

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sex, and age group, and relative risks per unit of exposure by systematically reviewing and synthesising published and unpublished data.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% [5·7–7·0]), and alcohol use (5·5% [5·0–5·9]). In 1990, the leading risks were childhood overweight (7·9% [6·8–9·4]), air pollution from solid fuels (HAP; 7·0% [5·6–8·3]), and tobacco smoking including second-hand smoke (6·1% [5·4–6·8]). Dietary risks and physical inactivity collectively accounted for 10·0% (95% UI 9·1–10·8) 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 overweight, 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, most of Latin America, and southern sub-Saharan Africa in 2010 was alcohol use; in most of Asia, 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 provided a comparative assessment of the importance of different exposures, particularly tobacco smoking, in causing cancer. Peto and colleagues subsequently estimated the effects of tobacco smoking on mortality in developed countries since 1950. Although these risk-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. However, different epidemiological traditions for different risks limited the comparability of the results. Subsequently, Murray and Lopez proposed a framework for global comparative risk assessment, which laid the basis for assessment of 26 risks in 2000. 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. Analyses have also been done for specific clusters of diseases, like cancers; or clusters of risk factors, like maternal and child under-nutrition. National comparative risk assessments (including in Australia, Iran, Japan, Mexico, South Africa, Thailand, USA, and Vietnam) have also been undertaken with similar approaches.

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, 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...
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 for 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) estimation 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.

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.19,10 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
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<th>Subgroup</th>
<th>Main data sources for exposure</th>
<th>Exposure estimation method</th>
<th>Theoretical-minimum-risk exposure distribution</th>
<th>Source of relative risks</th>
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<tbody>
<tr>
<td>1. Unimproved water and sanitation</td>
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<tr>
<td>1.1. Unimproved water source</td>
<td>Proportion of households using an unimproved water source (unprotected wells or springs, vendor-provided water, tanker trucks, surface water, and other unspecified sources)</td>
<td>Intestinal infectious diseases</td>
<td>All ages</td>
<td>Population surveys and censuses</td>
<td>Spatiotemporal Gaussian process regression&lt;sup&gt;19–21&lt;/sup&gt;</td>
<td>New meta-analysis</td>
</tr>
<tr>
<td>1.2. Unimproved sanitation</td>
<td>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)</td>
<td>Intestinal infectious diseases</td>
<td>All ages</td>
<td>Population surveys and censuses</td>
<td>Spatiotemporal Gaussian process regression&lt;sup&gt;19–21&lt;/sup&gt;</td>
<td>New meta-analysis</td>
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<tr>
<td>2. Air pollution</td>
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<tr>
<td>2.1. Ambient particulate matter pollution</td>
<td>Ambient concentration of particles with an aerodynamic diameter smaller than 2·5 μm, measured in μg/m&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Lower respiratory infections; trachea, bronchus, and lung cancers; IHD; cerebrovascular disease; COPD</td>
<td>Age &lt;5 years for lower respiratory tract infection; ≥25 years for all others</td>
<td>Surface monitor measurements, aerosol optical depth from satellites, and TM5 global atmospheric chemistry transport model&lt;sup&gt;22–26&lt;/sup&gt;</td>
<td>Average of satellite and chemistry transport estimates, calibrated to surface monitor measurements</td>
<td>3·8–8·8 μg/m&lt;sup&gt;3&lt;/sup&gt; Integrated exposure–response curve</td>
</tr>
<tr>
<td>2.2. Household air pollution from solid fuels</td>
<td>Proportion of households using solid fuels for cooking (coal, wood, charcoal, dung, and agricultural residues)</td>
<td>Lower respiratory infections; trachea, bronchus, and lung cancers; IHD; cerebrovascular disease; COPD; cataracts</td>
<td>Age &lt;5 years for lower respiratory tract infection; ≥25 years for all others</td>
<td>Population surveys and censuses</td>
<td>Mixed effect regression</td>
<td></td>
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<tr>
<td>2.3. Ambient ozone pollution</td>
<td>Ambient concentrations of ozone in air, measured in parts per billion</td>
<td>COPD</td>
<td>Age ≥25 years</td>
<td>TMS global atmospheric chemistry transport model&lt;sup&gt;22–26&lt;/sup&gt;</td>
<td>TMS global atmospheric chemistry transport model&lt;sup&gt;22–26&lt;/sup&gt;</td>
<td>33·3–41·9 parts per billion</td>
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<tr>
<td>3. Other environmental risks</td>
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<tr>
<td>3.1. Residential radon</td>
<td>Residential radon, measured in Bq/m&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Trachea, bronchus, and lung cancers</td>
<td>All ages</td>
<td>Direct household measurements from surveys</td>
<td>Mixed effect regression</td>
<td>10 Bq/m&lt;sup&gt;3&lt;/sup&gt; Darby and colleagues&lt;sup&gt;28&lt;/sup&gt;</td>
</tr>
<tr>
<td>3.2. Lead exposure</td>
<td>Blood lead (measured in μg/dL) and bone lead (measured in μg/g)</td>
<td>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</td>
<td>&lt;15 years for intellectual disability; ≥25 years for all others</td>
<td>Examination surveys and epidemiological studies</td>
<td>DisMod 3</td>
<td>Lanphear and colleagues&lt;sup&gt;30&lt;/sup&gt; Navas-Acien and colleagues&lt;sup&gt;31&lt;/sup&gt;</td>
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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
- Outcomes: Intestinal infectious diseases; the aggregate of lower respiratory infections, upper respiratory infections, and otitis media
- Subgroup: Age 0–5 months
- Main data sources for exposure: Population surveys
- Exposure estimation method: Spatiotemporal Gaussian process regression
- Theoretical-minimum-risk exposure distribution: All children exclusively breastfed for first 6 months
- Source of relative risks: Lamberti and colleagues.

