
GBD 2015 Risk Factors Collaborators

Summary

Background

The Global Burden of Diseases, Injuries, and Risk Factors Study 2015 (GBD 2015) provides an up to date synthesis of the evidence on risk factor exposure and the burden of disease attributable to these risks. By providing national and subnational assessments spanning 25 years, the GBD 2015 can help inform debates on the importance of addressing different risks in different contexts.

Methods

We used the comparative risk assessment (CRA) framework developed for previous iterations of the GBD study to estimate attributable deaths, DALYs, and trends in exposure by age group, sex, year, and geography for 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks over the period 1990 to 2015. The GBD 2015 study included 388 risk-outcome pairs which met World Cancer Research Fund-defined criteria for convincing or probable evidence. Relative risk estimates were extracted from published and unpublished randomised controlled trials, cohorts, and pooled cohorts. Risk exposures were estimated based on published studies, household surveys, census data, satellite data, and other sources. Statistical models were used to pool data from different sources, adjust for bias in the data, and incorporate explanatory covariates. We developed a metric that allows comparisons of exposure across risk factors – the summary exposure value (SEV) – which is scaled so that 100% is the entire population at maximum risk, and 0% is everyone at lowest risk. Using the counterfactual scenario of theoretical minimum risk level (TMREL) – the level for a given risk that could minimise population level risk if achieved – we estimated the portion of the burden (deaths and DALYs) that could be attributed to a given risk. We decomposed trends in attributable burden into contributions from population growth, population age structure, risk exposure, and risk-deleted cause-specific DALY rates. We characterized how risk exposures change as countries move through the development continuum. GBD 2015 follows the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER), and provides comprehensive and detailed
information for the data sources, estimation methods, computational tools, and statistical analysis used to generate estimates of attributable burden.

Findings

Between 1990 and 2015, global exposure to unsafe sanitation, household air pollution, childhood underweight, childhood stunting and smoking fell more than 25%. Global exposure for several occupational risks, high body mass index, drug use and ambient air pollution increased more than 25% over the same period. All risks jointly evaluated in 2015 accounted for 58.0% (56.9-59.0%) of global deaths and 41.3% (39.9-42.9%) of DALYs; the largest fraction of global DALYs was attributable to behavioural (30.3% [28.6-32.0%]). In 2015, the 10 largest Level 3 risks in terms of attributable DALYs at the global level were, in order: high systolic blood pressure (9.3% [8.3-10.3%] of global DALYs), smoking (6.0% [5.3-6.8%]), high fasting plasma glucose (5.8% [5.3-6.4%]), high body-mass index (4.9% [3.5-6.4%]), childhood undernutrition 4.6% [4.1-5.1%]), ambient particular matter (4.2% [3.6-4.8%]), high total cholesterol (3.6% [3-4.3%]), household air pollution (3.5% [2.6-4.4%]), alcohol use (3.5% [3.1-3.8%]) and diets high in sodium (3.4% [2.0-5.3%]). Decomposition analysis showed that from 1990 to 2015 the number of attributable DALYs declined for micronutrient deficiencies, childhood undernutrition, unsafe sanitation and unsafe water, and household air pollution but most of these declines were driven by reductions in risk-deleted DALY rates and not reductions in exposure. For a wide range of risks, increases in attributable burden were driven by population growth and aging exceeding reductions from risk-deleted DALY rates with exposure change having only a minimal contribution. Rising exposure has contributed to notable increases in attributable DALYs from high body-mass index, high fasting plasma glucose, occupational carcinogens, and drug use. Our assessments of the relationships between increasing development, measured using the Socio-demographic Index, showed that some environmental risks and childhood undernutrition decline steadily with development while a number of risks like low physical activity, high body-mass index, high fasting plasma glucose, smoking and others increase with development until the highest quintile. At the country level, metabolic risks such as high BMI and high fasting plasma glucose increasingly emerged as the leading risk factors for attributable DALYs in 2015. Nonetheless, regional risk profiles showed sizeable heterogeneity, with smoking still ranked among the leading five risk factors for attributable DALYs in 140 countries, and childhood underweight and unsafe sex enduring as primary drivers of early death and disability in much of sub-Saharan Africa.

Interpretation

Declines in some key environmental risks such as water, sanitation, and household air pollution have contributed to declines in critical infectious diseases such as diarrhoeal diseases. Many risks do not appear to change as countries move through the development continuum and have not
played a major role in trends of the last 25 years. Several key risks, including high BMI, high fasting plasma glucose, drug use, and some occupational exposures, are increasing and contributing to rising burden from some conditions; nevertheless these risks provide opportunities for intervention. Some highly preventable risks such as smoking remain major causes of attributable DALYs even as exposure is declining. Public policy needs to pay careful attention to the risks that are both major contributors to global burden and are increasing.

