

NATIONAL BURDEN OF DISEASE STUDIES: A PRACTICAL GUIDE

Edition 2.0

October 2001



World Health Organization
Global Program on Evidence for Health Policy
WHO, Geneva

ACKNOWLEDGEMENTS

This Manual was prepared by an editorial team comprising Colin Mathers, Theo Vos, Alan Lopez, Josh Salomon, and Majid Ezzati.

In preparing this manual, we drew on the experience and publications of the Global Burden of Disease Study, of various national burden of disease studies, and on teaching materials prepared for burden of disease training workshops. Chapter 7 draws heavily on guidelines for epidemiological reviews prepared by Edouardo Sabaté. We thank the many people who have contributed to these, but particularly Chris Murray, who has played a leading role in the development and promotion of burden of disease analysis and methodology and Rafael Lozano who contributed substantially to the Global Burden of Disease project at WHO over the last two years.

We also thank Jan Barendregt for development and documentation of the DISMOD II software program, and Abhaya Indrayan for his useful inputs and collaboration in preparation of this manual.

Suggested citation

Mathers CD, Vos T, Lopez AD, Salomon J, Ezzati M (ed.) 2001. National Burden of Disease Studies: A Practical Guide. Edition 2.0. Global Program on Evidence for Health Policy. Geneva: World Health Organization.

CONTENTS

1. INTRODUCTION.....	1
2. SUMMARY MEASURES OF POPULATION HEALTH	5
3. DISABILITY-ADJUSTED LIFE YEARS (DALYS)	9
4. PLANNING A NATIONAL BURDEN OF DISEASE STUDY.....	16
5. ESTIMATING MORTALITY BY AGE AND SEX AND CALCULATING A LIFE TABLE	24
6. ESTIMATING CAUSES OF DEATH	40
7. EPIDEMIOLOGICAL ESTIMATES – GENERAL APPROACH.....	51
8. DISEASE MODELLING USING DISMOD.....	64
9. HEALTH STATE VALUATION.....	80
10. SPECIFIC APPROACHES TO THE CALCULATION OF YLD.....	87
11. CALCULATING DALYS	111
12. CALCULATING HEALTHY LIFE EXPECTANCY	116
13. COMPARATIVE RISK ASSESSMENT.....	120
14. PROJECTIONS.....	131
15. PRESENTATION AND DISSEMINATION OF RESULTS.....	134

1. INTRODUCTION

1.1 PURPOSE OF THIS MANUAL

The purpose of this manual is to provide clear practical advice to people undertaking national or sub-national burden of disease studies using the methods developed for the Global Burden of Disease (GBD) Study (Murray and Lopez 1996a). This manual is not intended to provide detailed conceptual or theoretical background to the development of the measures of population health used in burden of disease analyses, such as DALYs or the rationale for burden of disease studies. For such material, you should refer to the GBD publications, and other published papers on burden of disease analysis (see Section 1.5 below for references and information on where to obtain this material).

1.2 BACKGROUND

Precise information about diseases and injuries, their incidences, their consequence, their causation and their trend is more than ever necessary to inform policy-making. In a context where increasingly vocal and well informed people demand more health services and interventions than available resources can finance, decision-makers at all levels are increasingly required to evaluate the impact of health policies, to justify the adoption of new ones and to ensure that information is available for inter-programme comparisons.

In 1993 the Harvard School of Public Health in collaboration with The World Bank and WHO assessed the global burden of disease. Aside from generating the most comprehensive and consistent set of estimates of mortality and morbidity by age, sex and region ever produced, GBD also introduced a new metric – disability adjusted life year (DALY) – to quantify the burden of disease. The use of DALY allows researchers to combine in a single indicator years of life lost from premature death and years of life lived with disabilities.

In recent years, considerable international effort has been put into the development of summary measures of population health that combine information on mortality and non-fatal health outcomes into a International policy interest in such indicators is increasing.

The World Health Organization is now undertaking a new assessment of the GBD for the year 2000.

The specific objectives of GBD2000 are:

- to quantify the burden of premature mortality and disability by age, sex, and region for 135 major causes or groups of causes;
- to analyze the contribution to this burden of selected risk factors using a comparable framework; and
- to develop various projection scenarios of the burden of disease over the next 30 years.

At the same time, WHO member States are increasingly requesting technical assistance and support to undertake country-level burden of disease measurement. Over 30 countries are in various stages of undertaking these assessments and WHO support to these efforts not only ensures better data for planning but also enables further development and testing of tools to facilitate burden of disease assessments. This iterative process builds a partnership between WHO and Member States, laying the groundwork for tackling the bigger challenge of integrating burden of disease data into country-level programming and health system performance assessment. In addition, this partnership contributes towards the ongoing updating of the 1990 estimates of the global and regional burden of disease to year 2000 estimates.

1.3 NATIONAL STUDIES CARRIED OUT TO DATE

With the publication of the original GBD Study in 1993-1996, there was immediate interest in applying the methods in countries. Since 1993, when the study in Andhra Pradesh in India started 35 national burden of disease (NBD) studies have been undertaken. Some have been completed and others are still in progress.

Although the majority have followed the essential principles and methodology initially proposed by Murray and Lopez (1996), they are not totally comparable to each other, because some have important modifications to the original procedures. For example, taking into account the valuation of health states as a criterion for classification of the studies, a first generation of NBD studies can be defined as those which used the map of disabilities published in the original version (Lozano et al 1994, 1995, Fundacion Mexicana Para La Salud 1995, Republica de Colombia Ministerio de Salud 1994, Concha et al 1996, Vos et al 1995). Another group of countries have validated the procedures followed at the international level by undertaking local valuations of health states. Yet another group of studies has developed their own procedures for health valuations (Ruwaard and Kramers 1998, Mathers et al 1999).

NBD studies have been undertaken primarily by Ministries of Health (planning or epidemiology departments) or by universities. Some of them have been financed by international agencies like the World Bank and others with local funding. These studies have proved to be of considerable usefulness in guiding health sector reform and for priority setting in countries.

1.4 ORGANIZATION OF CONTENTS

The content of this Manual has been organized to reflect as far as possible the sequential steps which need to be followed to carry out a national burden of disease study. Chapters 2 and 3 introduce the reader to the key issues and concepts in the construction of summary measures of population health. A choice of one or more of these measures is required as the basic metric to measure disease burden. This is followed by Chapter 4 on the various elements involved in planning an NBD study, including the set of specific choices that need to be made concerning the level and detail of the analysis. Once these decisions have been made, the first step in carrying out a study is to estimate the age-sex distribution of deaths. Guidance on methods to do this is given in Chapter 5. Chapter 6 then provides details on methods and approaches to estimating causes of death by age and sex. With Chapters 5 and 6, the basic epidemiological material for estimating the premature mortality component of DALYs can be assembled.

The next section of the Manual deals with the estimation of disease burden for non-fatal outcomes. Chapter 7 outlines the principles and key data sources needed to prepare systematic reviews of the epidemiological literature in order to estimate basic input parameters for calculating DALYs. Chapter 8 provides guidance on the use of disease modeling software (DISMOD) to prepare and ensure internal epidemiological consistency of estimates of incidences, prevalence, duration and death. Once these estimates have been prepared, they need to be converted into years of life lived with disabilities by weighting periods of life lived in less than perfect health. Techniques and approaches for doing this are given in Chapter 9. Chapter 10 provides basic information for the modelling of YLD for the most common causes included in NBD studies.

The organization and calculus of converting this information into final estimates of disease burden and health expectancy are described in Chapters 11 and 12.

The final substantive section of the book provides details on the approaches and methods used to assess disease and injury burden from major risk factors (Chapter 13) and to project disease burden into the future under various assumptions (chapter 14). These chapters cover critical policy-relevant components of any burden of disease assessment.

Finally, suggestions for the dissemination and use of the results of NBD studies for maximum policy effectiveness are given in Chapter 15.

1.5 OTHER RESOURCES AND REFERENCE MATERIAL

(a) *Global Burden of Disease publications*

The methods and results of the GBD study have been published in 3 volumes to date. The first volume (Murray and Lopez 1996a) describes methods and main results. The second volume (Murray and Lopez 1996b) documents the estimates of incidence, prevalence, duration and mortality for the various causes and sequela for each of 8 regions of the world. Volume 3 (Murray and Lopez 1998) documents the methods and data used to estimate the global burden of maternal, perinatal and congenital causes in 1990.

It is planned to release subsequent volumes documenting the methods and data used for the GBD 2000 study for communicable diseases, non-communicable diseases, mental health and injury.

The results of the GBD 1990 study have also been published in a number of journal articles (Murray and Lopez 1996c, 1997a, 1997b, 1997c, 1997d). A number of papers have also critically discussed the DALY methodology (Anand and Hansen 1997, Murray and Acharya 1997, Williams 1999, Murray and Lopez 2000).

Version 1.0 draft results of the GBD 2000 project are available on the WHO website at <http://www.who.int/evidence>. An accompanying Discussion Paper (Murray et al. 2001) gives details of analysis categories, principles, and summary results.

A book will be published by WHO at the beginning of 2002 on the conceptual, ethical and methodological issues underlying the development of summary measures of population health (Murray et al 2002).

(b) *Burden of Disease training*

WHO and the Harvard Burden of Disease Unit run an annual training workshop on burden of disease analysis (one week), cost-effectiveness analysis (one week) and health system performance analysis (one week) usually in September or October. Details of the next training workshop can be found on the Harvard website at <http://www.hsph.harvard.edu/organizations/bdu>

(c) *National Burden of Disease studies*

The Australian burden of disease studies completed in 1999 (Mathers et al 1999, Department of Human Services 1999a,b) have published detailed reports on the methods used and the results obtained. They have also made available the complete set of disease worksheets on the worldwide web. Examination of these worksheets will provide a useful introduction to the range of disease models and the types of data that are used in burden of disease analysis.

The Australian Burden of Disease Study reports are available at:
<http://www.aihw.gov.au/publications/health/bdia/index.html>

The Victorian Burden of Disease Study reports and the disease worksheets are available at:
http://www.dhs.vic.gov.au/phd/_9909065/index.htm

The US Burden of Disease Study has published one report already (Murray et al 1998) and the final report will be available in 2001.

(d) *Software*

DISMOD I. May be downloaded from Harvard Burden of Disease Unit website at <http://www.hsph.harvard.edu/organizations/bdu/dismod/index.html>

DISMOD II May be downloaded from the WHO website at <http://www.who.int/evidence>
(select the link to burden of disease, and follow links to DISMOD II)Life tables

WHO has constructed life tables for the year 2000 for all 191 Member States. These life tables will be made available on the WHO website <http://www.who.int/evidence> and may provide a useful starting point for countries without good mortality registration data for estimating total mortality by age and sex.

REFERENCES

- Anand S. Hanson K. (1997). Disability-Adjusted Life Years: A Critical Review. *Journal of Health Economics* 16(6): 685-702.
- Concha M, Aguilera, X, Albala C, et al (1996). Estudio ecarga de enfermedad informe final. Estudio Prioridades de Inversio en salud Minsterio de Salud.

- Department of Human Services (DHS) (1999a). The Victorian Burden of Disease Study: Mortality. Melbourne: Public Health and Development Division, Department of Human Services.
- Department of Human Services (DHS) (1999b). The Victorian Burden of Disease Study: Disability. Melbourne: Public Health and Development Division, Department of Human Services.
- Fundación Mexicana Para La Salud (1995). Health and the Economy: Proposals for Progress in the Mexican Health System. Mexico, Salud.
- Lozano R, Frenk J, Gonzalez MA (1994). El peso de la enfermedad en adultos mayores, Mexico 1994. *Salud Publica de Mexico*, 38: 419-429.
- Lozano R, Murray CJL, Frenk J, and Bobadilla J (1995). Burden of Disease Assessment and Health System Reform: Results of a study in Mexico. *Journal for International Development*, 7(3): 555-564.
- Mathers C, Vos T, Stevenson C (1999). The burden of disease and injury in Australia. Australian Institute of Health and Welfare, Canberra: AIHW. Also available on the worldwide web at www.aihw.gov.au.
- Murray CJL, Lopez, AD, eds. (1996a). The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020. *Global Burden of disease and Injury Series, Vol. 1*. Cambridge: Harvard University Press; 1996.
- Murray CJL, and Lopez A (1996b). *Global Health Statistics*. Cambridge, Harvard University Press (*Global Burden of disease and Injury Series, Vol. 2*).
- Murray CJL, and Lopez A (1996c). Evidence-based health policy—lessons from the Global Burden of Disease Study. *Science*, 274:740-743.
- Murray CJL, and Lopez A (1997a). Mortality by cause for eight regions of the world: Global Burden of Disease Study. *Lancet*, 349: 1269-1276.
- Murray CJL, and Lopez A (1997b). Regional patterns of disability-free life expectancy and disability-adjusted life expectancy: Global Burden of Disease Study. *Lancet*, 349: 1347
- Murray CJL, and Lopez A (1997c). Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. *Lancet*, 349: 1436-1442.
- Murray CJL, and Lopez A (1997d). Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. *Lancet*, 349: 1498-1504.
- Murray CJL, Acharya AK (1997). Understanding DALYs. *J Health Economics* 16: 703-730.
- Murray CJL, and Lopez A (1998). Health dimensions of sex and reproduction. Cambridge, Harvard University Press (*Global Burden of disease and Injury Series, Vol. 3*).
- Murray CJL, Michaud CM, McKenna MT, and Marks JS (1998). U. S. Patterns of Mortality by County and Race: 1965-1994. Cambridge: Harvard Center for Population and Development Studies and Centers for Disease Control, 1998.;
- Murray CJL, Lopez AD (2000). Progress and directions in refining the global burden of disease approach: response to Williams. *Health Economics* 9: 69-82.
- Murray CJL, Lopez AD, Mathers CD, Stein C (2001). *The Global Burden of Disease 2000 project: aims, methods and data sources*. Geneva, World Health Organization (GPE Discussion Paper No. 36).
- Murray CJL, Salomon J, Mathers CD, Lopez A, Lozano R (2002). Summary Measures of Population Health: concepts, ethics, measurement and applications. Geneva, World Health Organization.
- República de Colombia Ministerio de Salud (1994). La Carga de la Enfermedad en Columbia. Bogota, Ministerio de Salud, 1994.
- Ruwaard D. and Kramers PGN (1998). Public health status and forecasts. The Hague: National Institute of Public Health and Environmental Protection, 1998.
- Vos T, Timæus I, Gareeboo H, Roussety F, Huttly S, Murray C. (1995). Mauritius Health Sector Reform. National Burden of Disease Study. Final report of consultancy. London: London School of Hygiene and Tropical Medicine.
- Williams A. (1999). Calculating the global burden of disease: time for a strategic reappraisal? *Health Economics* 8:1-8.

2. SUMMARY MEASURES OF POPULATION HEALTH

2.1 OVERVIEW

Summary measures of population health are measures that combine information on mortality and non-fatal health outcomes to represent the health of a particular population as a single number (Field and Gold 1998). Why would we want a single number of this form?

The simplest and most widely used method for producing population health statistics is to aggregate data on individuals in order to generate statistics like the proportion of the population (or of a particular age–sex group) suffering from a particular health problem or in a particular health state. This approach rapidly becomes unwieldy when a number of problems are being monitored and we want to make comparisons over time, across population groups, or before and after some health intervention. We are then faced with an explosion in the numbers of statistics that must be compared. Summary measures of population health allow us to summarise all these numbers in a comprehensive and consistent manner.

Efforts to develop summary measures of population health have a long history and in the past decade, there has been a markedly increased interest in the development, calculation and use of summary measures. Their range of potential applications include:

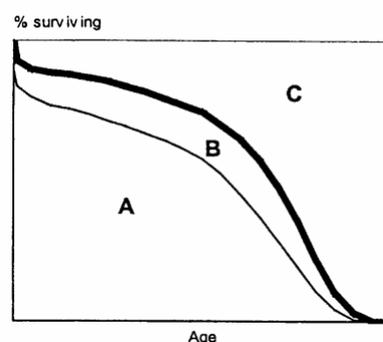
- comparison of health conditions or overall health status between two populations or the same population over time;
- quantification of health inequalities;
- inclusion of non-fatal health outcomes to ensure these receive appropriate policy attention;
- measurement of the magnitude of different health problems using a common currency;
- analysis of the benefits of health interventions for use in cost-effectiveness studies; and
- provision of information to assist in setting priorities for health planning, public health programs, research and development, and professional training (Murray, Salomon & Mathers 2000).

Two classes of summary measure have been developed: health expectancies and health gaps. Both classes of summary measure use time (lived in health states or lost through premature death) as an appropriate common metric for measuring the impact of mortality and non-fatal health outcomes.

2.2 A TYPOLOGY OF SUMMARY MEASURES OF POPULATION HEALTH

Summary measures of population health can be classified into two classes: *health expectancies* (e.g. disability-free life expectancy, disability adjusted life expectancy) and *health gaps* (disability-adjusted life years, healthy life years). These two classes of measures are complementary (see Figure 1).

Figure 1. The survivorship curve.



In the Figure, the bold line is the survivorship curve from a hypothetical life table population. The thin curve under B is a hypothetical curve of survivors to each age x in optimal health. Area A represents time lived in optimal health, area B time lived in suboptimal health, and area C represents time lost due to mortality. Total life expectancy at birth is given by the area under the bold curve:

$$LE = A + B$$

Health expectancies are population indicators that estimate the average time (in years) that a person could expect to live in a defined state of health. Examples include disability-free life expectancy (DFLE), active life expectancy and disability-adjusted life expectancy. These extend the concept of life expectancy to refer to expectations of various states of health, not just of life per se. In terms of Figure 1, health expectancy is given by:

$$HE = A + f(B)$$

where $f()$ is some function that assigns weights to years lived in suboptimal health (optimal health has a weight of 1).

Measures of potential years of life lost due to premature mortality have been used for many years to measure the mortality burden of various causes of death. These all measure the gap in years between age at death and some arbitrary standard (typically 65 years or 75 years).

Health gaps measure the difference between actual population health and some specified norm or goal.

$$\text{Health gap} = C + g(B)$$

where $g()$ is some function that assigns weights to health states lived during time B, but where a weight of 1 equates to time lived in a health state equivalent to death.

Time-based health gaps measures offer the possibility of using a common metric for population health and for the outcomes of interest in randomized control trials, in cohort studies and in some health services administrative datasets. A common metric is the key to linking economic evaluations of interventions, monitoring of health system outcomes, and the overall health burden of diseases, injuries and health determinants in the population.

2.3 HEALTH EXPECTANCIES AND HEALTHY LIFE EXPECTANCY

As a summary measure of the burden of disability from all causes in a population, healthy life expectancy (health-adjusted life expectancy – HALE) has two advantages over other summary measures. The first is that it is relatively easy to explain the concept of an equivalent “healthy” life expectancy to a non-technical audience. The second is that HALE is measured in units (expected years of life) that are meaningful to and within the common experience of non-technical audiences (unlike other indicators such as mortality rates or incidence rates).

During the 1990s, Disability-Free Life Expectancy (DFLE) and related measures were calculated for many countries (Mathers 2001, Robine et al 1999). However, these measures incorporate a dichotomous weighting scheme in which time spent in any health state categorized as disabled is assigned arbitrarily a weight of zero (equivalent to death). Thus, DFLE is not sensitive to differences in the severity distribution of disability in populations. In contrast, DALE adds up expectation of life for different health states with adjustment for severity weights. DALE has been calculated in the GBD for eight regions of the world and for 191 WHO Member States (WHO 2000, Mathers et al 2000), HALE has been calculated for 191 WHO Member States for the year 2000 (WHO 2001), for Canada based on population prevalence data for health states together with measured utility weights (Wolfson 1996) and for Australia using prevalence data from the Australian Burden of Disease Study and preference weights based on the GBD valuation methods (Mathers, Vos and Stevenson 1999). Burden of disease and DALE estimates have been made for 78 Local Government Areas in Victoria, Australia: the results are available at <http://hn01.dhs.vic.gov.au/bodw>

Chapter 12 gives guidelines for calculating healthy life expectancy in national burden of disease studies.

2.4 HEALTH GAPS

Following the pioneering work of Dempsey (1947), various measures of years of life lost due to premature mortality have been proposed. All are examples of “mortality gaps”, or the area labeled C in Figure 1. Health gaps extend the notion of mortality gaps to include time lived in states of suboptimal health (i.e. part of area B in Figure 1).

The principle characteristic defining a health gap measure is the population norm (age) chosen to define the period before which death or disability is considered premature. For some types of health gap measures, the implied target age may change as the mortality level changes, a highly undesirable property for comparisons.

Methods for defining health states and for eliciting health state valuations, as well as the incorporation of other social values also affect the calculation and interpretation of health gaps, as for health expectancies.

The following chapter describes the characteristics of the disability-adjusted life year (DALY), the best known of the health gaps, developed for use in burden of disease studies by Murray and Lopez (1996).

2.5 RELATING SUMMARY MEASURES TO CAUSES

One fundamental goal in constructing summary measures is to identify the relative magnitude of different health problems, including diseases, injuries and risk factors. There are two dominant traditions in widespread use for causal attribution: categorical attribution and counterfactual analysis.

In *categorical attribution*, an event such as death is attributed to a single cause according to a defined set of rules. Such rules inevitably involve grey areas and degrees of arbitrariness in dealing with multicausality and comorbidity.

In *counterfactual analysis*, the contribution of a disease, injury or risk factor is estimated by comparing the current and future levels of a summary measure with the levels that would be expected under some alternative hypothetical scenario. For example, we could ask what the burden of disease would be if no one in the Australian population had ever smoked. By comparing this estimate with the actual current burden, we can estimate the attributable burden of tobacco smoking.

Health gap measures use categorical attribution to attribute the fatal and non-fatal burden of diseases and injuries to an exhaustive and mutually exclusive set of disease and injury categories. They generally use counterfactual analysis to attribute the burden of disease to health determinants and risk factors.

Health expectancy measures do not naturally lend themselves to disaggregation by categorically defined causes. Instead, counterfactual methods, such as “disease elimination”, are required to quantify the contribution of disease causes to overall health expectancy measure, as well as for dealing with risk factors.

Counterfactual analysis of the disease burden associated with risk factors for national burden of disease studies is described in Chapter 14.

REFERENCES

- Dempsey M (1947). Decline in tuberculosis: the death rate fails to tell the entire story. *American Review of Tuberculosis*, 56: 157-164.
- Field MJ, Gold GM, eds. (1998). Summarizing population health: Directions for the development and application of population metrics. Institute of Medicine, Washington, D.C.: National Academy Press.
- Mathers C, Vos T, Stevenson C (1999). The burden of disease and injury in Australia. Australian Institute of Health and Welfare, Canberra: AIHW. Also available on the worldwide web at www.aihw.gov.au.
- Mathers CD, Sadana R, Salomon JA, Murray CJL, Lopez AD. *Healthy life expectancy in 191 countries, 1999. Lancet*, 2001, 357(9269): 1685-1691.

2 SUMMARY MEASURES OF POPULATION HEALTH

- Mathers CD (2002). Health expectancies: an overview and critical appraisal. In: Murray CJL, Salomon J, Mathers CD, Lopez A, Lozano R (2002). *Summary Measures of Population Health: concepts, ethics, measurement and applications*. Geneva, World Health Organization (in press).
- Murray CJL, Lopez, AD, eds (1996). *The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020*. Global Burden of disease and Injury Series, Vol. 1. Cambridge: Harvard University Press; 1996.
- Murray CJL, Salomon JA, Mathers C (2000). *A critical examination of summary measures of population health*. *Bulletin of the World Health Organisation* 78(8): 981-994
- Robine JM, Romieu I, Cambois E (1999). Health expectancy indicators. *Bulletin of the World Health Organisation* 77(2):181-185.
- Wolfson MC (1996). Health-adjusted life expectancy. *Health Reports* 8(1): 41-45.
- World Health Organization (2000). *World Health Report 2000*. Geneva: World Health Organization. Also available on the worldwide web at www.who.int/whr.

3. DISABILITY-ADJUSTED LIFE YEARS

3.1 INTRODUCTION

The DALY is a health gap measure that combines both time lost due to premature mortality and non-fatal conditions. This measure was used in The Global Burden of Disease and Injury (GBD), a joint study between the World Bank, the World Health Organization (WHO) and Harvard School of Public Health, which began in 1988 with the objective to quantify the burden of disease and injury of human populations and define the world's main health challenges.

The GBD study had three major objectives:

- a) to facilitate the inclusion of non-fatal health outcomes in the debate on international health policy which were all too often focused on mortality in children under 5 year of age;
- b) to decouple epidemiological assessment from advocacy so that estimates of mortality and disability from a condition are developed as objectively as possible. Decision-makers at the national and international level are frequently presented evaluations of the burden of disease or injury that have been produced by groups advocating a particular policy change. What they require are independent objective evaluations; and
- c) to quantify the burden of disease using a measure that could also be used for cost-effectiveness analysis. The power of using a common metric for burden assessment and economic appraisal of intervention options warranted the difficulties of crafting a measure for both purposes.

The DALY was designed to meet these objectives. Using DALYs, the GBD was measured for 1990 and projections were developed to 2020. This measure was also used in The World Development Report: Investing in Health (World Bank 1993) in order to define priorities for investments in health.

The DALY extends the concept of potential years of life lost due to premature death (PYLL) to include equivalent years of 'healthy' life lost by virtue of being in states other than good health. DALYs for a disease or health condition are calculated as the sum of the years of life lost due to premature mortality (YLL) in the population and the equivalent 'healthy' years lost due to disability (YLD) for incident cases of the health condition:

$$\text{DALY} = \text{YLL} + \text{YLD}$$

The loss of healthy life due to non-fatal health conditions requires estimation of the incidence of the health condition (disease or injury) in the specified time period. For each new case, the number of years of healthy life lost is obtained by multiplying the average duration of the condition (to remission or death) by a severity weight that measures the loss of healthy life using an average health state weight. The DALY is described in detail in Murray and Lopez (1996).

3.2 TIME AS THE COMMON METRIC FOR DEATH AND DISABILITY

The DALY is based on the premise that the best approach for measuring the burden of disease is to use units of time. Having chosen units of time as the unit of measure, the burden of disease can still be calculated using incidence or prevalence measures. Time lost due to premature mortality is a function of the death rate and the duration of life lost due to a death at each age. Because death rates are incidence rates, there is no obvious alternative for mortality using an incidence perspective. By contrast for non-fatal health outcomes both incidence and prevalence measures have been routinely used.

There are at least two ways of measuring the aggregate time lived with a disability. One method is to take point prevalence measures of disability, adjusting for seasonal variation if present, and estimate the total time lived with the disability as prevalence *times* one year. The alternative is to measure the incidence of disabilities and the average duration of each disability. Incidence *times* duration will then provide an estimate of the total time lived with disability.

For burden of disease analysis using the DALY, an incidence perspective has been chosen for three reasons.

- a) First, the method of calculating time lived with disability is consistent with the method for calculating time lost due to premature mortality.
- b) Second, an incidence perspective is sensitive to current epidemiological trends.
- c) Third, measuring incidence or deriving it from prevalence data and information on case-fatality and remission rates imposes a level of internal consistency and discipline that would be missing if prevalence data were used uncritically.

3.3 SOCIAL VALUE CHOICES

All summary measures of population health involve explicit or implicit social value choices. In particular, the DALY measures the gap between a population's actual health status and some 'ideal' or reference status. In developing the DALY indicator, Murray and Lopez (1996) identified five value choices that should be explicitly made:

- How long 'should' people in good health expect to live?
- Is a year of healthy life gained now worth more to society than a year of healthy life gained sometime in the future, for instance in 20 years' time?
- How should we compare years of life lost through death with years lived with poor health or disability of various levels of severity?
- Are lost years of healthy life valued more at some ages than others? The GBD chose to value a year of life at young adult ages more than in old age or infancy.
- Are all people equal? Do all people lose the same amount of health through death at a given age, even if there are variations in current life expectancies between population groups?

The Global Burden of Disease Study used the same values for all regions of the world. In particular, it uses the same life expectancy 'ideal' standard for all population subgroups, whether or not their current life expectancy is lower than that of other groups, it uses the same 'disability weight' for everyone living a year in a specified health state, and it gives equal value to a year of healthy life lost at any age (equal 'age weights').

The standard social value choices for an NBD Study are described below and calculation details given in Chapter 11.

3.4 DISABILITY WEIGHTS – MAKING TIME LIVED COMPARABLE TO TIME LOST

In order to use time as a common currency for non-fatal health states and for years of life lost due to mortality, we must define, measure and numerically value time lived in non-fatal health states. The 'valuation' of time lived in non-fatal health states formalises and quantifies social preferences for different states of health as health state *weights*. Depending on how these weights are derived, they are variously referred to as disability weights, quality-adjusted life year (QALY) weights, health state valuations, health state preferences or health state utilities. Most such weights are measured as a number on a scale of 0 to 1, where 0 is assigned to a state comparable to death and 1 is assigned to a state of optimal health. Because the DALY measures loss of health, the weights are inverted for DALY calculation with 0 representing a state of optimal health (no loss) and 1 representing a state equivalent to death.

While death is not difficult to define, non-fatal health states are. Non-fatal outcomes of disease are different from each other in their impact on the individual, and the impact on the individual is mediated by contextual factors including personal characteristics and the physical and social environment. Non-fatal outcomes of disease involve multiple domains of health. Disability weights provide the means to weight and then aggregate various aspects of an individual's health such as mobility, anxiety and pain.

Methods for measuring preferences for health states are described in Chapter 9.

The disability weights used in DALY calculations quantify societal preferences for different health states. These weights do not represent the lived experience of any disability or health state, or imply any societal value of the person in a disability or health state. Rather they quantify societal preferences for health states in relation to the societal 'ideal' of optimal health.

Thus a weight for paraplegia of 0.57 does not mean that a person in this health state is 'half dead', that they experience their life as halfway between life and death, or that society values them as a person less than anyone else. It means that, on average, society judges a year with blindness (weight 0.43) to be preferable to a year with paraplegia (weight 0.57), and a year with paraplegia to be preferable to a year with unremitting unipolar major depression (weight 0.76). It also means that, on average, society would prefer a person to have a year in good health followed by death than a year with paraplegia followed by death. As well, society would prefer a person to live three years with paraplegia followed by death than have one year of good health followed by death ($3 \text{ years} \times (1-0.57) = 1.3$ 'healthy' years is greater than 1 year of good health).

3.5 CONCEPTUALISATION, MEASUREMENT AND VALUATION OF HEALTH STATES

One common approach is to describe health as a profile of levels on a series of domains. The SF-36 is an example of such an instrument, with eight domains covering self-perceived health, vitality, bodily pain, mental health, physical functioning, social functioning, and role limitations (Ware & Sherbourne 1992). SF-36 domains are scored on continuous scales from 0 to 100, resulting in a large number of potential health states. Health state profiles intended for use with health state valuations tend to use a more limited number of levels in each domain.

Ideally, any weighting exercise for use in burden of disease analysis or economic evaluation should measure preferences for clearly defined health states. The Global Burden of Disease Study 1990 asked participants in weighting exercises to make a composite judgement on the severity distribution of the condition and the preference for time spent in each severity level. This was to a large extent necessitated by the lack of population information on the severity distribution of most conditions at the global and regional level. The Netherlands has also carried out a project to measure weights for 53 diseases of public health importance using a methodology consistent with the GBD study (Stouthard et al. 1997). This study used more specific disease stages or severity levels so that judgements were not required on the distribution of disease stages or severity levels in the population. In addition, the Dutch defined each disease stage in terms of the associated average levels of disability, handicap, mental wellbeing, pain and cognitive impairment using a modified version of the EuroQol health status instrument. The Global Burden of Disease 2000 project is adopting a similar approach to health state valuation, using a standard health state description based on 7 core domains of health. This health state description is being used in a standard WHO health status survey module currently under development.

Following the GBD terminology, and consistent with the WHO International Classification of Functioning, Disability and Health (ICF), the term *disability* is used broadly in burden of disease analysis to refer to departures from optimal health in any of the important domains of health. These include mobility, self-care, participation in usual activities, pain and discomfort, anxiety and depression, and cognition and social participation.

In some contexts, the word 'healthy' is understood to mean 'absence of illness'. In the context of summary measures of population health, *health* is given a broader meaning. As well as implying absence of illness there are also no impairments or functional limitations due to previous illness or injury.

We thus refer to *disability weights* and *years lost due to disability* (YLD) as shorthand terms for health state preferences and years of healthy life lost due to time lived in states other than the reference state of optimal health, respectively. A *year of healthy life* refers to a year lived in the reference state of optimal health. Note that disability (i.e. states other than ideal health) may be short-term or long-term. A day with a common cold is a day with disability.

3.6 DISCOUNTING

The DALY measures the future stream 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 applied a

3% 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 worth 24% less than one gained now.

Discounting of future benefits is standard practice in economic analysis and there are some specific arguments for applying discounting to the DALY in measuring population health (Murray and Acharya 1997):

- to be consistent with measurement of health outcomes in cost-effectiveness analyses;
- to prevent giving excessive weight to deaths at younger ages (without age weighting and discounting, a male death at age zero results in 44% more YLL than a death at age 25 and 97% more than a death at age 40; with discounting at 3% an infant death results in only 12% and 29% more YLL than a death at age 25 and age 40, respectively); and
- the disease eradication/research paradox: assuming that investment in research or disease eradication has a non-zero chance of succeeding, then without discounting, all current expenditure should be shifted to such investment because the future stream of benefits is infinite. This is a particular case of the excessive sacrifice argument.

A number of people have argued that discounting should not be applied to future health gains or losses and discounting is rarely used by epidemiologists and demographers for summary health measures. Murray and Acharya (1997) concluded that the strongest argument for discounting is the disease eradication/research paradox and that the social discount rate should be smaller than average individual discount rates. They noted, however, that the choice of a discount rate for health benefits, even if technically desirable, may result in morally unacceptable allocations between generations. Because the discount rate issue is not easily resolved, the GBD published discounted and undiscounted estimates of the global burden.

A discount rate of 5% per annum has been standard in much health economic and other social policy analyses for many years. Environmentalists and renewable energy analysts have argued in recent decades for lower discount rates for social decisions. The World Bank Disease Control Priorities Study and the Global Burden of Disease project both used a 3% discount rate. The US Panel on Cost-Effectiveness in Health and Medicine recently recommended that a 3% real discount rate be used in health economic analyses to adjust both costs and health outcomes (Gold et al. 1996), but that the sensitivity of the results to the discount rate should be examined.

Discounting has a profound effect on the estimated size of benefits. As shown in Figure 3.1, discounting alters the value attached to death at different ages. This is described in Section 3.8.

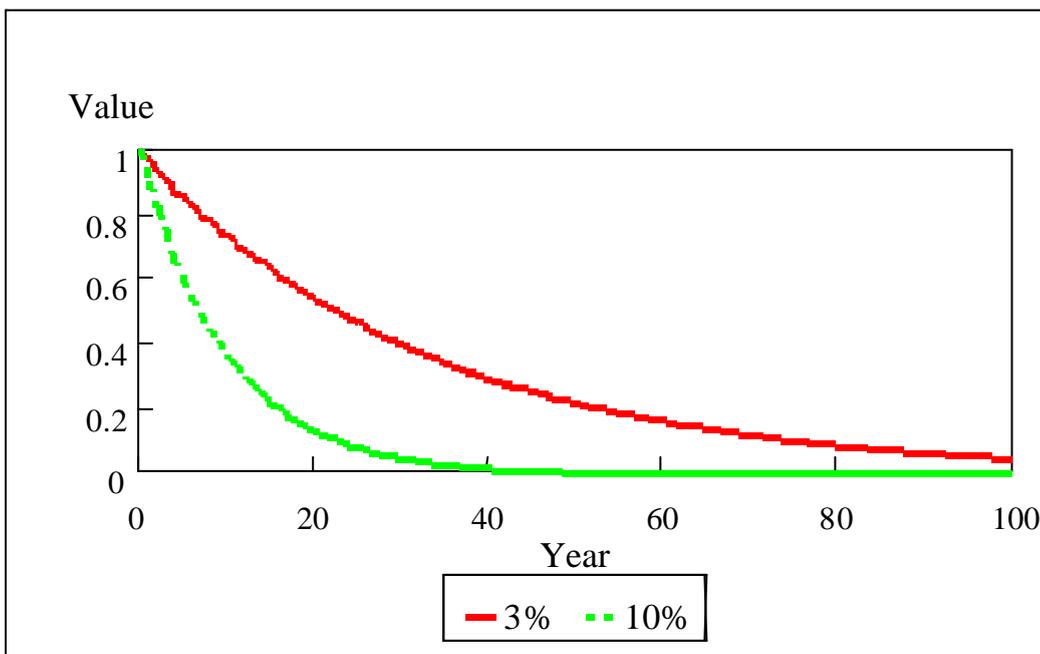


Figure 3.1 Effect of Discounting on the Value of a Year of Life Lost at Various Times in the Future.

For ease of calculation, the DALY formulae use a continuous discounting function of the form e^{-rt} where r is the discount rate and t is time. The rate (3% in this study) is not precisely the same as the annual discount rate used in the discrete form of the discount function $(1+r)^{-t}$. With a continuous discount rate of 3%, the corresponding annual discount rate is 2.96%. In order to make the discrete and continuous forms give the same result, the discount rate in the continuous form must be set equal to $\ln(1+r)$.

3.7 AGE WEIGHTING

The Global Burden of Disease Study weighted a year of healthy life lived at young ages and older ages lower than for other ages. This choice was based on a number of studies that have indicated there is a broad social preference to value a year lived by a young adult more highly than a year lived by a young child or at older ages (Murray and Lopez 1996). Not all such studies agree that young ages as well as older ages should be given less weight or on the relative magnitude of the differences.

The age weights are the most controversial value choice built into the DALY. Some find age weights unacceptable on equity grounds (every year of life is of equal value a priori), others on empirical grounds (that the standard age weights do not well reflect actual social values). Murray and Acharya (1997) have argued that age weights are not in themselves inequitable, because everyone potentially lives through every age, and that they do reflect legitimate societal priorities.

A number of studies of individual preferences for healthy life lived at different ages and the valuation derived from social roles yield a higher weight for life lived at younger adult ages as compared to younger or older ages (Murray 1996).

An exponential function can express this age-weighting:

$$Cxe^{-b \cdot x}$$

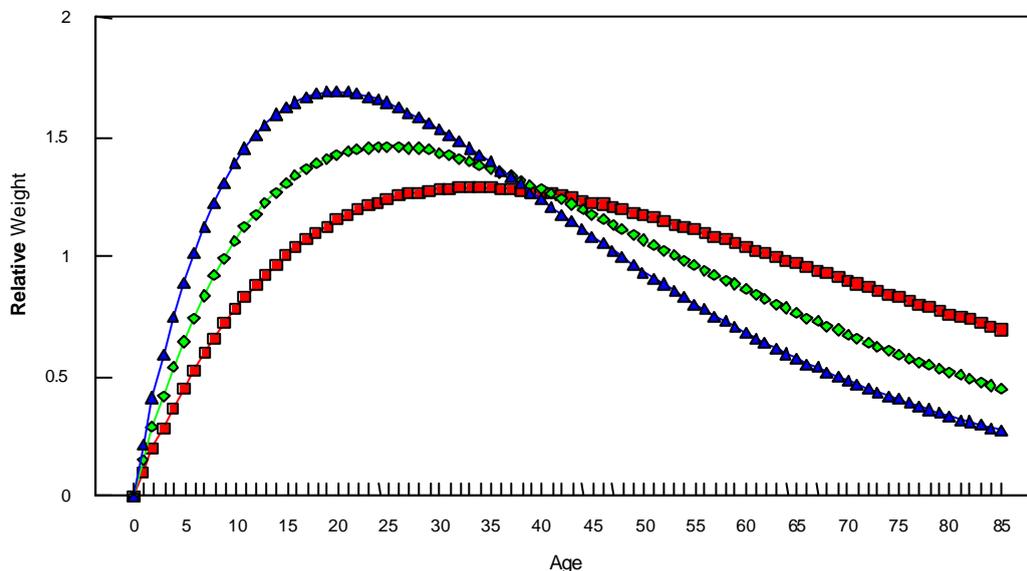


Figure 3.2 Value of a Year of Life Lived at Different Ages for Various Values of Beta

Such an exponential function captures the rising and then falling value of individual years of life lived at different ages. In the above equation, b determines the importance of age-weights and is chosen arbitrarily; C is an adjustment constant, chosen so that the introduction of age-weights does not alter the total number of years of life lost. The value of $C = 0.1658$ used in the GBD 1990 study was chosen to ensure that the total global burden with and without age weighting was the same. Clearly, if this approach is used to choose C for an NBD, then values of C will differ according to study population. It is recommended that the GBD 1990 values of $C = 0.1658$ and $b = 0.04$ be used for standard age weighting in NBDs for comparability with other studies. You are of course free to also compute burden with other age weights as relevant, and without age weighting.

3.8 ESTIMATING YEARS OF LIFE LOST DUE TO PREMATURE MORTALITY

For measuring the GBD due to premature mortality, the Standard Expected Years of Life Lost (SEYLL) method has been adopted. This uses the expectation of life at each age x based in some ideal standard to estimate the loss of years of life associated with a death. As a measure of the burden of premature mortality, SEYLL has several advantages: a) deaths at all ages contribute to the calculation of the burden of disease; and b) deaths at the same age contribute equally to the burden of disease.

To define the standard, the highest life expectancy observed for any nation (i.e. the 82.5 years life expectancy of women in Japan) was chosen. The standard expectations are therefore based on a model life table, namely Coale and Demeny West level 26, which have a life expectancy at birth for females of 82.5 years.

The male-female “biological” difference in survival potential was chosen as 2.5 years. As there is no male schedule with a life expectancy of 80 years, the standard life expectancy at birth for males of 80 years was based on the female schedule for Coale and Demeny model life table West level 25.

Figure 3.3 summarizes the contribution of deaths at each age to the burden of diseases in term of number of years of life lost. Standard life expectancy tables and methods for estimating years of life lost for average ages of death within specified study age groups are given in Chapter 11.

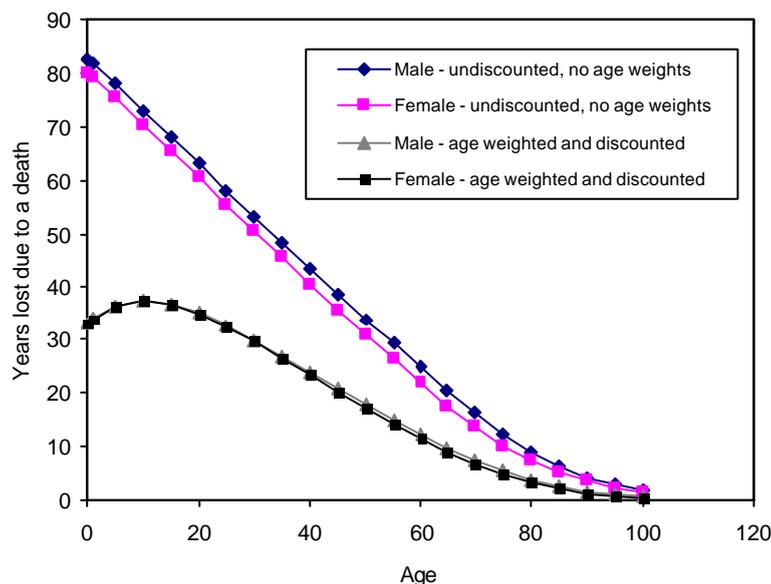


Figure 3.3 The Value of Years of Life Lost Due to a Death at Varying Ages by Sex, with and without Discounting and Age Weighting.

3.9 EPIDEMIOLOGICAL ESTIMATES FOR DISEASES

Years of Lost due to Disability (YLD) are the disability component of DALYs. Estimating YLD is the most difficult component of an NBD study. It will frequently require an in depth understanding of the epidemiology of particular diseases in order to identify alternative estimation methods and will involve the use of judgement and creativity. Various methods have been developed to reconcile often fragmented and partial estimates available from different studies. These are described in Chapters 7, 8 and 10. A specific software tool, DISMOD, was developed to ensure that the final product of this phase would be a set of internally consistent estimates (see Chapter 8).

. The data required to estimate YLD are: disability incidence, disability duration, age of onset, and distribution by severity class, all of which must be disaggregated by age and sex. These in turn require estimates of incidence, remission, case-fatality rates or relative risks, by age and sex. Data and methods useful for estimating these parameters are described in Chapters 7, 8 and 10. With zero discounting and uniform age weights, the basic formula for calculating YLD is:

$$YLD = I \times DW \times L$$

where I is the number of incident cases in the reference period, DW is the disability weight (in the range 0-1) and L is the average duration of disability (measured in years).

The full formula with non-uniform age weights and discounting is given in Chapter 11. Consistent and meaningful YLD estimates depend on a clear definition of the condition under consideration in terms of case or episode, and severity level or disease stage. It is then necessary to ensure that the disability weight and the population incidence or prevalence data relate to the same case definition. The most difficult step in estimating YLD for most diseases is matching existing population data to the disease stage or severity categories for which weights of different severity are available. Getting this wrong can result in substantial error in the YLD estimate.

REFERENCES

- Gold MR, Siegel JE, Weinstein MC, & Russell LB (1996). *Cost-effectiveness in health and medicine*. NY: Oxford University Press.
- Murray CJL, Lopez, AD, eds. (1996). *The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020*. Global Burden of disease and Injury Series, Vol. 1. Cambridge: Harvard University Press; 1996.
- Murray CJ (1996). Rethinking DALYs. In: Murray CJ, Lopez AD (ed.). *The Global Burden of Disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020*. Harvard: Harvard School of Public Health.
- Murray CJ & Acharya AK (1997). Understanding DALYs. *Journal of Health Economics*. 16:703–730.
- Stouthard M, Essink-Bot M, Bonsel G, Barendregt J & Kramers P (1997). *Disability weights for diseases in the Netherlands*. Rotterdam: Department of Public Health, Erasmus University.
- Ware JF & Sherbourne CD (1992). The MOS 36-item Short-Form Health Survey (SF-36): conceptual framework and item selection. *Medical Care* 30:473–483.
- World Bank (1993). *World Development Report 1993: investing in health*. New York: Oxford University Press.

4. PLANNING A NATIONAL BURDEN OF DISEASE STUDY

4.1 OBJECTIVES AND PURPOSES

All National Burden of Disease (NBD) studies should describe broadly the health conditions of the country using available information and justify the importance of a comprehensive assessment of the national burden of disease using summary measures that take into account both the fatal and non-fatal impacts of diseases and injuries, and of important risk factors.

