blood pressure, tobacco smoking including second-hand smoke, household air pollution, diets low in fruits, and alcohol use) are mainly causes of adult chronic disease, especially cardiovascular diseases and cancers (figures 1, 2). The burden of disease attributable to other chronic disease risk factors also increased substantially between 1990 and 2010; for example, the global disease burden attributable to high body-mass index increased from 52 million to 94 million DALYs and that of high fasting plasma glucose increased from 56 million to 89 million DALYs over this period.

The rise in global disease burden attributable to chronic disease risk factors has been accompanied by a decrease in the relative importance of risk factors that largely or exclusively cause communicable diseases in children. The global disease burden attributable to childhood underweight halved between 1990 (7·9% [6·8–9·4] of global DALYs) and 2010 (3·1% [2·6–3·7]; table 3). Although the fraction of disease burden attributable to iron deficiency fell relatively little, suboptimal breastfeeding, unimproved water, unimproved sanitation, vitamin A deficiency, and zinc deficiency all decreased substantially between 1990, and 2010.

The transition from childhood communicable to non-communicable disease burden is also exemplified by the fall in DALYs caused by household air pollution from solid fuels (despite the rise in its effects on cardiovascular diseases). Although the burden attributable to ambient particulate matter pollution has largely remained unchanged (3·2% [2·8–3·7] of global DALYs in 1990 *vs* 3·0% [2·6–3·4] in 2010), the contribution of lower respiratory tract infections had fallen sharply by 2010, with chronic diseases of adults being the dominant health outcome caused by this exposure.

Figure 4 shows the 95% uncertainty interval in global DALYs attributable to each risk factor and the overall rank for each risk factor. The uncertainty intervals for many risk factors overlap, especially those not in the top five. Unimproved water, unimproved sanitation, vitamin A deficiency, and zinc deficiency have large uncertainty, which reflects the substantial uncertainty in the estimates of etiological effect sizes for these risks.

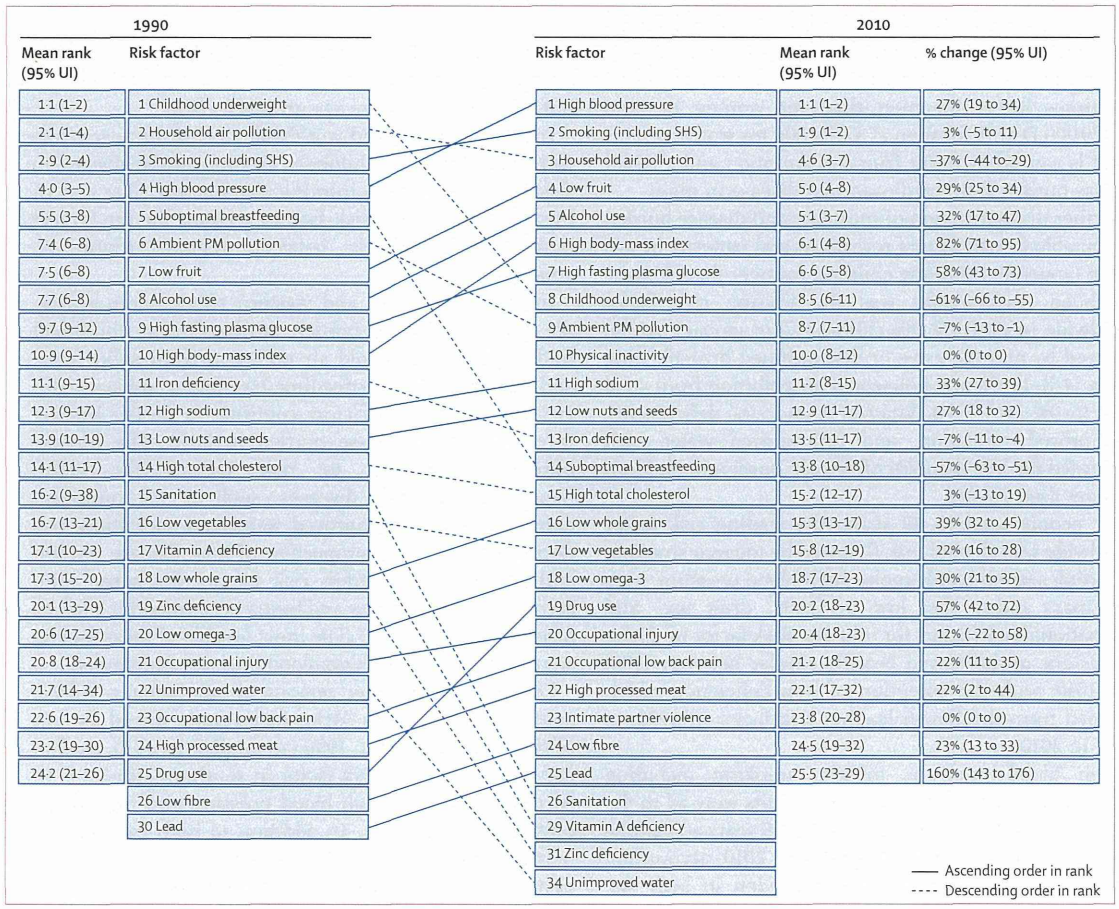


Figure 3: **Global risk factor ranks with 95% UI for all ages and sexes combined in 1990, and 2010, and percentage change**
PM=particulate matter. UI=uncertainty interval. SHS=second-hand smoke. An interactive version of this figure is available online at http://healthmetricsandevaluation.org/gbd/visualizations/regional.

Some risks were quantified for women only—for example, intimate partner violence, which accounted for 1·5% (1·0—2·1) of DALYs among women in 2010. Important differences between men and women also exist for disease burden attributable to other risk factors, most notably, for tobacco smoking including second-hand smoke and alcohol use (figures 1, 2). These risks cause substantially lower burden in women than in men, because women drink less and in less harmful ways than do men, and fewer smoke or have smoked for a shorter time than have men in most regions.[157] In 2010, tobacco smoking including second-hand smoke accounted for 8·4% of worldwide disease burden among men (the leading risk factor) compared with 3·7% among women (fourth highest risk factor). For alcohol use, these sex differences were similarly substantial: 5·4% (third) versus 2·0% (twelfth). The effect of occupational risk factors on population health also differed between sexes—for example, the fraction of disease burden attributable to occupational risk factors for injuries was 18·5 times higher for men than for women in 2010 (20 175 000 DALYs for men *vs* 1 090 000 for women). Dietary risk factors had broadly similar effects for men and women with the exception of diet low in fruits, for which the fraction of disease burden attributable was 1·5 times larger for men than for women in 2010 (47 979 000 DALYs for men *vs* 32 474 000 for women). This effect is caused by lower fruit consumption and a larger disease burden from cardiovascular disease in men.