**Funding:** Bill & Melinda Gates Foundation
Research in context

Evidence before this study

The most recent assessment of attributable deaths and DALYs at the global, regional and national level was the Global Burden of Disease (GBD) Study 2013 which covered 79 risk factors or combination of risks from 1990 to 2013 in 188 countries.

Added value of this study

The GBD 2015 study incorporates recently published studies, newly acquired data for exposure to relative risks, new risk-outcome pairs meeting study inclusion criteria. To enhance transparency of the supporting evidence, we provided an assessment of the strength of evidence supporting causality for all 388 risk-outcome pairs. For the first time, we separately assessed trends in risk exposure by computing a summary exposure value (SEV) which allows comparisons overtime and across place for dichotomous, polytomous and continuous risks. Quantification of exposure trends allowed decomposition of trends in attributable DALYs into the portion contributed by changes in population growth, population structure, exposure and risk-deleted DALY rates. We find that reductions in exposure have been key drivers of change for only a limited set of environmental risks including water, sanitation, household air pollution, and behavioural risks including undernutrition and smoking. For many risks, trends in attributable DALYs have been driven by the interplay between population growth, ageing and declines in risk-deleted DALY rates. For some risks including body-mass index, fasting plasma glucose, occupational carcinogens, and drug use, exposure is increasing and driving up attributable burden. While there is, on average, a risk transition as countries move through the development continuum, many risks initially increase and then decline at the highest development levels. We document leading risks for each country and territory included in the study. This study is compliant with the requirements of the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) adding greater transparency to the assessment or attributable burden.

Implications

Risk assessments allow us to identify several groups of risk factors that deserve policy attention. Risks such as smoking, unsafe sanitation, and childhood undernutrition still cause many attributable DALYs but recent trends show that exposure can be reduced. It also shows many large global risks where there are relatively slow changes in exposure – such as high systolic blood pressure, ambient air pollution, diets high in sodium, high cholesterol, and alcohol intake – highlighting huge opportunities for intervention that may not be happening. Two large risks – high BMI and high fasting plasma glucose – have particularly large and concerning increases in exposure.
Introduction

Analysing the causes of poor health – or more specifically, the connections between risk factors and the development of poor health – can provide insights into opportunities and priorities for prevention, research, policy, and development. One of the mainstays of modern epidemiology is the quantification of elevated risks for particular diseases or injuries from exposure to a given risk factor for groups of individuals. Quantifying elevated risk for exposed groups of individuals from an array of risk-outcome pairs is important in informing decision-making about individual health; however, public policy debates require the more comprehensive metric of population-level risk, which is a function of elevated risk in the exposed population and the fraction of the population exposed to a given risk. Efforts to measure population risk have combined data on excess risk with the number of individuals exposed to provide comparative quantification of different health risks for populations which have been influential in establishing policy priorities.1,2

The comparative risk assessment (CRA) approach developed for the Global Burden of Diseases, Injuries, and Risk Factors (GBD) study provides an overarching conceptual framework for population risk assessment across risks and over time.3,4 The scale of the GBD study required extensive work to develop exposure metrics, assess relationships, and compile health data from different parts of the world with differing levels of metadata and uncertainty and the unique contribution of this work has been broadly recognized.5–7 At the same time, a robust debate on specific risks and results emerged following the publication of GBD 2013.8 The inclusion and exclusion of particular risks and outcomes,3,4,9 the optimum targets for indicators such as high systolic blood pressure,10,11 cholesterol,11,12 diets high in sodium,13 and air pollution,4,14 and the certainty of some dietary components of risk8,15 were challenged in addition to some details of methods; underlying many of these discussions were heterogeneities in the strength of causal evidence for different risk-outcome pairs.8

The GBD 2015 comparative risk assessment, in addition to updating data and methods, adds new transparency about the evidence supporting causal connections for each of the 388 risk-outcome pairs included in the analysis, allows the quantification and reporting of levels and trends in exposure, decomposes changes in attributable burden into population growth, ageing, risk exposure, and risk-deleted disability-adjusted life year (DALY) rates, and examines how risks change in a systematic way with development. As with all iterations of the GBD study, GBD 2015 results presented here supersede all previously published GBD CRA estimates.

