A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010

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For **interactive versions of figures 3, 4, and 6** see http://healthmetricsandevaluation.org/gbd/visualizations/regional

Summary

Background Quantification of the disease burden caused by different risks informs prevention by providing an account of health loss different to that provided by a disease-by-disease analysis. No complete revision of global disease burden caused by risk factors has been done since a comparative risk assessment in 2000, and no previous analysis has assessed changes in burden attributable to risk factors over time.

Methods We estimated deaths and disability-adjusted life years (DALYs; sum of years lived with disability [YLD] and years of life lost [YLL]) attributable to the independent effects of 67 risk factors and clusters of risk factors for 21 regions in 1990 and 2010. We estimated exposure distributions for each year, region, sex, and age group, and relative risks per unit of exposure by systematically reviewing and synthesising published and unpublished data. We used these estimates, together with estimates of cause-specific deaths and DALYs from the Global Burden of Disease Study 2010, to calculate the burden attributable to each risk factor exposure compared with the theoretical-minimum-risk exposure. We incorporated uncertainty in disease burden, relative risks, and exposures into our estimates of attributable burden.

Findings In 2010, the three leading risk factors for global disease burden were high blood pressure (7·0% [95% uncertainty interval 6·2–7·7] of global DALYs), tobacco smoking including second-hand smoke (6·3% [5·5–7·0]), and household air pollution from solid fuels (4·3% [3·4–5·3]). In 1990, the leading risks were childhood underweight (7·9% [6·8–9·4]), household air pollution from solid fuels (HAP; 6·8% [5·5–8·0]), and tobacco smoking including second-hand smoke (6·1% [5·4–6·8]). Dietary risk factors and physical inactivity collectively accounted for 10·0% (95% UI 9·2–10·8) of global DALYs in 2010, with the most prominent dietary risks being diets low in fruits and those high in sodium. Several risks that primarily affect childhood communicable diseases, including unimproved water and sanitation and childhood micronutrient deficiencies, fell in rank between 1990 and 2010, with unimproved

water and sanitation accounting for 0·9% (0·4–1·6) of global DALYs in 2010. However, in most of sub-Saharan Africa childhood underweight, HAP, and non-exclusive and discontinued breastfeeding were the leading risks in 2010, while HAP was the leading risk in south Asia. The leading risk factor in Eastern Europe, Andean Latin America, and southern sub-Saharan Africa in 2010 was alcohol use; in most of Asia, most of Latin America, North Africa and Middle East, and central Europe it was high blood pressure. Despite declines, tobacco smoking including second-hand smoke remained the leading risk in high-income north America and western Europe. High body-mass index has increased globally and it is the leading risk in Australasia and southern Latin America, and also ranks high in other high-income regions, North Africa and Middle East, and Oceania.

Interpretation **Worldwide, the contribution of different risk factors to disease burden has changed substantially, with a shift away from risks for communicable diseases in children towards those for non-communicable diseases in adults. These changes are related to the ageing population, decreased mortality among children younger than 5 years, changes in cause-of-death composition, and changes in risk factor exposures. New evidence has led to changes in the magnitude of key risks including unimproved water and sanitation, vitamin A and zinc deficiencies, and ambient particulate matter pollution. The extent to which the epidemiological shift has occurred and what the leading risks currently are varies greatly across regions. In much of sub-Saharan Africa, the leading risks are still those associated with poverty and those that affect children.**

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Introduction

Measurement of the burden of diseases and injuries is a crucial input into health policy. Equally as important, is a comparative assessment of the contribution of potentially modifiable risk factors for these diseases and injuries. The attribution of disease burden to various risk factors provides a different account compared with disease-by-disease analysis of the key drivers of patterns and trends in health. It is essential for informing prevention of disease and injury.

Understanding the contribution of risk factors to disease burden has motivated several comparative studies in the past few decades. The seminal work of Doll and Peto[1] provided a comparative assessment of the importance of different exposures, particularly tobacco smoking, in causing cancer. Peto and colleagues[2] subsequently estimated the effects of tobacco smoking on mortality in developed countries since 1950. Although these risk factor-specific or cause-specific analyses are useful for policy, a more comprehensive global assessment of burden of disease attributable to risk factors can strengthen the basis for action to reduce disease burden and promote health. The Global Burden of Disease Study (GBD) 1990 provided the first global and regional comparative assessment of mortality and disability-adjusted life-years (DALYs) attributable to ten major risk factors.[3] However, different epidemiological traditions for different risks limited the comparability of the results. Subsequently, Murray and Lopez[4] proposed a framework for global comparative risk assessment, which laid the basis for assessment of 26 risks in 2000.[5–7] Since this work, WHO has provided estimates for some risks by the same methods but with updated exposures and some updates of the effect sizes for each risk.[8] Analyses have also been done for specific clusters of diseases, like cancers,[9] or clusters of risk factors, like maternal and child under-nutrition.[10] National comparative risk assessments (including in Australia, Iran, Japan, Mexico, South Africa, Thailand, USA, and Vietnam) have also been undertaken with similar approaches.[11–16]

GBD 2010 provides an opportunity to re-assess the evidence for exposure and effect sizes of risks for a broad set of risk factors by use of a common framework and methods. Particularly, since this work was done in parallel with a complete re-assessment of the burden of diseases and injuries in 1990 and 2010, for the first time changes in burden of disease attributable to different risk factors can be analysed over time with comparable methods. Since uncertainty has been estimated for each disease or injury outcome,[17,18] the comparative risk assessment for GBD 2010 has also enabled us to incorporate uncertainty into the final estimates. We describe the general approach and high-level findings for comparison of the importance of 67 risk factors and clusters of risk factors, globally and for 21 regions of the world, over the past two decades.

Methods

Overview

The basic approach for the GBD 2010 comparative risk assessment is to calculate the proportion of deaths or disease burden caused by specific risk factors—eg, ischaemic heart disease caused by increased blood pressure—holding other independent factors unchanged. These calculations were done for 20 age groups, both sexes, and 187 countries and for 1990, 2005 (results for 2005 not shown, available from authors on request), and 2010. We present aggregated results for 21 regions.

Table 1 shows the included risk factors and their organisation into a hierarchy with three levels. Level 1 risks are clusters of risk factors that are related by mechanism, biology, or potential policy intervention. Most risks are presented at level 2. For occupational carcinogens, a third level is included to provide additional detail about specific carcinogens. For suboptimal breastfeeding we

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also include a third level to distinguish between non-exclusive breastfeeding during the first 6 months and discontinued breastfeeding from 6 to 23 months.

We calculated burden attributable to all (67) risk factors and clusters of risk factors except for physiological risks and air pollution. These two clusters present analytical challenges for computation of the aggregate burden. For example, the effects of high body-mass index are partly mediated through high blood pressure, high total cholesterol, and high fasting plasma glucose, and household air pollution from solid fuels (wood, crop, residues, animal dung, charcoal, and coal) contributes to ambient particulate matter pollution.

We ranked results for 43 risk factors and clusters of risk factors, grouping together occupational carcinogens, non-exclusive and discontinued breastfeeding, and tobacco smoking with second-hand smoke on the basis of common exposure sources.

Our estimation of disease burden attributable to a risk factor had five steps: 1) selection of risk–outcome pairs to be included in the analysis based on criteria about causal associations; 2) estimation of distributions of exposure to each risk factor in the population; 3) estimation of etiological effect sizes, often relative risk per unit of exposure for each risk–outcome pair; 4) choice of an alternative (counterfactual) exposure distribution to which the current exposure distribution is compared. We selected an optimum exposure distribution, termed the theoretical-minimum-risk exposure distribution for this purpose; and 5) computation of burden attributable to each risk factor, including uncertainty from all sources. Further details about the data and methods used for specific risk factors are available on request.

Selection of risk–outcome pairs

The inclusion criteria for each risk–outcome pair that we applied were: 1) the likely importance of a risk factor to disease burden or policy based on previous work; 2) availability of sufficient data and methods to enable estimation of exposure distributions by country for at least one of the study periods (1990 and 2010); 3) sufficient evidence for causal effects based on high-quality epidemiological studies in which the findings were unlikely to be caused by bias or chance, analogous to the criteria used for assessment of carcinogens with convincing or probable evidence (panel). Sufficient data to estimate outcome-specific etiological effect sizes per unit of exposure were also needed; and 4) evidence to support generalisability of effect sizes to populations other than those included in the available epidemiological studies or satisfactory models for extrapolating them. Table 1 shows the risk–outcome pairs that were included in the final analysis, on the basis of these criteria.

Distribution of exposure to each risk factor

For most risk factors, a systematic search was done to identify published and, when possible, unpublished data sources to estimate risk factor exposure distributions in 1990 and 2010. Strategies to identify data sources included searching survey databases such as the WHO Global Database on Child Growth and Malnutrition, searching general citation databases such as Google Scholar and PubMed, manual searching of reference lists of articles and conference abstracts, and contacting experts in the relevant fields. Data sources included censuses, health examination and nutrition surveys, and community-based epidemiological studies.

Because data for risk factor exposure are often incomplete or missing for many populations, models were used to generate a complete set of current exposure distributions for risk factors for each country and for both years, including uncertainty. Table 1 shows for each risk factor the main sources of data and the modelling approach used for estimation of present risk factor exposure distributions. Briefly, risk factor models were designed to use available data and information for exposures in countries, for several years, and for different age groups to generate estimates for all countries, for both years, and for all relevant age groups. Estimation of exposure was done with statistical models that used predictors such as time, geography, and other variables that were relevant to the exposure of interest—eg, income per person.

For each risk factor, we tested a wide array of covariates for prediction of exposure distributions, drawing from covariates included in databases created or collated at the Institute for Health Metrics and Evaluation for GBD 2010. If relevant, the model also included age. Finally, each analysis accounted for important study characteristics such as national versus subnational representativeness, and the measures and instruments used for measuring exposure.

In addition to this general approach, specific methods were used for some risk factors. For tobacco including second-hand smoke, much scientific literature exists about alternative methods to estimate cumulative exposure, based on the premise that present prevalence and consumption data do not take into account likely variations in duration and intensity of smoking. In this case, we used the method of Peto and Lopez,[2] which uses lung cancer mortality as a marker (ie, smoking impact ratio) of cumulative population exposure to smoking for cancers and chronic respiratory disease. We used epidemiological data to estimate lung cancer mortality in non-smokers separately for China, other countries in the high-income Asia Pacific region, and all remaining countries.[119,120] For all other outcomes, we used 10-year lagged tobacco smoking prevalence. We also applied an approach analogous to the smoking impact ratio for occupational exposure to asbestos, for which we used mesothelioma mortality, separately estimated, as a marker of asbestos exposure.

For ambient particulate matter pollution, two complete, high resolution estimates exist of the concentration of particulate matter smaller than 2·5 μm in aerodynamic

	Exposure definition	Outcomes	Subgroup	Main data sources for exposure	Exposure estimation method	Theoretical-minimum-risk exposure distribution	Source of relative risks
1. Unimproved water and sanitation							
1.1. Unimproved water source	Proportion of households using an unimproved water source (unprotected wells or springs, vendor-provided water, tanker trucks, surface water, and other unspecified sources)	Intestinal infectious diseases	All ages	Population surveys and censuses	Spatiotemporal Gaussian process regression[19–21]	All households use an improved water source (household connection, a public tap or standpipe, a tubewell or borehole, a protected well or spring, or rainwater collection)	New meta-analysis
1.2. Unimproved sanitation	Proportion of households using unimproved sanitation (traditional latrines, open latrines without squatting slabs, bucket latrines, hanging latrines, open defecation or no facilities, and other unspecified facilities)	Intestinal infectious diseases	All ages	Population surveys and censuses	Spatiotemporal Gaussian process regression[19–21]	All households use improved sanitation (public sewers, septic systems, flush or pour-flush facilities, ventilated improved latrines, simple pit latrines with squatting slabs, and composting toilets)	New meta-analysis
2. Air pollution							
2.1. Ambient particulate matter pollution	Ambient concentration of particles with an aerodynamic diameter smaller than 2·5 μm, measured in μg/m^3	Lower respiratory infections; trachea, bronchus, and lung cancers; IHD; cerebrovascular disease; COPD	Age <5 years for lower respiratory tract infection; ≥25 years for all others	Surface monitor measurements, aerosol optical depth from satellites, and TM5 global atmospheric chemistry transport model[22–26]	Average of satellite and chemistry transport estimates, calibrated to surface monitor measurements	5·8–8·8 μg/m^3	Integrated exposure–response curve
2.2. Household air pollution from solid fuels	Proportion of households using solid fuels for cooking (coal, wood, charcoal, dung, and agricultural residues)	Lower respiratory infections; trachea, bronchus, and lung cancers; IHD; cerebrovascular disease; COPD; cataracts	Age <5 years for lower respiratory tract infection; ≥25 years for all others	Population surveys and censuses	Mixed effect regression	All households using clean fuels for cooking (vented gas, electricity)	Integrated exposure–response curve for lower respiratory tract infection, IHD, and stroke; new meta-analysis for cataracts, COPD, and lung cancer
2.3. Ambient ozone pollution	Ambient concentrations of ozone in air, measured in parts per billion	COPD	Age ≥25 years	TM5 global atmospheric chemistry transport model[22–24]	TM5 global atmospheric chemistry transport model[22–24]	33·3–41·9 parts per billion	Jerrett and colleagues[27]
3. Other environmental risks							
3.1. Residential radon	Residential radon, measured in Bq/m^3	Trachea, bronchus, and lung cancers	All ages	Direct household measurements from surveys	Mixed effect regression	10 Bq/m^3	Darby and colleagues[28]
3.2. Lead exposure	Blood lead (measured in μg/dL) and bone lead (measured in μg/g)	Intellectual disability; systolic blood pressure, which has effects on: RHD; IHD; ischaemic stroke; haemorrhagic and other non-ischaemic stroke; HHD; aortic aneurysm; the aggregate of cardiomyopathy and myocarditis and endocarditis; the aggregate of atrial fibrillation and flutter, PVD, other CVD; CKD	<15 years for intellectual disability; ≥25 years for all others	Examination surveys and epidemiological studies	DisMod 3	Bone lead level expected from age-specific cumulative exposure to blood lead of 0·09652 μmol/L[29]	Lanphear and colleagues,[30] Navas-Acien and colleagues[31]

