass index); (13) physical inactivity; (14) smoking; (15) unsafe sex; (16) unsafe water, sanitation, and hygiene; (17) urban air pollution; (18) vitamin A deficiency; (19) zinc deficiency.

Figure 5.11 Effects of Changes in Key DALY Parameters on Proportion of the Regional Disease Burden Attributable to Risk Factors for High-Income Countries

UNCERTAINTY ANALYSIS OF THE GLOBAL BURDEN OF DISEASE ESTIMATES

The 2001 GBD study estimated mortality and the burden of disease for a comprehensive set of disease and injury causes and for all regions of the world, including regions with limited, incomplete, and uncertain data. To allow users of the information to assess whether the information uncertainty range is compatible with the purpose at hand, providing some analysis and guidance on levels of uncertainty is important (Murray, Mathers, and Salomon 2003). This is difficult to do, because apart from the large number and disparate nature of the data sources used (see chapter 3), information or knowledge about the quality of and potential biases in the data is often limited. This and the following sections provide an overview of initial efforts to quantify the uncertainty associated with the estimation of deaths by cause, with disability weights, and with epidemiological estimates of incidence and prevalence for GBD 2001.

Sources of Uncertainty

Uncertainty in estimated disease burden may arise from the following sources:

- incomplete information, for example, when estimates for a population are based on observations from a sample;
- potential biases in information, for instance, issues concerning the representativeness for a whole population of estimates from a study of a subgroup or the validity of a survey instrument in addressing the quantity of interest;
- heterogeneity or from disagreements among information sources, as when several studies give different estimates for the same quantity of interest;
- model uncertainty, for example, the variables or functional form specified in a regression model;
- the data generation process itself; for instance, investigators may only infer risks from event counts in a population, which means that they can never know the risks themselves with certainty.

The most familiar and most commonly quantified kind of uncertainty arises from random error in the direct measurement of a quantity. An estimate of an epidemiological quantity for a population will have uncertainty arising from the finite sample used in the study as well as from random measurement error. The standard error of the mean or the confidence interval for such a quantity specifies the distribution of uncertainty in knowledge of the true mean value in the population (assuming no systematic error).

Most measurement involves not only random (stochastic) error, but also systematic error arising from biases in the measurement instrument, for instance, unrepresentativeness of a sampling frame for a survey, or from inaccuracies in the assumptions used to infer the actual quantity from the available data, for example, estimating the prevalence of a disease for a country from studies of representative subpopulations. Examinations of historical measurements reveal a consistent tendency to underestimate systematic error, perhaps because systematic error usually relates to sources of error that are unknown or about which little is known. Ignoring systematic error when estimating uncertainty is common, but this often results in substantial

underestimation of the true uncertainty (Morgan and Henrion 1990).

Putting upper and lower bounds on the systematic error component is often possible, for example, where a disease process has biological limits or where evidence from a range of populations provides likely upper and lower limits to an epidemiological parameter such as prevalence or case fatality. In addition, consistency analysis across the various inputs for the DALY calculation (incidence, prevalence, case fatality rates or relative risk of mortality, and remission rates) often helps identify sources of systematic error and provides some basis for quantifying them (Kruijshaar, Barendregt, and Hoeymans 2002; Mathers, Murray, and Lopez 2002). This is discussed further in chapter 3.

Much of the uncertainty in estimates of deaths or DALYs for the 2001 GBD study is associated with the assessment of systematic errors in primary data. Chapter 3 examined primary data sources and their reliability in some detail and provided summary tabulations of the numbers of data sources available across regions and causes. This review clearly indicated that even though most countries have some information about prevalence, incidence, and mortality from some diseases and injuries and about population exposures to risk factors, it is generally fragmented, partial, incomparable, and diagnostically uncertain. One of the explicit aims of the GBD approach is to provide a coherent framework for integrating, validating, analyzing, and disseminating fragmentary information on the health of populations so that it is truly useful for health policy and planning. An important aspect of this framework is to assess the reliability and validity of data, particularly in relation to systematic error, and hence to provide some guide to the uncertainty in the resulting estimates.

Describing and Quantifying Uncertainty

We follow Morgan and Henrion's (1990) approach toward interpreting and using probability to describe and quantify uncertainty. The classical or frequentist view of probability defines the probability of an event occurring in a particular trial or experiment as the frequency with which it would occur during a long sequence of similar experiments. For many quantities of real interest, it is difficult to imagine how to operationalize a long sequence of relevant, similar experiments. An example of such a quantity would be the probability, estimated in late 2005, that avian influenza will cause a major global epidemic with deaths exceeding, say, 1 million in 2006. One approach has been to distinguish events whose probabilities are knowable through a series of experiments from those whose probabilities are unknowable or uncertain because no unique and operationalizable set of similar experiments exists, but this essentially limits the use of probabilities to games of chance.

Alternatively, a Bayesian view of probability defines it as the degree to which a person believes that an event will occur, or that a parameter has a certain value, given all the relevant information currently known to that person. Because different people have different information, they may legitimately assign different probabilities to the same event. These subjective probabilities must obey all the same axioms and rules as frequentist probabilities. These conceptual distinctions do not usually affect the practice of statistical inference, and essentially the same formal inference models of probability may be applied (King, Tomz, and Wittenberg 2000; Morgan and Henrion 1990). Moreover, when an empirical series of data from trials becomes available, the Bayesian assessment of probability should converge to the frequentist assessment, assuming the Bayesian approach uses the data rationally to update the assessments.

Our general approach to describing and estimating uncertainty in quantities of interest is to express them as probability distributions using a Bayesian interpretation of probability as expressing uncertainty of an observed or hypothetical event given a set of assumptions about the world. Probability distributions can therefore be used to express uncertainty about epidemiological quantities, such as the prevalence of depression in a particular population, the population values reflected in health state valuations, or the underlying risk of mortality due to a specific cause in a specific population.

Advances in computer technology have facilitated analytical methods for dealing with uncertainty enormously. One general approach to combining the uncertainties of multiple inputs into estimates relies on numerical simulation methods. The simulation approach uses multiple samples from probability distributions around uncertain inputs to allow estimates of the probability distributions around quantities of interest that may be complicated functions of these inputs, without the need to solve difficult, or in many cases insoluble, mathematical equations (King, Tomz, and Wittenberg 2000; Vose 2000).

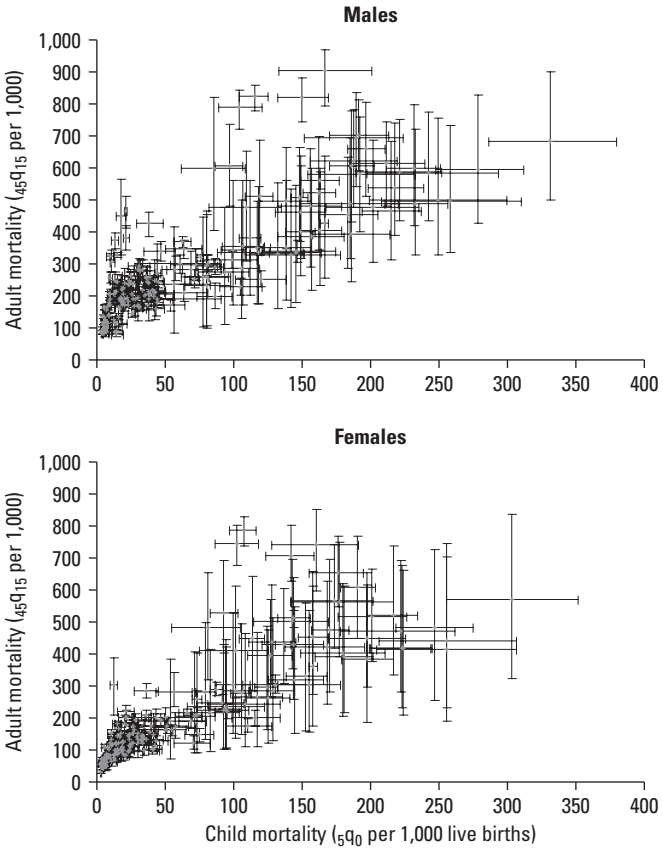
UNCERTAINTY ESTIMATES FOR ALL-CAUSE MORTALITY AND LIFE EXPECTANCIES

Chapters 2 and 3 describe methods for estimating life tables for each of 192 WHO member states. For those countries with vital registration data projected using time series regression

models on the parameters of the logit life table system, we accounted for uncertainty around the regression coefficients by taking 1,000 draws of the parameters using the regression estimates and variance-covariance matrix of the estimators. For each of the draws, we calculated a new life table. In cases where additional sources of information provided information on the limits of uncertainty ranges around ${}_5q_0$ (the mortality risk for children under five years of age) and ${}_{45}q_{15}$ (the mortality risk for adults between the ages of 15 and 60), the 1,000 draws were constrained so that each life table produced estimates within these specified ranges. The range of 1,000 life tables produced by these multiple draws reflects some of the uncertainty around the projected trends in mortality, notably, the imprecise quantification of systematic changes in the logit parameters over the time period captured in available vital registration data.