Several planning and evaluation objectives are possible for an NBD study. For example, the exercise might be a baseline study to identify health needs priorities or a baseline study to monitor the future performance of the health system. The data requirements will vary depending of the objectives and the type of study. Possible specific objectives for an NBD study include:

1. To carry out a comprehensive assessment of the burden of disease, injuries and important risk factors for the population in order to
 - (a) provide a baseline for assessing improvements in health and performance of health systems; and
 - (b) provide comprehensive data on health needs to support rational resource allocation and to address inequalities in health status across subpopulations
2. To carry out cost-effectiveness studies focussing on those conditions deemed as priorities by the NBD study, in order to:
 - (a) develop alternative packages of essential health services with the potential to significantly reduce the burden of disease within available resources;
 - (b) provide objective criteria for improving the effectiveness and efficiency of the health system; and
 - (c) provide key policy makers with clear options and the implications of those options for health sector performance and affordability.
3. To establish in the country, the technical and institutional capacity to carry out NBD and cost-effectiveness studies.

In developing objectives for an NBD, it is very important to remember that the priorities for action are not a simple function of the burden of disease but also depend on the cost-effectiveness of interventions and the capacity of the system to deliver these interventions.

Other issues to consider when planning an NBD study include:

- (a) *Inclusion of all Causes*
Even when data are poor, it is better to estimate the burden of a disease than to ignore it.
- (b) *Transparency of Analysis*
Value judgments and the steps in the analysis of the burden of a disease should be transparent and reproducible.
- (c) *Judgment*
An essential part of analyzing the burden of disease is judgment. An NBD study is not a mechanical analysis according to a set of cookbook rules.
- (d) *Focus on Consequential Variables*
The focus of analytical attention should be on the assumptions and estimates that make a difference to the results.

(e) *Expanded Ownership*

Whenever possible, expand the ownership of the exercise so that, when the study is complete, there is a ready-made constituency for its results.

4.2 CHOOSING LEVELS OF ANALYSIS – AGE, SEX, CAUSES, SUB-POPULATIONS

Key components to identify are the level of analysis (regional or national); the year of reference; the age groups to be included, and the scope of study. The levels of geographic analysis are of particular importance and should at minimum include several regions. The study will be of greatest use to assist health system planning if estimates are made at regional level. Other key decisions include the set of disease and injury categories to be used, and the risk factors for which burden analyses will be conducted (the latter may not be finalised until data sources have been reviewed).

REFERENCE YEAR FOR ANALYSIS.

Choose the most recent possible reference year for analysis, even if this means estimating trends in the epidemiology of some causes from older data. You will need to assess availability of data (particularly delays in availability of death registration data) and balance this against the need for burden of disease calculations to be timely and relevant to policy.

AGE GROUPS

These could be the same as those used in the GBD (0-4, 5-14, 15-44, 45-59, 60+) or more detailed age groups such as those used for the GBD 2000 (0-4, 5-14, 15-29, 30-44, 45-59, 60-69, 70-79, 80+).

DISEASE AND INJURY CATEGORIES

These should be based on the list used for the GBD 2000 (see Table 4.1 and full definitions given in Murray et al. 2001) but reviewed to amalgamate disease categories not relevant to the country and identify any additional categories of public health importance in the country.

For the Global Burden of Disease 1990 study (GBD 1990), Murray and Lopez (1996) proposed a tree structure of causes of death. This GBD list has four levels of disaggregation and includes 108 specific diseases and injuries. At the first level, overall mortality is divided into three broad groups of causes: Group I, consisting of communicable diseases, maternal causes, conditions arising in the perinatal period and nutritional deficiencies, Group II encompassing the non-communicable diseases; and Group III, comprising intentional and unintentional injuries.

Each group has been divided into several sub-categories of disease and injury that are mutually exclusive and exhaustive. Specifically, group I has been divided into 5 sub-categories (infectious and parasitic diseases, respiratory infections, maternal causes, conditions arising in the perinatal period and nutritional causes; Non-communicable diseases (group II) have been divided in 14 sub-categories and Injuries (Group III) have been divided in unintentional and intentional injuries.

A third level of disaggregation is used to identify more specific causes of death within each of the 21 sub-categories. For example, within the category of respiratory infections, specific causes such as, upper respiratory infections, lower respiratory infections and otitis media have been identified. Finally, for some diseases, such as sexually transmitted disease, a fourth level of disaggregation is provided, in this case syphilis, chlamydia, and gonorrhoea.

The 108 diseases and injuries studied in the GBD 1990 were selected on the basis of three criteria: a) the probable magnitude of the cause of death; b) level of health services provided for the cause; and, c) the attention attracted by the cause in current health policy debate. For the Global Burden of Disease 2000 Study being carried out by WHO, the cause list has been expanded to include additional causes (see Table 4.1).

Table 4.1: GBD 2000 cause categories

GBD Cause Name	
<p>I. Communicable, maternal, perinatal and nutritional conditions</p> <p>A. Infectious and parasitic diseases</p> <ol style="list-style-type: none"> 1. Tuberculosis 2. Sexually transmitted diseases excluding HIV <ol style="list-style-type: none"> a. Syphilis b. Chlamydia c. Gonorrhoea Other STDs 3. HIV/AIDS 4. Diarrhoeal diseases 5. Childhood-cluster diseases <ol style="list-style-type: none"> a. Pertussis b. Poliomyelitis c. Diphtheria d. Measles e. Tetanus 6. Meningitis 7. Hepatitis B Hepatitis C 8. Malaria 9. Tropical-cluster diseases <ol style="list-style-type: none"> a. Trypanosomiasis b. Chagas disease c. Schistosomiasis d. Leishmaniasis e. Lymphatic filariasis f. Onchocerciasis 10. Leprosy 11. Dengue 12. Japanese encephalitis 13. Trachoma 14. Intestinal nematode infections <ol style="list-style-type: none"> a. Ascariasis b. Trichuriasis c. Hookworm disease (Ancylostomiasis and necatoriasis) Other intestinal infections Other infectious diseases <p>B. Respiratory infections</p> <ol style="list-style-type: none"> 1. Lower respiratory infections 2. Upper respiratory infections 3. Otitis media <p>C. Maternal conditions</p> <ol style="list-style-type: none"> 1. Maternal haemorrhage 2. Maternal sepsis 3. Hypertensive disorders of pregnancy 4. Obstructed labour 5. Abortion Other maternal conditions <p>D. Conditions arising during the perinatal period</p> <ol style="list-style-type: none"> 1. Low birth weight 2. Birth asphyxia and birth trauma 	<p>I. Communicable, maternal, perinatal and nutritional conditions (continued)</p> <p>E. Nutritional deficiencies</p> <ol style="list-style-type: none"> 1. Protein-energy malnutrition 2. Iodine deficiency 3. Vitamin A deficiency 4. Iron-deficiency anaemia Other nutritional disorders <p>II. Noncommunicable diseases</p> <p>A. Malignant neoplasms</p> <ol style="list-style-type: none"> 1. Mouth and oropharynx cancers 2. Oesophagus cancer 3. Stomach cancer 4. Colon and rectum cancers 5. Liver cancer 6. Pancreas cancer 7. Trachea, bronchus and lung cancers 8. Melanoma and other skin cancers 9. Breast cancer 10. Cervix uteri cancer 11. Corpus uteri cancer 12. Ovary cancer 13. Prostate cancer 14. Bladder cancer 15. Lymphomas and multiple myeloma 16. Leukaemia Other malignant neoplasms <p>B. Other neoplasms</p> <p>C. Diabetes mellitus</p> <p>D. Endocrine disorders</p> <p>E. Neuropsychiatric disorders</p> <ol style="list-style-type: none"> 1. Unipolar depressive disorders 2. Bipolar affective disorder 3. Schizophrenia 4. Epilepsy 5. Alcohol use disorders 6. Alzheimer and other dementias 7. Parkinson disease 8. Multiple sclerosis 9. Drug use disorders 10. Post-traumatic stress disorder 11. Obsessive-compulsive disorder 12. Panic disorder 13. Insomnia (primary) 14. Migraine 15. Mental Retardation attributable to lead exposure Other neuropsychiatric disorders <p>F. Sense organ diseases</p> <ol style="list-style-type: none"> 1. Glaucoma 2. Cataracts 3. Vision disorders, age-related 4. Hearing loss, adult onset

Other perinatal conditions

Other sense organ disorders

Table 4.1: GBD 2000 cause categories (continued)

GBD Cause Name	
<p>II. Noncommunicable diseases (continued)</p> <p>G. Cardiovascular diseases</p> <ol style="list-style-type: none"> 1. Rheumatic heart disease 2. Hypertensive heart disease 3. Ischaemic heart disease 4. Cerebrovascular disease 5. Inflammatory heart diseases <p>Other cardiovascular diseases</p> <p>H. Respiratory diseases</p> <ol style="list-style-type: none"> 1. Chronic obstructive pulmonary disease 2. Asthma <p>Other respiratory diseases</p> <p>I. Digestive diseases</p> <ol style="list-style-type: none"> 1. Peptic ulcer disease 2. Cirrhosis of the liver 3. Appendicitis <p>Other digestive diseases</p> <p>J. Genito-urinary diseases</p> <ol style="list-style-type: none"> 1. Nephritis and nephrosis 2. Benign prostatic hypertrophy <p>Other genitourinary system diseases</p> <p>K. Skin diseases</p> <p>L. Musculoskeletal diseases</p> <ol style="list-style-type: none"> 1. Rheumatoid arthritis 2. Osteoarthritis 3. Gout 4. Low back pain <p>Other musculoskeletal disorders</p>	<p>II. Noncommunicable diseases (continued)</p> <p>M. Congenital anomalies</p> <ol style="list-style-type: none"> 1. Abdominal wall defect 2. Anencephaly 3. Anorectal atresia 4. Cleft lip 5. Cleft palate 6. Oesophageal atresia 7. Renal agenesis 8. Down syndrome 9. Congenital heart anomalies 10. Spina bifida <p>Other Congenital anomalies</p> <p>N. Oral conditions</p> <ol style="list-style-type: none"> 1. Dental caries 2. Periodontal disease 3. Edentulism <p>Other oral diseases</p> <p>III. Injuries</p> <p>A. Unintentional injuries</p> <ol style="list-style-type: none"> 1. Road traffic accidents 2. Poisonings 3. Falls 4. Fires 5. Drownings 6. Other unintentional injuries <p>B. Intentional injuries</p> <ol style="list-style-type: none"> 1. Self-inflicted injuries 2. Violence 3. War <p>Other intentional injuries</p>

For an NBD study, it is likely that some of the causes in the GBD list are not relevant to the country, and that there are other causes of importance that should be included. Therefore to start the diseases and injuries selection process for those countries with a vital registration system, it is important to analyze the local pattern of cause of death and compile the number of death coded to each 3 digit ICD-9 code or one letter and two number ICD-10 code. For all deaths causing more than 0.1% (or some other cutoff) check to see if the code is included in one of the GBD-specific categories or is in one of the GBD residual categories. Where there are garbage codes or causes of death not in the list that are locally important, the list approach to coding may need modification. This modification of the GBD list requires careful consideration of the consequences and judgments as to the likely reason for the garbage codes

It is recommended not to have more than 12% of total deaths in the sum of the residual categories within the 21 chapters of the BoD list.

For those countries without a good vital registration system, the study team has to analyze carefully the BoD list and determine which diseases and injuries should be excluded from the list and which diseases and injuries need to be included. For this task the study team should receive help from relevant local experts.

REGIONS FOR WHICH ESTIMATES WILL BE MADE

At the minimum, estimates should be made for a set of geographical regions based on broad regional zones. In planning the NBD study, you should also assess the feasibility of using available data and synthetic estimation techniques to produce estimates of burden of disease for

- health planning regions, if relevant, and
- other population subgroups of policy importance: eg. urban/peri-urban/rural populations and possibly subgroups based on a socioeconomic variable such as education level.

For the Victorian Burden of Disease Study, separate estimates were made for each of the 78 Local Government Areas using a mixture of observed data (mortality and injuries) and predicted values of disease occurrence in small areas based on socio-economic and urban/rural distributions of state-wide data. These results can be viewed at: <http://hn01.dhs.vic.gov.au/bodw>.

4.3 CHOOSING SOCIAL VALUES

The standard DALY incorporates a number of social value choices (see Chapter 3). In planning an NBD study, you will need to decide on the following value choices:

REMAINING LIFE EXPECTANCY

Loss of healthy life at each age is usually based on the "standard" life expectancy at each age in used in the GBD 1990 (Murray and Lopez 1996). This will ensure comparability with other burden of disease studies and is recommended as the standard for reporting main results.

DISCOUNT RATE

The GBD standard of 3% for time discounting is recommended. Calculations of burden of disease should be repeated using discount rates of 0%, and 6%; the report should discuss the sensitivity of the results to the choice of discount rate.

AGE WEIGHTS

Calculations of burden of disease should be repeated using:

- (a) uniform age weights and
- (b) the standard age weights used in the gbd study The NBD Study may elect to use a third set of age weights appropriate to the national situation if desired. The report should discuss the sensitivity of the results to the choice of age weights.

DISABILITY WEIGHTS

You need to decide whether the NBD will use existing international standard weights (such as those of the GBD 1990 or GBD 2000) or will include a component on health state valuations to obtain local weights.

STANDARD VALUE CHOICES

One set of values (discount rate, age weights, remaining life expectancy) should be chosen as the standard for the main reporting and presentation of results.

4.3 OTHER ANALYSES

A set of at least 6 risk factors should be chosen for analysis based on importance in size of attributable burden and public health importance. This will need to be balanced against the availability of population data on risk factor exposure and on the relative risks associated with exposure.

In planning the NBD, you should also consider the feasibility and policy relevance of other analyses such as trend analysis and/or projections (see Chapter 14), and cost-effectiveness analyses.

4.4 STAFFING AND RESOURCING

HUMAN RESOURCES

There are different kinds of participants in the study. Three to four full time staff usually form the core team with a secretary or administrative assistant. The skills required for a NBD study include demography, epidemiology, statistics, clinical medicine, public health and economics. It is recommended to include in the core group one or two computer analysts.

In case the core team does not have enough expertise, a network of experts can be useful and the core team can call on them occasionally to provide key inputs. The balance between a core team and the input of other experts (national and international) will need to emerge based on the human resources available, the study timeline, and political concerns.

(a) Core Group

Coordinator	1
Epidemiologist	1 or 2
Public health or health economist	1
Computer analyst	1
Secretary	1

(b) Part time consultants

Demographer
Clinical specialist

(c) Experts Network for consultation

Should include demographers, clinical specialists in major diseases, epidemiologists and public health experts

PHYSICAL SPACE, ADMINISTRATIVE SUPPLIES AND COMPUTER SUPPORT

Based on the human resources requirements and the study timeline, the team ideally needs a dedicated office space, administrative supplies (telephone, fax, email) and computer support to achieve the objectives. Computer requirements include:

Hardware: 2 or 3 Pentium with at least 64 in RAM memory and 6 gigabytes in hard disk, Laser printer.

Software: Microsoft Office, @Risk Uncertainty Analysis software, graphics software, DISMOD I or II, and Mortpack.

SPECIAL TRAINING FOR CORE TEAM MEMBERS

It is essential that there is a common language and minimum level of knowledge about the BoD methods among the core group participants at the beginning of the study.

In order to ensure this, a workshop should be organized to cover at least the following subjects: life table method, measures of years of life lost, measuring disability, preferences for health states, indirect methods to estimate mortality, cause of death certificates and coding, cause of death models, epidemiological description and internal consistency, attributable burden to risk factors, and projections.

The workshop should include an important component of practical exercises (life tables, DISMOD, spreadsheets for YLL and YLD calculations, etc.).

4.5 MAJOR TASKS TO BE UNDERTAKEN

These are not necessarily sequential and can run concurrently

DEMOGRAPHIC BASELINE

The demographic inputs to the study are usually required largely at the beginning. The demographic baseline must precede most of the work on the cause of death analysis and the epidemiological analysis.

The necessary baseline data are:

1. population by age, sex and geographical region, for the reference year; and
2. total mortality by age, sex and geographical region for the reference year.

Data sources for estimating child mortality include vital registration systems, sample registration systems, census or survey questions and birth histories.

Data sources for estimating adult mortality include vital registration systems, sample registration systems, census or survey questions on deaths in households during the past 12 months, census or survey questions on whether an individual's mother or father are alive, census or survey questions whether an individual's spouse is alive, census or survey questions whether a women's sister is alive.

Refer to Chapter 5 for further information.

CAUSE OF DEATH ANALYSIS

For countries with a good vital registration system, these data can be used with adjustments for incompleteness and misclassification. For countries without a good vital registration system, the following steps are recommended:

1. collation of all available data sources: health surveys, hospital discharges, medical registries, police records, etc;
2. definition of a list of diseases (number of diseases that has to be analyzed in detail); and
3. following the list of selected diseases, estimation of mortality rates by cause, age and sex

Refer to Chapter 6 for further information.

EPIDEMIOLOGICAL DESCRIPTION OF NON-FATAL OUTCOMES

The basic steps in describing the epidemiology of non-fatal health outcomes include:

- 1) systematic review of current knowledge of the selected disease and sequelae;
- 2) construction of a diagram of the natural history of the disease and sequelae;
- 3) identification of the epidemiological indicators to be estimated;
- 4) Review of the published and non-published epidemiologic data available; evaluation of the best available studies that provide information for the epidemiological indicators;
- 5) collation of all available data sources: health surveys, hospital discharges, medical registries, police records, etc.; and
- 6) creation of the first set of estimates.

Refer to Chapter 7 for further guidance.

INTERNAL CONSISTENCY OF EPIDEMIOLOGICAL ESTIMATES

- 1) using DISMOD, check of internal consistency of the first set of estimates (see Chapter 8);
- 2) expert consultation; and

- 3) production of a second set of estimates, which are internally consistent

CALCULATIONS OF YLL AND YLD

These are the components of DALYs. Calculation methods and available software are described in Chapter 11. DALYs are health gaps that summarise loss of health by cause. They incorporate social values (discount rate, age weighting) and disability weights (see Chapter 7).

CALCULATION OF OTHER SUMMARY MEASURES OF HEALTH

Chapter 12 describes how to calculate health expectancies from your DALY estimates.

COMPARATIVE RISK ASSESSMENT

- 1) Select a minimum of five risk factors for analysis
- 2) Gather information on prevalence and relative risk from local studies i.e. surveys, epidemiological studies
- 3) Search in the international literature for complementary information and relative risk data
- 4) Estimate the burden attributable to each selected risk factor

Refer to Chapter 14 for more details.

SENSITIVITY ANALYSIS

The sensitivity analysis of the final results to the social preferences used in YLL and YLD should be examined by recalculating the entire set of estimates using different values of discount rate and age weighting. Refer to Chapter 11 for a brief discussion of methods.

FINAL REPORT

Describe results and methods employed, noting the limitations of the study. Recommendations and policy implications should be included.

4.6 DISSEMINATION OF FINAL RESULTS.

This will involve careful planning to ensure maximum dissemination and understanding of results. Apart from preparation of an NBD report, there will be a need for seminars to explain findings to key government staff and health researchers and planners. Additionally, thought should be given to dissemination of results through the Internet and in electronic form.

In the interests of transparency and accountability, it is highly recommended to make YLD worksheets and documentation of disease models and assumptions publicly available. See Chapter 15 for more details.

REFERENCES

Murray CJL, Lopez, AD, eds. (1996). The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020. Global Burden of disease and Injury Series, Vol. 1. Cambridge: Harvard University Press; 1996.

5. ESTIMATING MORTALITY BY AGE AND SEX AND CALCULATING A LIFE TABLE

5.1 INTRODUCTION

The first analytical step in any burden of disease study is to estimate the age-specific death rates, by sex, for a given population for the reference year chosen for the study. This reference year should be chosen to be the most recent year for which data are available and might coincide, for example, with a census year, or a year for which extensive epidemiological and demographic data are available from other sources.

The need to reliably estimate age-specific mortality and population data cannot be overemphasized. The number of deaths, by age and sex, provides a convenient and essential “envelope” which constrains individual disease and injury estimates of deaths. The sum of deaths from all specific causes for any sex-age group must sum to the total number of deaths for that age-sex group.

From the estimated age-specific mortality rates, a life table for the population under study can be derived using standard methods described in this chapter. This life table forms the basis for the calculation of HALE (healthy life expectancy), one of the key summary measures of population health to be calculated in a Burden of Disease Study. The first part of this chapter provides practical advice on how to estimate age-specific death rates. The latter part of the chapter shows, using a detailed example, how to use these estimates to calculate a life table.

5.2 AGE-SPECIFIC DEATH RATES

A complete life table is built up from a set of age-specific death rates. It is essential that these death rates are calculated separately for males and females because there are generally substantial differences in mortality levels between the sexes.

We define the Age-Specific-Death-Rate (ASDR) at any age (x), as the number of deaths occurring in a given period (usually 1 year) at age x , divided by the size of the mid-year population at age x (taken as an estimate of the average population size exposed to risk of dying throughout the year). Algebraically, the ASDR at age x in year t is written as:

$$M_x^t = \frac{D_x^t}{P_x^t}$$

where D_x^t is the number of deaths at age x in year t

and P_x^t is the estimated population alive at age x on June 30 in year t .

A set of age-specific death rates forms the basis for the calculation of all summary indicators of the level of mortality in a population. Common measures include:

- life expectancy at birth: a non-linear function of death rates
- YLLs: sum of deaths at each age, weighted by the number of years lost due to premature mortality
- Age-standardized death rates: an artificial death rate calculated by weighting observed death rates at each age by an arbitrary "standard" population size to get the total expected number of deaths over all ages in the standard population, if it were exposed to the set of age-specific death rates. Dividing this sum by the number of people in the standard population yields the age-standardized death rate. This is called the direct age standardisation method. With the indirect age-standardisation method the mortality rates of a standard population are applied to the population figures of the country of interest to calculate the expected number of deaths if the country of interest would have had death rates similar to those of the standard population. The indirectly age-standardised mortality ratio (SMR) is calculated by dividing the observed deaths by the expected

number of deaths. These measures are used for mortality comparisons among populations with different age-structures.

The major challenge is to estimate the schedule of age-specific death rates. A step-by-step procedure is now presented according to the nature of the data source or sources available.

5.3 DATA SOURCES AND ESTIMATION APPROACHES

A. VITAL REGISTRATION

The “gold standard” data source for estimating age-specific mortality is a national vital registration system, which records all deaths occurring in the de-facto population (i.e. population actually resident in a country or area, irrespective of legal status) and issues a death certificate with accurate data on the age and sex of the deceased, as well as the underlying cause of death. By compiling this information into a table, complete data on the number of deaths by age (D_x) and sex can be obtained.

In order to convert mortality statistics into death rates, estimates of mid-year resident populations at risk are required by age (usually for five-year age groups) and sex. These estimates should be based on the latest available population census, adjusted for misreporting, with annual intercensal estimates of mid-year population based on statistics (or estimates) on births, deaths and migration, by age and sex.

Annual estimates of population age-sex composition are produced by the United Nations Population Division. If recent population estimates are not available for your population, the most recent UN estimates could be used (United Nations 2001; see also United States Bureau of the Census: International database available at <http://www.census.gov/ipc/www/idbnew.html>).

B. OTHER SOURCES

Other data collection systems have also been used successfully to compile data on the level of mortality in the absence of good vital registration systems. Modules on child and adult mortality can be added to household surveys; the data so derived can be used for estimation of mortality levels either directly or indirectly. For example, the Demographic and Health Survey programme has yielded comparable estimates of infant and child (under-five) mortality for more than 60 countries since 1985.

Data are generally collected on the number of children ever born and those still surviving, by age of mother. Indirect mortality methods can be used to estimate levels of child mortality. A complete birth history for each woman surveyed can also be asked from which child mortality can be estimated directly.

At other ages, death, particularly among adults of working age, is much rarer than among children and hence larger statistical samples are generally required. As for child mortality, levels of adult mortality can be estimated either directly from questions about deaths in the household over the past 24 months or indirectly from questions about orphanhood and the survival of siblings.

Indirect methods for estimating adult mortality are particularly prone to underestimation, frequently by as much as 50% to 60%. Great care is, therefore, needed in interpreting estimates of adult mortality and direct methods, with appropriate interview probes for misreporting are likely to yield more useful results.

If age-specific death rates are to be estimated from these sources, great care must be taken to ensure that the data are reasonably complete. This might involve re-sampling a subset of households or comparing rates from the surveys with levels suggested by model life tables.

In situations where vital registration cannot cover the entire population, sample registration systems or networks of disease-surveillance points have been used to collect data on defined (“catchment”) populations. Provided that these populations are chosen so as to be nationally representative and that the routine demographic and epidemiological surveillance is suitably rigorous, sample surveillance schemes can yield very useful data on age-specific death rates and causes of death. Since both deaths and population, by age and sex, are routinely reported, standard demographic techniques can be applied to adjust for underreporting of deaths (see below).

Sample-based schemes have been successfully used for demographic surveillance in India (0.6% sample) and for epidemiological surveillance in China (1% sample).

5.4 ASSESSING THE COMPLETENESS OF DEATH REPORTING

Irrespective of the source, under-reporting of deaths is unfortunately very common, particularly in developing countries. There are many reasons for this, including indifference to the need for reporting, recall lapse and dysfunctional vital registration systems.

Where vital registration or sample registration is thought to be incomplete, standard demographic techniques may be used to adjust for underreporting of deaths. These should ideally use data from two censuses not more than 10 years apart (for which five-year age detail is required) and recorded intercensal deaths (also with five-year age groups). If population data (by five-year age groups) are available for only one year, then registered deaths among adults (also by five-year age groups) can be evaluated for completeness of reporting using demographic methods.

Such estimates of completeness are then applied to all registered deaths over the age of 5 years to obtain corrected estimates of age-specific death rates.

Statistics on the number of deaths by sex and age should ALWAYS be subjected to methods to assess completeness unless there is unequivocal knowledge that the registration system is capturing all deaths.

The most common techniques for assessing the completeness of death registration are:

- 1) The Brass Growth-Balance Method
- 2) The Bennett-Horiuchi Method
- 3) The Generalized Growth-Balance Method.

Each of these techniques require data on at least one population distribution by age and sex, and registered deaths by age and sex. The Bennett-Horiuchi and Generalized Growth-Balance methods require data from two censuses (or other ways to get population estimates by age and sex) and hence may be more difficult to apply in practice. Their basic principles are the same as for the Growth-Balance method, but in addition, they assume that the intercensal growth rate (r) is not constant over all ages, but varies from age to age.

These procedures can only be applied when there are vital registration data available, which can be corrected using standard methods. In many countries this is not the case and other procedures are required to estimate a life table. Section 5.8 at the end of this Chapter describes methods for estimating age-specific mortality when vital registration data is non-existent, or too poor to adjust using standard methods.

A BRASS GROWTH-BALANCE METHOD

In 1975, William Brass proposed a method to estimate the completeness of adult death registration based on the "balancing" equation:

$$\frac{N(x)}{N(x+)} = r + \frac{D(x+)}{N(x+)}$$

This is of the form: Birth rate - Death rate = Population Growth Rate (r)

What is needed to apply the method? You will need the number of deaths registered by age in any year or period of years (i.e. 1991-95), as well as the mid-year population size by age. In both cases, 5-year age groups are sufficient.

What will the method do? The method yields an average estimate of the extent of under-reporting of deaths above age 5. Separate calculations should be made for males and females as under-reporting is generally different for the sexes. The method does NOT yield useful information on the under-reporting of child deaths.

The steps in the application of the method are illustrated in Tables 5.1 and 5.2 for the case of El Salvador in 1961.

Table 5.1 Female Deaths and Population, El Salvador, 1961

Age X (1)	Registered Female Deaths ${}_5D_x$ (2)	Reported Female Population ${}_5N_x$ (3)
0	6,909	214,089
5	610	190,234
10	214	149,538
15	266	125,040
20	291	113,490
25	271	91,663
30	315	77,711
35	349	72,936
40	338	56,942
45	357	46,205
50	385	38,616
55	387	26,154
60	647	29,273
65	449	14,964
70	504	11,205
75+	1360 ^a	16,193 ^a
Total	13,652	1,274,253

a For the open interval 75+

Source: United Nations, 1983

Table 5.2 Application of Brass Growth-Balance Method, El Salvador, Females, 1961

Age X (1)	Population at exact age x N(x) (2)	Population Aged x and over N(x+) (3)	Reported Deaths over Age x D(x+) (4)	Partial Death rate D(x+)/N(x+) (5)	Partial birth rate N(x)/N(x+) (6)
5	40 432.3	1 060 164	6 743	0.0064	0.0381
10	33 977.2	869 930	6 133	0.0070	0.0391
15	27 457.8	720 392	5 919	0.0082	0.0381
20	23 853.0	595 352	5 653	0.0095	0.0401
25	20 515.3	481 862	5 362	0.0111	0.0426
30	16 937.4	390 199	5 091	0.0130	0.0434
35	15 064.7	312 488	4 776	0.0153	0.0482
40	12 987.8	239 552	4 427	0.0185	0.0542
45	10 314.7	182 610	4 089	0.0224	0.0565
50	8 482.1	136 405	3 732	0.0274	0.0622
55	6 477.0	97 789	3 347	0.0342	0.0662
60	5 542.7	71 635	2 960	0.0413	0.0774
65	4 423.7	42 362	2 313	0.0546	0.1044
70	2 616.9	27 398	1 864	0.0680	0.0955

Source: United Nations, 1983

Step 1: From these data, we first need to calculate the population at each exact age x . This is called $N(x)$. We do this by adding the numbers alive in the two 5-year age intervals around the exact age, and divide by 10. For example, to get the population size at age 20 (ie. $N(20)$), we have

$$N(20) = ({}_5N_{15} + {}_5N_{20})/10 = (125,040+113,490)/10 = 23,853$$

These estimates of population at each age x are shown in column 2 of Table 5.2.

Step 2: Next, calculate the population at each age x , and above. Call this $N(x+)$. In other words, calculate $N(5+) =$ population aged 5 and over, i.e. Pop. (5–9) + Pop (10–14) + ...; $N(10+) =$ population aged 10 and over, etc.

In our example, the population alive above age 60 would be

$$N(60+) = 29,273+14,964+11,205+16,193 = 71,635$$

Step 3: Do exactly the same calculation for registered deaths aged x , and over. Call this $D(x+)$. So we calculate:

$D(5+) =$ deaths at ages 5 and over, i.e. deaths aged 5–9 + deaths aged 10–14 + ...

$D(10+) =$ deaths aged 10-14 + deaths aged 15-19+.....,etc.

Step 4: Calculate, for each age 5, 10, 15, 20, ... the following ratios.

$$\frac{D(x+)}{N(x+)} \text{ and } \frac{N(x)}{N(x+)}$$

In other words, you need to calculate:

$$\frac{D(5+)}{N(5+)}, \frac{N(5)}{N(5+)} \text{ and so on.}$$

For convenience, label each of these calculated pairs as: X_i, Y_i ,

where $X_i = \frac{D(i+)}{N(i+)}$ and $Y_i = \frac{N(i)}{N(i+)}$ for $i = 5, 10, 15, 20, \dots, 70, 75, 80$.

Note: Do not worry if your data stop at 70+ or 75+. Just calculate the set of pairs (X_i, Y_i) for as many ages as possible from your data set.

Step 5: Plot the set of points (X_i, Y_i) . If your data were perfect and there was no-under-reporting, the set of points would lie on a straight line. However, this is unlikely to be the case. You can see from the plot which ages do not lie on the line. (see Figure 5.1).

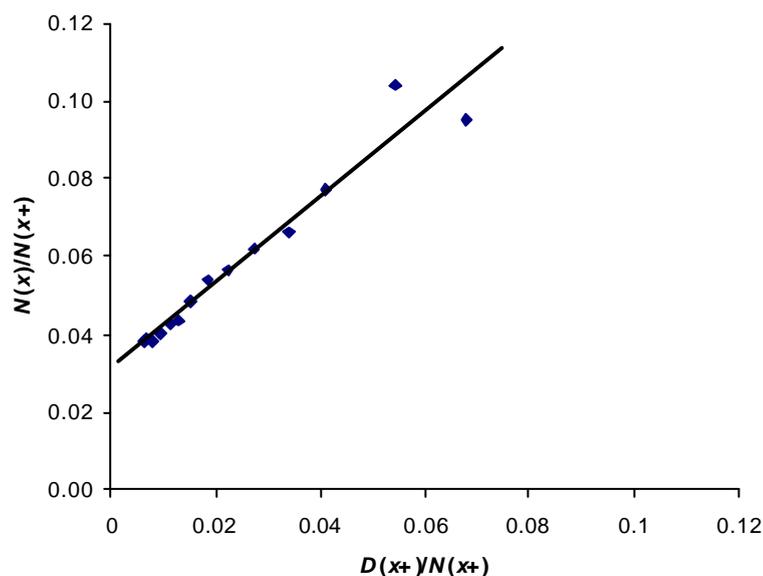


Figure 5.1 Plot of Partial Birth Rates, $N(x)/N(x+)$, Against Partial Death Rates, $D(x+)/N(x+)$, for Females, El Salvador 1961 (Source: United Nations, 1983)

We now describe a formal method to fit the line to these points.

Step 6: Group your data points (X_i, Y_i) into two subsets. Subset 1 groups together points for ages 5, 10, 15, 20, 25 and 30 (i.e. 6 points). Subset 2 groups together points for ages 35, 40, ..., 60. Calculate X_1, Y_1 and X_2, Y_2 as the average (mean) of the points in subset 1, and subset 2, respectively. (See Table 5.3).

Table 5.3 Fitting of a Straight Line by Group Means, Females, El Salvador, 1961

Age x (1)	Partial death rate $D(x+)/N(x+)$ (2)	Partial birth rate $N(x)/N(x+)$ (3)
(a) Group 1		
5	0.0064	0.0381
10	0.0070	0.0391
15	0.0082	0.0381
20	0.0095	0.0401
25	0.0111	0.0426
30	0.0130	0.0434
TOTAL	0.0552	0.2414
MEAN	$X_1 = 0.0092$	$Y_1 = 0.0402$
(b) Group 2		
35	0.0153	0.0482
40	0.0185	0.0542
45	0.0224	0.0565
50	0.0274	0.0622
55	0.0342	0.0662
60	0.0413	0.0774
TOTAL	0.1591	0.3647
MEAN	$X_2 = 0.0265$	$Y_2 = 0.0608$

Source: United Nations, 1983

Step 7: Calculate $K = \frac{Y_2 - Y_1}{X_2 - X_1}$

K should be a number greater than 1 e.g. $K = 1.191$ in this example.

Step 8: Next, calculate $C = \frac{1}{K}$

C is the final estimate of the completeness of your death registration. It should be a number smaller than 1. In the above example, if $K = 1.191$, then $C = 0.84$. In other words, your death registration is 84% complete.

Step 9: Multiply the number of deaths at each age above 5 (D_x) by K to get the corrected (adjusted) number of deaths by age and sex for your Burden of Disease Study.

Note of caution: No data are perfect. The Growth-Balance method will help you evaluate the extent of under-reporting. However, do NOT apply the technique without very careful consideration of the data plot

under Step 5. Think carefully about the line of "best fit" to your data points. You may need to exclude more points or weight the contribution of the error term for each point differently, depending on whether you judge it to be an "outlier" or not.

An example of the application of the Brass Growth Balance method is given on the accompanying CD (or may be downloaded from the WHO website at <http://www.who.int/evidence> (select the links to burden of disease, then National Burden of Disease Manual).

B THE BENNETT-HORIUCHI METHOD

This method requires two population censuses, preferably 5 or 10 years apart, as well as registered intercensal deaths by age.

In any population, the number of persons in a particular age group, say 25-29, at a particular time t , will be equal to the total number of deaths to those persons from time t , when its members are 25-29, until the last member has died. If, therefore, only 50% of the deaths in this age group are registered, then the ratio of the total number of deaths reported to the actual population will be 0.5, the value of **completeness of registration of deaths**.

Unfortunately, using this approach one would have to wait a long time in order to obtain an estimate of completeness, since all members of an age group have to die first. Since we cannot wait, it is more practical to use the number of deaths reported for a particular year or calendar period as an estimate of future deaths that will occur after time t .

A comparison of the reported number of persons in a particular age group with the estimated total number of future deaths to that age group should provide an estimate of the completeness with which deaths are registered. The Bennett-Horiuchi procedure is based on this simple idea.

In a **stable population** (i.e. a population with constant birth and death rates), there is a precise relationship between the numbers of current *deaths* and the numbers of *persons in the population*. The persons now aged x , to whom deaths are currently occurring, are the survivors of births x years ago, which, by the properties of stable populations, must have been smaller in number than the current births by a factor of e^{-rx} . Hence, the number of deaths that will occur to the current number of births when they are aged x will be larger than the current number of deaths to persons aged x by factor of e^{-rx} .

It follows, therefore, that the number of deaths that will be experienced by persons currently age x (theoretically equal to their number) can be estimated from the current number of deaths recorded at each age above x . Specifically, if $N(x)$ is the number of persons at age x in a stable population with growth rate r , and $D(x)$ is the number of deaths at age x , then an estimate of $N(x)$, $N'(x)$ can be expressed as follows:

$$N'(x) = \sum_a^w D(a) e^{r(a-x)}$$

If the population is genuinely stable, the rate of growth is correctly specified, and deaths and population accurately reported, then $N'(x)$ will equal $N(x)$. If, however, deaths are under-reported by some fixed proportion (say 20%), $N'(x)/N(x)$ will be 0.8. This ratio is a measure of the completeness of death registration in adults.

The Bennett-Horiuchi method is actually a generalization of the Preston-Coale method in that it does not assume stable population conditions and hence allows the growth rate r to vary by age. An example of the application of the method is given on the accompanying CD (or may be downloaded from the WHO website at <http://www.who.int/evidence> (select the links to burden of disease, then National Burden of Disease Manual).

5.5 THE LIFE TABLE

The life table provides the most complete description of mortality. The basic life table is made up of a set of columns most of which can be reproduced if one or more of the other columns are known.

Life tables have several uses in demography and public health. The basic summary statistic from a life table is the expectation of life at birth for a population. This is a convenient summary index of mortality conditions prevailing in a population.

There are two principal forms of the life table:

1. The Cohort life table
2. The Period life table

The **cohort** (or **generation**) life table records the actual mortality experience of a particular group of individuals from the birth of its first member to the death of its last member. Such data are hard to come-by, hence the cohort or generation life table is of limited practical interest.

The **period** (or **current**) life table is constructed from the conditions of mortality obtaining during a single year or a given period of years using the experience of a synthetic cohort.

It thus provides a cross sectional view of the mortality and survival experience of a given population during a single year, and is therefore, a more useful tool for mortality analysis.

A second distinction is made between complete and abridged life tables. A **complete** life table is built up from data on deaths and population at each single year of age 0, 1, 2, 3, ..., 99, 100+. An **abridged** life table is based on the assumption that death rates are similar at neighbouring ages and hence uses death rates calculated from groups of ages. The most common age groupings are 0, 1-4, 5-9, ..., 95-99, 100+ but other age categories are possible (e.g. 10-year age groups).

The following Table 5.4 is a display of an abridged period life table for French males for 1996. We will use this table to illustrate the calculation of an abridged life table.

5.6 CALCULATING THE LIFE TABLE

Step 1: q_x

Complete Life Tables

The first step in calculating a life table is to convert the set of age-specific death rates (M_x) into a set of probabilities of dying at each age, or age group. The *probability* of dying between exact age x and $x+1$ is defined as:

$$q_x = \frac{\text{Deaths during the year to persons aged } x \text{ at the start of the year } (D_x)}{\text{Population aged } x \text{ at the start of the year } (N_x)}$$

In general, tabulated population figures normally relate to the mid-year rather than the start of the year, hence, q_x cannot be calculated directly. It is estimated from the **age-specific death rates** M_x which is defined as follows:

$$M_x = \frac{\text{Deaths during the year to persons aged } x (D_x)}{\text{Population aged } x \text{ at mid - year } (P_x)}$$

Table 5.4 Abridged Life Table for French Males, 1996

x	Population		Deaths									
	n	${}_n P_x$	${}_n D_x$	${}_n M_x$	a	${}_n q_x$	${}_n p_x$	l_x	${}_n d_x$	${}_n L_x$	T_x	e_x
0	1	369300	2022	0.00548	0.1	0.00545	0.99455	100,000	545	99,510	7,471,253	74.71
1	4	1462700	467	0.00032	0.4	0.00128	0.99872	99,455	127	397,516	7,371,743	74.12
5	5	1755600	306	0.00017	0.5	0.00087	0.99913	99,328	87	496,425	6,974,227	70.21
10	5	1974200	394	0.00020	0.5	0.00100	0.99900	99,242	99	495,961	6,477,802	65.27
15	5	1997800	1315	0.00066	0.5	0.00329	0.99671	99,143	326	494,899	5,981,841	60.34
20	5	2041900	2377	0.00116	0.5	0.00580	0.99420	98,817	574	492,651	5,486,942	55.53
25	5	2155700	2824	0.00131	0.5	0.00653	0.99347	98,243	641	489,614	4,994,291	50.84
30	5	2193000	3659	0.00167	0.5	0.00831	0.99169	97,602	811	485,983	4,504,677	46.15
35	5	2150700	4764	0.00222	0.5	0.01101	0.98899	96,791	1,066	481,291	4,018,693	41.52
40	5	2114300	6906	0.00327	0.5	0.01620	0.98380	95,725	1,551	474,749	3,537,403	36.95
45	5	2167100	9944	0.00459	0.5	0.02268	0.97732	94,174	2,136	465,532	3,062,654	32.52
50	5	1608000	10873	0.00676	0.5	0.03325	0.96675	92,038	3,060	452,541	2,597,122	28.22
55	5	1341000	13304	0.00992	0.5	0.04840	0.95160	88,978	4,307	434,124	2,144,581	24.10
60	5	1362300	20756	0.01524	0.5	0.07338	0.92662	84,671	6,214	407,823	1,710,456	20.20
65	5	1266000	28937	0.02286	0.5	0.10811	0.89189	78,458	8,482	371,084	1,302,634	16.60
70	5	1056300	36075	0.03415	0.5	0.15733	0.84267	69,976	11,009	322,356	931,549	13.31
75	5	651300	33265	0.05107	0.5	0.22646	0.77354	58,967	13,353	261,450	609,193	10.33
80	5	409100	37544	0.09177	0.5	0.37323	0.62677	45,613	17,024	185,505	347,743	7.62
85+	5	346500	61059	0.17622			1	0.00000	28,589	28,589	162,238	5.67

To obtain q_x , the M_x values will need to be modified slightly. Thus:

$$q_x = \frac{D_x}{N_x}$$

$$M_x = \frac{D_x}{P_x}$$

$$N_x = P_x + 0.5D_x$$

$$\therefore q_x = \frac{D_x}{P_x + 0.5D_x} = \frac{D_x / P_x}{P_x / P_x + 0.5(D_x / P_x)} = \frac{M_x}{1 + 0.5M_x}$$

The equation $N_x = P_x + 0.5D_x$ assumes that those who died in the year lived on average a fraction of the year (denoted by a_x).

In this example $a_x=0.5$, i.e. each person who died in a given year lived, on average, half a year during that year. This assumption is fairly accurate for all ages except the very young and the very old. Death among the very young tends to be concentrated in the early part of life.

We can therefore generalize the last equation to:

$$q_x = \frac{M_x}{1 + (1 - a_x)M_x}$$

The values that a_0, a_1, \dots take vary from country to country depending on the level of mortality.

For countries with very high mortality, $a_0=0.3$, $a_1=0.4$ and $a_x=0.5$ for all other ages. For low mortality countries, a value of $a_0=0.1$ is typically used since infant mortality is low and those who die in infancy tend to die mainly from perinatal causes and therefore live for relatively short periods.

As a general rule, the value of a_x chosen is not critical, except for a_0 . In our example (France) $a_0 = 0.1$. So,

$$q_0 = M_0 / (1 + 0.9M_0) = 0.00548 / (1 + 0.00493) = 0.00545.$$

Special attention must be paid to the last (open-ended) age interval. Since all those alive at the beginning of the last age interval will die eventually, q_{x+} is always equal to 1.0.

There are other approaches for adjusting M_x values to q_x values. These include the Reed-Merrell and the Greville methods (Shyrock & Siegel, 1976). These alternatives are, however, not significantly easier or better than the above method.

Abridged Life Tables

These are far more common than complete or single-year life tables. They usually begin with the intervals 0, 1-4 followed by 5 year groups: 5-9, 10-14, ..., 85+.

They are constructed in a similar manner to that for the single-year life table, but instead of q_x , ${}_nq_x$ is calculated, where n is the length of the interval, not its start.

${}_nq_x$ in life table notation, represents the probability of dying between ages x and $x + n$, and is given by

$${}_nq_x = \frac{n \cdot {}_nM_x}{1 + n \cdot (1 - {}_na_x) \cdot {}_nM_x}$$

In the example life table for French males in 1996, the probability of dying between ages 30 and 34 (i.e. dead before age 35) is

$${}_5q_{30} = \frac{5(0.00167)}{1 + 5(1 - 0.5)(0.00167)} = 0.00831$$

Normally ${}_na_x$ is defined as the proportion of the interval lived by those who died. Thus, for $n=5$, and ${}_na_x=0.5$, each person who died in the interval would have contributed $0.5 \cdot 5 = 2.5$ years. The convention is to use ${}_na_0=0.1$ in low mortality countries, and 0.3 for high mortality countries. For ${}_na_1$, use 0.4 in all cases.

The converse of ${}_nq_x$ is ${}_n p_x$. This is defined as the probability of surviving between exact age x and $x+n$:

$$\begin{aligned} {}_n p_x &= 1 - {}_n q_x \\ \therefore {}_n p_x + {}_n q_x &= 1 \end{aligned}$$

Step 2: l_x

This is one of the most useful columns in a life table and is widely used for mortality estimation methods. l_x is the number of people alive at exact age x out of some arbitrarily defined number (l_0) at birth

Unlike the other functions of the life table discussed so far, this function refers to an exact age rather than an age interval. The first value, l_0 , is an arbitrary number called the **radix** or root. It is usually a round number such as 1, or 1000, or 100,000. By definition, the following relationships hold:

$$\begin{aligned}
 l_{x+n} &= l_x \cdot {}_n p_x = l_x \cdot (1 - {}_n q_x) \\
 {}_n d_x &= l_x - l_{x+n} \\
 &= l_x \cdot {}_n q_x
 \end{aligned}$$

where ${}_n d_x$ is the number of deaths in the life table population between exact ages x and $x + n$.

We start with $l_0 = 100,000$. Then $l_1 = l_0 \cdot ({}_1 p_0)$ = number alive at exact age 1 (l_0) times the probability of surviving to exact age 1 (${}_1 p_0$) = $l_0(1 - q_0) = 100,000(1 - 0.00545) = 99,455$

Next, calculate $l_5 = l_1 \cdot ({}_4 q_1) = 99,455(1 - 0.00128) = 99,328$

Next, calculate $l_{10} = l_5(1 - {}_5 q_5) = 99,242$ and so on. Notice that l_x is a decreasing function of x , i.e. as age increases, l_x must decrease.

l_x is an **imaginary** number of survivors from an initial **1000 or 100000 imaginary births**, assuming these imaginary births were to experience the same mortality rates as those underlying the current life table.

l_x bears no relation to the **actual number** of individuals aged x to $x+n$ in the real population.