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	Exposure definition	Outcomes	Subgroup	Main data sources for exposure	Exposure estimation method	Theoretical-minimum-risk exposure distribution	Source of relative risks
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4. Child and maternal undernutrition							
4.1. Suboptimal breastfeeding							
4.1.1. Non-exclusive breastfeeding	Proportion of children younger than 6 months with predominant, partial, or no breastfeeding	Intestinal infectious diseases; the aggregate of lower respiratory infections, upper respiratory infections, and otitis media	Age 0–5 months	Population surveys	Spatiotemporal Gaussian process regression[19–21]	All children exclusively breastfed for first 6 months	Lamberti and colleagues,[32] Black and colleagues[10]
4.1.2. Discontinued breastfeeding	Proportion of children aged 6–23 months with discontinued breastfeeding	Intestinal infectious diseases	Age 6–23 months	Population surveys	Spatiotemporal Gaussian process regression[19–21]	Continued breastfeeding until 2 years	Lamberti and colleagues,[32] Black and colleagues[10]
4.2. Childhood underweight	Proportion of children less than –3 SDs, –3 to –2 SDs, and –2 to –1 SDs of the WHO 2006 standard weight-for-age curve	Intestinal infectious diseases; measles; malaria; the aggregate of lower respiratory infections, upper respiratory infections, and otitis media; protein–energy malnutrition	Age <5 years	Examination surveys and epidemiological studies	Spatiotemporal Gaussian process regression[19–21]	Proportion of the WHO 2006 reference population in each SD range	Black and colleagues[10]
4.3. Iron deficiency	Haemoglobin, measure in g/L	The aggregate of maternal haemorrhage and maternal sepsis; iron-deficiency anaemia	All ages	Examination surveys and epidemiological studies	Mixed effect regression	Country-specific	Stoltzfus and colleagues[33]
4.4. Vitamin A deficiency	Proportion of children with serum retinol concentration <70 μmol/L	Intestinal infectious diseases; measles; vitamin A deficiency	Age 6 months to 5 years	Examination surveys and epidemiological studies	DisMod 3	No childhood vitamin A deficiency	Imdad and colleagues,[34,35] adjusted for background prevalence
4.5. Zinc deficiency	Proportion of the population with inadequate zinc intake based on estimated mean daily amount of absorbable zinc per head in the food supply compared with mean physiological requirements	Intestinal infectious diseases; lower respiratory infections	Age 1–4 years	Food and Agricultural Organization food balance sheets	Mixed effect regression	No inadequate zinc intake	Yakoob and colleagues,[36] adjusted for background prevalence
5. Tobacco smoking, including second-hand smoke							
5.1. Tobacco smoking	Smoking impact ratio for cancers and chronic respiratory disease, 10-year lagged tobacco smoking prevalence for all other causes including cardiovascular diseases	Tuberculosis; oesophageal cancer; nasopharynx cancer; pancreatic cancer; kidney and other urinary organ cancers; bladder cancer; stomach cancer; leukaemia; liver cancer; trachea, bronchus, and lung cancers; cervical cancer; colon and rectal cancer; mouth cancer; diabetes mellitus; IHD; cerebrovascular disease; the aggregate of HHD, atrial fibrillation and flutter, aortic aneurysm, PVD, and other CVD; COPD; the aggregate of pneumoconiosis, asthma, other interstitial lung disease, and other chronic respiratory diseases	Age ≥25 years	Mortality data including vital registration, verbal autopsy, and population surveys for smoking prevalence	CoDEM[37]	No tobacco smoking	Re-analysis of the Cancer Prevention Study 2[38–40]
5.2. Second-hand smoke	Proportion of children and non-smoking adults reporting exposure to second-hand smoke	The aggregate of lower respiratory infections, upper respiratory infections, and otitis media; trachea, bronchus, and lung cancers; IHD; cerebrovascular disease	Age <5 years for the aggregate of lower respiratory infections, upper respiratory infections, and otitis media, age ≥25 years for all others	Population surveys	Spatiotemporal Gaussian process regression[19–21]	No second-hand smoke exposure	US Department of Health and Human Services,[41] Oono and colleagues,[42] Jones and colleagues[43,44]

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	Exposure definition	Outcomes	Subgroup	Main data sources for exposure	Exposure estimation method	Theoretical-minimum-risk exposure distribution	Source of relative risks
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6. Alcohol and drug use							
6.1. Alcohol use	Average consumption of pure alcohol (measure in g/day) and proportion of the population reporting binge consumption of 0·06 kg or more of pure alcohol on a single occasion	Tuberculosis; lower respiratory infections; oesophageal cancer; the aggregate of mouth cancer, nasopharynx cancer, cancer of other part of pharynx and oropharynx; liver cancer; larynx cancer; breast cancer; colon and rectum cancers; diabetes mellitus; IHD; ischaemic stroke; haemorrhagic and other non-ischaemic stroke; HHD; atrial fibrillation and flutter; cirrhosis of the liver; pancreatitis; epilepsy; transport injuries; the aggregate of falls, drowning, fire, heat, and hot substances, poisonings, exposure to mechanical forces, intentional self-harm, and interpersonal violence; alcohol use disorders	All ages for alcohol use disorders, transport injuries, and interpersonal violence; ≥15 years for all others	Population surveys, alcohol sales, production, and other economic statistics	Mixed effect regression[45]	No alcohol consumption	Published studies[46-59]
6.2. Drug use	Proportion of the population reporting use of cannabis, opioids, and amphetamines, proportion of the population reporting use of injecting drugs	Drug use disorders; schizophrenia; HIV/AIDS; the aggregate of acute hepatitis B, liver cancer secondary to hepatitis B, and cirrhosis of the liver secondary to hepatitis B; the aggregate of acute hepatitis C, liver cancer secondary to hepatitis C, and cirrhosis of the liver secondary to hepatitis C; intentional self-harm	All ages	Population surveys, registries, and indirect measures	DisMod 3	No use of cannabis, opioid, or amphetamines, no use of injecting drugs	New meta-analyses, published studies[60,61]
7. Physiological risk factors							
7.1. High fasting plasma glucose	Fasting plasma glucose, measured in mmol/L	Diabetes mellitus; IHD; cerebrovascular disease; CKD; tuberculosis	Age ≥25 years	Examination surveys and epidemiological studies	Bayesian hierarchical regression[62]	Mean 4·9–5·3 mmol/L (SD 0·3 mmol/L)	Meta-regression of pooled prospective studies[63-66]
7.2. High total cholesterol	Total cholesterol, measured in mmol/L	IHD; ischaemic stroke	Age ≥25 years	Examination surveys and epidemiological studies	Bayesian hierarchical regression[67]	Mean 3·8–4·0 mmol/L (SD 0·9 mmol/L)	Meta-regression of pooled prospective studies[68,69]
7.3. High blood pressure	Systolic blood pressure, measured in mm Hg	RHD; IHD; ischaemic stroke, haemorrhagic and other non-ischaemic stroke; HHD; the aggregate of cardiomyopathy and myocarditis and endocarditis; the aggregate of atrial fibrillation and flutter, PVD, and other CVD; aortic aneurysm; CKD	Age ≥25 years	Examination surveys and epidemiological studies	Bayesian hierarchical regression[70]	Mean 110–115 mm Hg (SD 6 mm Hg)	Meta-regression of pooled prospective studies[71-73]
7.4. High body-mass index	Body-mass index, measured in kg/m^2	Oesophageal cancer; gallbladder and biliary tract cancer; pancreatic cancer; kidney and other urinary organ cancers; breast cancer; uterine cancer; colon and rectum cancers; diabetes mellitus; IHD; ischaemic stroke; HHD; the aggregate of cardiomyopathy and myocarditis and endocarditis; the aggregate of atrial fibrillation and flutter, PVD, and other CVD; CKD; osteoarthritis; low back pain	Age ≥25 years	Examination surveys and epidemiological studies	Bayesian hierarchical regression[74]	Mean 21·0–23·0 kg/m^2 (SD 1 kg/m^2)	Meta-regression of pooled prospective studies[75-78]

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	Exposure definition	Outcomes	Subgroup	Main data sources for exposure	Exposure estimation method	Theoretical-minimum-risk exposure distribution	Source of relative risks
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7.5. Low bone mineral density	Standardised bone mineral density measured at the femoral neck	Hip fracture falls; non-hip fracture falls	Age ≥50 years	Examination surveys and epidemiological studies	DisMod 3	90th percentile of NHANES-III cohort[79] by age	Johnell and colleagues[80]
8. Dietery risk factors and physical inactivity							
8.1. Diet low in fruits	Dietary intake of fruits (fresh, frozen, cooked, canned, or dried but excluding fruit juices and salted or pickled fruits)	The aggregate of oesophageal cancer, mouth cancer, the aggregate of nasopharynx cancer, cancer of other part of pharynx and oropharynx, and larynx cancer; trachea, bronchus, and lung cancers; IHD; ischaemic stroke; haemorrhagic and other non-ischaemic stroke	Age ≥25 years	Nutrition and health surveys	DisMod 3	Mean 300 g/day (SD 30 g/day)	New meta-analysis, published studies[81,82]
8.2. Diet low in vegetables	Dietary intake of vegetables (fresh, frozen, cooked, canned, or dried vegetables including legumes but excluding salted or pickled, juices, nuts and seeds, and starchy vegetables such as potatoes or corn)	The aggregate of mouth cancer, nasopharynx cancer, cancer of other part of pharynx and oropharynx, and larynx cancer; IHD; ischaemic stroke; haemorrhagic and other non-ischaemic stroke	Age ≥25 years	Nutrition and health surveys	DisMod 3	Mean 400 g/day (SD 30 g/day)	New meta-analysis, He and colleagues[81]
8.3. Diet low in whole grains	Dietary intake of whole grains (bran, germ, and endosperm in their natural proportions) from breakfast cereals, bread, rice, pasta, biscuits, muffins, tortillas, pancakes, and others	Diabetes mellitus; IHD; cerebrovascular disease	Age ≥25 year	Nutrition and health surveys	DisMod 3	Mean 125 g/day (SD 12·5 g/day)	Mellen and colleagues,[83] de Munter and colleagues[84]
8.4. Diet low in nuts and seeds	Dietary intake of nut and seed foods including, for example, peanut butter	IHD	Age ≥25 years	Nutrition and health surveys	DisMod 3	Mean 114 g per week (SD 11·4 g per week)	Kelly and colleagues[85]
8.5. Diet low in milk	Dietary intake of milk including non-fat, low-fat, and full-fat milk but excluding soya milk and other plant derivatives	Colon and rectum cancers	Age ≥25 years	Nutrition and health surveys	DisMod 3	Mean 450 g/day (SD 45 g/day)	World Cancer Research Fund and American Institute for Cancer Research[82]
8.6. Diet high in red meat	Dietary intake of red meat (beef, pork, lamb, and goat but excluding poultry, fish, eggs, and all processed meats)	Colon and rectum cancers; diabetes mellitus	Age ≥25 years	Nutrition and health surveys	DisMod 3	Mean 100 g per week (SD 10 g per week)	World Cancer Research Fund and American Institute for Cancer Research,[82] published studies[86,87]
8.7. Diet high in processed meat	Dietary intake of meat preserved by smoking, curing, salting, or addition of chemical preservatives, including bacon, salami, sausages, or deli or luncheon meats like ham, turkey, and pastrami	Colon and rectum cancers; diabetes mellitus; IHD	Age ≥25 years	Nutrition and health surveys	DisMod 3	No dietary intake of processed meat	World Cancer Research Fund and American Institute for Cancer Research,[82] Micha and colleagues[87]
8.8. Diet high in sugar-sweetened beverages	Dietary intake of beverages with ≥50 kcal per 226·8 g serving, including carbonated beverages, sodas, energy drinks, fruit drinks but excluding 100% fruit and vegetable juices	Diabetes mellitus and body-mass index with subsequent effects on: oesophageal cancer; gallbladder and biliary tract cancer; pancreatic cancer; kidney and other urinary organ cancers; breast cancer; uterine cancer; colon and rectum cancers; diabetes mellitus; IHD; ischaemic stroke; HHD; the aggregate of cardiomyopathy and myocarditis and endocarditis; the aggregate of atrial fibrillation and flutter, PVD, and other CVD; CKD; osteoarthritis; low back pain	Age ≥25 years	Nutrition and health surveys	DisMod 3	No dietary intake of sugar-sweetened beverages	New meta-analysis

