

***Uncertainty and data availability for  
the global burden of disease estimates  
2000-2002***

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## Executive summary

During the years 1998 to 2004, the World Health Organization (WHO) undertook a progressive re-assessment of the GBD for the years 2000 to 2002, with consecutive revisions and updates published annually in WHO's World Health Reports. These updates drew on a wide range of data sources to develop internally consistent estimates of incidence, health state prevalence, severity and duration, and mortality for over 130 major causes, for 17 sub-regions of the world. WHO program participation in the development and finalization of these estimates ensured that estimates reflected all information and knowledge available to WHO at the time, and to the extent possible. This working paper provides an overview of data availability, an examination of levels of uncertainty for GBD estimates for 2002, and a summary of the levels of evidence for country-level estimates of burden of disease.

While it is difficult to quantify the exact numbers of data sources used for the YLD estimates for GBD 2000-2002, an attempt has been made to provide an approximate count by region. Of the more than 8,000 datasets estimated to have been used for the GBD 2000-2002 estimation of YLD, nearly 6,600 relate to Group I causes, and only 18 datasets to Group III causes (injuries). Furthermore, one quarter of the datasets relate to populations in sub-Saharan Africa, and around one-fifth to populations in high income countries. Not counting again studies which also contributed to the estimation of cause-specific mortality rates, an additional 1,370 datasets were used for the estimation of YLL. In total, the GBD 2000-2002 has drawn on in excess of 10,000 datasets or studies.

The GBD 2000-2002 analyses have been used to prepare estimates of mortality and burden of disease for WHO Member States for the year 2002. Mortality estimates were based on analysis of latest available national information on levels of mortality and cause distributions as at mid-2004. YLD estimates were based on the GBD analyses of incidence, prevalence, duration and severity of conditions for the relevant epidemiological subregion, together with national and subnational level information available to WHO. Country-level estimates have been classified broadly into three classes according to the levels of evidence available.

Uncertainty in the GBD prior estimates for countries must be taken into account when making cross-national comparisons, and needs to be carefully communicated and interpreted by epidemiologists and policy makers alike. Estimates of mortality in countries where there is no functioning vital registration system for causes of death will always be substantially more uncertain than those derived from systems where all deaths are registered and medically certified. The same may be said for the quantification of disability due to various conditions, where the gap in data availability between rich and poor countries is likely to be even more extreme than for mortality.

This working paper summarizes provisional attempts to quantify the levels of uncertainty relating to all-cause and cause-specific estimates of mortality, and provides estimates of uncertainty ranges for total deaths by sex for WHO Member States in 2002. Relative uncertainty ranges varied from less than 1 per cent in countries with good death registration systems up to plus or minus 25 per cent in countries with limited information on mortality.

# 1. Introduction

In 1993 the Harvard School of Public Health in collaboration with WHO and the World Bank assessed the Global Burden of Disease (GBD). As well as generating comprehensive and consistent set of estimates of mortality and morbidity by age, sex and region for the world for the first time (Murray and Lopez 1996a; Murray and Lopez 1996b; Murray and Lopez 1996c; World Bank 1993), the GBD study also introduced a new metric – the disability adjusted life year (DALY) – to quantify the burden of disease.

During the years 1998 to 2004, the World Health Organization (WHO) undertook a progressive re-assessment of the GBD for the years 2000 to 2002, with consecutive revisions and updates published annually in WHO's World Health Reports. These updates drew on a wide range of data sources to develop internally consistent estimates of incidence, health state prevalence, severity and duration, and mortality for over 130 major causes, for 17 sub-regions of the world (Mathers et al. 2003a). WHO program participation in the development and finalization of these estimates ensured that estimates reflected all information and knowledge available to WHO at the time, and to the extent possible.

The original GBD study analysed and synthesized a large volume of data on population health to produce comprehensive and comparable information on the causes of loss of health globally, regionally and particularly for low and middle income countries, where there are considerable limitations in data availability and comparability. The GBD study made estimates even for causes of burden where there was limited data and considerable uncertainty, to ensure that causes with limited information were not implicitly considered to have zero burden and hence ignored by health policy makers (Murray, Mathers, and Salomon J.A. 2003).

The basic philosophy guiding the GBD approach is that there is likely to be information content in almost all sources of health data, provided they are carefully screened for plausibility and completeness; and that internally consistent estimates of the global descriptive epidemiology of major conditions are possible with appropriate tools, investigator commitment and expert opinion. This philosophy remains central to the GBD updates for 2000 to 2002, which have expanded the framework of the original GBD study in order

1. to quantify the burden of premature mortality and disability by age, sex, and region for 135 major causes or groups of causes;
2. to develop internally consistent estimates of the incidence, prevalence, duration, and case-fatality for over 500 sequelae resulting from the above causes;
3. to analyze the contribution to this burden of major physiological, behavioural, and social risk factors by age, sex and region.

Methods and data sources are discussed in detail in other working papers (Mathers et al. 2003a; Salomon et al. 2001); this working paper provides an overview of data availability and an examination of levels of uncertainty for GBD estimates for 2002.

## 2. GBD version changes

### GBD Version 1 estimates for 2000

Version 1 of the GBD estimates for the year 2000 were published in the World Health Report 2001. The data sources and methods for Version 1 estimates were documented in a discussion paper available on the WHO website (Murray et al. 2001b). Subsequent versions of the GBD estimates have been progressively made available in the World Health Reports 2002 to 2004 and are also available on the WHO website at [www.who.int/evidence/bod](http://www.who.int/evidence/bod). Apart from the incorporation of new epidemiological data for specific causes, later versions incorporated improvements in mortality data availability, and improvements in methods used for life table and cause of death analysis. These are summarized in a more detail below. For these reasons, the later Versions 4 and 5 GBD estimates for 2002 are not directly comparable with earlier versions, with non-minor changes in estimates for some causes and age groups.

### GBD Version 2 estimates for 2000

Version 2 estimates formed the basis for the comparative risk assessments for 26 major risk factors and the analyses of the cost-effectiveness of interventions for these risks which were the main topic of the World Health Report 2002 (World Health Organization 2002). Full details of the CRA analyses for these risk factors were published in book form in 2004 (Ezzati et al. 2004). A summary of the CRA methods is also available on the WHO website as a supplementary file to the World Health Report 2002.

### GBD Version 3 estimates for 2002

The World Health Report 2003 reported burden of disease estimates for 2002 based on Version 3 revisions of the GBD. The data sources and methods used for these Version 3 revisions were documented in Discussion Paper 54 (Mathers et al. 2003a). These estimates contained substantial revisions in some areas:

- Following the Scientific Peer Review (Anand et al. 2003), significant improvements were made in both data and methods used to calculate life expectancies for WHO Member States. There was a substantial effort to obtain recent death registration data, surveys and censuses, particularly from developing countries. This resulted in significant changes and improvements in estimates of child and adult mortality levels for some countries.
- The CODMOD model for estimation of the proportions of deaths across major cause groups was revised to take into account the much larger historical dataset on cause distributions of deaths. For countries without useable cause of death registration data, there were substantial revisions in the regional cause-of-death distributions used to estimate deaths for detailed cause groups within major cause groups.
- Version 3 of the GBD 2000 included new reviews of the epidemiological data and new or revised disease models for many causes. In particular, the age distribution of HIV/AIDS deaths was substantially revised to use the detailed age-specific estimates prepared by UNAIDS (Walker et al. 2003).
- The total war deaths of 310 million reported for 2000 in the World Health Report 2001 and in the World Report on Violence were substantially revised downwards to around 170

million in 2002. This revision resulted from a combination of correction of several errors (resulting in significant numbers of war deaths in several countries where there should have been few) and of a reduction in estimated numbers of deaths for a number of the larger conflicts, reflecting downwards revisions in several of the data sources.

As part of the analysis effort to produce the version 3 estimates, consistent back revisions of estimates for the year 2000 were also carried out. Version 3 estimates for the year 2001 were then interpolated between the estimates for the years 2000 and 2002. These version 3 estimates for 2001 were used to prepare the global burden of disease estimates and tabulations used in the Disease Control Priorities Project (Jamison et al. 2006; Lopez et al. 2006).

#### **GBD Version 4 estimates for 2002**

The GBD estimates for 2002 were updated and republished in the World Health Report 2004. These Version 4 estimates were updated only to incorporate new information received from Member States as a result of the consultations in 2003, but too late for inclusion in the *World Health Report 2003*. Life tables for eight countries were revised from those prepared for the *World Health Report 2003* to include new vital registration information received too late for inclusion in that report. Additionally, mortality and DALY estimates were revised to reflect new estimates from WHO programs and partners for mortality due to six causes, based on improved data and recent evidence:

- Latest provisional estimates of HIV/AIDS mortality available for countries as at the beginning of February 2004 were incorporated.
- TB prevalence and mortality for 2002 were also revised, as published in WHO's Global Tuberculosis Control report for 2004.
- Estimates of measles mortality were revised to take into account new information on the effects of supplemental immunization campaigns in reducing measles mortality.
- Estimates of deaths due to pertussis, polio and tetanus for 2002 were also revised to take into account new information on notifications and immunization coverage.

