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Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2015

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Published in:
The Lancet

DOI:
[10.1016/S0140-6736\(16\)31679-8](https://doi.org/10.1016/S0140-6736(16)31679-8)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2016

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Forouzanfar, M. H., Afshin, A., Alexander, L. T., Anderson, H. R., Bhutta, Z. A., Biryukov, S., Brauer, M., Burnett, R., Cercy, K., Charlson, F. J., Cohen, A. J., Dandona, L., Estep, K., Ferrari, A. J., Frostad, J. J., Fullman, N., Gething, P. W., Godwin, W. W., Griswold, M., ... GBD 2015 Risk Factors (2016). Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2015: A systematic analysis for the Global Burden of Disease Study 2015. *The Lancet*, 388(10053), 1659-1724. [https://doi.org/10.1016/S0140-6736\(16\)31679-8](https://doi.org/10.1016/S0140-6736(16)31679-8)

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Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013



GBD 2013 Risk Factors Collaborators*

Summary

Background The Global Burden of Disease, Injuries, and Risk Factor study 2013 (GBD 2013) is the first of a series of annual updates of the GBD. Risk factor quantification, particularly of modifiable risk factors, can help to identify emerging threats to population health and opportunities for prevention. The GBD 2013 provides a timely opportunity to update the comparative risk assessment with new data for exposure, relative risks, and evidence on the appropriate counterfactual risk distribution.

Methods Attributable deaths, years of life lost, years lived with disability, and disability-adjusted life-years (DALYs) have been estimated for 79 risks or clusters of risks using the GBD 2010 methods. Risk-outcome pairs meeting explicit evidence criteria were assessed for 188 countries for the period 1990–2013 by age and sex using three inputs: risk exposure, relative risks, and the theoretical minimum risk exposure level (TMREL). Risks are organised into a hierarchy with blocks of behavioural, environmental and occupational, and metabolic risks at the first level of the hierarchy. The next level in the hierarchy includes nine clusters of related risks and two individual risks, with more detail provided at levels 3 and 4 of the hierarchy. Compared with GBD 2010, six new risk factors have been added: handwashing practices, occupational exposure to trichloroethylene, childhood wasting, childhood stunting, unsafe sex, and low glomerular filtration rate. For most risks, data for exposure were synthesised with a Bayesian meta-regression method, DisMod-MR 2.0, or spatial-temporal Gaussian process regression. Relative risks were based on meta-regressions of published cohort and intervention studies. Attributable burden for clusters of risks and all risks combined took into account evidence on the mediation of some risks such as high body-mass index (BMI) through other risks such as high systolic blood pressure and high cholesterol.

Findings All risks combined account for 57·2% (95% uncertainty interval [UI] 55·8–58·5) of deaths and 41·6% (40·1–43·0) of DALYs. Risks quantified account for 87·9% (86·5–89·3) of cardiovascular disease DALYs, ranging to a low of 0% for neonatal disorders and neglected tropical diseases and malaria. In terms of global DALYs in 2013, six risks or clusters of risks each caused more than 5% of DALYs: dietary risks accounting for 11·3 million deaths and 241·4 million DALYs, high systolic blood pressure for 10·4 million deaths and 208·1 million DALYs, child and maternal malnutrition for 1·7 million deaths and 176·9 million DALYs, tobacco smoke for 6·1 million deaths and 143·5 million DALYs, air pollution for 5·5 million deaths and 141·5 million DALYs, and high BMI for 4·4 million deaths and 134·0 million DALYs. Risk factor patterns vary across regions and countries and with time. In sub-Saharan Africa, the leading risk factors are child and maternal malnutrition, unsafe sex, and unsafe water, sanitation, and handwashing. In women, in nearly all countries in the Americas, north Africa, and the Middle East, and in many other high-income countries, high BMI is the leading risk factor, with high systolic blood pressure as the leading risk in most of Central and Eastern Europe and south and east Asia. For men, high systolic blood pressure or tobacco use are the leading risks in nearly all high-income countries, in north Africa and the Middle East, Europe, and Asia. For men and women, unsafe sex is the leading risk in a corridor from Kenya to South Africa.

Interpretation Behavioural, environmental and occupational, and metabolic risks can explain half of global mortality and more than one-third of global DALYs providing many opportunities for prevention. Of the larger risks, the attributable burden of high BMI has increased in the past 23 years. In view of the prominence of behavioural risk factors, behavioural and social science research on interventions for these risks should be strengthened. Many prevention and primary care policy options are available now to act on key risks.

Funding Bill & Melinda Gates Foundation.

Lancet 2015; 386: 2287–323

Published Online
September 11, 2015
[http://dx.doi.org/10.1016/S0140-6736\(15\)00128-2](http://dx.doi.org/10.1016/S0140-6736(15)00128-2)

See [Comment](#) page 2235

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Introduction

The Global Burden of Disease, Injuries, and Risk Factor study 2013 (GBD 2013) is the first of a series of annual updates of the GBD. Quantification of functional health loss and mortality by disease and injury is an important input to more informed health policy, as is the contribution of different risk factors to patterns of disease and injury across countries. Risk factor quantification, particularly for modifiable risk factors, can help to identify emerging threats to population health and opportunities for prevention.

The Global Burden of Disease study 2010 (GBD 2010) provided the most comprehensive comparative assessment of risk factors covering 67 risk factors or clusters of risks for 21 regions from 1990 to 2010.¹ The GBD comparative risk assessment (CRA) brings together data for excess mortality and disability associated with risk factors, data for exposure to risks, and evidence-based assumptions on the desired counterfactual distribution of risk exposure to estimate how much of the burden observed in a given year can be attributed to risk exposure in that year and in all previous years. GBD 2010 generated broad interest in the scientific community and public health agencies.^{2–4} GBD 2010 also generated several scientific debates on topics such as the magnitude of burden related to diet, the low estimates of burden related to unsafe water and sanitation, and exclusion of some risk–outcome pairs from the analysis.^{2,5–10} Additionally, new studies have been

published since the release of GBD 2010 that inform both estimates of relative risks and exposure in different countries.^{11–15}

The GBD 2013 provides a timely opportunity to update each aspect of the CRA with new data for exposure, add new risk–outcome pairs meeting study inclusion criteria, and incorporate new data for relative risks and the appropriate counterfactual risk distribution. Important insights from scientific debates on GBD 2010 have been used in revised approaches. This analysis supersedes all previous GBD CRA results by providing a complete revised time-series of attributable burden from 1990 to 2013, for 188 countries, with consistent definitions and methods. This CRA also allows us to explore how much of the burden of disease around the world is not explained by the behavioural, environmental and occupational, and metabolic risks included in this study.

Methods

Overview

In general, this analysis follows the CRA methods used in GBD 2010.¹ Conceptually, the CRA approach evaluates how much of the burden of disease observed in a given year can be attributed to past exposure to a risk. Attributable burden is estimated by comparing observed health outcomes to those that would have been observed if a counterfactual level of exposure had occurred in the past. Given that different risks lead to different health

Research in context

Evidence before this study

As part of the Global Burden of Disease (GBD) 2010 study a revision of the global comparative risk assessment was undertaken, with an expanded list of 67 risks and risk clusters by 21 world regions, and comparable estimates made for the time period 1990–2010. Quantification of the burden that can be attributed to risk factors is important information to set priorities in prevention.

Added value of this study

The GBD 2013 comparative risk assessment is a further update to the GBD 2010 study in several ways: (1) addition of new risk factors (handwashing practices, occupational exposure to trichloroethylene, childhood wasting, childhood stunting, unsafe sex, and low glomerular filtration rate); (2) new data for exposure; (3) assumption of a lognormal rather than a normal distribution for most of the continuous risk factors to better represent the observed population distributions; (4) updates to the systematic reviews and meta-analyses of relative risks; (5) aggregation of the burden at multiple levels of risk factors, including the combined effect of all GBD risk factors and aggregates of three large classes—ie, behavioural, environmental and occupational, and metabolic risk factors; (6) systematic inclusion of mediation between major risk

factors in the quantification of the burden associated with joint risks; and (7) quantification of the risk burden for 188 countries. Furthermore, several major improvements to specific risk factors were implemented, such as use of the latest analytical instruments for multilevel analysis of exposure (DisMod-MR), as well as production of burden estimates for 5-year intervals from 1990–2010 plus 2013.

Implications of all the available evidence

Comparative risk assessment enables policy makers to prioritise prevention by addressing the most important risk factors at the population level. The burden by aggregations of risk categories, such as air pollution or dietary risks, provides the broad view of investment priorities, whereas the size of burden for individual risks can inform the potential elements of a broader intervention package. In 2013, we explain 41% of burden by the 79 GBD risk factors with a slight increase since 1990. This proportion varies between 28% and 61% between countries, highlighting the importance of making country estimates as the opportunities for intervention will vary accordingly. Unless new risk factors are identified, the proportion of burden that is not explained by GBD risk factors is likely to be less amenable to primary prevention but more of a concern for curative or rehabilitative services.

outcomes, assessments are undertaken separately for specific risk–outcome pairs.

For most risk–outcome pairs, we estimated the attributable burden using the following equations.

$$AB_{jasc} = \sum_{o=1}^w DALY_{oasc} PAF_{jasc}$$

Where AB_{jasc} is the attributable burden for risk factor j in age group a , sex s , country c and year t . $DALY_{oasc}$ is disability-adjusted life-years (DALYs) for cause o (of w relevant outcomes for risk factor j) in age group a , sex s , country c and year t . PAF_{jasc} is the population attributable fraction (PAF) for cause o due to risk factor j in age group a , sex s , country c and year t . Attributable deaths, years of life lost (YLLs), or years lived with disability (YLDs) are computed by substituting in the equation these metrics for DALYs.

Risks fall into three categories on the basis of how exposure is measured: dichotomous, polytomous, and continuous. High systolic blood pressure is an example of a risk measured on a continuous scale. The PAF_{jasc} for a continuous risk factor in each country is defined as:¹⁶

$$PAF_{jasc} = \frac{\int_{x=l}^u RR_{jasc}(x) P_{jasc}(x) dx - RR_{jasc}(TMREL_{jas})}{\int_{x=l}^u RR_{jasc}(x) P_{jasc}(x) dx}$$

$RR_{jasc}(x)$ is the relative risk as a function of exposure level x for risk factor j , cause o , age-group a , sex s , and country c . l is the lowest level of exposure and u is the highest level of exposure observed. $P_{jasc}(x)$ is the distribution of exposure for risk j in age-group a , sex s , country c , and year t . $TMREL_{jas}$ is the theoretical minimum risk exposure level for risk factor j , age group a , and sex s . The discrete version of this equation for polytomous and dichotomous risks is provided in the appendix (p 2).

The equations highlight the four key components by cause, age, sex, country, and year that go into estimations of the burden attributable to a risk factor: the number of deaths, YLLs, YLDs, or DALYs; exposure levels for a risk factor; relative risk of a given outcome due to exposure; and the counterfactual level of risk factor exposure. In the CRA approach, the counterfactual level of risk exposure is selected to be the risk exposure that is theoretically possible and minimises overall risk (theoretical minimum risk exposure level [TMREL]).¹⁷ The intention is to quantify how much disease burden could be lowered by shifting the distribution of a risk to the level that would lead to the greatest improvement in population health. GBD 2013 provides the rates of mortality, YLLs, YLDs, and DALYs by cause.^{18,19} We focus here on the data and methods used to estimate 79 behavioural, environmental and occupational, and metabolic risks and clusters of these risks, levels of exposure, relative risks, and the choice of TMREL (a more detailed presentation of methods is provided in appendix [pp 2–23]).

Risk–outcome pairs and risk factor hierarchy

In this analysis, we focus on three groups of risk factors: behavioural, environmental and occupational, and metabolic. Figure 1 shows a more complete causal web (not all the arrows detailing possible interconnections have been drawn) that recognises the role of four other sets of risks: genes; the microbiome and other host factors; public health and medical care interventions; and social, economic, and cultural factors. It is currently beyond the scope of this study to quantify these other categories of risks or causes; however, in future iterations of the GBD we intend to broaden the analysis to include at least some of these broader causes.

For the current assessment focused on behavioural, environmental and occupational, and metabolic risk factors, risk–outcome pairs have been included based on four criteria. These criteria take into account the importance of each risk factor to either disease burden, policy, or both; the availability of sufficient data to estimate risk factor exposure; evidence from epidemiological studies supporting a causal relation between risk factor exposure and the outcome and available data to estimate effect sizes per unit of exposure increase; and evidence that these effects can be applied to a general population. Following GBD 2010, we have adopted the World Cancer Research Fund grading of evidence supporting the causal relation between risk factor exposure and an outcome. They defined four levels of evidence: convincing, probable, possible, and insufficient. Only risk–outcome pairs judged to meet the criteria of convincing or probable were included. Convincing evidence is defined as “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 is defined as “evidence based on epidemiological studies showing

See Online for appendix

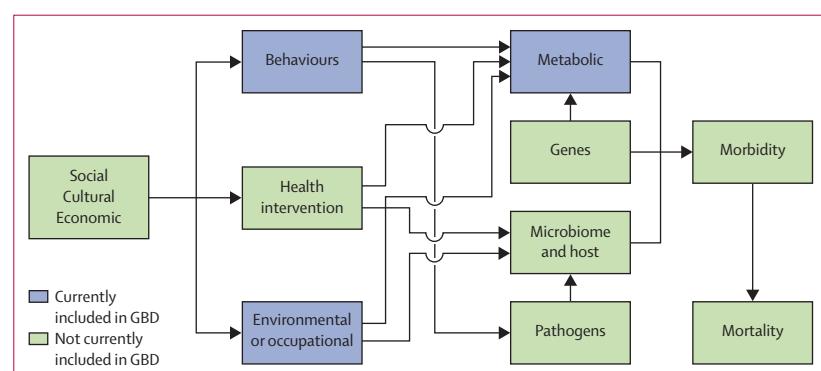


Figure 1: A more general causal web of the causes of health outcomes

Categories of causes included in this analysis shown in blue. GBD=Global Burden of Disease.

	Exposure definition	Theoretical minimum risk exposure level	Data representativeness index			
			<1998	1998–2005	2006–13	Total
All risk factors	100·0%	100·0%	100·0%	100·0%
Environmental and occupational risks	100·0%	100·0%	100·0%	100·0%
Unsafe water, sanitation, and handwashing			59·0%	72·3%	60·6%	80·3%
Unsafe water source	Proportion of households with access to different water sources (unimproved, improved except piped, piped water supply) and reported use of household water treatment methods (boiling or filtering; chlorinating or solar filtering; no treatment)	All households have access to water from a piped water supply that is also boiled or filtered before drinking	69·6%	84·2%	68·4%	91·8%
Unsafe sanitation	Proportion of households with access to different sanitation facilities (unimproved, improved except sewer, sewer connection)	All households have access to toilets with sewer connection	65·8%	81·6%	67·1%	91·1%
No handwashing with soap	Proportion of individuals who wash their hands with soap and water after potential faecal contact	All individuals wash hands with soap and water after potential faecal contact	1·1%	10·1%	25·5%	29·3%
Air pollution			100·0%	100·0%	100·0%	100·0%
Ambient particulate matter pollution	Annual average daily exposure to outdoor air concentrations of particulate matter (PM) with an aerodynamic diameter smaller than 2·5 µm, measured in µg/m³	Uniform distribution between 5·9 µg/m³ and 8·7 µg/m³	99·5%	99·5%	99·5%	99·5%
Household air pollution from solid fuels	Annual average daily exposure to household concentrations of particulate matter (PM) with an aerodynamic diameter smaller than 2·5 µm, measured in µg/m³ from solid fuel use (coal, wood, charcoal, dung, and agricultural residues)	No households are exposed to excess indoor concentration of particles from solid fuel use (assuming concentration of particulate matters, aerodynamic diameter smaller than 2·5 µg/m³, measured in µg/m³ in no fuel use is consistent with a TMREL of 5·9–8·7)	47·8%	83·3%	71·7%	94·2%
Ambient ozone pollution	Seasonal (3 month) hourly maximum ozone concentrations, measured in parts per billion (ppb)	Uniform distribution between 33·3 µg/m³ and 41·9 µg/m³, according to minimum/5th percentile concentrations	100·0%	100·0%	100·0%	100·0%
Other environmental risks			34·0%	38·8%	26·6%	49·5%
Residential radon	Average daily exposure to indoor air radon levels measured in becquerels (radon disintegrations per s) per cubic metre (Bq/m³)	10 Bq/m³, corresponding to the outdoor concentration of radon	19·7%	27·1%	11·7%	38·3%
Lead exposure	Blood lead levels in µg/dL of blood, bone lead levels in µg/g of bone	2 µg/dL, corresponding to lead levels in pre-industrial humans as natural sources of lead prevent the feasibility of zero exposure	29·3%	27·1%	20·2%	39·9%
Occupational risks			56·4%	64·4%	55·3%	72·3%
Occupational carcinogens	34·0%	56·9%	51·6%	62·8%
Occupational exposure to asbestos	Proportion of the population with cumulative exposure to asbestos	No occupational exposure to asbestos
Occupational exposure to arsenic	Proportion of the population ever exposed to arsenic at work/through their occupation	No occupational exposure to arsenic
Occupational exposure to benzene	Proportion of the population ever exposed to benzene at work/through their occupation	No occupational exposure to benzene
Occupational exposure to beryllium	Proportion of the population ever exposed to beryllium at work/through their occupation	No occupational exposure to beryllium
Occupational exposure to cadmium	Proportion of the population ever exposed to cadmium at work/through their occupation	No occupational exposure to cadmium
Occupational exposure to chromium	Proportion of the population ever exposed to chromium at work/through their occupation	No occupational exposure to chromium
Occupational exposure to diesel engine exhaust	Proportion of the population ever exposed to diesel engine exhaust at work/through their occupation	No occupational exposure to diesel engine exhaust
Occupational exposure to second-hand smoke	Proportion of the population ever exposed to second-hand smoke at work/through their occupation	No occupational exposure to second-hand smoke
Occupational exposure to formaldehyde	Proportion of the population ever exposed to formaldehyde at work/through their occupation	No occupational exposure to formaldehyde
Occupational exposure to nickel	Proportion of the population ever exposed to nickel at work/through their occupation	No occupational exposure to nickel