Further disaggregation of mortality and disease burden attributable to risk factors reveals several patterns by age group (appendix). Among children younger than 5 years, childhood underweight was the leading risk factor worldwide in 2010 (12·4% [10·4–14·7] of global DALYs), followed by non-exclusive or discontinued breastfeeding (7·6% [4·8–10·9]) and household air pollution from solid fuels (6·0% [4·3–7·7]). Vitamin A and zinc deficiencies, unimproved sanitation, and unimproved water each accounted for less than 2% of disease burden in children younger than 5 years.

For people aged 15–49 years, the leading risk factor worldwide was alcohol use, followed by tobacco smoking including second-hand smoke, high blood pressure, high body-mass index, diet low in fruits, drug use, and occupational risk factors for injuries. Risk factor rankings in this age group stayed broadly similar between 1990, and 2010, with the exception of iron deficiency, which dropped from the fourth leading risk factor in 1990, to tenth in 2010.

High blood pressure, tobacco smoking including second-hand smoke, and diet low in fruits were all in the top five risk factors for adults aged 50–69 years and adults older than 70 years, in both 1990, and 2010, accounting for a large proportion of disease burden in both age groups. Globally, high blood pressure accounted for more than 20% of all health loss in adults aged 70 years and older in 2010, and around 15% in those aged 50–69 years. Tobacco smoking including second-hand smoke accounted for more than 10% of global disease burden in each of these age groups in 2010.

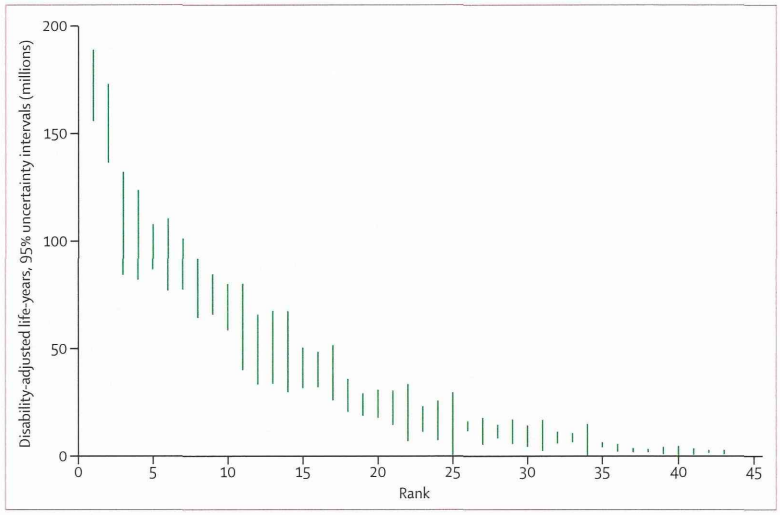


Figure 4: **95% uncertainty intervals for risk factors ranked by global attributable disability-adjusted life-years, 2010**
An interactive version of this figure is available online at http://healthmetricsandevaluation.org/gbd/visualizations/regional

In all 21 regions, and worldwide, a shift has occurred, from risk factors for childhood communicable disease to risk factors for non-communicable disease. The size of this shift and which risk factors account for the largest burden varies highly between regions (figure 5, appendix).

In central, eastern, and western sub-Saharan Africa, the share of disease burden attributable to childhood underweight, household air pollution from solid fuels, and suboptimal breastfeeding has fallen substantially. However, these risk factors continue to be the leading three causes of disease burden in 2010. The disease burden attributable to risk factors for childhood communicable diseases, such as micronutrient deficiencies and unimproved water and sanitation, has decreased, both as a proportion of total disease burden and in their rank order: risk factors for some non-communicable diseases and injury accounted for a larger disease burden in 2010. The most notable of these factors were alcohol use and high blood pressure (appendix).

Compared with other regions of sub-Saharan Africa, southern sub-Saharan Africa had a more mixed pattern of risk factor burden in 1990 (appendix). In 2010, alcohol use was the leading risk factor in southern sub-Saharan Africa, followed by high blood pressure and high body-mass index (figure 6). In addition to high exposure to harmful alcohol use, the effects of alcohol were particularly large because it increases the risk of road traffic and other unintentional and intentional injuries, as well as of tuberculosis,[47] all of which are large causes of disease and injury burden in this region.

