DALYs by nearly 50%. Declines in age-specific and sex-specific rates overall have meant that this group increased by 25%. Injury DALYs have increased more modestly, driven to a large extent by growth in population numbers and modest declines in rates.

These demographic and epidemiological changes have changed the age distribution of burden. In 1990, 41% of DALYs were due to deaths and disability in children younger than 5 years of age but by 2010, that had decreased to 25% (figure 4). Over the same interval, the burden of disease in the reproductive age-groups (15–49 years) increased from 27·0% to 35·0% of total DALYs. The shift to burden at older ages is also evident in the age groups 50–69 years and 70 years or older. The slight predominance of burden of 54·4% in male individuals in 1990 increased to 55·0% in 2010 (figure 4). Male burden is higher than female burden in all age groups except in the age groups 75–79 years in 1990 and 80 years or older in 1990 and 2010.

In 1990, 23·3% of DALYs were from YLDs. From 1990 to 2010, YLLs decreased from 1·919 billion to 1·713 billion, and YLDs increased 583 million to 777 million, so that by 2010, YLDs accounted for 31·2% of global DALYs, reflecting the relative increase of non-fatal versus fatal loss of healthy life years. As a consequence of these substantial structural changes in the burden of disease from younger to older ages and from YLLs to YLDs, the broad composition of the burden of disease has shifted from communicable, maternal, neonatal and nutritional disorders to NCDs and injuries. In 1990, 47% of DALYs were caused by communicable, maternal, neonatal and nutritional disorders, 43% from NCDs, and 10% from injuries. By 2010, this had shifted to 35% caused by communicable, maternal, neonatal, and nutritional disorders, 54% by NCDs, and 11% by injuries. The main changes from 1990 to 2010 are the reductions in infectious diseases, mostly among children, an increase in the HIV/AIDS and tuberculosis category, and increases in a diverse set of NCD and injury categories. Maternal disorders declined from 0·9% of DALYs in 1990 to 0·6% in 2010. From 1990 to 2010, mental and behavioural disorders increased from 5·4% to 7·4% and musculoskeletal disorders increased from 4·7% to 6·8%. Neurological disorders including dementia increased from 1·9% to 3·0% over the two decades. Increases in cardiovascular diseases were modest from 9·6% to 11·8%. Unintentional injuries including transport injuries increased from 7·6% to 8·1% in 2010.

Across the 1000 draws of the entire study results, each cause has been ordered in terms of total DALYs (figure 5). Causes in the figure are ordered by their mean rank across the 1000 draws. The order based on the mean rank across draws is not the same as the order based on the mean value of DALYs shown in table 1. For example, in 2010, malaria caused slightly more DALYs than HIV/AIDS in table 1; HIV/AIDS, however, in this figure ranks fifth and malaria seventh because across the 1000 draws HIV/AIDS is more likely to rank higher in the list than malaria because of the much greater uncertainty around

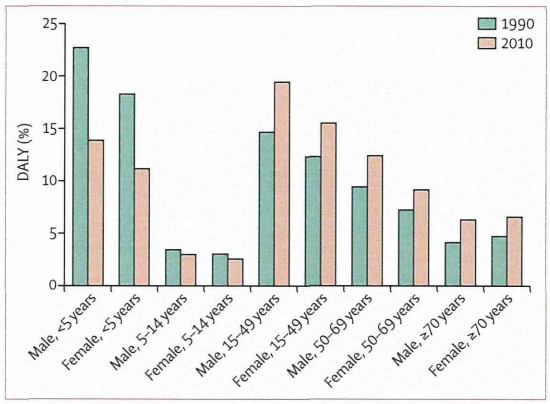

Figure 4: **Proportion of disability-adjusted life years (DALYs) by age and sex, 1990 and 2010**

the number of DALYs due to malaria. Causes in figure 5 are connected with lines to show changes in ranks over the two decades. Causes that moved into or dropped out of the top 25 ranks between 1990 and 2010 are listed at the bottom. Mean of the ranks of a disease across the 1000 draws of DALYs, the 95% UI in ranks, and the rank of the global mean value are shown for 1990 and 2010. The final column on the right-hand side provides the percentage change in the number of global DALYs for each cause from 1990 to 2010. As a general observation, most of the NCDs are rising in the rank list and most but not all communicable, maternal, neonatal, and nutritional disorders are declining. Notable exceptions are the stable and increasing ranks for malaria and HIV/AIDS, respectively. Among NCDs at a global level, only COPD and congenital anomalies have declined. Given that lung cancer is increasing from 24th to 22nd, the decline in COPD is worth noting. The decline is driven by the reduction of other determinants of COPD such as household air pollution in India and China, despite increasing cumulative exposure to tobacco.

In 1990, the leading cause of burden was lower respiratory infections, for which 81·4% of the total burden occurred among children younger than 5 years of age. The second leading cause was diarrhoeal diseases with 82·0% also occurring in children younger than 5 years of age. In 2010, these two causes remained among the top four causes of burden, but the absolute number of DALYs from these disorders has declined over the two decades by more than 40% in both cases. For the two cardiovascular causes now in the first and third slots, ischaemic heart disease and stroke, most of this burden is from YLLs not from YLDs, 93·2% and 95·7%, respectively. Both causes are increasing in absolute terms because of demographic changes; ischaemic heart disease increased by 29% and stroke by 19% over the two decades. HIV/AIDS went from the 33rd largest cause of burden in 1990 to the fifth largest cause in 2010. This rank is despite major declines in HIV/AIDS mortality since 2005. Malaria remains at

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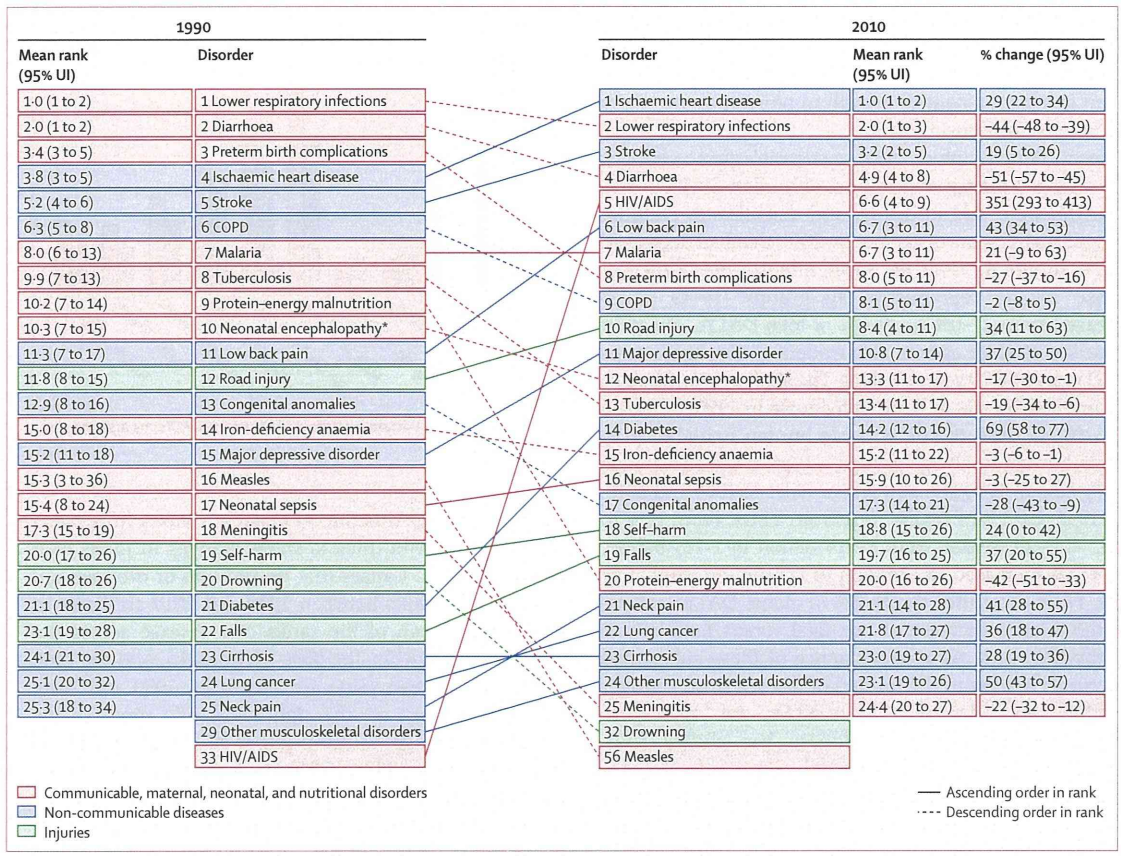