(Table 1 continues on next page)

	Exposure definition	Theoretical minimum risk exposure level	Data representativeness index			
			<1998	1998–2005	2006–13	Total
(Continued from previous page)						
Occupational exposure to polycyclic aromatic hydrocarbons	Proportion of the population ever exposed to polycyclic aromatic hydrocarbons at work/through their occupation	No occupational exposure to polycyclic aromatic hydrocarbons
Occupational exposure to silica	Proportion of the population ever exposed to silica at work/through their occupation	No occupational exposure to silica
Occupational exposure to sulphuric acid	Proportion of the population ever exposed to sulphuric acid at work/through their occupation	No occupational exposure to sulphuric acid
Occupational exposure to trichloroethylene	Proportion of the population ever exposed to trichloroethylene at work/through their occupation	No occupational exposure to trichloroethylene
Occupational asthmagens	Proportion of the population currently exposed to asthmagens at work/through their occupation	Background asthmagen exposures	41.0%	37.2%	36.2%	52.7%
Occupational particulate matter, gases, and fumes	Proportion of the population ever exposed to particulates, gases, or fumes at work/through their occupation	No occupational exposure to particulates, gases, or fumes	34.0%	56.9%	51.6%	62.8%
Occupational noise	Proportion of the population ever exposed to noise greater than 85 decibels at work/through their occupation	Background noise exposure	34.0%	56.9%	51.6%	62.8%
Occupational injuries	Proportion of the population at risk to injuries related to work/through their occupation	The rate of injury deaths per 100 000 person-years is zero	5.3%	17.0%	18.6%	20.7%
Occupational ergonomic factors	Proportion of the population who are exposed to ergonomic risk factors for low back pain at work/through their occupation	All individuals have the ergonomic factors of clerical and related workers	32.4%	58.5%	48.9%	63.3%
Behavioural risks	100.0%	100.0%	100.0%	100.0%
Child and maternal malnutrition			97.3%	97.9%	96.8%	98.9%
Suboptimal breastfeeding			44.7%	68.1%	55.9%	78.2%
Non-exclusive breastfeeding	Proportion of children younger than 6 months who receive predominant, partial, or no breastfeeding	All children are exclusively breastfed for first 6 months of life
Discontinued breastfeeding	Proportion of children aged 6–23 months who do not receive any breastmilk	All children continue to receive breast milk until 2 years of age
Childhood undernutrition			79.3%	72.3%	59.6%	86.7%
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	All children are above -1 SD of the WHO 2006 standard weight-for-age curve
Childhood wasting	Proportion of children less than -3 SDs, -3 to -2 SDs, and -2 to -1 SDs of the WHO 2006 standard weight-for-length curve	All children are above -1 SD of the WHO 2006 standard weight-for-height curve
Childhood stunting	Proportion of children less than -3 SDs, -3 to -2 SDs, and -2 to -1 SDs of the WHO 2006 standard height-for-age curve	All children are above -1 SD of the WHO 2006 standard height-for-height curve
Iron deficiency	Peripheral blood haemoglobin concentration in g/L	Country specific	40.4%	34.0%	22.3%	45.7%
Vitamin A deficiency	Proportion of children aged 28 days to 5 years with serum retinol concentration <0.7 µmol/L	No childhood vitamin A deficiency	22.9%	53.7%	45.7%	58.5%
Zinc deficiency	Proportion of the population with inadequate zinc intake versus loss	No inadequate zinc intake	89.9%	89.9%	91.0%	91.0%
Tobacco smoke			34.0%	91.0%	95.7%	98.4%
Smoking	Proportion of the population with cumulative exposure to tobacco smoking; proportion of the population who currently smoke	100% of population is lifelong non-smokers	34.0%	89.4%	93.6%	96.3%
Second-hand smoke	Average daily exposure to indoor air particulate matter from second-hand smoke with an aerodynamic diameter smaller than 2.5 µg, measured in µg/m³	No second-hand smoke exposure	8.5%	69.1%	87.2%	92.6%
Alcohol and drug use			100.0%	100.0%	100.0%	100.0%
Alcohol use	Average daily alcohol consumption of pure alcohol (measured in g/day) in current drinkers who had consumed alcohol during the past 12 months; binge drinking defined as proportion of the population reporting binge consumption of at least 60 g for males and 48 g for females of pure alcohol on a single occasion	No alcohol consumption	100.0%	100.0%	100.0%	100.0%

(Table 1 continues on next page)

	Exposure definition	Theoretical minimum risk exposure level	Data representativeness index			
			<1998	1998–2005	2006–13	Total
(Continued from previous page)						
Drug use	Proportion of the population dependent on opioids, cannabis, cocaine, or amphetamines; proportion of the population who have ever injected drugs	No use	28.7%	50.5%	54.3%	67.0%
Dietary risks						
Diet low in fruits	Average daily consumption of fruits (fresh, frozen, cooked, canned, or dried, excluding fruit juices and salted or pickled fruits)	Consumption of fruit between 200 g and 400 g per day	19.1%	38.8%	22.9%	56.4%
Diet low in vegetables	Average daily consumption of vegetables (fresh, frozen, cooked, canned, or dried vegetables, including legumes but excluding salted or pickled vegetables, juices, nuts and seeds, and starchy vegetables such as potatoes or corn)	Consumption of vegetables between 350 g and 450 g per day	88.8%	92.6%	90.4%	93.6%
Diet low in whole grains	Average daily consumption of whole grains (bran, germ, and endosperm in their natural proportion) from breakfast cereals, bread, rice, pasta, biscuits, muffins, tortillas, pancakes, and other sources	Consumption of whole grains between 100 g and 150 g per day	87.8%	89.9%	89.4%	89.9%
Diet low in nuts and seeds	Average daily consumption of nut and seed foods	Consumption of nuts and seeds between 12 g and 20 g per day	78.7%	85.1%	83.0%	86.7%
Diet low in milk	Average daily consumption of milk, including non-fat, low-fat, and full-fat milk, excluding soy milk and other plant derivatives	Consumption of milk between 425 g and 475 g per day	88.8%	91.0%	89.4%	91.0%
Diet high in red meat	Average daily consumption of red meat (beef, pork, lamb, and, goat but excluding poultry, fish, eggs, and all processed meats)	Consumption of red meat between 11.4 g and 17.1 g per day	88.8%	91.0%	89.4%	91.0%
Diet high in processed meat	Average daily consumption of meat preserved by smoking, curing, salting, or addition of chemical preservatives	Consumption of processed meat between 0 g and 14.3 g per day	14.4%	24.5%	6.9%	28.2%
Diet high in sugar-sweetened beverages	Average daily consumption of beverages with ≥50 kcal per 226.8 g serving, including carbonated beverages, sodas, energy drinks, and fruit drinks, but excluding 100% fruit and vegetable juices	Consumption of sugar-sweetened beverages between 0 g and 64.3 g per day	13.8%	23.9%	7.4%	27.1%
Diet low in fibre	Average daily intake of fibre from all sources including fruits, vegetables, grains, legumes, and pulses	Consumption of fibre between 28 g and 32 g per day	12.8%	19.7%	9.0%	27.1%
Diet suboptimal in calcium	Average daily intake of calcium from all sources, including milk, yogurt, and cheese	Consumption of calcium between 0 g and 0.77 g per day	15.4%	20.7%	11.2%	31.4%
Diet low in seafood omega-3 fatty acids	Average daily intake of eicosapentaenoic acid and docosahexaenoic acid	Consumption of seafood omega-3 fatty acids between 200 mg and 300 mg per day	87.7%	90.4%	88.8%	90.4%
Diet low in polyunsaturated fatty acids	Average daily intake of omega-6 fatty acids from all sources, mainly liquid vegetable oils, including soybean oil, corn oil, and safflower oil	Consumption of polyunsaturated fatty acids between 10% and 15% of total daily energy	9.0%	12.2%	5.3%	17.0%
Diet high in trans fatty acids	Average daily intake of trans fat from all sources, mainly partially hydrogenated vegetable oils and ruminant products	Consumption of trans fatty acids between 0% and 0.8% of total daily energy	8.5%	42.0%	42.0%	42.0%
Diet high in sodium	24 h urinary sodium measured in mg per day	Consumption of sodium between 1 g and 5 g per day	25.0%	18.6%	11.7%	33.5%
Sexual abuse and violence			17.6%	45.7%	53.2%	66.0%
Childhood sexual abuse	Proportion of the population who have ever experienced one or more acts of 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	No childhood sexual abuse	9.0%	25.5%	17.6%	37.8%
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 intimate partner since age 15 years	No intimate partner violence	13.8%	44.1%	47.3%	61.7%
Unsafe sex	Proportion of the population with exposure to sexual encounters that convey the risk of disease	No exposure to a disease agent through sex	14.4%	17.0%	43.1%	43.6%
Low physical activity	Average weekly physical activity at work, home, transport-related, and recreational measured by metabolic equivalent (MET) mins per week	Highly active, ≥8000 MET min per week	0.0%	50.5%	31.4%	63.3%

(Table 1 continues on next page)

	Exposure definition	Theoretical minimum risk exposure level	Data representativeness index			
			<1998	1998–2005	2006–13	Total
(Continued from previous page)						
Metabolic risks	68·1%	89·9%	87·8%	97·9%
High fasting plasma glucose	Serum fasting plasma glucose, measured in mmol/L	4·8–5·4	31·4%	38·3%	23·4%	54·3%
High total cholesterol	Serum total cholesterol, measured in mmol/L	3·0–4·8	23·9%	27·7%	22·3%	46·8%
High systolic blood pressure	Systolic blood pressure, measured in mm Hg	107–119	36·2%	45·7%	36·2%	71·8%
High body-mass index	Body-mass index, measured in kg/m ²	21–23	57·4%	87·8%	86·2%	97·3%
Low bone mineral density	Standardised mean bone mineral density values measured at the femoral neck in g/cm ²	99th percentile of NHANES 2005–10 by age and sex	14·9%	19·7%	6·9%	25·5%
Low glomerular filtration rate	Proportion of the population with a GFR <60 mL per min per 1·73 m ² , and excluding end-stage renal disease	>60 mL per min per 1·73 m ²	5·3%	12·2%	14·4%	21·8%

Table 1: GBD 2013 risk factor hierarchy, exposure definitions, theoretical minimum risk exposure level, and data representativeness index (DRI) for the entire period 1985–2013, pre-1998, 1998–2005, and 2006–13

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.”

Table 1 summarises the included risk factors; there are, counting risks and clusters of risks, 79 different risks in the hierarchy, including 13 level 2 groupings of risk factors and 63 individual risks. We have quantified the burden of each of the level 1, level 2, and level 3 groupings and an overall estimate of all risk factors combined. Risks are organised into a hierarchy with blocks of behavioural, environmental and occupational, and metabolic risks at the first level of the hierarchy. The next level in the hierarchy includes nine clusters of related risks and two individual risks, with more detail provided at levels 3 and 4 of the hierarchy. New risk–outcome pairs were added for risks already included in GBD 2010 due to new evidence, and some risk–outcome pairs were excluded because they did not meet the quality of evidence criteria.

Estimating risk factor exposure

Data and exposure categories

For each risk factor exposure, we began with the GBD 2010 sources and supplemented those by identifying and using published studies through systematic reviews of the literature, household survey data, census data, and satellite data (used for PM_{2·5} estimation). Our analyses for the GBD 2013 of tobacco smoking prevalence and obesity have been published.^{20,21} For some risks such as diet and alcohol consumption, we have also used administrative record systems. Appendix pp 88–475 provides citations for all sources used for estimating risk factor exposure organised by country.

We have computed a data representativeness index (DRI) for risk factor exposure estimation. The DRI for a risk factor is the fraction of countries for which we have identified any data for the risk factor. Table 1 also provides the DRI for the entire period 1985–2013 and the DRI calculated for three intervals: pre-1997, 1998–2005, and from 2006 to 2013. The overall DRI ranges from 17% for diet low in polyunsaturated fatty acids to 100% for ambient ozone pollution and ambient particulate matter pollution. The DRI for PM_{2·5} is 100% because data are available for all countries and all years, although direct satellite observations are unavailable before 1998.

Modelling strategies for exposure levels

Appendix pp 49–51 lists the modelling strategy used to estimate exposure for every risk factor. For 23 risks, we used DisMod-MR 2.0, which is a Bayesian meta-regression method used extensively in estimating the prevalence of diseases for GBD 2013. See Vos and colleagues¹⁹ for a detailed description of the likelihood used for estimation and an explanation of improvements in DisMod-MR 2.0 compared with DisMod-MR 1.0, used in GBD 2010. In brief, DisMod-MR 2.0 shows improvements over DisMod-MR 1.0 in computational speed, geographical disaggregation, and display capabilities. The advantage of DisMod-MR 2.0 is that it estimates both the age–sex pattern of a risk as well as different levels over time based on estimation for 1990, 1995, 2000, 2005, 2010, and 2013. For 12 risk factors modelled with DisMod-MR 2.0, we conducted cross-validation tests (appendix pp 476–78).

For 34 risks, we used spatiotemporal Gaussian process regression (ST-GPR), which was also used for multiple risk factors in GBD 2010.²¹ ST-GPR has been used for risk factors for which the data density is sufficient to estimate a very flexible time trend that does not vary over age. If the tabulated data were in standard age groups or at the household level, such as access to different levels of improved water and sanitation, exposure to radon, or

available zinc intake, we used ST-GPR; but if the data were available by different age intervals or mixed sex groups, we used DisMod-MR 2.0 because of its ability to integrate over age and adjust for different exposure definitions in the data.

For PM_{2.5}, estimates of annual concentrations were generated by combining data from atmospheric chemistry transport models and satellite retrievals of aerosols in the atmosphere.²² The combined PM_{2.5} concentrations were then calibrated against observations from ground-level monitoring of particles from more than 75 countries. For modelling the burden attributable to tobacco smoking, we used the smoking impact ratio (SIR) developed by Peto, Lopez, and colleagues²³ for cancers and chronic respiratory disease, and 5-year lagged smoking prevalence for all cardiovascular outcomes, tuberculosis, diabetes, and asthma. The SIR is used to reflect past exposure, duration, and intensity of smoking in a population.²³ Alcohol exposure estimation used both administrative and survey data to estimate levels of abstainers, former drinkers, binge drinkers, and drinks per day for regular drinkers. Physical activity exposure was modelled in terms of four categories of metabolic equivalent (MET) min per week (ratio of metabolic rate during a specific physical activity to a resting metabolic rate): inactivity, less than 600 MET min per week; low activity, 600–3999; moderate activity, 4000–7999; and high activity, greater than 8000. Exposure to occupational risks was estimated with data from labour force surveys and censuses on the economically active population available from the International Labour Organization (ILO; Geneva, Switzerland). The distribution of the economically active population across nine industries or eight occupational groups was used to measure exposure to occupational asthmagens, particulate matter, noise, and ergonomic factors.

To calculate the burden of every continuous risk factor, the distribution of exposure needs to be estimated, which includes central tendency and dispersion parameters. We modelled mean and SD because these can be derived from nearly all published studies. In GBD 2010, for computational simplicity, all continuous risks were assumed to be normally distributed, so mean and SD were used to simulate the population distribution in the PAF calculation. Considerable evidence suggests that most risks are not normally distributed, so we have devoted substantial effort to choosing appropriate distribution for each risk factor.^{24–27} First, we modelled the natural log of the SD using observed data as a function of the mean and fixed effects on risk and super-region. Second, we evaluated the likelihood value of fitting normal, lognormal, gamma, beta, and inverse Gaussian distributions to the US National Health and Nutrition Examination Survey (NHANES) micro-data for systolic blood pressure, body-mass index (BMI), fasting plasma glucose, and cholesterol. We found that the lognormal distribution fit the available data best for all but three risk

factors. For iron deficiency and low bone mineral density, the normal distribution had the best fit. For high BMI, we used a beta distribution for which BMI is first transformed to be on a 0 to 1 scale, and the α and beta parameters for the distribution are fit to the mean and SD with the constraint that skewness cannot be negative.

Relative risks for systolic blood pressure have been corrected for regression dilution bias.²⁸ To be consistent with the adjusted relative risks for regression dilution bias, we have corrected exposure SDs for a measure of intertemporal variance in blood pressure observed in cohort studies; this effectively ensures that our values reflect usual systolic blood pressure.

Estimating the effects of risk factors on disease and injury outcomes

For 59 component risk factors, for which we estimate attributable burden using the relative risk and exposure formula, we estimated relative risks of mortality and morbidity based on either published meta-analyses, meta-analyses updated with new studies, or new meta-regressions that include covariates such as age, sex, or country-level predictors for the GBD 2013.