#### **GBD Version 5 estimates for 2002**

The 2004 Report on the global AIDS epidemic (UNAIDS 2004) contained substantially revised estimates of HIV/AIDS mortality for many countries, taking into account new and different sources of data, such as national household surveys, as well as improved information on emerging epidemics in Eastern Europe, Asia and the Americas. For some countries, these estimates differed substantially from the draft estimates used in Version 4.

As well as updating HIV/AIDS mortality to reflect the 2004 Report estimates, further updates were also carried out for malaria, schistosomiasis and intestinal helminths. Country-specific estimates of malaria mortality and incidence were updated to reflect recent work carried out in collaboration with other WHO programs and external expert groups to refine and revise these country-specific estimates of malaria mortality (Korenromp et al. 2003; Rowe et al. 2005).

### **3. Availability of data for GBD estimates**

The GBD 2000-2002 incorporated a range of new data sources to develop internally consistent estimates of incidence, health state prevalence, severity and duration, and mortality for 135 major causes, by sex and by eight age groups.

#### **Data on mortality levels and causes of death**

According to data provided by 112 Member States to WHO, only about one third of the estimated 56 million deaths occurring annually are recorded in death registration systems (Mathers et al. 2005). If the sample registration systems of India and China are considered to provide information on their whole populations, then information is available for around 72 percent of the global population. In recent years, considerable attention has also been placed on obtaining data on child and maternal mortality through instruments such as the Demographic and Health Surveys (DHS) and UNICEF's Multiple Indicator Cluster Surveys (MICS).

The sources of information on levels of child and adult all-cause mortality used to construct life tables for 192 WHO Member States for the GBD 2002 are given in the Annex Tables to Discussion Paper 54 (Mathers et al. 2003a). These sources of information are summarized in Table 1 by region and by type of data. The regions used in this table are defined in Annex Table A-1.

In the last decade, computerization of death registration data at country level and electronic transmission to WHO have considerably improved the timeliness of information received. The number of countries submitting their underlying causes of death data to WHO using 10<sup>th</sup> revision of the International Classification of Diseases (ICD-10) has increased from 4 in 1995 to 75 in 2003. There are still around 50 countries reporting data using the ICD-9 (9<sup>th</sup> revision) and only one country using the 8<sup>th</sup> revision (Mathers et al. 2005).

**Table 1: Availability of data for the estimation of all cause mortality rates by age and sex, by type of data and region.**

<b>Type of data</b>	<b>East Asia and Pacific</b>	<b>Europe &amp; Central Asia</b>	<b>High income</b>	<b>Latin America &amp; Caribbean</b>	<b>Middle East &amp; North Africa</b>	<b>South Asia</b>	<b>Sub-Saharan Africa</b>	<b>Total</b>
<b>Number of countries with all cause mortality data:</b>								
Death registration data for 2001								
Complete	1	11	25	2	1	0	1	41
Incomplete (a)	1	6	2	5	0	1	0	15
Death registration data for years prior to 2001 (b)								
Complete	1	0	5	3	0	0	0	9
Incomplete (a)	3	9	2	13	1	1	2	31
Data for levels of child and adult mortality	12	1	3	6	9	4	2	37
Data for levels of child mortality only	4	0	0	3	4	2	42	55
<b>Number of data collections</b>								
Country-years of death registration data used								
2001 available	4	17	28	7	1	1	1	59
2001 not available (c)	89	132	114	279	45	23	29	711
Other sources of information on								
child and adult mortality	70	22	16	122	67	48	190	535
<b>Total data sets used</b>	<b>163</b>	<b>171</b>	<b>158</b>	<b>408</b>	<b>113</b>	<b>72</b>	<b>220</b>	<b>1305</b>

- (a) Completeness of death registration data assessed using standard demographic methods (see Lopez et al. 2002)
- (b) Includes countries where death registration data for years prior to 2001 were used to project levels of child and adult mortality to construct a life table based on a country standard derived from the death registration data.
- (c) Also includes countries where death registration data were used to project levels of child and adult mortality as inputs to the WHO logit life table system using a global standard.

**Table 2: Availability of data for the estimation of causes of death by age and sex, by type of data and region.**

<b>Type of data</b>	<b>East Asia and Pacific</b>	<b>Europe &amp; Central Asia</b>	<b>High income</b>	<b>Latin America &amp; Caribbean</b>	<b>Middle East &amp; North Africa</b>	<b>South Asia</b>	<b>Sub-Saharan Africa</b>	<b>Total</b>
<b>Number of countries</b>								
Death registration data (a) (coverage of 85% or more)	1	11	29	5	1	0	1	48
Death registration data (coverage <85%) – adjusted using cause of death models	5	16	5	25	3	1	3	58
Sample registration and surveillance (b)	2	0	0	0	1	1	1	5
No data- use of cause of death models and regional model pattern of causes of death	14	0	3	2	10	6	42	77
Epidemiological estimates for mortality due to specific causes used where applicable	(c)	(d)	(e)	(c)	(c)	(c)	(c)	(c)
<b>Per cent of population</b>								
Death registration data (a) (coverage of 85% or more)	0.0	52.7	94.4	13.0	0.1	0.0	0.2	19.5
Death registration data (coverage <85%) – adjusted using cause of death models	5.6	47.3	5.3	84.2	50.0	1.4	8.6	17.1
Sample registration and surveillance (b)	73.3	0.0	0.0	0.0	1.7	74.5	1.4	39.1
No data- use of cause of death models and regional model pattern of causes of death	21.1	0.0	0.3	2.9	48.1	24.2	89.8	24.3
<b>Total</b>	<b>100.0</b>	<b>100.0</b>	<b>100.0</b>	<b>100.0</b>	<b>100.0</b>	<b>100.0</b>	<b>100.0</b>	<b>100.0</b>

(a) The threshold of coverage of 85% used for causes of death differs from that used for registration of deaths (95%) since the biases from underreporting of the fact of death are more serious for assessing levels of all cause mortality than for assessing the distribution of causes.

(b) Includes countries with death registration or surveillance systems relying heavily on verbal autopsy methods for ascertaining causes of death.

(c) AIDS, tuberculosis, measles, pertussis, poliomyelitis, tetanus, acute lower respiratory infections, Chagas disease, maternal conditions, perinatal conditions, cancers, drug use disorders, rheumatoid arthritis and war

(d) AIDS, drug use disorders and war

(e) Drug use disorders and war

Death registration data containing useable information on cause of death distributions were available for 107 countries, the majority of these in the high income group, Latin America and the Caribbean and Europe and Central Asia (see Table 2). For more detailed information on these data sources, refer to the Annex Tables of Discussion Paper 54 (Mathers et al. 2003a). Where the latest available year was earlier than 2002, death registration data from 1980 up to the latest available year were analyzed as a basis for projecting recent trends for specific causes, and these trend estimates were used to project the cause distribution from the latest available year. When estimating cause of death

distributions for very small countries, an average of the three last years of data were used to minimize stochastic variation.

Specific epidemiological estimates for some causes were also taken into account in analysing causes of death for countries (Mathers et al. 2003a). Table 3 summarizes the numbers of studies (population-based epidemiological studies, disease registers and notifications systems) that contributed to the estimation of mortality due to 21 specific causes of death, including HIV/AIDS, malaria and tuberculosis. In excess of 2,700 datasets contributed to the estimates for these 21 causes of death, with almost one third of these relating to sub-Saharan Africa. Estimates of deaths by cause, age and sex were carried out for 226 countries and territories drawing on a total of 770 country-years of death registration data, as well as 535 additional sources of information on levels of child and adult mortality, and in excess of 2,700 data sets providing information on specific causes of death in regions not well covered by death registration systems.

**Table 3: Numbers of data sets (a) contributing to epidemiologically based estimates of deaths due to specific causes, by region and cause**

<b>Cause</b>	<b>East Asia and Pacific</b>	<b>Europe &amp; Central Asia</b>	<b>High income</b>	<b>Latin America &amp; Caribbean</b>	<b>Middle East &amp; North Africa</b>	<b>South Asia</b>	<b>Sub-Saharan Africa</b>	<b>Total</b>
Tuberculosis (b)	24	27	31	34	16	8	39	179
HIV/AIDS (b)	14	26	29	27	13	5	37	150
Diarrheal diseases		0	0	15	8	21	24	73
Childhood-cluster diseases								
Pertussis	14	33	124	64	14	8	45	302
Poliomyelitis	22	27	37	32	15	8	47	192
Diphtheria	12	25	8	2	14	8	46	115
Measles	22	18	22	32	12	8	47	127
Tetanus	48	23	34	27	40	32	79	289
Meningitis	23	18	43	30	12	4	27	157
Hepatitis B and C	40	27	113	47	43	18	67	355
Malaria	9	0	0	2	1	7	142	161
Tropical-cluster diseases								
Trypanosomiasis*	0	0	0	0	0	0	36	36
Chagas disease	0	0	0	31	0	0	0	31
Schistosomiasis	6	0	1	3	8	0	37	55
Acute lower respiratory infections	2	0	2	18	0	9	18	49
Maternal conditions (all causes)	6	0	1	9	5	4	20	45
Unsafe abortion	14	32	10	27	11	13	49	156
Perinatal causes	7	0	0	7	11	19	12	56
Malignant neoplasms	14	12	40	12	10	3	14	105
Drug use disorders	11	11	43	18	10	6	15	114
War	3	1	7	1	0	0	6	18
<b>Total</b>	<b>296</b>	<b>280</b>	<b>545</b>	<b>438</b>	<b>243</b>	<b>181</b>	<b>807</b>	<b>2,765</b>

(a) includes population-based epidemiological studies, disease registers, surveillance and notifications systems. Where possible, regional and global totals refer to numbers of separate studies, or country-years of reported data from surveillance or notifications systems.