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	Exposure definition	Outcomes	Subgroup	Main data sources for exposure	Exposure estimation method	Theoretical-minimum-risk exposure distribution	Source of relative risks
(Continued from previous page)							
8.9. Diet low in fibre	Dietary intake of fibre from all sources including fruits, vegetables, grains, legumes, and pulses	Colon and rectum cancers; IHD	Age ≥25 years	Nutrition and health surveys	DisMod 3	Mean of 30 g/day (SD 3 g/day)	World Cancer Research Fund and American Institute for Cancer Research,[82] Pereira and colleagues[88]
8.10. Diet low in calcium	Dietary intake of calcium from all sources, including milk, yogurt, and cheese	Colon and rectum cancers; prostate cancer	Age ≥25 years	Nutrition and health surveys	DisMod 3	Mean of 1200 mg/day (SD 120 mg/day)	World Cancer Research Fund and American Institute for Cancer Research,[82] Cho and colleagues[89]
8.11. Diet low in seafood omega-3 fatty acids	Dietary intake of eicosapentaenoic acid and docosahexaenoic acid, measured in mg/day	Death caused by IHD	Age ≥25 years	Nutrition and health surveys	DisMod 3	250 mg/day	Updated published review of Mozaffarian and colleagues[90]
8.12. Diet low in polyunsaturated fatty acids	Dietary intake of omega-6 fatty acids from all sources, mainly liquid vegetable oils, including soybean oil, corn oil, and safflower oil	IHD	Age ≥25 years	Nutrition and health surveys	DisMod 3	Substitution of present saturated fatty acid intake up to a mean intake of polyunsaturated fatty acids of 12% of energy (SD 1·2%)	Jakobsen and colleagues,[91] Mozaffarian and colleagues[92]
8.13. Diet high in trans fatty acids	Dietary intake of trans fat from all sources, mainly partially hydrogenated vegetable oils and ruminant products	IHD	Age ≥25 years	Nutrition and health surveys	DisMod 3	Mean of 0·5% of energy (SD 0·05%)	Mozaffarian and colleagues[93]
8.14. Diet high in sodium	24 h urinary sodium, measured in mg/day	Stomach cancer; systolic blood pressure which has effects on: RHD; IHD; ischaemic stroke, haemorrhagic and other non-ischaemic stroke; HHD; the aggregate of cardiomyopathy and myocarditis and endocarditis; the aggregate of atrial fibrillation and flutter, PVD, and other CVD; aortic aneurysm; CKD	Age ≥25 years	Nutrition and health surveys	DisMod 3	Mean of 1000 mg/day (SD 100 mg/day)	Re-analysis of observational studies for stomach cancer and randomised studies for blood pressure lowering[82,94]
8.15. Physical inactivity and low physical activity*	Proportion of the population in categories of physical activity: level 0, <600 MET-minutes per week (inactive); level 1, 600–3999 MET-minutes per week (low-active); level 2, 4000–7999 MET-minutes per week (moderately active); and level 3, ≥8000 MET-minutes per week (highly active)	Breast cancer; colon and rectum cancers; diabetes mellitus; IHD; ischaemic stroke	Age ≥25 years	Population surveys	DisMod 3	All individuals are highly active (level 3)	Danaei and colleagues[11]
9. Occupational risk factors							
9.1. Occupational carcinogens							
9.1.1. Occupational exposure to asbestos	Cumulative exposure to asbestos using mesothelioma in a smoking impact ratio analogue	Ovarian cancer; other neoplasms; larynx cancer; trachea, bronchus, and lung cancers	Age ≥15 years	Vital registration mortality data, asbestos production, import, and export statistics	Spatiotemporal Gaussian process regression[19–21]	No exposure to asbestos	Published studies[95–98]

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	Exposure definition	Outcomes	Subgroup	Main data sources for exposure	Exposure estimation method	Theoretical-minimum-risk exposure distribution	Source of relative risks
(Continued from previous page)							
9.1.2. Occupational exposure to arsenic	Proportion of population ever exposed (by taking into account worker turnover)[99,100] based on distribution of the population in nine industries†	Trachea, bronchus, and lung cancers	Age ≥15 years	Labour force surveys, censuses, and International Information System on Occupational Exposure to Carcinogens	Spatiotemporal Gaussian process regression[19–21]	No occupational exposure to carcinogens	Lee-Feldstein[101]
9.1.3. Occupational exposure to benzene	Proportion of population ever exposed (by taking into account worker turnover)[99,100] based on distribution of the population in nine industries†	Leukaemia	Age ≥15 years	Labour force surveys, censuses, and International Information System on Occupational Exposure to Carcinogens	Spatiotemporal Gaussian process regression[19–21]	No occupational exposure to carcinogens	Khalade and colleagues[102]
9.1.4. Occupational exposure to beryllium	Proportion of population ever exposed (by taking into account worker turnover)[99,100] based on distribution of the population in nine industries†	Trachea, bronchus, and lung cancers	Age ≥15 years	Labour force surveys, censuses, and International Information System on Occupational Exposure to Carcinogens	Spatiotemporal Gaussian process regression[19–21]	No occupational exposure to carcinogens	Schubauer-Berigan and colleagues[103]
9.1.5. Occupational exposure to cadmium	Proportion of population ever exposed (by taking into account worker turnover)[99,100] based on distribution of the population in nine industries†	Trachea, bronchus, and lung cancers	Age ≥15 years	Labour force surveys, censuses, and International Information System on Occupational Exposure to Carcinogens	Spatiotemporal Gaussian process regression[19–21]	No occupational exposure to carcinogens	Hutchings and colleagues[95]
9.1.6. Occupational exposure to chromium	Proportion of population ever exposed (by taking into account worker turnover)[99,100] based on distribution of the population in nine industries†	Trachea, bronchus, and lung cancers	Age ≥15 years	Labour force surveys, censuses, and International Information System on Occupational Exposure to Carcinogens	Spatiotemporal Gaussian process regression[19–21]	No occupational exposure to carcinogens	Rosenman and colleagues[104]
9.1.7 Occupational exposure to diesel engine exhaust	Proportion of population ever exposed (by taking into account worker turnover)[99,100] based on distribution of the population in nine industries†	Trachea, bronchus and lung cancers	Age ≥15 years	Labour force surveys, censuses, and International Information System on Occupational Exposure to Carcinogens	Spatiotemporal Gaussian process regression[19–21]	No occupational exposure to carcinogens	Lipsett and colleagues[105]
9.1.8. Occupational exposure to second-hand smoke	Proportion of population ever exposed (by taking into account worker turnover)[99,100] based on distribution of the population in nine industries†	Trachea, bronchus, and lung cancers	Age ≥15 years	Labour force surveys, censuses, and International Information System on Occupational Exposure to Carcinogens	Spatiotemporal Gaussian process regression[19–21]	No occupational exposure to carcinogens	Stayner and colleagues[106]
9.1.9. Occupational exposure to formaldehyde	Proportion of population ever exposed (by taking into account worker turnover)[99,100] based on distribution of the population in nine industries†	Leukaemia; nasopharynx cancer	Age ≥15 years	Labour force surveys, censuses, and International Information System on Occupational Exposure to Carcinogens	Spatiotemporal Gaussian process regression[19–21]	No occupational exposure to carcinogens	Collins and colleagues,[107] Hauptmann and colleagues[108]
9.1.10. Occupational exposure to nickel	Proportion of population ever exposed (by taking into account worker turnover)[99,100] based on distribution of the population in nine industries†	Trachea, bronchus, and lung cancers	Age ≥15 years	Labour force surveys, censuses, and International Information System on Occupational Exposure to Carcinogens	Spatiotemporal Gaussian process regression[19–21]	No occupational exposure to carcinogens	Grimsrud and colleagues[109,110]
9.1.11. Occupational exposure to polycyclic aromatic hydrocarbons	Proportion of population ever exposed (by taking into account worker turnover)[99,100] based on distribution of the population in nine industries†	Trachea, bronchus, and lung cancers	Age ≥15 years	Labour force surveys, censuses, and International Information System on Occupational Exposure to Carcinogens	Spatiotemporal Gaussian process regression[19–21]	No occupational exposure to carcinogens	Armstrong and colleagues[111]
9.1.12. Occupational exposure to silica	Proportion of population ever exposed (by taking into account worker turnover)[99,100] based on distribution of the population in nine industries†	Trachea, bronchus, and lung cancers	Age ≥15 years	Labour force surveys, censuses, and International Information System on Occupational Exposure to Carcinogens	Spatiotemporal Gaussian process regression[19–21]	No occupational exposure to carcinogens	Kurihara and colleagues[112]
9.1.13. Occupational exposure to sulphuric acid	Proportion of population ever exposed (by taking into account worker turnover)[99,100] based on distribution of the population in nine industries†	Larynx cancer	Age ≥15 years	Labour force surveys, censuses, and International Information System on Occupational Exposure to Carcinogens	Spatiotemporal Gaussian process regression[19–21]	No occupational exposure to carcinogens	Soskolne and colleagues[113]

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	Exposure definition	Outcomes	Subgroup	Main data sources for exposure	Exposure estimation method	Theoretical-minimum-risk exposure distribution	Source of relative risks
(Continued from previous page)							
9.2. Occupational asthmagens	Proportion of population exposed based on distribution of the population in eight occupational groups (professional, technical, and related workers; administrative and managerial workers; clerical and related workers; sales workers; service workers; agriculture, animal husbandry, and forestry workers, fishermen and hunters; production and related workers; and transport equipment operators and labourers)	Asthma	Age ≥15 years	Labour force surveys and censuses	Spatiotemporal Gaussian process regression[19–21]	Background asthmagen exposures	Published studies[114–116]
9.3. Occupational particulate matter, gases, and fumes	Proportion of population exposed based on distribution of the population in nine industries†	COPD	Age ≥15 years	Labour force surveys and censuses	Spatiotemporal Gaussian process regression[19–21]	No occupational exposure to particulates, gases, or fumes	New meta-analysis
9.4. Occupational noise	Proportion of population exposed based on distribution of the population in nine industries†	Hearing loss	Age ≥15 years	Labour force surveys and censuses	Spatiotemporal Gaussian process regression[19–21]	Background noise exposure	New meta-analysis
9.5. Occupational risk factors for injuries	Fatal occupational injury	..	Age ≥15 years	International Labour Organization injury database	Spatiotemporal Gaussian process regression[19–21]	Five injury deaths per 1 000 000 person-years	..
9.6. Occupational low back pain	Proportion of population exposed based on distribution of the population in eight occupational groups (professional, technical, and related workers; administrative and managerial workers; clerical and related workers; sales workers; service workers; agriculture, animal husbandry, and forestry workers, fishermen and hunters; production and related workers; and transport equipment operators and labourers)	Low back pain	Age ≥15 years	Labour force surveys and censuses	Spatiotemporal Gaussian process regression[19–21]	All individuals have the ergonomic factors of clerical and related workers	New meta-analysis
10. Sexual abuse and violence							
10.1. Childhood sexual abuse*	Proportion of the population who have ever experienced childhood sexual abuse, defined as the experience with an older person of unwanted non-contact, contact abuse, or intercourse, when aged 15 years or younger	Alcohol use disorders, unipolar depressive disorders, intentional self-harm	All ages	Population surveys and epidemiological studies	DisMod 3	No childhood sexual abuse	New meta-analysis
10.2. Intimate partner violence*	Proportion of the population who have ever experienced one or more acts of physical or sexual violence by a present or former partner since age 15 years	Abortion, unipolar depressive disorders, intentional self-harm, interpersonal violence	Age 15–49 years for abortion, ≥15 years for all others	Population surveys and epidemiological studies	DisMod 3	No intimate partner violence	New meta-analysis, Beydoun and colleagues[117]

IHD=ischaemic heart disease. COPD=chronic obstructive pulmonary disease. CVD=cardiovascular and circulatory diseases. RHD=rheumatic heart disease. PVD=peripheral vascular disease. CKD=chronic kidney disease. HHD=hypertensive heart disease *Not assessed for 1990 because of absence of exposure data. †Agriculture, hunting, forestry, and fishing; mining and quarrying; wholesale and retail trade and restaurants and hotels; manufacturing; electricity, gas, and water; transport, storage, and communication; construction; financing, insurance, real estate, and business services; and community, social, and personal services.

Table 1: **Risk factors included, exposure variables, theoretical-minimum-risk exposure distributions, and outcomes affected**

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diameter ($PM_{2.5}$) in ambient air: TM5 estimates—based on a nested three-dimensional global atmospheric chemistry transport model—which simulates both particulate matter and ozone at a high spatial resolution;[22,23,121] and satellite-based estimates, which are based on satellite observations of aerosol optical depth, a measure of light extinction by aerosols in the total atmospheric column.[25] TM5 and satellite-based estimates of $PM_{2.5}$, measured in μg/m³, were averaged at a 0·1°×0·1° grid cell resolution (equivalent to roughly 11 km×11 km at the equator) and linked to available measures of $PM_{2.5}$ from ground-based monitors. We used a regression model with the average of TM5 and satellite-based estimates as the predictor to estimate ground-based $PM_{2.5}$ for all grid cells.[26] For ozone, we relied solely on the TM5 model.

Few population-based surveys have measured zinc deficiency based on serum zinc concentration;[122] however, intervention trials show a benefit of zinc supplementation for reduction of diarrhoea and lower respiratory infections in populations that have high zinc deficiency.[10] Because of the paucity of data for serum zinc concentrations, we measured zinc deficiency at the population level on the basis of dietary sources of zinc, expanding on previous work of the International Zinc Nutrition Consultative Group.[123] This approach uses national food balance sheets produced by the UN Food and Agriculture Organization to estimate a country-specific mean fractional absorption of zinc. The estimated mean daily per person amount of absorbable zinc in the food supply was compared with the mean physiological requirements of the population to calculate the percentage of the population with inadequate zinc intake.

Panel: The World Cancer Research Fund grading system[118]

Convincing evidence
Evidence based on epidemiological studies showing consistent associations between exposure and disease, with little or no evidence to the contrary. The available evidence is based on a substantial number of studies including prospective observational studies and where relevant, randomised controlled trials of sufficient size, duration, and quality showing consistent effects. The association should be biologically plausible.

Probable evidence
Evidence based on epidemiological studies showing fairly consistent associations between exposure and disease, but for which there are perceived shortcomings in the available evidence or some evidence to the contrary, which precludes a more definite judgment. Shortcomings in the evidence may be any of the following: insufficient duration of trials (or studies); insufficient trials (or studies) available; inadequate sample sizes; or incomplete follow-up. Laboratory evidence is usually supportive. The association should be biologically plausible.

Possible evidence
Evidence based mainly on findings from case-control and cross-sectional studies. Insufficient randomised controlled trials, observational studies, or non-randomised controlled trials are available. Evidence based on non-epidemiological studies, such as clinical and laboratory investigations, is supportive. More trials are needed to support the tentative associations, which should be biologically plausible.

Insufficient evidence
Evidence based on findings of a few studies which are suggestive, but insufficient to establish an association between exposure and disease. Little or no evidence is available from randomised controlled trials. More well-designed research is needed to support the tentative associations.