For every risk factor, relevant outcomes meeting the World Cancer Research Fund criteria of convincing or probable evidence for a causal association were identified. We used almost all outcomes from GBD 2010 and added 35 new outcomes (appendix p 10) to them through a comprehensive review of the list. For risk-outcome pairs for which evidence is only available on either mortality or morbidity, we assumed that the estimated relative risks applied equally to both. Where there was evidence of statistically different relative risks for mortality and morbidity, we used different relative risks for each. Of note, relative risks were not consistently higher or lower for mortality compared with morbidity. Appendix pp 479–614 summarise the relative risks used by age and sex for each risk factor and outcome pair, and appendix pp 615–709 provide citations for all sources used for relative risks. We used relative risks from studies controlled for confounding but not controlling for factors along the causal pathway between exposure and outcome.

We used an updated meta-regression for water, sanitation, and handwashing with results from recently published studies.^{11,12} We conducted a new meta-regression for physical activity by converting the activity levels for which relative risk data are available to total MET mins of activity per week. DisMod-MR 2.0 was used to generate a continuous risk curve for every outcome as a function of MET mins activity per week. We updated the relative risks for childhood underweight, stunting, and wasting using a recently published study that did a pooled analysis of children enrolled in ten prospective cohorts in Africa, Asia, and South America.^{29,30} The updated relative risks for all three anthropometric indicators showed that they have no significant effect on malaria. Finally, we assumed that 100% of the burden of protein-energy malnutrition

was attributable to childhood underweight and wasting. The integrated exposure-response curve was used as a framework for ambient particulate matter pollution, household air pollution, secondhand smoke, and tobacco smoking in GBD 2010.³¹ For GBD 2013, we re-estimated these relations with recently published studies of relative risk and also extended their use to estimate the burden from secondhand smoke and household air pollution for chronic obstructive pulmonary disease.^{31–39}

In some cases, evidence of the direct relation between a risk factor and a disease outcome was lacking or extremely sparse. For three risk factors (lead, sugar-sweetened beverages, and sodium), we estimated relative risks through a two-stage process.^{40–42} For sodium and disease outcomes other than gastric cancer, we first estimated the relation between 24-h sodium excretion and change in systolic blood pressure. Second, we estimated the relation between change in blood pressure and disease outcomes to estimate the effect of sodium on outcomes. This two-stage approach was also used for chronic lead exposure on adults (effect of bone lead through blood pressure) and sugar-sweetened beverages (through BMI).

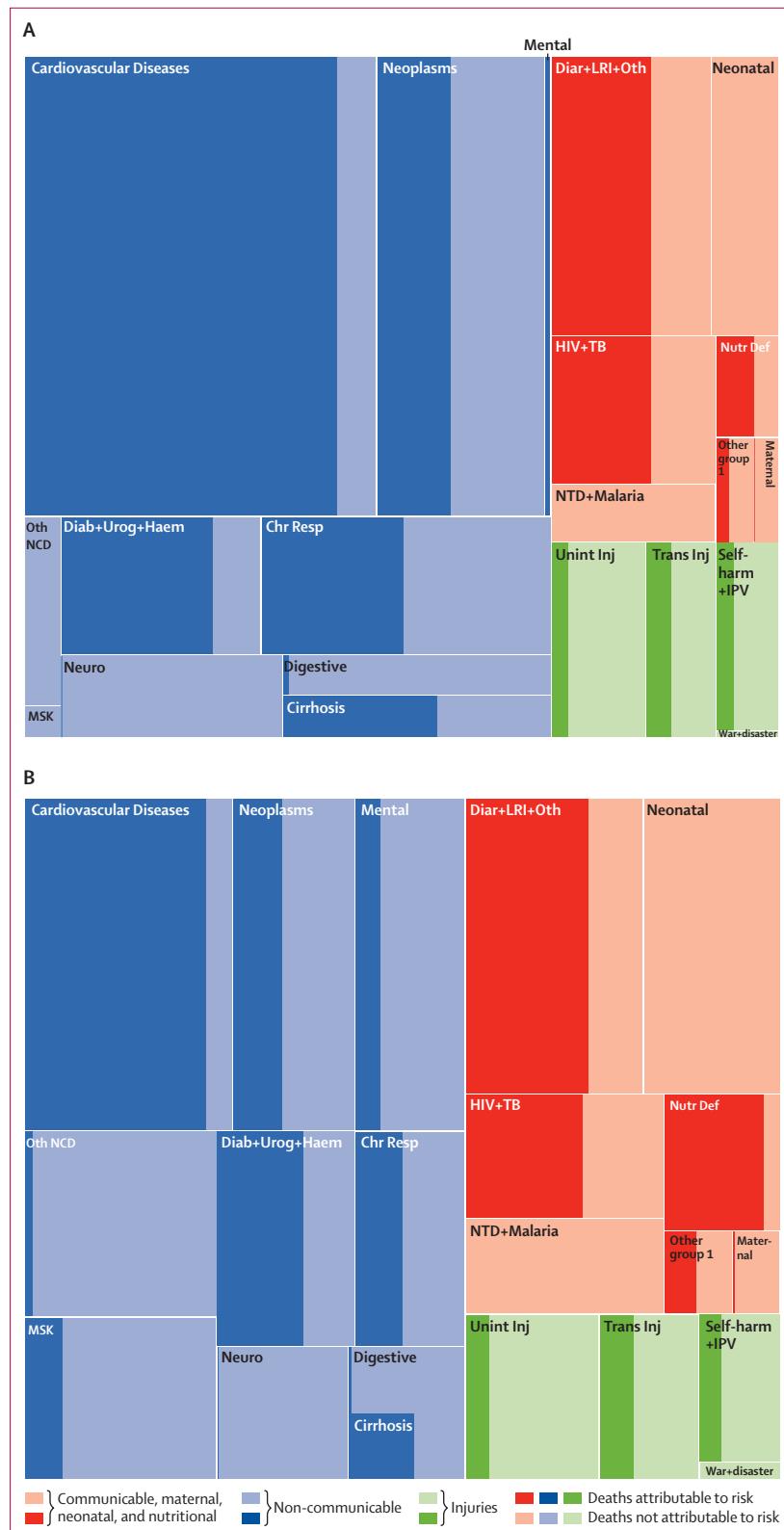
Alcohol and high BMI are the only risk factors included in our current analysis that show a significant protective effect for selected outcomes, and the protective effects are restricted to certain groups (ie, premenopausal women for high BMI) or levels of intake (ie, alcohol).^{43,44} Recent studies confirmed previous meta-analyses that indicated a protective effect of high BMI on breast cancer in premenopausal women outside Asia-Pacific countries.^{45,46} These protective effects were estimated and included as negative attributable burden in our calculations.

Theoretical minimum risk exposure level (TMREL)

In the CRA framework, attributable burden is calculated with respect to a counterfactual risk exposure (see equation 2). In GBD 2010, we used the exposure distribution that minimises risk for the population, termed the theoretical minimum risk exposure distribution (TMRED).¹⁷ Based on a consultation with risk factor epidemiologists, we have chosen to simplify the TMRED and to choose a single level of risk exposure that minimises risk from all causes of DALYs combined, which we term the theoretical minimum risk exposure level (TMREL). The TMREL by its definition should

Figure 2: Tree maps of global deaths (A) and global DALYs (B) for GBD level 2 causes for all ages, both sexes combined in 2013

The fraction of each cause attributable to all risk factors combined is shown with dark shading. DALYs=disability-adjusted life-years. GBD=Global Burden of Disease. Chr Resp=chronic respiratory diseases. Diab + Urog + Haem=diabetes, urogenital, blood, and endocrine diseases. Diar + LRI + Oth=diarrhoea, lower respiratory, and other common infectious diseases. HIV + TB=HIV/AIDS and tuberculosis. Mental=mental and substance use disorders. MSK=musculoskeletal disorders. Neuro=neurological disorders. Nutr Def=nutritional deficiencies. Oth NCD=other non-communicable diseases. Other group 1=other communicable, maternal, neonatal, and nutritional diseases. NTD + Malaria=neglected tropical diseases and malaria. Self-harm + IPV=self-harm and interpersonal violence. Trans Inj=transportation injuries. Unint Inj=intentional injuries.



minimise individual (and population level) risk and be theoretically possible to achieve, but not necessarily affordable or feasible to achieve. Table 1 shows the TMREL for each risk factor. In some cases, such as sodium consumption, the evidence supporting the selection of the TMREL is uncertain. In these cases, we include in the uncertainty estimation sampling a uniform distribution of different TMRELS.

As part of GBD 2013, we have modified the TMREL to be households with piped water connections and those who also boil or filter their water before drinking for unsafe water. Similarly, the TMREL for unsafe sanitation is now defined by the proportion of households that have access to sewer-connected toilet facilities.

In GBD 2010, a TMRED with a mean of 1 g per day of urinary sodium excretion was used for sodium intake. This value was supported by randomised clinical trials which showed that systolic blood pressure falls continuously as sodium is lowered to concentrations as low as 1 g per day.⁴⁷ The 2013 Institute of Medicine report, Sodium Intake in Populations: Assessment of Evidence, argued that the evidence of the benefit of lowering sodium below 2·3 g per day was unclear.⁴⁸ The PURE cohort study found a J-shaped association between urinary sodium excretion, mortality, and major cardiovascular events, with minimum risk of death and major cardiovascular events observed between 3 g and 6 g of sodium excretion per day.⁴⁹ Taking into account the potential overestimation of the Kawasaki formula used to estimate sodium excretion in PURE, the upper bound of minimum risk seems closer to 5 g per day. To account for the uncertainty surrounding the concentration of sodium that most minimises risk, we sampled a uniform distribution ranging from 1 g to 5 g per day to generate the TMREL. This choice, however, was controversial across the GBD investigators, with several diet collaborators proposing an uncertainty interval of 1–3 g per day. Following the GBD Study Protocol, the GBD Scientific Council made the final decision to use an uncertainty interval of 1–5 g per day.

For bone mineral density, we used the 99th percentile of age–sex subgroups of NHANES III studies between 2005 and 2010 data instead of 90th percentiles from NHANES III (used in GBD 2010). Use of the 99th percentile enables us to consider the bone density decrease by age, while capturing the excess risk of fracture caused by lower bone mineral density observed in elderly populations.

Attributable burden estimated using other approaches

For unsafe sex and occupational injuries for all outcomes, we did not use the relative risk and exposure method to estimate attributable burden. Because of absence of reliable relative risk estimates associating different occupations with injury outcomes, we used data for rates of fatal injuries reported by industry as related to occupation to calculate the PAF. This implicitly assumes that the TMREL would be zero for occupation-related

fatal injuries. In view of the difficulty of fitting unsafe sex in the exposure–risk framework, we took a direct attribution approach and modelled the PAFs directly in DisMod-MR 2.0 for HIV. Direct attribution was also used for intimate partner violence and homicide, as well as drug use and hepatitis B and C.

Burden attributable to clusters of risk factors

There is interest in what fraction of the burden of disease is attributable to various combinations of risk factors or to all risk factors combined.^{50,51} To compute the joint risk factor burden for metabolic risks and combinations of metabolic risk factors with other behavioural or environmental risk factors requires assumptions about how one risk factor is mediated through other risk factors—for example, what fraction of the hazard associated with obesity is mediated through blood pressure or cholesterol? Recent studies have examined the fraction of high BMI mediated through elevated cholesterol and systolic blood pressure.⁵² Consistent with this approach for every two risk factors for an outcome, we estimated the fraction of risk that is mediated through the other risk based on published studies (appendix pp 710–11). Using this matrix of parameters carrying every two by two combination of the risk factors, we have computed the aggregated burden of disease for every level including behavioural, environmental and occupational, and metabolic risks, and finally for all risk factors using the following formula:

$$PAF_{joasct} = 1 - \prod_{j=1}^J \left(1 - PAF_{joasct} \prod_{i=1}^J (1 - MF_{jio}) \right)$$

Where J is a set of risk factors for aggregation, PAF_{joasct} is the population attributable fraction for risk factor i , MF_{jio} is mediation factor for risk factor i mediated through j , cause o , age-group a and sex s , country c , and time t .

We estimated the joint burden of childhood wasting, stunting, and underweight. Published relative risks for wasting, stunting, and underweight, however, do not control for each other. We adjusted the published confounded relative risks for each indicator for the effect of the other two anthropometric indicators.²⁹ Using the adjusted relative risks for all three anthropometric indicators, we have calculated the joint PAF for all three indicators assuming they were independent.

Role of the funding source

The funder of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The authors had access to the data in the study and the final responsibility to submit the paper.

Results

The risk factors included in this analysis are estimated to account for a widely varying proportion of deaths and DALYs across causes at the global level. Figure 2 uses tree

maps to represent the PAFs for all risks combined for each disease and injury for level 2 causes in the GBD hierarchical cause list for deaths and DALYs. Across the level 2 causes, the attributable fractions for deaths range from 0% for neonatal disorders to 88·7% (95% UI 86·6–90·6) for cardiovascular and circulatory diseases. The next highest attributable fractions are 76·4% (95% UI 70·1–80·1) for diabetes, urogenital, blood, and endocrine disorders and 63·6% (61·2–66·1) for diarrhoea, lower respiratory infections, and other common infectious diseases. Table 2 shows that the attributable fraction for deaths due to all causes combined for all risk factors is 57·2% (95% UI 55·8–58·5) and the fraction for DALYs is 41·6% (40·1–43·0). The attributable fraction for YLDs due to non-communicable diseases for all risk factors combined (25·8% [24·0–27·6]) is much lower than for deaths or YLLs because some of the leading causes of YLDs such as mental and substance abuse disorders, musculoskeletal disorders, and other non-communicable diseases have low attributable fractions for the set of risks included in this study. For DALYs, in 2013 all risks explained a variable fraction

ranging from 25·8% (95% UI 24·0–27·6) for injuries, to 43·8% (41·1–46·3) for non-communicable diseases, and 42·3% (40·6–44·1) for communicable, maternal, neonatal, and nutritional diseases. Within each broad disease and injury group, there is also substantial variation. Risks account for only 5·8% (95% UI 2·6–8·6) for maternal disorders and 0% for neonatal disorders, but 87·0 (84·6–89·3) for nutritional deficiencies. Within non-communicable diseases, all risks account for less than 6% of DALYs for digestive diseases, neurological disorders, and other non-communicable diseases.

To help quantify how each large group of risk factors interacts, figure 3 shows the fraction of burden for different outcomes that is explained by eight exclusive groupings: not explained by risks included in this study; behavioural risks alone; behavioural risks and environmental and occupational risks; behavioural risks and metabolic risks; environmental and occupational risks alone; environmental and occupational and metabolic risks; metabolic risks alone; and the intersection of all three groups of risks (ie, behavioural, environmental and occupational, and metabolic). For all

	Deaths 2013	YLLs 2013	YLDs 2013	DALYs 2013
All causes	57·2% (55·8–58·5)	47·9% (46·6–49·0)	27·6% (26·6–28·5)	41·6% (40·1–43·0)
Communicable, maternal, neonatal, and nutritional diseases	44·1% (42·4–46·0)	40·8% (39·0–42·7)	51·8% (49·0–54·1)	42·3% (40·6–44·1)
HIV/AIDS and tuberculosis	59·8% (55·7–63·9)	58·5% (55·3–62·0)	62·5% (58·8–66·0)	58·7% (55·5–62·2)
Diarrhoea, lower respiratory, and other common infectious diseases	62·4% (60·0–64·8)	70·4% (67·6–73·0)	50·1% (41·3–57·6)	69·3% (66·5–71·9)
Neglected tropical diseases and malaria	0	0	0	0
Maternal disorders	6·1% (2·7–9·1)	6·1% (2·8–9·1)	1·4% (0·5–2·5)	5·8% (2·6–8·6)
Neonatal disorders	0	0	0	0
Nutritional deficiencies	56·8% (50·2–65·2)	78·2% (73·7–82·7)	94·2% (93·2–95·0)	87·0% (84·6–89·3)
Other communicable, maternal, neonatal, and nutritional diseases	33·0% (23·5–43·3)	47·6% (35·1–59·6)	38·0% (32·8–46·1)	46·5% (35·3–57·6)
Non-communicable diseases	64·0% (62·3–65·7)	58·9% (56·8–60·7)	23·1% (21·8–24·3)	43·8% (41·1–46·3)
Neoplasms	45·0% (42·1–47·7)	42·5% (39·8–45·1)	32·0% (29·9–34·0)	42·1% (39·4–44·7)
Cardiovascular diseases	88·5% (86·3–90·5)	88·7% (87·4–90·0)	76·5% (73·5–79·5)	87·9% (86·5–89·3)
Chronic respiratory diseases	49·3% (43·2–54·7)	45·3% (39·6–50·3)	44·1% (39·3–49·2)	44·9% (40·2–49·2)
Cirrhosis	57·3% (50·2–62·1)	56·8% (49·1–61·5)	44·3% (40·7–47·3)	56·6% (49·0–61·3)
Digestive diseases	2·0% (1·0–2·8)	2·7% (1·4–3·8)	1·3% (0·7–1·8)	2·4% (1·3–3·3)
Neurological disorders	0·6% (0·4–0·7)	1·9% (1·2–2·5)	1·3% (0·8–1·7)	1·5% (1·0–1·9)
Mental and substance use disorders	93·7% (90·8–94·8)	95·3% (93·1–96·0)	17·6% (16·0–19·4)	22·8% (20·7–25·4)
Diabetes, urogenital, blood, and endocrine diseases	77·6% (73·0–80·9)	64·5% (53·1–72·7)	64·8% (60·0–68·9)	64·5% (57·6–69·6)
Musculoskeletal disorders	0	0	19·9% (17·9–21·9)	19·4% (17·5–21·4)
Other non-communicable diseases	0	0	6·3% (5·4–7·3)	4·4% (3·6–5·2)
Injuries	26·9% (25·4–28·6)	23·3% (21·7–25·1)	38·7% (35·1–41·3)	25·8% (24·0–27·6)
Transport injuries	36·8% (34·3–39·5)	34·0% (31·2–37·0)	44·3% (42·1–46·7)	35·4% (32·7–38·4)
Unintentional injuries	20·0% (17·8–21·9)	12·3% (10·8–14·0)	43·3% (41·5–45·2)	19·1% (16·8–21·4)
Self-harm and interpersonal violence	27·9% (25·2–31·0)	28·2% (25·4–31·4)	26·6% (24·9–28·7)	28·1% (25·4–31·3)
Forces of nature, war, and legal intervention	0·3% (0·2–0·3)	0·1% (0·1–0·2)	1·5% (0·9–2·4)	1·0% (0·6–1·5)

Data are % (95% UI). YLLs=years of life lost. YLDs=years lived with disability. DALYs=disability-adjusted life-years. PAF=population attributable fraction.