Figure 5: **Global disability-adjusted life year ranks with 95% UI for the top 25 causes in 1990 and 2010, and the percentage change with 95% UIs between 1990 and 2010**

UI=uncertainty interval. COPD=chronic obstructive pulmonary disease. *Includes birth asphyxia/trauma. An interactive version of this figure is available online at http://healthmetricsandevaluation.org/gbd/visualizations/regional.

seventh rank from 1990 to 2010, although uncertainty around malaria burden is large, spanning from the third to the eleventh rank. Of the malaria burden, 22·6% occurs in adults over age 15 years, a previously unrecognised cause of adult disease burden.[94] Measles dropped from the 16th to the 56th cause.

Some causes not included in the top 25 list have changed substantially over the period 1990 to 2010. The 15 causes with the largest increases include two causes of blindness or low vision: glaucoma and macular degeneration. Age-sex specific prevalence rates for these disorders have not increased; the rise in burden is completely due to the increase in the world population in the oldest age groups. Two major neurological disorders concentrated in older age-groups are also in the list of top increases—dementia and Parkinson's disease. Atrial fibrillation, peripheral vascular disease, and benign prostatic hyperplasia also increased substantially over the two decades. Not surprisingly, in view of the time course of the epidemic, HIV/AIDS increased by 351%. Kidney cancer is the one cancer to be included in this list of top increases. Conversely, the largest declines have occurred for several of the infectious diseases including measles, tetanus, rabies, whooping cough, diarrhoeal diseases, lower respiratory infections, syphilis, leishmaniasis, and ascariasis. Large upward trends in exposure to forces of nature and downward trends in collective violence reflect the stochastic nature year by year in these causes.

East, southeast, and south Asia made up 52·7% of the global burden in 1990, declining to 48·3% in 2010 (table 3). The absolute number of DALYs has also declined in western and central Europe, central Asia, and Andean Latin America. Tropical Latin America, North Africa and Middle East, and eastern sub-Saharan Africa, have barely changed over the interval although in all three regions a substantial change in the age-structure and cause composition has occurred. Other regions have seen increases in the number of DALYs. The largest increases have been in western, southern, and central sub-Saharan Africa. The increase in the Caribbean is largely related to the Haiti earthquake in 2010 because of the increase in the death rate and the fact that Haiti accounts for 26·3% of the Caribbean population. Most high-income regions have also seen modest increases in

the number of DALYs. DALYs per 1000 confirm that these increases are largely driven by population growth; only in three regions, namely the Caribbean, southern sub-Saharan Africa, and eastern Europe, did the rate of DALYs per 1000 increase substantially over the 20-year period as a proportion of population. Declines in DALYs per 1000 have generally been larger in developing country regions than in high-income country regions. These declines are partly due to the effect of population ageing lowering DALYs per 1000 from communicable, maternal, neonatal, and nutritional disorders, which are highest in the young age groups.

The share of burden from non-fatal health outcomes has generally increased from 1990 to 2010 in nearly all regions (figure 6); declines in southern sub-Saharan Africa can be related to the large HIV-related increase in

	Total DALYs (thousands)			DALYs (per thousand)		
	1990	2010	%Δ	1990	2010	%Δ
High-income Asia Pacific	38 934 (35 997–42 301)	42 486 (38 842–46 586)	9·1	231 (213–250)	239 (218–262)	3·5
Western Europe	115 151 (106 794–124 174)	113 364 (103 991–123 930)	−1·6	302 (280–326)	272 (250–298)	−9·8
Australasia	5382 (4966–5853)	6101 (5538–6733)	13·3	264 (243–287)	235 (214–260)	−10·7
High-income North America	79 582 (74 150–85 639)	91 073 (84 342–98 239)	14·4	287 (267–309)	268 (248–289)	−6·6
Central Europe	43 442 (40 918–46 341)	38 978 (36 355–41 960)	−10·3	355 (335–379)	327 (305–353)	−7·9
Southern Latin America	14 626 (13 755–15 688)	15 562 (14 458–16 917)	6·4	299 (281–321)	259 (240–281)	−13·5
Eastern Europe	88 654 (84 173–93 891)	93 104 (88 367–98 267)	5·0	400 (380–424)	449 (427–474)	12·3
East Asia	379 565 (355 627–405 991)	332 437 (306 978–358 541)	−12·4	319 (299–342)	238 (220–257)	−25·5
Tropical Latin America	53 824 (50 633–57 102)	56 781 (52 636–61 338)	5·5	349 (329–371)	281 (261–304)	−19·5
Central Latin America	53 375 (50 672–56 555)	57 706 (53 753–61 997)	8·1	321 (305–340)	250 (233–268)	−22·2
Southeast Asia	192 296 (180 655–204 699)	188 512 (175 435–202 574)	−2·0	418 (392–444)	309 (287–332)	−26·0
Central Asia	30 298 (28 853–31 889)	28 539 (26 801–30 395)	−5·8	441 (420–464)	356 (334–379)	−19·3
Andean Latin America	16 513 (15 558–17 564)	14 164 (13 074–15 304)	−14·2	427 (402–454)	265 (244–286)	−38·0
North Africa and Middle East	123 183 (116 867–130 540)	124 617 (115 374–134 555)	1·2	408 (387–432)	279 (259–302)	−31·5
Caribbean	15 582 (14 757–16 483)	26 698 (21 182–39 812)	71·3	437 (414–462)	614 (487–915)	40·6
South Asia	747 529 (705 906–798 664)	680 859 (633 905–727 982)	−8·9	665 (628–710)	422 (393–452)	−36·5
Oceania	4015 (3527–4618)	4779 (3907–5825)	19·0	621 (546–714)	481 (393–586)	−22·6
Southern sub-Saharan Africa	23 794 (22 429–25 299)	44 027 (41 666–46 474)	85·0	452 (426–481)	625 (591–659)	38·1
Eastern sub-Saharan Africa	207 130 (196 459–219 636)	204 526 (193 904–216 317)	−1·3	994 (943–1054)	575 (546–609)	−42·1
Central sub-Saharan Africa	60 702 (56 022–66 082)	77 391 (71 187–83 385)	27·5	1132 (1044–1232)	802 (738–864)	−29·1
Western sub-Saharan Africa	209 023 (196 925–221 795)	248 683 (232 208–266 906)	19·0	1040 (980–1103)	740 (691–794)	−28·8

Data are DALYs (95% uncertainty intervals) or % change. DALY=disability-adjusted life years. %Δ=percentage change.