(b) Totals refer to numbers of countries for which data were available, not to total data sets or country-years.

Although these epidemiological studies allow estimation of deaths for certain causes in populations without death registration data, they do not cover many important causes of death in these populations, such as cardiovascular disease or injuries. In order to address these information gaps, models for estimating broad cause-of-death patterns were used as the starting point for indirect methods of estimating attributable mortality for a comprehensive list of detailed causes. The cause-of-death model used in the GBD 1990 was substantially revised and enhanced for estimating deaths by broad cause group in regions with limited information on mortality. The statistical model was enhanced by the adaptation of models for compositional data that were previously developed in other areas, and a substantially larger dataset of 1,613 country-years of observations used for analysis. Income per capita was added to the model as an explanatory variable, in addition to level of all cause mortality (Salomon and Murray 2002).

### **Data on incidence, prevalence, duration and severity of conditions**

Estimating the years lived with a disability (YLD) is the most complex component of burden of disease analysis, since it requires systematic assessments of the available evidence on incidence, prevalence, duration and severity of a wide range of conditions. Various methods have been developed to reconcile often fragmented and partial estimates available from different studies. A specific software tool, DisMod, has been developed to assist in the development of internally consistent estimates (Barendregt et al. 2003).

A wide range of data sources were used for the analysis of incidence, prevalence and YLD for the GBD 2000-2002. These included:

#### **(1) Disease registers**

Disease registers record new cases of disease based on reports by physicians and/or laboratories. Registers are common for infectious diseases (e.g. tuberculosis), cancer, congenital anomalies, a number of relatively rare diseases (e.g. cystic fibrosis or thalassaemia), and sometimes for conditions such as diabetes, schizophrenia and epilepsy. For some Group I conditions, WHO programs maintain up-to-date databases based on diseases registers, population surveys and epidemiological studies. These have been used where available.

#### **(2) Population surveys**

Interview surveys such as the National Health Interview Survey in the USA can provide self-reported information on disabilities, impairments and diseases. However, self-report data is generally not comparable across countries (Murray et al. 2002; Sadana et al. 2002). It is also often difficult to attribute impairment to the underlying causes, and, there are often considerable differences between lay self-reporting of disease causes and the actual underlying disease causes in terms of defined GBD disease categories.

In general, the results of health examination surveys have contributed more to YLD calculations than self-reported interview surveys. 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 in assessing YLD for mental disorders for the GBD 2000-2002.

#### **(3) Epidemiological studies**

Some of the most useful sources of information for the GBD 2000-2002 were population-based epidemiological studies. Particularly, longitudinal studies of the 'natural' history of a disease have provided 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 is needed to extrapolate results to the whole population.

#### **(4) Health facility data**

In the majority of cases, routine data on consultations by diagnosis was not found to be very helpful in estimating YLD. Facility based data — unless the coverage of the health system is near complete — will always be based on biased samples of the conditions present in the community. Likewise, hospital deaths are unlikely to be useful due to the same problems of selection bias. Examples of conditions that were estimated from hospital data with national or quasi-national population coverage include: perinatal and maternal conditions, meningitis, stroke, myocardial infarction, some sequelae identifiable via data on surgical interventions and injuries.

The epidemiological reviews underlying the GBD 2000-2002 estimates of YLD have been progressively documented and published in draft form on the WHO website ([www.who.int/evidence/bod](http://www.who.int/evidence/bod)) and in peer reviewed publication. Discussion Paper 54 provides an overview of data sources and methods for various specific causes together with references to more detailed documentation (Mathers et al. 2003a).

While it is difficult to quantify the exact numbers of data sources used for the YLD estimates for GBD 2000-2002, an attempt has been made to provide an approximate count by region (Table 4). This table counts numbers of data sources (registers, notifications, health facility and other official data sets, and epidemiological studies for each of the causes included in the GBD. For some causes, only counts were available of the numbers of countries in each region for which country-specific data were used. In some cases, it was not feasible to do an exact recount of studies by region, and an approximate regional break down was estimated from prior counts according to the 17 epidemiological subregions used in the GBD (Mathers et al. 2003b). Additionally, it was not always possible to be consistent in the counting of studies carried out across multiple countries or multiple years. Finally, it must be emphasized that there is huge variability in the information content across studies or data sets and that small epidemiological studies count equally in Table 4 with national hospital inpatient data on injuries for an entire population-year. Thus the counts in Table 4 should be treated as reasonably indicative of the empirical bases underlying the GBD 2000-2002 without over-interpreting differences between causes or regions.

That said, it is striking that of the more than 8,000 datasets estimated to have been used for the GBD 2000-2002 estimation of YLD, nearly 6,600 relate to Group I causes, and only 18 datasets to Group III causes (injuries). Furthermore, one quarter of the datasets relate to populations in sub-Saharan Africa, and around one-fifth to populations in High income countries. While this predominance of data relating to Group I conditions, and to sub-Saharan Africa, is not entirely surprising, the paucity of data for some of the leading noncommunicable diseases is more surprising. For example, for several of the leading causes of burden among mental disorders, one or no useable population-based studies were found for some regions. For ischaemic heart disease, very few studies of the incidence or prevalence of angina pectoris or acute myocardial infarction were found outside high income countries.

Assuming that for causes in Table 4 where the counts relate to countries rather than datasets, there are on average two datasets per country, then overall, approximately 8,700 datasets contributed to the estimation of YLD. Not counting again studies which also contributed to the estimation of cause-specific mortality rates, an additional 1,370 datasets were used for the estimation of YLL. In total, the GBD 2000-2002 has drawn on in excess of 10,000 datasets or studies.

**Table 4: Numbers of country data sources (a) contributing to the estimation of YLD, by region and cause.**

<b>GBD Cause Category</b>	<b>East Asia and Pacific</b>	<b>Europe &amp; Central Asia</b>	<b>High income</b>	<b>Latin America &amp; Caribbean</b>	<b>Middle East &amp; North Africa</b>	<b>South Asia</b>	<b>Sub-Saharan Africa</b>	<b>Total (a)</b>
<b>I. Communicable, maternal, perinatal and nutritional conditions</b>								
Tuberculosis (b)	24	27	31	34	16	8	39	179
Sexually transmitted diseases excluding HIV (c)	143	318	297	148	45	99	406	1,456
HIV/AIDS (b)	14	26	29	27	13	5	37	150
Diarrheal diseases	155	0	0	27	55	29	91	357
Childhood-cluster diseases (d)								
Pertussis	14	33	124	64	14	8	45	302
<i>Poliomyelitis</i>	22	27	37	32	15	8	47	192
Diphtheria	12	25	8	2	14	8	46	115
Measles	22	18	22	32	12	8	47	127
Tetanus	48	23	34	27	40	32	79	289
Meningitis	23	18	43	30	12	4	27	157
Hepatitis B	4	4	28	6	6	10	11	69
Hepatitis C (e)	36	23	85	41	37	8	56	286
Malaria	9	0	0	2	1	7	98	117
Tropical-cluster diseases								
Trypanosomiasis (b)	0	0	0	0	0	0	36	36
Chagas disease	0	0	0	31	0	0	0	31
Schistosomiasis	6	0	1	3	8	0	37	55
Leishmaniasis (f)	3	7	4	15	13	4	20	66
Lymphatic filariasis (b)	29	0	2	8	5	5	40	89
Onchocerciasis	0	0	0	6	0	0	26	32
Leprosy (b)	32	10	3	8	14	8	45	120
Dengue (g)	91	0	15	170	0	4	2	282
Japanese encephalitis (b)	10	1	4	0	0	3	0	18
Trachoma	11	0	0	4	5	4	19	43
Intestinal nematode infections	29	0	6	23	13	10	53	134
Acute lower respiratory infections	15	0	5	15	12	30	18	95
Otitis media	4	0	9	0	2	2	7	24
Maternal conditions								
Maternal haemorrhage	3	0	9	2	0	1	13	28
Maternal sepsis	2	0	11	3	0	1	14	31
Hypertensive disorders of pregnancy	1	0	2	1	0	2	12	18
Obstructed labour	2	0	2	2	0	1	14	21
Abortion	32	10	27	11	13	49	156	32
Perinatal conditions								
Low birth weight (i)	28	27	33	33	15	7	41	184
Birth asphyxia & trauma	7	0	0	7	11	19	12	56