For countries that did not have time series data on mortality by age and sex, the following steps were undertaken. First, point estimates and ranges around ${}_5q_0$ and ${}_{45}q_{15}$ for males and females were developed on a country-by-country basis as described in chapter 2 and elsewhere (Lopez and others 2002). For countries where the ${}_5q_0$ estimate for 2001 was based on an analysis of available data sources for earlier years, such as surveys and censuses, the uncertainty range for ${}_5q_0$ was typically dominated by the uncertainty resulting from the scatter of survey-based direct and indirect estimates of child mortality for earlier years and the uncertainty in extrapolation of the trend to 2001, rather than the sampling error associated with individual estimates. For countries without usable information on levels of adult mortality, ${}_{45}q_{15}$ was estimated, along with uncertainty ranges, based on regression models of ${}_{45}q_{15}$ versus ${}_5q_0$ as observed in a set of almost 2,000 life tables judged to be of good quality. Estimated levels of child and adult mortality were then applied to a modified logit life table model, using a global standard, to estimate the full life table in 2001; HIV/AIDS deaths and war deaths were added to total mortality rates where necessary. Uncertainty ranges for HIV/AIDS were estimated as described elsewhere (Grassly and others 2004). In countries with substantial numbers of war deaths, estimates of their uncertainty range were also incorporated into the life table uncertainty analysis.

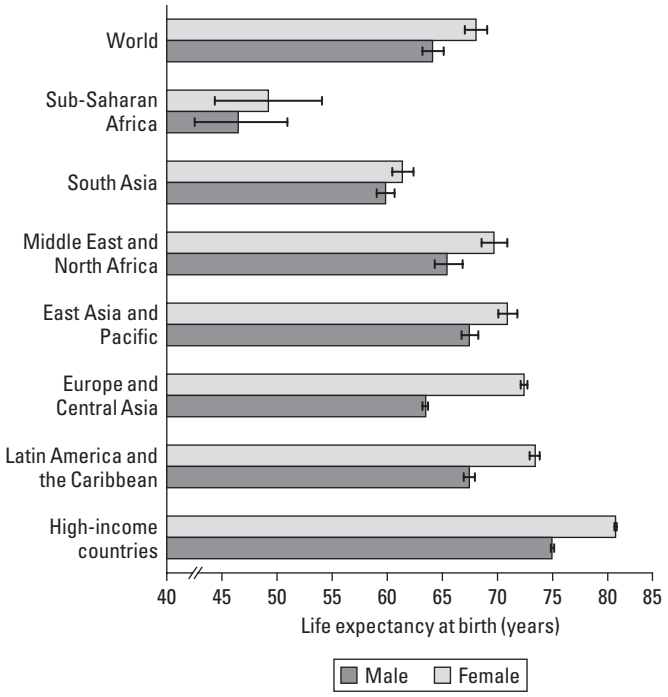
Figure 5.12 plots the final estimated uncertainty ranges for ${}_5q_0$ and ${}_{45}q_{15}$ for 192 WHO member states for males and females. Using Monte Carlo simulation methods, 1,000 random life tables were generated by drawing samples from normal distributions around these inputs with variances defined in reference to the defined ranges of uncertainty for ${}_5q_0$ and ${}_{45}q_{15}$. In countries where uncertainty around ${}_5q_0$ and ${}_{45}q_{15}$ was considerable because of a paucity of survey or surveillance information, the samples were drawn from wide distributions, but then constrained within prior specified maximum and minimum possible values for ${}_5q_0$ and ${}_{45}q_{15}$. For each country, the results of this analysis were 1,000 different simulated life tables that were then used to describe ranges around key indicators, such as life expectancy at birth and age- and sex-specific mortality rates.



Source: Authors' calculations.

Figure 5.12 Uncertainty Ranges for Child and Adult Mortality for WHO Member States, 2001

Figure 5.13 illustrates the resulting uncertainty ranges for life expectancy at birth for the World Bank regions (see map 1 inside the book's front cover). For high-income countries, where relatively complete death registration data are available, the uncertainty ranges for life expectancy at birth are around ± 0.07 years for females and ± 0.16 years for males. For regions such as Latin America and the Caribbean, where death registration data are available for most countries but are often incomplete, the uncertainty ranges are larger, typically around ± 0.5 years. For regions with partial data on child mortality only, where adult mortality is predicted from child mortality, the uncertainty ranges are much larger, and



Source: Authors' calculations.

Figure 5.13 Uncertainty in Average Life Expectancy at Birth, by Sex and DCPP Region, 2001

for Sub-Saharan Africa are typically around ±5.0 years. Across the regions, this translates to considerable heterogeneity in uncertainty ranges for life expectancies at birth and for estimates of all-cause mortality levels.

UNCERTAINTY ESTIMATES FOR REGIONAL MORTALITY BY CAUSE

We use a simulation approach to estimate uncertainty ranges for deaths by cause for GBD 2001. These uncertainty ranges take into account uncertainty in the expected number of total deaths (life table uncertainty); uncertainty in the estimated proportions of broad cause Groups I, II, and III (where relevant for countries without vital registration data or with incomplete coverage); uncertainty in the diagnosis of underlying cause; uncertainty arising from the miscoding of underlying cause; and fundamental Poisson uncertainty in the estimated death rate arising from the observation of a finite number of deaths in a fixed time interval. This analysis was carried out by country.

As described in the previous section, a total of 1,000 life tables were developed for each of the 192 WHO member states to quantify the uncertainty distribution of key life table parameters. We then used the age-specific mortality rates from the 1,000 life tables to estimate the uncertainty distribution for the expected number of total deaths for 2001. Uncertainty in the underlying cause attribution was estimated in terms of the relative uncertainty of the proportion of deaths due to each specific cause. The estimates of cause-specific relative uncertainty were based on advice from nosologists and experts in the area of cross-country mortality analysis on the general levels of uncertainty in the attribution of specific causes within Groups I, II and III, together with detailed advice on particular causes with known higher levels of attribution uncertainty according to the ICD. Information on the latter causes derives from comparative analyses across countries, across time periods, and across ICD revisions, together with information from a variety of country-specific coding quality studies involving recoding or dual coding of deaths and comparisons with the original attributed causes.

Based on this advice, for cause distributions derived from vital registration data coded using ICD-10 (the 10th edition of the ICD), we generally assumed that diagnostic uncertainty and coding uncertainty together resulted in approximate relative 95 percent uncertainty ranges of ±3 percent for Group I causes, ±7 percent for Group II causes, and ±2 percent for Group III causes. Larger uncertainty ranges were assumed for specific causes known to have greater levels of diagnostic or coding error; for WHO member states that have been using ICD-10 coding for less than three years; for member states still using ICD-9 coding (with particular attention to causes where coding rates between ICD-9 and ICD-10 are known to differ); and for member states using other cause coding systems or verbal autopsy methods, or where cause of death models were used to estimate death distributions across Groups I, II, and III. In the latter case, an additional relative uncertainty for the estimation of Group I, II, and III proportions was estimated from the prediction uncertainty ranges associated with the CodMod regression model (see chapter 3).

Uncertainty estimates also took into account the redistribution of general, cancer, cardiovascular, and injury ill-defined cause codes and incomplete coverage of vital registration data. The relative uncertainty range for each cause was then combined with the estimated uncertainty distribution for all-cause mortality to provide estimates of the uncertainty distributions of cause-specific mortality estimates for all ages and both sexes at the country level.

The analysis of uncertainty in cause of death estimates at the country level thus combines quantitative, country-specific information on uncertainty in all-cause mortality

and, in some cases, also in major cause group distributions, together with quantified average relative uncertainty ranges for specific cause attributions based on expert advice and adjusted for specific causes and for country-specific information on data sources, type of cause information available, and indicators of data quality. Here we summarize these uncertainty estimates at the regional level to provide some indication of the range of uncertainty for cause-specific mortality estimates across the World Bank regions as reported in chapter 3. This requires some additional assumptions about the cross-country correlations in uncertainty distributions.

At one extreme, if all country-level estimates have uncorrelated uncertainty because they are derived from completely independent data sets, then even with high levels of uncertainty at the country level, there will be considerably less uncertainty at the regional or global level. At the other extreme, if the uncertainty in country-level estimates for a cause derives predominantly from a single source or assumption, for example, about the case fatality rate of malaria, that is applied in deriving each country estimate, then the uncertainty distributions will be highly correlated and the regional uncertainty will be of a similar relative magnitude as each of the country uncertainty ranges.

With respect to cross-country correlations for life table and cause of death estimates based on death registration data, we assumed that even though life table uncertainties would be uncorrelated, relative uncertainties in cause of death attribution for specific causes were likely to be correlated because of systematic errors in ICD coding practices across countries for specific causes. We arbitrarily set this correlation at 25 percent. For life table estimates not based on death registration data, we assumed some correlation in uncertainty because even though estimates of childhood mortality came from independent sources, the method for determining adult mortality was similar across countries. We therefore set this correlation at 50 percent.