Table 3: **Disability-adjusted life years for 291 causes by region for 1990 and 2010, and the percentage change from 1990 to 2010**

Cruces, Barakaldo, Spain (F Perez-Ruiz MD); **Shanghai Mental Health Center, School of Medicine** (Prof M R Phillips MD), **School of Public Health, Shanghai Jiao Tong University, Shanghai, China** (Prof Z-J Zheng); **Brigham Young University, Provo, UT, USA** (Prof C A Pope III PhD); **Centre for Addiction and Mental Health, Toronto, ON, Canada** (S Popova MD, Prof J T Rehm PhD); **Hospital Universitario de Canarias, Tenerif, Spain** (E Porrini MD); **Faculty of Medicine, School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada** (F Pourmalek MD); **Vector Control Research Centre, Pondicherry, India** (K D Ramaiah PhD); **Center for Disease Analysis, Louisville, CO, USA** (H Razavi PhD); **University of California, Berkeley, Berkeley, CA, USA** (M Regan MPH); **NORC, University of Chicago, Chicago, IL, USA** (D B Rein PhD); **Complejo Hospitalario Caja De Seguro Social, Panama City, Panama** (F Rodriguez de Leòn MD); **Centre for Alcohol Policy Research, Turning Point Alcohol and Drug Centre, Fitzroy, SA, Australia** (Prof R Room PhD); **Vanderbilt University, Nashville, TN, USA** (Prof U Sampson MD); **University of Alabama at Birmingham, Birmingham, AL, USA** (Prof D C Schwebel PhD, J A Singh MBBS); **Ministry of Interior, Madrid, Spain** (M Segui-Gomez MD); **Health Canada, Ottawa, ON, Canada**

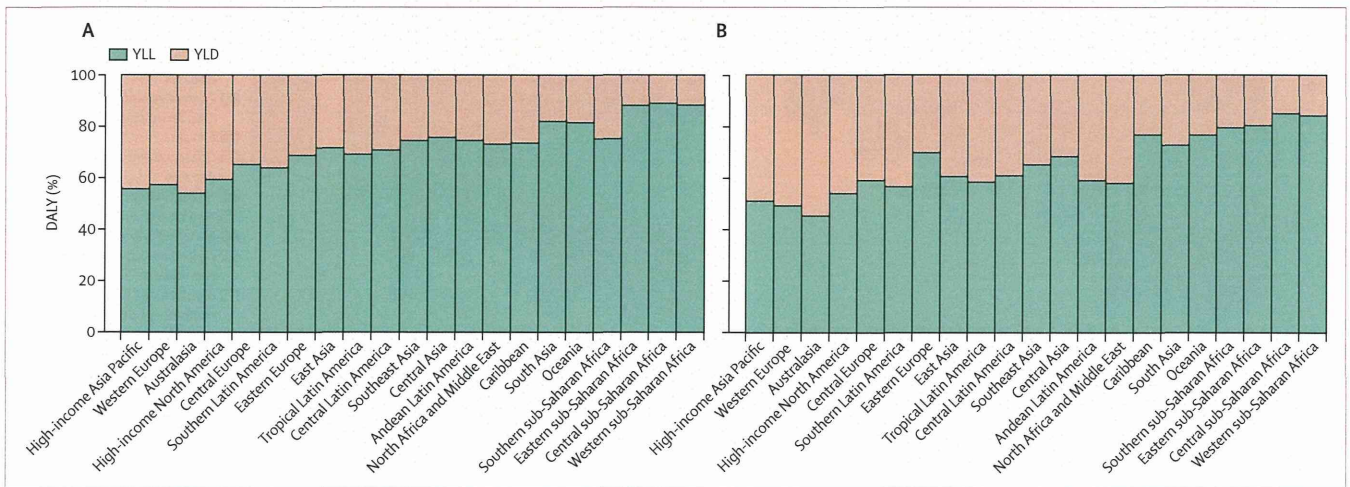

Figure 6: **Years of life lost due to premature mortality and years lived with disability composition of total disability-adjusted life years by region, 1990 and 2010**
Composition in 1990 (A) and 2010 (B). DALY=disability-adjusted life years. YLD=years of life lost due to premature mortality. YLL=years lived with disability.

(H Shin PhD); **Queens Medical Center, Honolulu, HI, USA** (D Singh MD); **Department of Neuroscience (Prof L J Stovner PhD), Norwegian University of Science and Technology, Trondheim, Norway** (Prof T Steiner PhD); **Aga Khan University, Karachi, Pakistan** (S Syed MBBS, A K M Zaidi MBBS); **Drexel University School of Public Health, Philadelphia, PA, USA** (J A Taylor PhD); **Alberta Kidney Disease Network** (Prof M Tonelli MD), **University of Alberta, Edmonton, AB, Canada** (N Wiebe BMath); **Cincinnati Children's Hospital, Cincinnati, OH, USA** (Prof J A Towbin MD); **Department of Neurology, Copenhagen University Hospital, Herlev, Denmark** (T Truelsen MD); **University of Crete Medical School, Crete, Greece** (Prof M K Tsilimbaris MD); **Instituto Nacional de Epidemiología, ANLIS, Malbran, Argentina** (C Ubeda MD); **KNCV Tuberculosis Foundation, The Hague, Netherlands** (M J van der Werf PhD); **Maastricht University Medical**

mortality and in the Caribbean due to mortality from the 2010 Haiti earthquake. Figure 6, in which the regions are ordered by the mean age of death, shows that in general the share of burden from disability increased with the demographic and epidemiological transition. In 2010, the fraction of DALYs due to YLDs varied widely, from 55% in Australasia to 15% in central sub-Saharan Africa. Australasia had a higher ratio than high-income Asia Pacific; both had low mortality levels but higher YLD rates prevailed in Australasia. In eastern Europe, the fraction due to YLDs has not increased noticeably from 1990 to 2010 because of the rise in adult mortality in the region over this period, especially for men.