The l_x value is only meaningful when related to the original radix.

For the last (open-ended) interval, the number of persons dying is the same as the number alive at its start:

$$d_{x+} = l_x$$

For example, $d_{85+} = l_{85}$

Step 3: ${}_n L_x$

In an abridged life table, each person who remains alive throughout a specified time interval contributes n years of life (n is the length of the interval). So someone alive at age 10, who is still alive at age 15, would contribute 5 years of life to the total lived by the l_0 'births' when they pass from ages 10 to 15.

Each person who dies in an interval contributes a fraction of the interval equivalent to ${}_n a_x \cdot n$ years.

The ${}_n L_x$ function is defined as the total number of person-years lived (contributed by those alive and those who died) between exact ages x and $x+n$.

By the above definition,

$${}_n L_x = n(l_{x+n} + {}_n a_x \cdot {}_n d_x)$$

By definition

$$l_{x+n} = l_x - {}_n d_x$$

$$l_x - l_{x+n} = {}_n d_x$$

$${}_n L_x = n(l_{x+n} + {}_n a_x \cdot (l_x - l_{x+n}))$$

$$= n(l_{x+n}(1 - {}_n a_x) + {}_n a_x \cdot l_x)$$

For ${}_n a_x = 0.5$,

$${}_n L_x = n(l_{x+n}(1 - 0.5) + 0.5 \cdot l_x)$$

$$= n(0.5 \cdot l_{x+n} + 0.5 \cdot l_x)$$

$$= \frac{n(l_{x+n} + l_x)}{2}$$

In other words, ${}_nL_x$ is obtained by a simple averaging of the l_x and l_{x+n} and multiplying by the interval width, n .

$$\text{In our example, } {}_5L_{50} = \frac{5}{2}(l_{50} + l_{55}) = \frac{5}{2}(92038 + 88978) = 452,541$$

This is, therefore, a much easier formula for computational purposes.

This simplification does not however apply in the case of L_0 , and ${}_4L_1$ as ${}_na_x$ is not equal to 0.5 at these ages. These are obtained using the following formulae:

$$\begin{aligned} L_0 &= l_1 + 0.1 \cdot d_0 \\ \text{For } a_0 &= 0.1 \\ {}_4L_1 &= 4 \cdot l_5 + 4(0.4 \cdot d_1) \\ \text{For } {}_4a_1 &= 0.4 \end{aligned}$$

The open-ended interval has no defined length, hence we need an assumption regarding how many more years (on average) individuals alive at the start of the interval live for.

The following formula, involving the life table deaths (${}_nd_x$) and the observed age-specific mortality rate (${}_nM_x$), generally provides a good approximation:

$$\begin{aligned} {}_nM_x &= \frac{{}_nd_x}{{}_nL_x} = \frac{\text{Life table deaths in the interval } x \text{ to } x+n}{\text{Person - years lived between } x \text{ and } x+n} \\ \therefore {}_nL_x &= \frac{{}_nd_x}{{}_nM_x} \\ \therefore L_{85+} &= \frac{d_{85+}}{M_{85+}} = \frac{l_{85}}{M_{85+}} \\ \text{i.e., } d_{85+} &= l_{85} \text{ since everyone eventually dies.} \end{aligned}$$

$$\text{In our example, } L_{85+} = 28\,589 / 0.176 = 162\,238$$

Step 4: T_x

This represents the total number of person-years lived after age x . It is obtained by cumulating the ${}_nL_x$ function from the bottom (highest age interval) up. Symbolically,

$$\begin{aligned} \text{For any age } x : \\ T_x &= T_{x+n} + {}_nL_x \\ \text{For } x &= 80 \\ T_{80} &= T_{85} + {}_5L_{80} \\ \text{For terminal age } w \\ T_w &= L_{w+} \\ \text{For } w &= 85 \\ T_{85} &= L_{85+} \end{aligned}$$

Thus in our example, start with

$$T_{85} = L_{85+} = 162,238$$

$$T_{80} = {}_5L_{80} + T_{85} = 185,505 + 162,238 = 347,743$$

And so on, until you calculate T_0 .

Note that T_x like l_x refers to exact age x , not an age interval.

Step 5: e_x

This is defined as the expected (average) number of years of life left for a person aged x . Thus, for the l_x people alive at age x , the total number of years left for them to live is given by T_x . Therefore, on average, each of these l_x individuals has, approximately T_x/l_x years to live. Hence,

$$e_x = \frac{T_x}{l_x}$$

For example, $e_{55} = \frac{T_{55}}{l_{55}} = \frac{2,144,581}{88,978} = 24.10 \text{ years}$

The average number of years available to a new born is generally referred to as the **expectation of life at birth** and is given by the ratio:

$$e_0 = \frac{T_0}{l_0}$$

In our example, $e_0 = 7,471,253/100,000 = 74.71 \text{ years}$

5.7 INTERPRETING THE LIFE TABLE

The Static Population (Person Year) Interpretation: In this interpretation, the cohort of 1000 or 100000 babies that are assumed to be born at the same instant are gradually killed off until the last person dies. Since everyone has exactly the same birthday, the l_x column then represents the number of persons alive at any given exact age x . The ${}_nL_x$ is the number of person-years lived.

The Stationary Population (or Dynamic) Interpretation: Instead of same-instant births, this approach assumes that the $l_0=1000$ or 100,000 babies are born at a constant rate during the each year. Using this assumption, the l_x and ${}_nL_x$ columns take on a slightly different meaning. The l_x column represents the number of persons celebrating their x^{th} birthday during the year. The ${}_nL_x$ is just the population aged between x and $x+n$. The population described by the ${}_nL_x$ column is, therefore, known as the *stationary population*. It has a constant age-structure and size ($=T_0$) with l_0 babies being born every year and exactly the same number dying. In general, most models fall between these two extremes, i.e., their basis is neither purely empirical nor purely theoretical.

5.8 ESTIMATING AGE-SPECIFIC MORTALITY WHEN VITAL REGISTRATION IS NON-EXISTENT, OR TOO POOR TO ADJUST USING STANDARD METHODS

A BACKGROUND

The above procedures only apply when there are vital registration data available, which can be corrected using standard methods. In many countries this is not the case and other procedures are required to estimate a life table.

In this case, you should apply the Brass logit approach. Brass found that the logits of the survivorship column (l_x) are linearly related to each other. Hence, if one chooses a 'standard' set of survivorship values (l_x^s) from some life table, then one can obtain all l_x values for a current life table provided estimates of the parameters α and β relating the logits are available.

The survivorship proportions from *birth* to age (l_x) in two tables are linearly related by

$$\text{logit}(l_x) = a + b \text{logit}\left(\frac{l_x^s}{l_x}\right)$$

where

$$\text{logit}(l_x) = \frac{1}{2} \ln\left(\frac{1-l_x}{l_x}\right)$$

The logit transformation is simply a specific transformation of the l_x values which varies from $-\infty$ (when $l_x = 1.0$) to $+\infty$ (when $l_x = 0$), assuming l_x is expressed as a proportion, not with an initial value of 100,000. When $l_x = 0.5$, the logit transformation equals 0.

This system is quite flexible since α , β and l_x can all be varied. Thus all life tables can be generated from a "standard" life table by changing the values of α and β used. The linearity assumption may not be true in every case. Still, the approximation is close enough to warrant the use of this relation to fit observed mortality schedules.

Analyses of registered mortality data over a period of 100 years or so show that the departures from linearity increase as you move further away from the standard population, and that these departures are most evident among children and older adults.

To correct for this bias, WHO has developed a modified Brass Logit system with two additional parameters (γ and θ) which are functions of age only and not specific to any given country.

However since α and β can be derived from l_5 and l_{60} , it remains a two parameter system.

This modified Brass model is of the form:

$$\text{Logit}(l_{xij}) = a_{ij} + b_{ij}\text{Logit}(l_x^S) + g_x \left(1 - \left(\frac{\text{Logit}(l_{5ij})}{\text{Logit}(l_5^S)}\right)\right) + q_x \left(1 - \left(\frac{\text{Logit}(l_{60ij})}{\text{Logit}(l_{60}^S)}\right)\right)$$

where x is age, i is the population of interest and j is the year(s).

To facilitate global application, WHO has developed a "global" standard set of l_x values based on mortality data from over 60 countries since the early 1900s. A spreadsheet containing the current standard set of l_x values is given on the accompanying CD (or may be downloaded from the WHO website at <http://www.who.int/evidence> (select the links to burden of disease, then National Burden of Disease Manual).

Since α and β are unique functions of l_5 and l_{60} (i.e. number of individuals surviving to age 5 (l_5) or age 60 (l_{60})), and since l_x^S , θ_x and γ_x are known, the model can be used to estimate l_x for any population provided l_5 and l_{60} can be estimated from survey or census data. The WHO modified logit approach is described further in Murray et al. (2000, 2001) and Lopez et al. (2000, 2001).

B STEPS IN PRACTICAL APPLICATION OF WHO LIFE TABLE APPROACH

Step 1: Calculate, from your data, appropriately adjusted based on the methods described in this chapter, 1) ${}_5q_0$, the level of child mortality in your population; 2) ${}_{45}q_{15}$, the probability of dying between ages 15 and 60 years.

Where estimates of adult mortality are based on vital registration (i.e. civil registration of death, sample demographic surveillance systems) or recall of deaths in households in the last 12 months from censuses of surveys, they should ALWAYS be subjected to data evaluation methods outlined in this chapter, and adjusted accordingly. Where adult mortality estimates are obtained from indirect techniques (see reading list) based on questions on the survival of relatives, even greater care is required in interpreting the data due to likelihood of serious reporting errors.

Note that there are numerous data sources and estimates of child mortality (${}_5q_0$) for most countries. You should carefully screen these in order to decide upon the most appropriate level of ${}_5q_0$ for your population. This will always involve some projection of ${}_5q_0$ to the year(s) to which your NBD Study refers.

An example of this procedure is given in Figure 5.2 for Indonesia.

Step 2: Based on your estimates of child mortality (i.e. a given value of l_5) and adult mortality, search among the space of WHO life tables to obtain the best-fitting value of l_{60} . A visual representation of the life table space of 50,000 life tables is shown in Figure 5.3.

Step 3: Use these values of $l_5 = (1 - {}_5q_0)$ and l_{60} (from matching on your ${}_{45}q_{15}$) and apply to the modified Brass model to estimate the set of l_x and hence the age-specific death rates.

Note:

1. If no reliable estimate of adult mortality is available (i.e. ${}_{45}q_{15}$), the WHO models may be used to estimate l_{60} from a given value of l_5 (i.e. child mortality). If you need to do this, please contact WHO for assistance with the application of this procedure.
2. Uncertainty around the level of child mortality may be used to estimate uncertainty bounds for adult mortality. When the latter is estimated from child mortality, uncertainty intervals might be quite large.

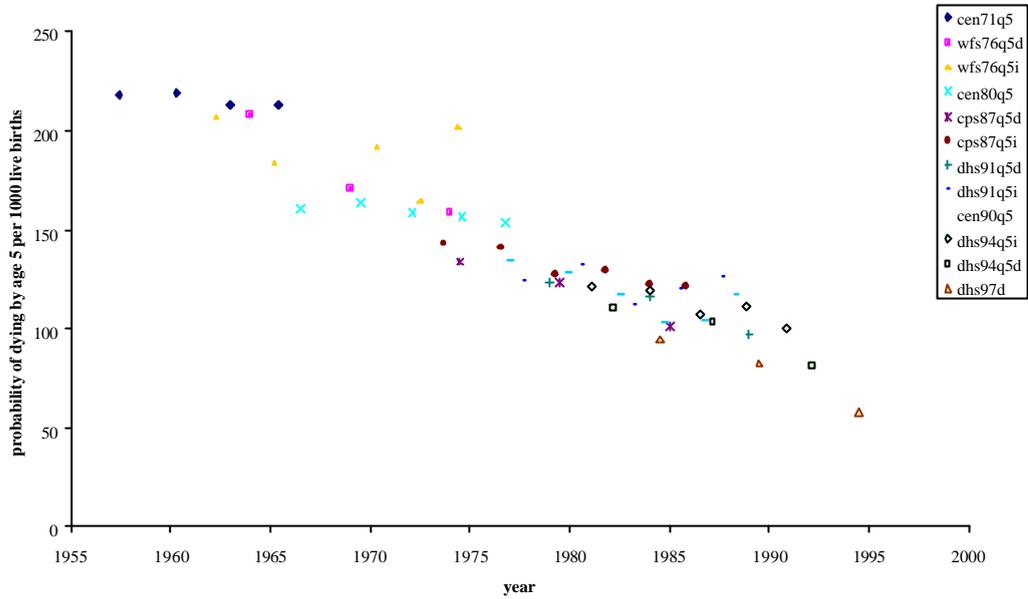


Figure 5.2 Various measurements of ${}_5q_0$, Indonesia 1955-1995.

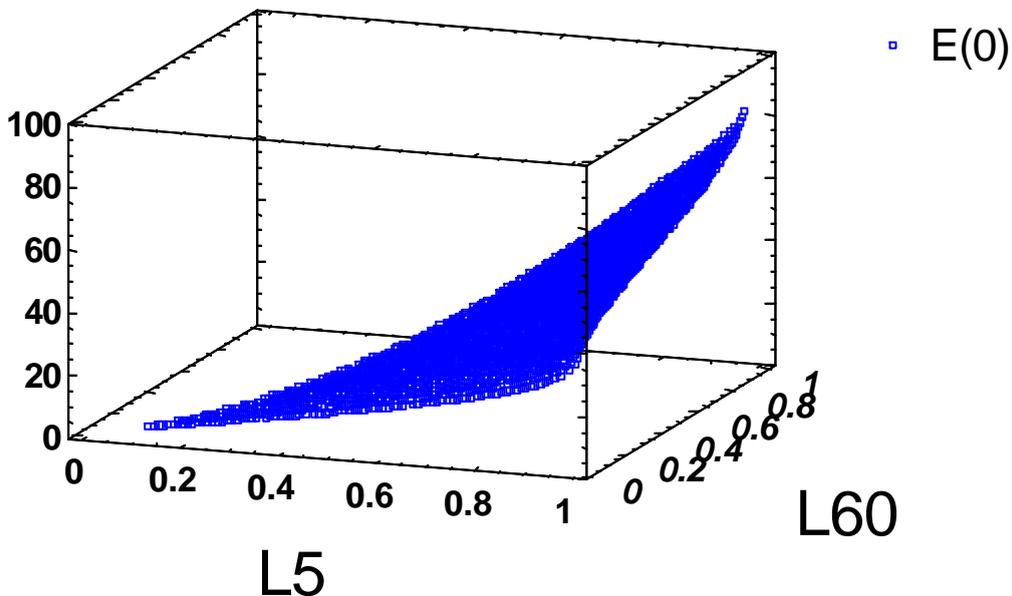


Figure 5.3 E_0 as a function of l_5 , l_{60}

REFERENCES

- Brass W, et al (1968). *The Demography of Tropical Africa*. Princeton: Princeton University Press.
- Coale AJ, Demeny P, Vaughan B (1983). Models of mortality and age composition. In: Coale, et al., eds. *Regional model life tables and stable populations*, 2nd ed. New York: Academic Press.
- Coale AJ, Demeny P (1966). *Regional Model Life Tables and Stable Population*. Princeton: Princeton University Press.
- Hill K, Yazbeck A. *Trends in Child Mortality, 1960-90: Estimates for 84 Developing Countries*.
- Hill, K (1987). *Estimating census and death registration completeness. Asian and Pacific Population Forum*, 1(3): 8-24.
- Ledermann S, Beas J. 1959. Les Dimensions de la Mortalité. *Population* (Paris), **14(4)**: 637-682.
- Ledermann S (1969). Nouvelles Tables-Types de Mortalité, *Travaux et Documents, Cahier (53)*. Paris: Institut National d'études démographiques.
- Lopez AD, Salomon J, Ahmad O, Murray CJL (2000). *Life tables for 191 countries: data, methods, and results*. Geneva: WHO (GPE Discussion Paper No. 9). Available online: http://www-nt.who.int/whosis/statistics/discussion_papers/discussion_papers.cfm
- Lopez AD, Ahmad O, Guillot M, Inoue M, Ferguson B (2001). *Life tables for 191 countries for 2000: data, methods, results*. Geneva, World Health Organization (GPE Discussion Paper No. 40). Available online: http://www-nt.who.int/whosis/statistics/discussion_papers/discussion_papers.cfm
- Murray CJL, Lopez A, Ahmad O, Salomon J (2000). *WHO system of model life tables*. Geneva: WHO (GPE Discussion Paper No. 8).
- Murray CJL, Ferguson B, Lopez AD, Guillot M, Salomon J, Ahmad O (2001). *Modified-logit life table system: principles, empirical validation and application*. Geneva, World Health Organization (GPE Discussion Paper No. 39). Available online: http://www-nt.who.int/whosis/statistics/discussion_papers/discussion_papers.cfm
- Newell C (1988). *Methods and models in demography*. New York: The Guilford Press.
- Palmore JA, Gardner RW (1983). *Measuring mortality, fertility and natural increase: a self-teaching guide to elementary measures*. Honolulu: East-West Population Institute.
- Pressat R (1961). *Demographic analysis*. Chicago: Aldine Atherton. Inc.
- Preston SH (1984). Chapter 8: Use of direct and indirect techniques for estimating the completeness of death registration systems. In: United Nations, *Data Bases for Mortality Measurement*. New York: United Nations.
- Shryock HS, Siegel et al. (1976). *Methods and materials of demography*. Condensed Ed. by Edward G. Stockwell. New York: Academic Press.
- United Nations (1955). *Age and Sex Patterns of Mortality: Model Life Tables for Under-Developed Countries*. New York: United Nations, Sales No. 55.XIII.9.
- United Nations (1983). Brass growth balance method. In: United Nations, *Manual X. Indirect Techniques for Demographic Estimation*. New York: United Nations.
- United Nations (1984). Chapter 5: Approaches to the collection of mortality data in the context of data needs. In: United Nations. *Data Bases for Mortality Measurement*. New York: United Nations.
- United Nations (1988). *Mortpak-Lite. The United Nations software package for mortality measurement*. New York: United Nations.
- United Nations (2001). *World population prospects: the 2000 revision (2001)*. New York, United Nations.

6. ESTIMATING CAUSES OF DEATH

6.1 INTRODUCTION

Careful estimation of the cause of death pattern in the base year selected for the NBD study is a critical component of any NBD exercise. Firstly, DALYs are cause-specific measures and hence we need to estimate the underlying pattern of causes of death by age and sex in order to calculate the years of life lost (YLL) component of DALYs. In addition, accurate estimates of causes of death are required as a basis for estimating or validating basic epidemiological inputs into DALYs such as disease incidence, prevalence, etc. Where no reliable data on incidence, for example, are available, you will need to estimate incidence from data on causes of death. Hence, cause of death data have multiple uses in an NBD Study and great care need to be taken to develop cause of death estimates. This chapter provides a step-by-step approach to estimating cause of death patterns, depending on data sources available.

The major sources of cause of death information mentioned earlier are:

- vital registration systems
- sample registration systems
- household surveys
- population laboratories and surveillance systems
- epidemiological estimates.

Most countries collect information on causes of death through some form of vital registration system. However, coverage varies from country to country. In a majority of countries, however, most deaths go unrecorded.

Many countries with inadequate vital registration systems have established sample registration systems or population laboratories with the potential to provide some useful information on local patterns of cause of death using a variety of verbal autopsy procedures.

For a number of causes of death, epidemiological estimates of cause-specific mortality are available. A wide range of data sources may be needed to estimate causes of death in data-poor environments. It is therefore important to appreciate the quality of different data sources.

There are three main determinants of the quality of cause of death coding:

- 1) The extent of information available at the time of attributing a death to a specific cause. The set of possible information includes the history of symptoms prior to death, the results of diagnostic tests undertaken, prior diagnoses, and, in rare cases, autopsy results.
- 2) The knowledge and training of the individual or group attributing a death to a specific cause. In different settings, this ranges from lay reporters who have less than primary-school education and are sometimes aided by algorithms to specialist physicians.
- 3) The extent of time that the certifier has known the patient: not at all, during the acute phase prior to death, or for a longer period.

The quality of the attribution of cause may also depend on patient characteristics. Autopsy studies have shown that it is harder to assign causes correctly to deaths in the elderly. The quality of the causes of death data is dependent on the extent of medical certification of deaths. In all systems outlined above, each death is either:

- i) certified by a medical practitioner
- ii) based on "verbal autopsies" or
- iii) not given a cause at all.

6.2 DATA SOURCES AND METHODS FOR ESTIMATING CAUSES OF DEATH

A VITAL REGISTRATION WITH CERTIFICATION OF CAUSE OF DEATH

The “gold standard” data source for estimating age-specific mortality is a national vital registration system, which records at least 70% (and ideally more than 95%) of all deaths occurring in the resident population. Such data should be cause-specific, with the cause medically certified, and permit the compilation of complete data on the number of deaths by age and sex.

B SAMPLE REGISTRATION SYSTEMS

In situations where vital registration cannot cover the entire population, sample registrations systems or networks of disease-surveillance points have been used to collect data on defined (“catchment”) populations. These can yield very useful data on age-specific death rates and causes of death, providing that the catchment population are nationally representative and the surveillance is rigorous (i.e. all or almost all deaths are registered). The quality of cause attribution ranges from medical certification to “verbal autopsy” methods (see Section 6.5 for a discussion of verbal autopsies). These schemes have been successfully used for demographic surveillance in India and for epidemiological surveillance in China.

C HOUSEHOLD SURVEYS

Modules on child and adult mortality can be added to household surveys and the data derived can be used for estimation of mortality levels either directly or indirectly. Cause of death can be ascertained from “verbal autopsies”. The Demographic and Health Survey programme has yielded comparable estimates of infant and child mortality for more than 60 countries since 1985. Levels of adult mortality can be estimated either directly from questions about deaths in the household over the past 24 months or indirectly from questions about orphanhood and the survival of siblings.

D POPULATION SURVEILLANCE SYSTEMS

A number of population laboratories have been established which provide vital registration of events (including causes of death) for a small population. Examples include Matlab, Niakar, Ifakara, Machakos and others.

E EPIDEMIOLOGICAL ESTIMATES

Estimates of mortality by age and sex from a cause can often be constructed based on knowledge of the cause’s epidemiology. For example, one can estimate incidence, remission and case-fatality rates and thus approximate mortality.

Epidemiological estimates for a cause often overestimate mortality, as compared to vital registrations of events. This is largely a reflection of co-morbidity where several co-existing pathologies contribute to and compete for the cause of death.

In general, epidemiological surveys of mortality due to a single cause probably also overestimate mortality due to that cause. At the margin, these studies tend to be inclusive rather than exclusive.

The use of critical judgment to analyse and adjust epidemiologically based estimates of mortality by cause in order to generate plausible estimates is one of the more difficult exercises in an NBD study.

F CAUSE-OF-DEATH MODELS

In the absence of any data to estimate mortality by cause, including epidemiological estimates, cause-of-death models may have to be used.

These are models that predict the cause structure of mortality based on other information such as income and the level of total mortality for a particular age and sex group.

6 ESTIMATING CAUSES OF DEATH

In a series of equations these models capture past patterns of the epidemiological transition in countries with good vital registration over previous decades. The models are most useful at the highest level of aggregation, such as determining the split between Groups I, II and III.

G DEATHS IN-HOSPITAL

Deaths in hospitals should not be used to estimate the cause of death pattern in the community, except in localities where a very high proportion of deaths occur in hospitals.

H CANCER REGISTRIES

The International Agency for Research on Cancer (IARC) has developed standards for operating a population based registry of cancer incidence and mortality. In some countries, these registries provide a rich resource from which mortality can be estimated.

6.3 PRACTICAL STEPS IN ANALYSING CAUSE OF DEATH DATA

Firstly, a list of causes of death must be decided upon.

The ICD lists hundreds of detailed causes; much of the detail is not relevant to policy choice.

A list is needed that captures the level of detail needed for planning and evaluating interventions, risk-factor changes, etc.

In the GBD Study a three-part tree-structure of cause of death classification was proposed:

Group I are the pre-transitional causes: communicable, maternal, perinatal and nutritional

Group II are the non-communicable causes

Group III are the intentional and unintentional injuries.

Note that ill-defined causes are NOT included in the list. They are of no direct programme relevance.

National Burden of Disease studies in countries with reasonable vital registration and cause-of-death coding have access to more detailed 3- and 4-digit ICD-9 or ICD-10 data. For these purposes, a more accurate and detailed list can be developed.

The current list used in the GBD 2000 is given in a Table on the accompanying CD together with two files that enable you to construct SPSS code to apply these cause classifications (or may be downloaded from the WHO website at <http://www.who.int/evidence> (select the links to burden of disease, then National Burden of Disease Manual).

A KEY STEPS IN ANALYSING LOCAL PATTERNS OF CAUSE OF DEATH

- 1) Compile the number of deaths coded to each 3-digit ICD-9 (or one letter and two number ICD-10 codes) code without regard to age or sex.
- 2) For all deaths causing more than 0.1% (or some other similar cutoff) check to see if the code is included in one of the NBD-specific categories or is in one of the NBD residual categories.
- 3) Where there are local garbage codes or causes of death not in the list that are locally important, the list and approach to coding may need modification.

Modification of the cause list and the coding structure requires careful consideration of the consequences and judgment as to the likely reason for a garbage code.

Tables 6.1 and 6.2 show summaries of this exercise for Mexico and Uruguay, where 81.4% and 80.4%, respectively, of deaths are captured in the GBD list without modification. As a rule of thumb, the specific codes in your list should cover 80% or more of all deaths.

Table 6.1 Classified Deaths in Mexico, 1992

	>0.1% of total	<0.1% of total	Total
Classified	76.6	4.8	81.4
Residual	14.3	4.3	18.6
Total	90.9	9.1	100

Table 6.2 Classified Deaths in Uruguay, 1992

	>0.1% of total	<0.1% of total	Total
Classified	77.5	3.9	80.4
Residual	15.4	3.2	19.6
Total	92.9	7.1	100

B CORRECTING CAUSE OF DEATH DATA FROM VITAL REGISTRATION

There are likely to be several problems with the validity and reliability of cause of death data, even those certified by medical practitioners.

The two major problems are:

- 1) not assigning a specific code, but using senility or some other ill-defined code; or
- 2) assigning the wrong code due to diagnostic fashions, carelessness, etc.

In many countries, a large proportion of deaths are coded to ICD-9 Chapter XVI (or Chapter R in ICD-10): Symptoms, Signs and Ill-defined Conditions.

If the accuracy of coding of these ill-defined deaths has increased over time, it can create false trends in the age-specific rates of other causes, such as cardiovascular diseases.

The variation in the percentage of ill-defined deaths among countries is substantial. On the one hand, there are countries with less than 1% ill-defined causes such as Hungary, New Zealand, Finland, Cuba, Romania; for other countries more than 15% of total deaths are coded under ill-defined codes. Ecuador, South Africa, Brazil, Guatemala, El Salvador, Peru are examples of this group. In some cases such as Syria or Thailand, more than 50% of total deaths are coded as ill-defined causes of death.

In addition to the chapter of ill-defined causes of death in the ICD, there are many codes that are used to code deaths to the residual of each group of diseases. In order to provide a true assessment of causes of death, these specific "garbage codes" need to be identified and their numerical importance for each chapter or group of diseases.

From the GBD and NBD studies, the most important specific groups of ill-defined cause-of-death (garbage codes) are in the categories of cardiovascular diseases (heart failure, cardiac arrest and ill-defined cardiovascular diseases); injuries (ill-defined injuries and injuries undetermined whether accidentally or purposely inflicted); and malignant neoplasm (cancers with site ill-defined).

NEVER accept cause of death data at face value. Always carry out the "check and correct" procedures outlined below.

C STANDARD ADJUSTMENTS FOR ILL-DEFINED DISEASES AND INJURIES

Injury Garbage Codes

In the Basic Tabulation List (BTL) of ICD-9, E560 (E980-E989 in the 3 digit ICD-9 codes or Y10–Y34 in ICD-10) is “Injury undetermined whether accidentally or purposely inflicted.” These codes can often represent a large share of injuries and, for policy purposes, we must attribute these deaths to specific injuries.

For the GBD study, we have proportionately allocated these deaths to all other injury causes of death. For an NBD study, there may be local information available that can guide the allocation of these deaths across the rest of the injury group in a more targeted manner.

When 4-digit ICD-9 data are available, E928.9, “Unspecified Accidents” is a major garbage code for unintentional injuries. It is advised that such deaths be redistributed proportionally across the other unintentional injury categories. In ICD-10, there is no code for unspecified accidents, forcing coders to at least specify a broad category of injury.

Chapter XVI. Signs, Symptoms and Ill-Defined Conditions

In the BTLs and the 3-digit data, this entire chapter should be allocated to specific causes of death. We presume that, in adults, most of these deaths are miscertified Group II deaths. In the GBD study we have proportionately allocated Chapter XVI deaths after age 5 to all other Group II causes.

In children under 5 years, we have chosen to proportionately allocate these deaths across Group I. This approach is based on the assumption that most Chapter XVI deaths in children are due to miscertified infectious diseases or conditions arising in the perinatal period. The choice of into which Group to reallocate Chapter XVI deaths should be made locally based on all information available. For instance, in the Zimbabwe NBD considerable numbers of deaths certified by lay-persons were classified as due to symptoms such as cough, headache and abdominal pain. After consultation with local experts, it was decided to redistribute these deaths proportionally by age and sex to the most likely underlying disease categories. Ill-defined respiratory deaths were redistributed across TB and pneumonia; ill-defined abdominal problems across diarrhoea, digestive disorders and pelvic inflammatory disease (STD); and headache across meningitis, stroke and malaria.

There may also be local evidence to suggest that deaths coded to ill-defined conditions, or even to specific diseases may in fact be due to an injury as the underlying cause. A recent study of 48,000 adult deaths in Chennai, India found that 2.5% of deaths coded to a disease were actually injury deaths.

6.4 ANALYSING CARDIOVASCULAR MISCERTIFICATION

Given the importance of CVD deaths in many countries, special procedures have been developed to adjust for variation in cardiovascular certification practice among countries. Within countries over time, there is clear evidence of shifts in cardiovascular certification practices. In many places, deaths previously assigned to related causes are increasingly assigned to ischaemic heart disease.

The two main causes of cardiovascular deaths are cerebrovascular accidents (stroke) and ischaemic heart disease. The proportion of cardiovascular deaths excluding stroke due to ischaemic heart disease is highly variable.

Four clusters of codes are likely to include miscertified ischaemic heart disease, which may explain some of the variation in the proportion of cardiovascular deaths (excluding stroke) assigned to ischaemic heart disease:

- heart failure (ICD-9 code 428; ICD-10 code I50);
- ventricular dysrhythmias (ICD-9 codes 427.1, 427.4, 427.5; ICD-10 codes I47.2, I49.0, I46.0–9);
- general atherosclerosis (ICD-9 440.9; ICD-10 code I70.9); and
- ill-defined descriptions and complications of heart disease (ICD-9 codes 429.0, 429.1, 429.2, and 429.9; ICD-10 codes I51.4–6 and I51.9).

Figure 6.1 shows that some countries, particularly Japan have a very high proportion of deaths assigned to these garbage codes. There is also a strong inverse relationship between the proportion of deaths assigned to the four cardiovascular garbage codes and the proportion assigned to ischaemic heart disease.

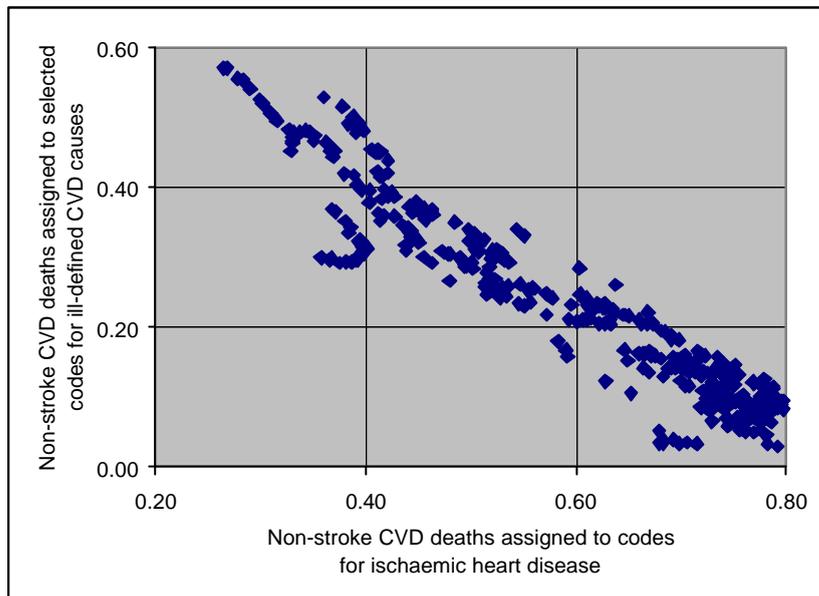


Figure 6.1 Proportions of Cardiovascular Disease Deaths (Excluding Stroke) Assigned to Selected Codes for Ill-Defined Causes and Directly to Ischaemic Heart Disease for selected countries, 2000.

ALGORITHMS TO CORRECT CARDIOVASCULAR MISCERTIFICATION

A correction algorithm was used in the GBD and has been elaborated as part of the US Burden of Disease Study. This is based on the assumption that true ischaemic heart disease rates are a function of some set of risk factors or exposures, that is:

$$IHD_T = f(\text{risk factors})$$

The true ischaemic heart disease mortality rate is the sum of mortality rates of observed IHD and IHD that gets coded to one of the cardiovascular garbage codes.

$$IHD_T = IHD_o + IHD_G$$

It follows from these two equations that:

$$IHD_o = f(\text{risk factors}) - IHD_G$$

By multiplying the IHD deaths coded to the cardiovascular garbage codes by the death rate from the total cardiovascular garbage codes (GAR), divided by the same GAR, we get:

$$IHD_o = f(\text{risk factors}) - \frac{IHD_G}{GAR} GAR$$

This relationship can then be estimated with observed ischaemic heart disease mortality rates, data on some set of risk factors for ischaemic heart disease, and the death rate from the combination of all cardiovascular garbage codes. The linear regression coefficient on the cardiovascular garbage codes is an estimate of the fraction of the garbage codes that is miscoded cardiovascular disease.

6 ESTIMATING CAUSES OF DEATH

A good proxy variable for the risk factor effect might be the lung cancer death rate, since smoking is a major cause of both IHD and lung cancer.

The GBD 2000 project has reanalyzed the WHO mortality database to construct an improved algorithm for re-assigning cardiovascular garbage codes (Lozano et al. 2001). Separate correction factors were derived for “high ill-defined coding” countries, where doctors certified, on average, more ill-defined CVD than IHD deaths, and “low ill-defined coding” countries, where doctors assign, on average, a small proportion of ill-defined CVD deaths. Table 6.3 defines the ICD codes for which deaths are classified as “ill-defined”. Table 6.4 shows the proportion of these deaths that should be added to IHD deaths by age and sex for the two groups of countries.

Table 6.3. Ill-defined cardiovascular diseases, ICD-9 and ICD-10

Disease	ICD-9	ICD-10
Paroxysmal ventricular tachycardia	427.1	I47.2
Ventricular fibrillation and flutter	427.4	I49.0
Cardiac arrest	427.5	I46
Heart failure	428	I50
Myocarditis, unspecified	429.0	I51.4
Myocardial degeneration	429.1	I51.5
Cardiovascular disease, unspecified	429.2	I51.6
Complications of heart disease, unspecified	429.9	I51.9
Atherosclerosis, generalized and unspecified	440.9	I70.9

Source: Lozano et al. (2001)

Table 6.4. Correction factors (Beta values) by age and sex, Low and high ill-defined coding countries. Beta values give the proportion of ill-defined CVD deaths to be re-allocated to IHD deaths.

Age group	Males		Females	
	Low ill-defined coding	High ill-defined coding	Low ill-defined coding	High ill-defined coding
35-39	0.000	0.000	0.000	0.000
40-44	0.107	0.107	0.000	0.000
45-49	0.039	0.273	0.000	0.041
50-54	0.040	0.696	0.101	0.446
55-59	0.203	0.941	0.139	0.689
60-64	0.160	0.754	0.119	0.660
65-69	0.253	0.827	0.251	0.615
70-74	0.264	0.732	0.202	0.469
75-79	0.233	0.576	0.170	0.358
80+	0.030	0.242	0.060	0.198

Source: Lozano et al. (2001)

6.5 VERBAL AUTOPSY

In a number of countries, medical certification of deaths or even a sample of deaths is not possible.

Because cause-of-death information is essential for planning health interventions, efforts have been made to develop instruments that can be used to assign each death to a cause based largely on a history provided by the individual's family, supplemented by medical records where available. This process is known as "verbal autopsy".

These verbal autopsy methods are based on two assumptions: (1) the symptom complex for each disease of interest is unique, and (2) family members can accurately recall symptoms and their timing.

Unique symptom complexes and histories exist for some diseases, such as neonatal tetanus or motor vehicle accidents, but for others — such as tuberculosis, lung cancer, and heart failure — they do not.

Recall has also been found to be poor for some symptoms. For example, maternal recall in rural East Africa was poor for pallor, splenomegaly, severe cough, jaundice, fever, chest indrawing, and nasal flaring.

6.6 PRACTICAL IMPLICATIONS OF USING VERBAL AUTOPSY DATA

Cause-of-death information from national household surveys (e.g., Indonesia's), sample registration systems (e.g., *Survey of Causes of Death (Rural) in India*), or population laboratories (e.g., in Navrongo, Ifakara or Matlab) that are based on verbal autopsy must be used with great caution.

For some causes -- measles, neonatal tetanus, maternal causes, and most injuries -- the estimates are probably reasonable.

The data may also be reasonable for establishing the split between Groups I, II and III. This in itself is a major contribution towards estimating cause of death patterns since it is likely to avoid under-estimation of Injuries (Group III).

For many detailed causes, however, estimates based on verbal autopsy should be examined for plausibility, based on available epidemiological estimates. In most cases, verbal autopsy data should not be used for detailed cause estimation.

Verbal autopsy data should not be used without a good understanding of how the data were collected and verified. For example, were all, or a sample of the verbal autopsy diagnoses checked by a medical officer? Was there any follow-back procedure for improbable or unclear diagnoses?

Information on validation exercises against hospital diagnoses should be exploited to adjust VA codes to give a more reliable estimate of cause of death patterns. The results from one study in Africa are shown in Table 6.5.

Great care must be taken to ensure that the sensitivity and specificity results from various studies can reasonably be extrapolated to local conditions. Selection bias of the causes of death in health establishments needs also to be considered since these might not be typical of the community as a whole.

Table 6.5 Sensitivities, Specificities, and Predictive Values of Verbal Autopsy Interviews compared with hospital derived diagnosis (Snow et al. 1992)

Cause of death diagnosis	Sensitivity (%)	Specificity (%)	Positive predictive value (%)
<i>Post-neonatal</i>			
Malnutrition	89	96	87
Malaria	46	89	57
Measles	90	96	84
ARI	28	91	29
Gastroenteritis	36	96	36
Anaemia	33	98	50

6 ESTIMATING CAUSES OF DEATH

Accidents	78	100	88
Meningitis	38	94	20
<i>Neonates</i>			
Sepsis	61	81	67
Tetanus	90	79	69

The results of verbal autopsy studies are usually summarized in terms of:

- i) *sensitivity*: the proportion of true deaths from a given cause identified as due to that cause from the VA. Sensitivity measures the probability that a given disease will be identified by the VA.
- ii) *specificity*: the proportion of deaths which are truly not due to the cause correctly identified as such by the VA.
- iii) *positive predictive value*: the proportion of all deaths assigned to a given cause by the VA which are actually due to that cause.

The adjusted cause-specific mortality fraction (CSMF) is then estimated as:

$$CSMF = \frac{VA + x - 1}{x + y - 1}$$

where x = specificity, y = sensitivity.

For example, from Table 6.5, if the VA fraction of all deaths due to measles was 10%, then the corrected rate would be:

$$CSMF(\text{measles}) = \frac{0.1 + 0.96 - 1}{0.96 + 0.90 - 1} = \frac{0.06}{0.86} = 0.07 \text{ or } 7\%$$

6.6 VALIDITY CHECKS

All data on causes of death should also be screened for demographic plausibility.

Certain causes (e.g. maternal deaths, cancer of prostate) are sex-specific.

Most major causes of death follow a well-defined age-pattern. Figure 6.2 shows the normalized age-pattern for all forms of cancer over the last 50 years. Departures from such standard patterns should be examined carefully. In some cases, these differences may be due to small numbers of deaths in some age groups.

If departures from regular age patterns cannot be explained, the cause of death data should NOT be used.

If a substantial fraction (>10%) of all deaths are coded to causes in Chapter XVI of the ICD-9 or Chapter R of ICD-10 (senility and ill-defined), then specific follow-back studies to conduct intensive investigations on a sample of such deaths should improve the reallocation algorithm.

This investigation might include reviewing:

- VA reports
- sequences on death certificates
- supplementary medical records

plus additional information from families and certifying medical practitioners.

In countries where such studies have been carried out, the reallocation of ill-defined deaths may differ from that resulting proportional reallocation. For example, in Thailand, the majority of the ill-defined codes among adults were re-assigned to HIV, cancer, cardiovascular disease and chronic respiratory disease; in Andhra Pradesh, most of these deaths were reassigned to chronic bronchitis and emphysema, ischaemic heart disease and stroke.

In situations where available data are of questionable reliability, it is useful to compare an observed pattern of Group-specific mortality rates with rates predicted by the cause-of-death model. These predicted values have been generated for each age, sex and cause Group, at each level of mortality, using Monte Carlo simulation. Table 5 of the Annex to Volume I of the *Global Burden of Disease Series* provides the reader with the predicted proportions of total mortality for Groups I, II and III, as well as predictions for -4, -3, -2, -1, 1, 2, 3 and 4 standard deviations.

6 ESTIMATING CAUSES OF DEATH

European standard population used

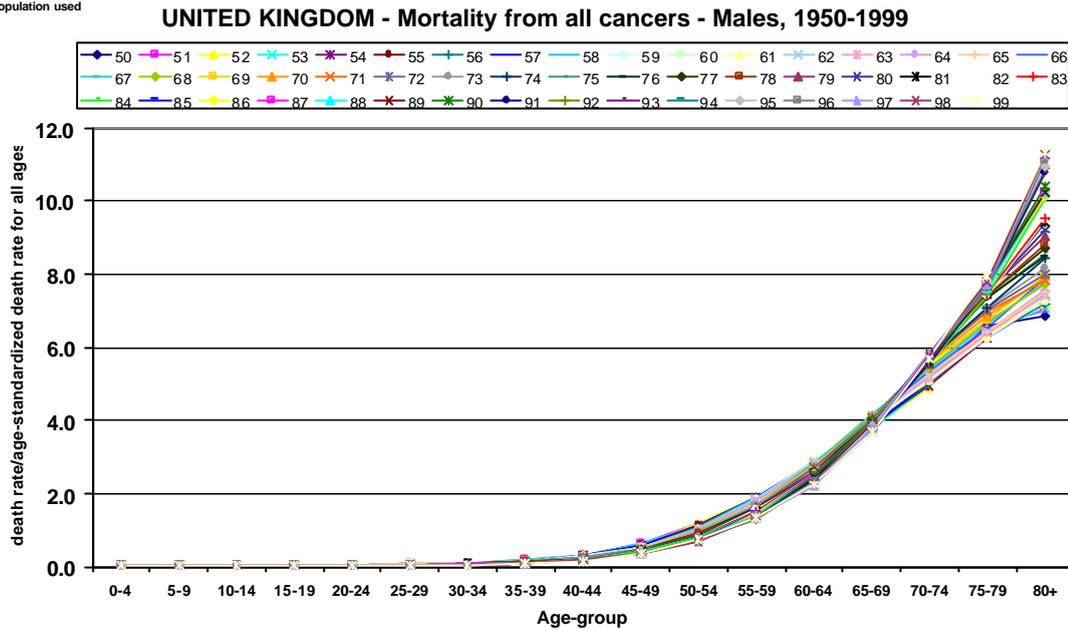


Figure 6.2 Age-Specific Death Rates for All Cancers, United Kingdom 1950–1999

Using this prediction table and a series of observed age-sex-cause-Group-specific estimates, one can measure how different the cause of death structure of a population is compared with that predicted by the models.

In rare situations, this table may even be used to predict the age-sex-specific mortality rates for more detailed causes (this has been done for ICD-9 coded mortality data). Such applications of the model are less reliable given that there are significant variations in coding practices among countries.

6.7 COMBINING MULTIPLE SOURCES

The standard deviation analysis can also be helpful at the phase of cause of death analysis when different sources are being integrated into a final set of cause of death estimates. For example, when some vital registration data and models have been used to generate an initial set of estimates and epidemiological estimates have been generated for selected causes.

If the epidemiological estimates imply substantial increases in the magnitude of Group I or Group II mortality for an age-group, then standard deviation analysis can be used to assess the plausibility of the proposed alteration in cause of death structure.

For the GBD study, we have used an arbitrary convention that epidemiological estimates cannot shift away from the predicted value for any given Group by more than 2 standard deviations beyond that initially estimated through causes of death sources.

The final step in estimating cause of death patterns is to integrate all sources into a final estimate by age and sex.

- a) If good quality vital registration data are available, then these should form the basis for the estimate, adjusted for specific "garbage" coding and redistributing ill-defined codes. Cause of death data from specific epidemiological studies should then be incorporated. However, adjustments to vital registration should only be made if these epidemiological sources strongly suggest under-reporting in the vital registration.

- b) If only partial vital registration, and/or verbal autopsy data are available, then first establish the proportion of Groups I, II and III for each age and sex group. Once this is fixed, use the available data sources to estimate the pattern for specific causes.

The results should be compared to the distribution of causes available from neighbouring countries or from other standards (e.g. WHO Regional patterns).

External validity checks should be applied wherever possible. For example, liver cancer mortality should be consistent with Hepatitis B prevalence, lung cancer mortality with cigarette consumption some decades earlier, motor vehicle accident mortality with police records, etc.