Methods

Overview
The CRA conceptual framework was developed by Murray and Lopez,\textsuperscript{16} who established a causal web of hierarchically organised risks or causes that contribute to health outcomes (Appendix Figure 1), which allows quantification of risks or causes at any level in the framework. In GBD 2015, as in previous iterations of the GBD study, we evaluated a set of behavioural, environmental and occupational, and metabolic risks, where risk-outcome pairs were included based on evidence rules (see Appendix p 7). These risks were organised in four hierarchical levels – described in Table 2. To date, we have not quantified the contribution of other classes of risk factors (illustrated in Appendix Figure 1); however, through an analysis of the relationship between risk exposures and development, measured using the Socio-demographic Index (see below for details), we provide some insights into the potential magnitude of distal social, cultural, and economic factors.

Two types of risk assessments are possible within the CRA framework: attributable burden and avoidable burden. Attributable burden is the reduction in current disease burden that would have been possible if past population exposure had shifted to an alternative or counterfactual distribution of risk exposure. Avoidable burden is the potential reduction in future disease burden that could be achieved by changing the current distribution of exposure to a counterfactual distribution of exposure. Murray and Lopez identified four types of counterfactual exposure distributions: (1) theoretical minimum risk; (2) plausible minimum risk; (3) feasible minimum risk; and (4) cost-effective minimum risk.\textsuperscript{17} To date in GBD studies and in this study, we focus on attributable burden using the theoretical minimum risk level (TMREL) which is the level of risk exposure that minimises risk at the population level, or the level of risk that captures the maximum attributable burden.

Overall, this analysis follows the CRA methods used in GBD 2013.\textsuperscript{4} The methods described here provide a high-level overview of the analytical logic with a focus on areas of notable change from the methods employed in GBD 2013 with details provided in the Appendix. This study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) statement, which include recommendations on documentation of data sources, estimation methods, and statistical analysis (Appendix Table 1).\textsuperscript{18}

Geographic units of analysis and years for estimation

In the GBD framework, geographies have been arranged as a set of hierarchical categories: seven super-regions; 21 regions nested within the seven super-regions; and 195 countries and territories nested in the 21 regions. Additionally, GBD collaborator interest and availability of data resulted in an expansion of countries for which we disaggregate our estimates at the subnational level. At the first level of subnational division, 256 geographic units are now included in GBD 2015. For this paper we present results for the 195 national and territory-level geographies. We produced a complete set of age-, sex-, cause-, and location-specific estimates.

**Attributable burden formula**

Four key components are included in estimation of the burden attributable to a given risk factor: the metric of burden being assessed (the number of deaths, years of life lost [YLLs], years lived with disability [YLDs], or DALYs [the sum of YLLs and YLDs]); the exposure levels for a risk factor; the relative risk of a given outcome due to exposure; and the counterfactual level of risk factor exposure. Estimates of attributable DALYs for a risk-outcome pair are equal to DALYs for the outcome times the population attributable fraction (PAF) for the risk-outcome pair for a given age, sex, location, and year. A similar logic applies for estimating attributable deaths, YLLs, or YLDs. Risks are categorised on the basis of how exposure was measured: dichotomous, polytomous, and continuous. The PAF represents the proportion of risk that would be reduced in a given year if the exposure to a risk factor in the past were reduced to a counterfactual level of exposure – see the Appendix for equations.

**Causal evidence for risk-outcome pairs**

In this study, as in GBD 2013, we have included risk-outcome pairs that we have assessed as meeting the World Cancer Research Fund (WCRF) grades of convincing or probable evidence (see Appendix p 7 for definitions of these grades). Table 1 provides a summary of the evidence supporting a causal relationship between a risk and an outcome for each pair included in GBD 2015. For each risk-outcome pair, we used recent systematic reviews to identify independent prospective studies (randomised control trials [RCTs], non-randomised interventions, and cohorts) that evaluated the putative relationship. For risk-outcome pairs for which no recent systematic review was available, we either updated reviews developed for GBD 2013 or conducted a new systematic search of literature (see appendix pps 35-158). Table 1 summarizes the evidence using multiple dimensions that supports our assessment that each included risk-outcome pair meets the criteria of convincing or probable evidence – see the Appendix for a justification of the criteria presented to support causality. In this summary of evidence, we have focused on randomized control trials (RCTs) and prospective observational studies, along with supporting evidence like dose-response relationships and biologically plausible mechanisms. Other evidence supporting causal connections, such as case-control studies, are not summarized in the table.

**Estimation process**
Information on the data sources, estimation methods, computational tools, and statistical
analysis employed in deriving our estimates are provided in the Appendix. Figure 2 in the
Appendix summarizes the analytical steps for estimating burden attributable to single or clusters
of risk-outcome pairs. Table 2 provides definitions of exposure for each risk factor, the TMREL
used, and metrics of data availability. For each risk, we estimated effect size as a function of age
and sex and exposure level, mean exposure, the distribution of exposure across individuals, and
the TMREL. The approach taken is largely similar to the GBD 2013 for each quantity for each risk.