Table 2: The age-standardised PAF attributable to the joint distribution of all risk factors for all ages, both sexes combined for each GBD level 1 and level 2 cause and all causes for 2013

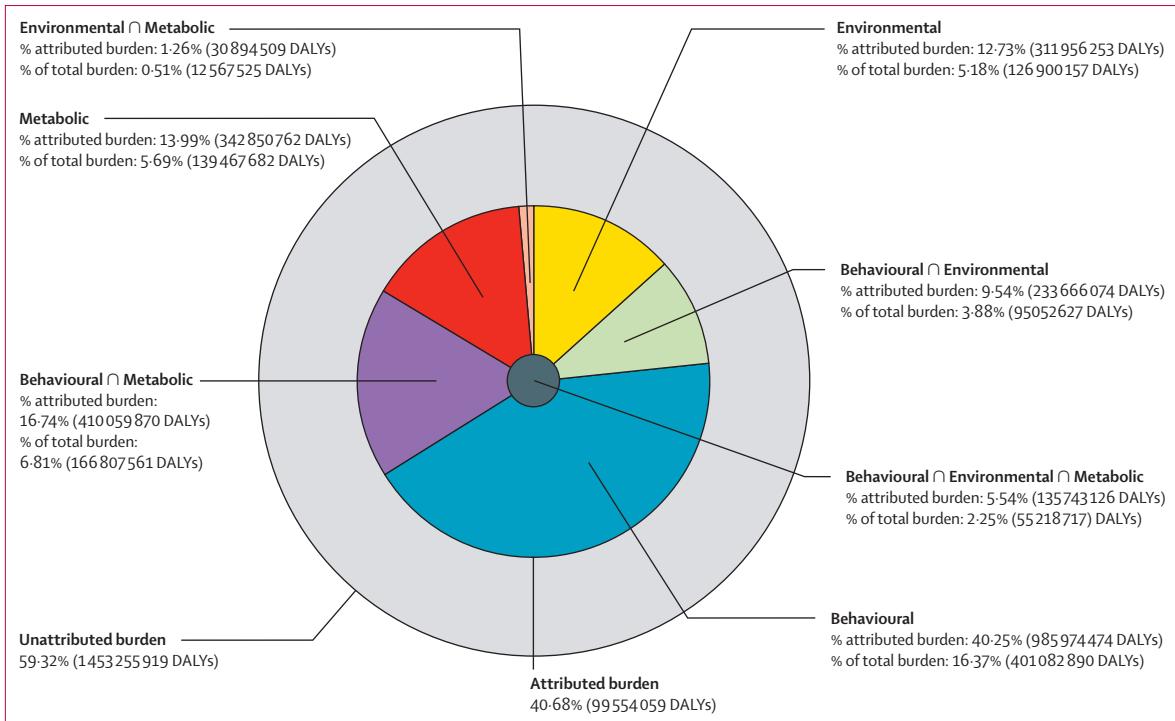


Figure 3: Proportion of all-cause DALYs attributable to behavioural, environmental and occupational, and metabolic risk factors and their overlaps for all ages in 2013
DALYs=disability-adjusted life-years. \cap =interaction.

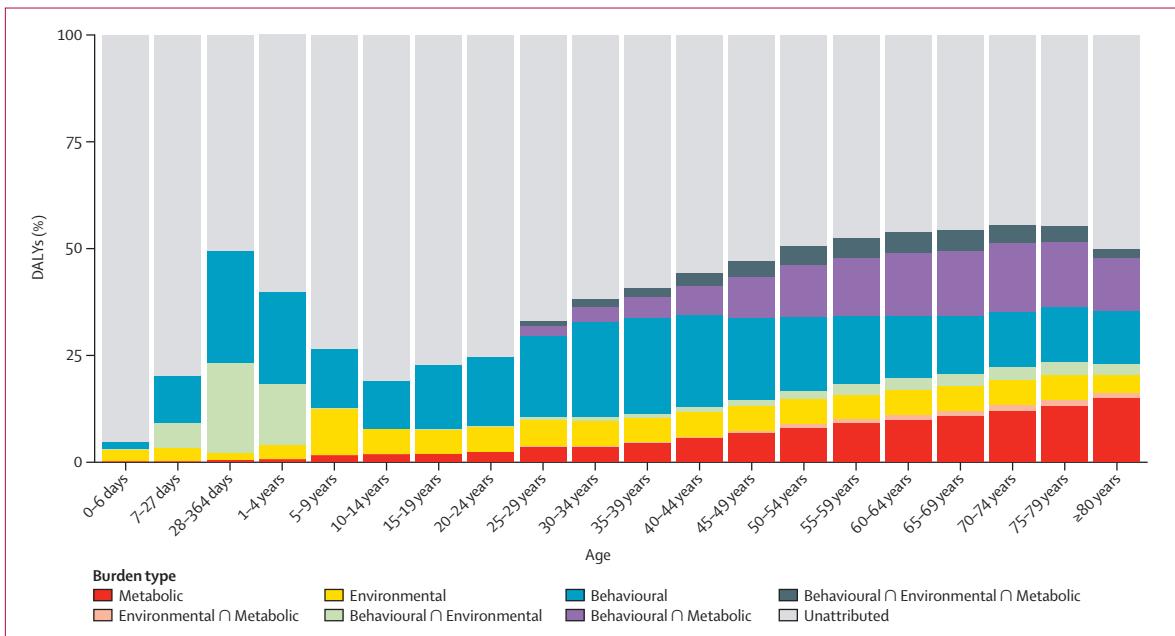


Figure 4: Proportion of global all-cause DALYs attributable to behavioural, environmental and occupational, and metabolic risk factors and their overlaps, by age for both sexes combined in 2013
DALYs=disability-adjusted life-years. \cap =interaction.

causes, all three primary clusters of risks have substantial overlap with the smallest proportional overlap being for environmental and occupational and metabolic risks. By contrast, cardiovascular diseases are dominated by

metabolic risks and their considerable overlap with behavioural risks and environmental and occupational risks plays a much smaller role. Behavioural risks with a substantial overlap with environmental risks are the key

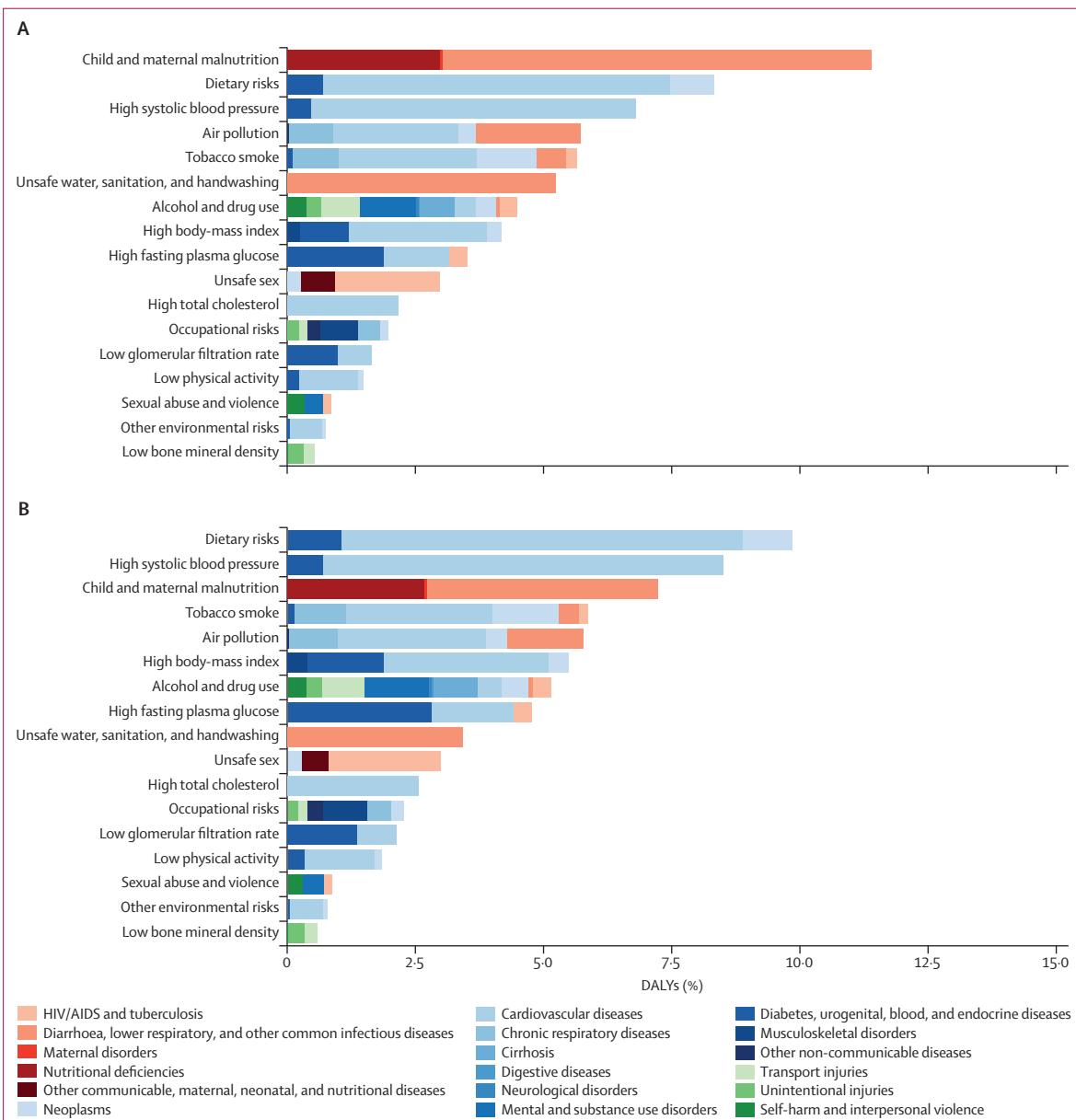


Figure 5: Global DALYs attributed to level 2 risk factors in 2000 for both sexes combined (A) and global DALYs attributed to level 2 risk factors in 2013 for both sexes combined (B)
DALYs=disability-adjusted life-years.

explanations for neoplasms. For the category of diarrhoea, lower respiratory infections, and other common infections, there is no contribution from the metabolic risks included in this study but environmental and occupational and behavioural risks are nearly equal with substantial overlap. Figure 4 shows the same breakdown of the overlap of the three clusters of risk factors by age. Because we have included no risk factors for major neonatal causes in this analysis, the fraction explained by the three clusters rises rapidly with age in children. The fraction explained declines again to a low at 10–14 years.

In young adults, behavioural risks are the dominant risks with an increasing component related to metabolic risks at older ages. Environmental risks explain a relatively constant share of burden in all age groups.

The leading risk factors globally have changed substantially from 2000 to 2013 (figure 5; see appendix pp 712–20 for 1990 and for results for males and females separately). In 2000, the leading cause of attributable DALYs (level 2 in the risk hierarchy) was child and maternal malnutrition for both males and females, accounting for more than one in ten DALYs. Other risks

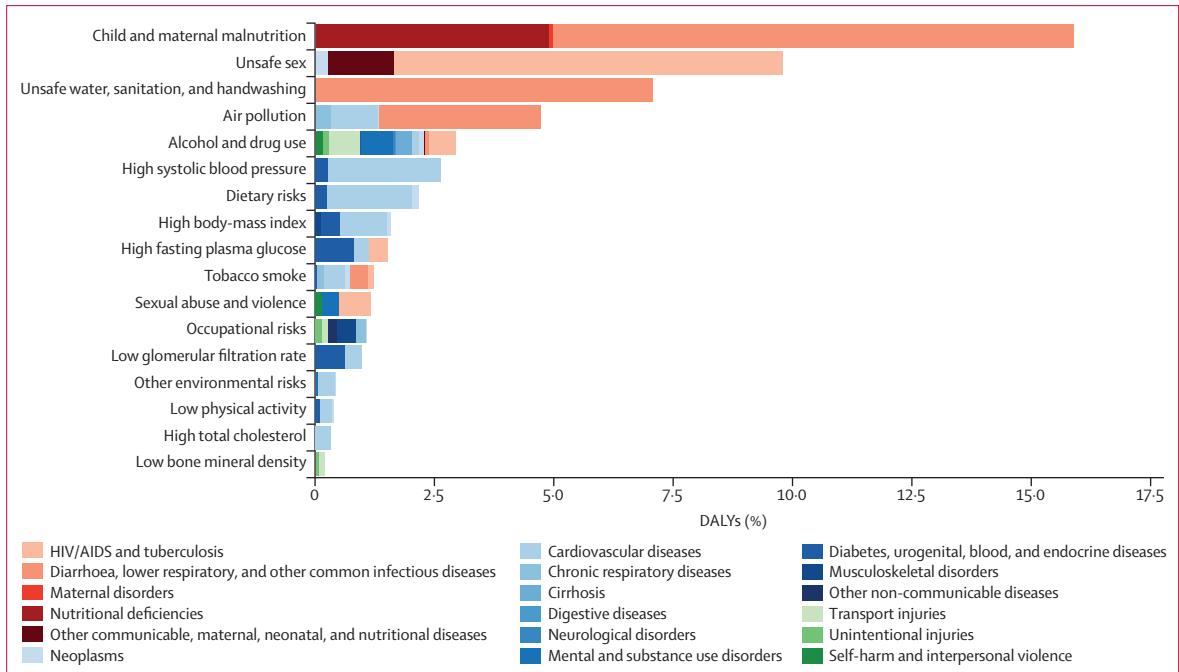


Figure 6: Global DALYs attributed to level 2 risk factors in 2013 for sub-Saharan Africa for both sexes combined
DALYs=disability-adjusted life-years.

that are characteristic of poor communities including unsafe water, unsafe sanitation and handwashing, and air pollution caused nearly 5% each of DALYs for males and females. By 2013, child and maternal malnutrition had dropped from 10·4% in males and 12·5% in females in 2000 to 6·55% and 8·02%, respectively. Risks for males at the global level in 2013 accounting for more than 5% of DALYs were the aggregation of dietary risks, high systolic blood pressure, tobacco smoke, alcohol and drug use, child and maternal malnutrition, air pollution, high fasting plasma glucose, and high BMI. In females, the risks in 2013 accounting for more than 5% of DALYs were dietary risks, child and maternal malnutrition, high systolic blood pressure, high BMI, and air pollution. Other risks that account for more than 2% of global DALYs in men and women include high fasting plasma glucose, unsafe water, unsafe sanitation, lack of handwashing, unsafe sex, and high cholesterol. The most notable differences in the magnitude of risk factors between males and females are the more prominent role for females of child and maternal malnutrition, high BMI, and sexual abuse and violence; whereas in males, tobacco, alcohol, and drug use are much more prominent than in females.

The global pattern masks tremendous regional variation in the profile of risks, particularly in sub-Saharan Africa compared with the rest of the developing and developed world. Figure 6 shows the leading risk factors in terms of attributable DALYs for sub-Saharan Africa in 2013 for both sexes combined: child and maternal malnutrition, unsafe sex, and unsafe water, sanitation, and handwashing

practices. In females, the next most important is air pollution (in this case mostly household air pollution) and high systolic blood pressure. In males, alcohol and drug use is also an important risk factor.