REFERENCES

- Battle RM et al. (1987). Factors influencing discrepancies between premortem and postmortem diagnoses.
- Britton M. (1974). Diagnostic errors discovered at autopsy.
- Bulatao RA. Mortality by cause, 1970-2015. In: JN Gribble, SH Preston, eds. *The Epidemiological Transition. Policy and Planning Implications for Developing Countries*
- Chandramohan D, Maude GH, Rodrigues LC, Hayes R. (1994). Verbal autopsies for adult deaths: Issues in their development and validation.
- Coale AJ, Demeny P, Vaughan B. Models of mortality and age composition. In: Coale et al., eds. *Regional model life tables and stable populations*, 2nd ed. (See Session 2)
- Espanshade, T. (1973). The cost of children in the urban united states, Population Monograph No. 14. Institute of International Studies, University of California, Berkeley.
- Frenk J, et al. (1991). Elements for a theory of health transition.
- Hakulinen T, Hansluwka H, Lopez AD, Nakada T. Global and regional mortality patterns by cause of death in 1980.
- Israel RA.(1990). Automation of mortality data coding and processing in the United States of America. *World Health Statistics Quarterly* ; 43(4):259-62
- Israel RA, Rosemberg H, Curtin L. (1986). Analytical potential for multiple cause of death *American Journal of Epidemiology*, 2:161-179.
- Jougla E, et al. (1992). Death certificate coding practices related to Diabetes in European Countries-The Eurodiab study. *International Journal of Epidemiology*, 21:343-351.
- Lozano R, Murray CJL, Lopez AD, Satoh T (2001). *Miscoding and misclassification of ischaemic heart disease mortality*. Geneva, World Health Organization (GPE Discussion Paper No. 12).
- Murray CJL, Lopez AD (1996). Estimating cause-of-death: new methods and global and regional applications for 1990. In: Murray CJL, Lopez AD, eds. *The global burden of disease*.
- Nicholson, JL. (1949). Variations in working class family expenditure. *Journal of the Royal Statistical Society, Series A*, 112 (Part IV), 359-411.
- Omran AR. The epidemiological transition. A theory of the epidemiology of population change.
- Preston SH. Mortality patterns in national populations -- with special reference to recorded causes of death.
- Shryock, HS, Siegel and Associates (1976). *Methods and Materials of Demography*. Condensed Edition by Edward G. Stockwell. Academy Press.
- Snow RW, et al. (1992). Childhood deaths in Africa: Uses and limitations of verbal autopsies.
- Snow RW, et al. (1993). Maternal recall of symptoms associated with childhood deaths in rural East Africa.
- Stehbens WE. (1987). An appraisal of the epidemic rise of coronary heart disease and its decline.
- World Health Organization. Measurement of overall and cause-specific mortality in infants and children: memorandum from a WHO/UNICEF meeting.

7. EPIDEMIOLOGICAL ESTIMATES—GENERAL APPROACH

Estimating the years lived with a disability (YLD) is the most difficult component of an NBD study. While the cause of death information largely relies on one data source, the estimation of YLD depends on a wide range of different data sources specific to each disease. It requires judgment on what the most plausible source of information is and which parameters best describe the disability caused by each disease. The basis of this is a good understanding of the epidemiology of the disease.

In reality, you will have a limited time to become an expert in the epidemiology of each of the diseases in your burden of disease list and you will find inconsistencies, uncertainty and gaps in the available data. Creativity and plausibility are the key themes. The 'art' of doing a good burden of disease study is to adopt the following characteristics appropriately:

- Courage but not recklessness
- Precision but not 'uncertainty-induced' paralysis
- Good listening skills in the contacts with disease experts but not blind acceptance of advocacy-driven estimates

The rest of this chapter provide a general step-by-step description of how to proceed with estimating YLD. The steps are summarised in the flowchart of Figure 7.1. Chapter 10 gives further details and tips specific to the major disease and injury categories.

7.1 STEP 1 RESEARCH CURRENT KNOWLEDGE OF THE DISEASE

Exhaustive and comprehensive knowledge is not required to develop epidemiological assessments. However, it is important to develop familiarity with the basic characteristics of a disease before investigating specific data sources, or trying to understand the detailed dynamics of a disease.

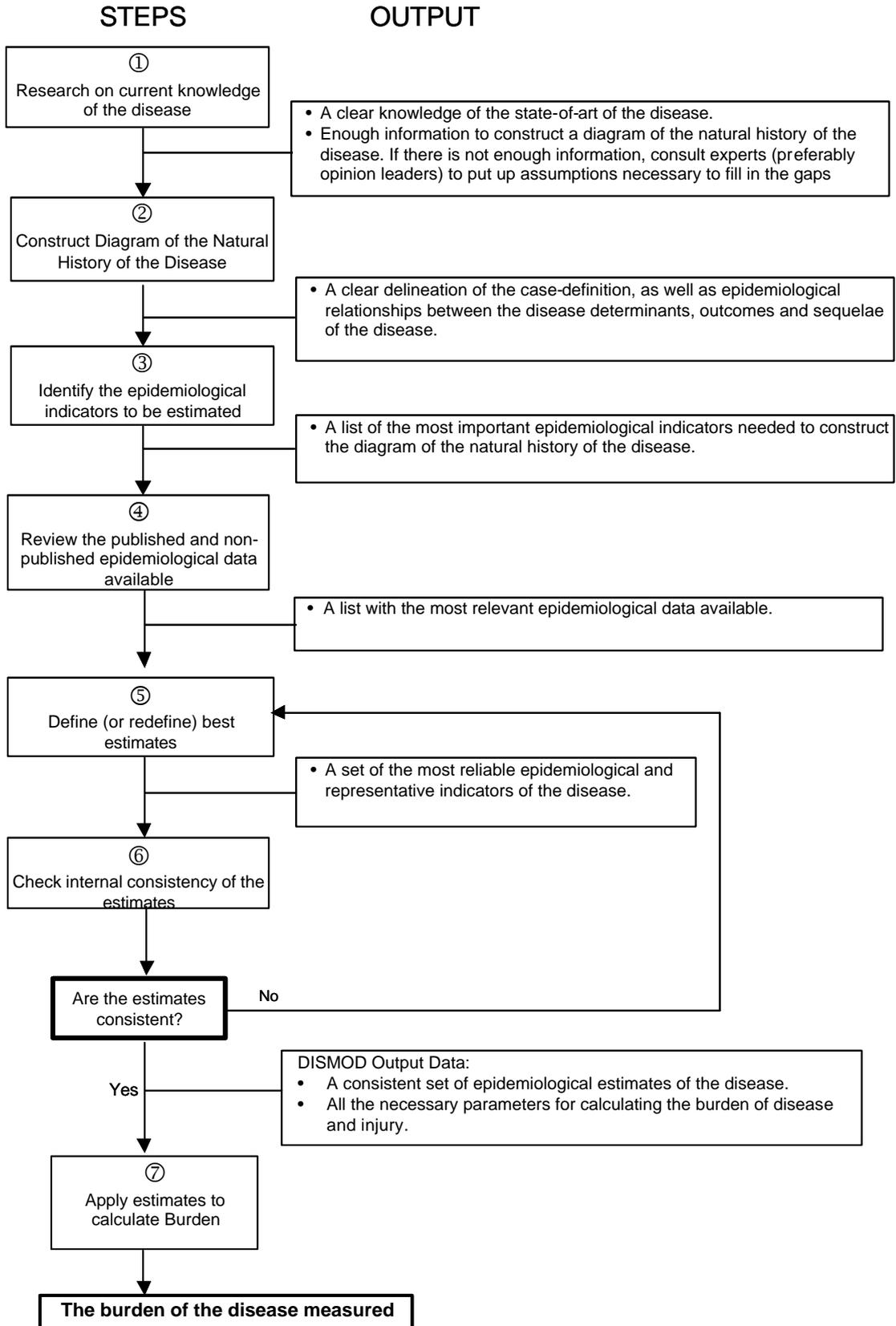
Actions to be undertaken:

- 1) Focus on what has been written about the definition, natural history, classification, severity and epidemiology of the condition studied and its disabling sequelae.
- 2) Acquire a general familiarity with the current knowledge on the condition, from major textbooks in the specialty, an authoritative review paper or scrutiny of attempts by GBD or other NBD studies to describe the disease

Output:

- 1) A clear knowledge of the state-of-art concerning the epidemiology of the disease and potential sources of data.
- 2) Enough information to construct a diagram of the natural history of the disease. If there is not enough information, consult experts (preferably opinion leaders) to put up assumptions necessary to fill in the gaps

Figure 7.1 Developing a Reliable and Internally Consistent Epidemiological Assessment



Questions to be addressed:

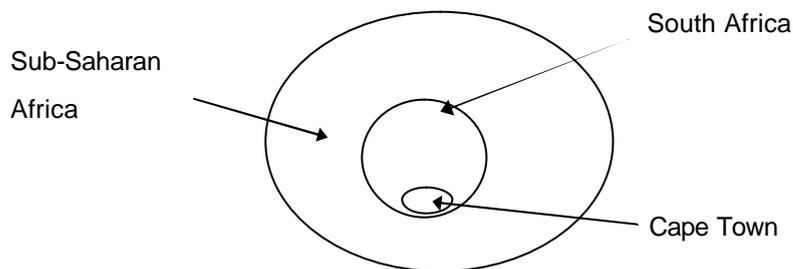
- 1) What is the current knowledge on the disease being studied?
- 2) What are the limitations of the current knowledge on the disease being studied?
- 3) What are the relevant data available on the natural history of the disease and its disabling sequelae? (prevalence, incidence, duration, age of onset, remission rate, and mortality rate, relative risk, level of severity and duration from disease onset to disabling sequela)
- 4) Is there any controversy where you have to search more in depth to find the data needed to construct a diagram of the disease?
- 5) If there are no precise data, is there at least a general consensus amongst opinion leaders?
- 6) If there is no clear consensus, do you think a panel of experts will be needed? If yes, how would you choose the expert panel?

7.2 STEP 2 CONSTRUCT DIAGRAM OF THE NATURAL HISTORY OF THE DISEASE.

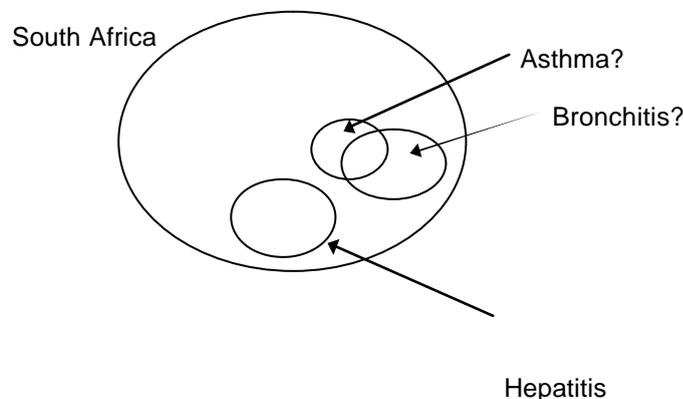
With a good understanding of the disease it is helpful to draw a diagram of the epidemiological dynamic. This will help to define the epidemiological estimates that will need to be developed for every component in the diagram.

Actions to be undertaken:

- 1) Define the population for which the estimates are being developed



- 2) Describe case definitions and relationships between the diseases

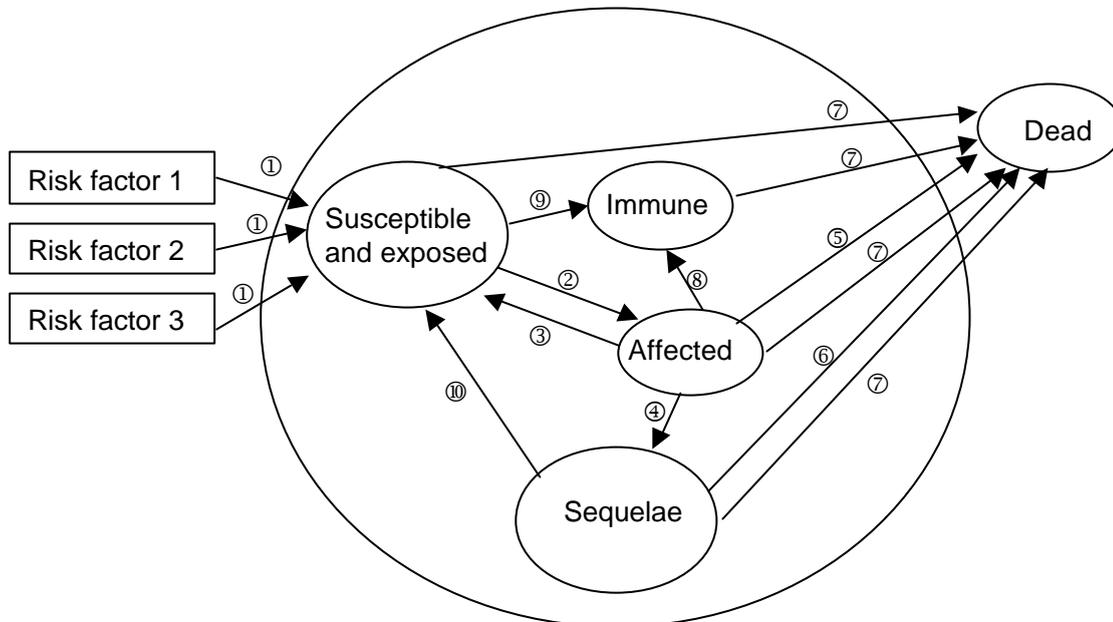


- Do they overlap?, e.g. TB and HIV
- How are they related?

- How are distinctions to be defined?, e.g. what is upper and what is lower respiratory infection?
- Is there misclassification, misdiagnosis or another problem?

3) Define and draw the natural history of the disease

Figure 7.2 Diagram of Dynamic Disease Model



Key to Figure 7.2:

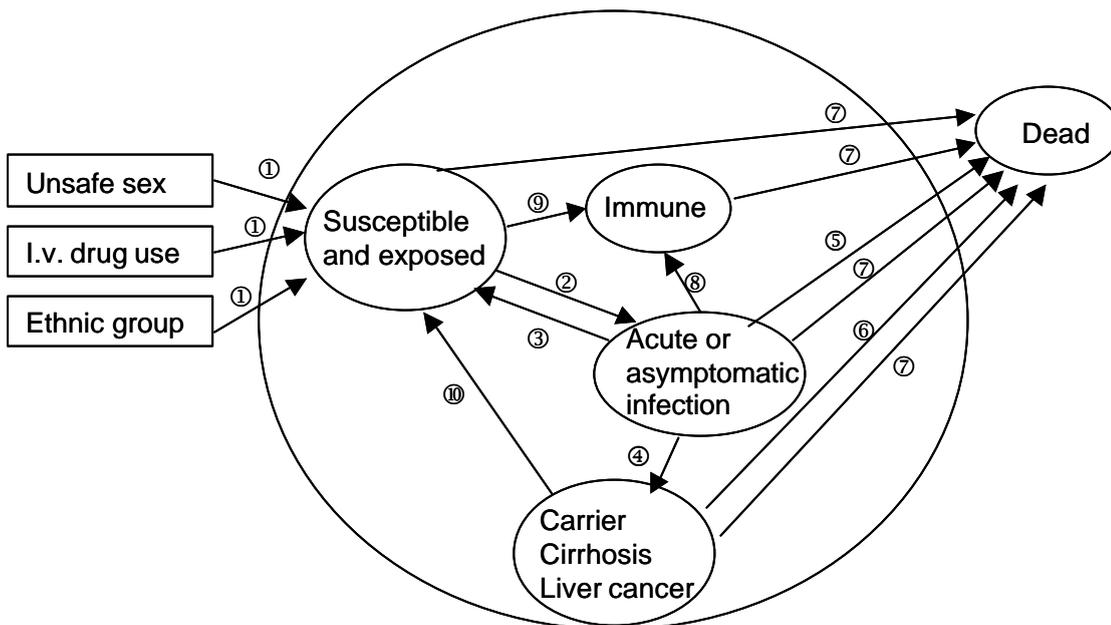
- ① Many risk factors can affect the exposed population. Some risk factors are actually diseases that increase the risk of experiencing the disease being investigated, e.g. diabetes and heart disease or depression and suicide.
- ② Incidence of the disease: the rate at which people become newly affected by the disease under study
- ③ Remission: the rate at which people with disease stop being a case of disease
- ④ Case-complication: the rate at which patients experience a complication of the disease or start to suffer from sequelae of the disease.
- ⑤ Case-fatality: the rate at which patients die from the disease under study.
- ⑥ Complication-fatality: the rate at which patients die as a result of a complication of the disease.
- ⑦ General mortality: the rate at which the population dies from any condition other than the one under study. The general mortality rate applied here excludes death from the disease under study. In practice, we input the all-cause mortality rate in our models and DISMOD calculates the general mortality hazard from other causes.
- ⑧ Patients who become immune to the disease and will not be susceptible to the disease again.
- ⑨ People who become immunized as a result of health intervention programs.
- ⑩ People with sequelae who are exposed to the risk factor(s) and are susceptible to acquire the disease again. For instance, women who have become infertile as a sequela to gonorrhoeal infection are still susceptible to a next episode of gonorrhoea.

This diagram can become even more complex if recurrences of the clinical events associated with an intermittently relapsing disease increase the severity of the sequelae and/or the risk of dying with every

new episode of the disease (i.e. rheumatic fever). Also, many diseases are interrelated and/or are risk factors for other diseases (e.g. diabetes is a risk factor for ischaemic heart disease and stroke). On the other hand, some of the parameters do not apply to certain diseases allowing a simpler disease diagram. For instance, immunity is only an issue in infectious disease and there is no remission from quite a few diseases, e.g. dementia, COPD and Parkinson. There are also diseases in which mortality is not higher than that in the general population, e.g. periodontitis or osteoarthritis.

Hepatitis B is an example of a disease in which most of the boxes and arrows drawn in figure 7.2 are relevant. The disease diagram for hepatitis B would look as follows (figure 7.3)

Figure 7.3 Diagram of Dynamic Disease Model for Hepatitis B

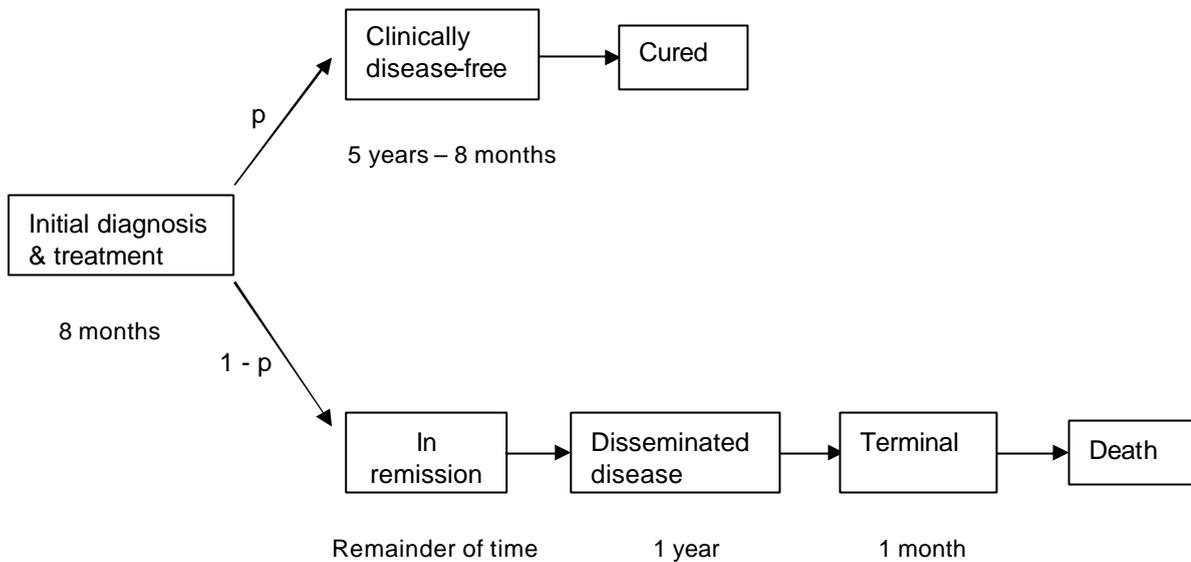


Key to Figure 7.3:

- ① Unsafe sex, i.v. drug use are important risk factors for infection with hepatitis B in adults. Ethnic group may be an important risk factor for the perinatal transmission of hepatitis B if the risk of being a carrier varies significantly between ethnic groups in a population
- ② Incidence of the disease: the rate at which the susceptible population becomes newly infected with hepatitis B; for burden of disease estimates you would need to know what proportion of infections lead to acute illness and what proportion of infections are asymptomatic
- ③ Remission: not relevant in hepatitis B; infection leads to immunity or becoming a chronic carrier
- ④ Case-complication: the rate at which patients experience complications or sequelae of hepatitis such as being a carrier, cirrhosis and liver cancer
- ⑤ Case-fatality: the rate at which patients die from the acute infection with hepatitis B.
- ⑥ Complication-fatality: the rate at which patients die as a result of complications such as cirrhosis and liver cancer
- ⑦ General mortality: the rate at which the population dies from any condition other than hepatitis B.
- ⑧ Patients who become immune to hepatitis B and will not be susceptible to the disease again.
- ⑨ People who become immunized as a result of health intervention programs.
- ⑩ People with sequelae who are exposed to the risk factor(s) and are susceptible to acquire the disease again. This is not relevant to hepatitis B

There are different ways in which a disease diagram can be drawn. Figure 7.4 gives an example of a diagram for a disease with progressive health states.

Figure 7.4 Disease Diagram for Breast Cancer with Tumour Larger than 5 cm at Diagnosis (from Australian Burden of Disease Studies).



Notes: p = proportion of cases who survive; $1 - p$ = proportion of cases dying

The period of disability was set to five years in survivors. Average duration of those who die is determined from follow-up data of cancer registry. The durations for initial diagnosis & treatment, disseminated disease and the terminal phase were set after discussions with cancer experts.

Output:

- 1) A clear delineation of the case-definition, as well as epidemiological relationships between disease determinants, outcomes, and sequelae.
- 2) A clear delineation of the epidemiological parameters needed to describe the dynamic of the disease.
- 3) A simple disease model which captures the important components of the disease (in terms of pathways, sequelae, stages etc) but is not too complex to estimate from available data.

Questions to be addressed:

- 1) Is the disease under study well represented by the diagram created? What evidence supports or is in conflict with this conclusion?
- 2) Is there any other factor not represented in the diagram that could be affecting the accuracy of this representation? Would the addition of this factor significantly alter the overall scheme?
- 3) Is the marginal effort associated with introducing a new factor in the diagram much bigger than the marginal benefit? Does the perfection matter here?

7.3 STEP 3 IDENTIFY THE EPIDEMIOLOGICAL INDICATORS TO BE ESTIMATED.

The data required to estimate YLD are: disability incidence, disability duration, age at onset (if age weights are applied), and distribution by severity class, all of which must be disaggregated by age and sex.

These in turn require estimates of incidence, remission, case-fatality rates or relative risks, by age and sex. For most diseases, information on incidence and duration is not available. Most commonly, the prevalence of a disease or its disabling sequelae is known. The estimation of incidence and average duration from prevalence figures requires additional information on remission and case fatality or relative risk of mortality.

Quite a few diseases that are large causes of disability occur at very different levels of severity. Such diseases include depression, anxiety disorders, dementia, COPD and arthritis all of which can present with symptoms ranging between mild and very severe. Using one estimate of incidence and one disability weight, as was done in the GBD 1990, assumes a constant distribution of severity over time and between countries. If these conditions are expected to contribute significantly to a country's disability burden it is advisable to consider modeling the diseases by different levels of severity. This also means that disability weights should be available or be obtained for each level of severity. If disability weights from elsewhere are used (e.g. the 'Dutch DWs') an additional problem arises to match the scanty epidemiological information on the population distribution by severity with the defined health states for which DWs are available.

Output:

A list of the most important epidemiological indicators needed to construct the diagram of the natural history of the disease

7.4 STEP 4 REVIEW THE PUBLISHED AND NON-PUBLISHED DATA AVAILABLE.

For each disease and the disabling sequelae identified in step 2, a review must be undertaken of available data sources to estimate each of the epidemiological parameters. There are many different data sources—some published, some unpublished—that need to be scrutinised. The main data sources will be described in the order in which they tend to be most useful. When starting a NBD for the first time, it may come as a surprise to note that health facility data which traditionally tend to be reported on in epidemiological surveillance activities, are not considered a very useful source of information for many of the conditions in a burden of disease list. If the collection and analysis of health facility data has been a major part of your activities before starting a NBD study, you will need to become receptive to examining a much wider range of data sources.

TYPES OF DATA

1) Disease registers

Disease registers record new cases of disease based on reports by physicians and/or laboratories. Registers are common in infectious diseases (e.g. tuberculosis), cancer, congenital anomalies, a number of relatively rare diseases (e.g. cystic fibrosis or thalassaemia), and conditions such as diabetes, schizophrenia and epilepsy. The main issues are the level of completeness and data quality. If a register is well kept and has good data in only part of the country, a judgment needs to be made how representative the information is for the whole country or how the data can be adjusted to better reflect population estimates.

2) Population surveys

Interview surveys such as the National Health Interview Survey in the USA or the National Disability Surveys and National Health Surveys in Australia can provide self-reported information on disabilities in key domains such as self-care, occupation, or recreation. Theoretically, such large and representative surveys of prevalent disabling states could provide the information needed to estimate YLD for the most common conditions as well as set bounds to the overall amount of disability in the population. However, there is no example where this was successfully done. In fact, the available interview data prove to be quite uninformative for estimating YLD. There are a number of reasons for that.

First, it is often difficult to attribute impairment to the underlying causes. Second, there are often considerable differences between the disease concept the 'general public' has and the 'medically' defined disease category for which information is intended to be collected. For instance, surveys of asthma based on questions about wheezing, and/or a doctor's diagnosis of asthma tend to report prevalence figures that are 2–3 times higher than surveys which use a positive airway hyperresponsiveness test in its diagnostic criteria. The likely explanation for such a large difference between the two types of surveys is that a lot of minor episodes of wheezing are reported as asthma. It does not imply that the self-reported information has no value. It would be unwise, though, to base

decisions on resource allocation to intervention options on estimates of disease that include a large proportion of misdiagnoses.

To give another example, in self-report surveys of chronic joint problems rheumatoid arthritis is over-reported probably because people tend to call joint aches 'rheumatic'. Self-report surveys do not always overestimate the true prevalence of disease. Typically, self-report surveys underestimate the prevalence of diabetes in comparison to measurement surveys using a glucose-tolerance test or fasting blood sugar because many people with diabetes in the population have not yet been diagnosed as such. Another classical example comes from the Australian National Nutrition Survey of 1995, in which respondents first reported their own weight and height and subsequently measurements were taken. On average, people overstated their height by 2 cm and understated their weight by 2 kg. As a result the prevalence of obesity (defined as a body mass index greater than 30 kg/m²) was 40 per cent higher when based on the measured height and weight.

In general, the results of measurement surveys contribute more to YLD calculations than self-reported interview surveys. This may even be the case if the measurement survey was conducted in only part of the country or in a specific subpopulation. The value of self-report surveys increases when a standard set of questions is used, particularly if the questionnaire has been validated against a gold standard measurement or at least a more valid measurement. The CIDI and DIS questionnaires used in mental health surveys are examples of standard questionnaires based on self-report that have undergone validity testing and have been used widely.

Besides the validity of survey results, it is important to critically examine the representativeness. Did the survey exclude certain groups of the population? For example, in household surveys the homeless and people in institutions such as prisons and old age homes tend to be excluded. If disease is much more prominent in these populations (such as tuberculosis in the homeless, HIV in prisoners and vision loss in residents of nursing homes) the overall population estimate could be seriously underestimated. When examining survey results always look at a description of the level of response and make a judgment how selection bias could have influenced the results.

Keeping the above reservations in mind, surveys are useful sources of information for important disabling conditions including mental disorders, asthma, COPD, musculo-skeletal diseases, hearing loss, vision loss, cognitive function, diabetes, HIV and malnutrition.

3) Epidemiological studies

If information from registers or good quality surveys is lacking, the next most useful source of information tends to come from epidemiological studies. Particularly, longitudinal studies of the 'natural' history of a disease can provide a wealth of information on the incidence, average duration, levels of severity, remission and case fatality. Such studies are rare because they are very costly to undertake. As they are often conducted in a particular region or town, judgment will be needed how results can be extrapolated to the whole population. For most diseases, there is so little known about parameters such as remission, relative risk of dying and average duration that we tend to rely in our YLD calculations on the few studies carried out around the world that provide these estimates.

Even if good survey or register data are available in a country it is good practice to search the national and international literature. Medline is the most important electronic source of information on health related publications. It is available without cost from a number of websites, one of which can be found at: http://www4.infotrieve.com/newmedline/adv_search.asp. The following search strategy is suggested:

a) Identify the topic

b) Enter a number of key words and try a number of different combinations. Useful key words are 'the name of the disease', review, prevalence, incidence, remission and mortality. An example of a search strategy is given below.

c) The search can be limited to the following fields by adding a slash and a two letter code:

- Epidemiology (ep)
- Mortality (mo)

- Complications (co)
- Therapy (th)

Table 7.1 An Example of a Medline Search Sequence

Search	Search	Results
#1	Depression/ep	2120
#2	Prevalence and depression/ep	2120
#3	Incidence and depression/ep	2120
#4	review and depression/ep	226
#5	Australia and depression/ep	55
#6	Australia and review and depression/ep	4

For example: A search for the complications of diabetes would be entered as: "diabetes/co". You may also limit the search results to the following selections in the screen:

- English language
- Human subjects

or by type of study:

- Meta-analysis
- Clinical trials
- Longitudinal studies
- Case-control studies
- Consensus development conferences, including NIH guidelines
- Meeting reports
- Monographs
- Practice guidelines
- Technical reports

From the abstracts retrieved from Medline, select the most relevant papers and try to locate the full papers. Full-length papers from some journals are freely available via the Internet (e.g. BMJ at www.bmj.com) while others can be ordered via the Internet but this tends to be rather expensive. If you have a good library at your disposal you will find yourself spending a lot of time in front of a photocopier!

4) Health facility data

In the majority of cases, routine data on consultations by diagnosis will not be very helpful in estimating burden. Facility based data — unless the coverage of the health system is nearly complete — will always be based on biased samples of the disability present in the community. Likewise, hospital deaths are unlikely to be useful due to the same problems of selection bias.

Examples of conditions that can be estimated from hospital data if there is good coverage and data are available include: perinatal and maternal conditions, meningitis, stroke, myocardial infarction, surgical conditions and the more serious injuries. A common problem in hospital admission databases is to distinguish between episodes and people affected. If the database does not contain a unique identifier much more difficult probabilistic matching techniques need to be applied to determine persons who have been admitted more than once. Counting episodes of care rather than persons admitted could lead to overestimation. Another potential problem in hospital databases is that they are commonly used to determine the flow of resources from government to hospitals. This may lead to certain diagnoses and procedure codes being favoured over others if they increase a hospital's reimbursement. Comparisons over time thus become distorted and codes that would indicate more serious disease may be overused.

There may be a wide range of values for the measures of interest. Choose the papers/data sources on the basis of study design quality and the relevance of the study population to the target population. Sometimes the disparity in the results between different studies is so large that the choice of values will result in large differences in the potential estimates. When such profound conflicts between studies/data sources arise the recommended approach is the following:

Table 7.2 Summary of Data on the Prevalence of Asthma in Australia

Author	Place of study	Year of study	Age group	Wheeze last 12 months	Wheeze last 12 months + AHT
Prevalence					
Bauman (1992)	Sydney	1990	5-12	22.4%	
Bauman (1992)	Eastern Australia	1990	5-12	19.5%	
	Melbourne			18.5%	
Peat (1994)	NSW 2 sites	1982	8-10		4.5% - 6.6%
		1992		23 - 27%	12.0% - 9.4%
Peat (1994)	NSW 2 sites	1991-92	8-10	22 - 26%	11.3% - 9.5%
Peat (1995)	NSW 7 sites	1991-93	8-11	24 - 38%	7.1% - 13.0%
Robertson (1992)	Rural Victoria	1990	7	23.6%	
	Melbourne	1990	7	23.1%	
			12	21.7%	
			15	18.6%	
Pearce (1993)	Adelaide & Sydney	1991	12-15	29 - 30%	
Robertson (1998)	Melbourne, Perth, Sydney, Adelaide	1994	6-7	24.6%	
			13-14	29.4%	
Leung (1994)	Melbourne	1991	<20	33.9%	
			20-40	11.2%	
			>40	12.5%	
Woolcock (1987)	Busselton	1981	18-55		5.4%
Bauman (1992)	Eastern Australia	1990	33-41	0.2	7.0%
Peat (1992)	Busselton	1990	18-55		6.3%
Male-to-female ratio					
Gergen (1988)	USA	1976-80	children		1.4 : 1
Burrows (1991)	USA	1971-84	adults		1 : 1.8
Remission					

Bronnimann (1986) USA	1972-83	Mean follow-up: 9.4 years
	<10	35%
	10-19	65%
	20-29	30%
	30-39	15%
	40-49	6%
	50-59	18%
	60-69	30%
	70-79	26%

Actions to be undertaken:

- 1) Organize the study results in a way that facilitates easy comparison of the results. For example, Table 7.2 has ordered the prevalence studies of asthma in Australia by age and also lists a few US studies on the sex differential in the prevalence of asthma and age-specific remission rates.
- 2) From the summary table choose the highest quality studies from populations similar to the target population. If there is not a study that you think could be credible, choose a value that makes sense based on the studies published and on your experience. If there is no information to support your experience, go to an expert panel procedure.

Output:

- 1) A set of estimates coming from the most valid and representative sources.

Questions to be addressed:

- 1) Are you sure that the data selected are the most reliable and representative?
- 2) Is the reason why other papers/data sources have been excluded clearly explained?
- 3) Which estimates are missing? Why could they not be found in Steps # 1 and # 4?

7.5 STEP 5 CHECK DATA CONSISTENCY AND QUALITY

INTERNAL CONSISTENCY: USING DisMod

Once all available data on a disease have been collated, the first task is to assess whether the observations are all internally consistent.

Analysing whether disparate sources of information on prevalence, incidence, and mortality are consistent with each other requires the aid of a computer. DISMOD is a computer software program developed for the GBD that allows the user to check if a set of assumptions on incidence, prevalence, remission, case-fatality rates and observed mortality numbers are consistent with one another. The use of DISMOD is described in detail in Chapter 8.

DISMOD allows you to change the number and size of the age groups for input and output variables as you require. This is particularly useful when your epidemiological parameters are listed in age groups that differ from the age groupings in which you want to present YLD results. With practice you will develop a feel for the relationship of the different parameters in DISMOD. In general, changes in incidence will have a major influence on prevalence but not much on mortality (unless case-fatality is very high), remission impacts particularly on duration and prevalence but less on mortality while changes in case-fatality rate have a big impact on death figures but not much on prevalence and duration.

Table 7.3 Relationship between Input and Output Parameters in DisMOD

Input \ Output	Output	Prevalence	Mortality	Duration
Incidence	↑	↑↑↑↑	↑	no change
Remission rate	↑	↓↓	↓	↓↓
Case-fatality rate	↑	↓	↑↑↑↑	↓

Usually, not all available data will be consistent with each other. Judgment is then required to choose which data source is more likely to represent the reality in a particular community. No hard and fast rules can be created to define how to choose one data source over another.

ADJUSTING FOR NON-REPRESENTATIVENESS

The only available data on a disability may be clearly biased — *e.g.*, skin test data on tuberculosis may only be available for one region which is known to be much more economically advanced than the rest of the country. In such situations, the estimates of incidence and duration must be adjusted to take into account the expected variation in the epidemiology in the community. For instance, you may consider scaling up the prevalence based on observed differences in TB mortality between the region studied and the whole of the country. If necessary, you can also take into account that access to treatment is greater in the study area and thus assume that case-fatality rate in the whole population is greater. DISMOD will help to examine different scenarios

When *ad hoc* adjustments must be made, the logic underlying these adjustments should be presented, justified, and subjected to consultation with national and — as necessary — international experts.

PLAUSIBILITY

Estimates of disability incidence, duration, age of onset, and severity class must be plausible.

Plausible estimates are estimates that are reasonably consistent with the known epidemiology of the disease and consistent with independent observations of the same phenomenon. For example, does the estimated average duration of the disease tally with what is known about the disease in the literature? Another example of a plausibility check is to make sure that estimates of infertility due to septic abortions, obstructed labour or sexually transmitted diseases do not exceed the total observed secondary infertility rate.

It is very easy to make mistakes when manipulating lots of different variables. Therefore, always recheck your calculations and let them be scrutinised by others before drawing conclusions. It is often easy to think of a possible explanation for an 'unusual' finding luring you into thinking that you have made an important discovery while all along it was a mistake in one of your spreadsheets.

EXPERT CONSULTATION

Consultations with experts to scrutinise the estimates of incidence, prevalence, age of onset, and duration of disability are essential for a NBD study to gain credibility.

The consultation process will uncover unused data sources, identify computational and analytical mistakes and broaden participation in the study. The latter is an important component of building group-ownership for the exercise.

Expert consultation can be organized through face-to-face interviews, small group meetings, or a larger review meeting. The most appropriate mechanism will depend on local circumstances. Consider meeting several times with each group of experts. At a first meeting you can explain the purpose of the NBD study, emphasise the important role of experts to develop plausible estimates and ask experts to advise on available data sources for conditions within their area of expertise. You may need a second meeting to obtain expert advice on your disease diagram or missing parameters. At a final meeting you can present your DISMOD and YLD calculations and step by step discuss all the assumptions and transformations of data you have made.

Based on the national (and possibly international) expert input, estimates of disability incidence, duration, age of onset, and severity distribution should be revised. It is important at any subsequent steps of revision to use DISMOD to re-analyse the relationships between incidence, prevalence, remission, duration, cause specific or cause-attributable deaths and case-fatality or relative risk of death.

Output:

- 1) A consistent set of epidemiological data.
- 2) All the necessary data to calculate YLD for the burden of disease and injury.

Questions to be addressed:

- 1) If data from the same source are not consistent, the question should be: how reliable is the data source?
- 2) If DISMOD produces estimates that are not consistent with available information, this may mean that the available set of data is not consistent with the natural history model developed for this disease. Which is more reliable?
- 3) If DISMOD provides right away a consistent set of epidemiological estimates based on different sources, the question should be: Is the disease so homogeneously distributed in the population, so stable and well-known as to explain this happy result or could this be the result of chance?
- 4) Do the numbers make sense? Are results consistent with the published literature? Does the expert panel agree with these numbers?

7.6 STEP 6 APPLY DATA TO CALCULATE YLD.

Actions to be undertaken:

Simply enter the appropriate DISMOD output into a YLD spreadsheet template as described in Chapter 11.

Output:

The burden of the disease measured in DALY units.

Questions to be addressed:

- 1) Was the epidemiological assessment well done?
- 2) Does the uncertainty of the assumptions made result in large variability in the burden outputs? (Sensitivity/uncertainty analysis)
- 3) Are experts and opinion leaders supporting this epidemiological assessment?
- 4) Does the result make sense when compared to other accepted sources of information? (e.g. global and regional burden, local published data, etc)

8. DISEASE MODELLING USING DISMOD

8.1 BRIEF OVERVIEW OF DISEASE MODELLING

The starting point for YLD calculation is to determine the number of new cases of a particular condition in the year of interest and to estimate or model disease duration, and in some cases, progression through disease stages or severity levels. While for some conditions, it is possible to derive numbers of incident cases directly from disease registers, routine databases or epidemiological studies, for most only prevalence data are available. Additionally, it is often necessary to estimate average duration from a knowledge of the rates of remission or death for a particular condition. A special tool, called DISMOD, is available, that allows us to supplement available data with expert knowledge, and to force the estimates to be internally consistent. The underlying model used by DISMOD is summarised in Figure 8.1.

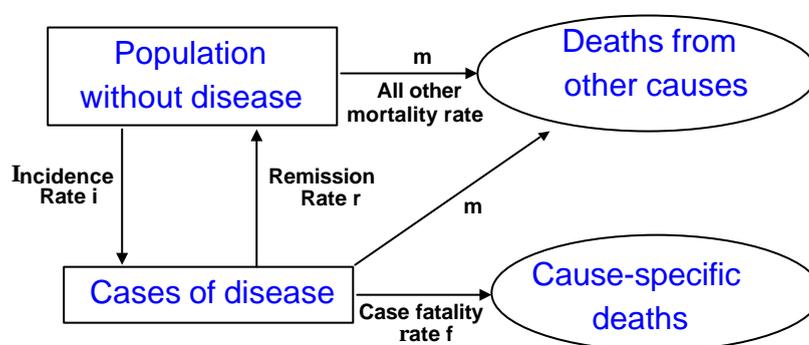


Figure 8.1 The Basic Disease Model Underlying DISMOD

A disease process can be described by a number of variables, like incidence, prevalence, remission, case fatality, duration, and mortality. These variables differ in nature: for example incidence and case fatality express transition from one state to another, while prevalence is a proportion. All of these variables can, in principle, be observed, but with a different degree of difficulty. Mortality, for example, can be relatively easily observed, but, depending on the disease, can be misclassified. Nevertheless, many countries have cause of death statistics, that usually constitute the most reliable source of disease data.

Observing prevalence and incidence is usually much harder than mortality. Data collection, when done, is often limited in time and geographical area. Problems of case definition abound. Not surprisingly, data are frequently incomplete, and when present, their validity may be in doubt. In particular, given the different nature of the disease variables and the differences in the way the data are collected it is inevitable that the observations are internally inconsistent. For example, when more incident cases than mortality are missed, the observed incidence will be too small for the observed mortality.

To get around these problems we exploit two kinds of additional knowledge. The disease characteristics, such as remission, case fatality, and duration, may be relatively constant between countries, and known from other countries or clinical studies. Supplementing observed data with such expert knowledge may help to overcome lack of data.

In addition to expert knowledge, we use the fact that a disease process causally links the various epidemiological variables. Any prevalent case must at some earlier point have been an incident case, and will go on to either recovery, death from the disease or death from other causes. A disease model that explicitly describes these causal pathways allows us to infer missing data if existing data are sufficient. For example, if incidence is not known, but mortality, case fatality and remission are, then incidence can be calculated

using such a disease model. Moreover, the results from the disease model are internally consistent by definition.

There are three common ways in which DISMOD is used:

- where we know prevalence but not incidence for a disease, we can use DISMOD to find a set of incidence rates by age that match observed prevalences, given estimates of remission rates and cause-specific mortality risk derived from population data or epidemiological studies;
- to check whether available data for a condition are consistent with each other, for example, if we have separate estimates of incidence and prevalence for the condition;
- to calculate average duration of incident cases, needed to calculate YLD for a condition; and
- to extrapolate estimates in desired age categories from epidemiological data presented in different age categories.

While different assumptions regarding remission and case fatality affect the age distribution of incident cases and YLD estimates, total YLD are relatively insensitive to these assumptions if matched to a fixed prevalence distribution. This is because YLD estimates are proportional to incidence multiplied by duration, which approximately equals the prevalence of the condition. In other words, for most conditions, the combination of incidence, case fatality and remission rates (and thus derived durations) used in the YLD calculations makes relatively little difference to total YLD across age groups assuming the same prevalence figures are used as the basis. The effect of discounting complicates this, however, with low incidence and long duration conditions being more discounted than high incidence but short duration conditions.

For the Global Burden of Disease study 1990 a software program called DISMOD was developed for the purpose of supplementing observations with expert knowledge and producing internally consistent estimates of disease epidemiology. Based on the experience with this tool a new one has been developed (called DISMOD II) that has a number of additional features to enhance usability, but its purpose is essentially the same. For clarity, we now refer to the original DISMOD program as DISMOD I. In order to use these tools, you must understand a number of concepts used to describe 'risk' in epidemiology.

8.2 RATES, RISKS AND PROBABILITIES

Working with a variety of data sources, it is important to clarify some basic definitions of rates, risks and probabilities. There is no one standard set of definitions. Different dictionaries define rates, risks and probabilities in different ways and these terms are used inconsistently in the epidemiological literature.

We clarify and define these terms using the example of a cohort study. Imagine a cohort of 1000 patients with smear-positive tuberculosis who are followed up over a period of 5 years. Three things can happen to individuals in the cohort: they can die, get better, or remain with smear-positive tuberculosis.

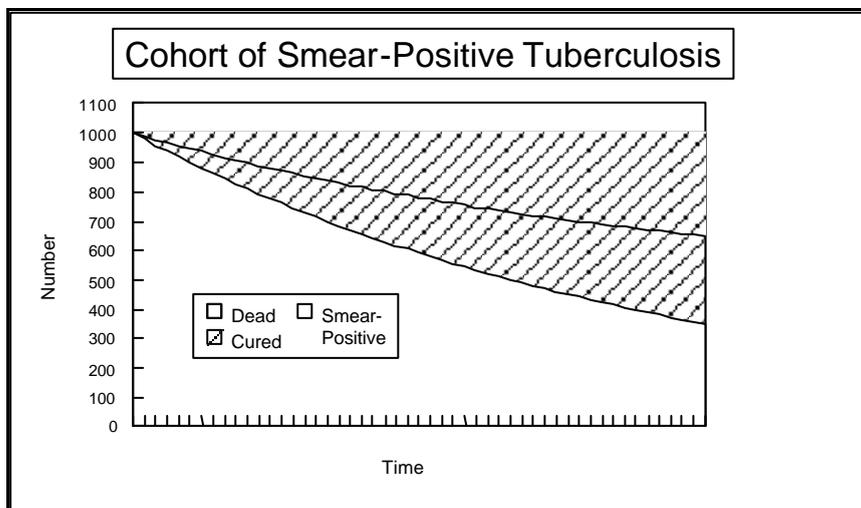


Figure 8.2 Evolution over Time of a Cohort of People Smear-Positive for Tuberculosis

Figure 8.2 shows the evolution of the cohort over the five year period. With time, an increasing proportion of the cohort is cured or dead. Let us define three variables: $D(t)$ is the number of the cohort dead at time t ; $C(t)$ is the number cured in the study at time t ; and $P(t)$ is the number of smear-positive tuberculosis cases left at time t . By definition, $P(0)$ is the number of individuals in the cohort at the beginning of the period of observation, which in our example is 1000.

The people in P face at any time two risks simultaneously: one is to die and one to be cured. The number of people still in cohort P at time t is determined by the combination of these two risks. How many people are dead at time t is determined by the risk of death, but also by the risk of being cured. When two or more risks are simultaneously determining the outcome, these risks are said to be 'competing'.

CONDITIONAL PROBABILITIES OF CURE AND DEATH

The proportion of the original cohort dead at a given time is called the cumulative death rate, proportion, or probability:

$$D(t)/P(0)$$

Likewise, the cumulative cure rate or probability would be:

$$C(t)/P(0)$$

These measures of the death and cure process are called conditional probabilities. They are conditional because the probability of being cured after 5 years must depend on the probability of dying after 5 years. These probabilities are easy to measure from a cohort study, but because of the conditional nature they are awkward to use in modeling, because when one probability changes all the competing probabilities change as well.