We assumed that cross-country correlation for relative cause of death uncertainties in the absence of vital registration data would vary depending on the method of causal attribution. Attributions based on some data and country-level predictions or assumptions were assumed to have less correlation than those based simply on regional patterns. In the case of the latter, we set the correlation at 75 percent; in the former, we set it at 50 percent or 25 percent depending on the degree of independence of the underlying inputs. We assumed greater independence for cancers and maternal conditions and less independence for tuberculosis, HIV/AIDS, sexually transmitted infections, diarrheal diseases, childhood-cluster diseases, meningitis, tropical-cluster diseases, lower respiratory infections, and perinatal conditions. We set cross-country correlations for war and drug use disorders at 25 percent for all countries, including those with vital registration data, to reflect the different methods used to obtain estimates for these causes.

We derived 95 percent uncertainty intervals by cause for World Bank regions in 2001 from the foregoing assumptions using simulation methods. We constructed 1,000 draws with the required correlation structure between countries separately for each cause, and the 2.5th percentile and the 97.5th percentile of expected deaths were taken to be the lower and upper bounds of the corresponding uncertainty interval. Note that these ranges provide guidance on uncertainty in the underlying cause-specific death rates, as expressed in terms of expected deaths in the population in 2001. Uncertainty in population estimates is not included, and the uncertainty ranges relate to underlying death rates, not to the numbers of deaths that actually occurred in 2001.

Table 5.5 summarizes regional uncertainty ranges for total estimated deaths for selected causes for 2001. Uncertainty ranges for estimated all-cause deaths increase from around ±1 percent for high-income countries to (−15 percent, +21 percent) for Sub-Saharan Africa. For specific causes, regional uncertainty ranges are generally higher, except for those causes for which cause-specific mortality estimates were available based on country-specific data from cause-specific surveillance systems (see chapter 3). For example, the uncertainty range for HIV/AIDS deaths in Sub-Saharan Africa is somewhat narrower than the all-cause mortality range, reflecting the substantial database for these estimates from antenatal clinic surveillance data and seroprevalence surveys, albeit still with considerable uncertainty arising from issues around the representativeness of the available data and the assumptions relating to survival and case fatality rates (Grassly and others 2004).

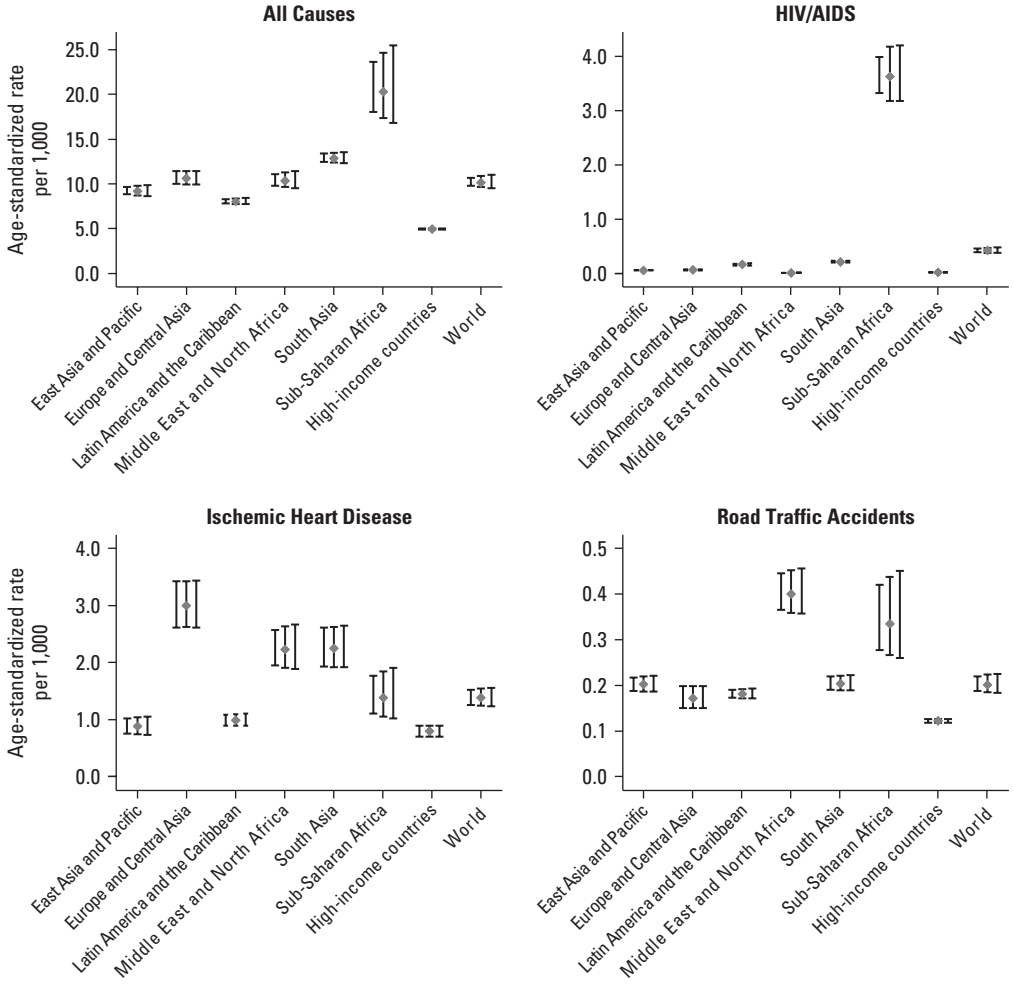
For most other causes, uncertainty ranges are greater than for the all-cause mortality estimates, because additional uncertainty is associated with cause attribution, as described earlier. For example, the relative uncertainty ranges for ischemic heart disease range from around ±12 percent for high-income countries to (−24 percent, +34 percent) for Sub-Saharan Africa (table 5.5). While the uncertainty range for high-income countries may seem surprisingly large, it reflects not only uncertainty in overall mortality levels, but also uncertainty in the attribution of

underlying cause and in the attribution of causes coded to cancer, cardiovascular, and injury ill-defined cause codes or to the ICD chapter for symptoms, signs, and ill-defined conditions. The proportion of deaths coded to these two groups of causes is surprisingly large for some high-income countries (Mathers and others 2005).

Figure 5.14 illustrates the relative insensitivity of the regional uncertainty ranges to the assumptions about cross-country correlation of uncertainty. The broad patterns of the uncertainty ranges for causes across regions provide useful additional guidance to policy makers in interpreting regional differences, particularly in judging which policy questions these estimates can help address and for which the uncertainty levels are too great to allow useful inferences.

UNCERTAINTY IN DISABILITY WEIGHTS

Although health state valuations are often treated as value parameters without uncertainty, we argue that unlike social choices such as the discount rate, no clear normative basis is available on which to assign relative values to the different dimensions of health that collectively define the universe of health states. Ideally, these values should be derived from empirical data among representative populations (Salomon and others 2003). Numerous challenges are associated with population-based data collection for the purpose of health state valuations, particularly given the broad scope of valuations required for a comprehensive assessment of disease burden. As a result, the current empirical base for disability weights remains well short of this ideal. Given the



Source: Authors' calculations.

Note: Cross-country correlations in uncertainty distributions for countries without vital registration data were varied from 0 percent (left-hand bar) to 25 percent (middle bar) and 50 percent (right-hand bar) for each region.

Figure 5.14 Sensitivity of Uncertainty Ranges to Changes in Between-Country Correlation Assumptions

Table 5.5 Estimated Total Deaths and 95 Percent Uncertainty Ranges for Selected Causes, by Region, 2001
(thousands)