Ranking legend
1–5 6–10 11–15
16–20 21–25 26–30
31–35 36–40 >40

Risk factor	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
High blood pressure	1	1	2	3	3	1	2	2	1	1	4	1	1	2	1	1	3	5	2	5	5	6
Tobacco smoking, including second-hand smoke	2	2	1	2	1	2	3	3	2	4	5	2	2	5	3	3	2	3	5	7	12	10
Household air pollution from solid fuels	3	42	..	..	..	14	23	20	5	18	11	3	12	7	25	8	1	4	7	2	2	2
Diet low in fruits	4	4	7	6	6	5	6	5	3	6	7	4	4	10	6	7	5	9	8	8	11	13
Alcohol use	5	5	6	9	7	4	4	1	8	2	2	6	5	1	18	9	10	7	1	6	10	5
High body-mass index	6	8	3	1	2	3	1	4	9	3	1	9	3	3	2	2	17	2	3	14	18	15
High fasting plasma glucose	7	7	5	5	4	7	5	10	7	5	3	5	7	6	4	4	7	1	6	10	13	11
Childhood underweight	8	39	38	37	39	38	38	38	38	32	23	13	25	18	20	14	4	8	9	1	1	1
Ambient particulate matter pollution	9	9	11	26	14	12	24	14	4	27	19	11	10	24	7	19	6	32	25	16	14	7
Physical inactivity and low physical activity	10	3	4	4	5	6	7	7	10	8	6	8	9	8	5	6	11	6	11	15	15	16
Diet high in sodium	11	6	10	11	11	9	11	9	6	9	13	7	6	13	8	15	14	16	13	21	17	18
Diet low in nuts and seeds	12	11	9	7	8	8	8	8	12	10	8	15	8	12	9	10	13	13	16	22	16	21
Iron deficiency	13	20	32	21	35	22	17	21	19	14	12	12	17	4	11	5	8	11	10	4	4	4
Suboptimal breastfeeding	14	..	..	..	..	..	27	..	24	22	15	14	16	9	13	13	9	10	4	3	3	3
High total cholesterol	15	12	8	8	9	10	9	6	13	11	10	16	14	16	10	16	20	14	19	28	27	30
Diet low in whole grains	16	10	16	16	17	11	12	11	11	12	14	26	13	17	12	12	15	15	32	24	19	24
Diet low in vegetables	17	14	13	12	13	13	10	12	15	16	20	10	11	14	16	11	16	12	15	23	23	20
Diet low in seafood omega-3 fatty acids	18	17	15	13	16	16	14	13	17	17	18	19	15	23	14	17	18	20	23	27	25	25
Drug use	19	13	14	10	10	20	13	17	18	13	16	18	20	11	17	18	22	19	12	19	24	22
Occupational risk factors for injuries	20	24	24	20	25	26	16	25	20	19	22	23	21	21	22	31	12	22	22	20	22	17
Occupational low back pain	21	15	17	15	23	18	20	24	14	15	24	17	24	22	19	26	23	17	24	17	21	19
Diet high in processed meat	22	22	12	14	12	15	18	15	29	7	9	27	19	15	27	24	25	27	28	31	28	28
Intimate partner violence	23	18	22	23	22	25	21	22	21	23	26	22	27	19	24	23	21	25	14	18	20	23
Diet low in fibre	24	16	18	18	18	19	15	16	16	25	28	20	18	28	21	22	33	21	33	36	34	36
Unimproved sanitation	25	38	39	39	41	42	40	40	40	40	38	30	37	31	32	28	19	18	18	9	7	9
Lead exposure	26	23	21	19	24	17	19	23	22	20	25	24	23	20	26	21	24	30	20	25	26	26
Diet low in polyunsaturated fatty acids	27	19	19	17	20	21	22	18	26	24	27	21	22	29	23	25	32	23	30	33	30	29
Diet high in trans fatty acids	28	29	23	24	15	23	28	19	28	21	21	33	26	27	15	38	28	34	35	37	36	37
Vitamin A deficiency	29	40	40	38	40	41	41	42	43	41	37	32	34	34	37	33	30	31	17	11	6	8
Occupational particulate matter, gases, and fumes	30	34	33	32	28	32	33	31	23	29	32	28	29	33	31	34	26	33	29	29	29	31
Zinc deficiency	31	37	37	36	37	39	39	39	39	39	29	29	28	25	35	27	31	28	21	13	9	14
Diet high in sugar-sweetened beverages	32	28	31	31	19	33	26	27	37	26	17	25	32	30	28	20	27	26	26	32	32	34
Childhood sexual abuse	33	26	25	22	21	30	25	26	30	28	30	37	30	26	29	30	29	35	31	26	31	27
Unimproved water source	34	41	41	40	38	40	42	41	42	42	40	31	36	35	30	29	34	24	27	12	8	12
Low bone mineral density	35	21	20	25	26	24	30	28	25	30	33	35	35	36	34	32	36	37	38	35	37	33
Occupational noise	36	33	35	34	36	35	35	35	33	33	31	34	31	32	36	35	37	36	34	30	33	32
Occupational carcinogens	37	31	26	29	31	34	32	34	27	38	35	38	33	40	38	40	39	41	37	41	42	42
Diet low in calcium	38	25	28	27	29	27	29	30	31	34	39	39	39	39	40	37	40	39	39	38	39	38
Ambient ozone pollution	39	36	36	41	33	36	43	37	34	43	43	43	43	43	43	43	35	43	43	42	38	41
Residential radon	40	32	27	35	27	28	36	33	32	36	41	41	38	42	41	42	41	42	42	43	43	43
Diet low in milk	41	27	29	30	30	29	34	32	35	37	42	40	41	41	42	39	42	40	41	39	41	39
Occupational asthmagens	42	35	34	33	34	37	37	36	41	35	36	36	42	37	39	36	38	29	36	34	35	35
Diet high in red meat	43	30	30	28	32	31	31	29	36	31	34	42	40	38	33	41	43	38	40	40	40	40

Figure 5: **Risk factors ranked by attributable burden of disease, 2010**
Regions are ordered by mean life expectancy. No data=attributable disability-adjusted life-years were not quantified.

In south Asia, the rise of risk factors for non-communicable diseases is shown by the substantial increase in the burden attributable to tobacco smoking including second-hand smoke, high blood pressure and other metabolic risk factors, dietary risk factors, and alcohol use. However, household air pollution from solid fuels was, despite decreases, the leading risk factor in 2010. Childhood underweight was still the fourth leading risk factor in 2010, despite its share of disease burden having more than halved from 11·9% [95% UI 10·1–14·4] of DALYs in 1990, to 4·0% [3·2–4·9] in 2010. Other risk factors for communicable disease, such as suboptimal breastfeeding and micronutrient deficiencies, fell substantially in the region as child mortality decreased.

In southeast, east, and central Asia, the epidemiological transition was already well advanced in 1990, and by 2010, high blood pressure (which is commonly associated with diets high in sodium as a prominent underlying cause[94,158]), tobacco smoking including second-hand smoke, and diets low in fruits were all among the five leading risk factors in these regions. The disease burden attributable to childhood underweight and suboptimal breastfeeding had been largely eliminated in east Asia by 2010, although they remain important in southeast Asia. In these three regions, despite decreases, household air pollution from solid fuels was still a leading risk factor in 2010, ranked third in southeast Asia, fifth in east Asia, and 12th in central Asia. Ambient particulate matter pollution accounted for a larger disease burden than did household air pollution in central and east Asia in 2010, although household solid fuels is an important source of ambient particulate matter pollution in these regions.

The North Africa and Middle East region also had a large shift from risk factors for communicable to non-communicable diseases. In 2010, risk factors for non-communicable disease almost exclusively dominated the region's causes of loss of health, with high blood pressure and high body-mass index each accounting for roughly 8% of disease burden, followed by tobacco smoking including second-hand smoke, high fasting plasma glucose, and physical inactivity or low physical activity. Ambient particulate matter pollution (seventh leading risk factor) is a notable cause of disease burden in this region, caused by a combination of polluted cities and dust from the Sahara desert.