POPULATION CURE AND DEATH RATES

Demographers and researchers using vital event registries often report population rates, which are the number of events (death or cure) in a time period divided by the mid-period population. Age-specific death rates are population rates—deaths in a year divided by mid-year population—for one age-group.

In the cohort of tuberculosis patients, we could calculate the analogous population death rate or cure rate over the time period t to be:

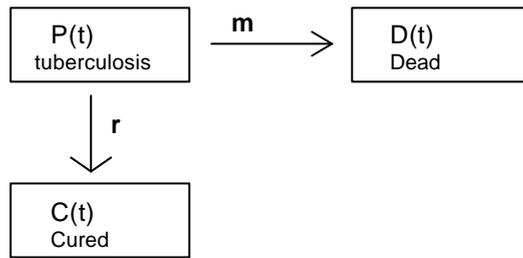
$$\frac{D(t)}{P(t/2) + C(t/2)}$$

While such a rate is rarely calculated for cohort studies, population rates are perhaps the most common measures of mortality and morbidity incidence.

INSTANTANEOUS RATES OR HAZARDS

When disease processes are modeled, it is common to make use of mathematical equations that include rates. By definition, these rates are instantaneous rates of cure or death, also commonly referred to as 'hazards', 'forces' or 'densities'. The main characteristic of hazards is that they describe risks continuously.

For the tuberculosis cohort example, we must first develop a simple model before calculating instantaneous rates of cure and death:



The three boxes represent the three possible outcomes: remaining with tuberculosis, death, and cure. m is the instantaneous rate at which individuals with tuberculosis die; r is the instantaneous rate at which individuals with tuberculosis are cured.

Using differential calculus, one can solve a set of equations that define how many individuals are in each box at each moment: $P(t) = P(0)e^{-(r+m)t}$

$$C(t) = \left(\frac{r}{r+m} \right) P(0) (1 - e^{-(r+m)t})$$

$$D(t) = \left(\frac{m}{r+m} \right) P(0) (1 - e^{-(r+m)t})$$

The rates m and r are the instantaneous death and cure rates, respectively. Instantaneous rates can be denominated in any units such as days, months or years. An everyday analogy to this are bank interest rates. When a bank offers a compound interest rate of 5%, it is offering an instantaneous interest rate. A 5% instantaneous interest rate will give an annual yield higher than 5%.

In epidemiology, instantaneous rates are also calculated. It can be shown that events divided by the number of exposure-years is the same as the instantaneous rate (as long as the instantaneous rate is constant over time). Such instantaneous rates or hazards in epidemiology may also be called 'forces' or 'densities', such as an 'incidence density' or 'force of infection'. Note that hazards, as opposed to probabilities, can be greater than 1: they range from 0 to ∞ .

ABSOLUTE PROBABILITIES

Some epidemiologists calculate the probability of being dead or cured at the end of time period assuming that all other rates are zero. These are absolute probabilities of cure or death as opposed to conditional probabilities.

A common example of an absolute probability is the cancer epidemiologist's calculation that the probability of a women dying from breast cancer by age 75 is 1 in 10. Ten percent of women do not actually die from breast cancer, because there are other causes of death decreasing the exposed population over time. For the tuberculosis cohort example, the equation for calculating an absolute probability of death at time t is simply:

$$\text{Absolute probability of death} = 1 - e^{-mt}$$

CALCULATING INSTANTANEOUS RATES FROM COHORT DATA

From a longitudinal epidemiological study, instantaneous rates or hazards can also be calculated. If we assume that the hazard has remained constant over time, it can be shown that the number of events in the population divided by the number of exposure-years (or person-years) is the same as the hazard.

Population rates are perhaps the most common measures of mortality and morbidity incidence. When the time period is not too long (for example the customary 1 year) and the death hazard is not too high, the mid-

period population is a reasonable approximation of the number of person-years. Therefore, these population rates can, under these circumstances, serve as a reasonable approximation of hazards.

8.3 DISMOD

DISMOD is based on a simple disease model, which describes the disease by an illness-death process with only one diseased state (see figure 8.1). There are four states: susceptibles (or non-diseased); cases (or diseased); cause specific deaths; and deaths from other causes.

Susceptibles become cases at an instantaneous rate i ; cases go back to being susceptible at remission rate r ; both susceptibles and cases are subject to a general instantaneous mortality rate m ; and the cases are subject to the instantaneous case-fatality rate f .

The set of differential equations implied in Figure 8.1 can be solved explicitly or computationally.

8.4 DISMOD I

The original version of DISMOD (DISMOD v1.0. President and Fellows of Harvard College. All rights reserved. 1994) is available from the Burden of Disease Unit, Harvard University. For downloading the software visit, <http://www.hsph.harvard.edu/organizations/bdu/dismod/index.html>

Installation instructions are also provided on the website. DISMOD I can be run under Windows 3.0, Windows 95, 98 or 2000 and Windows NT. If installing it on a Windows NT or Windows 2000 machine, it is necessary to create a folder called C:\WINDOWS\SYSTEM on the C drive. This folder is required in order to run the utility ENABLE.EXE which enables DISMOD I for use. The program will only run if it is installed in a directory C:\DISMOD.

DISMOD I takes a user-defined set of incidence, remission and case-fatality rates combined with either user-defined or regional general mortality rates to follow a cohort over time. The inputs to DISMOD I are instantaneous rates and the outputs are prevalence rates, population incidence rates, durations, ages of onset and cause-specific mortality rates. DISMOD I does not have facilities to print output or to transfer it to other databases or spreadsheets.

In order to model a disease in DISMOD I, it is necessary to define the population age structure and general mortality rates. These data are stored in region datasets in a folder called REGIONS in the DISMOD folder on the C drive. DISMOD I comes with predefined region data files for the 8 regions used in the GBD 1990. You can define your own region files using a text editor to create a text file containing total mortality rates (as a rate per person) by single year of age for ages 0 through to 90 followed by population numbers (in thousands) by single year of age for ages 0 through to 90. Examine one of the GBD region files to see the required format. Save your text files for your male and female populations the REGIONS folder with names of the form ppp_M.DAT and ppp_F.DAT.

When you open DISMOD I, you can choose a user-defined region in the first window, and when the DEFINE REGION window opens, specify region name ppp (the acronym used for your DAT files).

RUNNING DISMOD I

When you run DISMOD I, you can specify a new disease or open a file (with an extension .MOD) in which a disease model has been previously stored. The first window also allows you to define (or redefine) the region (population and mortality structure) that you wish to use, a disease name and sex.

The second window, shown in Figure 8.3 allows you to enter incidence rates, remission rates and EITHER case fatality rates or relative risks of mortality for people with the disease. All these rates are instantaneous rates. If you have estimates of annual incidence rates, then you may need to vary the instantaneous incidence rates (which will be slightly higher at older ages) until you get a match on the output estimates of average annual incidence rates.

The risk of mortality for cases may be specified either as a case fatality rate (an instantaneous rate of mortality for cases, where the denominator is the number of cases) OR as a relative risk of mortality compared to the background mortality for all other causes at that age. For example, a relative risk of 3 would

instantaneous incidence rates and see what the resulting prevalences are. You then iteratively change the incidence rates until you get a match of the calculated prevalence rates with the known prevalence rates. In many cases, it is not possible to exactly match a set of prevalence rates which vary by age without introducing large and implausible variations in incidence by age. In this case, it is necessary to use your knowledge of the natural history of the disease to develop a set of incidence and prevalence rates with plausible and smooth age patterns which provide a reasonable fit to the available data.

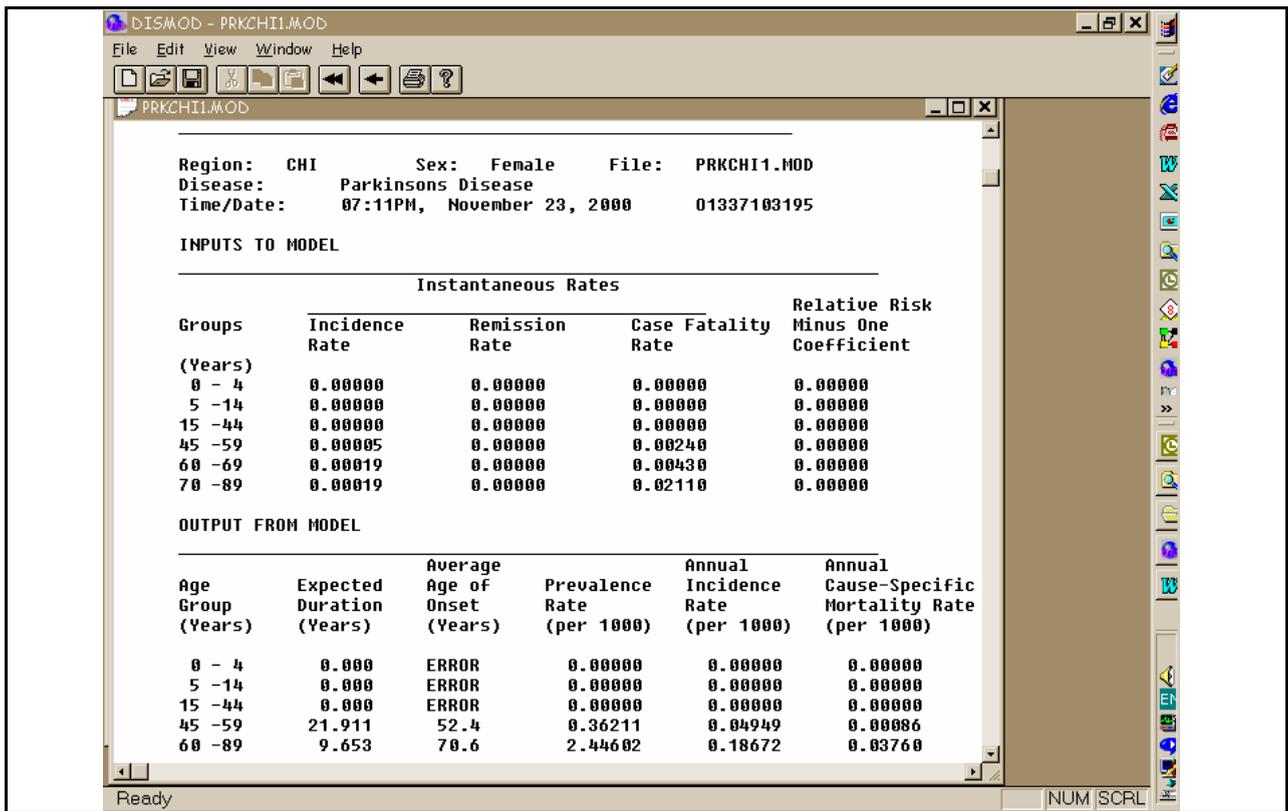


Figure 8.4 Output Window for DISMOD I. A Disease Model for Parkinson's Disease Based on Estimated Incidence, and Case Fatality Rates and Zero Remission Rates.

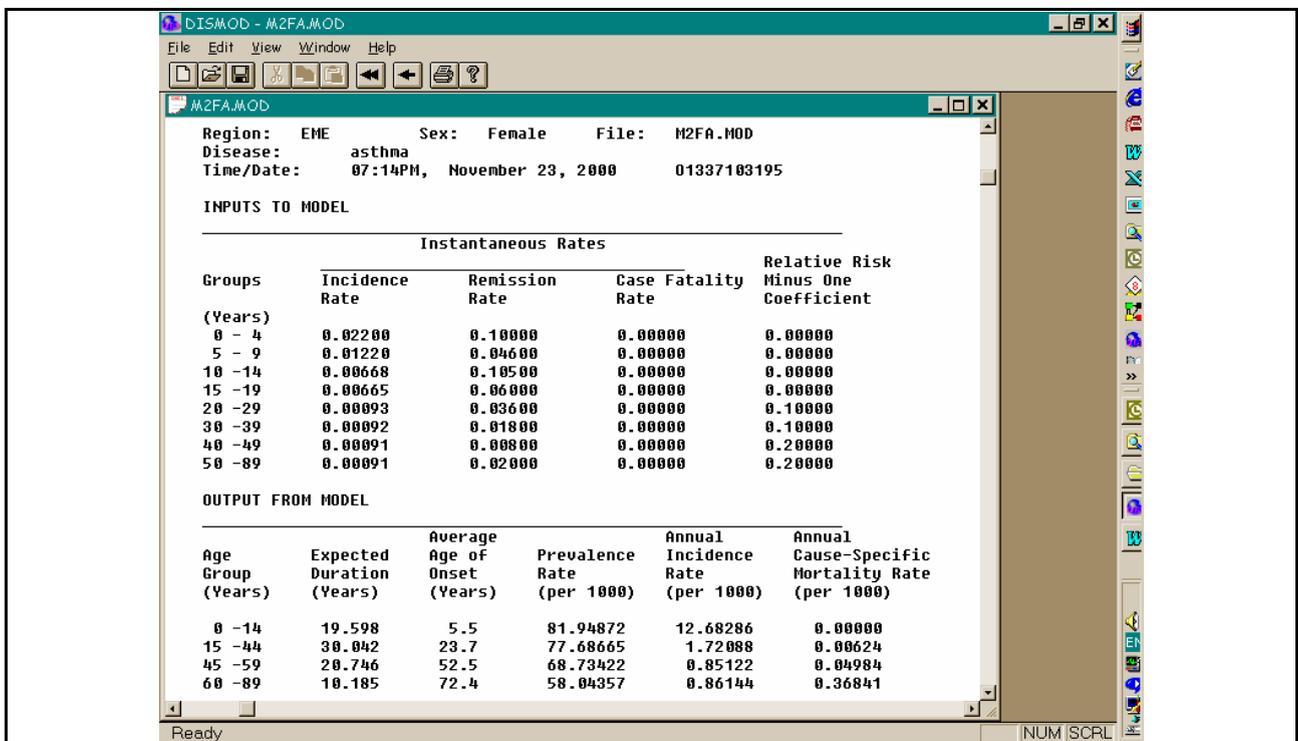


Figure 8.5 Output window of DISMOD I. A Disease Model for Asthma Based on Estimated Prevalence, Remission Rates and Cause-Specific Death Rates.

Figure 8.5 shows an example of the use of DISMOD to match available prevalence data, in this case for asthma. The remission rates entered in the model were based on measured age-specific proportion of cases remitted after a mean period of 9.4 years in a longitudinal study and the instantaneous remission rates calculated using the formula

$$\text{Instantaneous remission rate} = -\ln(1 - \text{Total fraction remitted in period } t) / t$$

Relative risks for asthma mortality were chosen to give an approximate match to observed asthma mortality rates. For many diseases, it is not possible to use cause-specific mortality data for the population to estimate case fatality or relative risks for cases. These rates specify the total excess risk of mortality, and for many diseases, cases have a raised risk of mortality for causes other than the cause being modelled. These excess risks must also be included in the model to obtain correct estimates of durations. Thus for example, people who have had a stroke not only have a risk of dying from stroke but also an excess risk of dying from coronary heart disease (because of common risk factors) and perhaps also from injuries and other causes (because they may have physical and cognitive disabilities that increase risk of injury). In the case of stroke, the cause-specific mortality rates may be up to twice the mortality rate due to stroke as main underlying case derived from vital registration data.

8.5 DISMOD II

DISMOD II has been developed to provide a full graphical interface, database storage capabilities and substantially enhanced features and options. It was developed by Jan Barendregt of Erasmus University in the Netherlands under contract to the World Health Organization. It is a very new software product and is still undergoing testing and refinement. It is being used as an analytical tool in the WHO Global Burden of Disease 2000 project.

Unlike DISMOD I, which used finite difference methods to “solve” the disease model, DISMOD II implements an exact solution to the underlying differential equations. As well as calculating solutions when the 3 hazard rates are provided as inputs, DISMOD II allows other combinations of inputs such as prevalence, remission and case fatality. In these cases, DISMOD uses the ‘downhill simplex method’ to fit hazards such that the model reproduces the available input variables.

DISMOD II has a range of advanced features including sensitivity analysis, uncertainty analysis, the ability to give different weights to the various inputs, and the ability to smooth inputs and specify age patterns for outputs.

INSTALLING DISMOD II

DISMOD II can be downloaded from the WHO website at <http://www.who.int/evidence>.

Once you have downloaded the installation files, double click on SETUP.EXE and you will be guided through the installation process. DISMOD II will be installed in the PROGRAM FILES folder on the C drive by default.

DISMOD II has help notes which include a tutorial. All new users, including those with experience of DISMOD I, are strongly recommended to go through the tutorial. The navigation chapter is something you might either read or get familiar with by using the context-sensitive help. The options chapter, in particular the topics on Calculation and on Smoothing and fitting, explains, in the course of describing these options, a lot of the inner workings of DISMOD. Those users determined to really understand DISMOD II and its possibilities and limitations will at some point have to read the technical background.

RUNNING DISMOD II

All data and results in DISMOD II are taken from and stored into databases, which use the MS Access '97 format. After starting DISMOD II the first thing to do is to open an existing database or create a new one using the ‘Dataset’ menu. DISMOD II operates on a disease by disease basis, and when a dataset is open the ‘disease identification’ section of the main form shows name and ICD codes of the current disease. Below the ‘disease identification’ section the database navigator buttons are visible: with these buttons the user can scroll through the database disease by disease, delete existing diseases, or add new ones.

The two main tasks to be performed using DISMOD II are respectively, data input, and processing the input data to produce internally consistent epidemiological estimates that can be saved as output. The main form reflects these tasks in an 'input' and a 'process and output' section.

But before we describe how these tasks are performed we would like to draw attention to the 'show notes' button at the bottom of the main form. Clicking this button will open up a window where users can type in comments and notes, which together with the disease data will be stored in the database. Proper use of this facility can help to keep track of where input data has come from, which expert knowledge has been added, etc.

It is strongly recommended to use this facility.

THE MAIN WINDOW

After starting up DISMOD II will just sit on your screen showing its Main window with almost all buttons and menus disabled. To get going you first have to open the data set 'Example', which belongs to the collection 'Local'. Choose 'Data|Collection|open' in the data menu, select 'Local' and click OK. The Data set window opens showing a list of available data sets, where currently only the 'Example' data set is present. Select it by clicking on it, and choose the 'Open' button. The Data set window will close, and in the Main window a disease name (Breast cancer) will appear in the Name field, and most of the buttons will become enabled.

The DISMOD data are organized in data sets. A data set is defined as a region or country with a population of which you want to describe the burden of disease. For example, in the Global Burden of Disease 1990 study regions as 'Latin America and the Caribbean' and 'Sub Saharan Africa' would have been considered a data set. Also the Mexican and Australian country studies would each be a DISMOD data set.

A data set contains:

- Total mortality rates by age and sex.
- Numbers of people by age and sex.
- Data for as many diseases as you want to describe.

Data sets themselves are organized in Collections. A collection consists of data sets that you for some reason want to group together. For example all data sets of the region 'Established Market Economies' might be grouped in a collection. Collections facilitate the management of large numbers of data sets.

The first step is to open an existing collection and select a dataset, or to define a new collection and/or dataset. This is explained further below. Figure 8.6 shows the main window of DISMOD II after a collection called GBD 2000 and a dataset called Amro A have been selected, and a disease model called 'Rheumatoid Arthritis' has been selected which is already in the dataset.

A DISMOD data set consists of as many diseases you want to describe. A disease must have a disease name (visible in the Name field), and optionally has an ICD code. If you want to do anything useful, a disease also has input data. There is a list of potential input data in the 'Input variables' section. For breast cancer the Incidence, Remission, and Mortality variables are checked, meaning that these inputs are present (only for women).

A note for users of the first DISMOD version: if no input for a variable is present this does not mean it is put to 0. It simply is not there.

Technically, each disease is a record in the database. This characteristic is emphasized by the Navigation buttons immediately below the disease Name and ICD code fields. With the Navigation buttons you can scroll through the data set disease by disease. Put the cursor over a specific button and in a few moments a tool tip will appear describing its purpose. Find the one that says 'Next disease' and click the button. The next disease turns out to be Ischaemic Heart Disease (IHD), with input variables Prevalence, Remission, and Mortality checked. Clicking a few more times will show that the other diseases in the data set Example are stroke (CVA) and dementia, each with different combination of input variables.

As an alternative to using the Navigation buttons you can use the 'Diseases|goto' command of the Diseases menu. This will produce a scrollable list of all diseases in the data set, where you can select the one you want.

DATA INPUT

There are 7 different possible input variables for DISMOD II . Four are hazards: incidence, remission, case fatality, and mortality. Prevalence is a proportion, duration is expressed in years, and 'RR Mortality' stands for the relative risk on total mortality. This latter input is useful for diseases that carry a considerable excess mortality from other causes of death, like for example diabetes, which causes mortality from cardiovascular disease.

The option of inputting durations has only been implemented for relatively short durations, where the durations at a particular age do not depend on the disease transition rates at older ages. It is not recommended to use durations as inputs in other cases.

Generally, three input variables are needed to calculate the output. When less than three variables are available, additional information, based on expert judgement, will have to be added during the processing of the data. When more than three input variables are available the model is over-identified, which means that there does not necessarily exist a solution consistent with all the inputs. Again expert judgement will have to decide which subset of 3 inputs will be considered best, or one can give different weights to the various inputs and all will be used in the analysis.

The 'input' section of the main form shows 7 checkboxes, one for each of the input variables. When input for that particular variable is present its box is checked, scrolling through the database shows different combinations of inputs. Also in the input section is a button 'Edit/Add Input'. Clicking this button will present the list of input variables. Selecting one and clicking 'OK' will open up the input form. Figure 8.7 shows an example where the incidence data for rheumatoid arthritis has been selected.

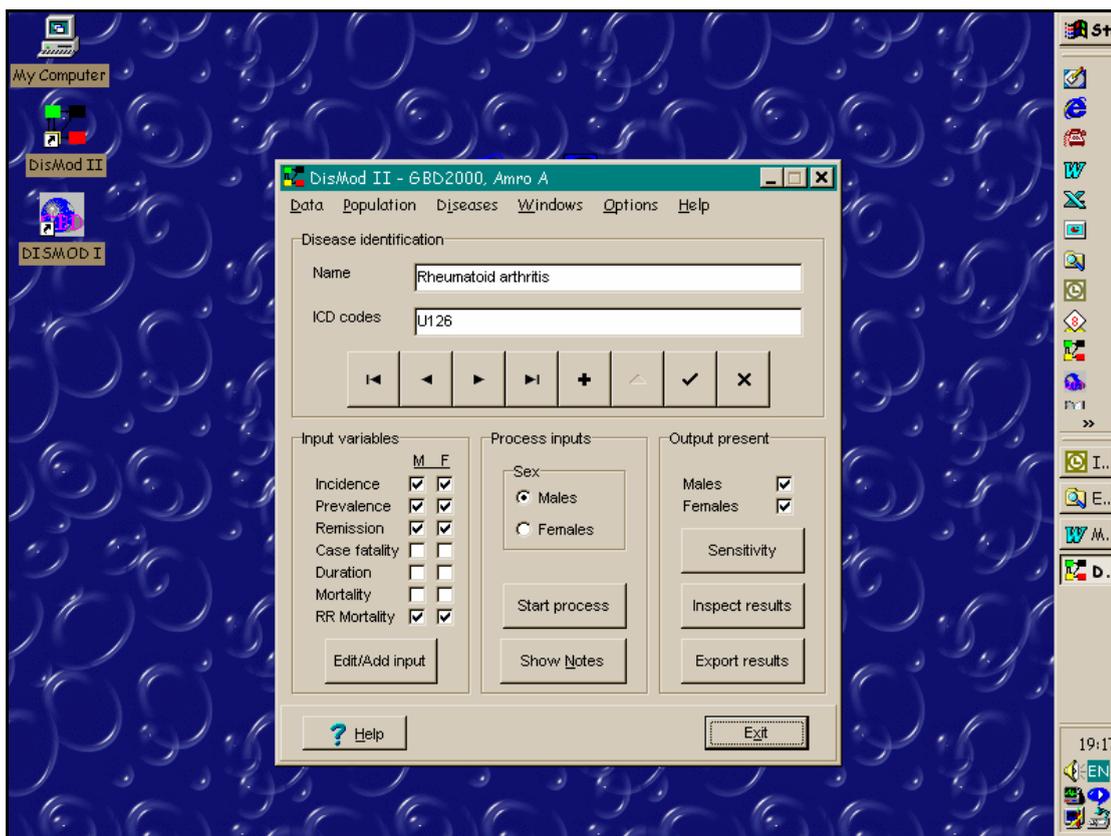


Figure 8.6 Example of Main Window for DISMOD II after a Collection and Dataset Have Been Opened.

In the input form the first task is to define an age group subdivision. Internally DISMOD II uses 1-year age groups: 0,1,2...up to the highest open-ended age group in the dataset, which can range from 65+ to 110+

Within this range any age group subdivision can be defined, and the subdivision may differ between input variables, and for a given input variable may differ between men and women. After defining the age groups, data can be typed into the input table. After typing in the values the user has to select 'Save' to commit the data to the database, and 'Close' to return to the main form.

PROCESSING THE INPUT

The 'process data and output' section of the main form contains a 'Process' button, which when clicked will bring up the process form. On this form an 'actions' section presents all the options to produce internally consistent estimates from the inputs: adjusting input data, setting calculation options, calculating the model, and inspecting results. Input and output can be inspected in both graphical and tabled form. When the user is satisfied with the output, clicking the save button will commit the results to the database.

As a rule, DISMOD needs at least three input variables to be present to be able to calculate the disease epidemiology. The exception to the rule is when you specify Case fatality and Relative risk on total mortality as inputs for the same disease: these inputs essentially concern the same variable, and therefore count for one. You can specify more than the minimum of three inputs

For the rheumatoid arthritis example shown above, incidence, prevalence, remission, and Relative risk are available, so there is more than sufficient input. To calculate the rheumatoid arthritis results, click the 'Process data' button. Two additional windows will open, one showing a lot of buttons (the Process window) and one showing a graph (Figure 8.8). The graph shows three lines, one for each input variable, with their names in the Label section followed by '(i)' for 'input'. The remission input is the yellow line at the top. Prevalence is the green line, and incidence is the blue line. Both these lines have a 'stepped' look: they were entered in 5-year age groups, which were interpolated to the 1-year age groups DISMOD uses for its calculations. The RR for mortality is not shown on the graph but can be added by clicking on the 'Options' button below the graph, highlighting 'RR Mortality' and clicking the box 'Visible' and 'Right axis'.

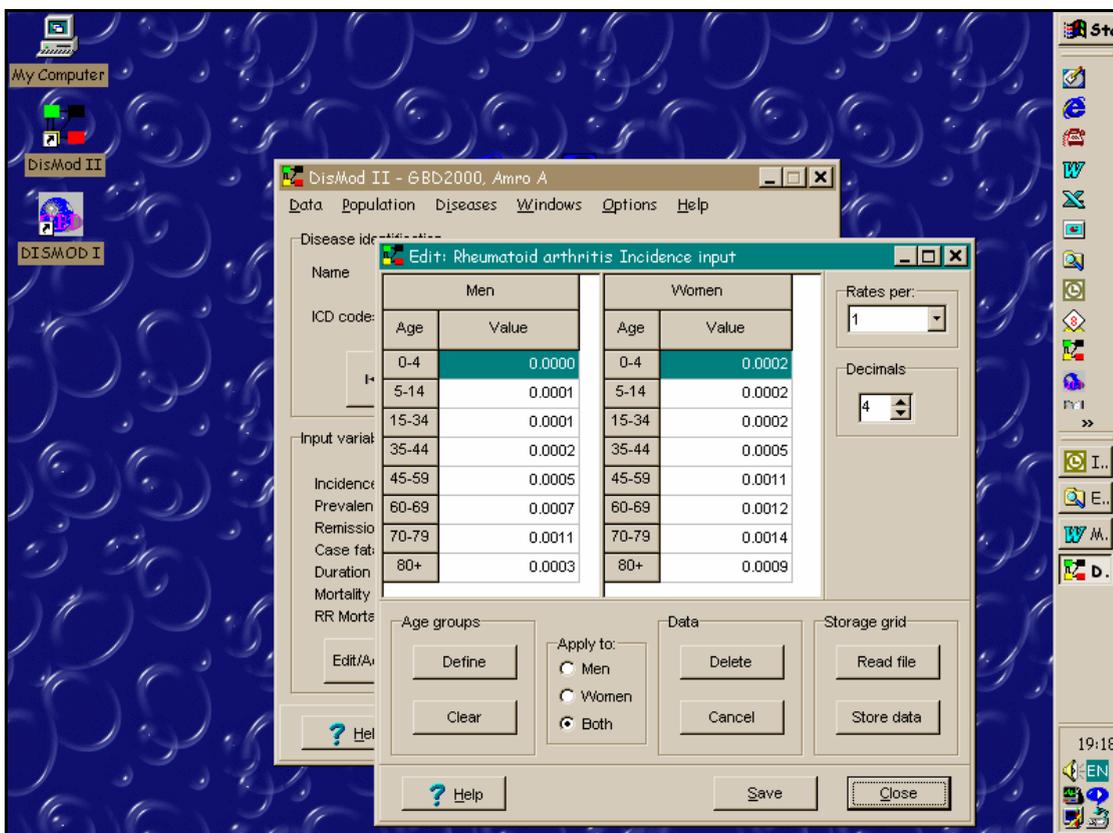


Figure 8.7 Example of DISMOD II Window for Editing Input Data (Incidence Hazards).

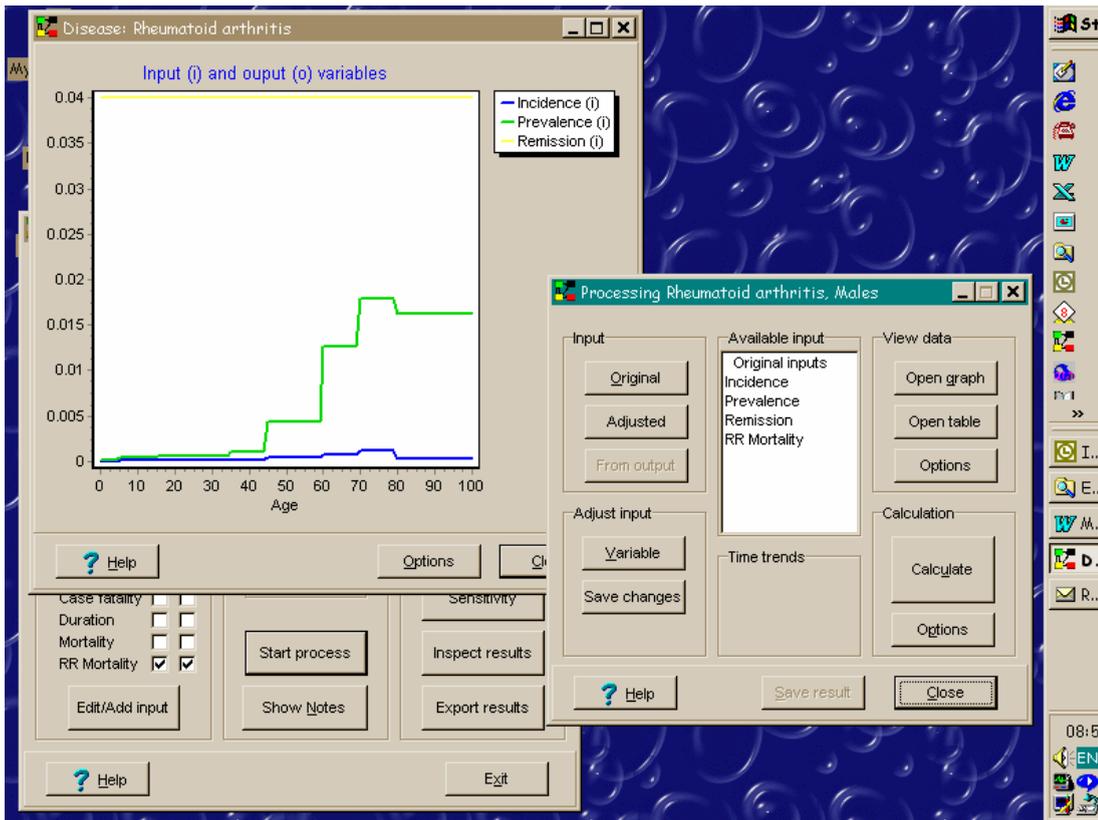


Figure 8.8. DISMOD II Window for Processing a Disease Model and Graph Window for Inputs.

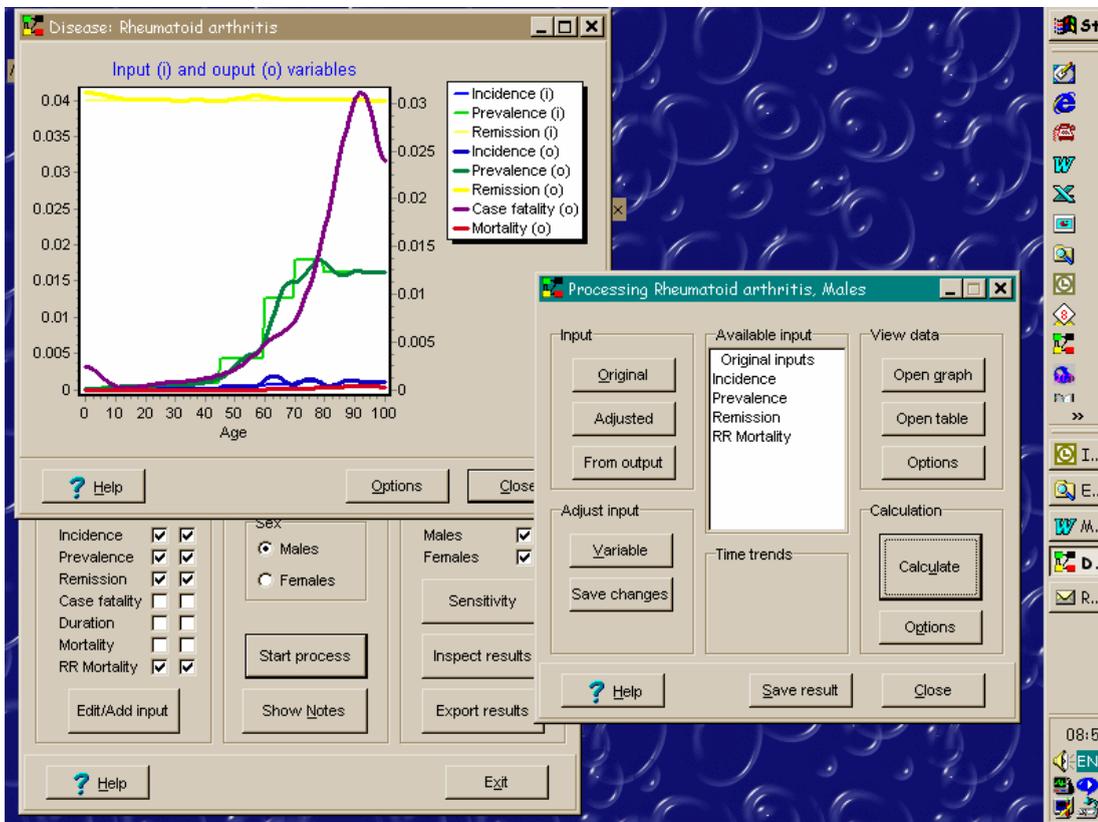


Figure 8.9. DISMOD II Output Windows after Calculation of a Disease Model.

CALCULATING THE MODEL AND ADJUSTING THE INPUTS TO IMPROVE IT

Given this input, the way to obtain output as such is simple: find the Calculate button on the Process window (it is the big one), and click it. After a few moments the graph window will show the results: five more lines, all labeled with '(o)' for 'output'. By default (but you can change that in the Graph options) output lines are a bit wider than, and have the same color (but in a richer shade) as the corresponding input. In addition to smoothed output versions of the three inputs the graph shows Case fatality (purple) and Incidence (blue) output. Please note that case fatality is by default on the right Y-axis, because it often has much higher values than incidence and mortality.

If you prefer numbers over (or in addition to) graphs you can open a table by clicking the Open table button on the Process window. The table has also duration of the disease as an output.

Underneath the Calculate button, there is a button labelled options which allows you to specify in more detail some of the parameters used to find the solution. The Calculation options window has several options divided over various tabs. Click the tab reading 'Weights', and you get a list of the DISMOD input variables with rulers to the right of them. Only the rulers of the available input are enabled.

These rulers enable you to give different weights to the various inputs in fitting the model. Thus, if you believe that the prevalence data is more reliable than the other inputs, you can give it greater weight. Additionally, there are check boxes which enable you to instruct DISMOD to ignore certain inputs.

In our rheumatoid arthritis example, we can tell DISMOD to ignore the incidence data inputs and calculate incidence rates to match the other inputs. We can then see whether the calculated incidence rates are similar to our empirical data on incidence. Figure 8.9 shows the graphical outputs from this calculation.

DISMOD II also allows you to experiment with other adjustments and options. For example, you might want to interpolate the input data in a more sophisticated way. This helps the optimization procedure (because the discontinuities are removed), and it also allows a better visual assessment of the divergence between input and output. To do this, choose the Variable button in the Adjust input section of the process window and then Prevalence and OK in the presented list. The Input adjustment window opens.

A more detailed description of this window is given in the help notes, here we note only some basic features. On the window is a display section, where a graph of the prevalence is shown. The label says there is a red line labeled 'original' and a blue one labeled 'Current', but only the blue line is visible. On the right is a row of buttons giving access to various adjustment actions. Choose the 'Interpolation' button, select 'Cubic spline' from the presented list, and click OK. The blue stepped prevalence line is now accompanied by a green smooth line, labeled 'Adjusted'. Next choose the button 'Keep result': the green line becomes blue, the blue line red, and no Adjusted line exists anymore. Leave the Input adjustment window by clicking the Apply button: the window closes and the input Prevalence curve in the Graph window has lost its stepped appearance.

In the Input adjustment window there are always at least two lines in the display section: the 'Original' and the 'Current' lines. The red line labeled 'Original' shows the input as it was entered in the Edits grids of the Edit window. The blue line labeled 'Current' shows what the input for further calculations will be when you leave the Input adjustment window by pressing the Apply button. The green line labeled 'Adjusted' shows the result of your latest manipulation of the data using the procedures accessible through the Adjustment actions buttons. If you like the result of that latest manipulation, you can make the 'Current' line equal to the 'Adjusted' line by pressing the 'Keep result' button.

When you opened the Input adjustment window only the blue 'Current' line was visible because it overlapped the 'Original' line: the 'Current' data then was equal the the 'Original'. After doing the interpolation, the green 'Adjusted' line showed its result. By pressing the 'Keep result' button, you made the 'Current line' equal to the 'Adjusted', and by choosing 'Apply' you made the interpolated data the basis for further calculations.

You can now choose the 'Calculate' button again to see whether the interpolation makes any difference for the outcome.

GETTING TO THE OUTPUT

To inspect your results in tabular form, click on the 'Open Table' button in the Processing window. The input and output variables will be displayed in a table as shown in Figure 8.10. You can change the way this table is displayed (e.g. rates per 1,000 and age groups used) using the Options button at the bottom. Note that this only affects the table displayed in the open window. To reset the default table options for all your calculations, you need to use the options button under the Open Table button in the Processing window, or the options menu in the main window.

You can paste results directly from this table into Excel, or you can use the Storage grid (called up within the Table Options button) to obtain a table with headings that can be pasted into Excel. DISMOD II does not have a print option, so to print your results you will need to transfer them to another program such as Excel.

DISMOD II saves the results from the input processing to the database in 1-year age groups. Export routines enable the user to produce results in various formats and age group subdivisions that can be used for burden of disease calculations, projections of future burden of disease, etc.

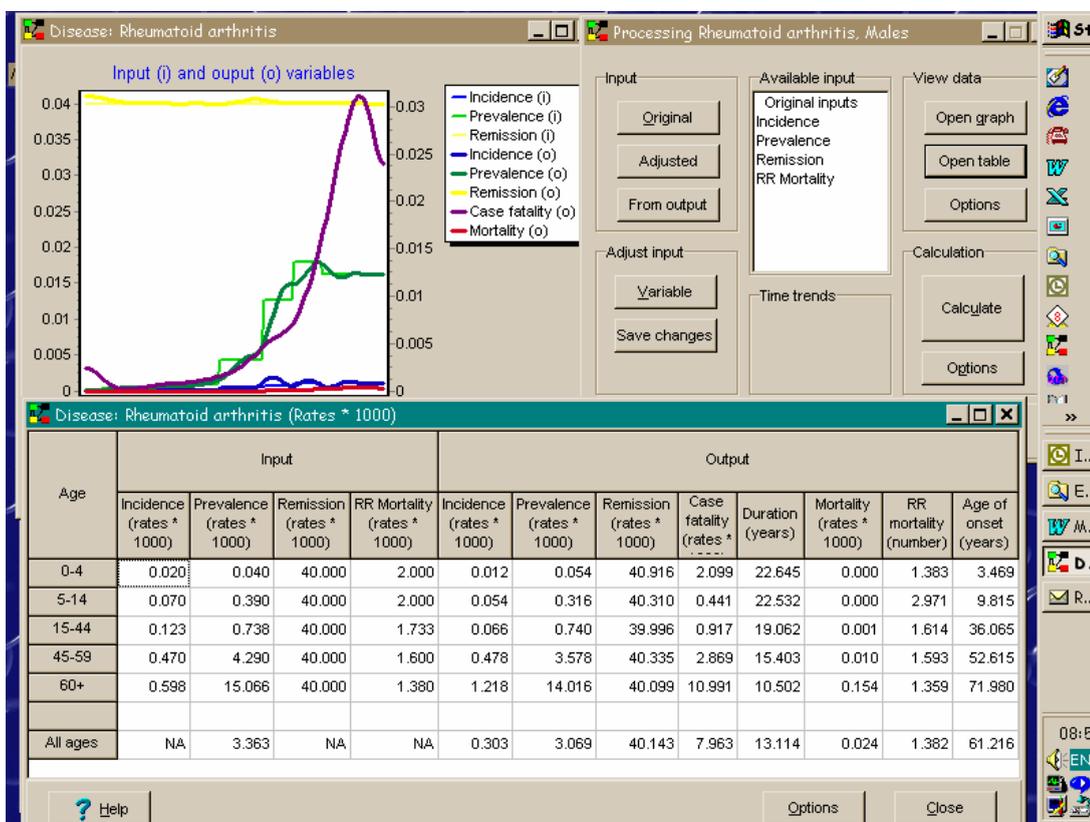


Figure 8.10 DISMOD II Output Table.

When you leave the Process window by clicking the Close button without saving, all the work will be lost. Of course this might just be what you want, but in case you want to save the fruit of your labors, there are two possible options.

- 1) You want to save the adjusted input data only. In that case choose the 'Save changes' button of the Adjust input section of the Process window. Saved adjusted input can, at a later moment, be recalled by choosing the 'adjusted' button in the Input section of the Process window. Note that calculation options such as weights on input variables are saved with the adjusted input data.
- 2) You want to save the output of the calculations. In that case choose 'Save result' before closing the Process window. Note that DISMOD saves together with the output results the (adjusted) inputs they are calculated from. Any adjusted inputs and any outputs you had saved before for this disease will be overwritten, DISMOD will ask you to confirm this beforehand.

The results from DISMOD typically form the basis for further work, such as calculation of disability adjusted life years (DALYs). DISMOD II therefore provides a number of formats to export the results from its database to other applications, or rather to files that other applications can read. Exporting results means defining which disease results you want to export, in what format (including in some cases the age group schedule), and to which file. You can export results only for the diseases for which you have previously calculated results and saved these. If you have not done that yet, you better first go to the Calculating results and Saving results sections of the tutorial.

ADDING A DISEASE

The DISMOD II help notes and tutorial contain detailed instructions for adding a new disease to your dataset. The basic steps are:

- First define disease name (and optionally ICD codes) and save it to the data set.
- Then for each of at least 3 input variables:
 - open the Edit window;
 - define an age group schedule (you can create and save your own);
 - type in the data in the data grids, or paste them from the Storage window or a spreadsheet; and
 - save the data to the data set.

CREATING A NEW DATA SET

A DISMOD II data set, as explained above, is defined as a region or country with a particular population, described by total mortality and population numbers. Since DISMOD results will be invalid without these population data, the first thing you are asked after creating a new data set is to provide the population data.

To create a new data set. Choose 'Data set | Select' in the data set menu. Up pops the Data set window, where you choose the 'Add/New' tab. This sub window shows a number of fields to be filled out. To enable the fields for editing, choose the 'Add/New' button. Then fill out the fields:

- Name. Type a meaningful name for the data set.
- File. Select the 'Browse' button and the standard Windows file dialog appears. The default file name is the same as the data set name with the MS Access extension '.mdb' added. Press 'Open'.
- Country, continent, region. Type whatever is appropriate here, or leave the default value.
- Highest age. This is the highest open ended age group of the population data, in the case of the Example data set 95.

Leave the 'Read only' box unchecked, and press 'Save'. After DISMOD is done, choose the 'Select' tab, select the new data set in the list, and choose the 'Open' button. Next a warning box pops up, informing you that 'Total mortality data is missing' and asking whether you want to provide it now. Click on 'Yes' to open up the Mortality window.

Now we first have to define age groups. Make sure the 'View' switch is on 'Original', and click the 'Define' button in the 'Age groups' section. In the 'Define age group' window you may read one of the stored age schedules from disk or create a new age schedule using the Define age groups option. When done, close the 'Define age group' window.

Back in the Mortality window, you can type in mortality data, paste it from another file, or read an existing file in comma separated value format. Save that data and continue. You will need to enter the population numbers using a similar procedure. Finally, you have a new data set, ready to be filled with diseases.

CREATING A NEW COLLECTION

To create a new, empty data set collection.

Choose 'Collection | New' from the Data set menu. A box will pop up asking to name the new data set collection. Type a name (for example 'Mycollection') and click OK. Next you are asked a file name,

which by default is the same as the name of the data set (with the extension 'mdb' added to it), but you may give it any name you like. After you click 'Open' in the file dialog it closes, the Data set window opens, showing you an empty list of data sets. You can now proceed by adding new or existing data sets.

It is possible to copy dataset files from one computer to another and to associate them with existing or new collections. In order to do this, you must copy the .mdb file for the dataset to an appropriate location. Open a new or existing collection and select Add/New dataset. Specify the name of the dataset file and click on 'browse' to find the existing file on your computer. Then press 'Save' and 'Close' to register the dataset in your collection.

COPYING DISEASE MODELS BETWEEN DATASETS AND COLLECTIONS

The Disease menu in the Main DISMOD II window has a copy option. This can be used to copy an entire disease model (including saved calculation options) from the open dataset to another dataset in the same or a different collection. This feature allows you to develop a disease model for one population and then transfer it to other populations in your study.