**4.1.2. Discontinued breastfeeding**
- Proportion of children aged 6–23 months with discontinued breastfeeding
- Outcome: Intestinal infectious diseases
- Subgroup: Age 6–23 months
- Main data sources for exposure: Population surveys
- Exposure estimation method: Spatiotemporal Gaussian process regression
- Theoretical-minimum-risk exposure distribution: Continued breastfeeding until 2 years
- Source of relative risks: Black and colleagues.

#### 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
- Outcomes: Intestinal infectious diseases; measles; malaria; the aggregate of lower respiratory infections, upper respiratory infections, and otitis media; malnutrition
- Subgroup: Age <5 years
- Main data sources for exposure: Examination surveys and epidemiological studies
- Exposure estimation method: Spatiotemporal Gaussian process regression
- Theoretical-minimum-risk exposure distribution: Proportion of the WHO 2006 reference population in each SD range
- Source of relative risks: Black and colleagues.

#### 4.3. Iron deficiency

- Haemoglobin, measure in g/L
- Outcomes: The aggregate of maternal haemorrhage and maternal sepsis; iron-deficiency anaemia
- Subgroup: All ages
- Main data sources for exposure: Examination surveys and epidemiological studies
- Exposure estimation method: Mixed effect regression
- Theoretical-minimum-risk exposure distribution: Country-specific
- Source of relative risks: Stoltzfus and colleagues.

#### 4.4. Vitamin A deficiency

- Proportion of children with serum retinol concentration <70 μmol/L
- Outcomes: Intestinal infectious diseases; measles; vitamin A deficiency
- Subgroup: Age 6 months to 5 years
- Main data sources for exposure: Examination surveys and epidemiological studies
- Exposure estimation method: DisMod 3
- Theoretical-minimum-risk exposure distribution: No childhood vitamin A deficiency
- Source of relative risks: Imdad and colleagues.

#### 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
- Outcomes: Intestinal infectious diseases; lower respiratory infections
- Subgroup: Age 1–4 years
- Main data sources for exposure: Food and Agricultural Organization food balance sheets
- Exposure estimation method: Mixed effect regression
- Theoretical-minimum-risk exposure distribution: No inadequate zinc intake
- Source of relative risks: Yakoob and colleagues.

#### 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
- Outcomes: 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
- Subgroup: Age ≥25 years
- Main data sources for exposure: Mortality data including vital registration, verbal autopsy, and population surveys for smoking prevalence
- Exposure estimation method: CoDEM
- Theoretical-minimum-risk exposure distribution: No tobacco smoking
- Source of relative risks: Re-analysis of the Cancer Prevention Study 2

#### 5.2. Second-hand smoke

- Proportion of children and non-smoking adults reporting exposure to second-hand smoke
- Outcomes: The aggregate of lower respiratory infections, upper respiratory infections, and otitis media; trachea, bronchus, and lung cancers; IHD; cerebrovascular disease
- Subgroup: Age <5 years for the aggregate of lower respiratory infections, upper respiratory infections, and otitis media, age ≥25 years for all others
- Main data sources for exposure: Population surveys
- Exposure estimation method: Spatiotemporal Gaussian process regression
- Theoretical-minimum-risk exposure distribution: No second-hand smoke exposure
- Source of relative risks: US Department of Health and Human Services, Oono and colleagues, Jones and colleagues.
### 6. Alcohol and drug use

#### 6.1. Alcohol use

Average consumption of pure alcohol (measured in g/day) and proportion of the population reporting binge consumption of 0.06 kg or more of pure alcohol on a single occasion

**Exposure definition:**
Exposure estimation method

**Theoretical-minimum-risk exposure distribution**

**Source of relative risks**

<table>
<thead>
<tr>
<th>Exposure definition</th>
<th>Outcomes</th>
<th>Subgroup</th>
<th>Main data sources for exposure</th>
<th>Exposure estimation method</th>
<th>Theoretical-minimum-risk exposure distribution</th>
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<tbody>
<tr>
<td>Alcohol use</td>
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<td>Mixed effect regression</td>
<td>No alcohol consumption</td>
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</tbody>
</table>

#### 6.2. Drug use

Proportion of the population reporting use of cannabis, opioids, and amphetamines, proportion of the population reporting use of injecting drugs

**Exposure definition:**
Exposure estimation method

**Theoretical-minimum-risk exposure distribution**

**Source of relative risks**

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<th>Drug use</th>
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<th>DisMod 3</th>
<th>No use of cannabis, opioid, or amphetamines, no use of injecting drugs</th>
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</thead>
</table>