Some methodological improvements have been implemented and many new data sources
incorporated. The Appendix provides details on each step by risk. Citation information for the
data sources used for relative risks are provided in searchable form through a new web tool
(http://ghdx.healthdata.org/). We estimate the joint effects of combinations of risks factors
using the same methods as GBD 2013, namely by using published studies to estimate the
fraction of a risk that was mediated through the other risk (Appendix pp 23-30). Relative risks by
age and sex for each risk factor and outcome pair are provided in Appendix Table 5.

All point estimates are reported with 95% uncertainty intervals (UI); estimates are statistically
significant where the UI does not include zero. Uncertainty intervals include uncertainty from
each relevant component including exposure, relative risks, TMREL, and burden rates. Where
percent change is reported (with 95% uncertainty intervals), it was computed as based on the
point estimates being compared. Here, we provide further methodological detail on new
extensions to the CRA analysis.

Summary exposure value calculation

In prior GBD studies, we did not report comparable exposure metrics for the risk factors included
because of the complexity of quantifying polytomous and continuous risks.\textsuperscript{19} Because of
substantial interest in the trends in exposure, we developed a summary measure of exposure for
each risk. This measure, called the summary exposure value (SEV), is the risk-weighted
prevalence of exposure. More formally, it is defined as:

\[
SEV = \frac{\sum_{i=1}^{n} Pr_i RR_i - 1}{RR_{max} - 1}
\]

where \(Pr_i\) is prevalence of category \(i\) exposure; \(RR_i\) is relative risk of the category \(i\); and \(RR_{max}\)
is the maximum relative risk observed (between categories). This quantity is estimated for each
age, sex, location, year, and outcome. For each risk factor, a single SEV is estimated by averaging
the outcome of specific SEV values for each age, sex, location, and year across outcomes. In the
case of dichotomous exposure, SEV is equal to prevalence. For continuous risks:

\[
SEV = \frac{\int_{x=l}^{u} RR(x) P(x) dx - 1}{RR_{max} - 1}
\]
where $P(x)$ is the density of exposure at level $x$ of exposure; $RR(x)$ is relative risk of the level $x$; and $RR_{max}$ is the highest relative risk that is supported by data and reflects a level where more than 1% of the population are exposed globally.

SEV takes the value zero when there is no excess risk for a population and the value one when the population is at the highest level of risk; we report SEV on a scale from 0% to 100% to emphasise that it is risk-weighted prevalence. We computed $RR_{max}$ as the level for exposure with the highest relative risk supported by cohort or trial data and for which at least 1% or more of the global population is exposed. For comparison purposes, we have also computed age-standardised SEVs for every risk factor from the most detailed level using the GBD population standard.

**Decomposition of changes in deaths and DALYs into the contribution of population growth, ageing, risk exposure, and risk-deleted DALY rates**

We conducted two related decomposition analyses of changes in DALYs from 1990 to 2015: (1) decomposing changes in cause-specific DALYs due to changes in population growth, population age structure, exposure to all risks for a disease, and risk-deleted death and DALY rates; and (2) decomposing changes in risk-attributable all-cause DALYs due to changes in population growth, population age structure, risk exposure to the single risk factor, and risk-deleted DALY rates. Risk-deleted rates are the rates after removing the effect of a risk factor or combination of risk factors; in other words, observed DALY rates multiplied by one minus the PAF for the risk or set of risks. Our decomposition analyses draw from methods developed by Das Gupta\textsuperscript{20} to provide a computationally tractable solution to estimating the contribution of multiple factors to an outcome – see the Appendix for details. For some risks where the PAF is 100%, such as fasting plasma glucose and diabetes, the methods have had to be further adapted. We were not able to include three outcomes in this analysis: cervical cancer, sexually transmitted diseases excluding HIV, and HIV/AIDS.

**Risk transition with development**

We examined how changes in risk exposure were related to changes along the development spectrum. Drawing from methods used to construct the Human Development Index,\textsuperscript{21} we constructed the Socio-demographic Index (SDI), a summary measure of overall development based on estimates of lag dependent income per capita (LDI), average educational attainment over age 15 years, and total fertility rate (TFR). SDI provides an interpretable scale spanning zero to one, such that zero reflects the lowest income per capita, lowest educational attainment, and highest TFR observed across geographies from 1980 to 2015, and one represents the highest values observed during this time period. For each risk, we calculated the average relationship between risk exposure, as measured by SEV, and SDI across all geography-years by age and sex.
using spline regression (Appendix pp 32-33). We then used this relationship to characterise how exposures to risk vary on the basis of SDI alone.

Role of the funding source

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

Results

We report summary global, regional and national results. Complete detail at the risk-outcome level across age groups, sex, and years used in this study can be explored at http://vizhub.healthdata.org/gbd-compare.