9. HEALTH STATE VALUATION

9.1 INTRODUCTION

In order to construct summary measures of health, it is necessary to assign values to time spent in different health states, relative to time spent in perfect health or time lost due to premature death. These weights provide the critical link between mortality and non-fatal health outcomes that allow the two to be combined in summary measures. All summary measures of population health require health state valuations as inputs. Likewise, cost-effectiveness analyses that measure the benefits of interventions in time-based units (such as QALYs) require health state valuations to assign weights to years spent in different states of health.

It is important to note the distinction between the measurement of health status along different domains of health and the valuation of different health states. While different health status instruments may be used to describe health states as stimuli for valuation, the purpose of health state valuations is to assign a single value to time spent in different health states, as compared to health status measurement, which seeks to describe the current health of individuals in terms of multiple dimensions.

A variety of issues around the measurement of health state valuations have been debated extensively from two major paradigms: health economics, where the focus has been on the formal theoretical basis of health state preferences; and psychometrics, which has emphasized empirical measurement issues. In this chapter, we begin by reviewing the major conceptual and methodological issues relating to health state valuation, then present the current strategy for measuring health state valuation in the Global Burden of Disease study.

For a national burden of disease study, it is useful to apply a standardized set of health state valuations consistent with the valuations used in the Global Burden of Disease in order to allow comparability of results. It is also possible, however, to investigate whether these valuations might differ in the local setting and to examine the sensitivity of the burden results to varying assumptions about health state valuations. This chapter therefore includes an overview of the recommended steps for collecting local data on health state valuations.

9.2 FOUNDATIONS FOR HEALTH STATE VALUATIONS IN SUMMARY MEASURES

The enterprise of measuring health state valuations for construction of summary measures relies on several basic assumptions:

- 1) A series of health states can be defined using an established instrument or other descriptors.
- 2) Individuals have preferences for time lived in different health state that may be expressed meaningfully in cardinal values.
- 3) These preferences may be measured through some form of interview or questionnaire.
- 4) The severity of a health state and the duration of time spent in a health state are assumed to be independent. For example, this assumption implies that the value an individual places on time spent bed-ridden is unrelated to the length of time under consideration.

While many of these basic assumptions may be challenged, they are adopted in nearly all of the research on health state valuations in summary measures. One important exception is the Healthy Year Equivalent (HYE) approach, which does not rely on the independence between severity and duration, but rather requires valuations for all possible combinations of health states and durations. In practice, the information requirements for implementation of an HYE approach to constructing summary measures are prohibitively demanding, so the independence assumption provides the only operationally feasible solution that has been proposed to date.

9.3 ISSUES IN DESIGNING A HEALTH STATE VALUATION STUDY

MEASUREMENT APPROACH

A burden of disease study requires health state valuations for each of the sequelae that will be included in the study. Given practical resource constraints, it would be impossible to elicit direct valuations for each of these states. It is therefore necessary to design a measurement approach that allows imputation of valuations for those health states not valued directly.

One approach to this problem is to describe states included in the valuation study according to a standardized descriptive system based on multiple domains of health, and then to estimate models that can predict valuations based on the different domain levels. This can be accomplished by defining a set of health state descriptions consisting of different profiles or combinations of domain levels, eliciting valuations for these states, and then applying econometric methods to estimate the relationships between domain levels and valuations.

An alternative to the direct measurement method has been applied in the Canadian work on the Health Utilities Index. This work is based on multiattribute utility theory, which takes an axiomatic approach to determining the structure of valuation functions. Thus, the way that different domain scores translate into valuations is not measured directly, but rather constructed based on certain assumptions about independence of different domains and measurement of preferences over the domains themselves rather than particular health states.

In either approach, two critical decisions involve the selection of the states that will be included and the number of states which each individual in the study will consider. Particularly if statistical inference will be used to estimate the valuation function, it is important to select a subset of states that span the full range of severity from very mild to very severe conditions. It is also essential to maximize the independent variation on each domain that is included in the descriptive system, in order to be able to estimate the independent effects of each domain on valuations and any interactions that are present.

In selecting the number of states to be valued by each individual, a tradeoff must be made between the cognitive demands of the interview and the need to include a range of states for each individual in order to improve reliability. Studies have shown that reliability of responses increases if respondents are simultaneously valuing more than 2 or 3 states, but there are also limitations as to how many different pieces of information an individual can consider effectively. Evidence that has been collected to date suggests that 10 to 12 states may offer a good balance between these twin demands, but this is likely to vary across groups according to various socio-economic factors.

DESCRIPTIONS OF HEALTH STATES

In order to elicit individuals' valuations of different health states, it is important to present each health state in a way that is standard, precise and comprehensible. One important challenge is to ensure, as much as possible, that all respondents are thinking about the same health state when they are giving valuations. A number of important methodological issues around the description of health states as stimuli for valuation remain controversial. For example:

Should health states be linked to specific disease states?

Disease labels can help people with the cognitive challenge of processing large amounts of information, particularly when a number of health states are being valued simultaneously. On the other hand, disease labels may also lead individuals to bring other information that varies across different individuals into their valuations, and therefore jeopardize standardization.

In selecting health states as stimuli for collection valuation information, it is important to consider whether individual perceptions of the state may be influenced by values other than the level of health in that state.

Should descriptions be limited to levels on standardized domains, or should other information be included?

The use of standardized domains as descriptive information for valuation can be useful, but there are questions about which domains are most relevant for valuation, and there are important tradeoffs between

parsimony and completeness of descriptions. Descriptions are sometimes based on existing classification systems, such as the Rosser/Kind matrix, the Health Utilities Index, or the EuroQol system. An alternative is to define health states *ad hoc* for a particular study, which is often the approach used for clinical decision analyses.

What other tools might be useful in description?

Different studies have explored the use of pictures, cartoons or multimedia presentations to aid in the description of health states. Some drawbacks, however, include added expense and potential biases regarding race, gender or other factors in depictions of different health states.

VALUATION TECHNIQUES

There are four major methods that are used to elicit health state valuations.

(a) *Rating Scale / Visual Analogue*

A typical rating scale consists of a line on a page with two clearly defined endpoints, such as death and perfect health. Respondents are asked to place other health states on the line representing their relative valuation of time spent in each health state.

Various alternatives where the line is broken into fixed categories or other visual aids have been employed. This approach is the easiest to explain to prospective respondents and may therefore be the only possible method for population-based data collection.

To obtain valid and reliable responses using a visual analog scale, it is important to include a sufficient number of different states on the same scale in order to ensure that respondents will minimize scaling distortions that have been observed when only a few states are considered. Respondents tend to use the entire scale no matter how many states are provided, so the inclusion of a range of different severity levels is essential.

It is also important to remind respondents that they should try to use the scale in such a way that the distances between states provide a meaningful representation of how similar or different the values for different states are, rather than a simple ordinal ranking.

(b) *Standard Gamble*

In a standard gamble, respondents are offered two alternatives. The first alternative is to live, with 100% certainty, for t years in a chronic state of reduced health. The second alternative is an uncertain prospect, with probability p of being restored to full health for those t remaining years, but with a complementary probability $(1-p)$ of immediate death. Respondents are asked a series of questions in which the value of p varies in order to identify the value for p that makes the two alternatives equally attractive. The level of risk that individuals will tolerate in order to be raised from some particular health state gives an indication of the value that they place on that health state.

Some health economists and decision scientists believe that the standard gamble is the gold standard measure of health state preference because it is formulated based on the von Neumann-Morgenstem axioms of expected utility. There have been a range of studies, however, that challenge the appropriateness of expected utility theory as a descriptive, prescriptive or normative basis for decision-making.

It is important to note that the standard gamble elicits responses that reflect not only the value that a person places on a health state but also the person's attitudes towards gambling or risk. For the construction of summary measures of population health, it may be necessary to extract out individual risk attitude from their standard gamble responses in order to obtain health state valuations that represent an appropriate quantity of interest.

(c) *Time Trade-Off*

In a time trade-off, respondents are asked to choose between living t years in state A or a smaller amount of time x in perfect health. The length of time in perfect health is varied until respondents are indifferent

between the two alternatives. The ratio of x to t then gives an indication of the valuation of state A relative to perfect health.

If a long period of time is used as the reference duration — for example years as opposed to months or days — responses will be confounded by individuals' time preference. The confounding effect of a positive rate of time preference will be greatest for mild conditions.

In addition, if severity and duration are not clearly separated in the minds of the respondents then the results will also be biased.

(d) *Person Trade-Off*

In the person trade-off, respondents are asked to choose between preventing deaths in X people in perfect health, or preventing the onset of some state A in a different number of people Y . The value of Y at which the respondent is unable to choose between the two options gives an indication of the valuation of state A relative to perfect health and death.

Preference for one's own health state may be different from the preferences revealed through a question eliciting an individual's social preferences for groups of people in different health. Some individuals may be less willing to trade-off quantity of life for quality of life when making decisions for others than when deciding for themselves.

One of the arguments that has been presented in favor of the person trade-off is that the method is closely linked to societal resource allocation decisions. For constructing summary measures of population health, however, it may be important to separate individual values regarding distribution issues from the question of how healthy a particular population is. Since resource allocation decisions in the real world depend on more than just the levels of health that result from different choices, the person trade-off may not be most appropriate for measuring the strength of preferences for different health states.

TYPES OF RESPONDENTS

There is extensive debate on whose preferences should be measured. The answer to this question depends critically on whether one is measuring individual values for clinical decisions or social valuations to construct summary measures of population health or to inform social policy making.

(e) *Individuals in a Health State*

In theory, individuals living in a health state have the most intimate knowledge of a health state and therefore are best able to make the most accurate assessment of the utility of living with the condition. On the other hand, these individuals may have different assessments than the general public would have even if they had full knowledge of a health state.

It has been observed that individual assessments of their own health state may change over time. For example, imagine an individual who suffers a spinal cord transection. The individual's initial valuation after the accident may assign a very low utility to living with a spinal cord transection. Repeated measurements of his or her health state preference, however, might show that over time, the valuation of the health state improves.

This improvement can be due to three different processes:

- **Adaptation** is the process by which individuals improve their functional performance in selected domains through learning or experience. These improvements can be observed and are also likely to be self-perceived and reported.
- Individuals may re-calibrate their expectations or norms for performance so that their self-perceived performance on selected domains may improve more than their observed performance. We can call this process of changing norms and thus increasing self-perceived performance **coping**. We expect that coping is heterogeneously distributed in the population, so that some individuals will cope more than others in the same context.
- Individuals may change their relative valuation of different domains of health status towards those domains where they have preserved or enhanced their function. So, for example, an avid skier who

puts a very high valuation of the domain for physical activity or mobility may, after a severe accident, shift her valuations of domains so that other domains such as cognitive function are valued much more highly than previously and physical domains less highly. This shift in the relative valuation of domains is called **adjustment** or domain valuation shift.

Individuals' valuation of their own health state will necessarily reflect adaptation, coping and adjustment. Individuals' valuations of hypothetical health states, if the individual making the valuation is provided with information on self-reported function alone, will reflect adaptation and coping but not adjustment. When individuals undertake social valuations, they may not want to incorporate coping and/or adjustment.

(f) *Health Care Providers*

Health care providers also have intimate knowledge of the consequences of health states and thus, in theory, can make judgments that are more informed than the general public. Some studies have found that health care providers rate health outcomes as being worse than how patients rate them.

(g) *The General Public*

In related debates about the appropriate respondents for health state valuation studies in clinical cost-effectiveness studies, some have argued that the values of the general public should be used as opposed to the values of patients or providers. The notion that the general public can make informed choices about health states that they have never experienced or with which they have never come in contact can be challenged.

(h) *Patients' Families*

Family members of patients have intimate knowledge about health states without actually suffering from a particular condition. In some surveys, they appear to rate health states as being worse than how patients rate them.

9.4 RECOMMENDATIONS

For the Global Burden of Disease Study 2000, WHO has developed a two-tiered data collection strategy that consists of:

1. Collection of health state valuations in the general population using a multiple state ordinal ranking and visual analog scale questionnaire;
2. Collection of health state valuations among educated respondents using a multistate, multimethod group exercise protocol.

The first part of the strategy is designed to address questions of variation in health state valuations across different types of respondents and settings. The results will be used to analyze the possible determinants of variance both across and within countries.

The second part of the strategy is required in order to translate responses obtained using the visual analog scale to an interval-scaled measure of strength of preference that may be used in constructing summary measures of population health.

POPULATION SURVEYS

For general population surveys, there is a standardized WHO health state valuation component with three parts:

- respondent-completed description of 11 health states in terms of 5 levels on 7 different domains of health, including mobility, self-care, usual activities, pain and discomfort, cognition, anxiety and depression, and social participation
- ordinal ranking exercise of these 11 health states with the aid of index cards

- valuation of these 11 health states using a visual analog scale anchored by the best imaginable health state at 100 and death at 0, and with 100 equally-spaced tick marks, labeled at every other mark.

Different sets of 11 health states have been developed, allowing randomisation of respondents to different groups, and all respondents also complete descriptions of their own current health using the same domains of health described above. The WHO health status and valuation survey modules may be found at <http://www.who.int/evidence/surveys>.

MULTIMETHOD PROTOCOL

The multimethod protocol is implemented among individuals with high levels of education attainment because it relies on valuation methods that are abstract and cognitively demanding. Previous empirical work suggests that these methods are not feasible for implementation in the general community. The goal of the multimethod approach is to have each individual provide valuations for a standard set of states using different valuation questions, and then to use this information to estimate the underlying strength of preference function that is reflected in responses on each of the different valuation tasks. Insights into the relationship between visual analog scale responses and strength of preference will then be used to calibrate results from the population-based surveys.

The exercise consists of 6 different tasks which are completed by each respondent for a set of 11 different health states. The first three tasks are the same as the ones in the general population survey described above:

- respondent-completed description of 11 health states in terms of levels on 7 different domains of health, including mobility, self-care, usual activities, pain and discomfort, cognition, anxiety and depression, and social participation
- ordinal ranking exercise of these 11 health states with the aid of index cards
- valuation of these 11 health states using a visual analog scale anchored by the best imaginable health state at 100 and death at 0, and with 100 equally-spaced tick marks, labeled at every other mark.
- valuation of these 11 health states using a time trade-off question and self-completed worksheets, followed by the opportunity to examine and revise all 11 TTO valuations
- valuation of these 11 health states using a standard gamble question and self-completed worksheets, followed by the opportunity to examine and revise all 11 SG valuations
- valuation of these 11 health states using a person trade-off question and self-completed worksheets, followed by the opportunity to examine and revise all 11 PTO valuations

Thus far, the protocol has been designed for implementation in a small group format, with instruction and discussion of each of the components guided by a facilitator, but individual completion of each task. Development of a variant of the protocol that may be administered in the format of an individual survey questionnaire is also underway.

Linked to the data collection strategy is a series of analytical methods that are used to estimate strength of preference based on multiple measurements of health state valuations that include other components or other values in addition to strength of preference. This is achieved by formalizing the relationship between each type of health state valuation response and some underlying strength of preference function using flexible parametric forms. For example, based on the common observation that the standard gamble includes both strength of preference for a health state as well as individual attitudes towards risk, we capture this relationship formally by specifying a model in which standard gamble responses are expressed as a function of the underlying valuation of the health state and a risk aversion parameter. Similar formal representations are developed for each type of valuation response. This allows estimation of both the underlying valuations for each health state and the values for each of the parameters relating the different responses to these underlying valuations.

HEALTH STATE VALUATIONS IN NATIONAL BURDEN OF DISEASE STUDIES

For countries undertaking national burden of disease studies, it is recommended that a baseline set of estimates should apply the weights used in the GBD, which are being updated as described above for GBD 2000.

For countries wishing to assess local health state valuations as well, we recommend using the same two-tiered data collection strategy following the standardized protocols developed at WHO. The required instruments and analytical tools will be finalized for the GBD 2000 study, which will facilitate collaborative efforts between WHO and national study teams on measuring reliable, valid and cross-culturally comparable health state valuations. For more information, contact Josh Salomon via email to salomonj@who.int.

REFERENCES

- Froberg DG, Kane RL. (1989). Methodology for measuring health state preference – I: measurement strategies. *Journal of Clinical Epidemiology*, **42(4)**: 345-354.
- Froberg DG, Kane RL. (1989). Methodology for measuring health state preference – II: scaling methods. *Journal of Clinical Epidemiology*, **42(5)**: 459-471.
- Froberg DG, Kane RL. (1989). Methodology for measuring health state preference – III: population and context effects. *Journal of Clinical Epidemiology*, **42(6)**: 585-592.
- Torrance GW. (1986). Measurement of health state utilities for economic appraisal: a review. *Journal of Health Economics*, **5**: 1-30.
- Nord E. (1992). Methods for quality adjustment of life years. *Social Science and Medicine*, **34(5)**: 559-569.
- Nord E. (1995). The person trade-off approach to valuing health care programs. *Medical Decision Making*, **15**: 201-208.
- Richardson J. (1994). Cost utility analysis: what should be measured? *Social Science and Medicine*, **39(1)**: 7-21.
- Gudex C. et al. (1996). Health state valuations from the general public using the visual analog scale. *Quality of Life Research*, **5**: 521-531.
- Dolan P. (1997). Modeling valuations for EuroQol health states. *Medical Care*, **35**: 1095-1108.
- Brazier J, et al. (1998). Deriving a preference-based single index from the UK SF-36 Health Survey. *Journal of Clinical Epidemiology*, **51(11)**: 1115-28.
- Patrick DL, et al. (1994). Measuring preferences for health states worse than death. *Medical Decision Making*, **14**: 9-18.
- Torrance GW, et al. (1996). Multiattribute utility function for a comprehensive health status classification system. *Medical Care*, **34**: 702-722.

10. SPECIFIC APPROACHES TO THE CALCULATION OF YLD

Chapter 7 described the general principals of assessing the burden of disease caused by disability. This chapter provides details and tips on how to proceed with the estimation of YLD for specific diseases. This information is by no means exhaustive and is meant to serve as 'a bit of good advice' from experienced burden of disease researchers.

It is good practice and helpful to examine the efforts of previous GBD and NBD studies in modelling particular diseases. However, you should remain critical about the plausibility and applicability of such efforts to the circumstances present in your country. The three GBD volumes are an important source of information. Even though the descriptions of most of the disease models have not been published, a lot of the assumptions can be deduced from the figures published. For instance, estimates of the proportion of cases with a particular disabling sequela can be deduced from the incidence figures of the disease and the sequela. Another available source of information is the website of the Department of Human Services of the state of Victoria in Australia which contains all the Excel and DISMOD (version 1) files used in the Victorian burden of disease study (<http://www.dhs.vic.gov.au/phd/9909065/filelist.htm>).

The information in this chapter is presented in tabular format. The diseases discussed are largely based on the GBD list of diseases. The table presents for each disease—or group of diseases—a list of the main health states and sequelae, data sources and comments on how to approach the disease modelling. If you consider adding conditions that have not previously been estimated in the GBD or another NBD study, you must be prepared to find the relevant epidemiological data for the disease as well find or create a set of appropriate disability weights.

<i>Condition</i>	<i>Main health states or sequelae</i>	<i>Data sources</i>	<i>Approach to modelling</i>
A Infectious and parasitic diseases			
1 Tuberculosis	Pulmonary Mild extrapulmonary (e.g. lymph glands, pleuritis, peritonitis) Severe extrapulmonary (e.g. miliary, spine or meningitis)	Notifications Registers (how complete?, % cured, % defaulters, % retreated)	Model treated and untreated cases separately because of different duration. Estimate the duration of those treated as in standard treatment regimen (e.g. 9 months?). Do you have historical data to estimate the average survival time of untreated TB? (e.g. 2–3 years?—consult local experts) Ignore HIV+ TB, assuming this is covered in calculations of symptomatic HIV and full blown AIDS as one of the opportunistic infections.
2 STDs (syphilis, chlamydia and gonorrhoea)	See GBD	Notifications (cave gross underreporting!) Health service contacts (e.g. PID cases, ectopic pregnancies)	See Volume III GBD series; check plausibility of assumptions with local expert. If independent source of (secondary) infertility is available, do the numbers of cases of infertility as a consequence of various diseases (STDs, maternal sepsis, septic abortion) add up?
3 HIV/AIDS	Asymptomatic—status not known Asymptomatic—status known Symptomatic HIV Full blown AIDS (criteria based on CD4 count or clinical picture?)	Notifications Prevalence surveys (general population, antenatal attenders) Disease register Local studies (how representative?)	Difficult to model because: - changing incidence over time, therefore hard to estimate incidence from prevalence figures - what is average duration? Particularly if anti-retroviral therapy is available; ask local experts (but be not surprised if they say they cannot guess); also note that average duration will vary with age of onset (shorter duration with increasing age except in perinatally infected children) - HIV in children: derive incidence from HIV prevalence in antenatal women using locally appropriate estimate of transmission (e.g. is AZT available and is there transmission via breastfeeding?); duration may be bimodal; in Zimbabwe it was estimated that two-thirds of children have fast progression (av. duration 1 year) and remainder progresses slowly (av. duration 8 years)

Condition	Main health states or sequelae	Data sources	Approach to modelling
4 Diarrhoea	Consider split in acute and chronic or complicated and uncomplicated episodes. Long term complications if amoebiasis prevalent?	Household surveys for frequency of simple diarrhoeal episodes Epidemiological studies	Very short duration (few days) for uncomplicated episodes; \pm 2 weeks for complicated episodes
5 EPI cluster	See GBD details	Notifications (how complete?) Surveillance (e.g. part of polio eradication programme) EPI coverage figures (e.g. if high, expect few cases)	Discuss GBD assumptions of some sequelae, e.g. 3/1000 mental retardation post-pertussis, 20% neurological complications for 2 months and 7.5% myocarditis for 3 months post-diphtheria Are there epidemic cycles (e.g. measles epidemic every few years: take average annual cases during one cycle)
6 Meningitis	See GBD details; consider adding 6 months of fatigue etc. after the acute episode, less severe developmental problems and the scarring/deformities post meningococcal skin necrosis	Notifications (how complete?) Health facility data (coverage?) Follow-up data on sequelae from epidemiological studies	Review assumptions of % with sequelae of GBD (in GBD Volume II divide incidence of sequela by incidence of acute episodes) Use international studies of follow-up of meningitis patients if no local data available
Consider adding septicaemia?	Similar sequelae as in meningitis		
7 Hepatitis	Symptomatic episodes hep A, B + C Cirrhosis Liver cancer	Prevalence studies (but evidence of past infection not an indication of symptomatic infection!)	What is main mode of transmission (e.g. in Asia high perinatal transmission and in Africa high childhood transmission; i.v. drug use for hep C; sexual transmission?) Estimate proportion of cirrhosis and liver cancer attributable to hep B, C from expert opinion?

10 CALCULATION OF YLD

Condition	Main health states or sequelae	Data sources	Approach to modelling
8 Malaria	Symptomatic episodes Anaemia Neurological sequelae	Health facility data (likely to be gross underestimate) Special studies Look for epidemics/seasonal variation	Short duration for episodes In endemic areas majority of symptomatic episodes in children Look at totals of anaemia (if prevalence of anaemia is known) from all causes (e.g. nutritional, maternal causes). GBD estimates in SSA: 50% of anaemia in children <5 and 25% 5-14 due to malaria GBD estimate of long-term neurological sequelae: 1.3 per 1,000 episodes
9 Tropical cluster	See GBD (Trypanosomiasis, Chagas, schisto, leishmaniasis, filariasis, oncho, dengue, Japanese encephalitis)	Notifications? Epidemiological studies?	See GBD
10 Leprosy	Cases Disabling leprosy	Notifications Disease registers	GBD gives DW=0 for cases (what about stigma?) If leprosy significant, consider more detail in modelling sequelae
11 Trachoma	Blindness Mild, moderate and severe vision loss	Registers? Special school attendance Disability pensions Surveys of disability Epidemiological studies	Do all causes of blindness add up to total prevalence (if data available), e.g. congenital, trauma, other infections, diabetic retinopathy, cataract, glaucoma, and macula degeneration?
12 Helminths	See GBD		See GBD assumptions; long-term sequelae modelled are not without controversy! Discuss with local experts if available
B Respiratory infections			
1 Lower respiratory infections	Episodes Chronic sequelae in children	Health facility data (coverage?)	Episodes of a week to 10 days on average Sequelae in GBD in 3.5/1000 episodes in 0-4 age group

Condition	Main health states or sequelae	Data sources	Approach to modelling
2 Upper respiratory infections	Episodes Pharyngitis/tonsillitis	Health facility data likely to be gross underestimate Surveys?	Several incident episodes per person per year, more in children Short duration, low severity
3 Otitis media	Episodes Deafness		Almost only in children Deafness often transient (duration a few years rather than rest of life as in GBD) but longer term consequences such as lesser school achievement should be considered
C Maternal conditions			
1 Haemorrhage	GBD volume III	Health facility data (coverage?) Special studies (e.g. abortions)	Comments on GBD assumptions: - Sheehan overestimated? - do all causes of (secondary) infertility add up to total prevalence (if known)? - stress incontinence shows only weak (if at all) link with obstructed labour; common after any birth; consider making new category under genitourinary disorders
2 Sepsis			
3 Hypertension in pregnancy			
4 Obstructed labour			
5 Abortion			
D Neonatal conditions			
1 Low birth weight	GBD lumps all sequelae	Health facility data (coverage?) Local or international epidemiological studies	Discuss plausibility of assumptions about sequelae with local experts For permanent disabling states consider modelling increased RR dying and thus shorter average duration (e.g. more severe intellectual disability, CP)
2 Birth trauma/asphyxia	Consider more detail: deafness, blindness, epilepsy, cerebral palsy, intellectual disability (by severity level?)		
3 Neonatal infections			
E Nutritional disorders			
1 Protein-energy malnutrition	Wasting, stunting and developmental disability	Nutritional surveys	GBD 1990 modelled wasting and stunting as prevalence x 1 year duration; developmental disability life-long

Condition	Main health states or sequelae	Data sources	Approach to modelling
2 Iodine deficiency	Goitre grade 0, 1, 2, mild developmental disability, cretinoidism and cretinism	Goitre surveys	Goitre YLD based on prevalence x 1 year duration calculation in GBD 1990 Consider RR mortality for life-long consequences
3 Vit A deficiency	Xerophthalmia, corneal scar	Vit A surveys Blindness survey/ epidemiological study	The excess mortality/morbidity in e.g. diarrhoea and pneumonia attributable to vit A could be part of a separate risk factor calculation but not as part of Vit A deficiency in overall BoD listing
4 Iron-deficiency anaemia	Mild, moderate, severe and very severe; cognitive impairment	Surveys, epidemiological studies?	Subtract other causes of anaemia (e.g. maternal or malaria) if overall prevalence of anaemia is known WHO classification of anaemia rather 'severe' GBD 1990 modelled anaemia YLD from prevalence Cognitive impairment following anaemia hard to quantify
F Cancers	<p>GBD has one weight for all stages of each cancer</p> <p>Consider more detailed health states (at least for 'big' cancers such as breast, bowel and prostate in EME; see example in Figure 7.4):</p> <ul style="list-style-type: none"> • Initial diagnosis and treatment • Disease free until considered cured (5 years; more for some longer lasting cancers such as breast, bowel, melanoma) • In remission • Disseminated • Terminal 	Cancer registry International cancer data	<p>If no or poor local data, look up international cancer databases and adopt figures from country/city most resembling local circumstances (http://www-dep.iarc.fr/dataava/infodata.htm)</p> <p>Redistribute ill-defined cancers and secondaries with unknown primary site across cancer sites (but do not redistribute cancers with specified site not included in BoD listing!)</p> <p>5-year survival often available; if not try and extrapolate from ratio of mortality and incidence (if available)</p> <p>exponential model of constant risk of dying over time often 'works': $e^{-\lambda t}$ describes survival and $1/\lambda$ is approximation of average duration (λ is the mortality rate); to calculate average survival of those who end up dying: $1/(\lambda * (1 - \text{proportion surviving}))$</p> <p>Determine duration of other stages (stage of initial diagnosis and R/, disseminated and terminal phase) after discussion with cancer experts. Subtracting those estimates from the overall estimate of duration of non-survivors gives you the duration of the 'in remission' period</p>

<i>Condition</i>	<i>Main health states or sequelae</i>	<i>Data sources</i>	<i>Approach to modelling</i>
G Benign neoplasms		Cancer registry? Health facility data (how complete?)	If wishing to model in detail consider separate calculations for brain tumours (with relatively high fatality for benign growths due to their location inside the skull; could consider lumping these together with malignant brain tumours), uterine myomata (fibroids) and neoplasms of uncertain nature (most of which in terms of deaths are neoplasms of the lymphatic and haematopoietic tissues)
H Diabetes mellitus	Diabetes per se Vision loss (retinopathy, glaucoma, cataract) Neuropathy Renal failure Peripheral vascular problems (diabetic foot and amputation) IHD Stroke	Prevalence surveys (underreporting of NIDDM if self-reported!) Blindness surveys Registry of renal failure? Epidemiological studies (local + international) Hospital data for amputations	It is ICD 'convention' to classify all CVD under CVD even if attributable to diabetes. Consider separate more inclusive calculation of DM with attributable fractions of IHD and stroke. Renal failure does not accrue many YLD unless patients have access to chronic dialysis. If transplant available, include this as 'remission' (though with considerable rest disability post-transplant) Do all causes of blindness add up? Calculate all cataract, glaucoma first, then apply attributable fractions Neuropathy (expert opinion and few studies): common problem, more in NIDDM than in IDDM; majority has mild symptoms, around 20% experiencing 'disability'; 1/3 remits after on average two years, 2/3 remains stable over time or gets worse

<i>Condition</i>	<i>Main health states or sequelae</i>	<i>Data sources</i>	<i>Approach to modelling</i>
I Mental disorders			
General issues:			
<ol style="list-style-type: none"> Several validated interview instruments that identify mental disorders into ICD (International Classification of Diseases; most current version is ICD–10) or DSM (Diagnostic and Statistical Manual of Mental Disorders of American Psychiatric Association; DSM–IV is the most current version) categories, are used in community surveys (e.g. CIDI, SCAN, DIS). There are also a number of screening instruments that are often used in general practice or outpatient settings to identify people at risk of having a mental disorders. In general, these screening instruments produce higher prevalence figures and if in your country only such survey information is available you will need to make a decision on how to adjust them downwards. All of these instruments have mainly been used in industrialised countries and may not be wholly appropriate in other cultures. For instance, in many non-western countries depression may present primarily as multiple physical complaints rather than guilt, worthiness or feeling blue that are essential elements of an ICD or DSM diagnosis of depression. Health facility data for most mental disorders are not very useful as many mental disorders are commonly not or insufficiently treated. Comorbidity between mental disorders is very common; this becomes more of an issue when including a larger number of mental disorders in your estimates; ignoring comorbidity could lead to considerable “double counting” with estimates of disability in one person exceeding the worst imaginable health state. Because comorbidity between depression and individual anxiety disorders is so common and because treatment options for anxiety disorders and depression are very similar, it may well be justified to estimate them as one entity. It is a common finding that the prevalence of most mental disorders is high in young and mid adulthood and much lower in the elderly; this may be a true finding but it may also be a problem of survey instruments not picking up mental disorders in the elderly; quite a few chronic physical disorders in the elderly are known to be associated with depression (e.g. Parkinson, dementia, stroke); assuming that the DWs for these common conditions incorporates the depression component of disability, the comorbidity between physical disorders and mental disorders is likely to lead to less ‘overcounting’ of YLD than the comorbidity between mental disorders themselves Age weighting has a great bearing on YLD for mental disorders as these are most prevalent at young and mid adulthood where age weights are high. 			

Condition	Main health states or sequelae	Data sources	Approach to modelling
1 Depression	Mild, moderate, severe major depressive disorder (MDD) Dysthymia Also mild depressive symptoms not qualifying for diagnosis of MDD?	Community surveys	Some consider MDD and dysthymia part of same disease entity Comorbidity between MDD and dysthymia is very common ICD-10 classification of mild, moderate and severe depression is based on (relatively) arbitrary cut-offs of the number of depressive symptoms Major depressive episodes on average last around 5-8 months but large variation exists (shorter in young adults, longer in mid adulthood?) There is also variation in the course of disease: ± 10% has MDD continuously over a long period; ± 15% experiences only one episode; the majority experiences multiple episodes of MDD (averaging 4-6 in a lifetime) MDD is difficult to model as chronic disease with symptomatic and asymptomatic periods; the alternative is to model MDD as episodes and dysthymia separately and then add YLD up to be presented as a single estimate for all depression
2 Anxiety disorders	Panic disorder, agoraphobia, social phobia, generalised anxiety disorder, obsessive-compulsive disorder, post-traumatic stress disorder and in children, separation anxiety disorder Each ranging between mild, moderate and severe symptoms	Community surveys	All of these are chronic conditions with periods of remission and relapses. The average duration in adults probably lies between 5 and 20 years (shorter for PTSD and longer for the other conditions). If one-year prevalence and current prevalence figures are known from a survey, one can take the ratio of current over one-year prevalence as a rough estimate of the proportion of time symptomatic.
3 Psychoses	Schizophrenia and other psychoses Exclude mania if bipolar disorder is included in NBD list Organic psychoses as a sequela of underlying disease	Community surveys	WHO has conducted surveys of schizophrenia/psychoses in a considerable number of developed and developing countries and has found a relatively similar prevalence of schizophrenia (about 3-6 per 1,000 adults) around the world. A few countries with much higher prevalence had used more inclusive diagnostic criteria. While treatment is effective in reducing/preventing symptoms of psychosis, many people with schizophrenia will continue to have relatively high levels of disability due to barriers to social participation and stigma. The WHO studies have also measured the proportion of time in psychosis in a wide range of countries (Leff et al 1992). In developed countries, schizophrenics have a RR of dying of around 1.5. This may be considerably higher in other countries.

Condition	Main health states or sequelae	Data sources	Approach to modelling
4 Bipolar disorder	Manic episodes, depressive episodes and relatively symptom-free periods in between	Community surveys, international studies	<p>Typical prevalence between 1 and 1.5% of adult population. Age at onset usually between 20 and 25 years of age. Chronic condition (average duration 20–25 years?).</p> <p>Bebbington and Ramana (1995) report a duration of 3.5 years between episodes. Assuming that the duration of a depressive and manic episode is similar to that of a major depressive episode, the Australian studies used the Dutch disability weight for moderate depression (0.34) for depressive episodes, an 'extrapolated' weight of 0.5 for manic episodes and argued that in between episodes there is 'rest' disability at the level of mild depression (0.14) due to stigma and the uncertainty about further episodes</p>
5 Substance use disorders	Alcohol dependence, harmful alcohol use	Community surveys	<p>Alcohol dependence is a chronic condition characterised by high levels of alcohol intake over a longer period leading to chronic physical and social problems. The category harmful alcohol use is used for the ill effects associated with binge drinking (e.g. acute intoxication, most of the alcohol-related injuries).</p> <p>Young people (especially males) may overstate alcohol problems in surveys ('bragging") while older people may be more likely to underreport alcohol problems ("denial").</p> <p>In the burden of disease list, we tend to include the mental and social problems in the category alcohol dependence/ harmful use but to count the alcohol-related sequelae of injuries, cirrhosis, pancreatitis and some cancers under separate categories. When estimating the burden due to alcohol as a risk factor attributable fractions are calculated for each of the associated conditions.</p>
	Heroin dependence	Community surveys	<p>dependence (underreporting due to stigma, higher refusal rate among heroin dependents and exclusion of heroin dependents who do not live in a household but are homeless or in prison). Also look at the numbers of people in treatment (e.g. methadone clinics, needle exchange programmes) and those in contact with the judiciary for heroin problems.</p> <p>Most heroin dependence starts in late teens and early twenties and after 15 to 25 years dependents tend to give up the habit. PTO</p>

<i>Condition</i>	<i>Main health states or sequelae</i>	<i>Data sources</i>	<i>Approach to modelling</i>
	Heroin dependence (continued)		<p>Household surveys tend to underestimate the prevalence of heroin</p> <p>Mortality in heroin dependent people can be significant with RRs of mortality in Australia as high as 10 to 20! Note that heroin overdose deaths may be classified under the ICD chapters for mental disorders (subsection on substance use disorders) as well as in the injury chapters under accidental poisoning with opioids. A further uncertainty is that there is not always enough information to distinguish accidental overdose deaths from intentional suicide by injection of large amounts of heroin.</p> <p>A considerable number of heroin dependents is able to hold down a job in spite of their habit. There tend to be a whole lot more addicts than the highly visible 'street junkies'.</p> <p>The consequences of i.v. drug use such as hepatitis B and C or HIV are included in the estimates for these conditions but can be grouped in a risk factor analysis of illegal drug use</p>
	Other legal and illegal drugs: marihuana, cocaine, stimulants, sedatives	Community surveys	One or more of these can be included in a national BoD study if they pose significant health problems and enough data to model the burden is available
6 Eating disorders	Anorexia and bulimia	Epidemiological studies, surveys	Rare in men. Average duration of anorexia 5–10 years and around 5 years in bulimia.
7 Childhood mental disorders	Autism, Asperger syndrome (as autism but not associated with intellectual disability)	Surveys, international studies	Three times more common in male children (Asperger even more common in males, M:F=1:8). Prevalence in industrialised countries between 2 and 13 per 10,000.

<i>Condition</i>	<i>Main health states or sequelae</i>	<i>Data sources</i>	<i>Approach to modelling</i>
J Neurological disorders			
1 Dementias	<p>Main types: Alzheimer's and vascular dementia; other types rare, e.g. congenital metabolic syndromes.</p> <p>Wide range in severity; if data are available it is useful to distinguish mild, moderate and severe dementia</p>	Local or international studies	<p>There are several meta-analyses of the prevalence of dementia in (mainly) EME countries (Jorm et al. 1987, Hofman et al. 1991 and Ritchie et al. 1992) and one meta-analysis of incidence (Jorm and Jolley 1998). The meta-analysis of incidence contains far fewer studies. There is a reasonable similarity in the prevalence of dementia across countries with the exception of prevalence estimates for the very old (85+ years). For the Australian study we could not create a DISMOD model that was consistent between the incidence and prevalence figures of the meta-analyses and decided to model incidence from the meta-analysis prevalence figures reported by Jorm et al.</p> <p>The Australian studies extrapolated a RR of dying of 1.8 up to age 75 and 1.6 in 75+ from available information on survival in dementia. Note that the number of deaths coded to dementia in the vital registration system will underestimate the 'true' number of attributable deaths (e.g. 'hidden' as a pneumonia death)</p>
2 Epilepsy	<p>Idiopathic epilepsy</p> <p>You may want to distinguish 'mild' and severe epilepsy, e.g. by the number of seizures per year</p>	Community surveys, treatment registers	<p>Treatment registers are likely to underestimate the true prevalence of epilepsy in countries with great stigma associated with the disease or a preference to treat epilepsy in the traditional medical system.</p> <p>There is one old study from the USA reporting remission rates, defined as 5 years seizure free (Annegers 1979) and relapse rates. From these figures, the Australian studies estimated a 'nett' remission rate (subtracting relapse from remission rates) of 0.136 in 0-15 yrs, 0.09 in 15-24 yrs, 0.046 in 25-64 yrs and .012 in 65+ yrs.</p> <p>The prevalence of epilepsy varies considerably between countries with some countries having much higher prevalence due to the existence of cystocercosis as a major contributing cause.</p>
3 Parkinson	Consider modelling as a progression thru mild, moderate and severe stages after incidence	Community survey, international studies	Prevalence 'similar' across different European countries (de Rijk et al. 1997). RR of dying 2.7 (Louis et al. 1997). Australian studies extrapolated from Tandberg et al. (1995) that 79% of time is spent in a mild health state, 14% in a moderate state and a remaining 7% of duration in a severe state (levels of severity as defined by descriptions of Dutch DWs)

Condition	Main health states or sequelae	Data sources	Approach to modelling
4 Multiple sclerosis	If possible distinguish between a relapsing/remitting phase and a progressive, more severe state	Epidemiological studies	80% of patients have an exacerbating-remitting clinical course in the early stage of the disease; the remaining 20% has a progressive course from onset. Patients with a relapsing-remitting course have earlier onset (29 years) than those with a progressive course (37 years). The mean duration from onset to death is more than 25 years, about 45% of patients having a benign course (i.e. only mild to moderate disability after a period of 15 years). Over 50% of patients in the community with MS are fully ambulatory. (McLeod 1994).
K Sense disorders			If a community prevalence survey of vision disorders is available make sure that estimates for all causes of blindness (including blindness as a sequela of other diseases such as trachoma, onchocerciasis, diabetic retinopathy, congenital anomalies or trauma) add up to grand total. In developing countries it may be necessary to model a RR of dying of 2 for blind people
1 Cataract	Blindness If data available, consider mild, moderate and severe vision loss	Surveys, epidemiological studies, hospital data on operations	Model remission from hospital figures on operations (but consider that most people will need surgery on both eyes and that number of operations may therefore be close to twice the number of people affected!). If lens implants are available, treatment gives full remission. If only cataract extraction is available consider awarding some rest disability for having to wear thick-lensed glasses with reduced vision. Diabetes is a risk factor for cataract (RR estimates around 4 in <55 yrs, 3 in 55-64 yrs and 2 in 65+ yrs).
2 Glaucoma	Blindness	Surveys, epidemiological studies	Diabetes is a risk factor for glaucoma with a RR of around 2.
3 Macula degeneration	Blindness	Surveys	An important cause of blindness in EME countries and other countries with a lot of elderly people

Condition	Main health states or sequelae	Data sources	Approach to modelling
4 Hearing loss	Acquired deafness (estimate other causes of deafness by underlying disease, e.g. meningitis; separate category for congenital deafness?) If possible: mild (25–34 dB), moderate (35–44 dB) and severe (45+ dB) hearing loss	Surveys, epidemiological studies	If overall prevalence of hearing loss is available, make sure that all estimates of causes of hearing loss (e.g. otitis, meningitis, congenital, trauma, age-onset hearing loss) add up to total
L Cardiovascular diseases			Heart failure is a sequela of many cardiovascular conditions: congenital heart disease, rheumatic heart disease, ischaemic heart disease, hypertensive heart disease and the heterogenous group of 'inflammatory' heart disease. Age-specific algorithms exist (GBD study, Mauritius and Australian BoD studies) to redistribute deaths coded to heart failure to the most likely underlying cause.
1 Rheumatic heart disease	Heart failure is the main disabling sequela	Epidemiological studies, hospital data on valve replacements	Untreated duration probably between 4 and 6 years as estimated by GBD 1990. Build in remission thru valve replacement based on hospital data.