	East Asia and Pacific		Europe and Central Asia		Latin America and the Caribbean		Middle East and North Africa	
Cause	**Deaths**	**Uncertainty**	**Deaths**	**Uncertainty**	**Deaths**	**Uncertainty**	**Deaths**	**Uncertainty**
All causes	13,070	12,379–13,866	5,669	5,334–6,122	3,277	3,166–3,411	1,914	1,790–2,088
Tuberculosis	534	497–578	66	58–76	45	41–50	23	21–26
HIV/AIDS	106	97–116	28	24–35	83	74–94	4	3–4
Diarrheal diseases	226	199–252	15	14–16	55	49–61	74	65–84
Pertussis	3	3–4	0	0–0	6	5–8	8	6–9
Diphtheria	1	1–1	0	0–0	0	0–0	0	0–0
Measles	76	66–85	8	7–8	0	0–0	15	13–18
Tetanus	27	25–30	0	0–0	1	1–1	4	3–5
Meningitis	33	29–39	14	13–15	17	15–20	10	9–11
Hepatitis B	32	29–36	3	3–4	4	4–5	6	5–7
Hepatitis C	13	12–15	1	1–1	2	2–2	3	3–3
Malaria	30	25–36	0	0–0	2	1–2	19	17–22
Schistosomiasis	3	3–4	0	0–0	1	1–1	8	8–9
Lower respiratory infections	544	449–655	104	94–116	157	140–177	108	90–130
Upper respiratory infections	27	25–30	4	4–5	3	2–3	2	2–3
Maternal conditions	37	23–56	3	2–4	16	12–21	15	10–22
Perinatal conditions	502	447–567	57	53–62	164	153–177	106	95–122
Stomach cancer	442	386–504	101	89–114	57	53–61	18	16–20
Colon and rectal cancers	159	142–179	96	87–106	37	34–39	10	9–11
Trachea, bronchus, and lung cancers	387	341–438	165	148–187	55	51–59	20	18–22
Breast cancer	93	83–103	63	59–68	37	34–40	14	13–15
Cervix uteri cancer	47	42–52	19	18–21	26	24–29	5	4–5
Corpus uteri cancer	8	7–9	17	15–18	12	11–12	1	1–1
Prostate cancer	16	14–17	25	23–29	37	34–39	6	5–7
Lymphomas, multiple myeloma	42	37–46	23	21–24	24	22–26	12	11–13
Leukemia	76	68–86	27	25–29	22	21–24	14	13–16
Diabetes mellitus	233	152–326	51	45–59	163	135–197	31	21–44
Alzheimer's and other dementias	58	37–82	10	8–11	14	12–16	3	2–5
Parkinson's disease	26	22–30	4	3–4	5	4–5	3	2–3
Drug use disorders	7	5–11	11	8–15	2	2–3	19	13–26
Ischemic heart disease	1,151	967–1,371	1,685	1,473–1,928	358	322–398	323	276–382
Cerebrovascular disease	1,902	1,606–2,236	1,029	888–1,189	267	240–298	130	111–153
Chronic obstructive pulmonary disease	1,415	1,218–1,634	130	119–143	99	92–109	41	35–47
Asthma	56	41–74	27	21–34	12	10–14	7	5–8
Cirrhosis of the liver	193	166–225	103	94–115	74	69–81	37	33–43
Nephritis and nephrosis	186	160–217	36	33–40	55	50–61	42	37–48
Road traffic accidents	361	334–394	83	73–96	88	83–93	99	88–112
Poisonings	83	78–90	106	90–127	3	3–4	7	7–8
Falls	122	114–132	35	32–40	15	14–16	12	10–13
Fires	36	33–41	20	16–24	5	4–5	13	12–15
Drownings	144	135–156	35	30–41	19	18–20	14	12–16
Other unintentional injuries	189	176–204	121	106–140	78	74–83	36	33–41
Self-inflicted injuries	323	294–356	121	105–141	30	28–32	14	13–17
Violence	103	93–117	68	57–81	130	123–138	10	9–12
War	14	9–20	17	13–23	6	6–7	8	5–12

Source: Authors' calculations.

Table 5.5 Continued
(thousands)

South Asia		Sub-Saharan Africa		High-income countries		World	
Deaths	**Uncertainty**	**Deaths**	**Uncertainty**	**Deaths**	**Uncertainty**	**Deaths**	**Uncertainty**
13,557	13,053–14,240	10,837	9,267–13,164	7,891	7,830–7,963	56,216	53,387–60,173
604	567–652	317	258–400	16	15–17	1,605	1,476–1,771
272	255–292	2,058	1,802–2,367	22	21–23	2,573	2,325–2,872
695	628–757	712	571–908	6	6–6	1,782	1,557–2,065
108	90–130	176	134–233	0	0–0	301	243–382
3	3–3	1	1–2	0	0–0	6	5–7
216	190–241	447	355–577	1	1–2	762	637–925
140	131–152	121	97–156	0	0–0	293	259–343
71	66–79	23	19–29	4	4–5	173	157–195
28	26–31	21	16–28	5	5–6	100	90–114
11	10–12	8	6–11	12	11–12	51	46–56
63	57–71	1,093	841–1,465	0	0–0	1,207	941–1,596
0	0–0	2	2–3	0	0–0	14	13–16
1,414	1,173–1,698	1,080	833–1,419	345	310–371	3,751	3,181–4,456
20	19–22	13	10–17	4	4–4	73	66–83
199	158–252	237	158–341	1	1–1	508	381–676
1,086	985–1,215	573	462–732	32	31–34	2,521	2,250–2,876
45	40–52	33	28–40	146	135–157	842	773–917
35	31–40	20	17–24	257	238–276	614	579–648
129	113–146	15	13–17	456	421–491	1,227	1,152–1,302
76	67–85	34	28–43	155	144–167	472	444–502
83	73–95	38	32–46	17	15–18	235	215–258
4	4–5	3	2–3	27	25–29	71	67–75
21	18–24	40	33–48	119	110–128	264	248–282
82	72–93	34	28–42	115	106–124	330	309–354
38	33–43	14	11–16	73	67–79	263	247–281
196	127–273	82	54–118	202	172–235	959	744–1,207
81	52–113	7	4–10	207	175–241	380	314–447
9	8–10	5	4–6	45	42–48	95	88–104
29	19–41	4	2–6	13	11–15	85	64–109
1,838	1,567–2,148	343	260–458	1,364	1,203–1,533	7,061	6,328–7,844
923	788–1,078	355	269–474	781	689–874	5,388	4,790–6,067
577	502–662	116	89–153	297	280–317	2,675	2,370–3,030
78	57–101	26	19–35	28	24–32	233	186–287
185	161–214	59	45–79	118	110–126	771	696–863
132	114–152	101	77–135	111	104–119	662	586–758
238	221–258	200	159–261	121	117–125	1,189	1,090–1,317
90	86–96	37	29–50	21	20–22	349	324–381
112	106–119	20	16–26	71	69–74	387	368–412
183	173–194	44	35–58	9	9–10	310	287–339
90	85–96	66	52–86	16	16–17	384	355–424
280	265–298	127	99–168	82	79–85	913	847–1,003
224	206–245	36	29–47	126	121–131	874	816–943
79	74–85	141	114–181	24	23–25	556	504–624
26	15–39	136	54–221	0	0–0	207	114–308

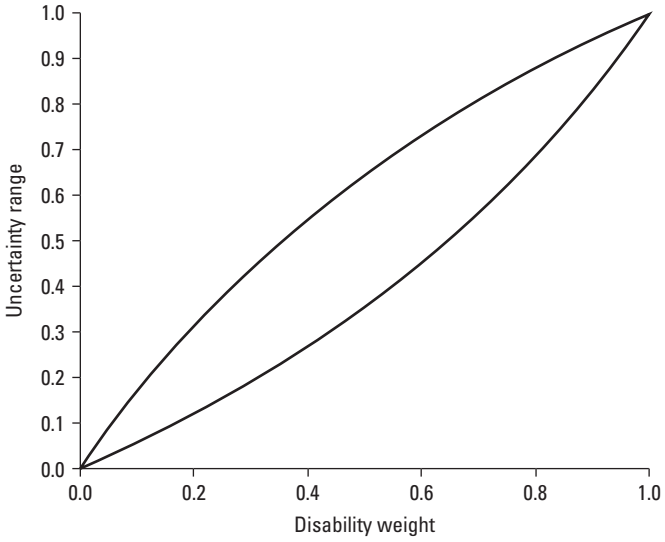
limitations in currently available information, an examination of the contribution of uncertainty around health state valuations to overall uncertainty in burden of disease estimates measured using YLD or DALYs is useful.

Conceptually, the basis for assigning disability weights to specific sequelae requires an understanding of (a) the distribution of health states among those living with the particular sequelae, where a health state is defined by the levels on the various dimensions that constitute health; and (b) a valuation function that provides a systematic way to aggregate across multiple dimensions of health in order to arrive at a single index value that captures the overall level of health associated with a given health state (Salomon and others 2003). While disability weights may vary across regions because of variation in either component, we have proposed elsewhere that for purposes of standardization and global comparisons, computing disability weights based on an average global valuation function is the most appropriate approach (Murray and others 2002). The need to understand variation in the distribution of health states among people living with given sequelae highlights the critical link between the epidemiological inputs of burden and the estimated disability weights.

In this section, we undertake a first analysis of the contribution of uncertainty in disability weights to uncertainty in the GBD DALY estimates. Given that the current set of disability weights reflects the accumulation of a wide array of different empirical inputs rather than the result of the comprehensive and standardized approach defined earlier as the ideal, we operationalize our analysis of uncertainty in terms of error around the disability weights by sequelae rather than in terms of the uncertainty arising from the constituent components, that is, the health state distributions and the valuation function. Based on this approach, the results offer guidance on the sensitivity of burden estimates to a certain degree of uncertainty around disability weights, but do not necessarily capture all sources of uncertainty and their covariance. As noted earlier, certain specific measurement methods for eliciting health state valuations, for example, the person trade-off or standard gamble, may have important normative implications that are orthogonal to the assessment of health levels. However, undertaking a sensitivity analysis that focuses on a specific measurement approach is not appropriate here, because the weights currently used in the GBD estimates have been derived from the synthesis of multiple data sources rather than from a single measurement method.