The global shift in the burden of disease from communicable, maternal, neonatal, and nutritional disorders to NCDs and injuries masks enormous epidemiological heterogeneity in the leading causes of burden in different regions. In the regions with an advanced demographic and epidemiological transition (high-income Asia Pacific, western Europe, Australasia, high-income North America, and central Europe), communicable, maternal, neonatal, and nutritional disorders account for less than 7% of DALYs (figure 7). Cancer and cardiovascular diseases account for a further 36% of DALYs. Mental and behavioural disorders account for 11% and musculoskeletal disorders account for 13%. Injuries make up about 11%. At the other end of the epidemiological transition, in eastern, western, and central sub-Saharan Africa communicable, maternal, neonatal, and nutritional disorders account for 67–71% of DALYs. A middle group of regions have a transitional volume of burden due to communicable, maternal, neonatal, and nutritional disorders. Comparison of 1990 and 2010 shows the most profound shifts in these transitional regions, moving from a profile with substantial burden from infectious diseases predominantly in children and neonatal causes, to a much greater dominance of injuries, musculoskeletal disorders, mental and behavioural disorders, as well as cancers and cardiovascular diseases. The great rise in HIV/AIDS and tuberculosis is also evident in southern and eastern sub-Saharan Africa. In 2010, deaths from the Haiti earthquake accounted for the substantial change in cause composition in the Caribbean from 1990 to 2010.

Although a strong tendency exists for the cancer DALY rate to increase with the demographic and epidemiological transition, there is notable variation. Oceania and the Caribbean seem to have higher than expected rates and central Latin America, lower rates (figure 8). Lung, colon and rectum, breast, and pancreatic cancers are associated with DALY rates that are generally higher in the high-income regions, while cervical cancer is lower. Liver, stomach, leukaemia, and skin cancers show strong geographic variation. Among high-income

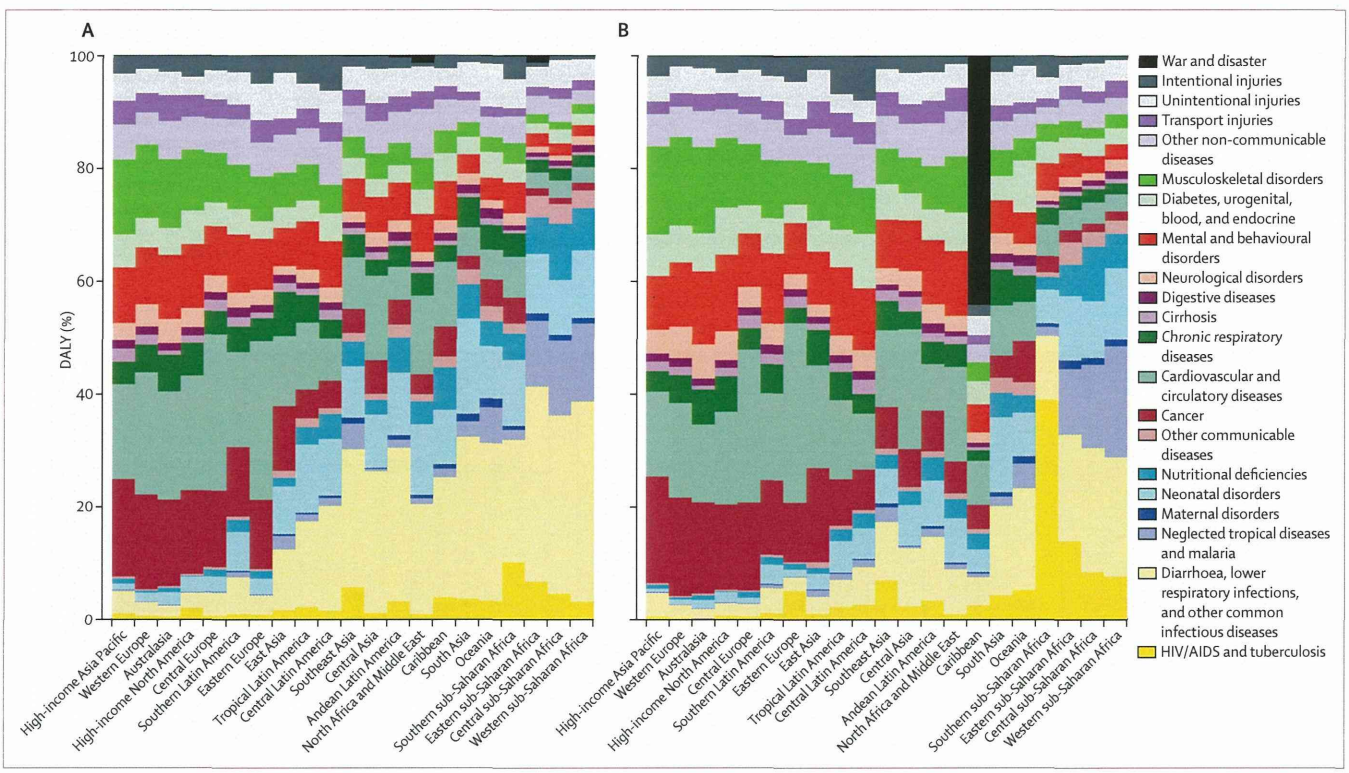

Figure 7: **Percentage of disability-adjusted life years by 21 main cause groupings and region, 1990 and 2010**
Proportion in 1990 (A) and 2010 (B). An interactive version of this figure is available online at http://healthmetricsandevaluation.org/gbd/visualizations/regional.

regions, Asia Pacific has a substantially different pattern with more stomach and liver cancer, and less breast cancer. Oceania has relatively high rates of liver, leukaemia, and cervical cancers.

The GBD study provides results for a set of diseases that are much smaller in magnitude at the global level but are important causes of burden in communities at risk. The neglected tropical diseases excluding malaria make up 1·0% of global DALYs (figure 9). Rates of neglected tropical diseases vary across regions by 961 fold. The highest rates were in central sub-Saharan Africa, largely because of the combination of schistosomiasis, onchocerciasis, African trypanosomiasis, and hookworm. Globally, leishmaniasis, schistosomiasis, hookworm, lymphatic filariasis, and food-borne trematodiases are the dominant causes in this grouping. In view of the focal nature of the transmission of many of these diseases, the regional pattern varies substantially. As most of these diseases cause limited mortality, the neglected tropical diseases highlight why quantification of the disability from diseases is important.

The order of causes in figure 10 follows the global ranking of burden shown in figure 5. All causes that appear in the top 25 in any region are included in figure 10. The cells in the figure have been colour coded to help identify different patterns in each region. Eight causes appear as the leading cause in at least one region. Ischaemic heart disease is ranked first in seven of 21 regions. Lower respiratory infections are ranked first in Andean Latin America, south Asia, and Oceania. Malaria is ranked first in two regions: western and central sub-Saharan Africa. HIV/AIDS is ranked first in eastern and southern sub-Saharan Africa. Interpersonal violence is ranked first in central Latin America and ranked second in tropical Latin America. Due to the Haiti earthquake in 2010, forces of nature ranks first for the Caribbean. Low back pain is a top ten cause in 15 regions. Falls are a top ten cause in three regions. A total of 33 causes appear in the top ten in at least one region. This extended list includes disorders such as chronic kidney diseases, drug use disorders, cirrhosis, dementia, meningitis, liver cancer, stomach cancer, and colon and rectum cancers.