Condition	Main health states or sequelae	Data sources	Approach to modelling
2 Ischaemic heart disease	Acute myocardial infarction (AMI) Angina pectoris (without having had an infarct and post-AMI) Heart failure post-AMI	Survey data for angina, hospital data for AMI, epidemiological studies for % post-MI developing HF	<p>are small in comparison to YLL but likely to rank among top twenty causes of YLD. It is not easy to model IHD with its three main disabling health states in one model, as this requires a lot of information on the average duration of health states and the probabilities of moving from one to another health state. It may be easiest to model each separately:</p> <ul style="list-style-type: none"> • AMI with a short duration (e.g. 6-8 weeks) and model first ever and repeat AMI together (if you discount this is not quite consistent with an incidence of disease approach but AMI do not contribute a lot to YLD because of the short duration and therefore the error of ignoring discounting of the disability of repeat events some time after the first event is not so great. • Heart failure post-AMI occurs in an estimated % of cases (e.g. 20%) with average duration as in GBD (e.g. 2–7 years depending on age)? • Angina regardless of it starting after or without an MI if survey prevalence data are available
2 Ischaemic heart disease (continued)			<ul style="list-style-type: none"> • A major cause of DALYs in all regions except sub-Saharan Africa. YLD <p>Prevalence of angina is not so easy to measure in community surveys. Validation studies of the Rose questionnaire show high false positive and false negatives, particularly in women.</p>

Condition	Main health states or sequelae	Data sources	Approach to modelling
3 Stroke	Mild, moderate and severe permanent impairments	Surveys, epidemiological studies, hospital admission data	<p>Half of men are symptom-free one year after a first episode of stroke. While the incidence of stroke is lower in women, they tend to have more severe disease (e.g. only about 1/3 symptom-free after a year). If not symptom-free at one year after stroke, permanent disability is assumed</p> <p>Mortality is high in first 28 days (29% of 75+ and 18% of <75 in New Zealand)</p> <p>It is not so easy to model stroke in DISMOD as the risk of mortality is not uniform over time. If prevalence figures of stroke are available and hospital incidence data incomplete or unavailable, it may be necessary to model symptomatic survivors past one year after event separately in DISMOD forcing you to make assumptions about the proportion of prevalent cases who are in their first year post-stroke and the proportion of stroke deaths that occur in survivors past one year after event.</p> <p>The observed deaths from stroke may underestimate the excess mortality in people with stroke (e.g. deaths coded as pneumonia)</p>
4 Inflammatory heart disease (cardiomyopathy, myocarditis, non-TB pericarditis and endocarditis)	Heart failure	Epidemiological studies, hospital admission data	<p>Cardiomyopathy and endocarditis are the most common of this group of conditions. Non-TB pericarditis is not so common and also does not contribute a lot of YLD because of the short duration (e.g. 1 month). There is not a whole lot of epidemiological information on these conditions. Routine hospital admission data in countries with good access to health care may give an indication of the magnitude but most likely you will need to examine the few international epidemiological studies.</p>
5 Hypertensive heart disease	Heart failure	Epidemiological studies, hospital admission data	<p>As with inflammatory heart disease, it may be hard to find local data on prevalence or incidence. A few international studies and hospital data (if good access) may help. If vital registration is of good quality you may consider using– in DISMOD –mortality (after redistribution of heart failure deaths!), remission (=0) and average duration (2–4 years) as input variables to derive incidence.</p>

M Respiratory diseases

Condition	Main health states or sequelae	Data sources	Approach to modelling
1 COPD	<p>Consider distinguishing mild, moderate and severe COPD.</p> <p>Shortness of breath is main complaint</p>	Epidemiological studies, surveys using spirometry	<p>Strongly linked with tobacco or chronic exposure to indoor air pollution. Incidence rises steeply with older age. There is a wide spectrum in the severity of symptoms. Therefore, if data allow it is preferable to distinguish different levels of severity.</p> <p>Self-reported prevalence of chronic bronchitis/emphysema may overestimate true prevalence. If survey data are available with spirometry this may be used in combination with answers to questions about the associated level of symptoms to determine different categories of severity. In general, symptoms start at FEV₁ (forced expiratory volume) < 70% of normal for age and will be more severe when FEV₁ < 50% of normal for age.</p> <p>Model incidence in DISMOD assuming no remission and mortality as observed for COPD (but consider that people with COPD are more likely to die from other e.g. tobacco related conditions than the general public and therefore you may want to use higher mortality rates than observed from COPD alone over and above the background mortality rate of the general population).</p>

Condition	Main health states or sequelae	Data sources	Approach to modelling																											
2 Asthma		Epidemiological surveys	<p>Surveys of self-reported asthma (via a set of questions about wheezing and shortness of breath as well as having been told a diagnosis of asthma by a doctor) overestimate the 'true' prevalence of asthma or if you accept the self-reported prevalence you must consider that a large proportion will have only minor symptoms (and therefore take this into account in your DW!). Australian survey results comparing the prevalence of self-reported asthma with that of a stricter definition of asthma including a positive airway hyperresponsiveness test show a difference by a factor 2–3 (see Table 7.2).</p> <p>Bronnimann (1986) is a useful reference for the remission of asthma in the US after a mean follow-up time of 9.4 years. The remission rate can be estimated from the % remitted during follow-up with the formula: remission rate = $-\ln(1 - \% \text{ remitted}) / 9.4 \text{ years}$:</p> <table border="1"> <thead> <tr> <th>Age group</th> <th>% remission</th> <th>remission rate</th> </tr> </thead> <tbody> <tr> <td>0-9</td> <td>35</td> <td>0.046</td> </tr> <tr> <td>10-19</td> <td>65</td> <td>0.112</td> </tr> <tr> <td>20-29</td> <td>30</td> <td>0.038</td> </tr> <tr> <td>30-39</td> <td>15</td> <td>0.017</td> </tr> <tr> <td>40-49</td> <td>6</td> <td>0.007</td> </tr> <tr> <td>50-59</td> <td>18</td> <td>0.021</td> </tr> <tr> <td>60-69</td> <td>30</td> <td>0.038</td> </tr> <tr> <td>70+</td> <td>26</td> <td>0.032</td> </tr> </tbody> </table> <p>Given the right epidemiological information and disability weights it would be useful to distinguish different levels of severity. There are two ways of doing this. First, together with an epidemiological estimate of the proportion of time symptomatic (e.g. from Bauman et al. 1992) the time spent with asthma can be valued separately for symptomatic time with a higher DW and asymptomatic time with a small DW (to account for the limitations imposed by a diagnosis of asthma even when not having symptoms). The second option is to define mild (e.g. less than 1 attack per month), moderate (e.g. between 1 and 10 attacks or symptomatic days a month) and severe asthma (e.g. more than 10 days a month symptomatic) and find the right epidemiological info to estimate the proportions mild/moderate and severe and apply appropriate DWs.</p>	Age group	% remission	remission rate	0-9	35	0.046	10-19	65	0.112	20-29	30	0.038	30-39	15	0.017	40-49	6	0.007	50-59	18	0.021	60-69	30	0.038	70+	26	0.032
Age group	% remission	remission rate																												
0-9	35	0.046																												
10-19	65	0.112																												
20-29	30	0.038																												
30-39	15	0.017																												
40-49	6	0.007																												
50-59	18	0.021																												
60-69	30	0.038																												
70+	26	0.032																												

Condition	Main health states or sequelae	Data sources	Approach to modelling
N Digestive diseases			
1 Peptic ulcer disease		Epidemiological studies, primary care data	New developments implicating <i>H Pylori</i> as the cause in the vast majority of cases of peptic ulcer disease have changed the way in which YLD from this disease are modelled. While as it was considered a chronic condition in the past (GBD estimated an average duration of 6 years) it can now be successfully cured with a short course of antibiotics. Estimation of YLD for PUD should therefore examine the exposure to antibiotic treatment and give short duration to those receiving curative treatment and reserve the longer duration for those not cured (including the 10-15% of largely elderly people who get PUD from chronic use of anti-inflammatory drugs and therefore are not curable with antibiotics).
2 Cirrhosis		Epidemiological studies	<p>Cirrhosis is a sequel of a number of diseases. In the GBD, cirrhosis due to hepatitis is counted under hepatitis but the remaining causes (mainly alcohol and a smaller rest group of metabolic and auto-immune causes) are counted in this category. If a credible estimate of the total number of cases of cirrhosis is available (which is not easily determined given that a liver biopsy is required for diagnosis!), make sure that the separate estimates for hepatitis and the main cirrhosis category add up.</p> <p>While the average duration for cirrhosis may be more in the direction of 15 years, it tends not to give disability until later in the disease. In Australia, disability was awarded to the last three years of life with cirrhosis with a greater weight for the last two months before dying. If liver transplants are done, a 'remission' can be built in based on hospital figures of transplants. However, one should consider that post-transplant there is considerable remaining disability.</p>

Condition	Main health states or sequelae	Data sources	Approach to modelling
O Genito-urinary diseases			
1 Nephritis and nephrosis	Renal failure	Register of renal failure, epidemiological studies	<p>Renal failure is also a sequela of diabetes, congenital disorders (dysplasia and polycystic kidneys) and poisoning (e.g. analgesic nephropathy). If you have an estimate of the overall number of people with renal failure, e.g. from a register, you want to make sure that the numbers of the different estimates of renal failure add up.</p> <p>While an important cause of mortality, renal failure does not cause much disability because duration is short (e.g. a year) unless chronic dialysis and/or transplants are available. The disability of chronic dialysis is considerable. As with liver transplants, rest-disability should be taken into consideration to account for complications and the side-effects of anti-rejection treatment.</p>
2 Benign prostatic hypertrophy		Hospital data on prostatectomy	<p>If there is good access to surgery, the recorded number of prostatectomies is a good starting point. In consultation with a local urology expert, you may get a feel for what proportion of men with BPH will end up with surgery and what proportion would not access treatment or be treated medically (with a lesser success rate of taking away symptoms). The operation carries a significant risk of side effects such as incontinence and impotence.</p>
3 Infertility		Family planning surveys, Demographic and Health Surveys	<p>Secondary infertility is a sequela of STD, septic abortion and maternal sepsis. You may want to consider estimating primary infertility as well. If there are figures on the prevalence of infertility, do all different estimates for infertility add up?</p>
P Skin diseases			
	Eczema	Survey	<p>There are many varied skin diseases and it will be hard to do justice to all. Eczema is probably the most common disabling condition. The prevalence is highest in young children but it remains a common problem at all ages. It is typically a condition with periods of remission and relapses.</p>
Q Musculoskeletal conditions			
1 Rheumatoid arthritis	If data and DWs are available consider distinguishing mild, moderate and severe	Epidemiological studies	<p>Self-report surveys may overestimate RA as joint problems other than RA are often labelled as 'rheumatism'. Remission is small. The disease is more common and starts at an earlier age in women. The RR of dying may be elevated (Pincus et al. 1994: 1.6)</p>

Condition	Main health states or sequelae	Data sources	Approach to modelling
2 Osteoarthritis		Epidemiological studies; hospital data on surgical interventions	Self-report surveys may not accurately estimate osteoarthritis (see remark under RA). There are a few studies of OA that have used a radiological classification of disease. X-ray findings do not always match symptoms but prevalence based on radiography is probably a reasonable population estimate. Osteoarthritis of the hip and the knee tend not to occur in the same person while the knee and hands/fingers are often affected simultaneously. If joint replacements are commonly performed, hospital figures may help to establish remission thru treatment. Otherwise this is a slowly progressive chronic condition with no or minimally added extra mortality. The incidence is higher in women, particularly at older ages.
R Congenital anomalies			Multiple anomalies in one child are not uncommon (around 25% of more serious malformations). Consider adjusting for comorbidity by awarding disability only to the more serious of comorbid anomalies.
1 Spina bifida		Birth registers, disability surveys	The five conditions listed below contribute most to disability. Consider adding estimates of congenital deafness and blindness. More than a third of children born with spina bifida are expected to die soon after birth. The majority of cases are at lumbar or thoracic level with considerable disability (paraplegia and incontinence). GBD 1990 estimated normal life expectancy for survivors of spina bifida. This may require scaling down particularly if services for disabled are poor.
2 Cleft palate and lip		Birth registers, surveys, hospital data on surgical corrections	After treatment, minimal disability remains (see GBD treated and untreated weights)
3 Congenital heart disease	Septum defects, Fallot's tetralogy, pulmonary stenosis, transposition. Heart failure and for some cyanosis	Birth registers, surveys, hospital data on surgical corrections	This category includes a range of different conditions with varying prognosis. Atrial and ventricular septum defects close spontaneously or if surgically corrected do not lead to reduced life expectancy. Transposition and Fallot's require multiple surgical interventions and survival is not so good. Around 80% of surgically corrected pulmonary stenosis leaves no rest disability.

Condition	Main health states or sequelae	Data sources	Approach to modelling
4 Down syndrome	Intellectual disability (mental retardation) Mild (IQ 50–69), moderate (IQ 35–49), severe (IQ 20–34) and profound (IQ <20)	Surveys, birth registers	Life expectancy is significantly reduced, even in countries with good access to medical care. The RR of dying is around 5 for those with mild IQ loss and as high as 15 for those with profound IQ loss. If an estimate of total prevalence of intellectual disability is available, make sure that the estimates made in different parts of your NBD schedule add up (e.g. the sequelae of meningitis, trauma, perinatal conditions, autism, poisoning, brain tumours and other congenital anomalies)
5 Other chromosomal anomalies	Intellectual disability (see above)	Surveys, birth registers	Intellectual disability is an important feature of most other chromosomal anomalies.
S Oral conditions			
1 Dental caries		Oral health survey (DMFT, dmft: number of decayed, missing and filled teeth)	Probably easiest to model as short episodes for each decayed tooth (GBD 1990 estimate: 2 weeks) with symptoms if access to treatment is good. The average duration in the absence of treatment may need to be quite a bit longer (discuss with local experts).
2 Periodontitis		Oral health survey	If prevalence available from survey, DISMOD can be used to derive incidence. The difficulty is to determine the average duration. GBD 1990 estimated 2–3 years per episode. Suggest consulting local experts.
3 Edentulism		Oral health survey	Big difference in disability between treated (false teeth) and untreated. Look for prevalence figures from surveys and use DISMOD to derive incidence assuming no remission and no mortality.

DISABLING SEQUELAE FROM INJURIES

The main sources of disability from injuries are road traffic accidents, falls, fires, other unintentional injuries and, in some countries, violence and war. The group of 'other unintentional injuries' is often the leading cause of YLD in injuries. It includes a wide variety of injuries. Being struck or crushed by an object, machinery accidents and sports injuries are important causes of YLD within this group. Poisoning, drowning and self-inflicted injuries mainly cause YLL and if disability is incurred, it is usually of short duration and therefore does not contribute significantly to YLD.

A meaningful estimation of YLD needs to take into account that in each injury category disability can occur from different impairments affecting different parts of the body. Therefore, information is required on both the type of injury and the nature of injury. Estimation of YLD for injuries was facilitated in Mauritius and Australia by the existence of databases of health facility data that had recorded both type and nature of injury codes. In Mauritius, only hospital data were available and inflation figures

Type of injury:	The cause of the bodily harm, e.g. road traffic accident, falls or fires
Nature of injury:	A description of the actual bodily harm caused by the type of injury, e.g. a fractured hip, brain injury or third degree burns over 20% of body surface

as a ratio for non-hospitalised cases to hospitalised cases were estimated. In the state Victoria of Australia, data were also available on injuries presented at emergency departments which deal with the vast majority of non-hospitalised injuries. The ratio of YLD caused by injuries that did not lead to a hospital admission and YLD resulting from injuries that did lead to an admission was 0.1 with a bit higher ratios for falls, fires and sports injuries. This indicates that if a country has hospital data on injuries only, most of the important disabling sequelae are likely to be covered.

The GBD 1990 made use of the data from Mauritius and added similar information from Chile and Sweden to develop death to incidence ratios and applied these to extrapolate YLD from injuries. Details of these calculations have not been formally published. If hospital and emergency department data on injuries are not available, injury YLDs can be extrapolated from the GBD figures using YLD to YLL ratios by age, sex and type of injury. If local information is available more accurate YLD calculations are possible (Figure 10.1).

The following steps are involved in the estimation of injury YLD from hospital data:

1. Extract incidence data on nature of injury categories by age and sex and type of injury category from the hospital admission database and, if available, an emergency department database. If you have both sources of data, consider how you can avoid double counting the same person who presented at the emergency department and was subsequently admitted (e.g. is there a variable in your emergency data base that indicates whether admission followed?). The GBD has published a list of 33 nature-of-injury categories largely based on work that was developed for the Mauritius National Burden of Disease Study. Table 10.2 reproduces this list with the corresponding ICD-9 codes and adds the ICD-10 codes to it. ICD-10 codes for nature of injury vary considerably from those in ICD-9 as they are grouped by body part affected rather than by the nature of injury.
2. Examine the GBD assumptions for the duration and disability weights associated with each of the nature of injury groups. These assumptions are published in table 4.4 on pages 214–217 of the GBD Volume I or the 'green book'. Some of the sequelae specify a duration for the disability associated by the immediate injury and a proportion of cases that will endure life long disabling states. For example, the short-term duration for intracranial injury is 0.067 years (or 3.5 weeks) while 5% of cases of intracranial injury is estimated to have life-long disability. There are not many follow-up studies of the 'natural history' of injuries and most of the GBD assumptions are based on expert opinion rather than evidence. It would be a good idea to discuss some of these assumptions with a group of local trauma experts. In particular, if a study is locally available on the downstream consequences of injuries examine how these results compare with the GBD assumptions.

Figure 10.1 Flow Chart for the Estimation of YLD from Injuries.

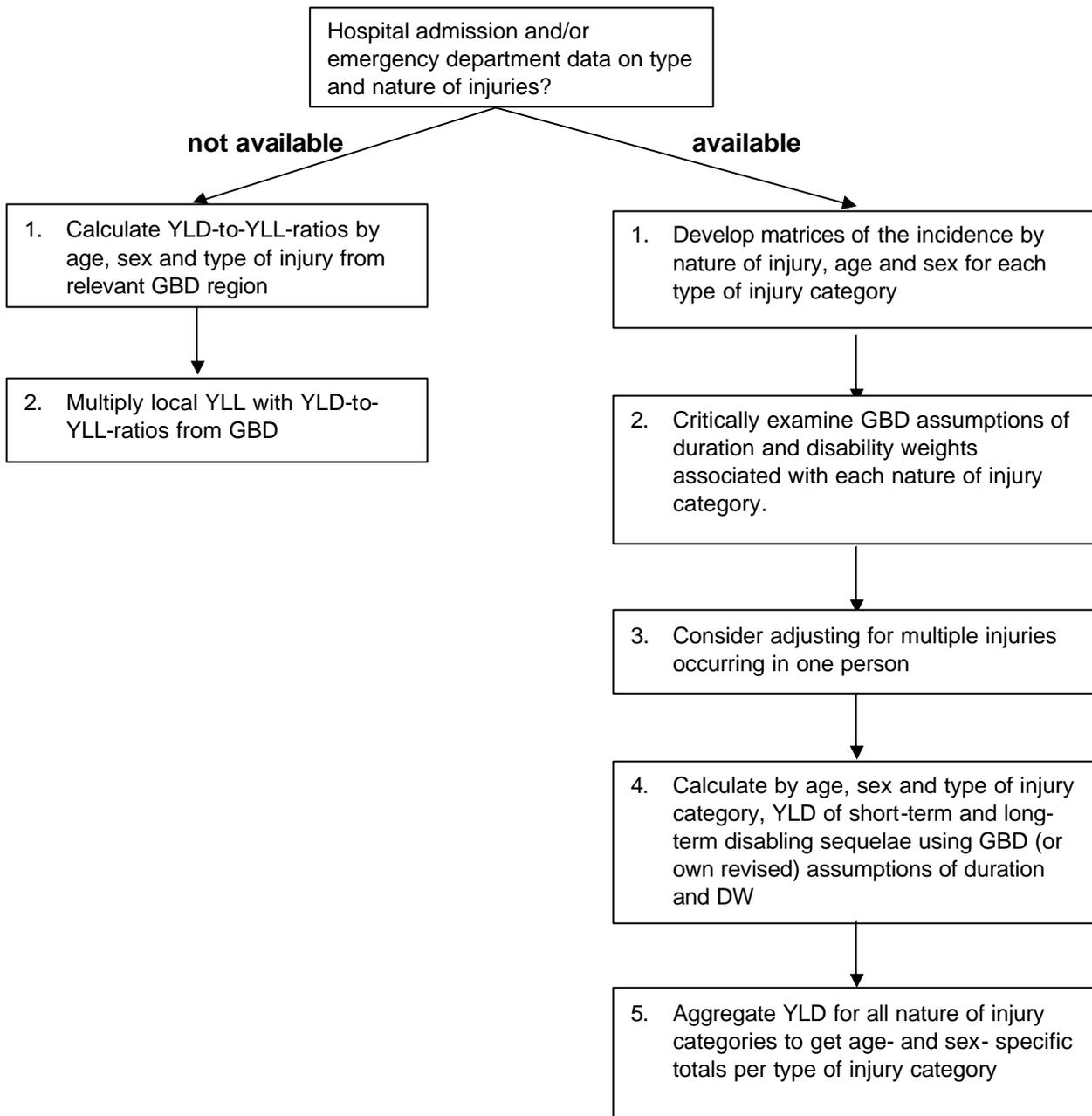


Table 10.2. GBD Short List of ICD–9 and ICD–10 Nature of Injury Codes

Name	N-code (ICD–9)	ICD–10 code
1 Fractured skull ¹	800 to 801	S02.0/1/7/9, T90.2
2 Fractured face bones ¹	802	S02.2/6/8
3 Fractured vertebral column	805	S12, S22.0/1, S32.0/7, T91.1
4 Injured spinal cord	806 and 952	S14, S24, S34, T06.0/1, T08, T91.3
5 Fractured rib or sternum ²	807	S22.2–9
6 Fractured pelvis ²	808	S32.1–5/8, T91.2
7 Fractured clavicle, scapula, humerus ³	810–812	S42, S49.7
8 Fractured radius or ulna ³	813	S52, S59.7, T10, T92.1
9 Fractured hand bones ³	814–817	S62, S69.7, T92.2
10 Fractured femur ⁴	820–821	S72, S79.7
11 Fractured patella, tibia, or fibula ⁴	822–823	S82.0–4, S82.7/9, S89.7, T12
12 Fractured ankle ⁴	824	S82.5–6/8
13 Fractured foot bones ⁴	825–826	S92, S99.7
14 Other dislocation	830,833–834, 836–839	S03.0–3, S13, S23, S33, S53, S63.0/1, S83.1–3, S93.1–3, T03, T11.2, T13.2, T14.3, T92.3, T93.3
15 Dislocated shoulder, elbow, hip	831,832,835	S43, S73
16 Sprains	840–848	S03.4/5, S16, S29.0, S39.0, S46, S56, S63.5–7, S66, S76, S83.4/7, S86, S93.4/6, S96, T06.4, T11.5, T13.5, T14.6, T92.5, T93.5
17 Intracranial injury	850–854	S06, T90.5
18 Internal injuries	860–869	S25–S27, S35–S37, S39.6, T06.4, T91.4/5
19 Open wound	870,872–884, 890–894	S01, S08, S11, S15, S21, S31, S41, S45, S51, S55, S61, S65, S71, S75, S81, S85, S91, S95, T01, T11.1/4, T13.5, T14.6, T90.1, T92.5, T93.5
20 Injury to eyes	871,950	S05, T90.4
21 Amputated thumb	885	S68.0
22 Amputated finger	886	S68.1/2
23 Amputated arm	887	S48, S58, S68.3–9, T05.0/2, T11.6
24 Amputated toe ⁵	895	S98.1/2
25 Amputated foot ⁵	896,897.0–1	S98.0/3/4, T05.3
26 Amputated leg ⁵	897.2–3	S78, S88, T05.4/6, T13.6
27 Crushing	925–929	S07, S17, S28, S38, S47, S57, S67, S77, S87, S97, T04, T14.7, T92.6, T93.6
28 Bums < 20% ⁶	940–947,948.0–1	T31.0/1
29 Bums 20–60% ⁶	948.2–5	T331.2/5
30 Bums > 60% ⁶	948.6–9	T31.6/9
31 Injured nerves	951,953–957	S04, S44, S54, S64, S74, S84, S94, T06.2, T11.3, T13.3, T14.4
32 Poisoning	960–979, 980–989	T36–T65, T96–T97

Name	N-code (ICD-9)	ICD-10 code
33 Residual	900-924, 930-939	S00, S09-S10, S20, S29.8/9, S30, S39.8/9, S40, S49.8/9, S50, S59.8/9, S60, S69.8/9, S70, S79.8/9, S80, S89.8/9, S90, S99.8/9, T00, T09, T11.0/8/9, T13.0/8/9, T14.0/2/8/9, T33-T35, T66-T88, T90.0/8/9, T92.0/8/9, T93.0/8/9, T98

- 1 The N-codes 803 and 804 were assigned to fractured skull following the distribution of N-codes 801 and 802.
 - 2 The N-code 809 was assigned to fractured rib, sternum, and pelvis following the distribution of N-codes 807 and 808.
 - 3 The N-codes 818 and 819 were assigned to fractured clavicle, scapula, humerus, radius, ulna and hand bones following the distribution of N-codes 810-817.
 - 4 The N-codes 827 and 828 were assigned to Fractured patella, tibia, fibula, ankle and foot bones following the distribution of N-codes 822-826.
 - 5 The N-codes 897.4 to 897.7 were assigned to Amputated toe, foot and leg following the distribution of N-codes 895, 896 and 897.0-897.3.
 - 6 The N-code 949 was assigned to Burns following the N-codes 940-948. In ICD-10, burns are classified by site (T20-T30) and/or proportion of body surface affected (T31). If there is no information given on the proportion of body surface affected, a decision will have to be made how to map the T20-T30 codes across.
 - 7 The N-codes 958-959 and 989-999 were assigned to all causes following their distribution after applying notes 1 through 6.
3. The same person may have multiple injuries from the same accident. Counting disability from each of the separate injuries could result in overcounting YLD. In the Australian studies a simple hierarchy was set up for people with multiple injuries counting only the most serious of concurrent permanent disabilities (Table 10.3).

Table 10.3. Hierarchy for Coexisting Injuries from Victorian Burden of Disease Study

Rank order of importance	Nature of injury	GBD weight	GBD duration
1	Spinal cord lesion	0.725	Lifelong
2	Brain injury	0.350	Lifelong (5% of incident cases)
3	Burns to >60% of body surface	0.255	Lifelong
4	Burns to 20-60% of body surface	0.255	Lifelong
5	Fractured skull	0.350	Lifelong (15% of incident cases)
6	Fractured femur	0.272	Lifelong (5% of incident cases)
7	Nerve injuries	0.064	Lifelong
8	All other injuries		

4. For each of the type of injury categories, by age and sex, calculate YLD for all of the 33 nature of injury categories.
5. Add up total YLD by age and sex for each type of injury category. This will become a very large spreadsheet. As an example, a zipped self-extracting file with the Victorian injury YLD Excel file can be downloaded from <http://www.dhs.vic.gov.au/phd/9909065/filelist.htm>

11. CALCULATING DALYS

11.1 OVERVIEW AND FORMULAE

Total DALYs for each cause-age-sex group are calculated as the sum of the non-fatal burden (YLD) and the burden of premature mortality (YLL):

$$DALY = YLD + YLL$$

CALCULATING YLL

Whatever are the age categories chosen for calculation of YLD and DALYs in your NBD, it is recommended that you calculate YLL using deaths tabulated by five year age groups, and preferably, to separate infant deaths from those at ages 1-4, e.g.

0, 1-4, 5-9, 10-14,, 80-84, 85+

For deaths in each age interval, the calculation of YLL requires estimation of the average age at death. If detailed data on all-cause deaths are available by single year of age, and by days and months for infant deaths, this can be calculated directly from the data for your population. If you have information on date of birth and date of death you can calculate the mean age at death in an interval accurately. Most of the time you will have the age at death in years. In that case, when calculating a mean age at death in an age interval, you need to add 0.5 years to the calculated mean. This is to take into account that for example, deaths at age 60 include deaths at true ages between 60 and 60.99 years. Otherwise, it is generally assumed that the average age at death is the mid-point of each five-year age group, apart from the infant deaths (where it is assumed to be 0.1 years in low mortality countries and 0.3 years in high mortality countries) and the 1-4 year age group (where it is assumed to be 2.6 years).

Standard life expectancies for these average ages at death must be calculated for each age-sex group by interpolation between the standard life expectancies at exact ages of death given in either the full Model West standard life tables by single year of age, or the abridged standard life tables by five-year age intervals. These standard lifetables are available on the CD that accompanies this Manual, and may also be downloaded from the WHO website at <http://www.who.int/evidence>.

YLL for deaths lost in each age-sex category can be estimated from the observed mean age at death in the age interval and the standard life expectancy figures at the exact ages defining the age interval. Use these standard life expectancies to interpolate the standard life expectancy L for the observed mean age at death in the interval. You can then calculate total YLL for a given cause, age and sex from the corresponding number of deaths N as follows:

Without discounting or age weights:

$$YLL = N * L \quad (11.1)$$

With 3% discounting and uniform age weights:

$$YLL = \frac{N}{0.03} \left(1 - e^{-0.03L} \right) \quad (11.2)$$

The full formula for non-zero discounting and age weighting is given by Murray and Lopez (1996) as follows:

$$YLL = N C e^{(ra)} / (b+r)^2 \left[e^{-(b+r)(L+a)} [-(b+r)(L+a)-1] - e^{-(b+r)a} [-(b+r)a-1] \right] \quad (11.3)$$

where r is the discount rate (GBD standard value is 0.03), C is the age-weighting correction constant (GBD

standard value is 0.1658), β is the parameter from the age-weighting function (GBD standard value is 0.04), a is the age of onset, and L is the duration of disability or time lost due to premature mortality.

However, you generally do not need to use this formula if you are using the standard life expectancies used in the GBD 1990. In this case, YLL can be calculated easily from numbers of deaths using discounted and age weighted life expectancies interpolated for the appropriate exact ages at death from the right-hand columns given in the standard life tables (full or abridged).

YEARS LOST DUE TO DISABILITY

YLD are the disability component of DALYs. The basic formula for calculating YLD is:

$$YLD = I * DW * L \quad (11.4)$$

where I is the number of incident cases in the reference period, DW is the disability weight (in the range 0-1) and L is the average duration of disability (measured in years). With discounting at a rate of 3 per cent, the formula becomes:

$$YLD = \frac{I \times DW \times (1 - e^{-0.03L})}{0.03} \quad (11.5)$$

The full formulae for YLD with non-uniform age weights are given by:

$$YLD = I DW C e^{(ra)} / (b+r)^2 [e^{-(b+r)(L+a)} [(b+r)(L+a)-1] - e^{-(b+r)a} [(b+r)a-1]] \quad (11.6)$$

where DW is the disability weight, r is the discount rate (GBD standard value is 0.03), C is the age-weighting correction constant (GBD standard value is 0.1658), β is the parameter from the age-weighting function (GBD standard value is 0.04), a is the age of onset, and L is the duration of disability.

Using a parameter K that specifies whether age-weighting is applied ($K=1$) or not ($K=0$), we can combine the formulae (11.5) and (11.6) into a single general formula for YLD:

$$YLD = I DW \left\{ K C e^{(ra)} / (b+r)^2 [e^{-(b+r)(L+a)} [(b+r)(L+a)-1] - e^{-(b+r)a} [(b+r)a-1]] + (1-K) (L/r) (1 - e^{-rL}) \right\} \quad (11.7)$$

11.2 SETTING UP WORKSHEETS AND MANAGING YOUR DATA

To date, national burden of disease studies have generally used spreadsheet software (Excel or Lotus) to calculate DALYs for each cause category and to summarise the results into tables for publication. The disease worksheets used in the Australian studies may be obtained from the website <http://www.dhs.vic.gov.au/phd/9909065/index.htm>

Figure 11.1 illustrates the layout used to calculate YLD for a disease sequela. This spreadsheet is also available on the accompanying CD to this Manual, and can be downloaded from the WHO website at <http://www.who.int/evidence>.

The YLD formula in cell H116 (circled) uses the data on incidence (column C), age at onset (column E), average duration (column F) and the disability weight (column G) to calculate the YLD as follows:

$$=IF(Rate=0,(\$C116*\$G116)*(Agewt*Const*((EXP(-Beta*\$E116))/Beta^2)*((EXP(-Beta*\$F116))*(-Beta*(\$F116+\$E116)-1)-(-Beta*\$E116-1))+((1-Agewt)*\$F116)),+\$C116*\$G116*(Agewt*((Const*EXP(Rate*\$E116))/(BplusR^2))*((EXP(BplusR*(\$F116+\$E116))*(BplusR*(\$F116+\$E116)-1))-$$

$$(EXP(BplusR*\$E116)*(BplusR*\$E116-1))+((1-Agewt)/Rate)*((1-EXP(-Rate*\$F116))))$$

This formula is the same as that given above in equation 11.7, but has been arranged in a form which is easier to enter in Excel or Lotus. The cell names Rate, Agewt etc in the formula refer to the named cells at the top of the spreadsheet which contain the parameters relating to age weights and discounting. Note that parameter K specifies whether age weighting is applied (K=1) or not (K=0). It is possible to apply fractional age weighting by specifying a value of K between 0 and 1.

11.3 RESIDUAL CATEGORIES

Because YLL are calculated for all deaths, they are as complete as the death registration data allow. Because the YLL are comprehensive, it is also necessary to estimate YLD for residual categories of disease and injury to ensure a balanced picture of the total burden of disease.

For the main disease categories for which there are substantial numbers of deaths, YLD for the residual category can be estimated for each age–sex group assuming that the YLD/YLL ratio is the same as that for the categories for which specific YLD models have been made to estimate YLD for all of these residual categories (see Global Burden of Disease Study Volume 1, page 211). In order to do this, YLL for each age–sex group are multiplied by the average YLD/YLL ratio for the combined set of disease categories within that main disease category for which individual YLD analyses have been carried out.

For main disease categories where there is a very small mortality burden, this method is not appropriate. In the GBD 1990, residual YLD were not estimated for these categories (eg. mental disorders, musculoskeletal disorders). In the Australian burden of disease studies, explicit YLD analyses were carried out for some of these residual categories using available prevalence or incidence data.

11.3 SENSITIVITY AND UNCERTAINTY ANALYSES

The GBD 1990 study and most NBD studies carried out to date have examined the sensitivity of the DALY estimates to the various social value choices, such as the standard life expectancies used, the disability weights, discounting and age weighting. In carrying out an NBD, the sensitivity of the final results to the social preferences used in YLL and YLD should be examined by recalculating the entire set of estimates using different values of discount rate and age weighting, and possibly other values, such as the disability weights.

Burden of disease estimates involve uncertainty of varying degrees in all the input data (in some cases very high degrees of uncertainty) and the use of judgement in achieving internal consistency. It would be highly desirable to provide estimates of the uncertainty associated with DALY estimates for each cause category in an NBD.

The calculation of the mortality burden (YLL) is generally straightforward, and the precision of the estimates is almost entirely dependent on the quality of the data on underlying cause of death and level of mortality. Techniques for estimating uncertainty in level of mortality and life expectancy are discussed by Salomon and Murray (2000). There may be additional sources of uncertainty in mortality associated with the redistribution of ill-defined and garbage codes, and for some particular causes of death where ICD coding on death certificates may underestimate the true numbers of deaths (e.g. HIV/AIDS and heroin overdose deaths).

The calculation of the disability burden (YLD) requires much more extensive epidemiological modelling drawing on a diverse range of data sources, research findings and expert opinion. Thus, the precision of the YLD estimates is not really quantifiable in the usual statistical sense of deriving a confidence interval. The precision varies between diseases and depends on the specific disease model applied and the source and nature of the data underlying the disease model. It is highly desirable to model the uncertainty of your burden of disease estimates using simulation modelling and sensitivity analyses. As a first step, you should determine which particular inputs and assumptions the resultant YLD estimates are highly sensitive to. It is often the case, that the YLD are quite insensitive to some of the inputs (eg. case fatality rates, when these are low and have little impact on average duration).

Although there is considerable uncertainty in YLD estimates for some causes, you will likely find that the uncertainty in the estimates of disease burden for many conditions is not excessive. Overall, about half or more of the burden is typically contributed by YLL, where estimates are generally fairly precise. Around 40 per cent of the YLD burden is contributed by a small number of diseases (including ischaemic heart disease, cancers, stroke, diabetes, affective and anxiety disorders, asthma, osteoarthritis and some Group I conditions in developing countries) where it will be important for you to concentrate your efforts to obtain local data. This leaves around 30 per cent of the total disease burden with varying higher levels of uncertainty.

Figure 11.1 Example of Excel Worksheet for Calculation of YLD for a Single Cause Sequela.

Column:	A	B	C	D	E	F	G	H	I
Cell name	DALY Parameters								
Rate	→	0.03	Discount rate (r)						
Beta	→	0.04	Beta (b)						
Const	→	0.1658	Constant (C)						
BplusR	→	-0.07	-(b+r)						
Agewt	→	1	K						
11. YLD for Alzheimer and other dementias									
Australia	Population	Incidence	Incidence	Age at	Duration	Disability	YLDs	YLD per	
	('00000)		per 100,000	onset		Weight		100,000	
Males									
0-4	6.66	0	0	2.5	0.0	0.512	0.0	0.0	
5-14	13.39	0	0	10	0.0	0.512	0.0	0.0	
15-24	13.64	0	0	20	0.0	0.512	0.0	0.0	
25-34	14.31	0	0	30	0.0	0.512	0.0	0.0	
35-44	14.03	0	0	40	0.0	0.512	0.0	0.0	
45-54	11.72	117	10	50	23.7	0.512	913.5	78.0	
55-64	7.74	665	86	59.9	14.5	0.512	3087.7	399.1	
65-74	6.14	1,828	298	69.8	9.2	0.512	4766.0	776.8	
75+	3.46	6,918	2001	80.7	3.8	0.512	6404.1	1852.2	
	91.08	9,529	105	76.8	5.8	0.51	15171	166.6	
Females									
0-4	6.31	0	0	2.5	0.0	0.512	0.0	0.0	
5-14	12.75	0	0	10	0.0	0.512	0.0	0.0	
15-24	13.12	0	0	20	0.0	0.512	0.0	0.0	
25-34	14.31	0	0	30	0.0	0.512	0.0	0.0	
35-44	14.08	0	0	40	0.0	0.512	0.0	0.0	
45-54	11.37	114	10	50	28.3	0.512	960.7	84.5	
55-64	7.64	657	86	60	18.4	0.512	3519.9	460.6	
65-74	6.82	2,052	301	69.9	11.9	0.512	6439.1	944.5	
75+	5.62	11,482	2043	81.3	4.3	0.512	11557.7	2056.5	
	92.03	14,305	155	78.4	6.2	0.51	22477.3	244.2	

It should also be noted that precise values of the DALY burden for many of the conditions lower down in the overall ranking of conditions will fluctuate from year to year due to variations in the incidence and mortality of such conditions. In particular, the estimates for many of the infectious diseases will vary from year to year depending on whether the year is an epidemic year or not. For this reason, precise ordering of the smaller causes of burden is not very useful.

DISMOD II provides a facility to estimate uncertainty in disease model outputs given specified levels of uncertainty in the inputs. This may be useful in deriving uncertainty ranges for inputs to the YLD calculation.

For calculating uncertainty intervals for YLD estimates given estimates of uncertainty ranges for the inputs to the calculation (incidence, average duration and disability weight primarily), you can use a simulation approach to estimate uncertainty intervals. This can be performed in a spreadsheet using the @RISK software program (Palisade 1996) to carry out Monte Carlo sampling of the inputs in order to generate the uncertainty distribution of the output YLD. @RISK allows you to calculate 'uncertainty' intervals for YLD and DALY estimates based on estimated ranges of uncertainty for various key parameters and assumptions built into the relevant disease models. An example of this type of uncertainty analysis for YLD due to dementia in Australia is given in Appendix B of the Australian burden of disease study report (Mathers, Vos and Stevenson 1999).

REFERENCES

- Mathers C, Vos T, Stevenson C (1999). The burden of disease and injury in Australia. Australian Institute of Health and Welfare, Canberra: AIHW. Also available on the worldwide web at www.aihw.gov.au.
- Murray CJL, Lopez, AD, eds (1996). The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020. Global Burden of disease and Injury Series, Vol. 1. Cambridge: Harvard University Press; 1996.
- Palisade (1996). @RISK: advanced risk analysis for spreadsheets. New York: Palisade.
- Salomon JA, Mathers CD, Murray CJL, Ferguson B (2001). *Methods for life expectancy and healthy life expectancy uncertainty analysis*. Geneva, World Health Organization (GPE Discussion Paper No. 10). Also available on the worldwide web at www.who.int/evidence.

12. CALCULATING HEALTHY LIFE EXPECTANCY

12.1 OVERVIEW

DALYs are a gap measure; they measure the gap between a population's actual health and some defined goal, while healthy life expectancy (HALE) belongs to the family of health expectancies, summarizing the expected number of years to be lived in what might be termed the equivalent of "full health". As described in Chapter 3, healthy life expectancy provides the best available single number SMPH for measuring the overall level of health for populations in a way that is appropriately sensitive to probabilities of survival and death and to the prevalence and severity of health states among the population. WHO has used healthy life expectancy as the measure of the average level of health of the populations of Member States in its World Health Report (WHR) for annually reporting on population health (WHO 2000, WHO 2001). Following feedback from WHO Member States and to better reflect the inclusion of all states of health in the calculation of healthy life expectancy, the name of the indicator used to measure healthy life expectancy was changed from disability-adjusted life expectancy (DALE) in the WHR 2000 to health-adjusted life expectancy (HALE) in the WHR 2001.

Two different types of methods have been used for calculating health expectancies: Sullivan's method and multistate life table methods. All healthy life expectancies calculated to date from burden of disease studies have used Sullivan's method. This involves using the observed prevalence of disability at each age in the current population (at a given point of time) to divide the hypothetical years of life lived by a period life table cohort at different ages into years with and without disability. Sullivan's method requires only a population life table and prevalence data for the health states of interest.

12.2 CALCULATING THE PREVALENCE OF DISABILITY

Murray and Lopez (1996) presented estimates of DFLE and DALE for each region of the world using Sullivan's method and the severity-weighted prevalence of disability derived from the YLD estimates in the Global Burden of Disease Study. For these calculations, severity-weighted disability estimates were not discounted or age weighted. Murray and Lopez calculated disability prevalences for seven disability classes with an adjustment to allow for independent co-disability between different disability classes.

The Australian Burden of Disease Study (Mathers, Vos and Stevenson 1999) also estimated DALE for Australia using Sullivan's method. Rather than estimate prevalence of seven disability classes, this study estimated undiscounted prevalence YLD per 1,000 population as a direct measure of severity-weighted disability prevalence and adjusted for comorbidity between disease and injury causal groups rather than for co-disability.

This second approach is recommended for use in National Burden of Disease Studies to calculate healthy life expectancy. In order to use this approach, it is necessary to calculate undiscounted and non-age-weighted prevalence YLD for each cause as well as the standard incidence-based YLD (which may include age weights and time discounting).

Prevalence YLD for a given sequela in age group x are calculated directly from the prevalence of that sequela as follows:

$$YLD_x = P_x * DW_x \quad (12.1)$$

where P_x is the number of cases in age group x prevalent at any point in time during the reference period, and DW_x is the disability weight (in the range 0-1). For diseases, where prevalence estimates were the basic data used as inputs to DISMOD for calculation of incidence and duration, these prevalence data should be used directly for the calculation of prevalence YLD.

Where prevalence data are not directly available, they should be derived using DISMOD where estimates of incidence, remission and case fatality are available.

There will be some diseases where DISMOD models may not have been constructed. These may be very short duration conditions (such as common cold) or very long duration conditions (such as injury sequelae). In these cases, it is possible to directly estimate prevalences as follows:

Short duration (<5 years): Prevalent YLD are equal to incident YLD[0,0] (undiscounted, no age weights)

Moderate duration (5 years to 50% of remaining life expectancy): Assume incident YLD[0,0] are evenly distributed across the age interval a to $a+L$, where a is average age of onset and L is average duration.

Long duration (50% or more of remaining life expectancy): Construct a life table for years lived with condition using the country life table and proportionately increasing mortality rates at all ages to match remaining life expectancy to the average duration of condition. Then use the L_x (years lived) column of the resulting life table to distribute incident YLD[0,0] across age groups.

12.3 DEALING WITH COMORBIDITY

Comorbidity refers to the not uncommon situation where a person has two or more health problems that result in disability (either dependently or independently of each other). It makes little sense to simply add the independently determined disability weights for conditions that are found to coexist as this can lead to the illogical possibility of having a combined weight of more than one (i.e. more disabling than death), particularly in the case of two heavily weighted conditions. The GBD made adjustments for comorbidity between 7 classes of disability. Both Australian studies made adjustments for comorbidity assuming that conditions occurred independently (ie. the probability of having 2 conditions was the product of the average probabilities for having each condition) and adjusted the disability weights for comorbid conditions assuming a multiplicative model. These studies took into account significant comorbidity between conditions within each major cause group (for example, between mental disorders or between injury types) but not between condition groups.

Assuming that your NBD has similarly accounted for comorbidity between conditions within major cause groups, but not between the cause groups themselves, you will need to correct for independent comorbidity between major condition groups as follows:

$$PYLD_{s,x} = 1 - \prod_g (1 - PYLD_{s,x,g}) \quad (12.2)$$

where $PYLD_{s,x,g}$ is the prevalence YLD per 100 population for sex s , age x and cause g .

The resulting PYLD per 100 population for sex s , age x gives the severity-weighted prevalence of disability by age and sex.

12.4 SULLIVAN'S METHOD

Sullivan's method uses a standard period life table for the population together with prevalence data for the health state (e.g. disability, severity-weighted disability) to calculate the expected years lived in the health state. Sullivan's method uses the life table functions:

l_x the number of survivors at age x in the hypothetical life table cohort.

L_x the number of years of life lived by the life table cohort between ages x and $x+5$

together with

D_x the severity-weighted prevalence of disability between ages x and $x+5$ in the population

to calculate

$YWD_x = L_x * (1 - D_x)$ Equivalent years of healthy life lived between ages x and x+5
 L_x is the total years lived by the life table population between ages x and x+5

DALE at age x is the sum of YWD_i from $i = x$ to w (the last open-ended age interval in the life table) divided by l_x (survivors at age x):

$$DALE_x = \left(\sum_{i=x}^w YWD_i \right) / l_x \quad (12.3)$$

$$DLE_x = \left(\sum_{i=x}^w YD_i \right) / l_x = LE_x - DALE_x \quad (12.4)$$

DLE_x , the equivalent years of healthy life lost, is the sum of YD_i from $i = x$ to w divided by l_x (survivors at age x).

12.5 WHO METHODS

For calculating health life expectancy for its Member States, WHO uses an approach that combines estimates from the Global Burden of Disease 2000 project with cross-population comparable data from representative population health surveys (Mathers et al. 2001a, 2001b)

REFERENCES

- Mathers CD, Murray CJL, Lopez AD, Salomon J, Sadana R, Ustun BL, Chatterji S (2001a). *Estimates of healthy life expectancy for 191 countries in the year 2000: methods and results*. Geneva, World Health Organization (GPE discussion paper No. 38).
- Mathers CD, Sadana R, Salomon J, Murray CJL, Lopez AD (2001b). *Healthy life expectancy in 191 countries, 1999*. The Lancet **357**: 1685-1691.
- Mathers C, Vos T, Stevenson C (1999). *The burden of disease and injury in Australia*. Australian Institute of Health and Welfare, Canberra: AIHW. Also available on the worldwide web at www.aihw.gov.au.
- Murray CJL, Lopez, AD, eds (1996). *The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020*. Global Burden of disease and Injury Series, Vol. 1. Cambridge: Harvard University Press; 1996.
- World Health Organization (2000). *World Health Report 2000. Health systems: improving performance*. Geneva, World Health Organization. Also available on the worldwide web at www.who.int/whr.
- World Health Organization (2001). *World Health Report 2001. Mental health: New Understanding, New Hope*. Geneva, World Health Organization. Also available on the worldwide web at www.who.int/whr.

13 COMPARATIVE RISK ASSESSMENT

13.1 INTRODUCTION

For strategies and policies to improve population health and allocation of resources, it is important to know not only the disease and injury burden for specific conditions (such as lung cancer, diarrhoeal diseases, or motor vehicle accidents), but also the burden associated with various underlying *risk factors* which cause disease and injuries (such as smoking, unsafe water and sanitation, or unsafe road conditions). Comparative Risk Assessment (CRA) is a systematic evaluation of potential changes in population health from altering the distribution of exposure to a risk factor or a group of risk factors, relative to other risk factors. It is important to note that CRA is different from intervention analysis which is the evaluation of the health benefits of a defined intervention, although the two may use similar methods at times.

The standard approach in epidemiology for estimating the health effects of a risk factor is to calculate the attributable fraction of a disease or injury due to the risk factor as a function of the prevalence of exposure (P) and the relative-risk (RR) compared to the non-exposed group. The basic statistic in such an “exposure-based” assessment is the *attributable fraction* (AF), defined as the percentage reduction in disease or death that would occur if exposure to the risk factor was reduced to zero, and is calculated by equation 1.

$$AF = \frac{P(RR - 1)}{P(RR - 1) + 1} \quad (13.1)$$

Alternatively, the contribution of a risk factor to disease burden can be estimated by comparing the burden due to the observed *exposure distribution* in a population (the first term in the numerator of Equation 2) with that from a hypothetical distribution defined according to some scenario or scenarios (the second term in the numerator of Equation 2). This hypothetical distribution of exposure to risk is called a *counterfactual distribution*.

The *attributable fraction* of a disease due to exposure to the risk factor is then defined by the following equation:

$$AF = \frac{\sum_{i=1}^n P_i RR_i - \sum_{i=1}^n P'_i RR_i}{\sum_{i=1}^n P_i RR_i} \quad (13.2)$$

where AF is the attributable fraction of disease burden, n the number of exposure categories or levels, P_i the fraction of population in exposure category i, RR_i is the relative risk for exposure category i, and P'_i the fraction of population in exposure category i in the counterfactual distribution. For a risk factor that is expressed in a continuous manner (such as the ambient concentration of particulate matter or blood pressure) the attributable fraction is given by:

$$AF = \frac{\int_{x=0}^m RR(x)P(x) - \int_{x=0}^m RR(x)P'(x)}{\int_{x=0}^m RR(x)P(x)} \quad (13.3)$$

where $RR(x)$ is the relative risk of death or disease for exposure level x , $P(x)$ is the distribution of the population by exposure level, $P'(x)$ is the counterfactual distribution of exposure for the population, and m is the maximum exposure level.

The *fraction* of burden from a cause (disease or injury) that is attributed to a risk factor (AF) can be multiplied by the total burden (B) due to that cause to obtain the *attributable burden* (AB), i.e. $AB = AF \times B$.