Global exposure to risks

Table 3 provides age-standardised SEVs for 61 risks at the global level, by sex for 1990, 2005, and 2015. SEV is a single, interpretable measure which captures risk-weighted exposure for a population, or risk-weighted prevalence of an exposure. The scale for SEV spans 0% to 100%, such that a SEV of 0% reflects no risk exposure in a population and 100% indicates that an entire population experiences maximum possible risk. A decline in SEV indicates reduced exposure to a given risk factor while an increase in SEV indicates greater exposure.

From 1990 to 2015, SEVs decreased by more than 30% for four risks – unsafe sanitation, childhood underweight, childhood stunting, and household air pollution. Exposure to unsafe sanitation declined the most from 1990, falling 38.3% (95% uncertainty interval 36.1–40.5%) for both sexes, followed by decreases in SEV for childhood underweight (34.2% [30.9–37.9%]), and childhood stunting (33.4% [30.3–37.4%]). The global SEV for smoking also decreased by 2015, dropping 27.5% (23.2–30.9%) for men and 28.7% (20.2–34.1%) for women; notably, smoking exposure among men still far exceeded exposure levels for women in 2015. Significant, although more moderate, reductions in global SEVs for both sexes occurred for second-hand smoke (12.2% [9.4–15.1%]), unsafe water (9.4% [5.3–13.0%]), and diet high in red meat (9.0% [7.6–10.3%]) from 1990 to 2015. Risk exposure for high total cholesterol significantly declined for both men and women during this time, though this decrease was somewhat smaller among men (3.2% [2.2–4.4%]) than for women (5.6% [4.6–6.7%]). For a subset of occupational risk factors, such as ergonomic factors and asthmagens, global SEVs fell between 1990 and 2015.

For a subset of risks, relatively minimal changes in exposure occurred between 1990 and 2015. This was particularly evident among a number of dietary risks (eg, diet low in fruits), and behaviours related to nutrition (eg, non-exclusive and discontinued breastfeeding). Discordant
trends emerged by sex for some risk factors, such as low physical activity, where global SEVs for men increased by 2.4% (1.8–2.9%) whereas the SEV for women declined 1.5% (1.0–2.0%).

Global SEVs significantly increased for 27 risk factors for both sexes combined between 1990 and 2015; significant increases occurred for 24 risks for men alone and 23 risks for women alone. The most pronounced rises were recorded for a number of occupational exposures, such as diesel engine exhaust, silica, and benzene. Global SEVs for high body mass index (BMI) increased 38.7% (29.9–55.6%) for men and 34.4% (27.7–45.7%) for women. For both sexes, other risks with large increases included drug use (30.2% [23.3–39.1%]), ambient ozone pollution (24.6% [15.0–31.9%]), and high fasting plasma glucose (23.8% [22.4–25.4%]).

Global attributable burden for all risk factors combined and their overlap

The proportion of deaths, YLLs, YLDs, and DALYs that could be jointly attributable to all risk factors combined differed by cause group and measure of health (Table 4). Globally, 58.0% (56.9–59.0%) of deaths, 48.5% (47.6–49.5%) of YLLs, 26.1% (25.1–27.1%) of YLDs, and 41.3% (39.9–42.9%) of DALYs could be attributed to the risk factors currently assessed as part of the GBD 2015 study. Across health outcomes, attributable DALYs were the highest for non-communicable diseases (NCDs), although this ranged from 20.9% (19.7–22.1%) for YLDs to 65.0% (63.6–66.4%) for deaths in 2015. Among NCD cause groups, attributable DALYs were as high as 86.1% (84.9–87.3%) for cardiovascular and circulatory diseases to relatively low attributable DALYs, even among leading causes of disease burden (ie, 16.0% [13.9–18.2%] for musculoskeletal disorders and 22.5% [20.1–25.4%] for mental and substance use disorders). In 2015, approximately 40% to 60% of DALYs due to cancers, cirrhosis, and chronic respiratory diseases could be attributed to risk factors assessed in this study. Except for YLDs, less than 50% of disease burden for Group 1 causes – communicable, maternal, neonatal, and nutritional diseases – could be attributed to analysed risk factors. Risk factors accounted for less than 10% of early death and disability from maternal disorders (eg, 10.2% [4.1–16.8%] of DALYs).