Effects of risk factors on disease outcomes

Table 1 shows the sources of effect sizes per unit of exposure for each risk factor. Some effect sizes were based on meta-analyses of epidemiological studies. For several risk factors without recent systematic reviews or for which evidence had not recently been synthesised, new meta-analyses were done as part of GBD 2010. We used effect sizes that had been adjusted for measured confounders but not for factors along the causal pathway. For example, effect sizes for body-mass index were not adjusted for blood pressure. For some risk–outcome pairs, evidence is only available for the relative risk (RR) of morbidity or mortality. In these cases, we assumed that the reported RR would apply equally to morbidity or mortality, unless evidence suggested a differential effect. For example, studies of ambient particulate matter pollution suggest a smaller effect on incidence of cardiovascular and respiratory disease than on mortality;[124–126] the published work on consumption of seafood omega-3 fatty acids suggests an effect on ischaemic heart disease mortality but not on incidence of ischaemic heart disease.[90]

Evidence for the RR of diarrhoea from unimproved water and sanitation is complicated by the complexity of available epidemiological studies, since the comparison groups varied greatly between studies. The comparison group used varied widely. For example, some studies compare an improved water source (eg, piped water) with an unimproved water source (eg, river water); in other studies the comparison is between two different types of improved water source (eg, piped water *vs* a protected well). Furthermore, studies often examine a combination of water, sanitation, and hygiene interventions. Previous reviews have yielded conflicting results about the magnitude of the effect sizes.[127–131]

We re-examined the epidemiological evidence for the effects of water and sanitation by reviewing the relation between water, sanitation and hygiene, and diarrhoea, starting with previous reviews.[128–131] We did a meta-regression of 119 studies that was designed to adjust for intervention and baseline group characteristics. First, we compared indicator variables for each of the intervention components (improved sanitation, hygiene, point-of-use water treatment, source water treatment, and piped water) with a reference category (improved water source). Second, we also included indicator variables for the baseline characteristics—ie, whether the baseline was an unimproved or improved water source or sanitation—as covariates to account for the heterogeneous control groups. Our analysis showed a significant effect of both improved water and improved sanitation compared with unimproved water and sanitation; we did not note a

significantly greater effect of piped water or point-of-use or source water treatment compared with improved water.

Particulate matter smaller than 2·5 μm is a common useful indicator of the risk associated with exposure to a mixture of pollutants from diverse sources and in different environments, including ambient particulate matter pollution from transportation, wind-blown dust, burning of biomass, and industrial sources; second-hand smoke; burning of biomass and coal for household energy; and active smoking.[132,133] However, existing studies cover only small concentration ranges—for example, ambient particulate matter pollution studies have been restricted to yearly average concentrations of particulate matter smaller than 2·5 μm of roughly 5 μg/m^3 to 30 μg/m^3[3,134–137] but much higher concentrations of ambient particulate matter have been recorded in polluted cities in Asia and elsewhere. The relation between concentration of small particulate matter and risk of disease is probably non-linear.[132,133]

To inform estimates of risk across the full range of concentrations, we used the approach of Pope and colleagues[132] and integrated epidemiological evidence for the hazardous effects of particulate matter at different concentrations from different sources and environments. Methods for estimation of the integrated exposure–response curves for each cause are described elsewhere.[138] Briefly, we compiled study-level estimates of the RR of mortality associated with any or all of ambient air pollution, second-hand smoke, household air pollution, and active smoking for the following outcomes: ischaemic heart disease, stroke, lung cancer, chronic obstructive pulmonary disease, and acute lower respiratory tract infection in children. We evaluated several non-linear functions with up to three parameters for fitting the integrated exposure–response relation and assessed them by calculation of the root mean squared error. An exponential decay with a power of concentration was the functional form that provided the best fit for all five outcomes. The integrated exposure–response curve was then used to generate effect sizes specific to the amount of ambient particulate matter smaller than 2·5 μm for each population. For ischaemic heart disease and stroke, evidence shows that household air pollution affects intermediate outcomes, such as blood pressure,[139] but not clinical events. For acute lower respiratory tract infection, the integrated exposure–response curve enabled us to extrapolate beyond the partial exposure–response measured in the RESPIRE trial.[140] For effects of household air pollution on chronic obstructive pulmonary disease and lung cancer we use the effect size based on new systematic reviews and meta-analyses.

Several dietary factors affect ischaemic heart disease and stroke, including consumption of fruits, vegetables, nuts and seeds, whole grains, processed meat, polyunsaturated fats, and seafood omega-3 fatty acids.[81,83,85,87,90–92,141,142] We updated earlier systematic reviews and meta-analyses for fruits, vegetables, and seafood omega-3 fatty acids, which included both observational and intervention studies if available. A systematic review[143] of randomised clinical trials of supplementation with seafood omega-3 fatty acids reported non-significant effects on several outcomes, and a significant effect for mortality from ischaemic heart disease—the primary outcome in GBD 2010. In view of this finding, we tested whether a significant difference exists between the randomised clinical trials of seafood omega-3 fatty acid supplementation and observational studies of seafood-omega 3 fatty acid intake. The effect of seafood omega-3 fatty acids tended to be lower in randomised controlled trials than in observational studies, however, this difference was not statistically significant (p=0·057). Therefore, we used the effect size based on the combination of randomised clinical trials and observational studies but also did a sensitivity analysis with the effect size based on randomised clinical trials.

Estimates of the RR associated with dietary risk factors are based largely on observational studies that control for age, sex, and other cardiovascular risk factors. However, some early observational studies do not fully control for other dietary components. Protective dietary risk factors such as consumption of fruits, vegetables, and whole grains, tend to be positively correlated with each other and negatively correlated with harmful dietary risk factors such as consumption of processed meat. Therefore, RRs estimated for single risk factors in observational studies could overestimate the protective or harmful effect of that risk factor. In effect, the partially adjusted RR will include some of the effects associated with other correlated diet components, particularly since the exposure measure for dietary risk factors is energy adjusted to a standard calorie intake.

To examine this issue, we did further empirical assessments using studies of dietary patterns and randomised controlled feeding studies. Studies of dietary patterns[144–148] have estimated the effects of beneficial diets (prudent or Mediterranean diets) and harmful diets (western diets); these studies capture the overall effects of differences in dietary components. For example, a prudent diet has lots of fruits, vegetables, fish, and whole grains. For each of the dietary pattern studies we computed the estimated RR for dietary pattern groups with the RRs from the meta-analyses of single dietary risk factors, the reported differences in dietary intake, and assuming a multiplicative relation between RRs for individual components. Results of this internal validation study show that overall, estimation of the effect of dietary pattern based on the RRs reported for single risk factors was much the same as the effect reported in the study; across four large cohort studies of seven dietary patterns the average ratio for the estimated RR reduction compared with the measured RR reduction was 0·98.

In addition to the dietary pattern studies, we also investigated the evidence for the effects of dietary risk factors from randomised controlled feeding studies, such as DASH[149] and OmniHeart,[150] which measured the effect of dietary changes on blood pressure and LDL cholesterol. We used meta-regression to estimate the pooled effect of

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fruits, vegetables, nuts and seeds, whole grains, fish, and dietary fibre on systolic blood pressure and LDL cholesterol, based on all randomised controlled feeding studies (six treatment groups from three studies for blood pressure and six treatment groups from two studies for cholesterol). When translated into an effect using the RRs of blood pressure and cholesterol for ischaemic heart disease, the average ratio of the estimated to measured RR reduction was 1·07 for all components and 0·85 when excluding fish, which has mechanisms additional to lowering blood pressure and cholesterol.[151] These two supplementary analyses suggest that the RRs estimated in the meta-analyses of single dietary risk factors are unlikely to be significantly biased because of residual confounding due to other diet components.

Pooled epidemiological studies of cardiovascular disease risks show that the RR decreases with age, and that the inverse age association is roughly log-linear. Based on a pooled analysis of several risk factors (high blood pressure, high fasting plasma glucose, high total cholesterol, and tobacco smoking), the age at which the RR reaches 1 is often between 100 and 120 years. We therefore estimated age-specific RRs for all cardiovascular risk factors by meta-regression of available data with logRR as the dependent variable and median age at event as the independent variable with an age intercept (RR=1) at age 110 years. Uncertainty in the RR was generated by simulation analyses.[152]

	Disability-adjusted life-years (%)
Physiological risk factors	
High blood pressure	53%
High total cholesterol	29%
High body-mass index	23%
High fasting plasma glucose	16%
Alcohol use	5%
Tobacco smoking, including second-hand smoke	31%
Dietary risk factors and physical inactivity	
Diet low in nuts and seeds	40%
Physical inactivity and low physical activity	31%
Diet low in fruits	30%
Diet low in seafood omega-3 fatty acids	22%
Diet low in whole grains	17%
Diet high in sodium	17%
Diet high in processed meat	13%
Diet low in vegetables	12%
Diet low in fibre	11%
Diet low in polyunsaturated fatty acids	9%
Diet high in trans fatty acids	9%
Diet high in sugar-sweetened beverages	2%
Air pollution	
Ambient particulate matter pollution	22%
Household air pollution from solid fuels	18%
Other environmental risks	
Lead exposure	4%

Table 2: **Proportion of ischaemic heart disease disability-adjusted life-years attributable to individual risk factors, worldwide, 2010**

The causal association between a risk factor and a disease outcome is often informed by a wider body of evidence than epidemiological studies of RRs for specific measures of exposure, especially when disease-specific and age-specific RRs are needed. For example, although smoking is an established cause of cardiovascular diseases, when cohorts are analysed in fine age groups, the 95% CI for the effect of smoking on stroke spans 1·0 in several age groups.[38] Similarly, randomised trials of zinc supplementation were designed to detect effects on total mortality.[36,153] Re-analysis of the same trials for disease-specific outcomes, which is necessary to extrapolate effects to populations with different causes of death, reduced their statistical power and gave 95% CIs that spanned 1·0. To use the broad evidence while accounting for the uncertainty of the subgroup RRs, we included in the uncertainty analysis all draws of the RR distribution, including those that show a protective effect as long as the overall relation for the risk factor across all ages is significant. In other cases, if there are different degrees of exposure for a risk factor, in some exposure categories the RR might not be significant. We have included draws from these posterior distributions if the mean values show a dose–response relation. To fairly represent the extent of our epidemiological knowledge, we have included in the uncertainty analysis draws from the posterior distribution for those exposure categories that show a protective effect.

Theoretical-minimum-risk exposure distributions for counterfactual comparison

In the comparative risk assessment framework, disease burden attributable to risk factors is calculated with reference to an alternative (counterfactual) distribution of exposure; in GBD 2010, we used an optimal exposure distribution (in terms of effect on population health), termed the theoretical-minimum-risk exposure distribution. For several risk factors, such as tobacco smoking, the choice of theoretical-minimum-risk exposure distribution is clear—ie, 100% of the population being lifelong non-smokers. However, for many of the other risk factors zero exposure is not possible (eg, blood pressure), or the lowest amount of exposure that is still beneficial is not yet established. In these cases the theoretical-minimum-risk exposure distribution was informed by two considerations: the availability of convincing evidence from epidemiological studies that support a continuous reduction in risk of disease to the chosen distribution; and a distribution that is theoretically possible at the population level (table 1).

For some risk factors, new evidence has resulted in a revision of the theoretical-minimum-risk exposure distribution compared to the previous comparative risk assessment. For example, the previous distribution for systolic blood pressure was a mean of 115 mm Hg (SD 6).[6] However, subsequent randomised trials[154] of blood

pressure-lowering medication suggest that the benefits of lowering blood pressure could continue to 110 mm Hg or lower. On this basis, we changed the theoretical-minimum-risk exposure distribution to a mean of 110–115 mm Hg (SD 6). For other exposures, the distribution was increased because of data from new epidemiological studies[75]—eg, for mean body-mass index we used 21–23 kg/m², compared with 21 kg/m² used previously.

For ambient particulate matter pollution, we did a sensitivity analysis with an alternative theoretical-minimum-risk exposure distribution that included the effect of regional dust particulate matter. We did so because although particulate exposure from dust could theoretically be reduced, it would probably be prohibitively expensive and could only be done over a very long period. This factor is particularly relevant in areas with high amounts of dust—eg, deserts. Dusty grid cells were identified as those with an ambient air concentration of $PM_{2.5}$ of 36 μg/m³ or more and where the dust fraction from the TM5 chemical transport model was 50% or more.

Mortality and disease burden attributable to individual and clusters of risk factors

We calculated the burden attributable to risk factors with continuous exposure by comparing the present distribution of exposure to the theoretical-minimum-risk exposure distribution for each age group, sex, year (1990 and 2010), and cause according to the following formula:

$$PAF=\frac{\int_{x=0}^{m} RR(x)P1(x)dx-\int_{x=0}^{m} RR(x)P2(x)dx}{\int_{x=0}^{m} RR(x)P1(x)dx}$$

Where PAF is the population attributable fraction (burden attributable to risk factor), RR(x) is the RR at exposure level x, P1(x) is the (measured or estimated) population distribution of exposure, P2(x) is the counterfactual distribution of exposure (ie, the theoretical-minimum-risk exposure distribution), and m the maximum exposure level.[4]

Burden attributable to categorical exposures was calculated by comparing exposure categories to a reference category for each age, sex, year, and cause according to the following formula:

$$PAF=\frac{\sum_{i=1}^{n} P_i(RR_i-1)}{\sum_{i=1}^{n} P_i(RR_i-1)+1}$$

Where RR_i is the RR for exposure category i, P_i is the fraction of the population in exposure category i, and n is the number of exposure categories.[4]

We calculated the burden attributable to clusters of risk factors by computing the combined population attributable fraction for risk factors for each age, sex, year, and cause according to the following formula:

$$PAF=1-\prod_{r=1}^{R}(1-PAF_r)$$

Where r is each individual risk factor, and R is the number of risk factors. This approach assumes that risk factors are independent—ie, it does not account for mediation, exposure correlation, or effect size modification that might exist between risk factors in a cluster.[155]

To represent uncertainty in the estimates we used simulation analysis to take 1000 draws from the posterior distribution of exposure, RR, and each relevant outcome for each age, sex, country, year. We accounted for the correlation structure of uncertainty (ie, whether exposure in a country, age group, and sex is high or low might be related to whether it is high or low in other subgroups) by use of the same draw of exposure across different outcomes and the same draw of RR across country, age, and sex subgroups when the RR does not vary by country, age, or sex. We otherwise assumed that the uncertainties in exposure, RR, and underlying burden attributable to the outcome were independent.