**Table 4 (continued): Numbers of country data sources (a) contributing to the estimation of YLD, by region and cause.**

<b>GBD Cause Category</b>	<b>East Asia and Pacific</b>	<b>Europe &amp; Central Asia</b>	<b>High income</b>	<b>Latin America &amp; Caribbean</b>	<b>Middle East &amp; North Africa</b>	<b>South Asia</b>	<b>Sub-Saharan Africa</b>	<b>Total (a)</b>
Nutritional deficiencies								
Protein-energy malnutrition (j)	61	28	15	116	37	30	132	419
Iodine deficiency	17	13	20	13	17	12	44	136
Vitamin A deficiency	10	2	8	12	4	4	29	67
Iron-deficiency anemia	14	1	0	1	15	5	33	69
<b>II. Noncommunicable diseases</b>								
Malignant neoplasms								
Incidence	11	8	25	11	10	2	14	81
Survival	3	4	15	1	0	1	0	24
Diabetes mellitus- Type I (l)	22	12	41	17	5	1	2	100
Diabetes mellitus- Type II	6	4	8	5	8	3	6	40
Neuro-psychiatric conditions								
Unipolar depressive dis.	5	5	27	6	3	4	6	56
Bipolar affective disorder	2	1	14	1	1	2	0	21
Schizophrenia	4	3	25	3	1	3	6	45
Epilepsy (k)	1	1	7	6	1	4	8	28
Alcohol use disorders	24	43	56	39	13	5	34	214
Alzheimer/other dementias	10	3	87	3	0	4	3	110
Parkinson disease (k)	2	1	7	1	0	1	1	13
Multiple sclerosis	4	24	116	3	5	1	1	154
Drug use disorders	11	11	43	18	10	6	15	114
Post-traumatic stress dis.	1	0	6	1	0	0	0	6
Obsessive-compulsive dis.	2	0	14	3	0	1	0	20
Panic disorder	2	0	22	3	1	0	2	30
Insomnia (primary)	2	2	9	5	1	1	1	21
Migraine	6	2	11	5	2	0	1	43
Mental retardation attrib. to lead exposure	10	12	23	21	4	14	9	93
Sense organ diseases								
Vision disorders (b)	11	3	9	4	5	4	19	55
Hearing loss, adult onset	5	0	12	1	1	5	1	25
Cardiovascular diseases								
Rheumatic heart disease	15	0	7	12	9	15	26	84
Ischemic heart disease	3	11	58	0	2	4	1	79
Cerebrovascular disease	4	8	28	1	5	0	6	52
Other forms of heart disease	0	0	5	0	0	0	0	5
Respiratory diseases								
COPD	24	10	32	10	4	16	8	104
Asthma	17	14	74	20	12	6	7	149
Musculoskeletal diseases								
Rheumatoid arthritis	4	1	9	4	4	2	5	29

Osteoarthritis	1	1	9	1	0	2	1	15
Congenital malformations	3	42	5	29	6	9	6	100
Oral conditions (f)	22	24	27	32	15	7	35	162
<b>III. Injuries</b>	<b>3</b>	<b>1</b>	<b>7</b>	<b>1</b>	<b>0</b>	<b>0</b>	<b>6</b>	<b>18</b>
<b>Total (m)</b>	<b>1,155</b>	<b>914</b>	<b>1,735</b>	<b>1,239</b>	<b>590</b>	<b>522</b>	<b>1,955</b>	<b>8,096</b>

(a) includes population-based epidemiological studies, disease registers, surveillance and notifications systems, but excludes death registration data (see Table 1 and 2). Where possible, regional and global totals refer to numbers of separate studies, or country-years of reported data from surveillance or notifications systems. Global total may include global review studies not counted in subtotals for regions. For some causes, regional subtotals were approximately estimated from subtotals for WHO regions and subregions.

(b) Totals refer to numbers of countries for which data were available, not to total data sets or country-years.

(c) Regional subtotals estimated from current distribution of studies in the WHO STI surveillance database

(d) Regional subtotals estimated from subtotals of numbers of studies by WHO region, rather than by re-accessing original databases.

(e) Count of country-years of data, data available for 133 countries.

(f) Approximate estimate from current WHO database, original extraction from surveillance data sources not available.

(g) Country years of surveillance reports (approximate minimum estimate for Latin America and Caribbean).

(h) Global total for number of countries with quantitative data, approximate regional subtotals pending detailed count.

(i) Approximate estimate based on finally published literature review.

(j) Regional distribution of the 419 national studies used assumed similar to that of the current 442 national studies in the WHO malnutrition database.

(k) Approximate minimum estimate. Several global reviews used and studies not separately counted.

(l) Total of 100 population-based registries in 50 countries.

(m) Actual numbers of studies used exceed the minimums shown here, based on summed table entries for specific causes irrespective of whether counts of data sets or countries.

## 4. GBD prior estimates for WHO Member States

The GBD 2000-2002 analyses have been used to prepare estimates of mortality and burden of disease for WHO Member States for the year 2002. These are available in summarized form by country and cause on the WHO website at [www.who.int/evidence/bod](http://www.who.int/evidence/bod) (select links to estimates, then to 2002 revised, then to country estimates). Mortality estimates were based on analysis of latest available national information on levels of mortality and cause distributions as at mid-2004. YLD estimates were based on the GBD analyses of incidence, prevalence, duration and severity of conditions for the relevant epidemiological subregion, together with national and subnational level information available to WHO (Mathers et al. 2003a). The GBD used the population estimates for WHO Member States prepared by the UN Population Division (2002 revision).

Initial WHO estimates and technical explanations were sent to Member States for comment in 2003. Comments or data provided in response were discussed with them and incorporated where possible. The prior estimates for countries should, however, still be interpreted as the best estimates of WHO, based on the evidence available to it in mid-2004, rather than the official estimates of

Member States. They have been computed using standard categories and methods to ensure cross-national comparability and may not be the same as official national estimates produced using alternate, potentially equally rigorous methods.

Where feasible, country-specific YLD estimates were made for a number of causes. For the estimates for 2002, these included childhood vaccine preventable diseases, malnutrition, HIV/AIDS, cancers, and diabetes (see Table 5). For other causes, regional YLD estimates were used, together with country-specific and regional cause of death information, to develop country-specific estimates of YLD by age and sex. The five methods used are described below and summarized in Table 5.

### Country-specific Data

For the causes listed in the first row of Table 5, YLD estimates were made directly for Member States using available data on the incidence or prevalence of each condition. For the Group I conditions, death registration data together with databases of country-level studies developed by WHO programmes and UNAIDS were used to estimate country-level incidences and prevalences. Methods used to estimate the prevalence of malignant neoplasms at the country level, based on national incidence, mortality and survival data, were described by Mathers et al (Mathers et al. 2002). Diabetes prevalence was based on updated country-level prevalence estimates prepared by the WHO Management of Non-communicable Diseases and Mental Health Programme (NMH) according to the revised WHO definition of diabetes cases (Wild et al. 2004). Variations in the prevalence of unipolar depressive disorders in some European countries, Australia, New Zealand, and Japan were estimated directly from relevant population studies for the GBD (Ustun et al. 2004). For other countries in the A (lowest mortality) regions, country-specific prevalences  $P_c$  for males and females aged 15-59 have been estimated using a regression model on suicide rates as follows:

$$P_c = P_R + 0.0919(S_C - S_R)$$

where  $P_R$  is the regional depression prevalence,  $S_C$  and  $S_R$  are the country and regional suicide rates (ages 15-59 both sexes combined). For other regions, it was assumed that the variation of depression prevalence with suicide rate was half that of A countries, and the range of variation was restricted from a minimum of one half the regional average to a maximum of twice the regional average.

### YLD/YLL Ratios

For specific disease and injury causes where mortality was responsible for a significant proportion of the total burden (incidence YLD/YLL ratio less than 5), regional estimates of incidence YLD/YLL ratios by age and sex together with country-level estimates of YLL were used to estimate country-level YLD. This process ensured that country-specific knowledge on the epidemiology of the disease (as reflected in the country-level mortality estimates of that disease) was used to adjust the regional-level patterns of disability due to that cause.

### Group cause YLD/YLL Ratios

For certain causes, regional age-sex specific incidence/mortality ratio for the overall cause group were applied to country-specific mortality for each cause in the group to estimate incidence and YLD (see Table 5). This avoided problems resulting from statistical fluctuations in countries with small numbers of deaths for certain cause-sex-age-groups.

### **Regional Prevalence YLD Rates**

For specific disease and injury causes where mortality is not responsible for a significant proportion of the total burden (incidence YLD/YLL ratio is 5 or higher), or where there is insufficient evidence to predict variations in YLD rates from variations in mortality rates, regional estimates of YLD rates per 1 000 population by age and sex were used together with country-level population distribution estimates to estimate YLD for each country.