Categories of risk factors – metabolic, environmental or occupational, and behavioural risks – often jointly contribute to disease burden. In 2015, 41.3% (39.9–42.9%) of global DALYs could be attributed to analysed risk factors, while 58.7% (57.1–60.0%) of global disease burden could not be explicitly attributed to specific risk factors. In terms of individual risk categories, behavioural risk factors accounted for 30.3% (28.6–32.0%) of attributable DALYs in 2015, followed by metabolic (15.8% [15.0–16.6%]) and environmental or occupational risk factors (13.0% [11.9–14.0%]). Regionally, total risk-attributable burden ranged from 59.0% (57.0–60.9%) in Southern sub-Saharan Africa to 33.6% (32.2–35.2%) in North Africa and Middle East; further, 10 regions had less than 40% of total DALYs attributable to risks under analysis (Figure 1).
Table 4 reports all-cause deaths and DALYs attributable to all risk factors from 2005 to 2015, including detail on attributable deaths and DALYs by risk-outcome pair. Globally, 32.3 million (31.6-33.1 million) deaths were attributable to all risk factors in 2015, a 4.9% (3.2-6.7%) increase since 2005; however, age-standardised attributable deaths declined from 2005 to 2015 (a 17.9% decrease [16.6-19.2%] to 499.3 [486.9-511.6]) deaths per 100,000. By contrast, total DALYs and age-standardised DALYs attributable to all risks decreased since 2005, 5.6% (3.8-7.5%) to 1.0 billion (0.96-1.09 billion) DALYs in 2015 and 20.9% (19.5-22.5%) to 14,448.9 (13,595.5-15,394.8) DALYs per 100,000 in 2015, respectively. Deaths and burden attributable to environmental and occupational risks significantly fell across measures, with age-standardised deaths dropping 22.7% (20.8-24.6%) to 141.9 (129.5-154.8) deaths per 100,000 in 2015 and age-standardised DALYs decreasing 24.9% (22.2-27.2%) to 4,499 (4,160.9-4,855.3) DALYs per 100,000 in 2015. Progress for environmental risks was mainly driven by sizeable reductions in mortality and disease burden attributable to unsafe water, sanitation, and hygiene, as well as declines in burden attributable to household air pollution. Between 2005 and 2015, global deaths attributable to unsafe water and no handwashing with soap fell more than 12%, while DALYs decreased more than 20%. Even faster declines in attributable deaths and burden occurred for unsafe sanitation (27.5% [22.3-32.7%] and 31.9% [25.7-37.4%], respectively) since 2005, to 807,904.2 (727,439.6-895,462.5) deaths in 2015 and to 46.3 million (41.1-51.8 million) DALYs in 2015 respectively. Reductions in attributable mortality and DALYs due to diarrhoeal diseases (associated with unsafe water, sanitation, and hygiene), were particularly prominent. Attributable deaths and disease burden due to household air pollution 13.0% (9.3-17.0%) and 20.3% (16.6-24.5%), respectively to 2.9 million (2.2-3.6 million) deaths in 2015 and to 85.6 million (66.7-106.1 million) DALYs in 2015 respectively, as well as large declines in age-standardised rates of attributable mortality and DALYs. Occupational risks factors generally accounted for a relatively smaller proportion of global deaths and disease burden; nonetheless, attributable mortality and DALYS due to a number occupational risk factors substantively increased between 2005 and 2015.

Behavioural risks can be grouped into four main categories: (1) generally large reductions for risk-attributable mortality and disease burden for risk factors associated with child and maternal malnutrition; (2) more mixed results for risk factors pertaining to alcohol and drug use; (3) rising attributable deaths and DALYs due to dietary risk factors; and (4) considerably varied trends for other behavioural risks, which span from sexual abuse and intimate partner violence to low physical activity.

Attributable deaths and disease burden due to metabolic risks have increased since 2005, particularly for high fasting plasma glucose for which all measures of attributable mortality and DALYs each increased by more than 19% between 2005 and 2015. These increases in attributable burden from high fasting plasma glucose were led by increased deaths and DALYs
from ischaemic heart disease, haemorrhagic stroke, chronic kidney disease (CKD), and diabetes. Attributable deaths and DALYs for high BMI also increased substantially, with 645,244 (457,647–862,412) more attributable deaths in 2015 than in 2005. Attributable mortality and DALYs due to low glomerular filtration rates also significantly increased from 2005 to 2015, with these primarily associated with rises in attributable deaths and burden due to cardiovascular and circulatory diseases, and CKD.

Global risk patterns by sex

In 2015, the relative ranks and attributable burden due to Level 2 risk factors varied between men and women (Figure 2). As the leading risk factor for both sexes, dietary risks accounted for 12.2% (10.8–13.6%) and 9.0% (7.8–10.3%) of total DALYs for men and women, respectively. These risks, which include diet high in sodium and diet low in fruit, contributed most to DALYs associated with three cause groups: cardiovascular and circulatory diseases; cancers; and diabetes, urogenital, blood, and endocrine diseases. In 2015, high systolic blood pressure also ranked among the leading risks for both sexes, contributing to 10.0% (9.0-11.0%) and 8.4% (7.5-9.4%) of DALYs for men and women, respectively. Air pollution was the fifth-leading risk for both sexes, largely contributing to DALYs associated with cardiovascular and circulatory diseases, as well as LRIs, diarrhoeal diseases, and other common infectious diseases. Child and maternal malnutrition, the leading global risk factor in 1990, was the third- and sixth-leading risk for women and men, respectively, in 2015.