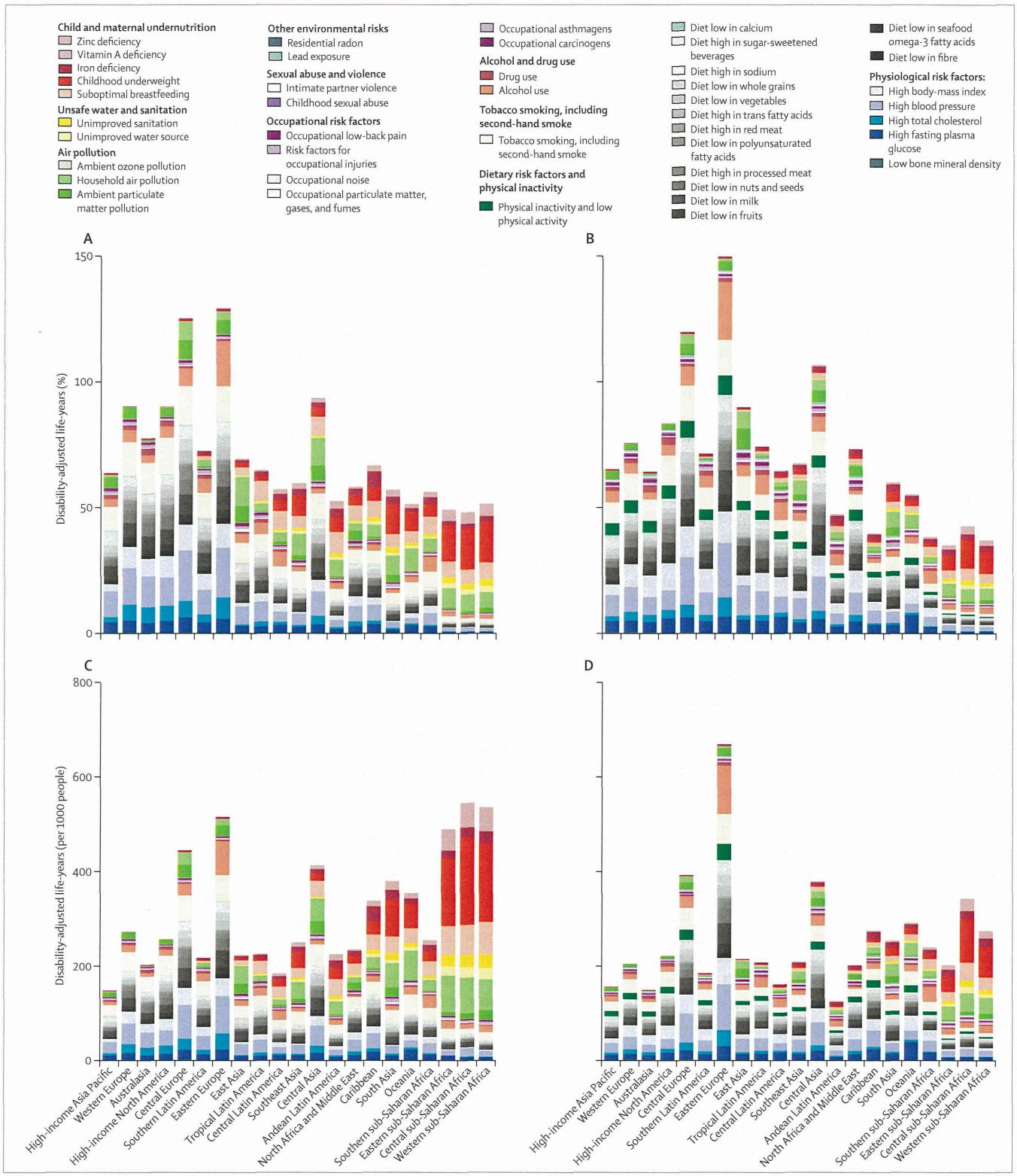
Alcohol use was an important cause of disease burden in most of Latin America. It was ranked second in central Latin America, fourth in tropical Latin America, and seventh in Andean Latin America in 1990. In 2010, it was ranked second in central and tropical Latin America, and first in Andean Latin Ameria. Risk factors for childhood communicable disease had been largely replaced by those causing non-communicable diseases in these regions by 2010, although household air pollution from solid fuels was still an important risk factor in Andean Latin America in 2010.

One of the most notable findings was the effect of alcohol use in Eastern Europe, where it accounts for almost a quarter of total disease burden. Other risk factors, such as high blood pressure, tobacco smoking including second-hand smoke, high body-mass index, and dietary risks, also feature prominently, underscoring the large underlying burden of cardiovascular disease in the region.

In North America, Australasia, southern Latin America, and western Europe, the share of disease burden attributable to tobacco smoking including second-hand smoke has fallen slightly; it has stayed almost constant in central Europe and high-income Asia Pacific. Tobacco smoking including second-hand smoke was still the leading risk factor in 2010 in North America and western Europe. Important decreases in disease burden are evident for high blood pressure and total cholesterol in North America, Australasia, and western Europe. High blood pressure is a leading risk for health in high-income Asia Pacific (accounting for 8·5% [95% UI 7·1–10·1] of disease burden) and central Europe (18·9% [16·8–20·8]); evidence from individual-level trials of salt and blood pressure and from cross-population studies indicates that this result is likely to be driven partly by high salt consumption in these regions.[94,158] Falls in disease burden attributable to tobacco smoking including second-hand smoke, high blood pressure, and high total cholesterol in high-income regions have been partly offset by the increasing burden caused by high body-mass index. In southern Latin America, high body-mass index accounted for almost 10% of overall disease burden in 2010, and is the leading risk factor in southern Latin America and Australasia.

Figure 6 summarises these regional patterns, in relation to the proportion of regional burden and attributable DALYs per 1000 people. Regions in figure 6 are ordered by mean age of death, a marker of the epidemiological transition. Figure 6 shows the clear transition away from risk factors for childhood communicable disease towards risk factors for non-communicable disease, with increasing mean age at death. This change is apparent from the decrease in burden of disease attributable to undernutrition and unimproved water and sanitation, with increased mean age at death, especially when the effect of risks is assessed by DALYs per 1000 people (figure 6C, D). A clear general shift occurs towards a larger proportion of overall burden arising from risk factors for non-communicable diseases, particularly metabolic risks and dietary risk factors (figure 6A, B). However, the absolute burden of risk factors for non-communicable disease does not increase with increasing mean age at death. Rather, its magnitude is lower in high-income regions than in sub-Saharan Africa and south Asia (figure 6C, D), showing the double burden of communicable and non-communicable disease in regions early in the epidemiological transition.