The period 2000–13 was characterised by a major shift in the size and relative magnitude of many risk factors (figure 7). Childhood undernutrition went from the number one global risk factor in terms of attributable DALYs to the fourth in 2013, a drop of 45% (39–51) in the number of DALYs. Unsafe water declined 37% (30–44) dropping from fourth to eighth; likewise unsafe sanitation dropped from ninth to 16th. Suboptimal breastfeeding declined 40% (32–47) from rank 11 to rank 19. Unsafe sex went from 10th to 9th from 2000 to 2013; it should be noted that the peak attributable burden associated with unsafe sex was in 2005. Several risks related to non-communicable diseases have risen in prominence. High systolic blood pressure increased from second to first. Smoking increased from third to second. High BMI increased from fifth to third and high fasting plasma glucose also increased from eighth to fifth. Ambient particulate matter pollution increased 6% (1–12) leading to a rank increase from 13th to 12th. Several diet components—most notably low fruit, high sodium, and low whole grains—increased in rank and absolute attributable burden over the period. We can isolate the impact of changes in population size and age composition by examining the change in the number of attributable DALYs compared with the change in the age-standardised rate of attributable DALYs. In fact, only five risk factors had increases in the age-standardised attributable DALY rate: unsafe sex, diet high in red meat,

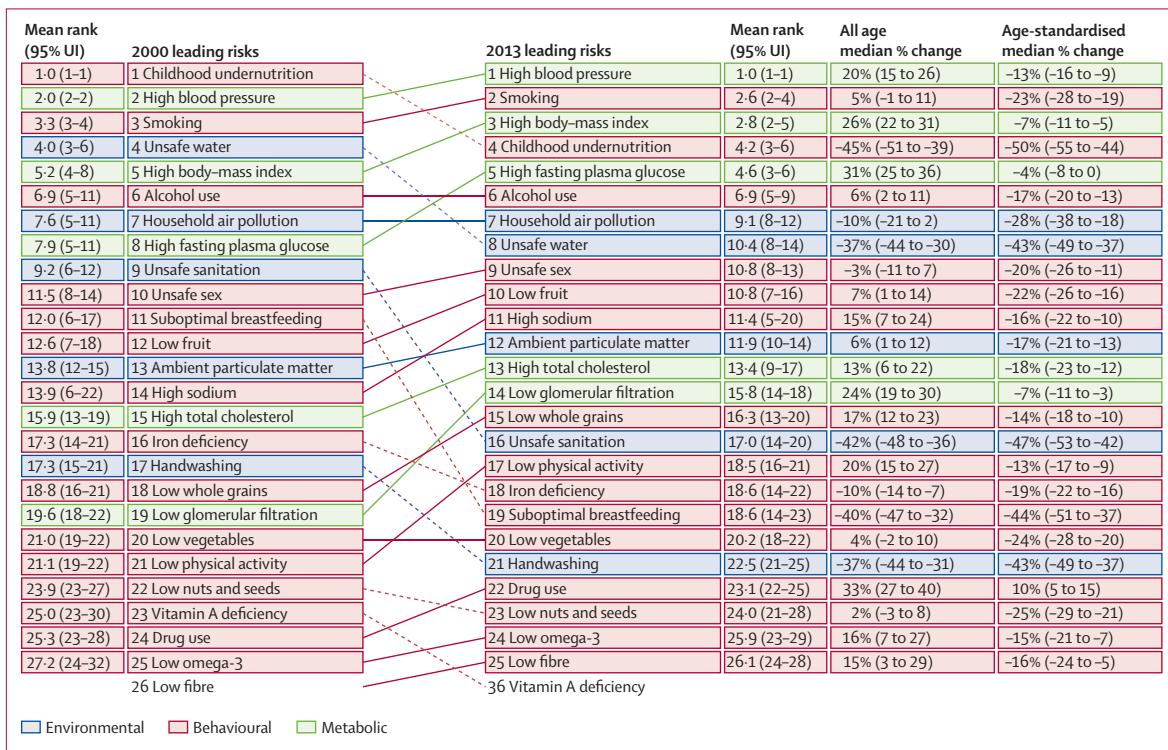


Figure 7: The 25 leading level 3 global risk factors for DALYs in both sexes combined in 2000 and 2013

diet high in sugar-sweetened beverages, occupational carcinogens, and drug use. In terms of the number of attributable DALYs, seven risks declined: vitamin A deficiency, childhood undernutrition, unsafe sanitation, secondhand smoke, no handwashing with soap, unsafe water, and suboptimal breastfeeding. Among the components of unsafe water, sanitation, and handwashing, the most important is unsafe water followed by unsafe sanitation and then no handwashing with soap.

Deaths and DALYs for all ages and both sexes combined for the full risk factor hierarchy are provided in table 3. Appendix pp 52–87 provides a further breakdown for each risk-outcome pair. All risk factors combined accounted for 25·1 million deaths in 1990, increasing by more than one-fifth to 30·8 million deaths in 2013. Although the number of deaths attributed to all risks increased substantially, the global all-risk all-cause PAF increased only 3·4 percentage points from 52·8% to 56·2%. The trends in DALYs attributed to all risk factors are quite different than those for deaths: total DALYs did not change from 1990 to 2013 and the PAF decreased by 0·05 of a percentage point. For most risks that affect non-communicable diseases, the number of deaths or DALYs that are attributable to those risks increased; however, the age-standardised PAF increased by more than 10% for a subset of risks, including most occupational carcinogens, occupational noise,

occupational ergonomic factors, alcohol use, drug use, diet low in whole grains, diet low in milk, diet high in red meat, diet high in processed meat, diet high in sugar-sweetened beverages, diet with suboptimal calcium, intimate partner violence, unsafe sex, low physical activity, high fasting plasma glucose, high systolic blood pressure, high BMI, and low glomerular filtration rate.

In most cases, the trend in the number of deaths attributed to a risk factor is similar to the trend in the number of DALYs attributable to the same risk from 1990 to 2013. Differences in the rates reflect the age pattern of the attributable events for a risk. An unusual case is air pollution, for which the number of attributable deaths increased but attributable DALYs declined. This finding is due to the trends for ambient particulate matter pollution, for which deaths increased from 2·2 million to 2·9 million deaths, and household air pollution from solid fuels for which deaths remained constant at 2·9 million. Because deaths due to household air pollution on average occur at much younger ages, the trend in this risk drives the overall trend in the joint risk of air pollution.

The combined effect of air pollution was 5·5 million deaths in 2013 and 141·5 million DALYs. There were roughly equal contributions from household air pollution (2·9 million deaths and 81·1 million DALYs in 2013) and ambient particulate matter pollution (2·9 million deaths and 69·7 million DALYs in 2013). Lead exposure accounted

	1990 deaths (in thousands)	2013 deaths (in thousands)	Median percent change deaths	Median percent change of age-standardised deaths PAF	1990 DALYs (in thousands)	2013 DALYs (in thousands)	Median percent change DALYs	Median percent change of age-standardised DALYs PAF
All risk factors	25 085 (24 385 to 25 821)	30 839 (29 719 to 31 949)	23.0% (19.0 to 27.3)	0.6% (-1.0 to 2.0)	1 035 987 (980 813 to 1 092 478)	996 554 (927 157 to 1 072 340)	-3.8% (-7.7 to -0.1)	-3.8% (-6.0 to -1.8)
Environmental risks	8 492 (8 036 to 8 953)	8 181 (7 651 to 8 726)	-3.7% (-9.6 to 2.4)	-15.5% (-19.8 to 11.1)	400 345 (374 489 to 424 432)	289 517 (265 778 to 312 094)	-27.7% (-32.1 to -23.2)	-22.6% (-26.1 to -19.1)
Unsafe water, sanitation, and handwashing	2 727 (2 530 to 2 952)	1 399 (1 237 to 1 576)	-48.8% (-53.6 to -43.7)	-44.9% (-49.6 to -40.0)	190 423 (174 685 to 208 033)	83 867 (72 879 to 95 568)	-56.0% (-60.6 to -50.9)	-45.6% (-50.8 to -40.1)
Unsafe water source	2 434 (1 971 to 2 763)	1 246 (989 to 1 464)	-48.8% (-53.7 to -43.9)	-45.0% (-49.7 to -40.1)	170 053 (137 216 to 193 963)	75 125 (59 952 to 89 756)	-55.9% (-60.4 to -50.8)	-45.5% (-50.7 to -40.0)
Unsafe sanitation	1 785 (1 613 to 1 959)	816 (707 to 921)	-54.4% (-58.8 to -49.8)	-51.1% (-55.5 to -46.9)	124 049 (111 394 to 137 303)	49 039 (41 770 to 56 227)	-60.5% (-64.8 to -56.0)	-51.3% (-56.3 to -46.4)
No handwashing with soap	1 010 (798 to 1 204)	517 (408 to 621)	-48.9% (-53.7 to -43.8)	-45.0% (-49.8 to -40.2)	70 389 (55 414 to 84 417)	30 721 (24 281 to 37 626)	-56.4% (-60.9 to -51.6)	-46.1% (-51.3 to -40.5)
Air pollution	4 808 (4 459 to 5 157)	5 527 (5 109 to 5 944)	14.8% (5.8 to 25.3)	-8.0% (-15.0 to -0.2)	157 831 (145 269 to 171 007)	141 456 (130 071 to 153 652)	-10.5% (-17.4 to -2.8)	-12.7% (-19.2 to -5.7)
Ambient particulate matter pollution	2238 (2 154 to 2 317)	2926 (2 777 to 3 066)	30.7% (25.2 to 36.5)	2.9% (0.7 to 5.1)	68 120 (64 972 to 71 405)	69 673 (65 585 to 73 552)	2.3% (-3.4 to 8.2)	-3.0% (-6.6 to 0.8)
Household air pollution from solid fuels	2857 (2 482 to 3 216)	2893 (2 463 to 3 303)	1.3% (-13.4 to 18.8)	-17.2% (-30.0 to -2.8)	101 643 (88 877 to 115 053)	81 087 (70 025 to 92 802)	-20.2% (-29.5 to -9.4)	-20.4% (-30.5 to -9.1)
Ambient ozone pollution	133 (105 to 162)	217 (161 to 272)	63.8% (14.5 to 125.1)	19.8% (-16.3 to 60.6)	3038 (2296 to 3814)	5073 (3576 to 6620)	66.9% (12.2 to 137.1)	32.5% (-11.0 to 84.6)
Other environmental risks	731 (523 to 965)	945 (663 to 1279)	29.2% (17.1 to 40.5)	-1.9% (-9.2 to 4.7)	17 015 (12 567 to 22 173)	18 822 (13 300 to 25 407)	10.5% (0.4 to 20.1)	-9.4% (-16.6 to -2.3)
Residential radon	63 (41 to 86)	92 (61 to 128)	46.3% (13.1 to 87.9)	13.8% (-11.7 to 44.3)	1503 (984 to 2086)	1979 (1331 to 2768)	31.7% (2.4 to 67.6)	7.1% (-17.0 to -36.9)
Lead exposure	668 (465 to 899)	853 (572 to 1181)	27.6% (15.1 to 39.1)	-3.3% (-10.8 to 3.7)	15 512 (10 967 to 20 727)	16 843 (11 494 to 23 505)	8.5% (-2.4 to 18.3)	-10.9% (-18.9 to -3.8)
Occupational risks	562 (509 to 629)	717 (641 to 803)	27.7% (13.4 to 42.5)	4.0% (-5.7 to 14.0)	43 879 (35 819 to 52 859)	55 352 (44 589 to 67 890)	26.2% (16.3 to 36.1)	10.2% (2.9 to 18.0)
Occupational carcinogens	152 (135 to 174)	304 (263 to 341)	100.7% (78.5 to 116.2)	52.4% (36.1 to 63.6)	3149 (2789 to 3543)	5803 (5076 to 6526)	84.7% (66.2 to 101.4)	48.5% (34.2 to 60.8)
Occupational exposure to asbestos	94 (76 to 116)	194 (155 to 233)	109.6% (72.4 to 132.2)	56.2% (28.9 to 74.2)	1773 (1425 to 2211)	3402 (2725 to 4113)	93.4% (63.5 to 117.3)	53.4% (29.9 to 72.4)
Occupational exposure to polycyclic aromatic hydrocarbons	3 (2 to 3)	6 (5 to 7)	120.2% (101.8 to 139.3)	71.4% (58.4 to 85.1)	60 (51 to 71)	125 (102 to 146)	105.9% (88.3 to 126.2)	67.4% (52.8 to 82.7)
Occupational exposure to silica	11 (10 to 12)	21 (19 to 24)	95.8% (78.9 to 112.6)	52.8% (41.3 to 64.1)	248 (223 to 274)	454 (404 to 509)	83.0% (67.3 to 100.1)	49.0% (35.8 to 61.9)
Occupational exposure to sulphuric acid	3 (2 to 4)	4 (3 to 5)	29.6% (16.8 to 48.3)	0.8% (-8.8 to 13.1)	68 (49 to 91)	83 (60 to 113)	21.3% (9.6 to 40.5)	-1.5% (-11.6 to 12.1%)
Occupational exposure to trichloroethylene	0 (0 to 0)	0 (0 to 0)	100.2% (88.5 to 112.2)	54.3% (46.1 to 62.7)	1 (0 to 2)	2 (0 to 3)	88.5% (77.3 to 100.2)	51.7% (42.9 to 61.1)
Occupational exposure to arsenic	2 (2 to 3)	4 (3 to 4)	72.7% (56.4 to 90.8)	34.7% (23.4 to 46.8)	47 (38 to 58)	76 (60 to 94)	61.3% (46.0 to 79.3)	31.3% (18.6 to 44.9)
Occupational exposure to benzene	2 (1 to 2)	3 (2 to 3)	66.2% (57.2 to 75.5)	32.3% (25.8 to 37.8)	59 (51 to 68)	95 (81 to 108)	59.4% (50.3 to 69.1)	36.8% (29.1 to 44.4)
Occupational exposure to beryllium	0 (0 to 0)	0 (0 to 0)	44.3% (30.6 to 62.7)	12.6% (3.0 to 25.3)	2 (2 to 3)	3 (3 to 4)	34.7% (21.6 to 53.2)	9.1% (-2.0 to 22.3%)

(Table 3 continues on next page)

	1990 deaths (in thousands)	2013 deaths (in thousands)	Median percent change deaths	Median percent change of age-standardised deaths PAF	1990 DALYs (in thousands)	2013 DALYs (in thousands)	Median percent change DALYs	Median percent change of age-standardised DALYs PAF
(Continued from previous page)								
Occupational exposure to cadmium	0 (0 to 0)	1 (1 to 1)	116.6% (97.0 to 137.4%)	68.6% (54.9 to 82.2)	8 (7 to 9)	16 (13 to 19)	102.8% (84.4 to 123.2)	64.9% (49.7 to 80.1)
Occupational exposure to chromium	1 (1 to 1)	3 (2 to 3)	116.2% (96.7 to 136.7)	68.3% (54.8 to 81.4)	28 (25 to 32)	57 (50 to 65)	102.3% (83.8 to 123.6)	64.6% (48.9 to 80.4)
Occupational exposure to diesel engine exhaust	17 (15 to 20)	37 (32 to 43)	116.6% (99.4 to 134.9)	69.1% (57.2 to 81.3)	394 (343 to 449)	797 (690 to 913)	102.0% (84.6 to 120.8)	64.4% (50.5 to 78.5)
Occupational exposure to second-hand smoke	19 (17 to 20)	34 (31 to 37)	80.5% (66.8 to 94.8)	40.6% (31.5 to 50.0)	431 (393 to 465)	725 (660 to 794)	68.1% (54.7 to 83.8)	36.7% (26.0 to 48.3)
Occupational exposure to formaldehyde	1 (0 to 1)	1 (1 to 1)	51.1% (34.2 to 67.8)	20.9% (9.3 to 32.2)	20 (16 to 25)	29 (23 to 35)	43.3% (26.9 to 59.7)	21.3% (8.6 to 34.3)
Occupational exposure to nickel	6 (4 to 8)	12 (9 to 16)	103.0% (82.2 to 123.6)	58.0% (42.7 to 73.1)	135 (103 to 173)	257 (193 to 326)	90.5% (70.8 to 110.7)	54.6% (38.4 to 71.0)
Occupational asthmagens	63 (48 to 93)	52 (42 to 70)	-18.4% (-32.9 to 5.2)	-34.2% (-46.8 to -17.1)	2903 (2310 to 3909)	2771 (2227 to 3521)	-4.7% (-18.1 to 12.0)	-18.1% (-30.5 to -4.4)
Occupational particulate matter, gases, and fumes	197 (161 to 236)	205 (164 to 251)	3.7% (-7.6 to 17.6)	-18.8% (-26.7 to -9.9)	7212 (5877 to 8545)	8802 (7012 to 10740)	22.0% (10.9 to 34.0)	-0.6% (-8.4 to 8.0)
Occupational noise	5039 (3268 to 7193)	7119 (4549 to 10329)	41.4% (33.9 to 48.0)	21.4% (15.1 to 27.8)
Occupational injuries	151 (122 to 197)	159 (127 to 206)	4.4% (-24.6 to 49.2)	-4.7% (-32.6 to 34.2)	9776 (7809 to 12884)	9947 (7886 to 12927)	1.3% (-26.0 to 42.5)	-2.9% (-29.9 to 34.2)
Occupational ergonomic factors	15 944 (10 747 to 22 276)	21 109 (14 206 to 29 304)	32.2% (28.0 to 37.7)	16.2% (11.2 to 21.8)
Behavioural risks	18 453 (17 419 to 19 480)	21 909 (20 446 to 23 383)	18.7% (14.5 to 23.1)	-0.7% (-2.4 to 1.0)	799 073 (753 589 to 844 178)	717 608 (667 831 to 771 924)	-10.2% (-14.1 to -6.1)	-7.4% (-9.8 to -5.1)
Child and maternal malnutrition	4254 (3937 to 4555)	1665 (1487 to 1840)	-60.8% (-65.0 to -57.1)	-50.5% (-55.9 to -45.5)	403 951 (371 608 to 432 910)	176 859 (156 431 to 199 831)	-56.1% (-60.6 to -52.2)	-43.2% (-47.9 to -38.9)
Childhood undernutrition	3635 (3341 to 3888)	1327 (1169 to 1481)	-63.4% (-67.6 to -59.6)	-53.2% (-58.6 to -48.1)	317 851 (292 419 to 339 549)	119 802 (106 565 to 133 359)	-62.2% (-66.3 to -58.5)	-49.9% (-55.1 to -45.0)
Childhood overweight	1080 (886 to 1288)	386 (309 to 463)	-64.2% (-70.5 to -57.9)	-54.0% (-62.1 to -45.8)	95 709 (79 446 to 113 315)	35 806 (29 108 to 42 575)	-62.5% (-68.9 to -56.3)	-50.2% (-58.3 to -42.4)
Childhood wasting	3295 (2802 to 3696)	1247 (1034 to 1413)	-62.0% (-66.5 to -57.4)	-51.4% (-57.1 to -45.2)	288 145 (246 038 to 322 526)	112 350 (94 437 to 127 169)	-60.9% (-65.4 to -56.3)	-48.2% (-53.8 to -42.2)
Childhood stunting	848 (474 to 1339)	218 (107 to 389)	-74.6% (-79.5 to -68.9)	-67.3% (-73.9 to -60.0)	73 355 (40 848 to 115 668)	19 291 (95 81 to 34 208)	-73.9% (-79.0 to -68.6)	-65.4% (-72.2 to -58.1)
Suboptimal breastfeeding	1344 (904 to 1834)	501 (318 to 697)	-62.8% (-67.5 to -58.0)	-52.1% (-58.3 to -45.5)	116 801 (78 740 to 158 958)	44 203 (28 205 to 61 650)	-62.3% (-66.8 to -57.6)	-49.6% (-55.7 to -43.4)
Non-exclusive breastfeeding	1155 (743 to 1606)	442 (264 to 641)	-61.9% (-66.8 to -56.9)	-50.7% (-57.3 to -43.9)	99 927 (64 457 to 138 645)	38 502 (23 037 to 55 565)	-61.7% (-66.5 to -56.7)	-48.7% (-55.1 to -42.1)
Discontinued breastfeeding	191 (65 to 349)	59 (20 to 110)	-69.3% (-74.6 to -63.0)	-60.5% (-67.3 to -52.5)	17 046 (5804 to 31 059)	5722 (1898 to 10 599)	-66.6% (-71.7 to -60.5)	-55.4% (-62.1 to -47.6)
Iron deficiency	241 (169 to 344)	199 (137 to 275)	-17.1% (-33.7 to -0.5)	-21.8% (-35.6 to -7.7)	53 019 (38 674 to 71 446)	44 651 (31 844 to 62 304)	-15.6% (-21.5 to -11.5)	-6.5% (-11.3 to -2.0)
Vitamin A deficiency	377 (247 to 522)	85 (51 to 125)	-77.4% (-82.9 to -71.5)	-71.0% (-78.2 to -63.7)	32 920 (21 694 to 45 629)	7875 (4758 to 11 541)	-76.1% (-81.6 to -70.3)	-68.3% (-75.6 to -60.9)
Zinc deficiency	221 (15 to 491)	66 (4 to 153)	-70.1% (-76.3 to -62.7)	-61.2% (-69.8 to -52.4)	19 188 (18 16 to 41 961)	5996 (745 to 13 267)	-68.4% (-74.4 to -56.7)	-57.3% (-66.1 to -42.6)