**Table 5. Methods used to estimate country-level YLD for 2002**

<b>Method</b>	<b>Imputation of country-specific incidence rates from regional incidence rates</b>	<b>Causes</b>
Country-specific data	Country-specific prevalence or incidence data used	Tuberculosis, HIV/AIDS, pertussis, diphtheria, measles, tetanus, schistosomiasis, lymphatic filariasis, onchocerciasis, trachoma, abortion, protein-energy malnutrition, iodine deficiency, diabetes mellitus, unipolar depressive disorders*, alcohol use disorders, drug use disorders, sense organ disorders excluding others, asthma
Incidence/ mortality ratio – short duration	Regional age-sex specific incidence/mortality ratio applied to country-specific mortality to estimate incidence. Same approach used for prevalence	Hepatitis B, hepatitis C, malaria, lower respiratory infections, malignant neoplasms, rheumatic heart disease, hypertensive heart disease, inflammatory heart disease, other cardiovascular diseases, peptic ulcer disease, cirrhosis of the liver, nephritis and nephrosis
Incidence/ mortality ratio – long duration	Regional age-sex specific incidence/mortality ratio applied to country-specific mortality to estimate incidence. Resultant country/regional sex specific all-ages YLD[0,0] ratio applied to regional prevalence YLD total for that sex to estimate country-specific prevalences by age and sex	Meningitis, endocrine disorders, ischaemic heart disease, cerebrovascular disease, COPD, other respiratory diseases, other digestive diseases, other genitourinary system diseases
Group cause incidence/ mortality ratio	Regional age-sex specific incidence/mortality ratio applied to country-specific mortality of the cause group to estimate incidence	Maternal haemorrhage and sepsis, hypertensive disorders of pregnancy, perinatal causes, congenital malformations excluding cleft lip and palate and Down syndrome, , road traffic accidents, poisonings, falls, fires, drownings, other unintentional injuries, self-inflicted injuries, violence, other intentional injuries
Regional rates	Regional age-sex specific incidence and prevalence rates applied to countries	Sexually transmitted diseases excluding HIV, diarrhoeal diseases, poliomyelitis, trypanosomiasis, Chagas disease, leishmaniasis, leprosy, dengue, Japanese encephalitis, intestinal nematode infections, other infectious diseases, upper respiratory infections, otitis media, obstructed labor, vitamin A deficiency, iron-deficiency anaemia, other nutritional disorders, other neoplasms, bipolar affective disorder, schizophrenia, epilepsy, Alzheimer and other dementias, multiple sclerosis, post-traumatic stress disorder, obsessive-compulsive disorder, panic disorder, insomnia (primary), migraine, mild mental retardation attributable to lead exposure, other neuropsychiatric disorders, other sense organ disorders, appendicitis, benign prostatic hypertrophy, skin diseases, musculoskeletal diseases, cleft lip and palate, Down syndrome, oral conditions
Average of ratio and rate method results	Regional age-sex specific incidence and prevalence rates and incidence and prevalence rates from the ratio methods are averaged and applied to countries	Other maternal conditions, Parkinson disease, war

\* Some country data plus regression model based on suicide rates.

### **Levels of evidence for country-level information on mortality and burden of disease**

Country-level estimates of deaths and DALYs by cause (for all ages and both sexes combined) have been made available on the WHO website at [www.who.int/evidence/bod](http://www.who.int/evidence/bod) with summary information on levels of evidence as follows.

The data sources and methods used for the estimation of total deaths (all causes) for each Member State are summarized into four levels of evidence:

- Level 1a Complete death registration data available for years 2001 and/or 2002.
- Level 1b Complete death registration data available for an earlier time period. All cause mortality projected to 2002.
- Level 2a Death registration data available for years 2001 and/or 2002. Completeness for latest year estimated using standard demographic methods for child deaths under age 5 and for deaths at ages 5 and over. Estimated completeness used to adjust death registration data.
- Level 2b Death registration data available for available for an earlier time period. Completeness for latest year estimated using standard demographic methods for child deaths under age 5 and for deaths at ages 5 and over. Estimated completeness used to adjust death registration data and then all cause mortality was projected to 2002.
- Level 3a Country information for years 2001 and/or 2002 available on levels of child mortality (between ages 0 and 5) and adult mortality (between ages 15 and 60). WHO modified logit life table system used with global standard to estimate all cause mortality.
- Level 3b Country information available for an earlier time period on levels of child mortality (between ages 0 and 5) and adult mortality (between ages 15 and 60). Child and adult mortality levels were projected to 2002 and the WHO modified logit life table system used with global standard to estimate all cause mortality.
- Level 4a Country information for years 2001 and/or 2002 available on level of child mortality (between ages 0 and 5) only. Levels of adult mortality excluding HIV/AIDS and war deaths predicted from child mortality. HIV/AIDS and war deaths added separately and WHO modified logit life table system used with global standard to estimate all cause mortality.
- Level 4b Country information prior to 2001 available on level of child mortality (between ages 0 and 5) only. Levels of adult mortality excluding HIV/AIDS and war deaths predicted from projected 2002 HIV/AIDS-free child mortality. HIV/AIDS and war deaths added separately and WHO modified logit life table system used with global standard to estimate all cause mortality.

The data sources and methods used for the estimation of deaths by cause for each Member State are also summarized into four levels of evidence. Additional information for estimating country-level deaths due to certain specific causes were obtained from studies, WHO technical Programmes and UNAids for the following conditions: AIDS, tuberculosis, measles, pertussis, poliomyelitis, tetanus, acute lower respiratory infections, Chagas, maternal conditions, perinatal conditions, cancers, drug use disorders, rhumathoid arthritis and war.

- Level 1a Complete death registration data with cause of death coded using ICD-9 or ICD-10 available for years 2001 and/or 2002. Less than 10% of deaths coded to ICD codes for “symptoms, signs, and ill-defined conditions”, injuries where the intent is not determined; cardiovascular "garbage" codes, and cancer deaths coded to categories for secondary or unspecified sites.
- Level 1b Complete death registration data available . Complete death registration data with cause of death coded using ICD-9 or ICD-10 available for for an earlier time

period. Less than 10% of deaths coded to ICD codes for “symptoms, signs, and ill-defined conditions”, injuries where the intent is not determined; and cardiovascular and cancer "garbage" codes.

- Level 2a Death registration data available for years 2001 and/or 2002. Adjustments to cause of death distribution required for incomplete registration and/or for use of non-ICD-9 or ICD-10 coding and/or for the more than 10% of deaths coded to ill-defined conditions, and cardiovascular, cancer and injury "garbage" codes.
- Level 2b Death registration data available for latest year earlier than 2001. Adjustments to cause of death distribution required for incomplete registration and/or for use of non-ICD-9 or ICD-10 coding and/or for the more than 10% of deaths coded to ill-defined conditions, and cardiovascular, cancer and injury "garbage" codes.
- Level 3 Country information on causes of death available based on verbal autopsy methods.
- Level 4 Country information on causes of death not available for most causes. Cause of death modelling used to estimate broad distribution of causes of death for Groups I, II and III by age and sex for the country level of all cause mortality and per capita income. Cause of death patterns within the three major cause groups based on death registration data from other countries in the region. Further country-level information and data on specific causes listed above was also used.

Two levels of evidence are distinguished for YLD estimates as follows:

- Level 3 Country data on causes of death (Levels 1 to 3) used to adjust regional YLD distributions for causes with significant case fatality. Partial country-specific information on incidence or prevalence of non-fatal causes available.
- Level 4. Level 4 information on causes of death and regional estimates of YLD used for most causes. Partial country-specific information on incidence or prevalence of some non-fatal causes available.

In the summary tables available on the WHO website, columns containing estimates of deaths or DALYs for WHO Member States in 2002 are colour-coded to summarize the levels of evidence and uncertainty. Three colour codes are used to denote the following levels:

Colour	Total mortality	Causes of death	YLD	
BLUE	Level 1 or Level 2	Level 1 or Level 2	Level 3	Death registration data, complete or incomplete, containing useable information on causes of death is available for the country, and used to adjust regional YLD distributions for causes with significant case fatality. Partial country-specific information on incidence or prevalence of non-fatal causes available.
YELLOW	Total mortality or causes of death have level 3 evidence, neither is level 4.			Other forms of information on child and adult mortality or causes of death (eg. verbal autopsy) available. Country-specific information on mortality for specific causes available. Partial country-specific information on incidence or prevalence of non-fatal causes available.
RED	Level 4 OR Level 4	Level 4	Level 4	Country information on level of adult mortality not available and it was predicted from child mortality level OR cause of death information for most causes not available, and cause pattern predicted using cause-of-death models. Partial country-specific information on incidence or prevalence of non-fatal causes available.

Estimated 95% uncertainty ranges for the expected number of total deaths for 2002 are also given for each country in the tables relating to deaths and provide some indication of the level of uncertainty for estimates in that country (see following section). Cause-specific estimates will generally have even greater relative uncertainty ranges, as will DALY estimates, with the possible exception of some causes such as HIV/AIDS where separate country-specific analyses have been used.

## 5. Uncertainty analysis

The GBD 2000-2002 estimated mortality and burden of disease for a comprehensive set of disease and injury causes and for all regions of the world, including regions with limited, incomplete and uncertain data. It is thus important to attempt to provide some analysis and guidance on levels of uncertainty in estimates, in order to allow the user of the information to assess whether the information uncertainty range is compatible with the purpose at hand (Murray, Mathers, and Salomon J.A. 2003). This is difficult to do, since apart from the large number and disparate nature of the data sources used, there is often limited information or knowledge of the quality and potential biases in the data. This section gives an overview of initial efforts to quantify the uncertainty associated with the estimation of deaths by cause, and with epidemiologic estimates of incidence and prevalence for the GBD.

Uncertainty may arise from incomplete information (e.g., when we base estimates for a population on observations from a sample), from potential biases in information (e.g., how representative for a whole population are estimates from a study of a subgroup, how validly does the survey instrument address the quantity of interest), from disagreements between information sources (e.g., when we have several studies giving different estimates for the same quantity), from model uncertainty (e.g., the variables or functional form specified in a regression model), or it may be inherent to the data generation process itself (e.g., we may only infer risks from event counts in a population, which means that we can never know the risks themselves with certainty).