Some risk factors deviated from the pattern of the proportional burden (percent of region-specifc DALYs


Child and maternal undernutrition
Zinc deficiency
Vitamin A deficiency
Iron deficiency
Childhood underweight
Suboptimal breastfeeding
Unsafe water and sanitation
Unimproved sanitation
Unimproved water source
Air pollution
Ambient ozone pollution
Household air pollution
Ambient particulate matter pollution
Other environmental risks
Residential radon
Lead exposure
Sexual abuse and violence
Intimate partner violence
Childhood sexual abuse
Occupational risk factors
Occupational low-back pain
Risk factors for occupational injuries
Occupational noise
Occupational particulate matter, gases, and fumes
Occupational asthmagens
Occupational carcinogens
Alcohol and drug use
Drug use
Alcohol use
Tobacco smoking, including second-hand smoke
Tobacco smoking, including second-hand smoke
Dietary risk factors and physical inactivity
Physical inactivity and low physical activity
Diet low in calcium
Diet high in sugar-sweetened beverages
Diet high in sodium
Diet low in whole grains
Diet low in vegetables
Diet high in trans fatty acids
Diet high in red meat
Diet low in polyunsaturated fatty acids
Diet high in processed meat
Diet low in nuts and seeds
Diet low in milk
Diet low in fruits
Diet low in seafood omega-3 fatty acids
Diet low in fibre
Physiological risk factors:
High body-mass index
High blood pressure
High total cholesterol
High fasting plasma glucose
Low bone mineral density
A
B
C
D
Disability-adjusted life-years (%)
Disability-adjusted life-years (per 1000 people)
0
50
100
150
200
400
600
800
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

attributable to a risk factor) being closely associated with epidemiological and demographic transition (shift from communicable to non-communicable disease with increasing mean age of death). The proportion of DALYs attributable to tobacco smoking including second-hand smoke was largest in North America—where smoking among women has generally been prevalent for a long time—and central and eastern Europe. Central and eastern Europe and central Asia also had the largest proportion of disease burden attributable to risk factors with large effects on cardiovascular diseases, which are disproportionately high in these regions. Exposure to particulate matter from household and ambient sources had the most varied pattern with respect to the epidemiological transition, partly because of the heterogeneous pattern of exposure and the effects on both children and adult causes of ill health. Household air pollution from solid fuels accounted for a large proportion of disease burden in central, eastern, and western sub-Saharan Africa and it is a leading risk factor in some Asian regions and Oceania. In central and east Asia in 2010, ambient particulate matter pollution surpassed household air pollution in terms of its burden.

Discussion

The results of GBD 2010 suggest that the contributions of risk factors to regional and global burden of diseases and injuries has shifted substantially between 1990, and 2010, from risk factors that mainly cause communicable diseases in children to risk factors that mainly cause non-communicable diseases in adults. The proportion of overall disease burden attributable to childhood underweight—the leading risk factor worldwide in 1990—had more than halved by 2010, making childhood underweight the eighth risk worldwide, behind six behavioural and physiological risks, and household air pollution from solid fuels. Other risks for child mortality, such as non-exclusive and discontinued breastfeeding, micronutrient deficiencies, and unimproved water and sanitation, have also fallen. However, child and maternal undernutrition risks collectively still account for almost 7% of disease burden in 2010, with unimproved water and sanitation accounting for almost 1%. Of the non-communicable disease risks, high blood pressure, high body-mass index, high fasting plasma glucose, alcohol use, and dietary risks have increased in relative importance. This overall shift has arisen from a combination of the ageing population, substantial achievements in lowering mortality of children aged younger than 5 years, and changes in risk factor exposure.

These broad global patterns mask enormous regional variation in risks to health. In sub-Saharan Africa, risks such as childhood underweight, household air pollution from solid fuels, and suboptimal breastfeeding continue to cause a disproportionate amount of health burden, despite decreasing. The shift to risk factors for non-communicable disease was clear in east Asia, North Africa and Middle East, and Latin America. This regional heterogeneity underestimates even greater differences in exposure to, and health effects of, risk factors in national and subnational populations. These differences should be further elucidated in country-specific analyses using the framework and methods reported here.

Our analysis shows the large burden of disease attributable to primary and secondary tobacco smoking and to particulate matter pollution in household and ambient environments. The magnitude of disease burden from particulate matter is substantially higher than estimated in previous comparative risk assessment analyses. For example, ambient particulate matter pollution was estimated in the previous comparative risk assessment[7] to account for 0·4% of DALYs in 2000 compared with 3·1% in GBD 2010 based on interpolating our 1990 and 2005 results; for household air pollution from solid fuels the comparison is 2·7% in the previous comparative risk assessment versus 5·4% based on GBD 2010.

Several reasons could account for this difference. First, accumulation of evidence from epidemiological studies about diseases caused by particulate matter, and the use of an integrated exposure–response curve, has led to the inclusion of more outcomes than before. For example, health effects for ischaemic heart disease and stroke were not previously included for household air pollution from solid fuels, and lung cancer was included for coal smoke only. Second, the previous assessment of ambient particulate matter pollution was restricted to medium and large cities. High-resolution satellite data and chemical transport models have enabled us to quantify exposure and burden for all rural and urban populations. Third, the previous assessment of ambient particulate matter pollution did not include additional increments of risk above a concentration of 50 μg/m^3 for $PM_{2·5}$, because of the narrow range of ambient particulate matter pollution levels reported in epidemiological studies. The use of an integrated exposure–response curve enabled us to estimate a continuous risk function across the full range of particulate matter concentrations, which covers the very high concentrations of ambient particulate matter exposure measured in, for example, parts of east Asia.

Our integrated exposure–response curve, however, does not address how different sources of particulate matter interact in terms of effects and overlapping exposures. Studies[124,159,160] have reported broadly similar effect sizes

Figure 6: **Attributable burden for each risk factor**
As percentage of disability-adjusted life-years in 1990 (A), and 2010 (B), and as disability-adjusted life-years per 1000 people in 1990 (C), and 2010 (D). Regions ordered by mean life expectancy. Burden of disease attributable to individual risk factors are shown sequentially for ease of presentation. In reality, the burden attributable to different risks overlaps because of multicausality and because the effects of some risk factors are partly mediated through other, more proximal, risks. An interactive version of this figure is available online at http://healthmetricsandevaluation.org/gbd/visualizations/regional.

for ambient particulate matter by smoking status (never, former, and current smokers). Other evidence[161] shows that the effects diminish with increasing exposure for active smoking, a pattern incorporated into our exposure–response curves. We applied the effects of ambient particulate matter to both smokers and non-smokers alike to be consistent with the epidemiological evidence that emphasises independent effects of ambient particulate matter. The reasons for the independent effects of different sources of particulate matter should be further investigated. They might include different compositions of particulate matter by source, or different time patterns of exposure[162]—eg, exposure to particulate matter from active smoking is characterised by episodic, high doses whereas exposure to ambient particulate matter is more constant over time.