(Table 3 continues on next page)

	1990 deaths (in thousands)	2013 deaths (in thousands)	Median percent change deaths	Median percent change of age-standardised deaths PAF	1990 DALYs (in thousands)	2013 DALYs (in thousands)	Median percent change DALYs	Median percent change of age-standardised DALYs PAF
(Continued from previous page)								
Tobacco smoke	5229 (4816 to 5681)	6149 (5587 to 6762)	17.8% (10.9 to 23.9)	-9.6% (-13.2 to -6.3)	142 341 (131 399 to 153 920)	143 512 (129 979 to 159 147)	0.7% (-5.5 to 7.5)	-14.5% (-18.9 to -10.2)
Smoking	4634 (4222 to 5079)	5818 (5258 to 6435)	25.7% (17.9 to 32.6)	-5.1% (-9.3 to -1.3)	115 910 (105 383 to 127 110)	134 196 (120 872 to 149 759)	15.8% (8.6 to 23.6)	-7.4% (-12.4 to -2.2)
Second hand smoke	595 (540 to 654)	331 (308 to 355)	-44.4% (-48.2 to -40.0)	-50.9% (-53.6 to -48.2)	26 431 (22 494 to 30 676)	9316 (8417 to 10,277)	-64.7% (-68.3 to -60.8)	-60.2% (-63.3 to -56.9)
Alcohol and drug use	2092 (1671 to 2438)	3163 (2537 to 3656)	51.3% (44.3 to 58.4)	19.4% (15.3 to 23.7)	89 844 (76 788 to 101 767)	126 053 (107 154 to 142 356)	40.2% (34.8 to 46.3)	23.5% (18.9 to 28.3)
Alcohol use	1977 (1555 to 2329)	2786 (2146 to 3287)	40.9% (33.2 to 47.9)	11.1% (6.9 to 14.8)	76 029 (63 443 to 87 186)	99 278 (81 295 to 113 616)	30.5% (23.9 to 37.0)	13.6% (8.6 to 18.1)
Drug use	132 (109 to 155)	429 (381 to 480)	224.8% (188.0 to 273.4)	179.5% (147.0 to 222.3)	14 481 (11 607 to 17 286)	28 578 (24 505 to 33 104)	97.4% (83.2 to 114.8)	89.3% (74.3 to 107.1)
Dietary risks	8068 (6991 to 9159)	11 274 (9656 to 12 957)	39.6% (34.1 to 46.2)	2.9% (0.3 to 5.8)	177 408 (154 661 to 200 097)	241 351 (209 634 to 273 339)	35.9% (29.8 to 43.0)	7.7% (4.1 to 12.0)
Diet low in fruits	2540 (1686 to 3367)	3413 (2207 to 4546)	33.9% (25.6 to 43.3)	0.1% (-5.2 to 5.9)	58 710 (39 575 to 76 928)	74 797 (49 434 to 98 791)	27.0% (19.0 to 36.0)	1.7% (-3.8 to 7.9)
Diet low in vegetables	1381 (1094 to 1684)	1782 (1405 to 2173)	28.9% (22.3 to 36.6)	-4.8% (-9.4 to -0.1)	31 283 (24 692 to 38 039)	39 176 (31 050 to 47 658)	25.2% (17.9 to 33.2)	-0.4% (-5.4 to 5.1)
Diet low in whole grains	1396 (1066 to 1728)	2049 (1575 to 2525)	46.8% (40.8 to 54.2)	9.2% (5.9 to 13.1)	34 807 (26 736 to 43 078)	51 411 (39 500 to 63 286)	47.6% (40.9 to 56.0)	18.0% (13.9 to 22.9)
Diet low in nuts and seeds	1012 (725 to 1304)	1195 (816 to 1578)	17.7% (10.5 to 25.0)	-13.3% (-18.7 to -8.5)	23 434 (16 643 to 30 134)	27 109 (18 408 to 36 030)	15.3% (8.0 to 22.8)	-8.5% (-13.7 to -3.3)
Diet low in milk	66 (19 to 111)	105 (30 to 177)	58.1% (51.9 to 63.8)	18.4% (14.6 to 22.2)	1515 (434 to 2538)	2218 (633 to 3713)	46.3% (39.8 to 52.5)	17.2% (12.6 to 21.6)
Diet high in red meat	62 (55 to 70)	102 (89 to 116)	64.1% (52.8 to 75.8)	23.0% (14.4 to 32.0)	2201 (1854 to 2585)	4147 (3349 to 5026)	88.2% (75.9 to 101.6)	50.7% (41.9 to 60.4)
Diet high in processed meat	457 (332 to 622)	644 (467 to 881)	41.4% (24.1 to 57.9)	4.4% (-8.6 to 17.1)	11 745 (8676 to 15 897)	17 380 (12 677 to 23 925)	47.9% (30.9 to 64.0)	17.3% (3.4 to 29.4)
Diet high in sugar-sweetened beverages	60 (44 to 82)	126 (96 to 166)	110.1% (88.7 to 141.4)	64.4% (45.7 to 87.2)	2712 (2006 to 3635)	6190 (4665 to 8142)	128.4% (105.4 to 159.0)	89.6% (70.2 to 115.3)
Diet low in fibre	716 (587 to 853)	1009 (817 to 1207)	40.6% (25.3 to 60.0)	4.2% (-7.4 to 18.0)	16 395 (13 496 to 19 433)	22 098 (17 996 to 26 349)	35.0% (18.6 to 52.4)	7.4% (-5.1 to 20.6)
Diet suboptimal in calcium	85 (74 to 97)	141 (122 to 160)	64.6% (53.6 to 80.4)	22.9% (15.2 to 33.1)	1870 (1605 to 2143)	2876 (2507 to 3258)	53.5% (42.8 to 66.9)	22.9% (15.5 to 33.0)
Diet low in seafood omega-3 fatty acids	712 (530 to 909)	1031 (769 to 1304)	44.6% (35.3 to 57.3)	7.5% (1.9 to 14.3)	16 285 (12 321 to 20 657)	22 448 (16 887 to 28 205)	37.6% (27.7 to 52.7)	10.1% (2.8 to 19.8)
Diet low in polyunsaturated fatty acids	447 (404 to 493)	581 (512 to 651)	29.6% (16.9 to 44.7)	-4.5% (-13.7 to 5.2)	10 033 (9051 to 11 040)	12 670 (11 103 to 14 342)	25.9% (13.0 to 41.8)	0.0% (-9.8 to 11.6)
Diet high in trans fatty acids	464 (311 to 650)	405 (218 to 645)	-15.0% (-34.0 to 3.7)	-38.3% (-52.2 to -24.5)	10 644 (7131 to 14 859)	9875 (5503 to 15 228)	-8.5% (-29.0 to 9.6)	-28.7% (-43.6 to -14.7)
Diet high in sodium	2562 (1377 to 4041)	3689 (2028 to 5810)	44.1% (33.8 to 57.1)	7.4% (1.3 to 15.5)	54 620 (29 271 to 86 008)	74 327 (40 615 to 116 717)	36.2% (26.5 to 48.7)	8.4% (1.5 to 17.5)
Sexual abuse and violence	163 (141 to 188)	257 (203 to 312)	57.5% (30.6 to 83.7)	36.7% (14.9 to 58.9)	15 133 (12 297 to 18 621)	21 290 (16 743 to 26 065)	40.6% (26.4 to 55.7)	31.8% (19.1 to 46.0)
Childhood sexual abuse	64 (53 to 78)	68 (55 to 82)	5.9% (-9.3 to 19.9)	-7.4% (-21.4 to 3.9)	6896 (5364 to 8667)	7682 (5910 to 9736)	11.4% (4.0 to 18.8)	5.8% (-1.6 to 12.6)
Intimate partner violence	106 (86 to 130)	197 (146 to 251)	85.9% (49.6 to 124.8)	60.9% (30.5 to 93.6)	9009 (7076 to 11 440)	14 454 (11 027 to 18 164)	60.6% (39.6 to 85.1)	48.8% (29.3 to 71.7)
Unsafe sex	679 (561 to 827)	1481 (1383 to 1621)	118.8% (86.2 to 158.1)	100.5% (76.6 to 129.3)	39 761 (30 789 to 52 320)	73 282 (67 015 to 82 478)	86.1% (51.7 to 127.0)	97.6% (68.3 to 131.3)

(Table 3 continues on next page)

	1990 deaths (in thousands)	2013 deaths (in thousands)	Median percent change deaths	Median percent change of age-standardised deaths PAF	1990 DALYs (in thousands)	2013 DALYs (in thousands)	Median percent change DALYs	Median percent change of age-standardised DALYs PAF
(Continued from previous page)								
Low physical activity	1489 (1257 to 1741)	2182 (1858 to 2555)	46·5% (40·9 to 52·9)	6·4% (4·0 to 9·2)	31247 (26556 to 36521)	45143 (38328 to 52671)	44·3% (37·2 to 52·8)	13·6% (9·4 to 18·3)
Metabolic risks	10398 (9811 to 11003)	15723 (14719 to 16767)	51·2% (46·2 to 57·0)	10·6% (8·8 to 12·6)	250957 (233711 to 267582)	373817 (343978 to 403889)	48·9% (43·1 to 54·9)	18·4% (15·3 to 21·7)
High fasting plasma glucose	2444 (2101 to 2853)	4014 (3499 to 4641)	64·4% (56·3 to 73·4)	21·8% (17·4 to 26·8)	68903 (60506 to 78071)	116893 (101592 to 133368)	69·6% (60·9 to 78·7)	37·0% (31·6 to 42·6)
High total cholesterol	2204 (1574 to 3126)	2830 (1966 to 4053)	28·0% (19·9 to 37·4)	-7·4% (-11·3 to -2·5)	49289 (38075 to 63764)	62715 (49244 to 80986)	26·9% (19·8 to 36·3)	-0·6% (-5·7 to 5·7)
High systolic blood pressure	6949 (6182 to 7665)	10364 (9178 to 11544)	49·1% (43·2 to 55·2)	8·8% (6·4 to 11·2)	143434 (130053 to 156023)	208129 (188307 to 227509)	45·1% (38·7 to 52·1)	14·1% (10·0 to 18·4)
High body-mass index	2724 (2263 to 3187)	4444 (3716 to 5169)	63·2% (57·8 to 69·5)	22·2% (19·0 to 25·4)	78310 (65436 to 92006)	134048 (112420 to 156787)	71·3% (64·4 to 78·0)	36·3% (32·3 to 40·1)
Low bone mineral density	176 (164 to 198)	334 (285 to 361)	92·1% (62·8 to 104·0)	35·4% (15·4 to 44·6)	10903 (8958 to 13231)	14249 (11658 to 17500)	30·6% (20·9 to 40·7)	-1·8% (-9·4 to 6·9)
Low glomerular filtration rate	1310 (1176 to 1480)	2164 (1960 to 2387)	65·6% (54·5 to 74·5)	18·9% (11·1 to 24·8)	34159 (30499 to 38394)	51906 (46246 to 57573)	52·0% (43·5 to 59·3)	25·5% (18·4 to 31·3)

DALYs=disability-adjusted life-years. PAF=population attributable fraction.

Table 3: Global, all-age, all-cause deaths, and DALYs for both sexes combined attributable to each risk factor in 1990 and 2013 with 95% uncertainty intervals

for an increased number of deaths in 2013 as compared with 1990 (853 000 compared with 668 000). Taken together, occupational carcinogens caused 304 000 deaths globally in 2013 and 5·8 million DALYs; asbestos exposure accounted for nearly two-thirds of the burden of all occupational carcinogens. In total, occupational risks accounted for 55·4 million DALYs, of which occupational ergonomic factors accounted for 38·1%. As a cluster, childhood undernutrition accounted for 1·3 million child deaths in 2013 and 120 million DALYs. Iron deficiency, vitamin A deficiency, and zinc deficiency each accounted for less than 200 000 deaths; however, iron deficiency is a major cause of DALYs due to its crucial role as a cause of anaemia.

The number of deaths attributable to tobacco smoking continued to increase from 4·6 million in 1990 to 5·8 million in 2013, and from 115·9 million DALYs to 134·2 million DALYs over the same period. Secondhand smoke accounted for an additional 331 000 deaths and 9·3 million DALYs. Alcohol use accounted for 2·8 million deaths and 99·3 million DALYs in 2013, with both deaths and DALYs increasing over time. Among the components of diet, the most important in terms of deaths and DALYs in 2013 were diets high in sodium and low in fruit, followed by low whole grains and low vegetables. Among the metabolic risks, high systolic blood pressure is more than twice as important as the next most important factor—high BMI, followed by high fasting plasma glucose.

One simple way to examine the complex results by country is to examine the leading risk factor in terms of DALYs with risk factors broken down to level 3 in the risk factor hierarchy (figure 8). For men (figure 8A), a large set of countries from North Africa and the Middle East through to south Asia and east Asia and into Eastern

Europe have high systolic blood pressure as their leading risk. Another broad set of countries in west, east, and central sub-Saharan Africa have childhood undernutrition as the leading risk. Unsafe sex is the leading risk in a set of countries in east and southern Africa with large HIV epidemics. Tobacco is the leading risk in most high-income countries and alcohol use is the leading risk in many countries in Latin America. For women (figure 8B), the pattern is notably different. High BMI is the leading risk for most countries in North and South America with only three exceptions (Canada, Guatemala, and Uruguay). High BMI is also the leading risk in Spain, France, Switzerland, Belgium, most of North Africa and the Middle East, Australia, and New Zealand. High systolic blood pressure is the leading risk in most of Central and Eastern Europe, central Asia, south Asia, and east Asia. Cambodia stands out as having household air pollution as the top risk factor for women. In sub-Saharan Africa, the leading risks are undernutrition and unsafe sex for both men and women in sub-Saharan Africa.