We computed the mean deaths and DALYs attributable to each risk factor and risk factor cluster from the 1000 draws. The 95% uncertainty intervals (95% UI) were calculated as the 2·5th and 97·5th percentiles of the 1000 draws. We also computed the mean rank and 95% UI for the 43 risk factors included in the ranking list. The mean of the ranks for a risk factor was not necessarily equivalent to the rank of the mean deaths or mean DALYs attributable to the risk factor.

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Results

Quantification of risk factors in this analysis represents the effects of each individual risk factor, holding all other independent factors constant. The effects of multiple risk factors are not a simple addition of the individual effects and are often smaller than their sums,[156] especially for cardiovascular diseases, which are affected by several risk factors (eg, table 2). The sum of the individual effects of just the metabolic risk factors at the global level is 121% and the summation of all the risks is greater than 400%.

We estimated global attributable mortality and DALYs with uncertainty for 1990, and 2010, for each of the 67 risk factors and clusters of risk factors (table 3, 4). The appendix shows full results by region, year, age, and sex for attributable deaths and DALYs. Because of the interest in

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	Men		Women		Both sexes	
	1990	2010	1990	2010	1990	2010
Unimproved water and sanitation	365 244 (18 940–662 551)	171 097 (6841–326 262)	350 629 (17 531–638 433)	166 379 (6690–326 989)	715 873 (36 817–1 279 220)	337 476 (13 150–648 205)
Unimproved water source	147 857 (10 566–282 890)	59 463 (3880–120 264)	140 150 (10 042–271 546)	56 663 (3604–115 704)	288 007 (20 641–553 293)	116 126 (7518–233 136)
Unimproved sanitation	252 779 (8032–480 822)	123 255 (2924–242 588)	244 207 (7348–460 913)	120 851 (3104–242 452)	496 986 (15 380–927 845)	244 106 (6027–478 186)
Air pollution	..	..	..	..	..	..
Ambient particulate matter pollution	1 549 448 (1 345 894–1 752 880)	1 850 428 (1 614 010–2 082 474)	1 360 712 (1 166 992–1 559 747)	1 373 113 (1 187 639–1 563 793)	2 910 161 (2 546 184–3 286 508)	3 223 540 (2 828 854–3 619 148)
Household air pollution from solid fuels	2 251 932 (1 677 785–2 743 681)	1 867 043 (1 359 090–2 452 588)	2 221 558 (1 862 975–2 581 337)	1 611 730 (1 243 516–2 027 067)	4 473 490 (3 651 253–5 206 632)	3 478 773 (2 638 548–4 386 590)
Ambient ozone pollution	77 087 (25 256–134 021)	86 335 (30 551–153 776)	66 274 (22 424–116 663)	66 100 (21 362–115 225)	143 362 (47 539–251 885)	152 434 (52 272–267 431)
Other environmental risks	109 224 (91 805–131 511)	426 280 (341 744–541 465)	100 699 (82 720–119 745)	346 751 (281 555–413 370)	209 923 (177 673–243 565)	773 030 (640 893–929 935)
Residential radon	..	70 014 (9140–154 460)	..	28 978 (4098–64 387)	..	98 992 (13 133–215 237)
Lead exposure	109 224 (91 805–131 511)	356 266 (292 587–435 046)	100 699 (82 720–119 745)	317 772 (265 722–376 431)	209 923 (177 673–243 565)	674 038 (575 858–779 314)
Child and maternal undernutrition	1 805 224 (1 479 043–2 219 888)	739 863 (570 560–909 248)	1 668 365 (1 396 689–1 986 532)	698 442 (569 013–832 012)	3 473 589 (2 906 896–4 175 138)	1 438 305 (1 175 257–1 713 103)
Suboptimal breastfeeding	693 103 (427 028–972 440)	293 449 (175 623–429 772)	581 921 (370 598–814 551)	251 368 (155 884–359 651)	1 275 024 (802 142–1 772 745)	544 817 (338 453–775 077)
Non-exclusive breastfeeding	612 059 (354 236–875 230)	257 771 (143 116–382 459)	505 849 (302 585–720 858)	218 117 (126 383–319 470)	1 117 908 (663 274–1 576 633)	475 888 (272 493–684 422)
Discontinued breastfeeding	81 044 (8643–178 237)	35 678 (3475–79 940)	76 073 (7809–165 395)	33 251 (3091–73 804)	157 117 (16 188–341 702)	68 929 (6445–153 290)
Childhood underweight	1 198 178 (997 627–1 484 105)	458 639 (366 866–561 352)	1 065 774 (898 859–1 299 715)	401 478 (325 516–484 452)	2 263 952 (1 927 356–2 735 821)	860 117 (715 742–1 033 573)
Iron deficiency	39 409 (30 677–47 108)	32 287 (21 925–37 449)	128 675 (92 036–156 884)	87 321 (62 505–107 021)	168 084 (130 444–197 085)	119 608 (93 261–139 985)
Vitamin A deficiency	181 151 (85 775–341 439)	63 291 (32 070–104 030)	168 203 (80 696–298 163)	56 472 (28 192–91 464)	349 354 (170 504–632 149)	119 762 (61 723–191 846)
Zinc deficiency	143 518 (27 797–276 850)	52 390 (9382–105 728)	132 071 (23 716–253 841)	44 940 (7696–87 711)	275 590 (51 274–529 451)	97 330 (17 575–190 527)
Tobacco smoking (including second-hand smoke)	3 680 571 (3 213 427–4 229 530)	4 507 059 (3 757 779–5 092 460)	1 649 238 (1 380 504–2 144 408)	1 790 228 (1 278 666–2 094 260)	5 329 808 (4 778 526–6 049 296)	6 297 287 (5 395 769–7 006 942)
Tobacco smoking	3 332 192 (2 871 957–3 840 033)	4 251 424 (3 503 674–4 850 554)	1 244 106 (961 356–1 781 819)	1 443 924 (920 763–1 743 849)	4 576 298 (4 068 753–5 312 438)	5 695 349 (4 755 779–6 421 611)
Second-hand smoke	348 378 (273 555–425 310)	255 634 (191 587–314 541)	405 132 (310 224–500 100)	346 304 (252 702–439 439)	753 510 (585 131–912 313)	601 938 (447 705–745 328)
Alcohol and drug use	1 345 743 (1 196 535–1 513 476)	1 925 525 (1 712 465–2 132 787)	702 071 (570 285–844 382)	956 819 (793 785–1 121 300)	2 047 814 (1 831 313–2 270 020)	2 882 343 (2 601 098–3 161 618)
Alcohol use	1 305 926 (1 156 571–1 466 638)	1 824 119 (1 613 616–2 029 574)	682 576 (551 702–825 112)	911 393 (748 254–1 076 004)	1 988 502 (1 772 115–2 214 916)	2 735 511 (2 464 575–3 006 459)
Drug use	46 682 (33 063–78 398)	109 420 (82 297–152 421)	21 895 (15 984–31 023)	48 385 (36 780–64 303)	68 577 (50 706–102 395)	157 805 (124 639–209 873)
Physiological risk factors						
High fasting plasma glucose	1 051 401 (865 949–1 250 550)	1 749 058 (1 455 169–2 039 206)	1 052 773 (881 704–1 230 327)	1 607 214 (1 367 465–1 839 764)	2 104 174 (1 797 633–2 401 170)	3 356 271 (2 917 520–3 782 483)
High total cholesterol	936 749 (767 684–1 128 051)	961 614 (714 774–1 236 023)	1 009 172 (829 163–1 218 442)	1 057 196 (793 595–1 350 633)	1 945 920 (1 625 929–2 318 054)	2 018 811 (1 572 853–2 479 097)
High blood pressure	3 412 588 (3 089 548–3 769 223)	4 750 581 (4 272 529–5 273 576)	3 880 598 (3 559 634–4 250 099)	4 645 279 (4 198 029–5 092 003)	7 293 185 (6 701 203–7 859 894)	9 395 860 (8 579 630–10 147 805)
High body-mass index	887 047 (698 599–1 079 235)	1 632 766 (1 328 501–1 941 988)	1 076 502 (878 065–1 286 482)	1 738 466 (1 454 008–2 036 059)	1 963 549 (1 590 282–2 345 133)	3 371 232 (2 817 774–3 951 127)
Low bone mineral density	52 816 (43 822–69 605)	103 440 (67 743–124 596)	50 455 (40 408–62 110)	84 146 (57 863–102 441)	103 270 (90 672–124 230)	187 586 (140 636–219 906)

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	Men		Women		Both sexes	
	1990	2010	1990	2010	1990	2010
(Continued from previous page)						
Dietary risk factors and physical inactivity	4 473 276 (4 110 262–4 852 556)	6 687 621 (6 172 230–7 206 283)	4 057 558 (3 704 325–4 431 571)	5 815 748 (5 380 274–6 261 225)	8 530 835 (7 907 898–9 150 862)	12 503 370 (11 710 741–13 324 770)
Diet low in fruits	2 013 415 (1 570 347–2 435 112)	2 837 481 (2 203 651–3 414 649)	1 653 787 (1 269 335–2 006 693)	2 064 761 (1 593 495–2 507 876)	3 667 202 (2 870 267–4 394 152)	4 902 242 (3 818 356–5 881 561)
Diet low in vegetables	779 747 (535 472–1 041 517)	1 017 500 (687 787–1 378 721)	674 309 (441 649–910 150)	779 754 (521 285–1 040 304)	1 454 057 (978 665–1 924 334)	1 797 254 (1 205 059–2 394 366)
Diet low in whole grains	649 676 (503 984–787 057)	963 640 (748 116–1 162 721)	580 600 (447 140–706 303)	762 171 (592 879–919 709)	1 230 276 (958 136–1 489 812)	1 725 812 (1 342 896–2 067 224)
Diet low in nuts and seeds	1 041 726 (667 481–1 349 266)	1 389 433 (890 869–1 817 734)	872 483 (541 757–1 147 258)	1 082 390 (663 158–1 441 054)	1 914 209 (1 216 363–2 487 874)	2 471 823 (1 559 603–3 226 994)
Diet low in milk	34 838 (10 464–58 211)	54 093 (16 106–91 527)	33 312 (9745–57 799)	46 858 (13 085–80 413)	68 150 (20 479–114 435)	100 951 (29 728–171 340)
Diet high in red meat	13 888 (3859–23 763)	21 330 (6175–37 340)	12 551 (3425–22 054)	16 762 (4306–29 007)	26 439 (7374–45 232)	38 092 (10 749–65 727)
Diet high in processed meat	397 198 (85 536–688 905)	473 562 (103 608–842 923)	334 476 (71 692–584 050)	367 296 (83 446–637 120)	731 675 (158 044–1 257 423)	840 857 (188 952–1 460 279)
Diet high in sugar-sweetened beverages	100 250 (69 485–134 139)	161 042 (111 700–219 563)	83 548 (53 949–117 567)	138 480 (91 257–203 236)	183 799 (127 938–240 028)	299 521 (212 310–403 716)
Diet low in fibre	333 603 (149 007–521 712)	441 895 (201 062–693 234)	250 541 (111 867–394 088)	300 994 (134 201–470 634)	584 144 (260 065–914 729)	742 888 (334 379–1 166 933)
Diet low in calcium	48 975 (32 814–66 562)	76 413 (51 653–103 188)	33 330 (23 008–43 904)	49 181 (34 016–63 592)	82 305 (57 324–108 535)	125 594 (88 323–164 800)
Diet low in seafood omega-3 fatty acids	576 646 (418 376–735 746)	793 650 (574 241–1 010 930)	466 440 (337 205–601 988)	596 246 (437 287–764 762)	1 043 085 (757 418–1 327 627)	1 389 896 (1 010 300–1 781 401)
Diet low in polyunsaturated fatty acids	248 677 (117 929–381 787)	306 296 (140 873–473 149)	199 388 (95 418–305 733)	227 307 (108 675–350 194)	448 065 (213 262–687 396)	533 603 (245 096–820 854)
Diet high in trans fatty acids	202 725 (144 395–260 843)	293 087 (209 155–371 284)	164 736 (117 395–211 588)	222 173 (160 511–283 740)	367 461 (265 936–467 609)	515 260 (371 081–649 451)
Diet high in sodium	1 197 713 (776 962–1 589 448)	1 732 870 (1 122 107–2 301 781)	1 047 642 (666 779–1 397 486)	1 371 438 (878 780–1 834 541)	2 245 355 (1 459 900–2 966 107)	3 104 308 (2 016 734–4 105 019)
Physical inactivity and low physical activity	..	1 547 833 (1 264 464–1 835 192)	..	1 636 107 (1 369 722–1 899 182)	..	3 183 940 (2 657 204–3 718 963)
Occupational risk factors	694 403 (541 113–858 435)	749 857 (580 954–941 322)	116 743 (74 642–164 679)	102 250 (68 744–140 097)	811 146 (623 674–1 010 107)	852 107 (659 652–1 062 443)
Occupational carcinogens	55 306 (37 867–80 887)	92 154 (57 261–127 678)	16 766 (11 866–24 842)	25 943 (15 498–37 074)	72 073 (50 753–101 233)	118 097 (77 249–160 431)
Occupational exposure to asbestos	17 024 (11 044–26 605)	26 563 (14 454–36 593)	6033 (4012–9397)	7047 (3312–9681)	23 057 (16 939–33 009)	33 610 (20 317–43 647)
Occupational exposure to arsenic	1155 (446–2210)	1915 (717–3496)	463 (176–915)	747 (275–1402)	1618 (622–3039)	2662 (1011–4860)
Occupational exposure to benzene	993 (426–1757)	1542 (618–2706)	770 (292–1422)	1189 (434–2156)	1764 (741–3085)	2731 (1111–4811)
Occupational exposure to beryllium	61 (24–110)	114 (44–192)	26 (10–47)	49 (19–86)	87 (35–152)	163 (65–276)
Occupational exposure to cadmium	214 (97–370)	410 (179–670)	74 (33–130)	145 (62–245)	288 (131–494)	555 (249–901)
Occupational exposure to chromium	729 (431–1133)	1361 (720–2014)	293 (171–490)	570 (295–858)	1022 (618–1578)	1931 (1140–2799)
Occupational exposure to diesel engine exhaust	10 979 (6241–17 555)	18 773 (9641–28 714)	2060 (1180–3422)	3413 (1709–5262)	13 040 (7494–20 486)	22 187 (12 180–33 213)
Occupational exposure to second-hand smoke	10 171 (6878–15 272)	17 189 (10 127–23 037)	3854 (2637–6207)	7046 (3935–9630)	14 025 (10 058–19 715)	24 235 (16 094–31 803)
Occupational exposure to formaldehyde	299 (117–584)	486 (185–939)	179 (77–325)	245 (97–456)	478 (202–877)	731 (301–1361)
Occupational exposure to nickel	3578 (935–7585)	6443 (1616–13 317)	1425 (369–3031)	2702 (743–5679)	5004 (1331–10 489)	9145 (2449–18 834)