These limitations aside, the large attributable burden documented in our analysis represents a major shift in our understanding of disease burden arising from particulate matter and emphasises the need to design alternative fuels for household cooking and heating,[163] implement more stringent regulation of vehicle and industrial emissions,[164–166] reduce agricultural burning or land clearing by fire,[167] and curb and reverse deforestation and desertification to reduce ambient particulate matter from dust.[168–171] A large share of ambient particulate matter in Asia and sub-Saharan Africa originates from solid fuel.[172,173] Therefore the two exposures are related, and alternative cooking and heating fuels would have benefits for people who currently use solid fuels as well as those who do not, but live in the same community.[173]

Unimproved water and unimproved sanitation together accounted for 0·9% of DALYs in 2010, compared with 2·1% in 1990. These proportions are substantially smaller than the 6·8% for 1990, and 3·7% for 2000, estimated in previous GBD studies for water, sanitation, and hygiene combined.[3,7] The relatively small burden estimated for 2010 is partly related to decreases in diarrhoeal disease mortality since 1990, and partly to differences in the distributions of deaths by underlying cause of death. We have also done an updated meta-analysis of quasiexperimental and experimental studies. Historical demographic analyses suggest that the introduction of piped water into cities in the late 19th and early 20th centuries had a large beneficial effect on mortality.[174] However, our re-analysis both when restricted to experimental studies and when also including quasiexperimental studies did not detect a significantly improved effect of household water connections over improved water sources. Similarly, we did not find a significantly improved effect of water quality interventions, consistent with the findings reported by Cairncross and colleagues,[128] which showed that masked point-of-use water quality interventions did not have a significant effect on self-reported diarrhoea. As a result of this reassessment, we restricted our analysis to improved water and improved sanitation compared with unimproved sources following the MDG definitions. However, the interventions used in previous studies might not have achieved their full efficacy because of the quality of implementation. The real burden from water and sanitation could therefore be underestimated if well-implemented household connections and water quality interventions have a larger effect than improved water sources alone, and if the combination of poor water and sanitation has a larger effect than a sample interaction of individual effects. More definitive epidemiological evidence is needed to assess the effects of low quality versus high quality water, household connections versus improved water sources, and exposure based on travel time to water source.[175] Also, we could not include an assessment of personal hygiene because of the paucity of national exposure data.

Our findings on the burden of micronutrients are also substantially smaller than those in the previous comparative risk assessment for 2000 and in estimates for 2004 by Black and colleagues[10] in *The Lancet*'s Maternal and Child Undernutrition Series. For example, Black and colleagues estimated 668 000 deaths caused by vitamin A deficiency in 2004; we estimated a quarter (168 000 deaths) for 2005; for zinc deficiency, the differences are similarly large (453 000 *vs* 120 000). These differences stem from many sources. First, the estimates of Black and colleagues were based on 10·3 million child deaths worldwide, itself based on WHO estimates of global child deaths for 2004. This estimate is substantially larger than those reported by UNICEF[176] and the Institute for Health Metrics and Evaluation[177] at the time of Black and colleagues' publication.

Large differences also exist for cause-specific mortality, especially in relation to diarrhoea and lower respiratory tract infections (which can be affected by both of these risks) versus malaria (which is not).[176] The estimates also differ because of differences in the availability and interpretation of epidemiological evidence for disease outcomes and effect sizes. Maternal mortality and malaria as outcomes of vitamin A deficiency were included in the 2000 comparative risk assessment but they were not included in the present report because recent epidemiological evidence did not show a significant effect of supplementation on these outcomes. Furthermore, we excluded neonatal vitamin A deficiency since it is the subject of three ongoing randomised trials. The age at which the effects of zinc deficiency begin was increased from birth in the 2000 comparative risk assessment, to 6 months in 2004,[10] and to 12 months in the present analysis based on a reassessment of existing and new supplementation trials. Furthermore, we quantified the proportion of the population who are vitamin A or zinc deficient instead of classing whole countries as exposed or non-exposed. The evolving epidemiology of exposure to micronutrient deficiency and the subsequent health effects suggests a need to systematically reconsider most single nutrient supplementation for children in preventive strategies to lower child mortality, as suggested

by the 2000 comparative risk assessment and later analyses.[10] Therapeutic zinc supplementation in health-care settings is feasible, as is iron supplementation during pregnancy.[174–179] Our findings support the need for strengthened policy about promotion of optimal breastfeeding practices and nutritional programmes that improve child growth. The estimated number of child deaths caused by underweight has also changed substantially over successive studies: in GBD 1990 it was estimated to be 5·9 million deaths in 1990,[180] in the comparative risk assessment study for 2000 as 3·7 million deaths,[7] and 1·9 million deaths in 2004.[10] In GBD 2010 we estimated 2·3 million deaths for 1990 and 0·9 million deaths for 2010.

The evolution of estimates for deaths caused by childhood underweight is because of improvements in assessment of the population at risk. These improvements come from systematic analysis of the available data on underweight, a major modification of RRs after the change in the WHO standard in 2006, and differences in estimates of total and cause-specific mortality. We have also assessed the burden attributable to childhood wasting and childhood stunting. These analyses produce quite similar findings, for example, worldwide, childhood wasting accounted for 0·7 million deaths in 2010, and childhood stunting for 0·9 million deaths, compared with 0·9 million deaths for childhood underweight (the effects of these risks cannot be added).

The global burden of disease attributable to tobacco smoking including second-hand smoke has changed little, with decreases in high-income regions offset by increases in regions such as southeast Asia and, to a lesser extent, east and south Asia. The burden attributable to alcohol use has increased substantially in eastern Europe since 1990, mainly because of a rise in the effects of heavy drinking on cardiovascular diseases.[181] The high burden in eastern Europe was also identified in the 2000 comparative risk assessment but the data for patterns of alcohol consumption and their effects were weaker, whereas now they are supported by more surveys and epidemiological studies.[182] High blood pressure, high body-mass index, and high fasting plasma glucose are leading risk factors for disease worldwide, with blood pressure having large effects on population health in all regions, including low-income regions in sub-Saharan Africa and south Asia. This finding is consistent with previous comparative risk assessment analyses. The disease burden in south Asia and sub-Saharan Africa, caused by increased blood pressure,[70] has increased its absolute and relative importance in risk factor rankings. The large burden of high blood pressure emphasises the importance of implementing both population-wide and high-risk approaches to reduction of blood pressure.[183,184] The worldwide increase in body-mass index and blood glucose is of particular concern in view of the absence of effective interventions.[62,74] In contrast to these risks, the burden of high total cholesterol is lower than that estimated in the 2000 comparative risk assessment, because the effects on ischaemic stroke were negligible at old ages when data from the Asia-Pacific Cohort Studies Collaboration and Prospective Studies Collaboration were pooled,[68,185] and because exposure has fallen in high-income countries.[67]