Smoking was the third-leading risk factor for men in 2015, contributing to 9.6% (8.5-10.7%) of DALYs and a large proportion of male disease burden from cardiovascular and circulatory diseases, cancers, and chronic respiratory conditions. As the fifth-leading risk for men, alcohol and drug use was associated with 6.6% (6.1-7.1%) of disease burden in 2015, primarily due to mental and substance use disorders, as well as cirrhosis and other chronic liver diseases; the burden attributable to these risk factors was far less for women (Figure 2). In 2015, high fasting plasma glucose was associated with 6.0% (5.4-6.6%) and 5.6% (5.1-6.2%) of DALYs for men and women, respectively. For women, 3.8% (3.4-4.3%) of burden was attributable to unsafe sex, largely from HIV/AIDS and cervical cancer.

Changes in leading risk factors in 1990, 2005, and 2015

Rising total attributable DALYs amid declines between 1990 and 2015 for age-standardised DALY rates was evident for a number of metabolic and behavioural risks, emphasising the need to parse out the effects of demographic and epidemiological factors on global risk profiles (Figure 3). In 1990, childhood undernutrition, high systolic blood pressure, and unsafe water were the leading three risk factors for attributable DALYs. Of these risks, only high systolic blood pressure ranked among the leading three risks in 2015. Large reductions in both total attributable DALYs
and age-standardised DALY rates from 1990 resulted in childhood undernutrition and unsafe water being ranked as the fifth- and fourteenth-leading risk factors in 2015.

Environmental risk factors, including household air pollution and unsafe sanitation, decreased in terms of total attributable DALYs, age-standardised DALY rates, and relative ranks between 1990 and 2015. Over the period 1990-2005, attributable total DALYs for occupational risk factors, such as ergonomic factors, rose more than 20% from 1990 to 2005, though age-standardised rates decreased 9.5% (7.2–11.6%) over the same time period. Similar patterns occurred for most behavioural risk factors between 1990 and 2005, with significant increases in total attributable DALYs occurring for many of these risks at the same time age-standardised DALY rates significantly fell (eg, smoking, low physical activity, and most dietary risks, including diet high in sodium). Unsafe sex, drug use, and intimate partner violence were exceptions, with each measure of attributable burden significantly increasing since 1990. For unsafe sex and drug use in particular, this rapid rise corresponded with the global HIV/AIDS epidemic.

For most risk factors, the time period of 2005 to 2015 resulted in an extension of earlier trends, with continued gains in reducing attributable DALYs due to various environmental risk factors and more varied patterns for many metabolic and behavioural risks. Yet some important changes occurred between 2005 and 2015, including the large reductions in attributable total DALYs and age-standardised DALY rates to unsafe sex (29.5% [26.8-32.0%] and 37.5% [35.2-39.8%], respectively) and intimate partner violence (10.5% [2.8-17.8%] and 23.2% [16.8-29.1%], respectively).

Contrasting global changes in risk exposure and attributable burden

Comparing percent change in risk exposure from 1990 to 2015 with the level of attributable DALYs in 2015 helps identify large risks for which there is a long-term increase in global exposure (Figure 4). While disease burden attributable to unsafe sanitation, household air pollution, stunting and underweight cause more than 10 million DALYs in 2015, exposure to these risks decreased for both sexes between 1990 and 2015 by more than 25%. At the other extreme, two risks causes more than 100 million DALYs and increased more than 20%: high fasting plasma glucose and high BMI. Other risks with large increases in exposure but cause less than 10 million DALYs include a number of occupational exposures, drug use, ozone, second hand smoke, and diets low in PUFA. For a large group of risks at the global scale, exposure increased or decreased less than 10% from 1990 to 2015. These included many component of diet, high SBP, ambient air pollution and alcohol use.