Figure 9 provides the ten leading risk factors in terms of attributable DALYs (level 3 in the risk hierarchy) for each country in 2013 for both sexes combined. The top 15 global risks have been coloured to highlight where country and regional patterns diverge from global patterns. In high-income regions, most countries had high BMI, high systolic blood pressure, and smoking as the top three risks. Brunei, Singapore, and Japan had high fasting plasma glucose in the top three. Alcohol use was the second leading risk in South Korea. Low glomerular filtration rate was an important risk in several countries such as Italy. In Central Europe,

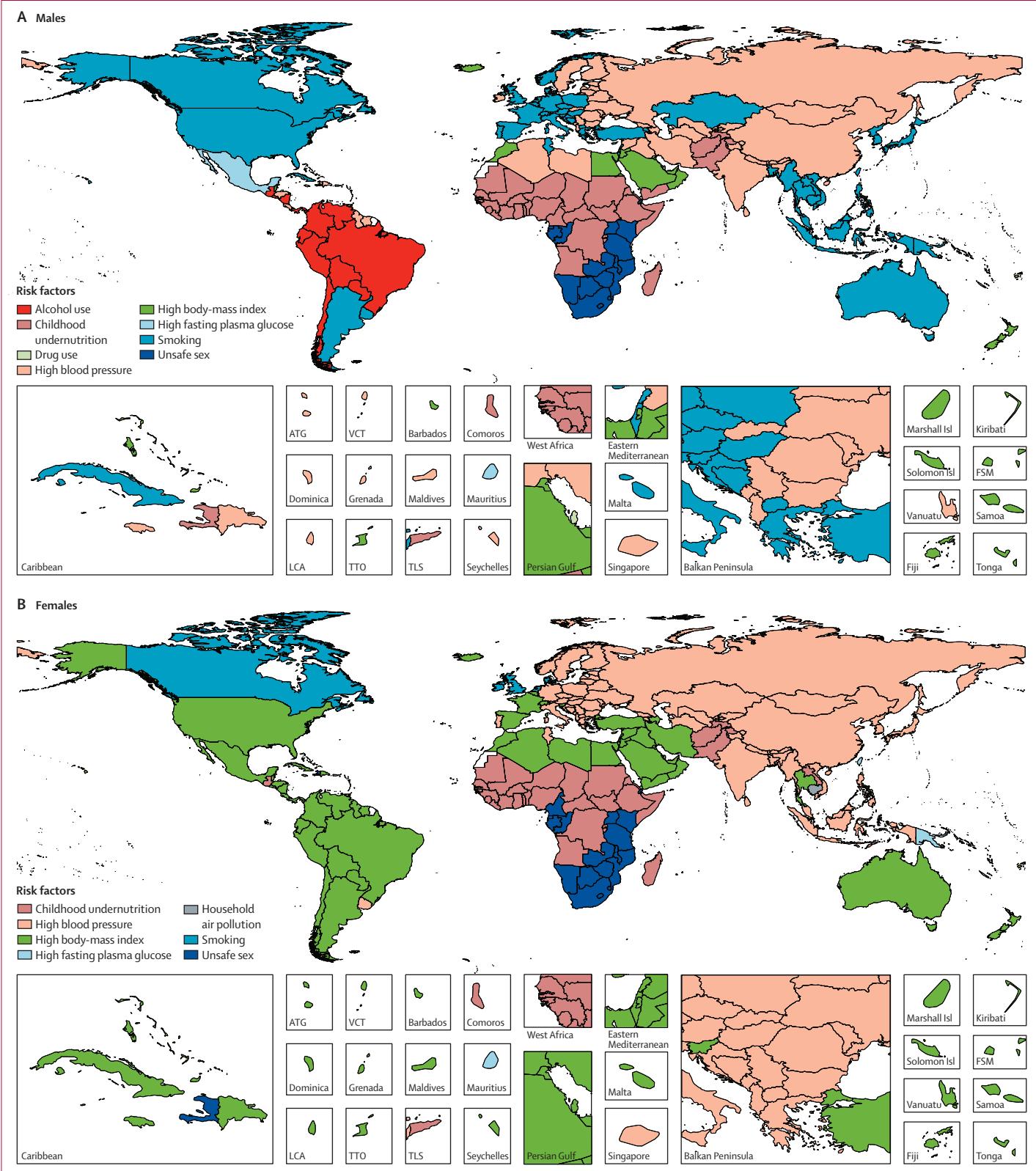


Figure 8: Global maps for level 3 risk factors in 2013 of attributable DALYs for males (A) and females (B)

DALYs=disability-adjusted life-years. ATG=Antigua and Barbuda. VCT=Saint Vincent and the Grenadines. FSM=Federated States of Micronesia. LCA=Saint Lucia. TLS=Timor-Leste. TTO=Trinidad and Tobago. Isl=Islands.

Eastern Europe, and central Asia, the leading risk factor for both sexes combined was high systolic blood pressure, followed by smoking or high BMI. In Mongolia, Belarus, and Russia, alcohol was the second leading risk factor. Childhood undernutrition remained a top five risk in Tajikistan, Turkmenistan, and Uzbekistan. In Latin America and the Caribbean, high systolic blood pressure or high BMI were the leading risks in most countries. Notable exceptions are in Haiti and Guatemala, where childhood undernutrition was the leading risk. Haiti also stands out with unsafe sex as the second leading risk factor. In this region, either high fasting plasma glucose or alcohol use were top five risks in nearly every country. Unsafe water was a top five risk in Haiti and Guatemala. In east Asia, the leading risks were high systolic blood pressure, tobacco smoking, and high sodium intake. In Oceania, high BMI and high fasting plasma glucose were the leading risks in all countries, except in Papua New Guinea where smoking and childhood undernutrition were most important and Vanuatu where high systolic blood pressure was the top risk, followed by high BMI. In southeast Asia, high systolic blood pressure and smoking were dominant risks, except in Laos and Timor-Leste where childhood undernutrition was the leading risk. Household air pollution was a top five risk in many countries in the region. In south Asia, high systolic blood pressure was the leading risk, except for in Afghanistan and Pakistan. In India, high fasting plasma glucose was the second leading risk followed by household air pollution, unsafe water, and childhood undernutrition. In North Africa and the Middle East, high BMI was the leading risk in nearly all countries, and most countries had high fasting plasma glucose and high systolic blood pressure as top three risks. Sudan and Yemen stand out with childhood undernutrition and unsafe water as top three risks. In sub-Saharan Africa, there are four patterns: countries where the leading risks were childhood undernutrition, unsafe water, and unsafe sanitation; countries where the leading risks were unsafe sex, childhood undernutrition, and unsafe water; countries in southern Africa with unsafe sex and alcohol use as leading risks, and island nations such as the Seychelles and Cape Verde with high systolic blood pressure as leading risk. South Africa is notable for the top three risks being unsafe sex, high BMI, and alcohol use.

Discussion

Our analysis of 79 risks divided into three broad groups of behavioural, environmental and occupational, and metabolic risk factors shows that together they explain slightly greater than 57% of global deaths and more than 41% of global DALYs. Each of the risk factors included in this analysis is modifiable, pointing to the huge potential of prevention to improve human health. Globally, behavioural risk factors are the most important followed by metabolic and environmental and occupational risk factors. This pattern varies substantially: in many countries in sub-Saharan Africa, environmental risk factors, mainly water, sanitation, no handwashing, and household air pollution, are more important than metabolic risks. By 2013, the six most important risk factors globally were dietary risks, high systolic blood pressure, child and maternal malnutrition, tobacco, air pollution, and high BMI.

Since 1990, there has been a profound change in risk factors associated with the global epidemiological transition. In 1990, child and maternal malnutrition and unsafe water, sanitation, and handwashing were the leading risks for global DALYs, but now these have been replaced by dietary risks and high systolic blood pressure. A large group of risk factors recorded declines of more than 10% in age-standardised PAFs from 1990 to 2013, including unsafe water, sanitation, and handwashing; household air pollution; suboptimal breastfeeding; childhood undernutrition; vitamin A deficiency; secondhand smoke; and diet high in trans fats. By contrast, for several risk factors, age-standardised PAFs are increasing: intimate partner violence, drug use, high BMI, high fasting plasma glucose, low glomerular filtration rate, unsafe sex, and several components of diet (ie, low whole grains, high red meat, and high sugar-sweetened beverages). This transition in risks reflects a general shift from environmental risks towards behavioural and metabolic risks. These insights should strengthen our understanding of the epidemiological transition and our capacity to forecast population health.

The risk factors included in this study are those that met our inclusion criteria. After removing the effect of these risks, a substantial fraction of global deaths and DALYs remain. What might account for the unexplained component of death rates and the even greater unexplained component for YLDs? Risk-deleted death rates (not shown in this paper) vary substantially across countries. Other environmental risks, such as soil and water contamination, or behavioural risks, such as lack of sleep, could explain a component of the unexplained variation.^{53–55} Inclusion of new risk factors in future iterations of the GBD might reduce the unattributed fraction. Social, economic, and cultural factors could be an important part of the explanation, but only the components of these risks expressed through differential behaviours or environmental risks have been incorporated in the GBD CRA work so far. Higher

Figure 9: The ten leading level 3 risks in 2013 in terms of DALYs by location for both sexes combined

The 15 leading risk factors are coloured. Subopt=Suboptimal. Occ=occupational. DALYs=disability-adjusted life-years. Bone mineral density=low bone mineral density. Handwashing=no handwashing with soap. Int partner violence=intimate partner violence. Nuts and seeds=diet low in nuts and seeds. Occ ergonomic=occupational ergonomic factors. Particulate matter=ambient particulate matter pollution. Physical activity=low physical activity. Processed meat=diet high in processed meat. Subopt breastfeeding=suboptimal breastfeeding. Sweetened beverages=diet high in sugar-sweetened beverages. Vegetables=diet low in vegetables.

risk-adjusted age-specific death and DALY rates are seen in low-income countries and those countries with lower educational attainment. Parts of both effects would be mediated through access to care and coverage with curative interventions. From a quarter to half of the decline in cardiovascular and circulatory diseases in high-income countries have been attributed to treatments.^{56–58} Another aspect of understanding the unexplained morbidity is that epidemiological studies have studied fewer of, and yielded fewer insights into, the drivers of key contributors to YLDs, such as mental and substance use disorders, musculoskeletal disorders, and neurological disorders. More research on the areas we know less about might redress this imbalance.

The behavioural risk factors included in this study range from explaining fewer than 19% of DALYs in 2013 in the Maldives to more than 54% in South Africa. There is substantial scope through changing behaviours to improve individual and population health. Although there is a role for drugs and vaccines to mitigate the harmful effects of some behaviours, interventions to affect and change behaviours must be the primary mechanisms to reduce this burden. In view of their large role, funding for research on interventions to change health behaviours by major research funders has been scarce. Intellectual property rights are harder to establish for behavioural change interventions so there are fewer incentives for the private sector to pursue this type of investigation. One exception to the absence of private sector engagement in this arena is the recent rise of personal health mobile device applications. More behavioural and social science research into solutions for behavioural risks, particularly those that are increasing such as the nexus of diet, physical activity, and BMI, is urgently needed.

Shifting from the behavioural, environmental and occupational, and metabolic risk factors to a more comprehensive view of risks including genes, the microbiome, public health, and medical care interventions, and distal social, economic, and cultural factors, would provide a more coherent account of health and its causes. The GBD has sought to provide a standardised framework, an evidence-based accounting, of the contribution of diseases and injuries and selected risks to deaths, YLLs, YLDs, and DALYs. It is natural to extend this framework progressively to quantify the broader set of risks for health outcomes. The rules of evidence, however, used so far in the CRA studies might need to be modified to allow this expansion. Social, economic, and cultural factors, for example, are mediated through several interactive pathways in the causal web; we would not expect that effect sizes would be consistent across contexts. This expansion will not be a quick undertaking, but the annual revisions of the GBD will provide an opportunity to encompass this broadened vision progressively.

The aggregation of the 14 specific components of diet accounted for nearly one tenth of global DALYs in 2013.

At the global level, the most important contributors to the overall burden of diet are low fruit, high sodium, low whole grains, low vegetables, and low nuts and seeds. But diet patterns vary greatly across countries and as a result the most important diet components vary substantially by country. Our diet estimates do not reflect the total effect of diet on health. Dietary risk factor exposures reflecting the literature on diet epidemiology are standardised to a 2000 calorie diet, resulting in dietary exposures that reflect diet composition rather than direct caloric contribution for each risk factor. This holds true for all dietary risks except for sugar-sweetened beverages, for which the effect of calories is captured through effects on BMI. Other dietary components probably affect overweight and obesity, in both protective and detrimental directions.^{59,60} If one were to quantify the contribution of diet mediated through weight gain and BMI, the overall effect of diet would be much larger than is estimated here. Since GBD 2010, the PREDIMED randomised clinical trial reported an effect of nut consumption that was quite consistent with the estimated effect from cohort studies.^{61,62} Yet criticism of dietary studies and the effects derived from them abounds.^{63,64} A considerable challenge in the diet estimation is that component exposures are also likely to be interrelated within individuals. There are correlations across individuals in the intake of different diet components, and there might also be synergistic or antagonistic effects of dietary components that are consumed together. Furthermore, various methods for diet recall all have substantial measurement error and biomarkers to measure recent diet have not been operationalised to date. In view of the importance of diet in this analysis, more attention should be paid to quantifying the correlation structure of diet components and the effects of different diet components on weight gain, including the effect of total caloric intake. Although there are many opportunities to improve the estimation of the burden attributable to diet, the potential magnitude of the benefits of shifting to a more optimum diet justify concerted examination of policy options to shift individual and national diets now.

After diet, high systolic blood pressure is the next most important global risk factor accounting for 9·6% of all DALYs, up from 5·6% in 1990, making high systolic blood pressure larger than ischaemic heart disease and three times larger than HIV/AIDS in terms of DALYs. Our estimates for DALYs attributable to high systolic blood pressure in 2010 are 15% higher than in the GBD 2010 analysis for two primary reasons: new estimates of the mean blood pressure for each country, age, and sex reflecting new data and an improved model; and the shift to use of the lognormal distributional assumption, which more closely follows the available data. Despite its importance, there has been comparatively little global health policy discussion or initiatives focused on blood pressure. The WHO voluntary targets for

non-communicable diseases have called for a 25% reduction in the prevalence of high blood pressure by 2025. For World Health Day 2013, WHO issued a global brief calling for salt reduction and integrated primary care management as cost-effective routes to address the burden of high blood pressure. Although these efforts are welcome, high blood pressure needs a stronger and more coherent global response; one that will both monitor the burden of high blood pressure and provide policy guidance for the most effective intervention strategies tailored to different contexts.

One key component of diet related to systolic blood pressure is high sodium intake; we find that 3·0% of global DALYs can be related to sodium intake (95% UI 1·8–5·3). The wide UI reflects the uncertainty in the sodium TMREL from 1 g to 5 g per day. This widening of the TMREL compared with that in GBD 2010 of 1 g per day reflected the growing debate on the optimum level of sodium intake. On the one hand, the PURE cohort study found a J-shaped association between sodium, mortality, and major cardiovascular events among 101 945 individuals in 17 countries. On the other hand, the J-shaped curve could be due to residual confounding or reverse causation. The findings from PURE have generated much debate on the methods used to measure sodium intake, as well as the potential for low sodium intake to reduce blood pressure but raise mortality through some aspect of the renin–aldosterone system.^{49,65,66} While the debate on optimum sodium intake is likely to continue, even with a much wider TMREL, high sodium intake is a major global risk. If the optimum sodium intake is 5 g, we still estimate that sodium accounts for at least 1·6% of global DALYs, which is more than the global DALYs caused by tuberculosis. Voluntary and mandatory reductions in sodium content of processed foods have been tried and found to be cost effective in some settings.^{67,68} Salt substitutes such as potassium chloride or blends of sodium and potassium chloride are being tested in randomised trials.^{69,70} Even as the science on how far individuals should reduce their sodium consumption will continue to evolve, the argument for a population-level strategy to reduce sodium intake is compelling.

Maternal and child undernutrition was the leading global risk in this analysis in 1990 and remains the third most important in 2013, causing 6·8% (95% UI 6·2–7·4) of global DALYs. This cluster of risks includes in terms of importance childhood undernutrition, iron deficiency, suboptimal breastfeeding, vitamin A deficiency, and zinc deficiency. Compared with the GBD 2010 analysis, this cluster of risks is estimated to account for more DALYs primarily because for childhood undernutrition we have computed the joint distribution of child stunting, wasting, and underweight. In the GBD 2010, only child underweight was computed. By examining the combined effects of all three anthropometric measures, we have increased the estimated burden by 71%. In sub-Saharan

Africa, childhood undernutrition remains the leading risk factor emphasising the strong link of this risk to socioeconomic development; by contrast, in developing countries outside sub-Saharan Africa, childhood undernutrition has declined profoundly. By estimating the combined effects of stunting, wasting, and underweight, we have documented the enormous burden still caused by these risks in the poorest countries. The joint estimation, however, is based on back-calculating the relative risks for stunting, wasting, and underweight from published risks that are confounded by each other. These estimations will be strengthened by pooled analysis of available cohort data that directly computes the independent relative risks and their joint distribution.

Particulate matter pollution from both ambient sources and from household use of solid fuels is a major risk. Our estimates for DALYs attributable to ambient particulate matter air pollution are slightly lower than those in GBD 2010, but our estimates for household air pollution are lower by 22% for 2010. The reduction reflects the much larger number of studies used to map household fuel use to PM_{2·5} exposure levels in different settings. Regardless of the exact values of these estimates, both ambient particulate matter pollution and household air pollution are estimated to be major risk factors, particularly for non-communicable diseases. These environmental risks are classic examples for which public policy is required to mitigate risk.⁷¹ Because of the concave relation between PM_{2·5} concentration and relative risk, the benefits of reducing exposure per unit of exposure to PM_{2·5} are greater at lower levels of exposure than at higher levels. This benefit puts a premium on reducing exposure down to low levels near the TMREL. Both for ambient and household air pollution, the full implications of the concave nature of the risk curve need to be factored into policy interventions.