A recent study estimated that 5·3 million deaths were attributable to physical inactivity in 2008.[186] This number, which has been widely quoted and equated with the number of deaths attributable to tobacco smoking,[187] used effect sizes for all-cause mortality obtained from cohorts of adults mainly from North America and Europe and applied these effects to deaths at all ages. This approach not only assumes that the cause distribution is the same in all populations, irrespective of region and age structure, but also extends the effects to people younger than those in the cohort study, including to infants and children. In other words, a proportion of deaths from maternal causes, neonatal causes, and children's infectious diseases and HIV were attributed to physical inactivity.[186] The prevalence of inactivity also included people who had sedentary patterns as well as those in the low (insufficient) activity group. By contrast, our approach—calculating attributable burden by cause and age group, and accounting for exposure in four categories—estimated substantially fewer attributable deaths: 3·2 million (2·7 million to 3·7 million) in 2010, 56% of what we attribute to tobacco smoking when second-hand smoke is excluded. This discrepancy shows the importance of comparable risk factor assessments and the importance of estimation of attributable burden taking into account differences in underlying disease and injury patterns across populations.

We have expanded the set of components of diet included from a combined category of fruits and vegetables in the 2000 comparative risk assessment to 15 components in GBD 2010; together these dietary risk factors account for a tenth of global disease burden. Of the dietary risk factors, the aetiological effect sizes for sodium, polyunsaturated fatty acids replacing saturated fatty acids, and seafood omega-3 fatty acids were informed fully (for sodium) or partly by randomised controlled trials. Disease burden attributable to diet high in sodium was a third of that for high blood pressure. The theoretical-minimum-risk exposure distribution was selected on the basis of values reported in randomised trials; studies of populations with low prevalence of cardiovascular disease suggest that benefits are likely to continue to lower levels.[158]

The large attributable burden for dietary risk factors such as diets low in fruits, vegetables, whole grains, nuts and seeds, and seafood omega-3 fatty acids might surprise some readers. The large burden is caused by both high exposure—eg, low intake of fruits in many regions—and large effect sizes. We did supplementary analyses using information from studies of dietary patterns and randomised controlled feeding studies to examine the robustness of the effect sizes used in GBD 2010. The

findings of these supplementary analyses were consistent with those from the meta-analyses of single risk factors. However, we stress that these results should still be interpreted with caution, particularly because of the debate surrounding the effects of seafood omega-3 fatty acids.[143,188] Empirical assessments show that the pooled effect of risks and interventions trends towards a null result over time[189,190] and this pattern could apply to seafood omega-3 fatty acids since the earlier, primarily observational effect sizes tended to show a larger effect than did the more recent randomised controlled trials. Because the difference between results of observational studies and randomised controlled trials is not statistically significant we have quantified the attributable burden by use of the combined effect size. However, the validity of this approach could change as new evidence accumulates. Also, evidence from randomised controlled trials does not exist for several of the dietary components with a large attributable burden—fruits, vegetables, and nuts and seeds—although, as previously noted, evidence from randomised controlled trials does exist for intermediate outcomes. Further work is needed to confirm the effect size of dietary components and to establish to what degree the benefits continue, preferably through intervention studies of fatal and non-fatal events.

The extended analysis of components of diet does not include saturated fat beyond its replacement by polyunsaturated fats. Ecological studies suggest that saturated fat intake is a significant risk factor for mortality from ischaemic heart disease.[191] However, observational studies indicate that there might be no benefits if saturated fat reduction is associated with an increase in carbohydrates,[91] which is also supported by the absence of benefits from a low fat diet in the Women's Health Initiative.[192] Together with data for seafood omega-3 fatty acids, these findings show the complexity of the relation between dietary fat and health and suggest that the traditional health education message focused on lowering saturated fat alone needs to be expanded greatly to encompass several other key components of diet, including increased consumption of healthy foods that are presently missing from most diets.

The strengths of our study include a more comprehensive set of risk factors than any previous global or national analysis, consistent analyses in 1990, and 2010, which enables assessment of changes in risk factor burden, the incorporation of substantially more data for risk-factor exposure, improved methods to deal with missing and incomparable data, strong emphasis on comparability of methods related to exposure, disease outcomes, and effect sizes, and use of theoretical-minimum-risk exposure distribution as the consistent alternative exposure distribution with which current exposures are compared.

Like all population-based analysis, our study also has some limitations. First, despite the massive improvement in the availability of exposure data and methods, exposure estimates for many risk factors are affected by data limitations, especially for 2010, since fewer data could be included. This limitation will become even more salient in applications of our methods to individual countries and shows the importance of surveillance of national risk factors as a crucial component of national health information systems. More importantly, for some risk factors we have less direct measures of exposure than for others. For example, for household air pollution from solid fuels we measured exposure on the basis of household fuel use rather than personal exposure to particulate matter; for other risks, such as blood pressure, we have direct biological measurements of exposure.

Second, the presence of residual confounding in the estimates of effect sizes cannot be definitively ruled out, particularly for those without evidence from intervention studies, either because they have not yet been done or the risk is not amenable to intervention. For example, no large-scale trials have been done of interventions for high body-mass index that measured cause-specific deaths although effects on disease incidence have been investigated in trials.[193] Observational studies of the effect sizes for body-mass index have controlled for some potential confounders.[75–77] As noted, the pooled effect of risks and interventions trends towards the null result over time;[189,190] the implication being that risks for which only a few studies have been done might have their effect overestimated compared with risks for which a large body of evidence exists.

Third, with the exception of risk factors for which much evidence has been accumulated across diverse populations and age groups, such as the metabolic risks, uncertainty remains as to the extent to which effect sizes are generalisable to different populations. Similarly, the large body of epidemiological evidence for cardiovascular risk factors shows a relation between age and the effect size of risk factors for cardiovascular disease. Such age-related changes might be present for other outcomes. Fourth, we have combined epidemiological evidence for effect sizes using studies across different periods, which could mask underlying temporal changes in risk; no data presently exist to enable an examination of the extent to which effect sizes might change over time.