Discussion

The GBD 2010 estimates that the number of DALYs for the world in 1990 was 2·503 billion, having decreased by 0·5% in 2010. Relatively small changes in the number of DALYs have occurred because the increase in global population has been largely balanced by a decrease in age-sex-specific DALY rates. The differential effect of population growth, population ageing, and changes in age-sex-specific rates have led to striking changes in the profile of burden in every dimension. Over two decades, the burden has shifted substantially from communicable, maternal, neonatal, and nutritional disorders towards NCDs. A much larger fraction of the burden is now caused by disability rather than premature mortality. Burden has shifted away from death of children younger than 5 years of age to death and disability in the reproductive age groups; nonetheless, a quarter of the burden is still caused by disease and injury in children younger than 5 years of age. Because of the richer dataset, improved methods, and more extensive cause list, our results for 1990 to 2010 supersede and replace previous GBD studies; comparisons with previous studies to assess change over time would not be valid.

Centre, Maastricht, Netherlands (Prof J van Os PhD); National University of Singapore, Singapore (N Venketasubramanian FRCP); Beijing Neurosurgical Institute, Capital Medical University, Beijing, China (Prof W Wang MD); Brown University, Providence, RI, USA (Prof M A Weinstock MD); Royal Children's Hospital and

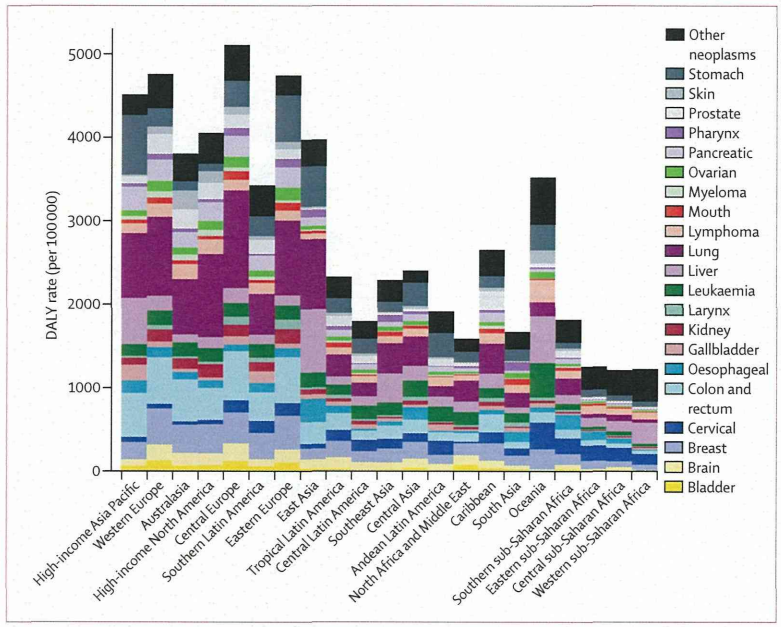

Figure 8: **Cancer disability-adjusted life years per 100 000 by cause and region in 2010**

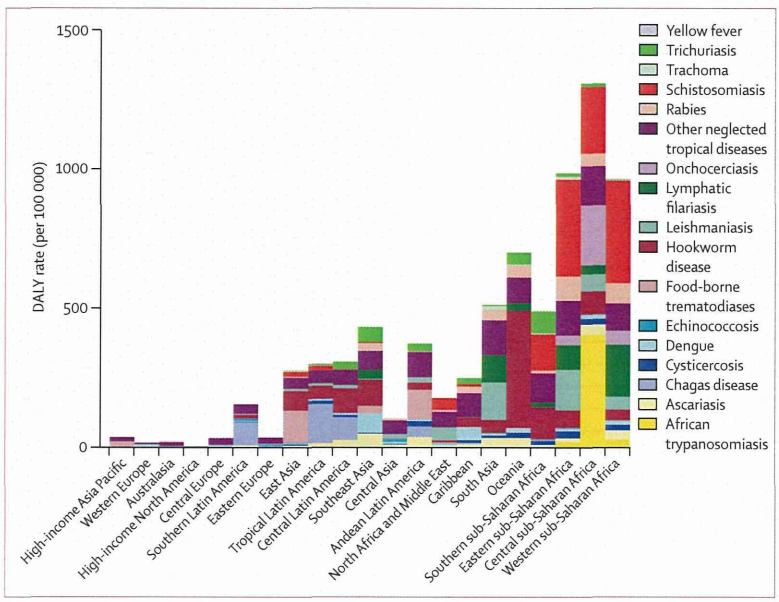

Figure 9: **Neglected tropical disease disability-adjusted life year rates by cause and region in 2010**
This figure excludes malaria.