Most measurement involves not only random (stochastic) error but also systematic error, arising from biases in the measurement instrument (e.g., unrepresentativeness of a sampling frame for a survey), or from inaccuracies in the assumptions used to infer the actual quantity from the available data (e.g., estimating prevalence of a disease for a country from studies of representative subpopulations). Much of the uncertainty in estimates of deaths or DALYs is associated with the assessment of systematic errors in primary data. While most countries have some information about prevalence, incidence and mortality from some diseases and injuries, and some information on population exposure to risk factors, it is generally fragmented, partial, incomparable and diagnostically uncertain.

The general approach of the GBD to describing and estimating uncertainty in quantities of interest is to express them as probability distributions using a Bayesian interpretation of probability as expressing uncertainty of an observed or hypothetical event given a set of assumptions about the world (Morgan and Henrion 1990). Probability distributions can thus be used to express uncertainty about epidemiologic quantities such as the prevalence of depression in a particular population, or the underlying risk of mortality due to a specific cause in a specific population.

Analytic methods for dealing with uncertainty have been facilitated enormously by the revolution in computer technology. Using such technology, the general approach to propagating uncertainty in estimates relies on numerical simulation method (King, Tomz, and Wittenberg 2000; Salomon et al. 2001; Vose 2000).

### **Uncertainty estimates for all cause mortality and life expectancies**

Methods for estimating life tables for each of 192 WHO Member States are described elsewhere (Lopez et al. 2002). For those countries with vital registration data projected using time series regression models on the parameters of the logit life table system, uncertainty around the regression coefficients was accounted for by taking 1000 draws of the parameters using the regression

estimates and variance covariance matrix of the estimators. For each of the draws, a new life table was calculated.

For countries that did not have time series data on mortality by age and sex, point estimates and ranges around  ${}_5q_0$  and  ${}_{45}q_{15}$  for males and females were developed on a country-by-country basis as elsewhere (Lopez et al. 2002). For countries without useable information on levels of adult mortality,  ${}_{45}q_{15}$  was estimated, along with uncertainty ranges, based on regression models of  ${}_{45}q_{15}$  versus  ${}_5q_0$  as observed in a set of almost 2000 life tables judged to be of good quality (Murray et al. 2001a). Estimated levels of child and adult mortality were then applied to a modified logit life table model, using a global standard, to estimate the full life table, and HIV/AIDS deaths and war deaths added to total mortality rates where necessary. Estimates of uncertainty ranges for HIV/AIDS and war deaths were also incorporated into the life table uncertainty analysis where necessary.

The final estimated uncertainty ranges for  ${}_5q_0$  and  ${}_{45}q_{15}$  for 192 WHO Member States are plotted in Figure 1 for males and females. Using Monte Carlo simulation methods, 1000 random life tables were generated by drawing samples from normal distributions around these inputs with variances defined in reference to the defined ranges of uncertainty for  ${}_5q_0$  and  ${}_{45}q_{15}$ . In countries where uncertainty around  ${}_5q_0$  and  ${}_{45}q_{15}$  was considerable due to a paucity of survey or surveillance information, the samples were drawn from wide distributions but then constrained within prior specified maximum and minimum possible values for  ${}_5q_0$  and  ${}_{45}q_{15}$ . For each country, the results of this analysis were 1000 different simulated life tables which were then used to describe ranges around key indicators such as life expectancy at birth and age and sex-specific mortality rates (Table 6).

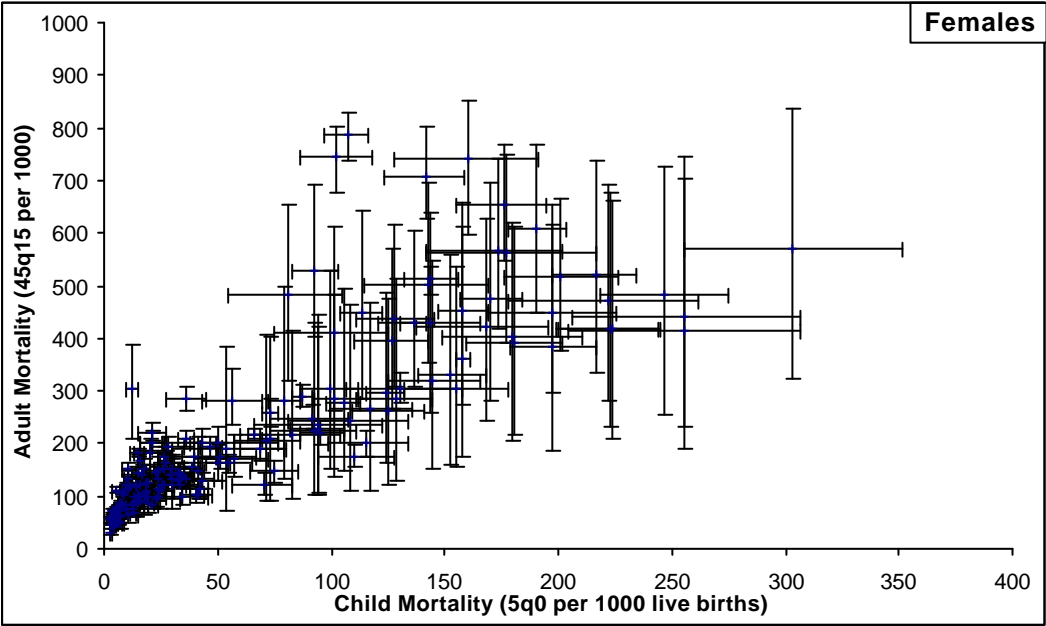
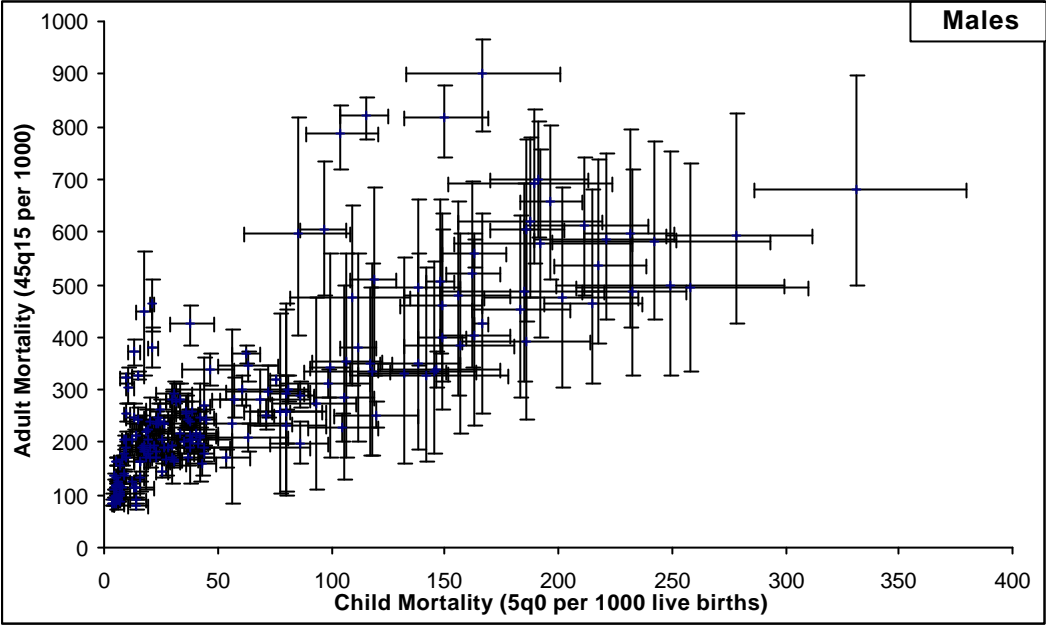
For high income countries where relatively complete death registration data was available, the uncertainty ranges for LE at birth were typically around  $\pm 0.1$  to  $0.2$  years. For regions such as Latin America and the Caribbean, where death registration data was available for most countries but was often not complete, the uncertainty ranges were larger, typically around  $\pm 0.5$  years. For regions with partial data on child mortality only, where adult mortality was predicted from child mortality, the uncertainty ranges were much larger, and for sub-Saharan Africa were typically around  $\pm 5$  to  $\pm 10$  years. This translated to considerable heterogeneity in uncertainty ranges for LE for estimates of all cause and cause-specific mortality levels across WHO Member States.

### **Uncertainty estimates for country-level estimates of mortality**

Provisional attempts were made to estimate indicative uncertainty ranges for the estimates of death by cause for the GBD in 2002. These uncertainty ranges took into account uncertainty in the expected number of total deaths for 2002 (life table uncertainty), uncertainty in the estimated proportions of broad cause groups I, II and III (where relevant for countries without vital registration data or with incomplete coverage), uncertainty in the diagnosis of underlying cause, uncertainty arising from the miscoding of underlying cause, and fundamental Poisson uncertainty in the estimated death rate arising from the observation of a finite number of deaths in a fixed time interval. This analysis was carried out country by country.