Fifth, we have excluded risks for which insufficient information exists to enable estimation of exposure, or for which the evidence of effect sizes is scarce. This approach excludes several risk–outcome pairs that have been previously included in global and regional assessments of risk factor attributable burden, such as unsafe sex and global climate change. Unsafe sexual practices were included in the 2000 comparative risk assessment but we excluded it because of the absence of robust estimates of exposure or available approaches to determine the proportion of HIV infection that is attributable to unsafe sexual practices by country over time. If quantifiable, unsafe sexual practices would probably account for a large fraction of global health burden; the direct burden of HIV is 3·3% of DALYs in

2010; other sexually transmitted infections account for 0·4% of DALYs. Similarly, we have been unable to control for confounding in observational studies of late initiation of breastfeeding, which is associated with an increased risk of neonatal mortality. Infants who might too ill or weak to breastfeed are more likely to die. In our analysis, we could not assess low birthweight as an outcome for maternal iron deficiency, despite evidence from randomised trials. Similarly, we could not assess low birthweight as an outcome for maternal alcohol use. Low birthweight was not a disease outcome in GBD 2010 but is associated with an increased risk of neonatal mortality. We excluded several other risk–outcome pairs that had insufficient evidence to estimate effect sizes or that had substantial potential of residual confounding—eg, the effect of addictive drugs (cannabis, amphetamines, and opioids) on unintentional and intentional injuries; or the effects of intimate partner violence, on HIV or other sexually transmitted infections.

Sixth, we included few risks that affected three of the leading communicable diseases—HIV/AIDs, tuberculosis, and malaria (beyond deaths in childhood). Overall, we have not included risks for 126 of the 241 most detailed causes included in the GBD, which account for 26·3% of global disease health burden. This shortcoming emphasises the need for a more deliberate research focus to identify and quantify risk factors for the outcomes for which there are presently no risks or few large risks.

Seventh, we have quantified the attributable burden of risk factors, holding all other independent factors constant. For clusters of risk factors we have approximated the joint effects, assuming that risk factors within each cluster are independent. A more accurate quantification of the joint effects of multiple risk factors is an important area for future research. Finally, it is important to stress that the size of the attributable risk factor burden does not equal priority for action since prioritisation also depends on availability, cost, and effectiveness of intervention strategies to reduce exposures to these risks.

Public policy to improve the health of populations will be more effective if it addresses the major causes of disease burden. Even small reductions of population exposure to large risks will yield substantial health gains.[194] The principal advantage of doing a comprehensive and comparable scientific assessment of disease burden caused by different risk factors is that it provides the evidence base for informing discussion about policy. Coupled with evidence of their present burden, most of the leading risk factors, except high body-mass index and high fasting plasma glucose, have decreased in at least some regions and countries, showing that substantial reduction of their effect through targeted prevention strategies is feasible. If predictions about huge increases in disease burden worldwide are to be proved wrong, then countries, with appropriate global public health leadership, must urgently implement measures to control exposure to leading hazards, particularly risks for non-communicable diseases.

Contributors

CJLM, SSL, and ME wrote the first draft. SSL, TV, AF, GD, KS, ADL, CJLM, and ME revised the report. ME, CJLM, and ADL designed the study and provided overall guidance. SSL, EC, GF, CA, ESa, KA, REE, and LCR did comparative analyses of risk factors. All other authors developed the estimates of risk-specific exposure, theoretical-minimum-risk exposure distribution, and RR inputs, and checked and interpreted results.

Conflicts of interest

A Davis is employed by the NHS on works for the UK Dept of Health as lead adviser on audiology. E R Dorsey has been a consultant for Medtronic and Lundbeck and has received grant support from Lundbeck and Prana Biotechnology. M Ezzati chaired a session and gave a talk at the World Cardiology Congress (WCC), with travel cost reimbursed by the World Heart Federation. At the WCC, he also gave a talk at a session organised by Pepsico with no financial remuneration. G A Mensah is a former employee of PepsiCo. D Mozaffarian has received: ad hoc travel reimbursement and/or honoraria for one-time specific presentations on diet and cardiometabolic diseases from Nutrition Impact (9/10), the International Life Sciences Institute (12/10), Bunge (11/11), Pollock Institute (3/12), and Quaker Oats (4/12; modest); and Unilever's North America Scientific Advisory Board (modest). B Neal is the Chair of the Australian Division of World Action on Salt and Health. He has consulted to Roche and Takeda. He has received lecture fees, travel fees, or reimbursements from Abbott, Amgen, AstraZeneca, George Clinical, GlaxoSmithKline, Novartis, PepsiCo, Pfizer, Pharmacy Guild of Australia, Roche, Sanofi-Aventis, Seervier, and Tanabe. He holds research support from the Australian Food and Grocery Council, Bupa Australia, Johnson and Johnson, Merck Schering-Plough, Roche, Servier, and United Healthcare Group. He is not employed by a commercial entity and has no equity ownership or stock options, patents or royalties, or any other financial or non-financial support that might be viewed as a conflict of interest. L Rushton received honorarium for board membership of the European Centre for Ecotoxicology and Toxicology of Chemicals and research grants to Imperial College London (as PI) from the European Chemical Industry Council and CONCAWE.

Acknowledgments

We thank the countless individuals who have contributed to the Global Burden of Disease Study 2010 in various capacities. We specifically acknowledge the important contribution to this work from multiple staff members of the World Health Organization. We also thank the following organisations that hosted consultations during the final stages of the analytical process, providing valuable feedback about the results and the data to improve the study's findings overall: Pan American Health Organization; Eastern Mediterranean Regional Office of WHO; UNAIDS; Ministry of Health, Brazil; China Centers for Disease Control; and the University of Zambia. We thank Regina Guthold, Jördis Ott, Annette Pruss-Ustun, and Gretchen A Stevens for their collaboration and input into the analyses and estimates. Finally, we acknowledge the extensive support from all staff members at the Institute for Health Metrics and Evaluation and specifically thank: James Bullard, Andrew Ernst, and Serkan Yalcin for their tireless support of the computational infrastructure required to produce the results; Linda A Ettinger for her expert administrative support to facilitate communication and coordination amongst the authors; Peter Speyer, Abigail McLain, Katherine Leach-Kemon, and Eden Stork for their persistent and valuable work to gain access to and catalogue as much data as possible to inform the estimates; and Erin C Mullany for her systematic efforts in organising drafts of papers, formatting correspondence with expert groups, and preparing the final manuscript. J Balmes, Z Chafe, and K R Smith acknowledge that their aspects of the research were also supported by USEPA and the Shell Foundation, neither of which had any role in design, data collection, analysis, interpretation, or decisions related to publication. R Bourne acknowledges Institutional Support: Vision & Eye Research Unit, Postgraduate Medical Institute, Anglia Ruskin University, Cambridge, UK. Funding support: Fight for Sight (Dr Hans and Mrs Gertrude Hirsch award). R Buchbinder was partially supported by an Australian National Health and Medical Research