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	Men		Women		Both sexes	
	1990	2010	1990	2010	1990	2010
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Occupational exposure to polycyclic aromatic hydrocarbons	1638 (772–2817)	3092 (1394–5028)	492 (230–864)	993 (441–1661)	2130 (1018–3613)	4086 (1909–6567)
Occupational exposure to silica	7870 (5154–11 902)	14 205 (8244–19 702)	1185 (797–1975)	2072 (1102–2948)	9056 (6140–13 213)	16 277 (9875–22 272)
Occupational exposure to sulphuric acid	1964 (531–4383)	2606 (718–5761)	193 (55–452)	239 (74–509)	2157 (626–4707)	2845 (833–6109)
Occupational asthmagens	31 666 (15 305–62 856)	25 364 (15 642–48 748)	10 485 (5116–19 129)	8352 (4854–13 425)	42 151 (24 425–76 872)	33 716 (22 844–58 659)
Occupational particulate matter, gases, and fumes	207 366 (92 516–320 244)	171 553 (79 656–270 369)	68 281 (29 408–112 504)	47 311 (20 330–77 499)	275 647 (121 774–429 427)	218 864 (100 403–344 633)
Occupational noise	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Occupational risk factors for injuries	400 064 (308 482–507 787)	460 785 (343 904–618 319)	21 211 (16 479–27 705)	20 644 (15 628–27 414)	421 275 (329 209–529 004)	481 429 (363 778–639 590)
Occupational low back pain	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Sexual abuse and violence	..	37 429 (21 366–56 607)	..	200 930 (113 070–292 802)	..	238 359 (143 200–325 690)
Childhood sexual abuse	..	37 429 (21 366–56 607)	..	27 009 (14 290–43 424)	..	64 438 (37 339–94 174)
Intimate partner violence	..	..	..	186 365 (92 028–280 059)	..	186 365 (92 028–280 059)

No data indicates that attributable deaths were not quantified.

Table 3: **Deaths attributable to risk factors and risk factor clusters, worldwide**

Africa (Prof S Seedat PhD); **National Center for Injury Prevention and Control** (D A Sleet PhD), **Centers for Disease Control and Prevention, Baltimore, MD, USA** (S T Wiersma MD); **Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway** (Prof L J Stovner PhD); **New York University, New York City, NY, USA** (Prof G D Thurston ScD); **Voluntary Health Services, Sneha, Chennai, India** (Prof L Vijayakumar MBBS); **Royal Children's Hospital and Critical Care and Neurosciences Theme, Murdoch Children's Research Institute, Melbourne, VIC, Australia** (R Weintraub); **University of Nottingham, Nottingham, UK** (Prof H C Williams PhD); **National Acoustic Laboratories, Sydney, NSW, Australia** (W Williams PhD); **Royal Cornwall Hospital, Truro, UK** (Prof A D Woolf MBBS); **and Centre for Suicide Research and Prevention, The University of Hong Kong, Hong Kong, China** (Prof P Yip PhD)

the combined effects of multiple risk factors, we have approximated the joint effects of clusters of risk factors assuming that risk factors included in each cluster are independent. However, risk factors included in a cluster are not necessarily independent; for example, a substantial part of the burden attributable to high body-mass index is mediated through high blood pressure and high fasting plasma glucose. Others act together and risk factor exposures might be correlated at the individual level,[155] especially household air pollution and ambient particulate matter pollution, which might have common sources.

For these reasons we have not computed the joint effects for physiological risk factors or air pollution. However, the combined effects of physiological risk factors are probably large, with high blood pressure the leading single risk factor globally, accounting for 9·4 million (95% UI 8·6 million to 10·1 million) deaths and 7·0% (6·2–7·7) of global DALYs in 2010, followed by high body-mass index (3·4 million [2·8 million to 4·0 million deaths] and 3·8% [3·1–4·4] of global DALYs in 2010), high fasting plasma glucose (3·4 million [2·9 million to 3·7 million] deaths and 3·6% [3·1–4·0] of DALYs), high total cholesterol (2·0 million [1·6 million to 2·5 million] deaths and 1·6% [1·3–2·0] of DALYs), and low bone mineral density (0·2 million [0·1 million to 0·2 million] deaths and 0·21% [0·17–0·25] of DALYs).

The joint effects of air pollution are also likely to be large. Household air pollution from solid fuels accounted for 3·5 million (2·6 million to 4·4 million) deaths and 4·3% (3·4–5·3) of global DALYs in 2010 and ambient particulate matter pollution accounted for 3·1 million (2·7 million to 3·5 million) deaths and 3·1% (2·7–3·4) of global DALYs. For ambient particulate matter pollution, we also did a post-hoc sensitivity analysis excluding the effects of dust, which had a small effect worldwide—attributable global DALYs decreased by 2%—but large effects in north Africa and Middle East. Household air pollution is an important contributor to ambient particulate matter pollution; we estimate that it accounted for 16% of the worldwide burden from ambient particulate matter pollution in 2010. The effects of ambient ozone pollution, which increases the risk of chronic obstructive pulmonary disease, were smaller than those of household air pollution from solid fuels or ambient particulate matter pollution (0·2 million [0·1 million to 0·3 million] deaths and 0·1% [0·03–0·2] of global DALYs in 2010).

For other clusters of risk factors for which we approximated the joint effects assuming independence, dietary risk factors and physical inactivity were responsible for the largest disease burden: 10·0% (9·2–10·8) of global DALYs in 2010. Of the individual dietary risk factors, the largest attributable burden in 2010 was associated with diets low in fruits (4·9 million [3·8 million to 5·9 million] deaths and 4·2% [3·3–5·0] of global DALYs), followed by diets high in sodium (4·0 million [3·4 million to 4·6 million]; 2·5% [1·7–3·3]), low in nuts and seeds (2·5 million [1·6 million to 3·2 million]; 2·1% [1·3–2·7]), low in whole grains (1·7 million [1·3 million to 2·1 million]; 1·6% [1·3–1·9]), low in vegetables (1·8 million [1·2 million to

	Men		Women		Both sexes	
	1990	2010	1990	2010	1990	2010
Unimproved water and sanitation	27 045 (1409–49 439)	11 022 (458–21 162)	25 123 (1262–45 792)	10 165 (428–19 650)	52 169 (2700–93 073)	21 187 (866–40 957)
Unimproved water source	11 075 (792–21 250)	4080 (266–8172)	10 097 (722–19 424)	3694 (242–7511)	21 172 (1517–40 491)	7775 (514–15 705)
Unimproved sanitation	18 610 (593–35 486)	7735 (190–15 338)	17 441 (522–32 889)	7192 (187–14 099)	36 050 (1115–66 871)	14 927 (377–29 705)
Air pollution	..	..	..	..	..	..
Ambient particulate matter pollution	46 667 (40 185–53 381)	46 732 (41 393–52 602)	35 032 (29 974–40 402)	29 431 (25 722–33 273)	81 699 (71 012–92 859)	76 163 (68 086–85 171)
Household air pollution from solid fuels	91 432 (71 850–109 298)	60 170 (45 087–75 153)	79 261 (64 684–93 004)	47 914 (37 929–58 289)	170 693 (139 087–199 504)	108 084 (84 891–132 983)
Ambient ozone pollution	1409 (460–2456)	1440 (506–2563)	1125 (375–1990)	1016 (331–1758)	2534 (851–4426)	2456 (837–4299)
Other environmental risks	2876 (2406–3459)	9434 (7476–12 045)	2489 (1974–3015)	6617 (5322–7938)	5365 (4534–6279)	16 051 (13 212–19 503)
Residential radon	..	1514 (191–3383)	..	600 (84–1355)	..	2114 (273–4660)
Lead exposure	2876 (2406–3459)	7920 (6491–9683)	2489 (1974–3015)	6017 (4915–7231)	5365 (4534–6279)	13 936 (11 750–16 327)
Child and maternal undernutrition	175 366 (146 049–211 406)	83 202 (67 963–99 704)	164 599 (139 926–192 077)	82 894 (69 171–98 757)	339 965 (289 845–402 489)	166 095 (139 685–193 981)
Suboptimal breastfeeding	59 902 (36 953–84 059)	25 572 (15 540–37 260)	50 359 (32 186–70 526)	21 965 (13 717–31 340)	110 261 (69 615–153 539)	47 537 (29 868–67 518)
Non-exclusive breastfeeding	52 729 (30 540–75 288)	22 258 (12 464–32 936)	43 601 (26 173–62 072)	18 850 (10 926–27 569)	96 330 (57 274–135 861)	41 108 (23 668–58 913)
Discontinued breastfeeding	7173 (767–15 819)	3314 (324–7377)	6758 (696–14 710)	3114 (296–6915)	13 931 (1443–30 062)	6429 (605–14 426)
Childhood underweight	104 713 (87 668–128 697)	41 270 (33 478–50 007)	93 028 (78 656–112 766)	36 045 (29 430–43 394)	197 741 (169 224–238 276)	77 316 (64 497–91 943)
Iron deficiency	21 451 (14 947–30 321)	19 974 (13 595–28 289)	30 390 (22 473–40 703)	28 251 (20 195–39 063)	51 841 (37 477–71 202)	48 225 (33 769–67 592)
Vitamin A deficiency	15 689 (7475–29 165)	5672 (2904–9348)	14 598 (7068–25 637)	5098 (2566–8168)	30 288 (14 884–54 488)	10 770 (5625–17 149)
Zinc deficiency	12 666 (2938–23 883)	4880 (1203–9316)	11 709 (2640–22 049)	4256 (1131–7821)	24 375 (5385–45 685)	9136 (2458–16 903)
Tobacco smoking (including second-hand smoke)	104 840 (91 849–119 255)	115 496 (98 595–130 090)	46 926 (39 634–58 092)	41 342 (30 473–48 563)	151 766 (136 367–169 522)	156 838 (136 543–173 057)
Tobacco smoking	84 956 (73 038–97 937)	105 635 (88 332–120 347)	28 784 (21 829–40 090)	31 272 (19 859–38 467)	113 740 (100 454–131 675)	136 907 (117 201–153 778)
Second-hand smoke	19 884 (14 493–25 591)	9861 (7669–12 312)	18 142 (13 748–22 355)	10 070 (7931–12 429)	38 026 (28 832–47 544)	19 931 (15 707–24 223)
Alcohol and drug use	65 660 (57 545–73 925)	90 578 (79 476–101 772)	22 851 (19 812–26 197)	30 033 (26 232–34 432)	88 510 (78 717–98 794)	120 611 (107 670–134 693)
Alcohol use	55 770 (49 280–62 723)	74 662 (65 764–83 831)	17 945 (15 470–20 768)	22 575 (19 542–25 693)	73 715 (66 090–82 089)	97 237 (87 087–107 658)
Drug use	10 178 (7787–13 073)	16 248 (12 679–20 132)	4993 (3811–6417)	7562 (5922–9471)	15 171 (11 714–19 369)	23 810 (18 780–29 246)
Physiological risk factors	..	..	..	..	..	..
High fasting plasma glucose	30 177 (25 148–34 980)	49 148 (41 619–57 197)	26 181 (22 243–30 349)	39 864 (34 103–45 972)	56 358 (48 720–65 030)	89 012 (77 743–101 390)
High total cholesterol	22 519 (18 230–27 029)	23 179 (17 148–29 650)	17 006 (13 940–20 640)	17 721 (13 153–22 508)	39 526 (32 704–47 202)	40 900 (31 662–50 484)
High blood pressure	73 120 (65 538–81 302)	99 566 (88 193–110 943)	63 897 (57 903–70 789)	73 991 (66 161–81 931)	137 017 (124 360–149 366)	173 556 (155 939–189 025)
High body-mass index	25 391 (19 752–31 108)	48 310 (39 429–57 750)	26 174 (20 911–31 642)	45 300 (37 218–54 219)	51 565 (40 786–62 557)	93 609 (77 107–110 600)
Low bone mineral density	1764 (1448–2208)	3105 (2295–3831)	1361 (1102–1686)	2111 (1627–2618)	3125 (2589–3811)	5216 (4133–6418)