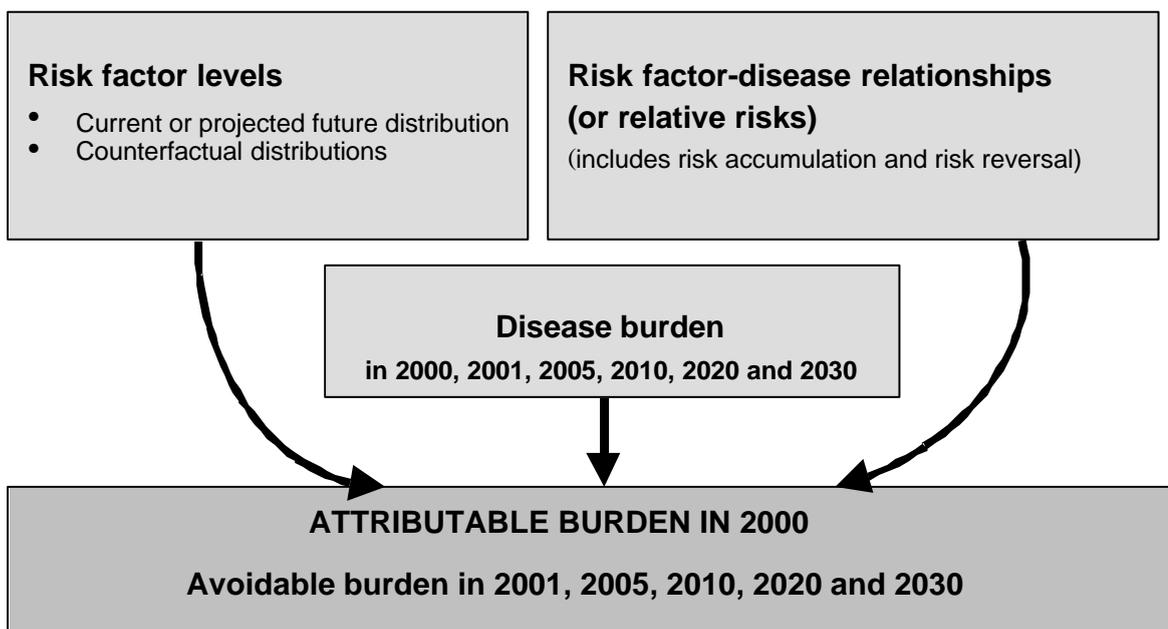
13.2 WHAT STAGES ARE INVOLVED IN A COMPARATIVE RISK ASSESSMENT EXERCISE?

The stages of a comparative risk assessment exercise are as follows:

1. Choice of risk factors
2. Choice of relevant diseases and injuries caused by the risk factor
3. Choice of appropriate exposure variable
4. Collection of data on population distribution of exposure for No. 1
5. Specification of the risk factor - disease relationship for each disease and injury in No.2 due to exposure to the risk factor in No. 1. To do this, you will need to systematically review the epidemiological literature.
6. Choice of counterfactual distribution of exposure
7. Calculation of the burden of disease or injury due to each cause in No.2
8. Analysis of uncertainty

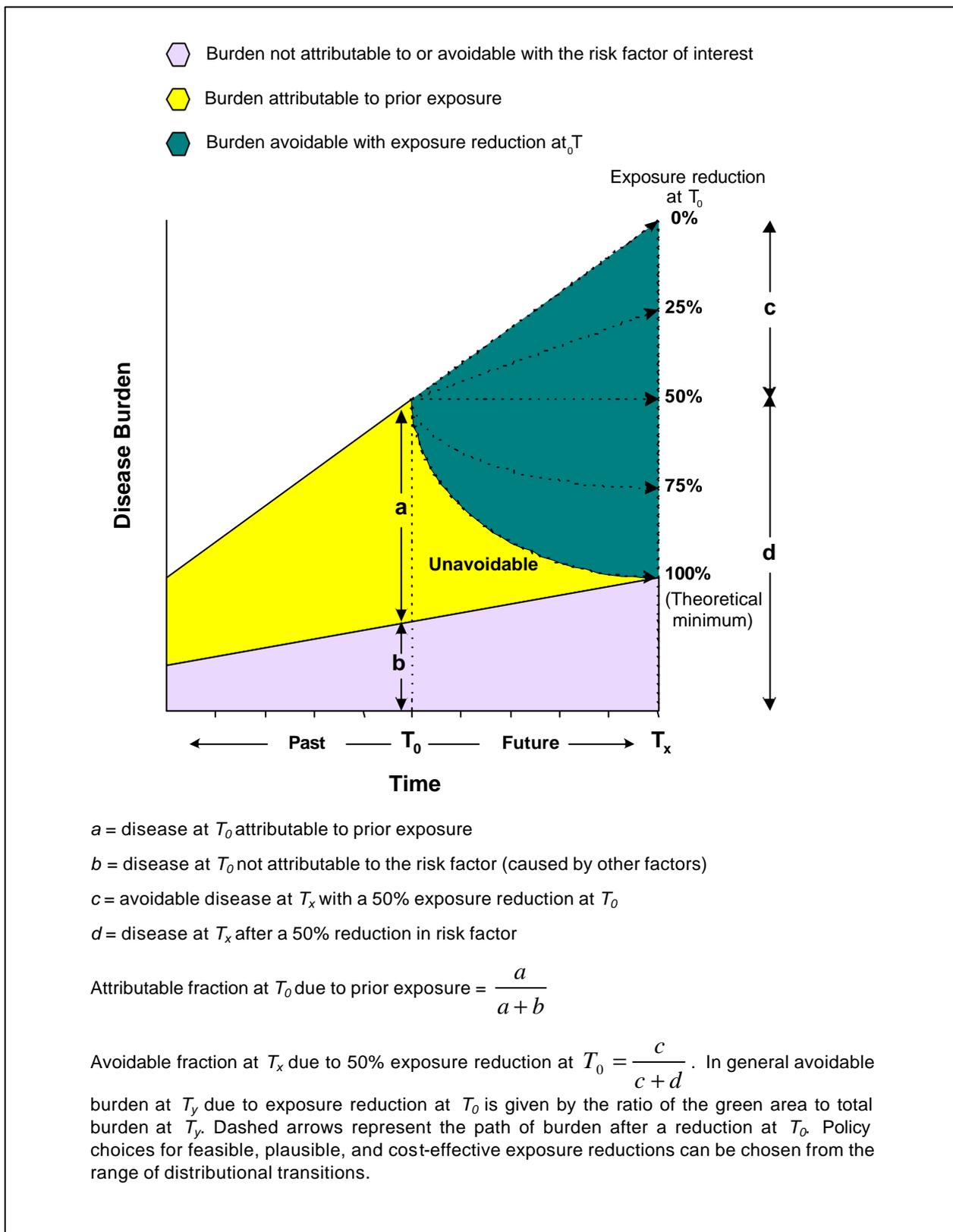
Stages 1 - 6 together with Equation 2, will allow you to calculate the *attributable fraction*. This result together with stage 7 gives the *attributable burden*. This process is shown in Figure 13.1. An additional feature of Figure 13.1 is the distinction between *current burden* of premature death and disability due to *past or current exposure* and *future burden* due to *current and future exposure*. To make this distinction explicit, *attributable burden* is defined as the reduction in current burden that would have been observed if

Figure 13.1 Key Data Inputs and Outputs in Comparative Risk Assessment



past levels of exposure had been equal to some counterfactual distribution of exposure (Figure 13.2). *Avoidable burden* is the reduction in future burden that would be observed if current and/or future levels of exposure were (reduced to those specified by some counterfactual distribution).

Figure 13.2: Attributable and Avoidable Burden



Note that the burden not attributable to our risk factors (striped grey area) may be decreasing, constant, or increasing over time. The last case is shown in the figure.

When the time between exposure and disease or death is short, this distinction is not critical. For some risk factors such as tobacco, hypertension, physical inactivity, some occupational exposures, and alcohol, the lag can be long. When there is considerable time lag between exposure and outcome there will be a substantial difference between attributable and avoidable burden. The trade-off between attributable and avoidable burdens is that while the former is easier to measure, the latter is more useful for policy.

13.3 HOW TO CALCULATE ATTRIBUTABLE FRACTIONS

The following sections of this manual provide a step-by-step guide in conducting the process described above. Quantitative risk assessment will always involve assumptions and uncertainty. It is essential to document such assumptions and sources of uncertainty so that readers of the assessment can be aware of these in interpreting the results.

(i) *Choice of Risk Factor*

The risk factors which you choose for analysis should be selected based on:

- Potential national or sub-national impact: covering all major causes of death and disability, and likelihood to be among the leading causes of disease burden
- High likelihood of causality
- Potential for modification through policy
- Requirement not to be too specific (such as a specific pathogen in water) or too broad (such as environmental hazards as a whole).
- Availability of reasonably complete data on risk factor distributions and risk-factor disease relationships

Some trade-off will be unavoidable in selecting risk factors based on any criteria. For example, some risk factors such as climate change may be of such potential importance that they will be estimated based on scenarios and theoretical models. These trade-offs will be made clear when the data sources, methods and results are reported in detail, including estimation of uncertainty.

(j) *Choice of Disease and Injuries Caused by the Risk Factor*

For each risk factor-disease relationship, there should be a systematic and documented assessment of the likelihood of causality. Mechanisms of causality and population distribution of exposure to risk factors are often known only partially. It is therefore important to make judgement based on best available science and data and document all assumptions and sources of uncertainty.

Many approaches have been proposed in the assessment of causality. One approach that might be most appropriate for this purpose, being widely known and reasonably well accepted, is the set of "standards" proposed by Bradford Hill to be considered when attempting to distinguish between causal and non-causal associations. These are not indisputable rules for causation and Bradford Hill (1965) emphasized that they should not be taken directly as a score. Also some of the standards are less useful than others, and none (except temporality) are absolute. However, it is widely agreed that a judgement of causality should be increasingly confident with the accumulation of satisfied standards such as:

- **Temporality:** Cause must precede effect in time.
- **Strength:** Strong associations are more likely to be causal than weak associations, the argument being that if a strong association were wholly due to some other factor (i.e. confounding) then that other factor would be more likely to be apparent. But, a weak association does not rule out a causal connection, and the impact of confounders must be considered and adjusted for in all estimates.
- **Consistency:** Repeated observations of associations in different populations under different circumstances. But, lack of consistency does not rule out a causal association as some effects are produced by their causes only under unusual circumstances.

- **Biologic gradient:** Presence of a dose-response curve (monotonic trend). But, some causal associations do show a single jump (threshold), or other relationships such as the J-shaped curve.
- **Plausibility:** Biologic plausibility of a causal relationship is important. But, it is not absolute, as it is based on current level of knowledge and beliefs, which may change over time.
- **Experimental evidence:** Randomized experiments can provide strong evidence of causality. But, evidence from human experiments is often not available for ethical and logistical reasons.

Experimental evidence, which is widely regarded as the most convincing proof of causality, will not be available for most risk factors. Other criteria may also not be relevant or available for other risk factors less amenable to traditional epidemiological study methods such as environmental health risks where measurement of exposure is complex or where there are long delays between exposure and effects. While it is essential that causal assessments are made in a systematic fashion for each risk factor and that they accompany the results, it is also important that CRA is not restricted to those risk factors with unequivocal proof of causality through traditional epidemiology.

Finally, disease and injuries should be selected to as much as possible to match the causes on the national burden of disease study. At the same time, epidemiological studies sometimes use different groupings (such as all vascular diseases or all injuries) which would have to be matched to aggregate class of causes on the NBD list.

(k) *Choice of Exposure Variable*

Before estimates can be undertaken, two key initial steps are required:

1. The risk factor must be clearly defined in terms of an exposure variable, including the units of measurements. For example, if the risk factor is alcohol use, the exposure variable might be average number of alcoholic drinks per day or grams of alcohol per day.
2. The method of describing risk factor levels or distributions can be decided in terms of either:
 - continuous data (with mean and standard deviations), or
 - categorical data (with a set number of defined categories).

The most fundamental criterion for choosing the exposure variable is to allow obtaining meaningful data on population distribution of exposure and on relative risks. For example, if the risk of lung cancer or COPD due to smoking depends on duration and intensity of smoking, using current prevalence of smoking will be an insufficient measure of exposure since it does not show whether smoking is an established or new phenomenon in the population. Therefore, the choice of exposure variable should be made in light of:

- The most commonly reported descriptions and methods of analyses of risk factor levels in the literature.
- The requirement to choose risk factor categories for which relative risks are available. Also note that it is essential that the exposure definition and units are suitable for reporting relative risks. For example, one cannot report risk factor levels by 5 categories and relative risk by 3 different categories since the relative risks may become irrelevant to the exposure categories.
- If data can be described by a mean, standard deviation and continuous relative risks, then they should be reported in this way. If risk factor distributions are not described well by mean and standard deviation (i.e. they are skewed), they may be best reported categorically.
- The trade-off between the improved estimation allowed by greater numbers of categories to describe risk factor distributions and the problems introduced by not including data from studies that reported fewer risk factor categories.

13.4 CURRENT POPULATION DISTRIBUTION OF EXPOSURE

The first of the three main data inputs into the potential impact fraction are estimates of current risk factor levels by age, sex and region. Extensive searches will be required to estimate risk factor levels by the age, sex and sub-national groups. This may well be the most time consuming part of the data collection process for CRA.

Some sources of information that could be used include:

- Date-bases such as Medline, Current Contents, and Social Science Index;
- Other national or sub-national ministries and departments such as water, transportation, agriculture, industry;
- WHO web site;
- Country- or region-specific societies, such as cancer control groups, national heart foundations, environmental monitoring groups, and local development organizations;
- Authors of relevant papers;
- Relevant academic institutions and experts in the field;
- National and sub-national surveys;
- Regional trade information (for risk factors such as tobacco or alcohol).

It will be important to record these search strategies as details will be required in the documentation of estimates.

13.4.1 OBTAINING DATA BY THE REQUIRED AGE AND SEX GROUPS

Data may not be reported in the required format. Different scenarios are described below, along with some suggestions for obtaining the necessary data by extrapolation or interpolation. For each risk factor, the investigator should make a choice as to whether the likely errors in including data from studies with non-ideal reporting of risk factor prevalence are greater than the errors introduced by excluding such data. Some of the scenarios which may be encountered when collecting risk factor data are:

- Data reported for different age categories and/or for males and females combined. For example, age standardized prevalence are often reported for age groups that are truncated such as “35% prevalence of hypertension for the age group 35 to 64 standardized to Segi world population, for men and women combined.” Ideally, attempts should be made to contact original investigators to obtain data broken down by the relevant age groups or sexes. However often this will not be available soon enough, if at all, and so indirect estimates may be required. In these instances it will be necessary to disaggregate the standardized estimates, which will typically require the use of two sources of data:
 - The age-sex breakdown of the reference population for standardization.
 - Information about the relationship of risk factor levels with age and sex from other studies
- Data reported categorically when mean and standard deviation required: Data may be available in categorical form for variables being described in continuous form. To estimate risk factor levels in terms of mean and standard deviations from categorical data requires estimates of typical standard deviations, which can often reasonably be generalised. For example, if 10% of people in a population are reported to have diastolic blood pressure $\geq 95\text{mmHg}$ and one knows that the standard deviation for diastolic blood pressure is typically 10mmHg, then a reasonable estimate for the mean DBP in that population is approximately 82mmHg (in a normal distribution 90% of values fall below the mean plus 1.28 times the standard deviation, hence the mean= $95-10*1.28=82$).
- Data reported as mean and standard deviation when categories are required: Data may be presented with a mean and standard deviation if the risk factor follows an approximately normal distribution. If this normal distribution is determined, then data may be grouped into the appropriate categories (the NORMDIST function in Excel is a useful tool to convert categorical values into normal distributions and vice versa).
- Data reported in differing categories: Frequently descriptive data will be available for categories other than the ones required. For example, frequency of drinking alcohol may be reported by 5 categories but 4 categories have been chosen for risk assessment due to the availability or relative risk estimates. In this instance some generalisable form of the alcohol drinking frequency distribution should be applied so that four category data can be estimated from the reported five category data.

13.4.2 EXTRAPOLATING DATA TO AGE, SEX, REGION GROUPS FOR WHICH DIRECT DATA ARE NOT AVAILABLE

For all risk factors there will inevitably be a requirement to extrapolate data to some age, sex, and region group for which direct data are not available. This extrapolation may be based on generalising from a particular subgroup that has similar health, demographic, geographical, or socio-economic indicators (such as infant mortality, adult mortality, population density, income, education, energy use, agricultural practice, level of industrialization, etc.).

13.5 RISK FACTOR - DISEASE RELATIONSHIP

The other important parameter input into attributable fractions is the estimates of risk factor-disease relationships by age, sex and region. This is a critical component of CRA analysis and great care and judgement is required to adequately estimate what are the effects of a particular exposure in your population. For example, if the relative risk of lung cancer for smokers in the US or the UK is larger than 20, this does not mean it will be as high in a population which has been smoking for a much shorter time than the US or UK. Appropriately detailed guidelines on methods for reliably characterising such relationships are given in textbooks on general epidemiology as well as other disciplines relevant to the risk factor of interest. Some broad headings, based on those developed for systematic reviews of trials and other epidemiological studies are:

- Criteria for identifying relevant studies
- Search strategy for studies
- Characteristics of excluded studies
- Description of studies, including methodological qualities
- Characteristics of included studies such as sample size and region
- Standard errors reported by studies
- Steps to assess and reduce random error
- Reported standard errors and other measures of uncertainty due to variability
- Meta-analysis if appropriate
- Steps to assess and reduce bias and to assess causality
- Confounding
- Selection bias
- Information bias (exposure and outcome measurement error)

Two particular issues are worth emphasizing in the assessment of risk factor-disease relationships for a CRA exercise: generalisability and risk reversibility

13.5.1 ASSESSING GENERALISABILITY

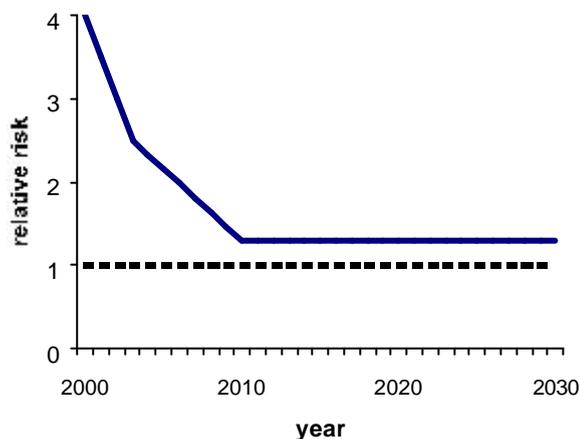
Consistency between the results of reliable studies conducted in different settings is a key component of establishing causality. Assessing generalisability is also important for extrapolations to age, sex and region groups for which direct evidence is not available. For risk factor levels, there is often no particular reason to expect levels to be consistent between regions. However, risk factor-disease relationships will often be more generalizable, especially if they are intrinsic biological relationships common to humans in many different settings. Also the "representativeness" of a study population is an essential component of extrapolating results for risk factor levels. However, for risk factor-disease relationships it will often be more important to assess study reliability than study population representativeness. Likelihood of causality is increased by consistency between reliable studies, even (and perhaps especially) if they are from highly selected populations. To maximize this generalizability, it will be important to report the most generalizable entity, which is often the relative risk or similar association. When relative risk per unit exposure does vary between populations, it will be important to document how this occurs. For example, the relative risk for current

tobacco smoking and chronic obstructive pulmonary disease appears to be less in China in 1990 than North America and Europe due principally to a shorter history of smoking.

13.5.2 ASSESSING RISK REVERSIBILITY

To estimate the avoidable burden with changes in risk factor distribution, it is necessary to provide information on "risk reversibility". This "reversibility" of risk may occur to differing extents and over different time frames for various risk factor-burden relationship. After some time, the relative risk of a "previously exposed" group may reach that of the "never exposed" group, or their risk may not be completely reversible and they have a remnant risk. Figure 13.3 illustrates graphically the way that the relative risk for an exposed population may decrease after a distributional transition that removes exposure in the year 2000. In this example there is a remnant relative risk in the year 2030, as the RR has not reached 1.0 (the relative risk in the non-exposed group).

Figure 13.3: Risk reversibility



Time trends of the risk 'reversibility' may vary with:

- Different population sub-groups. For example, reversibility may differ in older age groups
- Different initial exposure level. For example, reversibility at high exposure level may be less than reversibility at a lower exposure level.

It may therefore be necessary to provide information for each risk factor-disease relationship on whether this reversibility varies by age, sex, region or starting level of exposure. Note also that for many diseases RR tends to decrease with increasing age, due to the rapidly increasing level of background mortality from other causes.

13.6 CHOICE OF COUNTERFACTUAL DISTRIBUTION OF EXPOSURE

Analysis using counterfactual exposure distribution requires that the current distributions of exposure to risk factors be compared to some alternative distribution. Many different counterfactuals are potentially of interest, including four types described by Murray and Lopez (1999) – theoretical, plausible, feasible and cost-effective minima.

- **Theoretical minimum risk distribution** is the distribution of exposure which would yield the lowest population risk (for example, zero tobacco use). This risk distribution is more complicated for risk factors for which zero is not possible (such as cholesterol), in which case a distribution or level will have to be estimated that has lowest overall risk using empirical evidence.

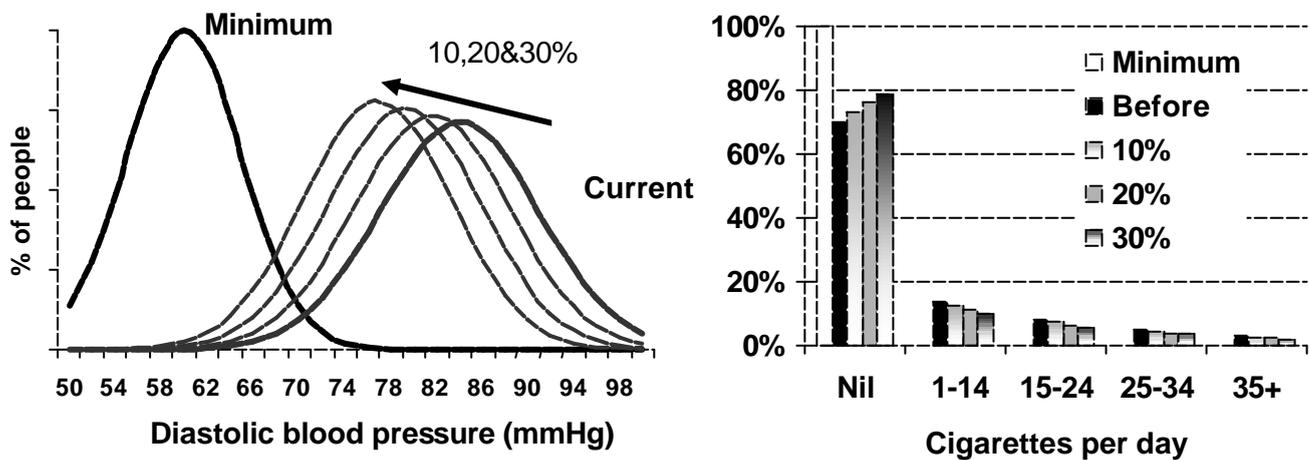
- **Plausible minimum risk** is the distribution of exposure among the set of plausible distributions that would minimize overall population risk. Plausible implies that the shape of the distribution is imaginable or possible in a society.
- **Feasible minimum risk** is the distribution of exposure that exists or has existed in a population. Note that plausible means that the distribution is imaginable or possible, whereas feasible means that it has been achieved in some population.
- **Cost-effective minimum risk** is the distribution of exposure that would result if all cost-effective interventions (against some reference value) could be implemented. This distribution will depend on what might be considered cost-effective in different populations and is therefore not uniformly applicable to all populations.

As a very minimum, for CRA analysis, you will need to specify the theoretical minimum distribution in order to apply equation (2). This is a complex and difficult choice for some risk factors. Since this minimum risk distribution is likely to be the same throughout the world for most (but not all) risk factors, WHO has already defined it for about 20 risk factors. These choices are available by contacting WHO.

CHARACTERISING THE DISTRIBUTIONAL TRANSITION

Risk factor distributions that are plausible, feasible, etc. should lie somewhere between the current risk factor levels and the theoretical minima chosen. Also, plausible, feasible and cost-effective reductions are likely to vary by age, sex or region. Therefore, after estimating the burden attributable to exposure that was greater than that of the theoretical minimum, a range of estimates should be made for counterfactual distributions at set intervals between the current and the theoretical minimum. This range has been termed the *distributional transition* (Figure 13.4).

Figure 13.4: Distributional Transition



NB: For categorical variables, different distributional transitions can be defined in terms of either shifting to the category below or to the baseline category.

In many instances the counterfactual of most relevance will involve small to moderate distributional transitions (for example 10%, 20%, or 30%) as these are most likely to be feasible, cost-effective, etc. Two other advantages of concentrating such small-to-moderate transitions are:

- First, these estimates are likely to be most reliable, as the dose-response is often least certain at low exposure levels. Large distributional transitions (such as 80% risk factor reduction) would require estimates of dose-response associations at these low levels of exposure.
- Second, small shifts are less susceptible to the influence of arbitrary choices of theoretical minima.

For each risk factor - disease pair an attributable fraction is calculated using the current and counterfactual distributions (sections 13.4 and 13.6) of exposure and the risk factor - disease relationship (section 13.5). Multiplying the attributable fraction with the burden of disease due to each cause gives the attributable burden of that cause due to the risk factor of interest.

13.7 THE ANALYSIS OF UNCERTAINTY

Quantitative risk assessment is almost always affected by uncertainty and addressing this issue can add greatly to the applicability of the results for policy purposes. Various taxonomies of uncertainty have been used in risk assessment including dividing uncertainty into *model uncertainty* and *parameter uncertainty*.

13.7.1 MODEL UNCERTAINTY

Model uncertainty is defined as uncertainty due to gaps in scientific theory. In other words, model uncertainty is in those aspects of the analysis which are not (currently) quantifiable using random-variable statistical methodology. It includes uncertainty in causal links and in the analytical relationship which characterizes the exposure-response relationship (threshold versus continuous, linear versus non-linear, etc.). In the context of population risk assessment, model uncertainty, broadly defined, also includes cases where exposure distributions for one region or demographic group are not known and are extrapolated from other regions while making assumptions about the similarity between the two.

For each risk factor the risk factor – disease pairs should be chosen (section 13.2) based on the scientific material available and any uncertainty and assumptions that surround these choices, including uncertainty in evidence for causality should be recorded. Also, the most plausible exposure-response relationships and population distribution for the respective risk factor(s) should be chosen again recording all assumptions and uncertainties.

13.7.2 PARAMETER UNCERTAINTY

Continuous risk factors

For each continuous risk factor, in addition to the best estimate population distribution of exposure, the uncertainty interval for mean and standard deviation should be reported. Note that this may not to be a 95% confidence interval in its conventional sense, since for some risk factors statistical analysis of the population distribution has not been conducted and the range is obtained using evidence other than statistical analysis.

Categorical risk factors

For each categorical risk factor, in addition to the best estimate of the population distribution of exposure, the uncertainty in the fraction of population belonging to each category should be reported.

Risk factor – disease relationship and risk reversibility

This uncertainty is reported as the 95% confidence interval in the exposure-response relationship coefficients (continuous) or relative risks (categorical).

13.7.3 UNCERTAINTY ANALYSIS

Through the use of simulation methods such as Monte Carlo simulations (using a program such as @RISK), estimates of uncertainty for each source of data will be varied separately and then simultaneously to construct intervals of the final estimates. Sources of data that will be included in these analyses include (as described in section 13.7.2):

- risk factor levels

- relative risk estimates
- risk reversibility

13.8 COMMUNICATING RESULTS

Finally, it is critical to remember that the sum of attributable burden for various exposures is unbounded: death and disability from many diseases and injuries can result from several exposures acting simultaneously, such as coronary heart disease which has been linked to smoking, alcohol, diet, and physical inactivity among others. This implies great caution when presenting and communicating interpreting attributable fractions. I

It is not possible to simply add the attributable fractions for a number of risk factors. For instance, it is not correct to state that the sum of attributable burden calculated separately for cholesterol, obesity, physical inactivity, hypertension and smoking represents the burden attributable to all of these risk factors taken together. This is because there are complex interactions between these risk factors. Summing the attributable fractions for a number of such risk factors would lead to overstating the size of the burden attributable to the combined set of risk factors.

REFERENCES

- Rothman, K. J. (1976). "Causes." *American Journal of Epidemiology* **104**:587-592.
- Bradford Hill, A (1965). "The Environment and Disease: Association or Causation?" *Proceedings of the Royal Society of Medicine* **58**:295-300.
- Mathers CD, Vos T, Stephenson CE, Begg SJ. (2000). The Australian burden of disease study: measuring the loss of health from diseases, injuries and risk factors. *Medical Journal of Australia*, **172**: 592-596.
- Murray CJL and Lopez AD. (1999). On the quantification of health risks: lessons from the Global Burden of Disease Study. *Epidemiology*, **10(5)**: 594-605.
- Peto, R., A. D. Lopez, J. Boreham, M. Thun, and C. Heath, Jr. (1992). "Mortality from Tobacco in Developed Countries." *The Lancet* **339**:1268-1278.
- Rodgers A, Lawes C, MacMahon S. (2000). The global burden of cardiovascular disease conferred by raised blood pressure: benefits of reversal of blood pressure-related cardiovascular risk in Eastern Asia. *Journal of Hypertension*. **18(suppl)**: S3-S6.
- Rothman KJ, Greenland S. (1998). *Modern Epidemiology 2nd ed.* Philadelphia: Lippincott-Raven (Especially Recommended: Chapters 2 and 4).

14. PROJECTIONS

14.1 INTRODUCTION

Projections or forecasts can be a useful input into the health policy debate on infrastructure, human capital and research investments. There has been an extensive literature on health projections, with a range of different types of approaches. A set of alternative projection scenarios were developed as part of the GBD 1990 study, and efforts are currently underway to build on these previous efforts with an expanded data set and improved statistical methods.

In this chapter we present a brief overview of the 1990 projection effort and a preview of some of the ongoing work on extending the exercise for the GBD 2000.

For researchers undertaking a national burden of disease study, we do not recommend independent efforts to include projections in these projects, as the analyses must draw on extensive databases from all countries for which data is available in order to fit models that may be used for developing forecasts.

14.2 GBD 1990 PROJECTION APPROACH

REGRESSIONS

For the GBD 1990 projections, a simple regression model was developed relating age- and cause-specific mortality rates to a short-list of distal socio-economic determinants and one major risk factor (smoking). The models in the GBD 1990 exercise were fit as follows:

Causes of death were divided into **nine clusters of causes**: Group I (communicable, maternal, perinatal and malnutrition), malignant neoplasms, cardiovascular diseases, digestive diseases, chronic respiratory diseases, other Group II diseases (noncommunicable), road traffic accidents, other unintentional injuries, and intentional injuries. These clusters were selected because mortality trends over the last 40 years in countries with good vital registration data suggest that the more specific causes within each cluster have followed a similar time trend.

Equations were developed relating age, sex and cause-specific death rates to the following explanatory variables:

- GDP per capita
- Human capital – average number of years of schooling
- Smoking intensity – based on lung cancer death rates
- Time – used as a proxy for technological progress.

A log-log functional form has been used for most causes:

$$\ln M_{a,k,i} = C_{a,k,i} + b_1 \ln Y + b_2 \ln HC + b_3 T \quad (14.2)$$

where $C_{a,k,i}$ is a constant term; $M_{a,k,i}$ is the mortality level for age group a , sex k , and cause i ; and Y , HC and T denote GDP per capita, human capital and time, respectively.

We omitted some of the variables where we thought epidemiological relation would not be sensible; for example mortality rate from infectious diseases for children would likely to be not affected by smoking intensity. A further selection of variables proceeded after F-tests were used to weed out insignificant variables. For some causes we posited quadratic relation with income and for nearly all we had a constant term.

A panel data set of age, sex and cause-specific mortality rates for 47 countries from 1950-1990 was used to estimate these regression equations.

PROJECTING INDEPENDENT VARIABLES

Alternative projection scenarios were constructed by projecting the independent variables over the projection period. For the 1990 GBD, we constructed baseline, pessimistic and optimistic scenarios. Many more scenarios including some lower probability scenarios could be constructed.

Regional **income per capita** projections, were based on the World Bank *Global Economic Prospects* estimates of expected growth over the period 1995-2004.

Forecasts for the period 2005 to 2020 were constructed assuming that the growth rate of income per capita would tend toward the historical average of EME over the last 40 years (around 3% per year). Optimistic and pessimistic scenarios were constructed by examining the highest and lowest regional growth rates over the last 40 years and selecting a plausible but arbitrary rate.

For projections of **human capital**, we first estimated the growth rate in human capital as a function of level of human capital that has been achieved.

$$r = 0.043 - 0.004HC$$

Projections assumed that this relationship would hold over the projection period. Optimistic and pessimistic variants were developed by arbitrarily modifying the coefficient on *HC*.

1. The GBD 1990 projections of **smoking intensity** were patterned after the evolution of the smoking epidemic in the UK from 1900 to 1990. We assume that the lagged relationship between cigarettes consumed per capita and the lung cancer rate minus the non-smoker lung cancer rate would be maintained in each region as in the UK. The 1990 consumption of cigarettes is thus used to estimate the smoking intensity in 2020. This presumes that the relationship between 1990 consumption and 2020 lung cancer incidence is fully determined.
2. The residual shift in the relationship between income, education and smoking with mortality rates was modeled by including **time** in the regressions, which captures the effects of technological improvements.

PROJECTING MORTALITY FROM DETAILED CAUSES

Once mortality projections for the nine cause clusters were developed, projections for the detailed causes within each cluster were developed in one of two ways:

1. Regression models were estimated relating rates for detailed causes to the rates for the cause cluster. Where these models were good predictors, the regression results were used.
2. For other causes, we assumed that the relative distribution of mortality within each cause cluster would be maintained over the projection period.
3. HIV was treated as a special case because the regression model was fit to data that dated, for the most part, from the pre-HIV era. Separate models of HIV trends were adapted from those used by the former Global Programme on AIDS. In India and sub-Saharan Africa, tuberculosis projections were also modified based on projections of large HIV epidemics in these regions and the important interactions between HIV and TB.

YLL AND YLD PROJECTIONS

YLL projections were calculated based on the mortality projections. YLDs were then added assuming, depending on the cause, either that the ratio of YLD to YLL would remain constant, that age specific YLD rates would decline faster than the mortality trend, or that these rates would remain constant.

14.3 NEW PROJECTION MODELS FOR GBD 2000

Ongoing work on extending previous projection models is being undertaken as part of the GBD 2000 project, using a substantially expanded data set on mortality by country, age, sex and cause that has been compiled at WHO. In addition, new statistical methods have been developed to address some of the major shortcomings of the previous efforts.

In terms of statistical methods, the regression models used in the GBD 1990 left a number of opportunities for improvements:

- Listwise deletion was applied for missing observations.
- The regression models did not include time series processes, i.e., death rates for one year were not used in predicting death rates for the following year.
- It was assumed that the same relationships between mortality rates and income, education, smoking and time would apply to all countries.
- Separate models were estimated for each age, sex and cause cluster, which does not take advantage of different degrees of relatedness along each of these dimensions.

A number of improvements have been realized since the GBD 1990 project was completed, including the development of algorithms for imputing missing data and more sophisticated statistical techniques to reduce the bias created by pooling observations from different countries, and to take advantage of the hierarchical data structure. Another important area of work is in providing meaningful measures of the uncertainty around projections. This work is currently ongoing for the GBD 2000 study.

The weakest aspect of the projection method developed for the GBD 1990 is the simple approach to projecting YLDs, which assumes in many cases that the relationship between mortality and non-fatal health outcomes will remain constant. There is some cross-sectional evidence that the ratio of YLDs to YLLs may decline as mortality declines. In addition, for some causes of disability there may be predictable trends independent of mortality trends. For example, the decline in heart disease mortality during the 80s and 90s in many western countries is mostly due to improved survival with heart disease, thus inflating the numbers of heart disease patients. On the other hand, due to better treatment possibilities, e.g. for heart failure, the YLD may actually be dropping. In current work, additional disease specific projection sub-models are being considered.

The final output of the ongoing projections work for the GBD 2000 will be the first set of country-specific projections of mortality and burden of disease. For research teams undertaking a national burden of disease exercise, revised projections may be developed in collaboration with WHO by including the results from the national burden study as the baseline from which forecasts extend.

REFERENCES

- Bulutao R. Mortality by cause, 1970-2015. in Gribble JN, Preston SH, eds. *The epidemiology transition. Policy and Planning Implications for developing countries. Work shop Proceedings*
- Lopez, AD and Hakama M. Approaches to the Projection of Health Status. in World Health Organization, *Health Projections in Europe: Methods and Applications*
- Murray CJL and Lopez AD. *The global burden of disease*
- Summers R and Heston A. *The Penn World Table* (version 5.5).
- World Bank. *The Adult Health Policy Challenge*

15. PRESENTATION AND DISSEMINATION OF RESULTS

This is the most important part of any NBD study. If you fail to interest policy makers and the community in the results of your study, your endeavours will remain 'academic' (in the negative sense of the word meaning ignored by those who matter) and largely a wasted exercise even if the quality of your study is very high. The opposite, doing a poor study that attracts a lot of attention of policy makers, the media and or community groups may lead to short term fame and influence but is likely to have an even worse outcome in the end: not only failed but also denounced.

15.1 TARGET AUDIENCES

At the start of your study you should already plan a strategy of dissemination of results. From the way you state your objectives, it should already become clear who your audience is and what content you want to provide. Let us examine a set of objectives as an example:

1. To provide internally consistent estimates of the burden of fatal and non-fatal health events (in numbers of deaths, incident and prevalent cases and DALYs) for the 100 most important conditions in country
2. To describe differentials in the burden of disease between x number of small areas/regions, rural and urban areas, between socio-economic strata and between ethnic groups in country
3. To describe the burden of disease attributable to 10 major risk factors of disease in country
4. To project the burden of disease 20 years into the future in country
5. To construct detailed disease models that describe the natural history of the 50 most important conditions that can be used as a basis for cost-effectiveness analyses which are planned after completion of the NBD
6. To provide policy makers, planners and the community with an understanding of the size of health problems and the distribution of health problems in country

From these objectives, target audiences for different elements of the results of your NBD study are apparent. Table 15.1 gives examples of the areas of interest in the NBD results to different stakeholders.

15.2 METHODS OF DISSEMINATION

Every NBD study produces a large amount of results. Some of your stake holders will be interested in a few summary findings while others will want to scrutinise and make use of very detailed descriptions of the methods and results. This means that you should plan a number of dissemination strategies that will satisfy the information demands of your target audiences. You may want to involve someone in your organisation who is a specialist in publishing and disseminating research findings.

Taking the principal of *transparency* to heart you should plan to make all your calculations available for public scrutiny. This can be done by providing all your worksheets on CDs or more conveniently by putting your work up on the Internet. When doing so, provide a contact address—often by e-mail—to receive feedback. Submitting papers to scientific journals for peer review is another method of seeking approval and legitimacy for the quality of your study.

However, as mentioned earlier, the main aim of doing a NBD study is to inform and influence policy and planning and to involve the community in thinking about health problems. Many of the stakeholders will not have the time or inclination to examine your worksheets and long tables of results. Give careful thought to the best way to get your target audiences interested and choose appropriate methods of dissemination which may include one or more of the following:

Table 15.1 Stakeholders Interests in NBD Results

Stake holders	Areas of interest
Policy makers	
Those involved in resource allocation	Health inequalities as a guide to funding formulas by region or sub-population The size of health problems: to identify 'neglected' areas which in turn may lead to an analysis of intervention options and/or research priorities The results of cost-effectiveness analyses that you may plan as a follow-up
Public health managers	Risk factor analyses, infectious diseases
Hospital managers	Number of prevalent and incident cases as a guide to potential demand for services
Planners	Projections of disease burden Number of incident/prevalent cases
Clinicians	A population health perspective to the health problems they deal with on a doctor to patient basis
Media	Striking differentials in health Projections Risk factor analyses
Community	'Neglected' health problems Striking differentials in health Projections Risk factor analyses
Disease advocacy groups	Estimates of size of the burden for the health problem of their interest
Academics	Methods, innovations, particular findings

PRINTED PUBLICATION

Most NBD studies will produce a written report. You can use the GBD books and published NBD studies as examples¹. Try to get an influential person, such as the Minister of Health, to write a foreword. The main body of such a report typically will contain 3–8 pages of executive summary, up to 5 pages of background & justification & objectives, a methods section of 20–60 pages, 20–60 pages of results, and up to 20 pages of discussion and recommendations. This can be followed by tables of summary results and appendices with e.g. your list of diseases with ICD–codes, the disability weights and examples of one or two of your worksheets. The whole report should probably not exceed 200–300 pages.

SUMMARY REPORT

Many people interested in your study will not be able to or want to read a full report. You may refer these people to the executive summary of the report but it may be better to produce a small summary booklet of

¹ For example, reports on the Australian Burden of Disease study and the study in the state Victoria can be found on the internet: www.aihw.gov.au/publications/health/bdia.html and www.dhs.vic.gov.au/phd/9909065/index.htm

30–40 pages. The style of such a booklet can be ‘looser’ than that of the full report or a paper in a scientific journal. Short sentences with clear simple language, separate text boxes to highlight an issue or explain a concept and lots of graphic images are strategies for a booklet that is accessible to a wide audience.

PRESENTATIONS

While you are doing your study you will probably want to present interim results. Typically, you will do most of the mortality analyses first and be able to show interesting results to kindle interest for the study. On completion of the study, it is likely that you will already have quite a collection of different presentations depending on the audience you were talking to. It is helpful to organise your visual aids in such a way that for each new request for a presentation you can easily pull together a set of slides, overheads or Powerpoint slides relevant to the occasion. Give your slides a similar look (same background colour/design, similar font, similar headings and preferably a logo for the study or the organisation you work for).

15.3 PRESENTATION OF RESULTS

It is not so easy to decide on which of the many results of your NBD study you will want to present and how best to present results. It often helps to use a variety or a combination of methods:

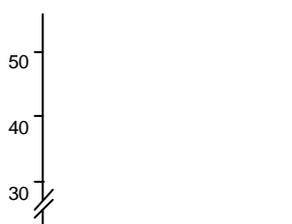
- a good description of the most important points in text
- a graph
- a table

Try to develop a certain common look to your tables and graphs. This will help your audience to recognise that the different components of your study hang together. You may want to talk to a professional designer how you can develop such a common style of presentation. Give each table and figure a self-explanatory heading that—using few words—describes the contents of the table or figure to a reader who may not take the time to read your text. Use the same fonts throughout for your headings, legends and labels.

Avoid putting too many things in one table or one graph. In principle, each table or graph should have one main message. If there are more messages on the same topic, it is best to create a second graph or table. Also, avoid presenting a graph and a table with the same information. If you feel the need to add a table to a graph, you probably should just use the table or add value labels to your graph. The text accompanying your tables and graphs in the main body of a report should not repeat what is shown already but should direct the reader to the important message(s) of the table or graph.

In NBD studies you will often want to present separate graphs for men and women or for other comparisons of health status between sub-populations. When doing this in a set of graphs, make sure that

- the measure shown is comparable (e.g. age standardised, a rate rather than absolute numbers)
- the categories of comparison are clearly shown on (usually) the X-axis
- the scale of the measurement (usually the Y-axis) is the same; for instance, if you are comparing DALY rates by age group between one ethnic group and another in two graphs, the Y-axis should run to the same number even if the DALY rates in one of the ethnic groups are much lower.
- you start the scale of your Y-axis at 0, or if you have good reasons not to do so indicate this clearly, e.g.:



The choice of type of graph (pie chart, line graph, area graph, 2-D or 3-D, etc.) depends on what you want to show. Again, you will find it helpful to look at how others have done this but you may want to venture in some creative designs that you think best conveys your message.

15.4 DEALING WITH CRITICISM

Summary measures of population health such as the DALY include a number of social value choices (discounting, age weights, disability weights, valuing deaths by the years of life lost) that can stir up heated and sometimes emotional debates. Some of this is a useful way of exploring common ground and trying to reach a consensus that most interested parties in the health sector accept. Some of the more emotional arguments are often based on incomplete understanding of the methods. It is important for the success of your study to be prepared to respond to criticism and to take away misunderstandings.

A good way of pre-empting criticism is to openly describe the social value choices in your reports and talks. It helps also if you can demonstrate that you have gone through a process of consultation with prominent health experts about these value choices during your NBD study and if you mention that WHO is actively encouraging a lively international debate.

The most common criticism concerns:

- confusion about the term disability. In many health systems, disability has become a term reserved for chronic disabling health states —often linked to eligibility to receive government support. Disability advocacy groups endeavour to take away the stigma and discrimination of disability in society. This leads to statements such as: “Persons with a disability can be healthy”. In the broad sense in which disability is used in the burden of disease terminology, any departure from full health is counted.
- equating a disability weight to a value judgment on a person with a disability. This is probably the most emotional criticism of DALYs. If the opportunity is there for discussion, it helps to explain that burden of disease assessments and cost-effectiveness analyses that use DALYs intend to reflect a societal willingness to prevent, cure or treat a health problem and not a judgement on the value of individuals with or without varying degrees of illness and disability. In fact, if a person with a disability (such as deafness) considers him/herself completely healthy this does not mean that society would not want to prevent others from becoming deaf. Thus, identifying the disability as a departure from full health indicates a willingness to invest resources in the prevention and or treatment of persons in that health state.
- disputes by disease advocacy groups about the estimates for a particular condition. It is not for nothing that *decoupling advocacy from epidemiology* is an important principle of burden of disease studies. Your NBD estimates of the prevalence of a condition are often considerably smaller than those put out by disease experts or advocacy groups. To an extent, this is a consequence of more liberal inclusion criteria while in a NBD study you endeavour to avoid double counting. There is often also an element of exaggeration or choosing the highest estimates to influence policy makers to provide more resources. In these debates it often helps to show your criteria of inclusion and exclusion, and to provide information on the data sources and data transformations that led to your estimates.
- unease about the uncertainty of burden of disease estimates. Statisticians and a lot of epidemiologists are averse to uncertainty and may challenge you on the grounds that there is so much uncertainty in your estimates that you cannot possibly present them, let alone base decisions on them. Again, giving full transparency of what you have done is an important first step in reply. Another helpful line of argument is to say that it may be better to produce uncertain results rather than ignoring a health problem if available data sources are poor. Moreover, in the absence of evidence about the size and distribution of health problems policy decisions are being made. Therefore, the extent to which decision-making can be informed by your NBD results should not be compared with an ideal of complete knowledge of every disease but against making decisions in the absence of this information. It helps if you can indicate that you have done or are planning to do sensitivity analyses (to evaluate the impact on results of varying the social value choices) and uncertainty analyses (exploring the impact of epidemiological uncertainty on the end results).