### 7. Physiological risk factors

#### 7.1. High fasting plasma glucose

Fasting plasma glucose, measured in mmol/L

**Outcomes:**

- Diabetes mellitus
- IHD
- Cerebrovascular disease
- CKD
- Tuberculosis

**Subgroup:**

- Age ≥25 years

**Main data sources for exposure:**

- Examination surveys and epidemiological studies

**Exposure estimation method:**

- Bayesian hierarchical regression

**Theoretical-minimum-risk exposure distribution:**

- Mean 4.9–5.3 mmol/L (SD 0.3 mmol/L)

**Source of relative risks:**

- Meta-regression of pooled prospective studies

#### 7.2. High total cholesterol

Total cholesterol, measured in mmol/L

**Outcomes:**

- IHD
- Ischaemic stroke

**Subgroup:**

- Age ≥25 years

**Main data sources for exposure:**

- Examination surveys and epidemiological studies

**Exposure estimation method:**

- Bayesian hierarchical regression

**Theoretical-minimum-risk exposure distribution:**

- Mean 3.8–4.0 mmol/L (SD 0.9 mmol/L)

**Source of relative risks:**

- Meta-regression of pooled prospective studies

#### 7.3. High blood pressure

Systolic blood pressure, measured in mm Hg

**Outcomes:**

- RHD
- IHD
- Ischaemic stroke
- Haemorrhagic and other non-ischaemic stroke
- CKD
- The aggregate of cardiomyopathy and myocarditis and endocarditis
- The aggregate of atrial fibrillation and flutter
- PVD
- Other CVD
- Aortic aneurysm
- CKD

**Subgroup:**

- Age ≥25 years

**Main data sources for exposure:**

- Examination surveys and epidemiological studies

**Exposure estimation method:**

- Bayesian hierarchical regression

**Theoretical-minimum-risk exposure distribution:**

- Mean 110–115 mm Hg (SD 6 mm Hg)

**Source of relative risks:**

- Meta-regression of pooled prospective studies

#### 7.4. High body-mass index

Body-mass index, measured in kg/m²

**Outcomes:**

- 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
- The aggregate of cardiomyopathy and myocarditis and endocarditis
- The aggregate of atrial fibrillation and flutter
- PVD
- Other CVD
- CKD
- Osteoarthritis
- Low back pain

**Subgroup:**

- Age ≥25 years

**Main data sources for exposure:**

- Examination surveys and epidemiological studies

**Exposure estimation method:**

- Bayesian hierarchical regression

**Theoretical-minimum-risk exposure distribution:**

- Mean 21.0–23.0 kg/m² (SD 1.0 kg/m²)

**Source of relative risks:**

- Meta-regression of pooled prospective studies

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### Exposure definition

**7.5. Low bone mineral density**

Standardised bone mineral density measured at the femoral neck

### Outcomes

- Hip fracture falls; non-hip fracture falls

### Subgroup

- Age ≥50 years

### Main data sources for exposure

- Examination surveys and epidemiological studies

### Exposure estimation method

- DisMod 3

### Theoretical-minimum-risk exposure distribution

- 90th percentile of NHANES-III cohort by age

### Source of relative risks

- Johrell and colleagues

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### 8. Dietary 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)**

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<th>Source of relative risks</th>
<th>Relative Risk</th>
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#### 8.2. Diet low in vegetables

**Dietary intake of vegetables (fresh, frozen, cooked, canned, or dried vegetables including legumes but excluding salted or pickled, jucies, nuts and seeds, and starchy vegetables such as potatoes or corn)**

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<th>Source of relative risks</th>
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#### 8.3. Diet low in whole grains

**Dietary intake of whole grains (bar, germ, and endosperm in their natural proportions) from breakfast cereals, bread, rice, pasta, biscuits, muffins, tortilla, pancakes, and others**

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<th>Source of relative risks</th>
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#### 8.4. Diet low in nuts and seeds

**Dietary intake of nut and seed foods including, for example, peanut butter**

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#### 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**

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<th>Source of relative risks</th>
<th>Relative Risk</th>
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#### 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)**

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<th>Source of relative risks</th>
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#### 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**

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<thead>
<tr>
<th>Source of relative risks</th>
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#### 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**

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<thead>
<tr>
<th>Source of relative risks</th>
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### Exposure definition

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<tr>
<td>8.9. Diet low in fibre</td>
<td>Dietary intake of fibre from all sources including fruits, vegetables, grains, legumes, and pulses</td>
<td>Colon and rectum cancers; IHD</td>
<td>Nutrition and health surveys</td>
<td>DisMod 3</td>
<td>Mean of 30 g/day (SD 3 g/day)</td>
<td>World Cancer Research Fund and American Institute for Cancer Research, Pereira and colleagues</td>
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<tr>
<td>8.10. Diet low in calcium</td>
<td>Dietary intake of calcium from all sources, including milk, yogurt, and cheese</td>
<td>Colon and rectum cancers; prostate cancer</td>
<td>Nutrition and health surveys</td>
<td>DisMod 3</td>
<td>Mean of 1200 mg/day (SD 120 mg/day)</td>
<td>World Cancer Research Fund and American Institute for Cancer Research, Pereira and colleagues</td>
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<td>8.11. Diet low in seafood omega-3 fatty acids</td>
<td>Dietary intake of eicosapentaenoic acid and docosahexaenoic acid, measured in mg/day</td>
<td>Death caused by IHD</td>
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<td>Updated published review of Mozaffarian and colleagues, Jakobsen and colleagues, Mozaffarian and colleagues</td>
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<td>8.12. Diet low in polyunsaturated fatty acids</td>
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### 9. Occupational risk factors