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	Men		Women		Both sexes	
	1990	2010	1990	2010	1990	2010
(Continued from previous page)						
Dietary risk factors and physical inactivity	102 663 (94 539–111 011)	149 576 (138 035–160 263)	74 611 (68 196–81 173)	104 757 (97 047–112 535)	177 274 (164 710–190 286)	254 333 (237 748–270 495)
Diet low in fruits	47 979 (37 530–57 842)	65 523 (51 056–78 959)	32 474 (25 061–39 155)	38 573 (29 923–46 512)	80 453 (63 298–95 763)	104 095 (81 833–124 169)
Diet low in vegetables	18 755 (12 859–24 939)	24 169 (16 503–32 480)	12 803 (8412–17 503)	14 389 (9434–19 284)	31 558 (21 349–41 921)	38 559 (26 006–51 658)
Diet low in whole grains	17 033 (13 513–20 522)	24 881 (19 486–29 709)	12 370 (9625–14 895)	15 881 (12 615–18 949)	29 404 (23 097–35 134)	40 762 (32 112–48 486)
Diet low in nuts and seeds	24 918 (16 268–31 946)	32 615 (21 258–41 958)	15 607 (9915–20 208)	18 674 (11 716–24 404)	40 525 (26 308–51 741)	51 289 (33 482–65 959)
Diet low in milk	818 (248–1366)	1171 (350–1977)	710 (210–1210)	931 (264–1605)	1527 (461–2555)	2101 (619–3544)
Diet high in red meat	642 (306–1014)	1026 (484–1629)	566 (263–903)	827 (374–1362)	1208 (571–1909)	1853 (870–2946)
Diet high in processed meat	10 477 (2801–17 479)	12 901 (4012–21 421)	6882 (2340–11 119)	8038 (2932–12 685)	17 359 (5137–27 949)	20 939 (6982–33 468)
Diet high in sugar-sweetened beverages	3085 (2120–4151)	4858 (3154–6549)	2358 (1586–3484)	3695 (2356–5255)	5443 (3769–7373)	8553 (5823–11 418)
Diet low in fibre	8485 (3787–13 262)	10 893 (4903–17 191)	4862 (2188–7562)	5559 (2500–8639)	13 347 (5970–20 751)	16 452 (7401–25 783)
Diet low in calcium	1083 (752–1406)	1570 (1113–2058)	753 (521–975)	1019 (720–1319)	1836 (1316–2368)	2590 (1873–3322)
Diet low in seafood omega-3 fatty acids	13 620 (9915–17 307)	18 300 (13 267–23 201)	8120 (5900–10 388)	9899 (7241–12 596)	21 740 (15 869–27 537)	28 199 (20 624–35 974)
Diet low in polyunsaturated fatty acids	6185 (2891–9362)	7521 (3455–11 583)	3727 (1788–5709)	4159 (1973–6396)	9912 (4655–14 976)	11 680 (5360–17 798)
Diet high in trans fatty acids	4979 (3571–6413)	7339 (5240–9300)	3085 (2226–3944)	4253 (3106–5416)	8064 (5893–10 305)	11 592 (8395–14 623)
Diet high in sodium	26 807 (17 646–35 273)	37 378 (24 639–49 428)	19 376 (12 521–25 596)	23 852 (15 544–31 682)	46 183 (30 363–60 604)	61 231 (40 124–80 342)
Physical inactivity and low physical activity	..	37 007 (30 583–43 466)	..	32 311 (27 698–37 217)	..	69 318 (58 646–80 182)
Occupational risk factors	42 660 (35 146–50 545)	48 317 (38 407–58 677)	12 754 (9357–16 658)	14 171 (10 344–18 842)	55 414 (45 312–66 718)	62 488 (49 471–76 240)
Occupational carcinogens	1346 (917–1958)	2087 (1315–2928)	412 (284–611)	594 (368–855)	1758 (1220–2477)	2681 (1773–3689)
Occupational exposure to asbestos	362 (236–555)	521 (279–709)	122 (78–189)	132 (61–184)	484 (354–695)	653 (389–840)
Occupational exposure to arsenic	29 (11–56)	45 (17–84)	12 (5–24)	18 (7–33)	41 (16–77)	63 (24–114)
Occupational exposure to benzene	36 (15–64)	52 (21–92)	28 (11–52)	40 (15–72)	65 (27–112)	92 (39–163)
Occupational exposure to beryllium	2 (1–3)	3 (1–5)	1 (0–1)	1 (0–2)	2 (1–4)	4 (2–6)
Occupational exposure to cadmium	5 (2–9)	10 (4–16)	2 (1–3)	3 (1–6)	7 (3–12)	13 (6–21)
Occupational exposure to chromium	18 (11–28)	32 (17–48)	8 (4–13)	13 (7–21)	26 (16–40)	45 (27–66)
Occupational exposure to diesel engine exhaust	278 (158–436)	442 (232–682)	54 (31–88)	81 (42–126)	332 (192–517)	523 (292–789)
Occupational exposure to second-hand smoke	257 (173–383)	405 (244–544)	100 (69–162)	167 (95–228)	358 (255–500)	572 (386–762)
Occupational exposure to formaldehyde	11 (4–20)	17 (6–31)	7 (3–13)	9 (4–16)	18 (8–32)	25 (11–47)
Occupational exposure to nickel	90 (24–191)	151 (38–312)	37 (10–79)	64 (18–132)	128 (34–266)	215 (58–443)

(Continues on next page)

	Men		Women		Both sexes	
	1990	2010	1990	2010	1990	2010
(Continued from previous page)						
Occupational exposure to polycyclic aromatic hydrocarbons	41 (19–71)	73 (33–119)	13 (6–23)	23 (10–39)	54 (26–92)	96 (45–156)
Occupational exposure to silica	199 (129–297)	333 (199–463)	31 (21–52)	49 (26–71)	230 (154–328)	382 (239–526)
Occupational exposure to sulphuric acid	52 (14–114)	66 (19–143)	5 (1–12)	6 (2–13)	57 (16–122)	71 (21–152)
Occupational asthmagens	1467 (874–2439)	1359 (917–2153)	662 (366–1062)	661 (407–994)	2129 (1419–3222)	2020 (1441–2871)
Occupational particulate matter, gases, and fumes	6808 (3162–10 425)	6682 (3293–10 311)	2745 (1216–4406)	2460 (1105–4025)	9552 (4385–14 636)	9142 (4377–14 250)
Occupational noise	1936 (1149–3103)	2284 (1348–3649)	933 (550–1489)	1167 (696–1870)	2869 (1698–4582)	3451 (2072–5574)
Occupational risk factors for injuries	20 175 (15 588–25 639)	22 434 (16 711–29 943)	1090 (836–1437)	1010 (771–1331)	21 265 (16 644–26 702)	23 444 (17 736–30 904)
Occupational low back pain	10 929 (7340–15 116)	13 471 (8968–18 945)	6912 (4487–9835)	8279 (5502–11 602)	17 841 (11 846–24 945)	21 750 (14 492–30 533)
Sexual abuse and violence	..	3588 (2669–4679)	..	19 931 (14 524–26 397)	..	23 519 (17 961–30 322)
Childhood sexual abuse	..	3588 (2669–4679)	..	4244 (3082–5533)	..	7833 (5964–10 005)
Intimate partner violence	..	..	..	16 794 (11 373–23 087)	..	16 794 (11 373–23 087)

No data indicates that attributable disability-adjusted life-years were not quantified. Total disability-adjusted life-years (in 1000s) in 1990 were 1 360 569 for men, 1 142 032 for women, and 2 502 601 for both. In 2010, they were 1 370 177 for men, 1 120 208 for women, and 2 490 385 for both.

Table 4: **Disability-adjusted life-years (1000s) attributable to risk factors and risk factor clusters, worldwide**

2·3 million]; 1·5% [1·0–2·1]), and low in seafood omega-3 fatty acids (1·4 million [1·0 million to 1·8 million]; 1·1% [0·8–1·5]). Our sensitivity analysis of omega-3 fatty acids using relative risks from randomised trials reduced the attributable burden by more than half, to 0·6 million (–0·6 million to 1·7 million) deaths, and 0·5% (–0·5 to 1·4) of global DALYs in 2010. Physical inactivity and low physical activity accounted for 3·2 million (2·7 million to 3·7 million) deaths, and 2·8% (2·4–3·2) of DALYs in 2010.

Child and maternal undernutrition was responsible for the next largest attributable burden of the risk factor clusters (1·4 million [1·2 million to 1·7 million] deaths; 6·7% [5·7–7·7] of global DALYs in 2010), with childhood underweight the largest individual contributor (0·9 million [0·7 million to 1·0 million]; 3·1% [2·6–3·7]), followed by iron deficiency (0·1 million [0·09 million to 0·14 million]; 1·9% [1·4–2·6]), and suboptimal breastfeeding (0·5 million [0·3 million to 0·8 million]; 1·9% [1·2–2·7]). Vitamin A and zinc deficiencies amongst children accounted for less than 0·8% of the disease burden.

The burdens of disease attributable to tobacco smoking including second-hand smoke (6·3 million [5·4 million to 7·0 million] deaths and 6·3% [5·5–7·0] of DALYs) as well as alcohol and drug use (2·9 million [2·6 million to 3·2 million] deaths and 4·8% [4·3–5·4] of DALYs) were substantial in 2010. These burdens are mainly driven by active smoking, which accounts for 87% of the combined burden with second-hand smoke, and alcohol use which accounted for 2·7 million (2·5 million to 3·0 million) deaths and 3·9% (3·5–4·3) of global DALYs in 2010. Of the remaining risk factor clusters, occupational risk factors accounted for 0·9 million (0·7 million to 1·1 million) deaths and 2·5% (2·0–3·0) of global DALYs in 2010, followed by sexual abuse and violence (0·2 million [0·1 million to 0·3 million] deaths and 0·9% [0·7–1·2] DALYs), unimproved water and sanitation, (0·3 million [0 to 0·6 million] deaths and 0·9% [0·04–1·6] DALYs), and other environmental risks (0·7 million [0·6 million to 0·9 million] deaths and 0·6% [0·5–0·8] DALYs).

The rest of the results section refers to the 43 risk factors and clusters of risk factors in the rank list. The predominance of non-communicable disease risks in 2010 highlights the global epidemiological transition that has occurred since 1990 (figures 1, 2, 3). In 1990, the leading risks were childhood underweight (7·9% [6·8–9·4] of global DALYs), household air pollution from solid fuels (7·0% [5·6–8·3]), and tobacco smoking including second-hand smoke (6·1% [5·4-6·8]), high blood pressure (5·5% [4·9–6·0]), and suboptimal breastfeeding (4·4% [2·8–6·1]). With the exception of household air pollution, which is a significant contributor to childhood lower respiratory tract infections, the five leading risk factors in 2010 (high

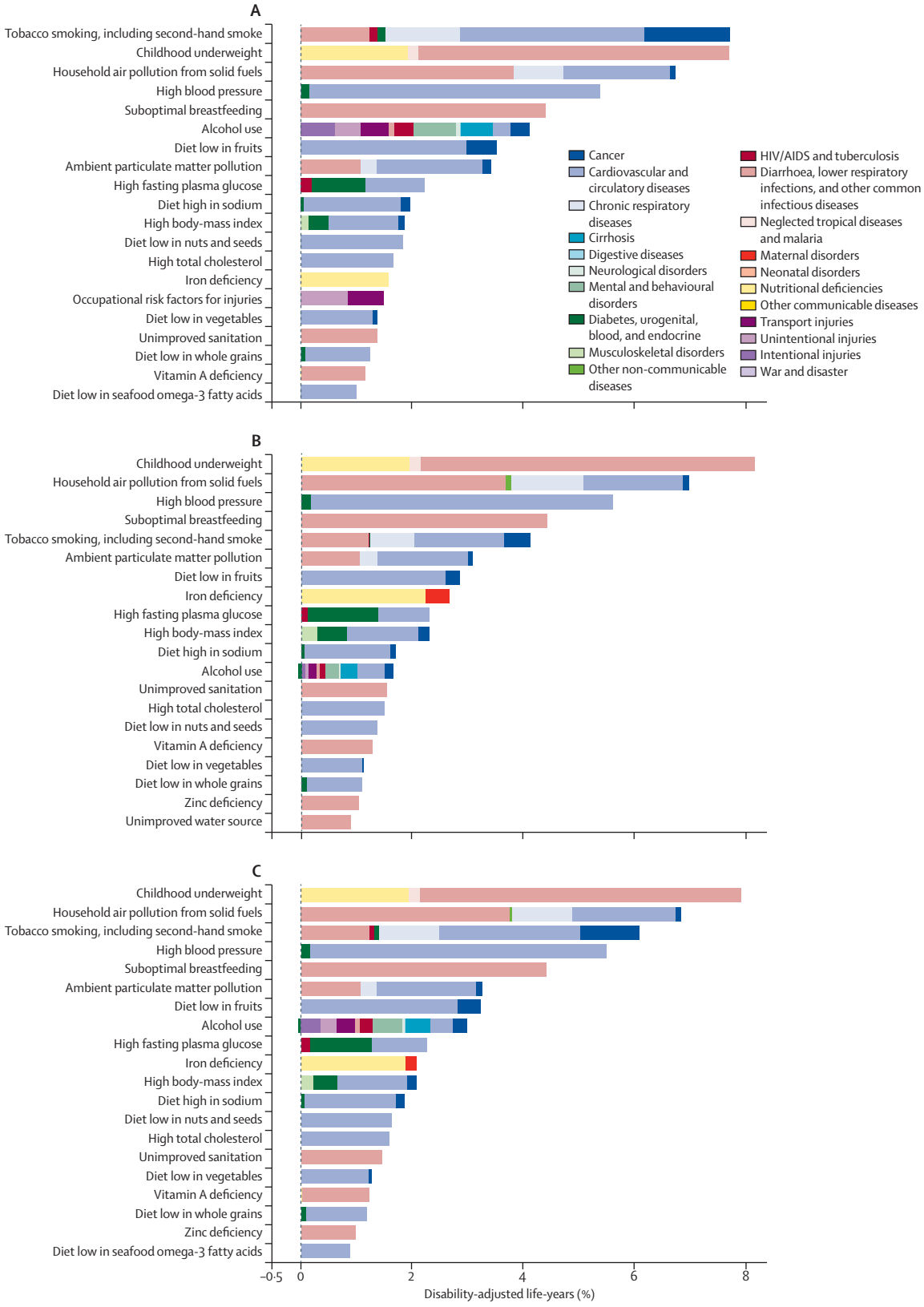


Figure 1: **Burden of disease attributable to 20 leading risk factors in 1990, expressed as a percentage of global disability-adjusted life-years**
For men (A), women (B), and both sexes (C).