Tobacco use remains a major determinant of global health, ranking second in terms of risk in 2013, although the age-standardised DALY rate has fallen by 32% since 1990. Although the prevalence of smoking seems to be declining or stable in most countries, the burden of tobacco suggests that it ought to remain a key focus of global health policy debates.²⁰ Continued vigilance is absolutely required to ensure that women in developing countries, particularly in those with rapidly growing economies, do not begin to smoke in large numbers as women have done in some high-income countries. Equally, the failure of societies to bring down tobacco use among men faster than what has been observed over the past three to four decades, when the magnitude of the hazards had been well established, is of great public health concern. The experience of countries such as Australia, the UK, and USA, where male smoking prevalence has fallen from 70% post war to 15–20% today, provides clear evidence that targeted tobacco control strategies can work, but are likely to require a

combination of strong government commitment, fiscal measures, and an informed and active civil society and non-governmental organisation sector to advocate effectively for comprehensive tobacco control measures.^{33,72} Without all of these ingredients, now facilitated by WHO's stewardship and private philanthropy driving the MPOWER programme, progress will be slow, difficult, and at risk of reversals.^{73,74}

Alcohol remains a major risk, ranking sixth among level 3 global risk factors, whereas all illicit drug use combined ranks 22nd. Yet, although drugs are internationally controlled by treaties and a UN agency, there is no international public health treaty on alcohol. The WHO voluntary targets for non-communicable diseases have called for a 10% reduction in the volume of alcohol consumption by 2025 where this is nationally appropriate, but this is a substantially more modest target than those for other leading NCD risk factors, and policy initiatives for alcohol are recommended only in general terms.⁷⁵ There is a need for a more coherent and effective global response, including detailed policy guidelines based on the substantial evidence available on effective intervention strategies.

Our estimates for the burden attributable to high BMI are substantially higher than those in GBD 2010 for two reasons. First, based on new published pooled cohort or meta-analyses, we added several new outcomes related to high BMI. Second, we have more accurately captured the fraction of the population with high BMI using the beta distribution compared with the assumption of a normal distribution. There remains some debate in the literature on the risks associated with overweight. Flegal and colleagues⁷⁶ reported in a meta-analysis of studies reporting on broad categories of BMI that risk is lowest in the category of overweight.²¹ Pooled cohort analysis with more detailed BMI categories with a much larger number of person-years of exposure found a regular association with rising BMI from 23 onwards.⁷⁷ Part of the discrepancy in the findings is also related to how many years of observation are excluded from the analysis to remove the bias of sick individuals having lowered BMIs. Stokes and colleagues showed that re-analysing NHANES follow-up data by maximum lifetime BMI suggested that people in the overweight category were at substantially elevated risk (relative risk 1·28) compared with normal weight individuals.^{78–81} We believe that the balance of the evidence clearly supports our TMREL of 21–23 and that the pooled cohort studies provide the most robust relative risks available to date for this analysis. Regardless of this debate, however, the burden attributable to high BMI more generally is large and increasing at the global level. Intensified research and policy experimentation into the options to reduce BMI or to slow its increase is needed.

Our estimates of the burden attributable to unsafe water, unsafe sanitation, and no handwashing with soap are substantial: 38 countries have more than 5% of DALYs attributable to these risks, rising as high as 16% in Chad.

Redefining the risk to be unsafe water and unsafe sanitation, and adding in the risk from lack of handwashing with soap, increases the burden attributable to the cluster of water, sanitation, and hygiene. It also has important policy implications: in terms of risk reduction, achieving the MDG targets of improved water and sanitation would have little effect on reducing diarrhoea morbidity and mortality. Based on new meta-regressions, much of the potential benefit of water and sanitation is through achieving levels of access that are far higher than those in the MDG category of improved water or sanitation.¹² These findings are reflected in the much larger attributable fractions for unsafe water and unsafe sanitation as compared with improved water and improved sanitation. We believe that future monitoring efforts related to water, sanitation, and hygiene, such as those that might emerge from the sustainable development goals, should take into account the levels of risk associated with different levels of access. Setting the goal to be minimum risk, the approach taken here, would also mean that many countries, including some middle-income countries, have a great distance to go. The finding that no handwashing with soap is a global risk present in all regions is a reminder that this nexus of risks is relevant to all countries, not just the poorest.

An important aspect of the GBD 2013 has been the attempt to estimate the joint counterfactual for metabolic risks and all risks together, taking into account mediation of some risks through others such as BMI through systolic blood pressure. We assume that the fraction mediated through another risk is the same across countries based on the available literature.⁵² A more precise approach would be to estimate the correlation of the risks directly in each population and, through pooled studies, analyse the relative risks for the full joint distribution of each combination of risks—eg, BMI and blood pressure. Administrative data such as electronic medical record data might provide a useful database to understand the correlation of risks in different populations. Use of the average level of mediation noted in studies probably means that, at the global level, our results are not biased up or down, but in specific countries our results could be either too high or too low for the joint distribution of risks. We propagated the uncertainty in the fraction mediated into the final results, but this might still underestimate uncertainty because we only incorporated the uncertainty in the mean estimate of mediation. However, because the joint PAF for cardiovascular disease across all risks is so large—ranging from 63·5% in Chad to 94·3% in Belarus in 2013—these limitations of the mediation analysis would have only a minimum effect on the cardiovascular disease PAF due to all risk factors. Mediation for other major outcomes plays a much smaller part than it does for cardiovascular diseases.

In GBD 2010, the integrated exposure-response curve for PM_{2.5} was introduced to take a more unified view of

risk exposure across different sources of PM_{2·5}.^{31,82} The crucial assumption is that the PM_{2·5} is a robust indicator of the risk associated with a mixture of pollutants from ambient air pollution, tobacco smoking, secondhand smoke exposure, and household air pollution exposure to PM_{2·5}. This simplifying assumption has received substantial attention.^{83,84} In GBD 2013, we have more consistently mapped the outcomes across this set of sources of PM_{2·5}: pneumonia has been added as an outcome of tobacco smoking, which has been supported by tobacco cohort studies.^{85,86} We have expanded PM_{2·5} to cover child and adult lower respiratory infections. In view of the crucial importance of the integrated exposure-response curve to the validity of estimates for household air pollution particularly, further research on this is required. For household air pollution, one of the crucial steps in the analysis is to map from the proxy measure of exposure to the level of PM_{2·5} that is actually experienced, to estimate the relative risk from the integrated exposure-response curve. In GBD 2010, this was mapped using a large study from India and no uncertainty in this mapping was incorporated into the final results. For GBD 2013, we have based this on 67 studies from eight regions and have propagated uncertainty in this mapping into the final results. The net effect of these changes has been to widen uncertainty and capture regional variation in the level of PM_{2·5} exposure in households using solid fuels.

A major improvement for CRA implemented in the GBD 2013 has been the use of exposure distributions across individuals that are more consistent with the available survey data. The shift from assuming normal distributions to lognormal distributions has important effects on metabolic risks, as does the use of the beta distribution for BMI. Fasting plasma glucose has an unusual distribution that is not well represented by any of the parametric distributions that we tested. In future research, it will be important to explore the use of alternative methods such as mixture distributions or non-parametric approaches. More attention to the consistency of the distribution of exposure across populations conditional on mean and SD is warranted in future cycles of the GBD.

At the global level, the correlation of the number of DALYs attributable to the same risks for the year 2010 across GBD 2010 and GBD 2013 is 0·97. There are several notable changes detailed above for risks such as high BMI, high systolic blood pressure, and unsafe water, sanitation, and handwashing. For other risks there are also changes, but, globally, they are generally smaller than 10% in the year 2010. At the country level, however, there are more important changes. The correlation coefficient for PAFs at the country level is 0·84. These changes can be traced to changes in exposure where newer data or model revisions have altered the assessments.

The attributable burden of disease formula (equation 1) multiplies PAFs by deaths, YLLs, YLDs, or DALYs. All the

limitations of the estimates of deaths, YLLs, YLDs, and DALYs apply to this analysis.^{18,19} There are, however, several important limitations that relate to the components of the PAF analysis. First, for most outcomes, cohort or randomised controlled trial data are available for either mortality or morbidity, but rarely both. Second, we apply relative risks from meta-analyses or meta-regressions for a disease category such as ischaemic heart disease to all the sequelae of that disease, but more detailed studies might reveal different relative risks. Third, the data representativeness index for some risk factors is quite low—eg, handwashing and diet low in polyunsaturated fatty acids. Our modelling strategies attempt to quantify uncertainty as captured in the available data, but it remains possible that new data collected in countries without data might reveal levels of exposure that are outside the uncertainty intervals that we have estimated. Fourth, for unsafe water and unsafe sanitation, we assess the availability of infrastructure not the use of the infrastructure. Our estimates are not biased because the relative risks are derived from similar exposure definitions. Fifth, some risk factors are measured with very coarse proxies for exposure. The most extreme example is zinc deficiency, for which we analysed Food and Agriculture Organization of the United Nations food balance sheets for absorbable zinc and estimated the balance between theoretical intake and physiological requirements. Although the proportion of people with estimated inadequate zinc intake is a proxy of zinc deficiency, it lacks the anchor to individual level measurement of the exposure as a gold standard to estimate the number of people at risk. Other examples of the use of exposure proxy measurements are the proportion of the population in coarse occupational categories as a proxy for exposure to specific carcinogens, and the type of fuel used as a proxy for household air pollution. Capturing geographical variation and uncertainty in the mapping from household solid fuel use to PM_{2·5} exposure enhances the validity of our findings and uncertainty intervals. Nevertheless, more direct PM_{2·5} measurement in households to calibrate the more widely available data for fuel use would be strongly preferable. Sixth, robust models to estimate variation in the SD of risk exposure are harder to develop than are estimations of the mean. In many cases, we are only able to capture regional variation in the SD. Measured SDs from studies are an overestimate of the true SDs, because they include the effects of measurement error. We have not in this study corrected SDs for measurement error except for correcting observed systolic blood pressure to usual blood pressure.

Seventh, we have not systematically corrected relative risks for publication bias. In some cases, there are not enough studies to do this. Eighth, relative risks have not been corrected for non-masking in studies. For example, if the meta-regression of handwashing studies is corrected for non-masking, the effect size would be

non-significant. Many risks, however, cannot be studied in a masked fashion, such as tobacco smoking. Correction of some risks but not others could introduce worse issues of comparability so we have chosen for this study to not correct for non-masking in study design.

Ninth, with few exceptions, we assume that relative risks are universal across countries for a given age–sex group with few exceptions.^{45,46} Some studies have argued that the BMI relative risk curve and TMREL might vary geographically, but there was insufficient evidence to date to identify statistically significant differences in relative risks, except in the case of breast cancer. Generally, as further evidence accumulates, we might find more examples of non-universal relative risks. We have not incorporated into our uncertainty intervals any qualitative assessment of the potential for non-universal risks.

Tenth, some heterogeneity remains around the implementation of the TMREL concept. For example, for exposure to ambient particulate matter pollution, the TMREL has been chosen as between 5·9 µg/m³ and 8·7 µg/m³, but zero PM2·5 arguably might be the lowest risk. Cohort data to support the notion that the relative risk continues to decline below 5·8 µg/m³, however, are limited. Eleventh, for unsafe sex, HIV risk from injecting drug use, and occupational injuries, we have not used the relative risk and exposure PAF calculation. Attributable fractions of HIV for unsafe sex and injecting drug use have been based on direct evidence of the attributable fraction. These direct or categorical approaches might not yield results that are strictly comparable to the risks estimated with the relative risk and exposure model.

Twelfth, for risk factors for which we do not correct for mediation, we assume their joint effect can be estimated with the multiplicative risk model. This model, while plausible, might not accurately capture how all risks interact. Unfortunately, there are no cohort studies available of sufficient size to study the nature of these interactions in more detail. Thirteenth, the fraction of a risk factor mediated through another risk factor might be underestimated because of measurement error in both risk factors (similar to the case of regression dilution bias due to the exposure measurement error).²⁸

Fourteenth, for air pollution, there are few studies that allow estimation of the quantitative contribution of household air pollution to ambient air pollution or vice versa.⁸⁷ As such we might have underestimated the burden of household air pollution as a single risk factor; we might also have overestimated the burden of air pollution combined. Lastly, estimating burden for risks divided into polytomous risks might underestimate their burden compared with estimating burden with a continuous risk variable.

Strategies and policies to improve the health of populations should be guided by the comparative importance of health loss arising from exposure to major risk factors, whatever their position in the causal chain. It is the underlying causes of diseases and injuries that

ought to guide prevention efforts, and knowing their comparative magnitude and trends in causing health loss is arguably among the most important information required by countries to prioritise health programmes and policies. The comprehensive assessment of risk factors presented in this study provides a clear indication of where prevention programmes aimed at risk factor modification can have major effects on health. The challenge for governments and the health development community more broadly is to heed this knowledge about the comparative effect of health risks more assiduously, and orient health policies towards their mitigation with much greater conviction than that currently observed. Yet our findings that the list of risk factor–outcome pairs that meet the bar of convincing or probable evidence account for slightly less than 40% of the entire GBD strongly suggest that massive health gains could be expected from adoption of policies to avoid what is avoidable. Certainly, there are more risk factors yet to be discovered and some well known risks such as poverty and education have not yet been quantified according to this framework. But such unknowns should not impede a much greater response from countries and donors to implement policies that are known to work in controlling diseases and injuries, and which have demonstrably led to much improved health outcomes in countries that have adopted them.

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Declarations of interest

RA-C has been employed by GSK, activities not related to this manuscript. JP is supported by a career development fellowship from the Wellcome Trust, Public Health Foundation of India, and a consortium of UK Universities. CK receives research grants from Brazilian public funding agencies Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), and Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (FAPERGS). He has also received authorship royalties from publishers Artmed and Manole. RSP Jr has been medical director for United Laboratories Consumer Health Division—United Laboratories Inc. GVP is employed by University of São Paulo and receives research support from the National Council for Scientific and Technological Development (CNPq), the São Paulo Research Foundation (FAPESP), Grand Challenges Canada, Fundação Maria Cecília Souto Vidigal, and the University of São Paulo. He has served as a consultant and speaker to Shire and has received royalties from Manole Editors. HJL, in addition to grant funding from the Bill & Melinda Gates Foundation, EU, WHO and Novartis, has done some consulting for GSK and on the Merck Vaccines Global Strategic Advisory Board outside of this report. All other authors declare no competing interests.

Acknowledgments

We thank the countless individuals who have contributed to the Global Burden of Disease Study 2013 in various capacities. We acknowledge the extensive support from all staff members at the Institute for Health Metrics and Evaluation and specifically thank James Bullard, Serkan Yalcin, Evan Laurie, Andrew Ernst, Elizabeth Roberts, and Peter Speyer for their tireless support of the computational infrastructure required to produce the results and production of visualisations to review the results; Abigail McLain for her guidance on organising data; Caitlyn Steiner for her management of the GBD estimation; Adrienne Chew for her editorial assistance; Kelsey Pierce for her valuable guidance; and Linda A Ettinger for her expert executive support. We would also like to thank Ivan Ivanov for his contributions. The following individuals acknowledge various forms of institutional support: HC is supported by the Intramural Program of the NIH, the National Institute of Environmental Health Science; KD is supported by a Wellcome Trust Research Training Fellowship (grant number 099876); KBG received the NHMRC-Gustav Nossal scholarship sponsored by CSL 2015 (his award is peer-reviewed through the standard NHMRC peer-review process; CSL played no part in selection of the awardee); HH's contribution of this effort was partially supported by NIH ROI ES021446; NK received funding from the Japan Society for the Promotion of Science (JSPS) KAKENHI (grant number 25253045); YK would like to thank the National Heart Foundation of Australia for its financial support for work on modelling cardiovascular disease and risk factors at the University of Canberra; SJL is supported in part by the Intramural Research Program of the NIH, National Institute of Environmental Health Sciences; KM reports personal fees from Mitsubishi Tanabe Pharma, Kyowa Hakko Kirin, and MSD outside the submitted work; WM is program analyst at the UNFPA country office in Peru, which does not necessarily endorse the study; FC-L is partially supported by the PROMETEOII 2015 program/Conselleria d'Educació, Investigació, Cultura i Esport, Generalitat Valenciana and the CIBERSAM/Institute of Health Carlos III, Spanish Ministry of Science and Innovation; DM reports ad-hoc honoraria or consulting from Bunge, Haas Avocado Board, Nutrition Impact, Amarin, Astra Zeneca, Boston Heart Diagnostics, and Life Sciences Research Organization; and is on the scientific advisory board for Unilever North America; UM gratefully acknowledges funding from the German National Cohort Consortium; CDP, in the past 3 years has received consultancy payments from Pfizer and from Nutricia; DAQ was supported by The Eunice Kennedy Shriver National Institute of Child Health and Human Development of the National Institutes of Health under award number 5T32HD057822; KR was funded by the UK NIHR Oxford BRC and NIHR CDF; IR is required to include the following statement: The authors alone are responsible for the views expressed in this Article and they do not necessarily represent the views, decisions or policies of the institutions with which they are affiliated; JR received additional funding from the WHO for the work on alcohol as a risk factor; SS received a research support grant from NIH and the National Research Foundation and has received pharmaceutical sponsorship from Pfizer, AstraZeneca, Servier, and Dr Reddy's, speakers honoraria from Pfizer and Lundbeck, and honoraria from the Discovery Foundation and Cambridge University Press; DJS, in the past 3 years, has received research grants and/or consultancy honoraria from AMBRF, Biocodex, Cipla, Lundbeck, National Responsible Gambling Foundation, Novartis, Servier, and Sun; AGT acknowledges a senior research fellowship from the National Health & Medical Research Council (Australia; 1042600); and GDT was supported by a Center Grant from the National Institutes of Environmental Health Sciences (ES00260).

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