#### 9.1. Occupational carcinogens

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<td>Sokolne and colleagues123</td>
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### Exposure definition

#### 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)

**Outcomes**

Asthma

**Subgroup**

Age ≥15 years

**Main data sources for exposure**

Labour force surveys and censuses

**Exposure estimation method**

Spatiotemporal Gaussian process regression

**Theoretical-minimum-risk exposure distribution**

Background asthmagen exposures

**Source of relative risks**

Published studies

#### 9.3. Occupational particulate matter, gases, and fumes

Proportion of population exposed based on distribution of the population in nine industries†

**Outcomes**

COPD

**Subgroup**

Age ≥15 years

**Main data sources for exposure**

Labour force surveys and censuses

**Exposure estimation method**

Spatiotemporal Gaussian process regression

**Theoretical-minimum-risk exposure distribution**

No occupational exposure to particulates, gases, or fumes

**Source of relative risks**

New meta-analysis

#### 9.4. Occupational noise

Proportion of population exposed based on distribution of the population in nine industries†

**Outcomes**

Hearing loss

**Subgroup**

Age ≥15 years

**Main data sources for exposure**

Labour force surveys and censuses

**Exposure estimation method**

Spatiotemporal Gaussian process regression

**Theoretical-minimum-risk exposure distribution**

Background noise exposure

**Source of relative risks**

New meta-analysis

#### 9.5. Fatal occupational injury

**Outcomes**

Low back pain

**Subgroup**

Age ≥15 years

**Main data sources for exposure**

Labour force surveys and censuses

**Exposure estimation method**

Spatiotemporal Gaussian process regression

**Theoretical-minimum-risk exposure distribution**

All individuals have the ergonomic factors of clerical and related workers

**Source of relative risks**

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

**Outcomes**

Alcohol use disorders, unipolar depressive disorders, intentional self-harm

**Subgroup**

All ages

**Main data sources for exposure**

Population surveys and epidemiological studies

**Exposure estimation method**

DisMod 3

**Theoretical-minimum-risk exposure distribution**

No childhood sexual abuse

**Source of relative risks**

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

**Outcomes**

Abortion, unipolar depressive disorders, intentional self-harm, interpersonal violence

**Subgroup**

Age 15–49 years for abortion, ≥15 years for all others

**Main data sources for exposure**

Population surveys and epidemiological studies

**Exposure estimation method**

DisMod 3

**Theoretical-minimum-risk exposure distribution**

No intimate partner violence

**Source of relative risks**

New meta-analysis, Beydoun and colleagues

---

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

<table>
<thead>
<tr>
<th>Exposure definition</th>
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<td>9.2. Occupational asthmagens</td>
<td></td>
<td>Age ≥15 years</td>
<td>Labour force surveys and censuses</td>
<td>Spatiotemporal Gaussian process regression</td>
<td>Background asthmagen exposures</td>
<td>Published studies</td>
</tr>
<tr>
<td>9.3. Occupational particulate matter, gases, and fumes</td>
<td></td>
<td>Age ≥15 years</td>
<td>Labour force surveys and censuses</td>
<td>Spatiotemporal Gaussian process regression</td>
<td>No occupational exposure to particulates, gases, or fumes</td>
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</tr>
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<td>9.4. Occupational noise</td>
<td></td>
<td>Age ≥15 years</td>
<td>Labour force surveys and censuses</td>
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<td>Background noise exposure</td>
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<tr>
<td>9.5. Fatal occupational injury</td>
<td></td>
<td>Age ≥15 years</td>
<td>International Labour Organization injury database</td>
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<td>Five injury deaths per 1 000 000 person-years</td>
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<tr>
<td>9.6. Occupational low back pain</td>
<td></td>
<td>Age ≥15 years</td>
<td>Labour force surveys and censuses</td>
<td>Spatiotemporal Gaussian process regression</td>
<td>All individuals have the ergonomic factors of clerical and related workers</td>
<td>New meta-analysis</td>
</tr>
<tr>
<td>10.1. Childhood sexual abuse*</td>
<td></td>
<td>All ages</td>
<td>Population surveys and epidemiological studies</td>
<td>DisMod 3</td>
<td>No childhood sexual abuse</td>
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<tr>
<td>10.2. Intimate partner violence*</td>
<td></td>
<td>Age 15–49 years for abortion, ≥15 years for all others</td>
<td>Population surveys and epidemiological studies</td>
<td>DisMod 3</td>
<td>No intimate partner violence</td>
<td>New meta-analysis, Beydoun and colleagues</td>
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</table>

**References:**

- 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.
Insufficient evidence
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.

Panel: The World Cancer Research Fund grading system

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.