Ranking legend: 1–10, 11–20, 21–30, 31–50, 51–90, 91–176

Cause	Global	High-income Asia Pacific	Western Europe	Australasia	High-income North America	Central Europe	Southern Latin America	Eastern Europe	East Asia	Tropical Latin America	Central Latin America	Southeast Asia	Central Asia	Andean Latin America	North Africa and Middle East	Caribbean	South Asia	Oceania	Southern sub-Saharan Africa	Eastern sub-Saharan Africa	Central sub-Saharan Africa	Western sub-Saharan Africa
Ischaemic heart disease	1	3	2	2	1	1	1	1	2	1	2	3	1	4	1	2	4	6	14	21	19	20
Lower respiratory infections	2	7	21	30	21	17	6	13	15	7	6	4	2	1	5	4	1	1	2	3	4	2
Cerebrovascular disease	3	1	3	5	7	2	3	2	1	4	11	1	3	11	4	3	12	11	7	16	14	16
Diarrhoeal diseases	4	46	52	53	48	77	44	49	49	26	14	8	18	8	11	8	3	3	3	4	2	3
HIV/AIDS	5	108	59	87	37	72	34	4	38	12	13	13	31	13	58	9	17	9	1	1	5	4
Low back pain	6	2	1	1	3	3	2	3	5	3	7	7	7	5	2	13	10	14	15	17	23	13
Malaria	7	163	162	157	155	163	166	163	169	145	154	22	162	142	66	58	44	5	20	2	1	1
Preterm birth complications	8	58	44	29	26	37	12	35	27	9	9	11	8	6	8	11	2	7	6	5	6	7
Chronic obstructive pulmonary disease	9	18	7	3	2	7	7	10	3	10	16	9	11	18	13	22	5	18	9	20	20	22
Road injury	10	16	12	9	10	8	5	7	4	5	4	5	5	2	6	10	11	15	13	11	12	9
Major depressive disorder	11	12	4	4	5	5	4	5	8	6	5	6	6	3	3	7	14	12	10	13	17	19
Neonatal encephalopathy*	12	84	66	50	54	66	42	40	24	20	20	12	4	9	18	15	6	19	12	9	10	10
Tuberculosis	13	42	107	123	124	55	65	17	37	46	44	2	15	21	33	17	8	4	4	7	7	12
Diabetes	14	10	10	14	8	9	9	15	10	8	3	10	12	15	9	6	16	2	8	29	28	26
Iron-deficiency anaemia	15	39	84	36	117	29	27	29	32	18	17	14	13	7	10	5	9	21	11	12	11	11
Sepsis and other infectious disorders of the newborn baby	16	119	120	113	99	114	49	82	132	27	29	34	53	17	22	14	7	25	29	8	13	5
Congenital anomalies	17	41	35	27	30	32	13	25	16	11	10	16	10	10	7	16	15	17	17	18	8	18
Self-harm	18	5	15	18	14	11	14	6	13	29	25	29	14	32	38	33	13	26	27	32	37	69
Falls	19	11	6	7	15	6	17	14	11	23	28	21	20	28	19	21	20	32	43	33	32	21
Protein–energy malnutrition	20	114	119	129	116	122	80	123	99	59	34	49	68	35	37	32	19	20	36	6	3	6
Neck pain	21	9	8	10	9	14	10	18	9	13	18	25	17	16	15	23	32	35	21	31	33	31
Trachea, bronchus, and lung cancers	22	6	5	8	4	4	15	9	6	30	39	26	28	48	28	27	49	58	45	95	75	96
Cirrhosis of the liver	23	17	19	37	16	10	16	11	21	19	12	15	9	22	17	34	22	16	37	30	27	25
Other musculoskeletal disorders	24	4	9	6	6	13	8	16	14	16	15	23	19	19	21	24	31	27	26	35	36	36
Meningitis	25	91	102	92	91	84	59	78	73	52	45	37	34	39	30	29	21	10	24	10	9	8
Anxiety disorders	26	21	14	12	13	15	11	30	26	14	19	27	16	12	12	20	26	33	30	25	29	35
Interpersonal violence	27	70	65	60	25	42	22	12	47	2	1	24	24	14	32	12	34	31	5	23	21	30
Asthma	28	26	23	15	22	33	24	42	53	15	26	18	40	20	20	19	25	8	22	26	26	29
Chronic kidney diseases	29	20	24	22	18	30	21	39	28	24	8	17	27	23	24	30	33	13	25	42	44	39
Migraine	30	23	18	17	29	18	29	26	36	21	22	20	22	27	26	25	23	41	38	60	41	34
Drug use disorders	31	25	20	11	11	28	18	23	35	22	24	33	26	25	16	28	35	40	18	39	49	47
Drowning	32	48	88	64	64	49	48	28	19	35	32	31	23	30	41	50	24	37	35	28	22	38
Liver cancer	33	13	37	52	49	39	54	60	7	56	47	28	45	50	47	49	84	24	62	64	66	40
Fire, heat, and hot substances	34	71	94	84	73	74	55	34	79	74	71	56	43	54	42	37	18	34	33	22	24	17
Alcohol use disorders	35	28	22	21	19	21	19	8	23	17	23	42	21	24	65	31	42	44	39	68	65	84
Epilepsy	36	50	50	55	52	38	37	44	44	33	21	35	25	26	31	41	43	28	19	19	25	14
Other cardiovascular and circulatory diseases	37	31	17	26	27	16	20	53	31	32	40	32	39	36	14	36	46	46	34	41	38	44
Osteoarthritis	38	15	25	23	24	20	30	24	17	25	27	41	33	31	25	35	54	50	44	48	60	51
Stomach cancer	39	8	29	48	56	23	32	20	12	40	35	51	30	29	46	54	61	39	75	74	80	82
Maternal disorders	40	128	133	132	109	133	91	119	80	77	65	38	76	44	55	46	29	23	28	14	15	15
Other hearing loss	41	27	30	28	36	25	31	31	25	36	33	36	38	34	39	45	37	59	42	37	50	41
Hypertensive heart disease	42	37	32	68	33	19	28	36	29	28	37	30	32	43	23	26	39	70	23	50	47	64
Schizophrenia	43	29	39	20	23	27	33	38	20	34	30	39	36	33	29	43	48	51	40	53	57	50
Colon and rectum cancers	44	14	13	16	17	12	23	21	22	37	46	46	47	55	53	42	78	69	60	81	91	94
Exposure to forces of nature	45	124	123	122	123	105	77	69	109	132	107	110	106	101	96	1	125	122	119	118	119	112
Breast cancer	47	30	16	19	20	22	25	27	39	39	43	45	41	51	43	44	65	48	57	66	78	79
Exposure to mechanical forces	48	76	92	75	75	71	64	19	54	75	56	50	29	45	36	57	36	42	16	38	30	53
Alzheimer's disease and other dementias	49	19	11	13	12	24	26	33	41	44	50	70	58	62	64	39	88	81	66	98	101	91
Cardiomyopathy and myocarditis	50	52	42	49	32	26	35	22	58	31	59	57	37	47	27	53	52	53	31	44	40	49
Typhoid and paratyphoid fevers	52	150	158	151	149	161	79	161	74	98	88	19	165	83	57	104	28	109	32	36	46	37
Syphilis	55	148	148	135	146	137	122	144	121	96	96	75	104	49	79	38	60	55	41	15	16	23
Measles	56	157	156	152	154	156	157	160	162	157	149	54	128	98	151	155	27	74	47	24	48	28
Oesophageal cancer	57	36	51	54	55	69	51	64	18	57	108	84	48	116	98	82	64	83	49	63	81	126
Poisonings	58	107	105	74	42	73	102	32	40	135	94	88	49	91	60	101	41	22	64	40	34	59
Benign prostatic hyperplasia	62	22	27	24	28	48	56	68	42	65	67	71	75	74	61	69	93	99	88	109	108	105
Pancreatic cancer	64	24	26	31	31	31	38	37	48	60	62	77	64	75	88	62	117	114	80	132	130	137
Sickle cell disorders	71	90	57	105	43	124	123	140	159	58	51	164	146	125	69	47	97	153	134	67	18	24
Adverse effects of medical treatment	82	80	73	77	69	98	63	70	94	84	90	78	100	77	80	18	90	49	63	57	52	75
Prostate cancer	88	56	28	25	34	41	39	61	122	51	55	122	93	63	95	40	150	91	68	117	126	120

Figure 10: **Regional ranking of leading causes of disability-adjusted life years in 2010**
Causes in the figure are ordered according to global ranks for causes. The figure shows all causes that are in the 25 leading causes in at least one region. Ranks are also colour-shaded to indicate rank intervals. *Includes birth asphyxia/trauma. An interactive version of this figure is available online at http://healthmetricsandevaluation.org/gbd/visualizations/regional.

On top of a general pattern of the demographic and epidemiological transition associated with both mortality decline and fertility decline, substantial regional heterogeneity exists in the diseases and injuries that cause burden. HIV/AIDS is one vivid example that has come to be the dominant cause of burden in eastern and southern sub-Saharan Africa. Interpersonal violence is a leading cause in central Latin America (rank 1) and tropical Latin America (rank 2), and in southern sub-Saharan Africa (rank 5); the pattern of interpersonal violence across regions is unrelated to metrics of the epidemiological and demographic transition. Self-harm is a top ten cause of burden in high-income Asia Pacific (rank 5), eastern Europe (rank 6) and central Europe (rank 11). Cirrhosis is an important cause in central Asia (rank 9), central Europe (rank 10), eastern Europe (rank 11), and central Latin America (rank 12). Drug use disorders are especially important in Australasia (rank 11) and high-income North America (rank 11). Site-specific cancers show substantial regional heterogeneity. The leading cancer across regions ranges from lung to liver to stomach and colon and rectum.

Some diseases show a strong relation between prevalence and mortality with age. As the number of individuals aged 75 years and older in the world increased from 119 million in 1990 to 206 million in 2010, it has driven up the burden of these diseases substantially. The most notable diseases include the various causes of blindness and low vision but also several neurological disorders. The rise of dementia and Parkinson's disease is almost entirely attributable to population ageing because age-specific rates have remained constant. In view of the global shifts in fertility and declines in age-specific mortality, we can expect the numbers of individuals with age-related disorders to increase substantially in coming decades. This shift in numbers of people with certain disorders will have substantial implications for health-service planning.