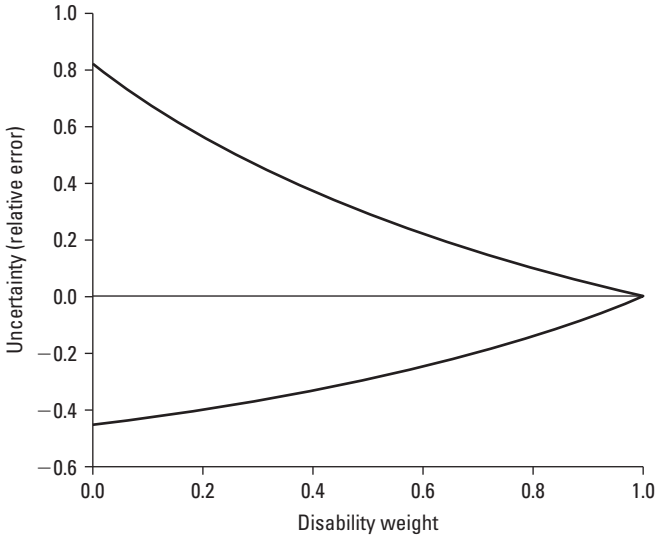
Because of the natural constraints on the range of values that disability weights may assume, we have incorporated normal distributions with constant variance in the space of the logit of disability weights. The logit transformation is given by $\text{logit}(x) = \ln[x/(1-x)]$. By allowing for normally distributed error in logit space, ranges in the natural space of valuations are constrained to fall between 0 and 1. We chose a value of 0.6 for the standard deviation of the logits, based on the standard deviations observed across the mean valuations by country for an array of conditions included in the WHO multicountry survey study from 2000–1 (with valuation modules implemented in 14 countries) (Salomon and others 2003; Ustun and others 2003). Although the variability in country means may reflect a range of different factors, including the possibility of real valuation heterogeneity, we use this value to approximate the average level of uncertainty around the set of disability weights used in the GBD study. A constant value in logit space yields absolute ranges that widen at the midpoint of the interval and narrow as the disability weight approaches 0 or 1 (figure 5.15). In relative terms, the uncertainty is greatest for the smallest disability weights and narrows as more severe weights are attained (figure 5.16).

To trace the implications of this uncertainty through to the calculation of DALYs(3,0) used in the DCPP, we took 100 draws from each of 622 independent normal distributions with a mean of 0 and a standard deviation of 0.6 (for the 622 sequelae included in the calculations). For each of the sequelae we applied a given sampled value as a perturbation of all age, sex, and region estimates of logit-transformed



Source: Authors' calculations.

Figure 5.15 Assumed 95 Percent Uncertainty Ranges for Disability Weights Based on Constant Variance Distribution for Logit of Disability Weight



Source: Authors' calculations.

Figure 5.16 Relative 95 Percent Uncertainty Ranges for Disability Weights Based on the Assumption of a Constant Variance Distribution for Logit of Disability Weight across All Disability Weights

disability weights pertaining to that sequela, and recomputed YLD(3,0) based on the disability weight plus the random perturbation (after reversing the transformation for the sum). We estimated uncertainty ranges by taking the 2.5th and 97.5th percentiles across the 100 values of the various quantities of interest based on the random draws of error around the disability weights. This method implies the simplifying assumption that errors are uncorrelated between sequelae but perfectly correlated for all estimates within a sequela. In addition to YLD(3,0) numbers, we recomputed YLD ranks resulting from each set of sampled values, and also calculated DALY numbers and ranks by adding each YLD(3,0) draw to constant YLL(3,0) estimates by sequela. Our intent is only to provide an indication of the sensitivity of the YLD and DALY results to disability weight uncertainty. We did not attempt either to carry out a full empirically based analysis of this issue or to combine this source of uncertainty with mortality uncertainty and uncertainty in epidemiological estimates to give a comprehensive uncertainty analysis for the DALY estimates.

Table 5.6 presents the resulting uncertainty ranges for YLD and DALYs by cause for low- and middle-income countries. As would be expected, DALY uncertainty ranges due to disability weight uncertainty are generally largest for those causes dominated by YLD and smallest for those causes dominated by YLL. Uncertainty ranges are also large for those YLD-dominated causes with high prevalence and low disability weight (with high relative uncertainty), such as hearing loss and anemia. Figure 5.17 summarizes in graphical form the uncertainty in total DALYs for low- and middle income countries for the 20 highest-ranked causes.

Table 5.7 presents the resulting 95 percent uncertainty ranges for the 40 leading causes of the burden of disease in low- and middle-income countries. Taking into account uncertainty in disability weights does not result in significant uncertainty in the ranking of the top four causes, with only the third (ischemic heart disease) and fourth (HIV/AIDS) possibly changing places. The total estimated DALYs for these two causes differ by less than 2 percent, so this is not surprising. Among the other top 10 causes, the disability weight uncertainty could change the rankings of individual causes by up to two ranks, with the exception of depressive disorders, which could change by up to four ranks. This reflects both the high relative uncertainty in the disability weight for mild depression and the fact that YLD are responsible for almost all depression DALYs. Among conditions ranked 20th to 30th in table 5.7, uncertainty ranges for most ranks are relatively narrow with the exception of nonfatal, high-prevalence conditions such as hearing loss and osteoarthritis, where the uncertainty in rank may be as much as ±15 places.

This analysis confirms the importance of efforts to improve the measurement of disability weights for health states close to full health, that is, with disability weights close to zero, particularly for health states with high prevalence in many populations, such as mild to moderate sense organ impairment or mild to moderate anemia. Unfortunately, most of the available choice-based or trade-off methods involving comparison in some form with death or survival present greater cognitive challenges to respondents when applied to health states close to full health.

UNCERTAINTY ARISING FROM EPIDEMIOLOGICAL ESTIMATES

Uncertainty in YLD estimates is mainly determined by the uncertainty in (a) epidemiological estimates for the prevalence and/or incidence of disability associated with specific causes or cause groups; and (b) disability weights arising from uncertainty in health state valuations and, in some cases, also in the disability severity distribution associated with a condition.

For a subset of the GBD causes, analysts carrying out reviews and analyses for the estimation of YLD also estimated

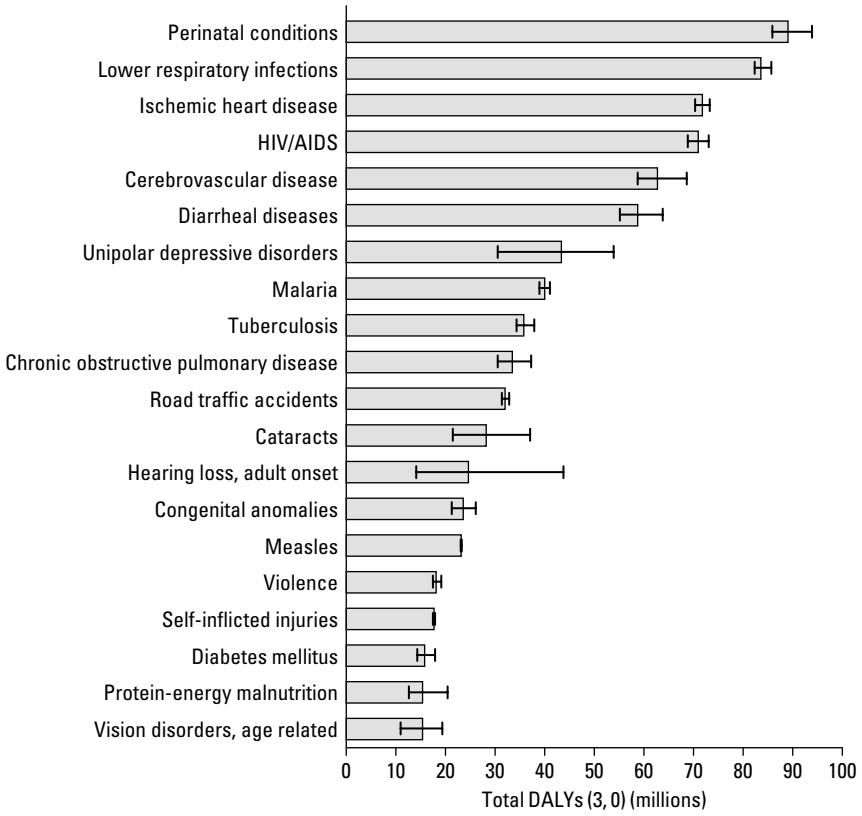
Table 5.6 Estimated 95 Percent Uncertainty Ranges for YLD and DALYs Arising from Uncertainty in Disability Weights for Selected Causes for Low- and Middle-Income Countries, 2001
(thousands)