University of Western Australia, Perth, WA, Australia (Prof F Bull PhD); Health Canada, Ottawa, ON, Canada (R T Burnett PhD); J M Zielinski PhD, Colorado School of Public Health, Aurora, CO, USA (Prof T E Byers MD); National Institute of Environmental Health Sciences, Research Triangle Park, NC, USA; Institute of Biomedical Sciences, Academia Sinica, Taipei, Taiwan (Prof A T A Cheng MD); Health Effects Institute, Boston, MA, USA (A Cohen MPH); Victorian Infectious Diseases Reference Laboratory, Melbourne, VIC, Australia (B C Cowie MBBS); Clinical Trial Services Unit (P McGale PhD), Oxford University of Oxford, Oxford, UK (Prof S Darby PhD); MRC Hearing and Communication Group, Manchester, UK (Prof A Davie PhD); European Commission, Joint Research Centre, Brussels, Belgium (F Dentener PhD); R Van Dongen PhD; Beth Israel Medical Center, New York City, NY, USA (D C Des Jarlais PhD); Federal Ministry of Health, 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,122,123 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 \(\mu g/m^3\), 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;12 however, intervention trials show a benefit of zinc supplementation for reduction of diarrhoea and lower respiratory infections in populations that have high zinc deficiency.29 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.13 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.

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;140-148 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.30

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.10,11 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/m³ to 30 μg/m³,12-17 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.10,11

To inform estimates of risk across the full range of concentrations, we used the approach of Pope and colleagues18 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.18 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 RRs from the meta-analyses of single dietary risk factors, the reported differences in dietary intake, and assuming a multiplicative relation between RR values for individual components. Results of this internal validation study show that overall, estimation of the effect of dietary factors from randomised controlled feeding studies, such as DASH149 and OmniHeart,150 which measured the effect of single risk factors 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 patterns148-149 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 DASH18 and OmniHeart,18 which measured the effect of dietary changes on blood pressure and LDL cholesterol. We used meta-regression to estimate the pooled effect of
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. 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.

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. Similarly, randomised trials of zinc supplementation were designed to detect effects on total mortality. 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 I).

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). However, subsequent randomised trials of blood pressure lowering demonstrated a significant benefit in reducing the risk of cardiovascular disease at younger SBP levels. The theoretical-minimum-risk exposure distribution has therefore been updated to reflect this new evidence.
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—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/m$^3$ 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:

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

Where PAF is the population attributable fraction (burden attributable to risk factor), RR 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.

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:

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

Where RR, is the RR for exposure category i, P, is the fraction of the population in exposure category i, and n is the number of exposure categories.

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:

$$\text{PAF} = 1 - \prod_{i=1}^{R} (1 - \text{PAF}_i)$$

Where 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.

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.

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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, 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...
<table>
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<th>Articles</th>
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### Air pollution
- **Ambient particulate matter pollution**
  - Men: 1,549,448 (1,345,894–1,752,880)
  - Women: 1,850,428 (1,614,010–2,082,474)
- **Household air pollution from solid fuels**
  - Men: 2,309,166 (1,720,246–2,824,893)
  - Women: 1,900,443 (1,738,832–2,518,572)
- **Ambient ozone pollution**
  - Men: 77,087 (25,258–134,021)
  - Women: 86,355 (30,551–1,537,766)

### Other environmental risks
- **Residential radon**
  - Men: 100,699 (872,200–1,179,475)
  - Women: 100,699 (872,200–1,179,475)
- **Lead exposure**
  - Men: 199,224 (91,805–1,315,111)
  - Women: 356,266 (292,587–435,046)

### Child and maternal undernourishment
- **Childhood underweight**
  - Men: 119,178 (99,767–1,481,105)
  - Women: 458,639 (366,866–611,352)
- **Iron deficiency**
  - Women: 21,287 (19,235–47,442)
- **Vitamin A deficiency**
  - Men: 181,511 (85,775–341,439)
  - Women: 857,340 (82,019–1,626,299)
- **Zinc deficiency**
  - Men: 143,518 (78,392–265,788)
  - Women: 52,390 (49,380–55,728)

### Tobacco smoking
- **Smoking**
  - Men: 3,322,192 (2,871,957–3,840,033)
  - Women: 2,551,248 (2,534,974–2,567,505)
- **Second-hand smoke**
  - Men: 348,378 (273,555–425,310)
  - Women: 255,534 (191,587–314,541)

### Alcohol and drug use
- **Alcohol use**
  - Men: 2,125,747 (2,007,763–2,255,818)
  - Women: 22,433 (2,024,281–3,948,873)
- **Drug use**
  - Men: 46,682 (33,661–78,265)
  - Women: 109,420 (82,973–152,421)

### Physiological risk factors
- **High fasting plasma glucose**
  - Men: 1,051,401 (886,949–1,250,550)
  - Women: 1,749,058 (1,455,169–2,039,206)
- **High total cholesterol**
  - Men: 926,749 (767,684–1,128,051)
  - Women: 961,514 (744,714–1,262,038)
- **High blood pressure**
  - Men: 3,412,588 (3,089,483–3,769,223)
  - Women: 4,750,581 (4,227,529–5,273,576)
- **High body-mass index**
  - Men: 887,047 (698,599–1,079,235)
  - Women: 1,632,766 (1,280,301–1,941,988)
- **Low bone mineral density**
  - Men: 52,816 (43,822–69,605)
  - Women: 103,440 (67,743–124,596)