At least partly viewed through the lens of the Millennium Development Goals (MDGs), the world has paid increased attention to the mortality of children younger than 5 years of age, maternal mortality, HIV/AIDS, tuberculosis, and malaria. Collectively the MDG-related causes of burden account for 742 million DALYs in 2010, or 29·8% of the total burden of disease—this burden includes YLLs from all causes in children younger than 5 years of age and DALYs from maternal disorders, HIV/AIDS, tuberculosis, and malaria. Progress has clearly been made. In 1990 these disorders accounted for 1096 million DALYs or 43·8% of the total burden. Although we are unlikely to achieve most of the health-related MDG targets by 2015, the burden of these disorders has declined by nearly 32·0% from 1990 to 2010 and will probably decline further by 2015 in view of current trends. More than two-thirds of global DALYs now arise from disorders not targeted in the MDGs. As 2015 nears and the world is discussing goals for the post-MDG period, addressing the leading, and often largely preventable, causes of the non-MDG health spectrum, especially NCDs and injuries, should be given greater priority than hitherto. When examined at a regional level (figure 11), the issue is even starker. In 2010, the fraction of the burden of disease that is related to disorders targeted in the MDGs ranges from 68·9% in western sub-Saharan Africa to 1·7% in high-income Asia Pacific. In five of 21 regions, the burden of MDG-related disorders exceeds a third of regional DALYs: the four sub-Saharan Africa regions, and south Asia. This regional heterogeneity shows how it will be important for post-2015 development goals to reflect the widely differing disorders across regions in setting targets.

The findings from this study have implications for health system investment decisions, including health manpower needs and the content of medical education. Many systems are already grappling with the challenges posed by rising numbers of cardiovascular events and cancers; these findings also highlight the importance of health-care professionals who will service the specialties of trauma, rehabilitation, mental health, musculoskeletal disorders, and diabetes. More generally, the shifting burden of disease driven by population ageing and differential rates of decline in age-specific rates that are greater for communicable, maternal, neonatal, and nutritional disorders than for NCDs also has implications for any health system's capital investments. These investments will often be used over decades so that they need to reflect future burden. Within professions, the shifting burden should also be reflected in the content of education for health professionals. The pace of demographic and epidemiological change is fast enough that a forward-looking assessment of the burden should be incorporated in the reform of health professional education on a region-by-region basis.[95]

The burden of musculoskeletal disorders is much larger than in previous GBD assessments. In the 2004 revision of the GBD study, this group of disorders was estimated to

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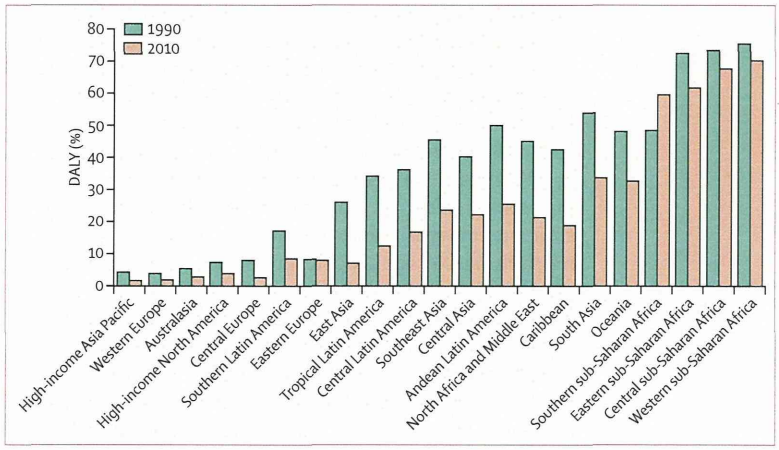

Figure 11: **Disability-adjusted life years (DALYs) related to Millennium Development Goals 4, 5, and 6 as a proportion of the total burden, by region, 1990 and 2010**

account for 2·0%, compared with 6·8% in this study. This much higher share relates to three factors. First, there has been a much more comprehensive and systematic assessment of the epidemiological data. These data show that low back pain, neck pain, osteoarthritis, and other musculoskeletal disorders are extremely common in nearly all populations. Second, the disability weights assigned to these disorders—which cause pain, discomfort, lack of mobility, anxiety, and sleeplessness—in the population-based surveys are higher than those based on the judgment of health-care professionals. Finally, in previous assessments that focused on incidence, the duration of symptoms was probably systematically underestimated. These disorders account for a substantial number of health-care visits and cost in populations with access to medical care.[96,97] The burden is likely to grow steadily because of rising rates with age, little change over time, and an ageing world population. In view of the epidemiological pattern and associated costs, health-care systems will need to develop a coherent policy for dealing with musculoskeletal disorders. Prioritisation of research on the most effective and affordable strategies is urgently needed to deal with these disorders.

A key finding of the GBD 1990 and 2000 studies was the large unrecognised burden of mental illness in developed and developing countries—8·5% of DALYs in the GBD 1990 study and 10·1% in the GBD 2000 study. These results were reported for DALYs with discounting and age-weighting. Age-weighting assigns maximum value to young and middle-aged adults in whom the prevalence of mental illness is high. Without age-weighting and discounting, the burden of mental illness in the GBD 1990 study was 5·7%. Despite the switch in the GBD 2010 study to a base case for DALY computation of no discounting and no age-weighting, mental and behavioural disorders account for 7·4% of global DALYs in 2010. This study has expanded the set of disorders carefully assessed to include many disorders previously crudely estimated in a residual category. Newly added disorders include all anxiety disorders compared with only three in the earlier studies, childhood disorders, and eating disorders. Some disorders such as major depressive disorder have a higher prevalence than previously estimated. Using consistent definitions in this study over time for the mental and behavioural disorders, the number of DALYs for this group increased by 38% from 1990 to 2010. The drivers of the increase are the combination of population growth, shift in age structure towards the age groups at highest risk, and relatively stable age-specific prevalence rates—although notable fluctuations exist in drug use disorders over time. We can expect that the absolute number and share of burden attributable to mental and behavioural disorders, already substantial, will probably steadily increase in the future. Despite increased global attention to mental health in the past decade,[17] practical strategies for managing these disorders in low-income and middle-income countries are urgently needed.

Road injury accounts for 75·5 million DALYs in 2010, up from 56·7 million in 1990. To put road injury in context, it accounts for 53% more burden than tuberculosis. Road injury shows a classic inverted U-shaped pattern with the largest DALY rates and highest rank as a cause of burden in regions that are upper low-income or middle-income. Nevertheless, even in the demographically and epidemiologically advanced regions, road injury is in the top 16 causes. The distribution of road injury by specific subcause is also important for policy: in seven developing regions more than 40% of road injury deaths are in pedestrians including all sub-Saharan African regions, south and east Asia, and Andean Latin America. Motorised two-wheel vehicles account for more than 20% of road injury deaths in southeast and east Asia and tropical Latin America. The local patterns of road injury and publications on road safety[98,99] argue that most road injury is preventable. Some high-income countries such as Australia have been able to reduce the death rate from road injuries by 43·7% since 1990, providing a population level demonstration that many deaths are preventable. Various global initiatives on road safety have been launched[100,101] but they remain relatively weakly funded and are yet to have a demonstrable effect on the rising burden from road injury globally. Continued attention from both the health sector and the transport sector will be needed to address this growing challenge.