Cause	YLD(3,0)	Uncertainty range	DALYs(3,0)	Uncertainty range
Group I				
Tuberculosis	4,134	2,706–6,219	35,882	34,400–37,900
Syphilis	407	310–574	4,122	4,021–4,286
Chlamydia	2,255	1,766–3,073	2,438	1,949–3,256
Gonorrhea	2,530	2,038–3,369	2,550	2,058–3,390
HIV/AIDS	5,973	4,142–8,195	70,857	68,900–73,000
Diarrheal diseases	7,836	4,236–12,900	58,685	55,100–63,800
Pertussis	2,291	1,763–2,986	11,408	10,900–12,100
Poliomyelitis	126	84–170	136	94–180
Diphtheria	0	0–1	164	164–164
Measles	193	113–319	23,097	23,000–23,200
Tetanus	14	10–16	8,337	8,329–8,335
Meningitis	1,131	915–1,416	5,477	5,255–5,756
Hepatitis B	52	28–96	2,082	2,056–2,124
Hepatitis C	21	11–39	844	832–860
Malaria	4,501	3,521–5,672	39,944	39,000–41,100
Trypanosomiasis	72	49–101	1,333	1,310–1,361
Chagas' disease	358	275–501	584	500–727
Schistosomiasis	1,313	727–2,563	1,525	938–2,774
Leishmaniasis	411	291–610	1,757	1,636–1,955
Lymphatic filariasis	4,446	3,365–6,947	4,455	3,374–6,956
Onchocerciasis	439	361–541	439	361–541
Leprosy	93	56–142	191	154–239
Dengue	5	3–10	529	526–533
Japanese encephalitis	231	187–276	598	554–644
Trachoma	2,618	2,023–3,192	2,621	2,025–3,195
Ascariasis	1,311	707–2,190	1,413	808–2,291
Trichuriasis	713	518–1,000	800	604–1,087
Hookworm disease	7	4–13	63	60–69
Lower respiratory infections	4,430	3,128–6,525	83,579	82,300–85,700
Upper respiratory infections	181	108–318	1,680	1,609–1,819
Otitis media	1,336	811–2,136	1,424	899–2,224
Maternal hemorrhage	232	61–162	3,923	3,750–3,851
Maternal sepsis	3,290	827–2,048	5,269	2,804–4,025
Hypertensive disorders	—	0–0	1,890	1,888–1,888
Obstructed labor	1,349	842–1,477	2,495	1,988–2,622
Abortion	1,732	1,034–2,344	3,503	2,803–4,112
Perinatal causes	13,525	10,300–18,100	89,121	85,900–93,800
Protein-energy malnutrition	9,337	6,616–14,300	15,450	12,700–20,400
Iodine deficiency	2,685	1,617–2,206	2,875	1,807–2,396
Vitamin A deficiency	58	34–88	711	685–740
Iron-deficiency anemia	6,736	4,782–10,300	9,488	7,530–13,000
Group II				
Mouth and oropharynx cancers	107	80–127	4,079	4,049–4,097
Esophageal cancer	42	29–56	5,251	5,235–5,262
Stomach cancer	124	95–160	9,613	9,577–9,643
Colon and rectal cancers	241	179–315	5,058	4,993–5,128
Liver cancer	49	37–63	7,943	7,926–7,952
Pancreas cancer	18	16–19	1,621	1,617–1,620
Trachea, bronchus, and lung cancers	137	117–155	10,697	10,700–10,700
Melanoma and other skin cancers	10	6–15	501	497–505
Breast cancer	308	226–386	5,527	5,440–5,600
Cervix uteri cancer	205	140–282	3,800	3,732–3,875
Corpus uteri cancer	276	200–416	908	831–1,046
Ovarian cancer	98	71–138	1,488	1,460–1,527

Table 5.6 Continued
(thousands)

Cause	YLD(3,0)	Uncertainty range	DALYs(3,0)	Uncertainty range
Prostate cancer	91	63–109	1,479	1,448–1,494
Bladder cancer	104	76–134	1,504	1,474–1,532
Lymphomas, multiple myeloma	69	49–98	3,770	3,746–3,795
Leukemia	58	33–86	3,964	3,936–3,989
Diabetes mellitus	5,662	4,229–7,736	15,806	14,400–17,900
Endocrine disorders	7,581	4,447–12,700	10,947	7,814–16,100
Unipolar depressive disorders	43,223	30,400–53,600	43,429	30,600–53,800
Bipolar affective disorder	8,676	5,636–12,100	8,681	5,642–12,100
Schizophrenia	10,156	7,419–12,800	10,530	7,793–13,200
Epilepsy	2,942	1,541–5,758	5,759	4,356–8,573
Alcohol use disorders	9,808	6,086–15,700	11,009	7,286–16,900
Alzheimer's and other dementias	8,172	6,690–9,790	9,641	8,158–11,300
Parkinson's disease	767	513–1,085	1,239	984–1,557
Multiple sclerosis	770	501–1,039	916	647–1,185
Drug use disorders	2,736	1,693–3,825	4,406	3,361–5,493
Post-traumatic stress disorder	2,013	1,217–3,918	2,013	1,218–3,919
Obsessive-compulsive disorder	3,136	1,726–5,532	3,136	1,726–5,532
Panic disorder	4,017	2,530–6,052	4,017	2,530–6,052
Insomnia (primary)	2,219	1,314–3,883	2,219	1,314–3,883
Migraine	4,851	2,720–7,503	4,851	2,720–7,503
Mental retardation, lead-caused	8,474	5,358–12,100	8,601	5,484–12,300
Glaucoma	4,110	2,986–5,393	4,111	2,987–5,395
Cataracts	28,155	21,500–37,100	28,155	21,500–37,100
Vision disorders, age-related	15,360	10,900–19,400	15,360	10,900–19,400
Hearing loss, adult onset	24,610	14,000–43,800	24,610	14,000–43,800
Rheumatic heart disease	607	404–863	6,152	5,945–6,404
Hypertensive heart disease	888	542–1,358	9,969	9,612–10,400
Ischemic heart disease	3,921	2,525–5,369	71,874	70,400–73,300
Cerebrovascular disease	11,096	7,209–17,100	62,652	58,700–68,600
Inflammatory heart diseases	1,309	765–1,908	5,812	5,263–6,406
Chronic obstructive pulmonary disease	8,473	5,670–12,400	33,457	30,600–37,300
Asthma	7,713	4,479–13,600	11,513	8,277–17,400
Peptic ulcer disease	1,154	556–1,737	4,802	4,203–5,383
Cirrhosis of the liver	2,329	1,391–3,289	13,635	12,700–14,600
Appendicitis	60	42–81	377	358–397
Nephritis and nephrosis	546	288–869	9,078	8,811–9,392
Benign prostatic hypertrophy	2,304	1,229–3,999	2,613	1,538–4,308
Skin diseases	2,924	1,764–4,425	3,697	2,535–5,197
Rheumatoid arthritis	3,433	2,132–5,436	3,645	2,344–5,648
Osteoarthritis	13,651	8,636–22,400	13,667	8,652–22,400
Gout	2,768	1,697–4,053	2,785	1,714–4,070
Low back pain	1,676	1,093–2,670	1,692	1,109–2,685
Congenital anomalies	9,295	7,047–11,700	23,538	21,300–26,000
Dental caries	4,752	2,771–8,429	4,752	2,771–8,429
Periodontal disease	206	124–368	207	125–369
Edentulism	2,293	1,349–3,476	2,293	1,349–3,476
Group III				
Road traffic accidents	7,195	6,489–8,063	32,022	31,300–32,900
Poisonings	135	107–170	7,119	7,088–7,151
Falls	8,055	7,035–9,203	13,582	12,600–14,700
Fires	2,719	2,199–3,286	10,081	9,557–10,600
Drownings	37	33–41	9,389	9,379–9,387
Self-inflicted injuries	1,236	1,040–1,489	17,677	17,500–17,900
Violence	5,405	4,734–6,420	18,135	17,500–19,100
War	1,569	1,321–1,887	6,496	6,240–6,806

Source: Authors' calculations.



Source: Authors' calculations.

Figure 5.17 Estimated 95 Percent Uncertainty in Total DALYs(3,0) Due to Uncertainty in Estimation of Disability Weights, Top 20 Causes, Low- and Middle-Income Countries

levels of uncertainty in regional prevalences. These assessments took into account not only typical levels of measurement error in the input data sets, but also expert judgment on the degree of uncertainty arising from the lack of representativeness of the available data for each region. The resulting uncertainty ranges vary considerably across causes, ranging from relatively certain estimates for some causes such as polio, for which intensive surveillance systems are in place, to highly uncertain estimates for other causes such as osteoarthritis, where for some regions not a single usable dataset was found, and where for others the latest available data were decades old. The summary tables provided in chapter 3 for numbers of data sources used for YLD estimates by cause and region provide one indication of the relative uncertainty associated with YLD estimates for different causes.

For some causes, such as stroke and ischemic heart disease, YLD estimates were essentially derived from estimates of cause-specific mortality by means of models of regional variations in case fatality rates. In such cases, YLD uncertainty will be significantly higher than the uncertainty associated with cause-specific mortality estimates given the considerable uncertainty in case fatality rates for most low- and middle-income countries and in models used to infer the burden of nonfatal disease from mortality. YLD uncertainty will generally be greater than YLL uncertainty, and will also vary across causes according to both the typical uncertainty associated with the measurement of incidence or prevalence according to GBD case definitions and with the number and representativeness of available studies. For a subset of 16 major causes of YLD for which analysts estimated indicative uncertainty ranges, the typical uncertainty for regional prevalence estimates ranged from ± 10 percent to ± 90 percent, with a median value of ± 41 percent. Uncertainty ranges were generally higher for low- and middle-income countries than for high-income countries.