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### Dietary factors and physical inactivity

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<tr>
<td>Low in fruits</td>
<td>203 415</td>
<td>274 286</td>
<td>407 558</td>
<td>581 748</td>
<td>853 835</td>
<td>12 903 707</td>
</tr>
<tr>
<td>Diet low in vegetables</td>
<td>779 747</td>
<td>1 075 500</td>
<td>674 309</td>
<td>779 754</td>
<td>1 464 057</td>
<td>179 754</td>
</tr>
<tr>
<td>Diet low in whole grains</td>
<td>649 676</td>
<td>963 640</td>
<td>580 600</td>
<td>762 171</td>
<td>1 220 276</td>
<td>1 725 812</td>
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<tr>
<td>Diet low in nuts and seeds</td>
<td>1 041 726</td>
<td>1 389 333</td>
<td>872 483</td>
<td>1 082 390</td>
<td>1 914 209</td>
<td>2 471 823</td>
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<tr>
<td>Diet low in milk</td>
<td>34 838</td>
<td>54 093</td>
<td>33 312</td>
<td>46 858</td>
<td>68 150</td>
<td>100 951</td>
</tr>
<tr>
<td>Diet high in red meat</td>
<td>12 888</td>
<td>21 330</td>
<td>12 551</td>
<td>16 762</td>
<td>26 439</td>
<td>38 092</td>
</tr>
<tr>
<td>Diet high in processed meat</td>
<td>397 198</td>
<td>473 562</td>
<td>334 476</td>
<td>367 296</td>
<td>731 675</td>
<td>840 857</td>
</tr>
<tr>
<td>Diet high in sugar-sweetened beverages</td>
<td>100 250</td>
<td>161 042</td>
<td>83 548</td>
<td>138 480</td>
<td>183 799</td>
<td>299 521</td>
</tr>
<tr>
<td>Diet high in fish</td>
<td>333 603</td>
<td>441 895</td>
<td>250 541</td>
<td>300 994</td>
<td>584 144</td>
<td>742 888</td>
</tr>
<tr>
<td>Diet high in calcium</td>
<td>48 975</td>
<td>76 413</td>
<td>33 230</td>
<td>49 181</td>
<td>82 305</td>
<td>125 594</td>
</tr>
<tr>
<td>Diet high in antioxidants</td>
<td>576 666</td>
<td>793 650</td>
<td>466 440</td>
<td>596 246</td>
<td>1 043 085</td>
<td>1 389 896</td>
</tr>
<tr>
<td>Diet high in polynsaturated fatty acids</td>
<td>248 674</td>
<td>306 296</td>
<td>199 388</td>
<td>227 307</td>
<td>484 065</td>
<td>533 603</td>
</tr>
<tr>
<td>Diet high in trans fatty acids</td>
<td>202 725</td>
<td>293 087</td>
<td>164 736</td>
<td>222 173</td>
<td>367 461</td>
<td>515 260</td>
</tr>
<tr>
<td>Diet high in n6 fatty acids</td>
<td>1 199 733</td>
<td>1 728 870</td>
<td>1 047 642</td>
<td>1 371 438</td>
<td>2 245 355</td>
<td>3 104 208</td>
</tr>
<tr>
<td>Diet high in n3 fatty acids</td>
<td>776 962–1 589 448</td>
<td>1 122 107–2 301 781</td>
<td>666 779–1 397 846</td>
<td>87 808–1 834 451</td>
<td>1 459 900–2 966 107</td>
<td>3 104 208</td>
</tr>
<tr>
<td>Physical inactivity</td>
<td>1 547 833</td>
<td>1 264 464–1 825 192</td>
<td>1 639 107</td>
<td>(1 264 712–1 899 182)</td>
<td>(Continued on next page)</td>
<td></td>
</tr>
</tbody>
</table>
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, 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 0·2% [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 (2·7 million to 4·4 million) deaths and 4·5% (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.

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 estimated 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.