Uncertainty in the underlying cause attribution of total deaths was estimated in terms of the relative uncertainty of the proportion of deaths due to each specific cause. The estimates of cause-specific relative uncertainty were based on advice from nosologists and experts in the area of cross-country mortality analysis on the general levels of uncertainty in attribution of specific causes within the major Groups I, II and III, together with detailed advice on particular causes with known higher levels of attribution uncertainty under the International Classification of Diseases (ICD). Information on the latter causes derived from cross-country, cross-time and cross-ICD-revision comparative analyses, together with information from a variety of country-specific coding quality studies involving recoding or dual coding of deaths and comparisons with the original attributed causes.

Figure 1. Adult mortality versus child mortality for 191 WHO Member States, 2002



**Table 6. Estimated 95% uncertainty ranges for total deaths in 2002, WHO Member States**

Member State	Estimated total deaths ('000)			Relative uncertainty (a)
	Total	Lower uncertainty bound	Upper uncertainty bound	
Afghanistan	485	348	696	36
Albania	22	19	28	20
Algeria	173	158	188	9
Andorra	1	1	1	7
Angola	307	255	435	29
Antigua and Barbuda	1	1	1	8
Argentina	281	277	287	2
Armenia	26	24	34	19
Australia	127	124	129	2
Austria	70	69	72	2
Azerbaijan	64	60	70	7
Bahamas	2	2	2	1
Bahrain	2	2	3	11
Bangladesh	1107	1030	1184	7
Barbados	2	2	2	1
Belarus	144	138	148	4
Belgium	103	101	105	2
Belize	1	1	2	8
Benin	87	69	123	31
Bhutan	21	15	30	36
Bolivia	73	49	104	38
Bosnia and Herzegovina	35	31	38	10
Botswana	41	34	45	14
Brazil	1225	1180	1262	3
Brunei Darussalam	1	1	1	2
Bulgaria	107	104	112	4
Burkina Faso	250	213	337	25
Burundi	120	104	174	29
Cambodia	160	123	219	30
Cameroon	236	188	330	30
Canada	222	220	225	1
Cape Verde	2	2	3	24
Central African Republic	76	60	99	26
Chad	149	109	192	28
Chile	84	81	87	4
China	9135	8712	9528	4
Colombia	244	231	257	5
Comoros	5	4	8	40
Congo	44	33	62	32
Cook Islands	0	0	0	1
Costa Rica	18	19	21	5
Croatia	50	49	52	4
Cuba	77	75	78	2
Cyprus	7	7	8	12
Czech Republic	103	101	105	2
Côte d'Ivoire	259	217	386	33
Democratic People's Republic of Korea	204	116	314	49
Democratic Republic of the Congo	986	797	1294	25
Denmark	57	57	57	0
Djibouti	8	7	13	34
Dominica	1	1	1	1

Dominican Republic	57	53	60	6
Ecuador	77	72	81	5
Egypt	495	485	505	2
El Salvador	41	37	43	8
Equatorial Guinea	8	5	9	26
Eritrea	41	27	55	34

**Table 6 (continued). Estimated 95% uncertainty ranges for total deaths in 2002, WHO Member States**

Member State	Estimated total deaths ('000)			Relative uncertainty (a)
	Total	Lower uncertainty bound	Upper uncertainty bound	
Estonia	18	18	19	0
Ethiopia	1060	818	1464	30
Fiji	5	5	6	7
Finland	49	48	49	1
France	499	495	517	2
Gabon	15	10	21	35
Gambia	16	11	22	34
Georgia	61	54	70	13
Germany	815	801	830	2
Ghana	209	138	289	36
Greece	114	111	116	2
Grenada	1	1	1	6
Guatemala	82	74	88	8
Guinea	114	86	151	29
Guinea-Bissau	27	21	34	25
Guyana	7	6	8	14
Haiti	112	91	158	30
Honduras	42	34	51	20
Hungary	122	120	125	2
Iceland	2	2	2	0
India	10378	9979	10678	3
Indonesia	1626	1541	1711	5
Iran (Islamic Republic of)	384	356	412	7
Iraq	213	191	237	11
Ireland	31	30	32	4
Israel	35	36	38	3
Italy	571	553	588	3
Jamaica	20	18	21	7
Japan	973	973	1018	2
Jordan	23	23	26	7
Kazakhstan	184	168	197	8
Kenya	407	287	521	29
Kiribati	1	1	1	1
Kuwait	5	4	5	11
Kyrgyzstan	45	42	48	7
Lao People's Democratic Republic	67	59	76	13
Latvia	33	33	33	1
Lebanon	24	22	26	7
Lesotho	46	36	60	26
Liberia	69	53	94	29
Libyan Arab Jamahiriya	23	18	30	26
Lithuania	41	41	42	2
Luxembourg	3	3	3	0
Madagascar	201	146	265	30
Malawi	258	220	330	21

Malaysia	119	115	122	3
Maldives	2	2	2	6
Mali	243	191	315	26
Malta	3	3	3	4
Marshall Islands	0	0	1	8
Mauritania	40	31	55	30
Mauritius	8	8	8	2
Mexico	470	442	489	5
Micronesia (Federated States of)	1	1	1	13
Monaco	0	0	0	3
Mongolia	19	19	20	2

**Table 6 (continued). Estimated 95% uncertainty ranges for total deaths in 2002, WHO Member States**

Member State	Estimated total deaths ('000)			Relative uncertainty (a)
	Total	Lower uncertainty bound	Upper uncertainty bound	
Morocco	154	139	169	10
Mozambique	385	293	476	24
Myanmar	520	344	757	40
Namibia	28	22	38	28
Nauru	0	0	0	24
Nepal	233	222	245	5
Netherlands	139	136	142	2
New Zealand	27	27	28	3
Nicaragua	26	24	28	9
Niger	245	177	350	35
Nigeria	2006	1456	2528	27
Niue	0	0	0	2
Norway	45	44	46	2
Oman	8	6	11	29
Pakistan	1386	1247	1526	10
Palau	0	0	0	1
Panama	14	13	15	6
Papua New Guinea	47	41	52	11
Paraguay	27	25	28	6
Peru	170	159	182	7
Philippines	448	421	477	6
Poland	352	344	360	2
Portugal	94	92	97	2
Qatar	1	1	2	5
Republic of Korea	275	266	284	3
Republic of Moldova	48	47	49	3
Romania	259	247	271	5
Russian Federation	2406	1973	2757	16
Rwanda	131	116	190	28
Saint Kitts and Nevis	0	0	0	1
Saint Lucia	1	1	1	1
Saint Vincent and the Grenadines	1	1	1	1
Samoa	1	1	1	6
San Marino	0	0	0	2
Sao Tome and Principe	1	1	2	35
Saudi Arabia	97	73	128	28
Senegal	103	75	145	35
Serbia and Montenegro	121	118	124	3
Seychelles	1	1	1	1
Sierra Leone	132	102	202	38

Singapore	18	17	19	6
Slovakia	50	49	51	3
Slovenia	18	18	18	1
Solomon Islands	3	3	3	13
Somalia	175	151	249	28
South Africa	680	513	816	22
Spain	356	343	368	4
Sri Lanka	146	127	163	12
Sudan	346	244	479	34
Suriname	3	3	4	8
Swaziland	26	22	32	19
Sweden	91	89	93	2
Switzerland	61	59	63	3
Syrian Arab Republic	71	67	75	6
Tajikistan	54	48	60	10
Thailand	419	387	453	8

**Table 6 (continued). Estimated 95% uncertainty ranges for total deaths in 2002, WHO Member States**

Member State	Estimated total deaths ('000)			Relative uncertainty (a)
	Total	Lower uncertainty bound	Upper uncertainty bound	
The former Yugoslav Republic of Macedonia	19	18	20	6
Timor-Leste	7	4	10	43
Togo	62	50	85	28
Tonga	1	1	1	4
Trinidad and Tobago	12	10	11	4
Tunisia	56	53	59	6
Turkey	437	407	464	7
Turkmenistan	42	41	43	3
Tuvalu	0	0	0	1
Uganda	388	311	470	20
Ukraine	783	760	809	3
United Arab Emirates	9	9	10	2
United Kingdom	599	577	623	4
United Republic of Tanzania	596	587	661	6
United States of America	2421	2372	2472	2
Uruguay	31	30	31	1
Uzbekistan	172	165	179	4
Vanuatu	1	1	1	12
Venezuela (Bolivarian Republic of)	115	109	120	5
Viet Nam	516	487	543	5
Yemen	171	125	233	31
Zambia	232	190	282	20
Zimbabwe	284	270	335	12

Based on this advice, for cause distributions derived from vital registration data coded using ICD-10, it was generally estimated that diagnostic uncertainty and coding uncertainty together resulted in approximate relative 95% uncertainty ranges of  $\pm 3\%$  for Group I causes (communicable diseases, maternal and perinatal conditions and nutritional deficiencies),  $\pm 7\%$  for Group II causes (non-communicable diseases), and  $\pm 2\%$  for Group III causes (injuries). Uncertainty ranges will be larger for some specific causes known to have greater levels of diagnostic or coding error, and for certain Member States using older ICD or other cause coding systems or verbal autopsy methods, or where

cause of death models were used to estimate death distributions across Groups I, II and III. In the latter case, an additional relative uncertainty for the estimation of Group I, II and III proportions would arise from the prediction uncertainty ranges associated with the CODMOD regression model. Additional uncertainty arises from the redistribution of general, cancer, cardiovascular, and injury ill-defined cause codes and incomplete coverage of vital registration data.