UNCERTAINTY IN THE DISEASE BURDEN ATTRIBUTABLE TO RISK FACTORS

The assessments of the disease burden attributable to selected risk factors reported in chapter 4 are affected by

Table 5.7 Estimated 95 Percent Uncertainty Ranges Arising from Uncertainty in Disability Weights for the Top 40 Causes of the Burden of Disease in Low- and Middle-Income Countries, 2001

Rank	Uncertainty range	Cause	DALYs (thousands)	Uncertainty range
1	1–1	Perinatal conditions	89,121	85,900–93,800
2	2–2	Lower respiratory infections	83,579	82,300–85,700
3	3–4	Ischemic heart disease	71,874	70,400–73,300
4	3–4	HIV/AIDS	70,857	68,900–73,000
5	5–6	Cerebrovascular disease	62,652	58,700–68,600
6	5–6	Diarrheal diseases	58,685	55,100–63,800
7	7–11	Unipolar depressive disorders	43,429	30,600–53,800
8	7–9	Malaria	39,944	39,000–41,100
9	8–10	Tuberculosis	35,882	34,400–37,900
10	9–12	Chronic obstructive pulmonary disease	33,457	30,600–37,300
11	10–13	Road traffic accidents	32,022	31,300–32,900
12	9–14	Cataracts	28,155	21,500–37,100
13	8–21	Hearing loss, adult onset	24,610	14,000–43,800
14	12–15	Congenital anomalies	23,538	21,300–26,000
15	13–15	Measles	23,097	23,000–23,200
16	15–18	Violence	18,135	17,500–19,100
17	16–19	Self-inflicted injuries	17,677	17,500–17,900
18	17–22	Diabetes mellitus	15,806	14,400–17,900
19	15–25	Protein-energy malnutrition	15,450	12,700–20,400
20	16–27	Vision disorders, age-related	15,360	10,900–19,400
21	16–36	Osteoarthritis	13,667	8,652–22,400
22	20–25	Cirrhosis of the liver	13,635	12,700–14,600
23	20–24	Falls	13,582	12,600–14,700
24	18–38	Asthma	11,513	8,277–17,400
25	23–29	Pertussis	11,408	10,900–12,100
26	19–40	Alcohol use disorders	11,009	7,286–16,900
27	18–40	Endocrine disorders	10,947	7,814–16,100
28	25–31	Trachea, bronchus, and lung cancers	10,697	10,700–10,700
29	22–39	Schizophrenia	10,530	7,793–13,200
30	27–34	Fires	10,081	9,557–10,600
31	27–34	Hypertensive heart disease	9,969	9,612–10,400
32	26–38	Alzheimer's and other dementias	9,641	8,158–11,300
33	29–36	Stomach cancer	9,613	9,577–9,643
34	25–40	Iron-deficiency anemia	9,488	7,530–13,000
35	31–37	Drownings	9,389	9,379–9,387
36	33–38	Nephritis and nephrosis	9,078	8,811–9,392
37	27–46	Bipolar affective disorder	8,681	5,642–12,100
38	24–47	Mental retardation, lead-caused	8,601	5,484–12,300
39	36–39	Tetanus	8,337	8,329–8,335
40	37–41	Liver cancer	7,943	7,926–7,952

Source: Authors' calculations.

additional sources of uncertainty, beyond the uncertainty in DALY estimates for specific disease and injury outcomes discussed earlier. A full uncertainty analysis of such burden estimates has not yet been carried out, but would involve assessment of the following additional types of uncertainty:

- uncertainty in the estimated distributions of population risk exposure;
- uncertainty in estimates of relative risks for cause-specific mortality and incidence associated with specific exposures, for which a significant source of uncertainty is the extrapolation of relative risks measured at other ages to older age groups;
- uncertainty associated with estimating joint effects of risk factors.

Uncertainty in exposure and in both the existence and magnitude of hazardous effect always affects quantitative risk assessment. In one taxonomy, risk assessment uncertainty can be divided into parameter uncertainty and model uncertainty

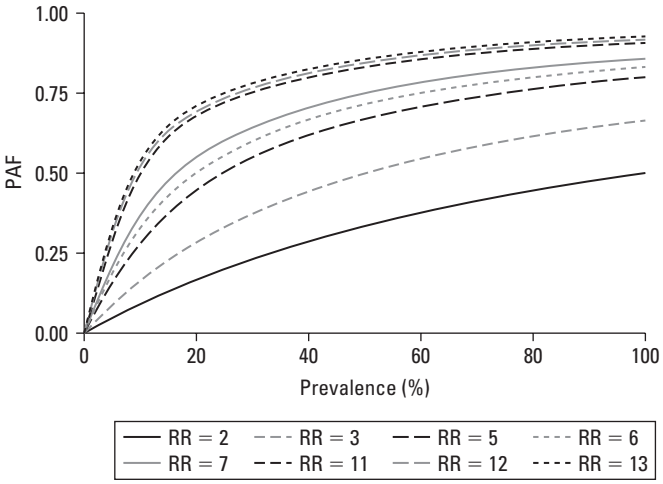
(National Research Council 1994). Parameter uncertainty is often quantifiable using random variable methods, for example, uncertainty due to sample size or measurement error. Model uncertainty is due to gaps in scientific theory, measurement technology, and data. It includes uncertainty in causal relationships or the form of the exposure-response relationship (for instance, threshold versus continuous or linear versus nonlinear), the level of bias in measurement, and so on. Defined broadly, model uncertainty also includes extrapolation of exposure or hazard from one population to another. Model uncertainty dominates uncertainty in risk assessment, a result of difficulty in carrying out direct studies on exposure, hazard, and background disease burden. This has motivated innovative assumptions and extrapolations even in the case of the most widely studied risk factors like smoking (Peto and others 1992).

Uncertainty around disease causation (Evans 1978; Hill 1965) was, in practice, secondary to uncertainty around hazard size, for example, relative risk, because when causality was uncertain, the estimates of relative risk needed for risk assessment were also unknown or uncertain. For example, whether the relationships between physical inactivity and lower back pain or between alcohol and violence are causal has equivalent questions on the magnitude of hazard of each risk for the disease outcome. Collective scientific knowledge from disciplines such as social and behavioral sciences, physiology and neuroscience, and epidemiology would confirm the possibility of a causal relationship in the foregoing cases, but would shift the uncertainty to hazard size. As a result, for some risk factors, we could only quantify the contribution to a subset of disease outcomes because epidemiological studies did not provide enough information for all risk factor and disease pairs, even when the causal relationship was believed or suspected.

Estimates of hazard in individual epidemiological studies were adjusted for confounding as much as possible. Extrapolation of hazard from a limited number of studies to other populations has received less attention. While the robustness of proportional measures of risk has been confirmed for more proximal factors in studies across populations (Eastern Stroke and Coronary Heart Disease Collaborative Research Group 1998; Horton 2000; Law, Wald, and Thompson 1994), their extrapolation is an important source of uncertainty for more distal risks (such as childhood sexual abuse) or those whose effects are heterogeneous (for example, alcohol and injuries versus alcohol and cancer).

Direct exposure data for many risk factors are limited both because of measurement difficulties and because of underinvestment in risk factor surveillance. To allow maximum use of available data, such risk factors were represented using indirect or aggregate indicators, for instance, smoking impact ratio for accumulated hazards of smoking, weight-for-age for childhood undernutrition, and use of solid fuels for indoor air pollution. Furthermore, for some risks multiple data sources allowed limiting the range of exposure estimates. For example, in the absence of alcohol surveys, information on total alcohol production, trade, and unrecorded consumption provided upper bounds on the fraction of the population that would be in the highest consumption category. Finally, some of the risk factors examined in chapter 4 were represented using continuous exposure variables such as high blood pressure. Others used categorical variables, for example, indoor smoke from household use of solid fuels, childhood underweight, and physical inactivity, even though the health effects occur along a continuum. This choice reflected the availability of exposure data and hazard estimates in categories. In such cases, the contribution to disease within the baseline category would not have been captured.

In addition to uncertainty in exposure and hazard, the uncertainty of estimated population attributable fractions (PAFs) is determined by the analytical properties of the PAF relationship. In particular, the PAF relationship is an increasing concave function of relative risk and exposure level, approaching 100 percent asymptotically, that is, the rate of increase declines with increasing relative risk or prevalence (figure 5.18). Therefore, if a risk factor or group of risk factors individually or jointly account for large



Source: Authors' calculations.

Note: The population attributable fraction (PAF) relationship is an increasing concave function of both prevalence (seen in the shape of each curve) and relative risk, *RR* (seen in the declining distance between each adjacent pair of curves). This limits the sensitivity of individual or joint PAFs to uncertainty in input parameters, when PAFs are relatively large.

Figure 5.18 PAF Sensitivity to Exposure and Relative Risks

fractions of specific diseases, the PAFs are more robust to uncertainty in inputs. Finally, there is uncertainty in mortality and disease burden estimates to which the estimated PAF are applied (see the previous section).

The findings in chapter 4 should therefore be considered within the context of limited available data and viewed as subject to uncertainty, which varies across risk factors and geographical regions. For further discussion of sources and quantification of uncertainty for specific risk factors see Ezzati and others (2004).

DISCUSSION

As described in chapter 3, the data requirements for adequate measurements of the global burden of disease are substantial and include information about age at death, cause of death, age-specific incidence of diseases and injuries, typical duration of life lived with the sequelae of diseases and injuries, and some quantification of the severity of disability assessed according to a common framework. While the ethical, philosophical, and conceptual issues involved in quantifying states of health other than perfect health are still very much a matter of debate, a substantial body of empirical evidence on the variations across individuals and populations in health state valuations is now available.