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

<table>
<thead>
<tr>
<th>Risk factor cluster</th>
<th>1990</th>
<th>2010</th>
<th>1990</th>
<th>2010</th>
</tr>
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<tbody>
<tr>
<td>Occupational exposure to polycyclic aromatic hydrocarbons</td>
<td>1638</td>
<td>3092</td>
<td>492</td>
<td>993</td>
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<tr>
<td>Occupational exposure to silica</td>
<td>7870</td>
<td>14205</td>
<td>1185</td>
<td>2072</td>
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<tr>
<td>Occupational exposure to sulphuric acid</td>
<td>1964</td>
<td>2606</td>
<td>193</td>
<td>239</td>
</tr>
<tr>
<td>Occupational asthmaemeges</td>
<td>31666</td>
<td>25264</td>
<td>10485</td>
<td>8352</td>
</tr>
<tr>
<td>Occupational particulate matter, gases, and fumes</td>
<td>207366</td>
<td>371535</td>
<td>68281</td>
<td>47311</td>
</tr>
<tr>
<td>Occupational noise</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
</tr>
<tr>
<td>Occupational risk factors for injuries</td>
<td>400706</td>
<td>460785</td>
<td>21211</td>
<td>20644</td>
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<tr>
<td>Occupational low back pain</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
</tr>
<tr>
<td>Sexual abuse and violence</td>
<td>37429</td>
<td>200930</td>
<td>113070</td>
<td>238359</td>
</tr>
<tr>
<td>Childhood sexual abuse</td>
<td>37429</td>
<td>20700</td>
<td>14290</td>
<td>64438</td>
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<td>Intimate partner violence</td>
<td>186355</td>
<td>92028</td>
<td>92028</td>
<td>186356</td>
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No data indicates that attributable deaths were not quantified.
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<tr>
<td>High fasting plasma glucose</td>
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<tr>
<td>Low body mass index</td>
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<tr>
<td>Low bone mineral density</td>
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<tr>
<td>High total cholesterol</td>
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<tr>
<td>High blood pressure</td>
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<td>High blood pressure</td>
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<tr>
<td>High body mass index</td>
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<tr>
<td><strong>Air pollution</strong></td>
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<td>Ambient particulate pollution</td>
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<td>Household air pollution from solid fuels</td>
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<td>Ambient ozone pollution</td>
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<tr>
<td>Residential radon</td>
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<td>Lead exposure</td>
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<td><strong>Other environmental risks</strong></td>
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<td>Low bone mineral density in young men</td>
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<td>Low bone mineral density in young women</td>
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<td>Low bone mineral density in middle-aged men</td>
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<td>Low bone mineral density in both sexes</td>
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### Articles

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<td>Diet low in fruits</td>
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<td>Diet low in vegetables</td>
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<td>Diet low in whole grains</td>
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<td>Diet low in nuts and seeds</td>
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<tr>
<td>Diet low in milk</td>
<td>818</td>
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<tr>
<td>Diet high in red meat</td>
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<td>Diet high in processed meat</td>
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<td>Diet high in sugar-sweetened beverages</td>
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<tr>
<td>Diet low in fibre</td>
<td>8 485</td>
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<td>Diet in calcium</td>
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<td>Diet in seafood</td>
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<td>Diet in vitamin A</td>
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<tr>
<td>Diet low in whole grains</td>
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</table>

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active smoking, which accounts for 87% of the combined burden with second-hand smoke, and alcohol use which accounted for 4·9 million (4·5 million to 5·2 million) deaths and 5·5% (5·0–5·9) 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 [0·04–1·6] 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

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>1990 (Men)</th>
<th>2010 (Men)</th>
<th>2010 (Women)</th>
<th>2010 (Both sexes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occupational exposure to polycyclic aromatic hydrocarbons</td>
<td>41 (19–71)</td>
<td>73 (33–119)</td>
<td>13 (6–23)</td>
<td>23 (10–39)</td>
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<tr>
<td>Occupational exposure to silica</td>
<td>199 (129–297)</td>
<td>333 (199–463)</td>
<td>31 (21–52)</td>
<td>49 (26–71)</td>
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<tr>
<td>Occupational exposure to sulphuric acid</td>
<td>52 (14–134)</td>
<td>66 (19–143)</td>
<td>5 (1–12)</td>
<td>6 (2–13)</td>
</tr>
<tr>
<td>Occupational particulate matter, gases, and fumes</td>
<td>6808 (1622–10425)</td>
<td>6682 (3292–1031)</td>
<td>2745 (1216–4406)</td>
<td>2460 (1105–4025)</td>
</tr>
<tr>
<td>Occupational noise</td>
<td>1936 (1149–3103)</td>
<td>2284 (1348–3649)</td>
<td>933 (550–14483)</td>
<td>1167 (696–1870)</td>
</tr>
<tr>
<td>Occupational risk factors for injuries</td>
<td>20175 (15588–25639)</td>
<td>22434 (16711–29492)</td>
<td>1090 (836–14427)</td>
<td>1010 (771–1223)</td>
</tr>
<tr>
<td>Occupational low back pain</td>
<td>16929 (7340–15116)</td>
<td>13471 (8968–18945)</td>
<td>6912 (4487–8435)</td>
<td>8279 (5502–11602)</td>
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<tr>
<td>Sexual abuse and violence</td>
<td>3588 (2669–4679)</td>
<td>-</td>
<td>19931 (14524–26397)</td>
<td>23519 (17961–3022)</td>
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<tr>
<td>Childhood sexual abuse</td>
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<td>-</td>
<td>4244 (3082–5533)</td>
<td>7833 (5964–10005)</td>
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<tr>
<td>Intimate partner violence</td>
<td>-</td>
<td>-</td>
<td>16794 (12173–23087)</td>
<td>16794 (11373–23087)</td>
</tr>
</tbody>
</table>

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
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, alcohol use, household air pollution, and diets low in fruits) 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.
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. 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: 7.4% (third) versus 3.0% (eighth). 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 (6.3% [4.4–8.1]). 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 ninth in 2010.

High blood pressure, tobacco smoking including second-hand smoke, alcohol use, 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.