The analysis of uncertainty in cause-of-death (COD) estimates at country level thus combined quantitative country-specific information on uncertainty levels in all-cause mortality and, in some cases also in major cause group distributions, together with quantified average relative uncertainty ranges for specific cause attributions based on expert advice and adjusted for specific causes and also for country-specific information on data sources, type of cause information available and indicators of data quality.

For most causes, uncertainty ranges were greater than those of the all cause mortality estimates, since there is additional uncertainty associated with cause attribution, as described above. For example, the relative uncertainty ranges for ischaemic heart disease ranged from around  $\pm 12\%$  for high-income countries to  $(-24\%, +34\%)$  for Sub-Saharan Africa. While the uncertainty range for high-income countries may seem surprisingly large, it reflects not only uncertainty in overall mortality levels, but also uncertainty in the attribution of underlying cause, and in the attribution of causes coded to garbage codes or to the ICD chapter for 'symptoms, signs and ill-defined conditions'. The proportion of deaths coded to these two groups of causes is surprisingly large for some high-income countries (Mathers et al. 2005).

### **Uncertainty arising from epidemiological estimates**

Uncertainty in YLD estimates is mainly determined by the uncertainty in

- (a) epidemiologic estimates for prevalence and/or incidence of disability associated with specific causes or cause groups,
- (b) disability weights arising from uncertainty in health state valuations and, in some cases, also in the disability severity distribution associated with a condition.

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

For a subset of the GBD causes, analysts carrying out reviews and analyses for the estimation of YLD also undertook an estimation of levels of uncertainty in regional prevalences. These uncertainty levels took into account not only typical levels of measurement error in the input data sets but also semi-qualitative judgements on the uncertainty arising from the lack of representativeness of the available data for each region. The resulting uncertainty ranges varied considerably across causes, ranging from relatively certain estimates for some causes such as polio for which there are intensive surveillance systems in place, to highly uncertain estimates for other causes, such as osteoarthritis where for some regions, not a single useable dataset was found, and for others, the latest available

data was decades old. Table 4 summarizing numbers of data sources used for YLD estimates by cause and region provides one indication of the relative uncertainty associated with YLD estimates for different causes.

For some causes, such as stroke and ischaemic heart disease, YLD estimates were essentially derived from estimates of cause-specific mortality, via models of regional variations in case fatality rates. In such cases, YLD uncertainty will be significantly higher than the uncertainty ranges associated with cause-specific mortality estimates, as there is also considerable uncertainty in case fatality rates for most low- and middle-income countries, and in models used to infer non-fatal disease burden from mortality. In general, we can conclude that YLD uncertainty will generally be greater than YLL uncertainty, and also varies across causes according to both the typical uncertainty associated with measurement of incidence or prevalence according to GBD case definitions, and also with the number and representativeness of available studies. For a subset of 16 major causes of YLD for which indicative uncertainty ranges were estimated by analysts carrying out revisions and updating of YLD estimates, the typical uncertainty ranges for regional prevalence estimates ranged from  $\pm 10\%$  to  $\pm 90\%$ , with a median value of  $\pm 41\%$ . Uncertainty ranges were generally higher for low- and middle-income countries than for high income countries.

## 6. Discussion and conclusions

Uncertainty in the GBD prior estimates for countries must be taken into account when making cross-national comparisons, and needs to be carefully communicated and interpreted by epidemiologists and policy makers alike. Estimates of mortality in countries where there is no functioning vital registration system for causes of death will always be substantially more uncertain than those derived from systems where all deaths are registered and medically certified. The same may be said for the quantification of disability due to various conditions, where the gap in data availability between rich and poor countries is likely to be even more extreme than for mortality.

The GBD project has attempted to maximize the use of available population-based data, and, even for regions and causes where data are sparse, to use the available evidence and the best available methods to make inferences. In excess of 770 country-years of death registration data and over 3,000 additional sources of information on levels of child and adult mortality and on specific causes of death were used to estimate global and regional patterns of mortality. Together with the more than 8,700 data sources used for the estimation of YLD, the GBD 2000-2002 has incorporated information from over 10,000 datasets relating to population health and mortality. This represents the largest synthesis of global information on population health carried out to date.

Despite the perceptions of some critics that the Global Burden of Disease study is inadequately empirically based for some regions, and particularly in Africa (Cooper et al. 1998), it is notable that fully one third of the more than 10,000 data sources used by the GBD 2001 relate to sub-Saharan African populations, albeit with the serious limitations in the information available on mortality noted above. The fact that estimates are possible does not obviate the need to put higher priority on addressing the serious lack of information on levels of adult mortality and causes of death in some regions of the world, particularly Sub-Saharan Africa. Low- and middle-income countries can benefit from the advantages of death registration without fully implementing a system of complete population coverage and medical certification (Rao, Bradshaw, and Mathers 2004; Setel et al. 2005; Yang et al. 2005).

There is also a massive lack of good population-based epidemiological data for developing regions, particularly for non-communicable diseases. Despite the fact that ischemic heart disease and stroke

are among the leading causes of burden of disease in most regions of the world, there are very few recent and reliable sources of information on the prevalence and severity distribution of chronic cardiovascular conditions and long-term disability following stroke. Similarly, there are very few population-based studies, even in high income countries, of the prevalence of chronic lung disease or musculoskeletal conditions. Cross-national surveys such as the WHO's World Health Survey, conducted during 2002 and 2003 in 73 countries, will fill some gaps in information for some chronic diseases and mental disorders (Ustun et al. 2003). However, there remain significant issues with the comparability of prevalence data derived from self-report questionnaires on symptoms for mental disorders, angina, and other chronic diseases, which will need to be addressed.

With increasing pressure on resources for health in all countries, priority setting in the health sector will depend more and more on comprehensive, comparative information about the impact of diseases, injuries and risk factors on population health. To improve the usefulness of the Global Burden of Disease results for setting and monitoring global health priorities, a much more concerted effort is needed to obtain, uncover and critically assess data sets on the health of populations in all countries. This must be a key focus of future efforts to assess the burden of disease.

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**Annex Table A-1: Regional reporting categories for GBD 2002 data sources.**

<b>Region</b>	<b>Countries included</b>
East Asia and Pacific	American Samoa, Cambodia, China, DPR Korea, Fiji, Indonesia, Kiribati, Lao People's Democratic Republic, Malaysia, Marshall Islands, Micronesia (Federated States Of), Mongolia, Myanmar, Palau, Papua New Guinea, Philippines, Samoa, Solomon Islands, Thailand, Timor-Leste, Tonga, Vanuatu, Viet Nam
Europe and Central Asia	Albania, Armenia, Azerbaijan, Belarus, Bosnia And Herzegovina, Bulgaria, Croatia, Czech Republic, Estonia, Georgia, Hungary, Isle of Man, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Poland, Republic of Moldova, Romania, Russian Federation, Serbia and Montenegro, Slovakia, Tajikistan, The Former Yugoslav Republic Of Macedonia, Turkey, Turkmenistan, Ukraine, Uzbekistan
High Income	Andorra, Aruba, Australia, Austria, Bahamas, Bahrain, Belgium, Bermuda, Brunei Darussalam, Canada, Cayman Islands, Channel Islands, Cyprus, Denmark, Faeroe Islands, Finland, France, French Polynesia, Germany, Greece, Greenland, Guam, Iceland, Ireland, Israel, Italy, Japan, Kuwait, Liechtenstein, Luxembourg, Monaco, Netherlands, Netherlands Antilles, New Caledonia, New Zealand, Northern Mariana Islands, Norway, Portugal, Qatar, Republic of Korea, San Marino, Singapore, Slovenia, Spain, Sweden, Switzerland, United Arab Emirates, United Kingdom, United States of America, United States Virgin Islands
Latin America and Caribbean	Antigua and Barbuda, Argentina, Barbados, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, El Salvador, Grenada, Guatemala, Guyana, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, Puerto Rico, Saint Kitts And Nevis, Saint Lucia, Saint Vincent And The Grenadines, Suriname, Trinidad And Tobago, Uruguay, Venezuela
Middle East and North Africa	Algeria, Djibouti, Egypt, Iran (Islamic Republic Of), Iraq, Jordan, Lebanon, Libyan Arab Jamahiriya, Malta, Morocco, Occupied Palestinian Territory, Oman, Saudi Arabia, Syrian Arab Republic, Tunisia, Yemen
South Asia	Afghanistan, Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, Sri Lanka
Sub-Saharan Africa	Angola, Benin, Botswana, Burkina Faso, Burundi, Cameroon, Cape Verde, Central African Republic, Chad, Comoros, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Eritrea, Ethiopia, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mauritius, Mozambique, Namibia, Niger, Nigeria, Rwanda, Sao Tome and Principe, Senegal, Seychelles, Sierra Leone, Somalia, South Africa, Sudan, Swaziland, Togo, Uganda, United Republic of Tanzania, Zambia, Zimbabwe
Other	Anguilla, British Virgin Islands, Cook Islands, Falkland Islands, French Guiana, Gibraltar, Guadeloupe, Holy See, Martinique, Montserrat, Nauru, Niue, Pitcairn, Réunion, Saint Helena, Saint Pierre et Miquelon, Tokelau, Turks and Caicos Islands, Tuvalu, Wallis and Futuna Islands, Western Sahara