We have shown in this chapter that the distribution of the global burden of disease and the overall rankings of various conditions in terms of their contribution to it are largely insensitive to alternative assumptions about the discount rate and age weighting. The major effect of discounting and age weighting is to enhance the importance of neuropsychiatric conditions and sexually transmitted infections. While disease rankings are relatively unaffected, the share of the burden due to disability, the age distribution of the burden, and the distribution of the burden by broad cause group are sensitive to the discount rate but less affected by age weighting.

When compared with the discounted and age-weighted DALY used in the 1990 GBD study and the WHO updates for 2000–2, the DCPP's use of discounted but not age-weighted DALYs results in somewhat more weight being given to the chronic diseases of older ages and somewhat less weight being given to mental disorders and injuries, which affect younger adults disproportionately. Of the value choices incorporated into the standard DALYs(3,1), the nonuniform age weights have been the most controversial. Apart from the DCPP, a number of national burden of disease studies, including those in Australia and Canada (Mathers, Vos, and Stevenson 1999; Public Health Agency of Canada 2005), have chosen not to apply the nonuniform age weights, presumably on equity grounds. In contrast, some investigators concerned with the inequitable health burden of the low- and middle-income countries have argued for ignoring all deaths over a certain age on the grounds that they are not premature—an extreme form of age weighting (Williams 1997). Chapter 6 presents some empirical evidence in making the case for a stronger form of age weighting for infants and younger children, that is, age weights that depart further from unity than the standard age weighting used in the DALY.

Although the choices for discounting and age weighting do affect the cause and age distributions of the burden of disease to some extent, and the results of specific cost-effectiveness studies may be even more sensitive to these choices, we conclude that the uncertainty of the underlying epidemiological choices is vastly more consequential than these social preferences when interpreting the results of burden of disease analysis. The validity and reliability, and hence the utility, of burden of disease studies for public policy depend much more strongly on the quality and availability of the underlying epidemiological data.

The GBD study has been criticized for making estimates of mortality and burden of disease for regions with limited, incomplete, and uncertain data (Cooper and others 1998; Gupta, Sankaranarayanan, and Ferlay 1994). Murray and Lopez describe the GBD approach as a "'meta-synthesis,' or in other words, the construction of a comprehensive and comparable view of health problems using all available sources of information" (Murray and Lopez 1996b, p. 289). The incorporation of many types of information about a comprehensive set of causes of death and disability results in estimates that are much less likely to be biased than those that emerge from an examination of specific health conditions in isolation. It also avoids the tendency to assume that if no data are available or the data are highly uncertain, then there is no disease burden.

We argue that including uncertain results (with quantified uncertainty to the extent possible) is far preferable than leaving blank cells in tables intended to provide policy makers with an overall assessment of the burden of disease in populations. We maintain that providing large volumes of unsynthesized, biased, and incomplete data relating to population health does not generally allow policy makers to make the best use of such information. Unless they have considerable analytic resources of their own, the unsynthesized products of the research enterprise are of little help to decision makers, who will often then resort to decisions on the basis of ideology, of their own beliefs about what is important, or of political imperatives.

The quantities of interest for the GBD study are the underlying rates of incidence, remission, and mortality for defined causes for whole populations for a specified time period, and the assessment of these often requires synthesizing data from multiple studies or making adjustments for biases in relation to population, age groups, or time periods. A major source of uncertainty for the GBD estimates is the uncertainty associated with extrapolating from one or more subgroups to a regional population. For example, how representative of the incidence and prevalence patterns of dementia in Sub-Saharan Africa are two or three population-representative studies of rural or urban populations in specific regions of specific countries? The uncertainty associated with extrapolating from a set of studies in subpopulations to the regional population is related to potential systematic (selection) biases and is much more difficult to quantify than the uncertainty associated with stochastic variation due to sample size or measurement error.

Estimates of deaths from specific causes undergo continual revision as new data and syntheses become available, yet drawing a time cutoff is a necessary (if somewhat arbitrary) condition for preparing any volume such as this which reports comprehensive and consistent global and regional estimates of deaths and burden of disease (see also annex 6C). During 2001 WHO established the Child Health Epidemiology Reference Group (CHERG) to review and synthesise data on cause of deaths under age 5. While early CHERG results contributed substantially to the GBD analyses in this volume, much of their work became available well after the cutoff date for this publication. While CHERG has published revised estimates of the distribution of child deaths by cause (Bryce and others 2005), based on recent comprehensive reviews of epidemiological data, these analyses used cause categories not consistent with the GBD (including use of incompatible cause categories for neonatal and other child deaths), fewer cause categories than the GBD, and left study deaths assigned to ill-defined categories in the 'Other' category. Additionally, at the date of writing, the CHERG evidence has not been brought into the GBD analytic and consistency framework, involving consistent mapping to causal categories and checking of internal consistency between incidence, prevalence and mortality estimates for specific causes.

To the extent that they can be compared with the GBD 2001 estimates, the WHO/CHERG estimates at the global level are differ substantially for tetanus (46% higher), lower respiratory infections (56% higher), and are somewhat lower for measles, malaria, low birthweight and noncommunicable diseases. It is not possible at this stage, to conclude whether or how much the WHO/CHERG analyses would modify the GBD 2001 results reported in this volume, when they are properly brought into the GBD analytic framework. However, they do give some indications that new evidence is becoming available for child deaths, and that uncertainty ranges for GBD estimates of child deaths may be greater for some causes than indicated by the analyses presented in this chapter.

The 1990 GBD study and GBD 2001 were both meta-syntheses of the available data, using the best models and tools available at the time, whose primary aims were to provide a comprehensive assessment of the current burden of disease. The assessment of trends between 1990 and 2001 is a much more difficult task, as discussed in chapter 2. The comparability of best point in time estimates is difficult to assess given changes in both the availability of data and in the methods used to synthesize those data for many of the causes. Murray, Mathers, and Salomon (2003) discuss this issue in more detail and conclude that to assess change or evaluate programs, extrapolating current levels of burden of disease from past measurements is inadequate, and that the assessment must include measurements carried out at both points in time or explicit measurement of the relevant trends or rates of change.

CONCLUSIONS

The 2001 GBD study uses a summary measure of population health, the DALY, that explicitly incorporates several important social values. This has the advantage that the effects of changing preferences can be readily explored through sensitivity analysis, as illustrated in this chapter. Another advantage of the burden of disease approach is that it entails a data audit, whereby the completeness, reliability, and consistency of routinely collected data are assessed and critical gaps in health data collection are identified. One implication is that periodic quality assessments of, say, routine cause of death data are needed to ensure their continued relevance and reliability for public policy (Mathers and others 2005). Another is the need for a more rational assessment of priority data for the health care sector that places greater emphasis on data collection and data linkage to facilitate burden of disease studies rather than on routine collection of statistics of limited relevance to public health. The burden of disease framework, based on the estimated distribution and duration of health states resulting from incident cases, would benefit greatly from wider availability of linked data sets on health outcomes and further longitudinal

research into health state transition probabilities following on from specific disease or injury causes (Kelman and Bass 2002).

A major advance with GBD 2001 has been the systematic, though as yet incomplete, attempt to quantify uncertainty in both national and global assessments of the disease burden. This uncertainty must be taken into account when making cross-national comparisons, and needs to be carefully communicated and interpreted by epidemiologists and policy makers alike. Estimates of mortality in countries without functioning vital registration systems for causes of death will always be substantially more uncertain than those derived from systems where all deaths are registered and medically certified. The same may be said for the quantification of disability due to various conditions, where the gaps in data availability across countries are likely to be even more extreme than for mortality.

Despite the progress of the past decade, the incremental gains in advancing knowledge and understanding of global descriptive epidemiology have been modest. A globally coordinated research and development effort is urgently needed to devise and implement cost-effective approaches to data collection and analysis in poor countries that are targeted to their health development needs, and that can routinely yield comparable information of sufficient quality to establish how the disease and risk factor burden is changing in populations (Murray, Lopez, and Wibulpolprasert 2004).

Much can be learned about the health of populations from relatively modest investments in sample registration systems, provided these are designed to reliably measure the causes of death in sample areas and have sufficient resources to do so. China's Disease Surveillance Points system is a good example of what can be done to improve knowledge about disease and injury control priorities in low-income countries at a modest cost (Lopez 1998; Yang and others 2005). Greater investments in getting the descriptive epidemiology of diseases and injuries correct in poor countries will do vastly more to reduce uncertainty in disease burden assessments than philosophical debate about the appropriateness of social value choices. Just as the production of global and regional estimates should not create the impression that the descriptive epidemiology of disease and injury is reliably known, so the uncertainties around these estimates must not create the impression that not enough is known reliably enough to usefully inform health priorities and programs. Health intelligence is an essential ingredient of the health development process. Those engaged in collecting, analyzing, and disseminating population health information have a responsibility to develop this evidence base using novel methods that communicate what we do know, as well, if not more convincingly, than what we do not know.

Information for policy purposes will never be perfect, but good policy makers will want to benefit from all available information to guide priority setting and action. We might well take solace in the comments of a prominent medical statistician who once cautioned that "Making the best the enemy of the good is a sure way to hinder any statistical progress. The scientific purist who will wait for medical statistics until they are nosologically exact is no wiser than Horace's rustic waiting for the river to flow away" (Greenwood 1948, p. 28).

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