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

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

Compared with other regions of sub-Saharan Africa, southern sub-Saharan Africa had a more mixed pattern of risk factor burden in 1990 (appendix). In 2010, alcohol use was the leading risk factor in southern sub-Saharan Africa, followed by high blood pressure and high body-mass index (figure 6). In addition to high exposure to harmful alcohol use, the effects of alcohol were particularly large because it increases the risk of road traffic and other unintentional and intentional injuries, as well as of tuberculosis,” all of which are large causes of disease and injury burden in this region.
<table>
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<th>Risk factor</th>
<th>Global</th>
<th>High-income Asia Pacific</th>
<th>Western Europe</th>
<th>High-income North America</th>
<th>Central Europe</th>
<th>South Africa and Latin America</th>
<th>Eastern Europe</th>
<th>South Asia</th>
<th>Southeast Asia</th>
<th>Central Asia</th>
<th>South and Central America</th>
<th>High-income Asia Pacific</th>
<th>Australasia</th>
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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 cause45), 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, sixth 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 first in central Latin America, fourth in tropical Latin America, and sixth in Andean Latin America in 1990, and first in all these regions in 2010. 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.46,47 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-specific DALYs attributable to a risk factor) being closely associated with epidemiological and demographic transition (shift from...
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

Dietary risk factors and physical inactivity
- Physical inactivity and low physical activity

Other factors
- Tobacco smoking, including second-hand smoke
- Tobacco smoking, including second-hand smoke

Physiological risk factors:
- High body-mass index
- High blood pressure
- High total cholesterol
- High fasting plasma glucose
- Low bone mineral density

Diet low in:
- Calcium
- Sugar-sweetened beverages
- Sodium
- Whole grains
- Vegetables
- Trans fatty acids
- Red meat
- Polyunsaturated fatty acids
- Processed meat
- Nuts and seeds
- Milk
- Fruits
- Seafood omega-3 fatty acids
- Fiber

Diet high in:
- Calcium
- Sugar-sweetened beverages
- Sodium
- Whole grains
- Vegetables
- Trans fatty acids
- Red meat
- Polyunsaturated fatty acids
- Processed meat
- Nuts and seeds
- Milk
- Fruits
- Seafood omega-3 fatty acids
- Fiber

Environmental risks:
- Residential radon
- Lead exposure
- Sexual abuse and violence
- Intimate partner violence
- Childhood sexual abuse

Occupational risks
- Occupational low-back pain
- Risk factors for occupational injuries
- Occupational noise
- Occupational particulate matter, gases, and fumes

Tobacco smoking
- Smoking, including second-hand smoke

Alcohol and drug use
- Drug use
- Alcohol use

Other factors
- Tobacco smoking, including second-hand smoke

Drug use
- Drug use

Alcohol use
- Alcohol use
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 assessment7 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 5.3% 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 PM₂.⁵, 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. Studies⁶⁶,⁶⁷,⁶⁸ have reported broadly similar effect sizes for ambient particulate matter by smoking status (never, former, and current smokers). Other evidence⁶⁹ 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—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, implement more stringent regulation of vehicle and industrial emissions, reduce agricultural burning or land clearing by fire, and curb and reverse deforestation and desertification to reduce ambient particulate matter from dust. A large share of ambient particulate matter in Asia and sub-Saharan Africa originates from solid fuel. 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.

Unimproved water and unimproved sanitation together accounted for 0·9–9·% 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. 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. 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, 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. 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 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 and the Institute for Health Metrics and Evaluation 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). 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, 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. Therapeutic zinc supplementation in health-care
settings is feasible, as is iron supplementation during pregnancy.\textsuperscript{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,\textsuperscript{186} in the comparative risk assessment study for 2000 as 3·7 million deaths,\textsuperscript{180} and 1·9 million deaths in 2004.\textsuperscript{187} 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.\textsuperscript{188} 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.\textsuperscript{189} 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,\textsuperscript{189} 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.\textsuperscript{190,191} The worldwide increase in body-mass index and blood glucose is of particular concern in view of the absence of effective interventions.\textsuperscript{192–194} 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.\textsuperscript{195–197} and because exposure has fallen in high-income countries.\textsuperscript{198}

A recent study estimated that 5·3 million deaths were attributable to physical inactivity in 2008.\textsuperscript{199} This number, which has been widely quoted and equated with the number of deaths attributable to tobacco smoking,\textsuperscript{200} 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.\textsuperscript{201} 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, polynsaturated 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.\textsuperscript{202}

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. Empirical assessments show that the pooled effect of risks and interventions trends towards a null result over time 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. However, observational studies indicate that there might be no benefits if saturated fat reduction is associated with an increase in carbohydrates, which is also supported by the absence of benefits from a low fat diet in the Women’s Health Initiative. 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. Observational studies of the effect sizes for body-mass index have controlled for some potential confounders. As noted, the pooled effect of risks and interventions trends towards the null result over time; 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 be 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—e.g., 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 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 equate to 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. 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 Heart Federation 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 (11/10), 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, Arrgen, AstraZeneca, George Clinical, GlaxoSmithKline, Novartis, PepsiCo, Pfizer, Pharmacy Guild of Australia, Roche, Sanofi-Aventis, Servier, 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. I 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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