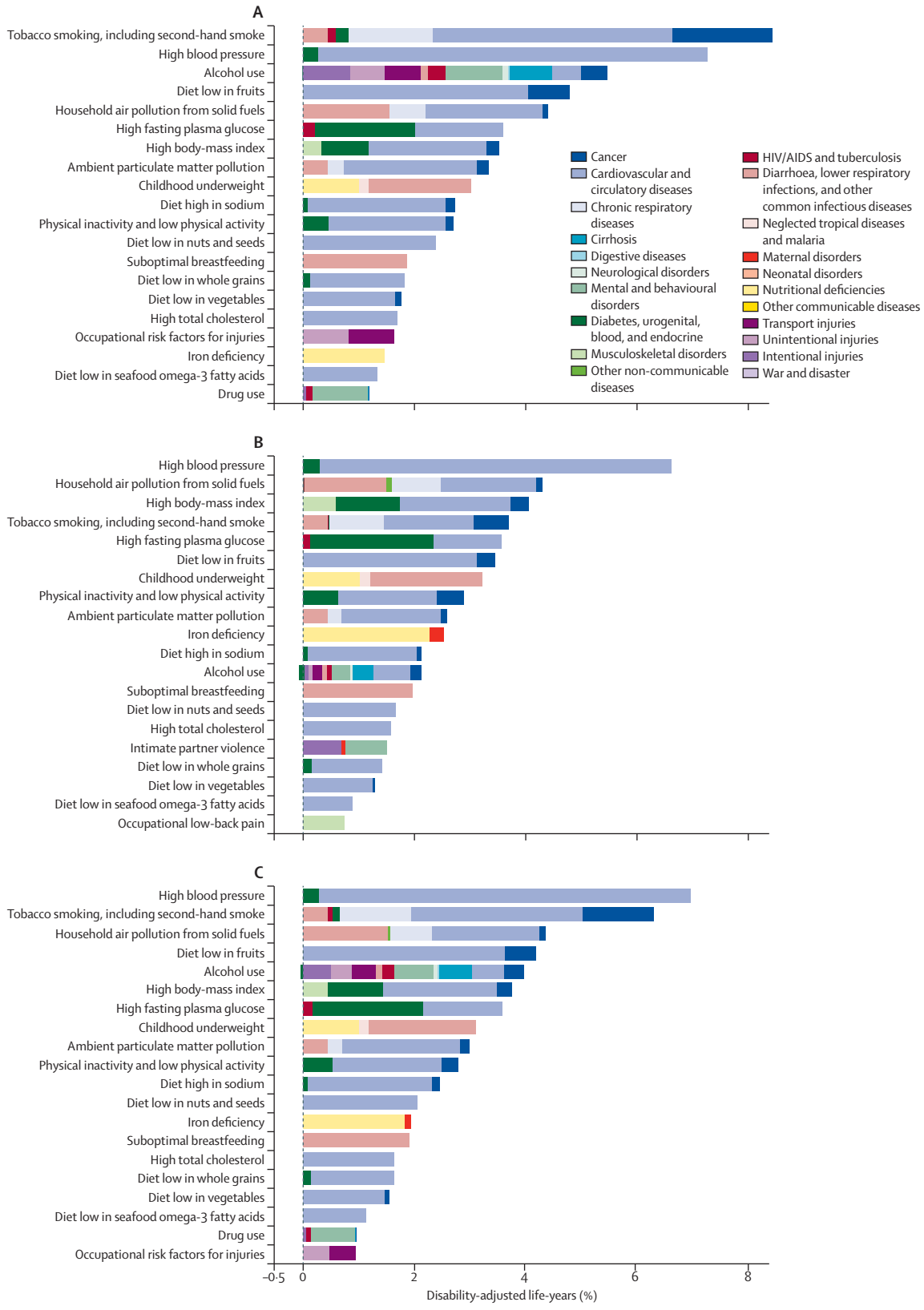


Figure 2: **Burden of disease attributable to 20 leading risk factors in 2010, expressed as a percentage of global disability-adjusted life-years**
For men (A), women (B), and both sexes (C).

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.

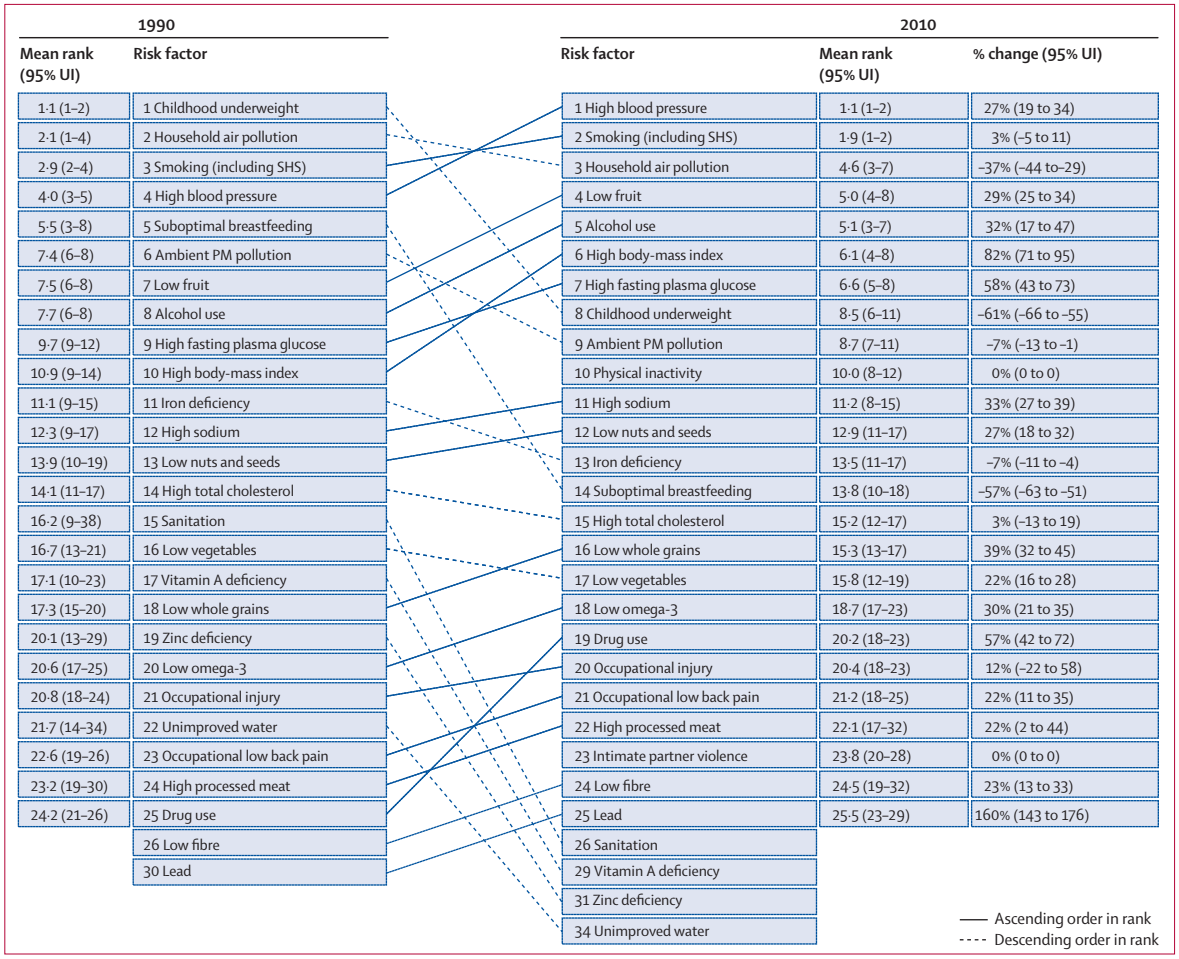


Figure 3: **Global risk factor ranks with 95% UI for all ages and sexes combined in 1990, and 2010, and percentage change**
PM=particulate matter. UI=uncertainty interval. SHS=second-hand smoke. An interactive version of this figure is available online at http://healthmetricsandevaluation.org/gbd/visualizations/regional.

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.

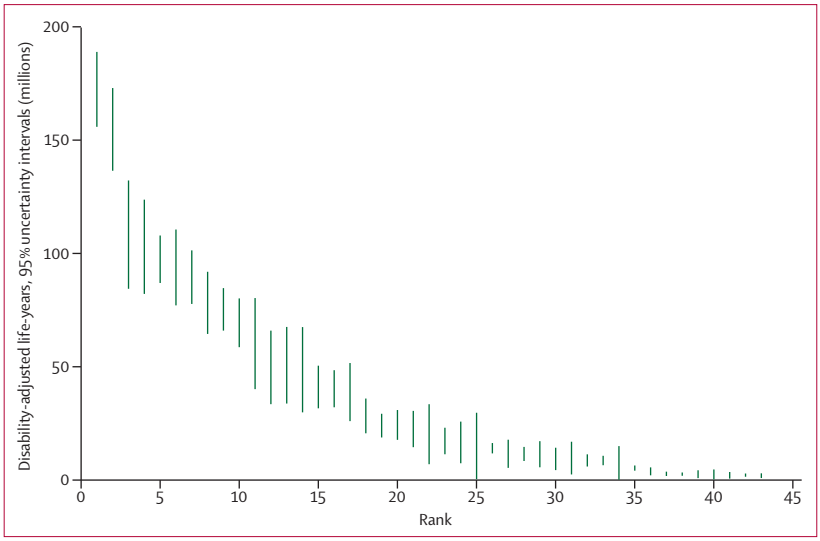


Figure 4: **95% uncertainty intervals for risk factors ranked by global attributable disability-adjusted life-years, 2010**
An interactive version of this figure is available online at http://healthmetricsandevaluation.org/gbd/visualizations/regional

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 child-hood 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.

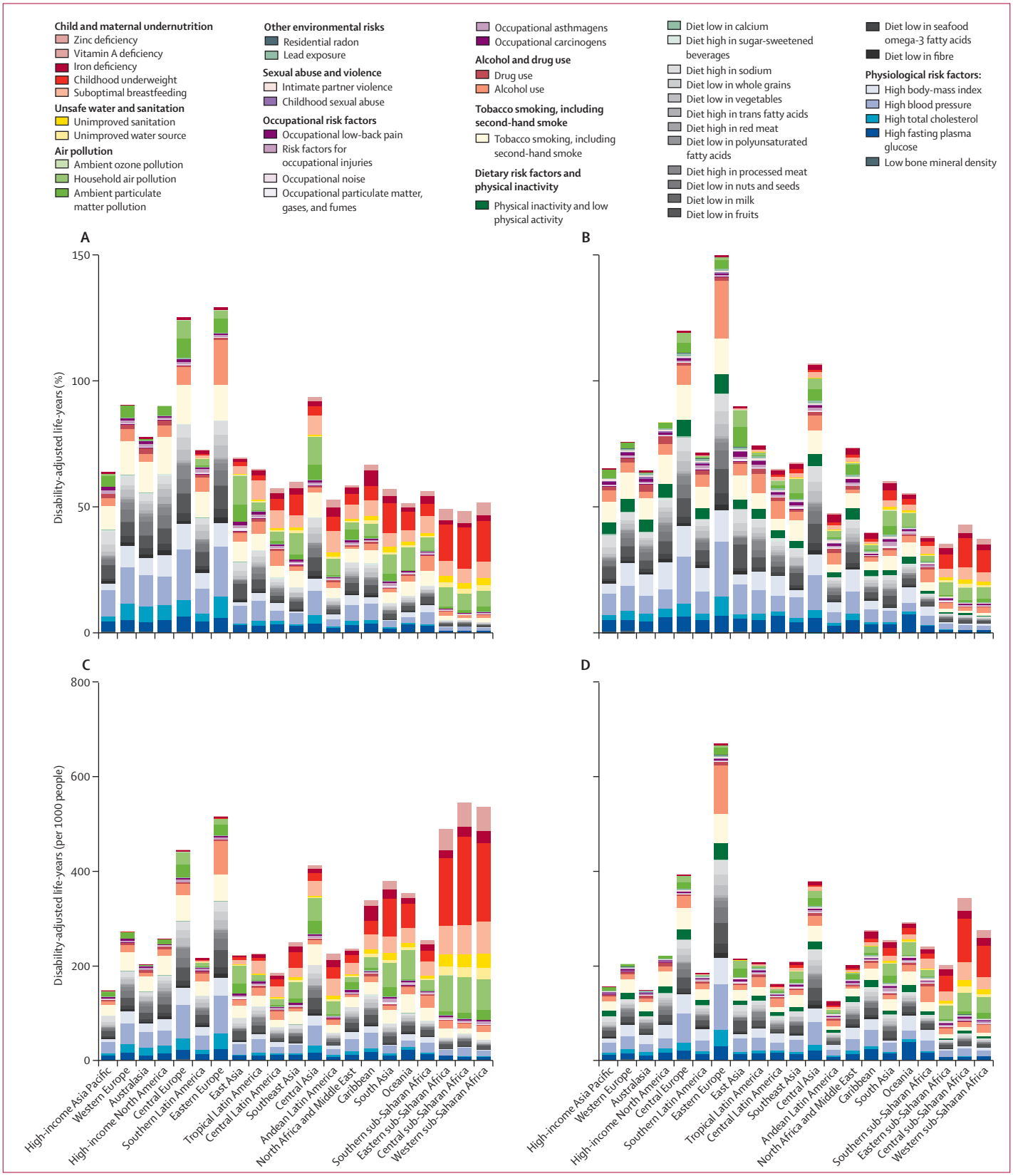
Alcohol use was an important cause of disease burden in most of Latin America. It was ranked second in central Latin America, fourth in tropical Latin America, and seventh in Andean Latin America in 1990. In 2010, it was ranked second in central and tropical Latin America, and first in Andean Latin Ameria. 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/m³ 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.

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