Interpersonal violence in 2010 ranks 27th across causes at the global level; in view of the fact that 81% of the DALYs due to interpersonal violence are in male individuals, it is the 21st ranked cause in male individuals and 49th in female individuals. This global figure masks enormous inter-regional variation in the extent of interpersonal violence. Three regions—central and tropical Latin America and southern sub-Saharan Africa—have violence as a top five cause of burden. Ecological analyses of the root causes of violence[102–106] have helped elucidate risk factors for different forms of violence and have been useful for exploring the determinants of within-country variation.[107] Few studies, however, help to explain why violence is such a dominant factor in population health in specific countries and regions. More robust research on this topic, as well as its relation to social and political changes and drug markets, would be a valuable addition to the public health literature. Increased links between public health researchers and social scientists working in this complex field could make this research more productive. A key challenge for this area, nevertheless, will be proposing, testing, and assessing effective policy interventions that stem from increased understanding of the broader determinants.

Among the top cancer causes of DALYs, liver cancer and pancreatic cancer DALYs have increased the most. Stomach cancer is declining, and lung, colon and rectum, breast, and brain cancer increased by about 35% from 1990 to 2010. For smaller causes, kidney cancer, prostate cancer, liver cancer secondary to

hepatitis C, and non-melanoma skin cancer are the only causes of cancer that have increased by more than 50% from 1990 to 2010. Many researchers might have expected the burden of liver cancer secondary to hepatitis B to decrease because of expansion of hepatitis B vaccine coverage. Burden, however, has increased from 1990 to 2010 by over 45%. The increase can be understood in terms of population growth in areas with substantial prevalence of hepatitis B and the long lag between childhood immunisation for hepatitis B and reductions in adult liver cancer deaths some 30–50 years later. Increases are also in part related to other causes of liver cancer, including hepatitis C and alcohol.

The downward trend in COPD rates in east Asia and upward trend in lung cancer in this region need explanation. In addition to tobacco consumption, other factors probably contribute to levels and trends in COPD possibly including exposure to particulates from biomass and coal fuels.[108–110] Relations might exist between exposure to respiratory infections as a child and adult COPD that can also alter secular trends.[111] Historical analysis, for example, for the UK and Australia also suggests that cause of death declined from 1900 to 1940 then increased until the 1980s from rising tobacco consumption.[112,113] The same set of determinants that account for the downward trend in high-income countries could be occurring in Asia.

In a study covering 291 diseases and injuries, 1160 sequelae, 20 age groups, both sexes, and 21 regions, many limitations reflect the availability, representativeness, and broad quality of the data. It is beyond the scope of this summary article to describe all the specific limitations associated with data availability, efforts to enhance quality and comparability of data, and model specification for estimation. More detail is provided in accompanying articles on all-cause mortality, causes of death, disability weights, and YLDs.[3,11,90,92] Future cause-specific publications will also provide a forum for exploring disease or injury-specific limitations. More generally, we have tried for the first time to quantify uncertainty as a way to inform the user of the strength of the evidence on the burden of a given disease or injury. Relative uncertainty varies widely across causes. For example, only four studies are available on onchocercal skin disease but for epilepsy there are 353 studies. For some causes of death like ischaemic heart disease, the models have very small prediction error whereas for others like dengue or rabies it is very large. The width of the UIs is a useful guide to where the limitations of the analysis are greatest. Of course, we might be missing sources of uncertainty for some disease and injury sequelae. As with any systematic analysis, selection bias in data collection can lead to systematic biases in the results that are not reflected in the statistical UIs. In computing UIs, we assumed that uncertainty distributions for YLLs and YLDs were independent; this assumption, however, could be incorrect. Countries with poor data on mortality and causes of death might be more likely to have poor data on the prevalence of sequelae. Empirical information to establish the correlation, however, is extremely limited. If data quality between causes of death and prevalence are correlated, our UIs could be underestimated. For the YLD component, disability weights play a crucial role; to the extent that lay descriptions used in the measurement of disability weights do not reflect the average experience of an individual with a sequela then the YLDs could be overestimated or underestimated. The shift in burden towards YLDs from 1990 to 2010 is not a function of the disability weights because the same weights are used for computing 1990 and 2010 burden. However, since the disability weights for this study are on average somewhat lower than the GBD 1990 disability weights, this shift would have seemed greater with the older, larger weights. For the first time in the GBD study, we have taken into account comorbidity. These corrections have reduced the number of YLDs that would be estimated without taking into account comorbidity. Because of limitations of data, we have only been able to take into account independent comorbidity within an age-sex group.

The heterogeneity across the 21 regions in the burden of disease highlights how important it will be to make estimates at the national level. Two strategies exist for national estimation: using the information collected in the GBD 2010 to report national burden results, and national burden of disease studies that start with collection and analysis of all local sources. Both strategies are useful. The wealth of data on causes of death and within-region variation in prevalence of disease and injury sequelae can be used to generate informed national estimates building on the GBD 2010 results. These estimates can be immediately useful for enriching a range of national policy debates but can also serve as an informative starting point for an in-depth national burden of disease study. Many countries will also be keenly interested in estimating disease burden for subpopulations on the basis of geography, ethnic group, and socioeconomic status. Capacity and methods to undertake this type of analysis need to be created or strengthened through appropriate training. The new generation methods and standardisation of approaches will make it easier than in the past to undertake comparable, comprehensive, and consistent national assessments.

The results of the GBD study show a truism known to everyone trained in clinical practice that also applies to population health: that individuals and communities suffer from a wide range of disorders. Clinical subspecialties have emerged in modern medicine to deal with some of this complexity at the level of individual patients. One of the fundamental challenges for the global health system and for national health systems is responding to the diversity of urgent health needs for communities. The GBD study provides quantification of this diversity and reminds us that the organised social

response to health problems must deal with a wide array of medical and public health priorities for action. Regular updating of the GBD study is an important way that the world can track many different health problems without the risk of a limited set of temporary priorities capturing all of our attention. Regular updates would provide a mechanism both to assess the latest evidence but also to promote accountability of health systems for achieving reductions in the burden of disease. Furthermore, despite this complexity and diversity, important health challenges are readily identifiable for which technologies and knowledge exist to substantially reduce or eliminate their impact on burden of disease rankings. The sustained commitment of governments, donors, and the public health community to do so is crucial, on the basis of the essential health intelligence that regular burden of disease updates can provide.

Contributors

CJLM and ADL prepared the first draft. CJLM, TV, RL, MN, AF, CM, ME, KS, JS, and ADL finalised the draft based on comments from other authors and reviewer feedback. CJLM and ADL conceived the study and provided overall guidance. CJLM, TV, RL, MN, AF, CM, ME, KS, JS, and ADL oversaw the implementation of the work. All other authors developed cause-specific models, reviewed results, provided guidance on the selection of key covariates, and reviewed the manuscript.

Conflicts of interest

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