Decomposition of changes in risk-attributable DALYs to population growth, aging, risk exposure and risk-deleted DALY rates

Drivers of global changes in overall DALYs attributable to risk factors varied (Figure 5). Across
GBD Level 3 risk factors, overall changes in all-cause attributable DALYs ranged from declines exceeding 50% for seven risk factors, including childhood undernutrition, suboptimal breastfeeding, and unsafe sanitation, to increases near to or exceeding 100% (ie, high BMI, occupational carcinogens, and drug use). Of these 46 Level 3 risk factors, attributable all-cause DALYs decreased significantly for 10 risk factors between 1990 and 2015, whereas 34 risk factors increased significantly over this same period. Population ageing led to increased attributable all-cause DALYs for most risk factors, with a relative contribution that spanned from lower than 10% (for household air pollution from solid fuels and occupational injuries), to greater than 60% (for occupational carcinogens). Population ageing contributed to reductions in all-cause DALYs attributable to eight risk factors, namely among environmental risks (eg, a 13.5% [6.0-19.9%] decrease for no handwashing with soap) and those associated with nutritional deficiencies or behavioural risks (eg, a 17.6% [12.6-24.0%] decline for childhood undernutrition and a 22.0% [10.9-31.4%] decline for suboptimal breastfeeding). Changes in risk-deleted DALY rates since 1990 were primary drivers of reductions in all-cause, risk-attributable burden, with decreases in underlying DALY rates exceeding 50% for 13 risks by 2015. By contrast, changes in risk exposure varied markedly, with risk exposure contributing to declines in all-cause DALYs for ten risks (eg, 30.0% [29.0-38.0%] and 21.7% [17.5-30.4%] due to declines in risk exposure for household air pollution and iron deficiency, respectively) at the same time change attributable to risk exposure increased for 16 risk factors to more than 25%, including high fasting blood glucose (25.1% [19.7-27.9%]), ambient ozone pollution (37.5% [31.5-42.7%]), occupational carcinogens (40.1% [28.5-50.8%]), occupational injuries (41.1% [37.0-48.1%]), high BMI (60.0% [54.9-69.2%]), and drug use (70.0% [65.5-73.6%]).

Decreases in underlying cause-specific DALY rates – as opposed to other factors – were generally the main drivers of overarching reductions in cause-specific burden attributable to all risk factors (Appendix Figure 4). From 1990 to 2015, 36 causes decreased in terms of associated risk exposure, including a number of communicable causes, nutritional deficiencies, and COPD. Notably, risk exposure was the only factor that improved between 1990 and 2015 for a subset of causes, with changes in population growth, ageing, and underlying cause-specific DALY rates all contributing to rising cause-specific disease burden; this was most evident for tracheal, bronchus, and lung cancer, as well as cirrhosis and other chronic liver diseases due to alcohol use.

The risk transition and development

Figure 6 shows the evolution of SEV by region for the 10 leading global risk factors in terms of attributable DALYs as SDI changes, and also provides the expected SEV level based on SDI alone. Two main trends emerged: (1) increasing and then leveling of SEVs for most metabolic and dietary risks; and (2) reductions in SEV for environmental risks and those associated with childhood undernutrition after reaching mid-levels of SDI. For the former, above an SDI of approximately 0.80, expected levels of risk exposure either moderately dropped or remained relatively constant. An exception was alcohol use, for which SEVs increased with each increment
of SDI. By contrast, SEVs for ambient particulate matter pollution did not substantively decline until after an SDI of 0.60, and the pace of SEV reductions for household air pollution accelerated after an SDI of about 0.40. These patterns reflect the complex shifts in risk exposure that accompany changes in development, which are further emphasised by regional SEV trends by risk factor.

Two risk factors related to nutrition or diet – childhood wasting and diet high in sodium – reflected the nuances of changing risk exposure and levels of development. Particularly among regions with an SDI below 0.8, SEVs for childhood wasting decreased over time and with rising SDI; nonetheless, a subset of regions, including South Asia and Western sub-Saharan Africa, had consistently higher-than-expected SEVs for childhood wasting on the basis of SDI. For diet high in sodium, most regions saw relatively minimal changes in exposure over time, even amid increases in SDI. In East Asia, SEVs for diet high in sodium were consistently above expected levels of exposure given SDI, whereas the opposite trend was found for Oceania and Central Latin America. Across the development spectrum – including high-income Asia Pacific, Southeast Asia, and Eastern Sub-Saharan Africa – exposure for diet high in sodium was at least moderately higher than expected based on the SDI for a given region. Heterogeneous risk patterns occurred for two leading environmental risks – household air pollution and ambient particulate matter pollution – particularly in terms of the relationship between SEVs and increasing SDI. For smoking and alcohol use, strikingly different trends for SEV and SDI occurred. While nearly every region recorded declines in SEVs for smoking, how quickly these reductions took place alongside changes in SDI varied.

Regional and national risk profiles

Leading risk factors for early death and disability, as measured by attributable DALYS, varied by region, level of SDI, and sex in 2015 (Figure 7). In high-income North America and the UK, smoking was the leading risk for attributable DALYS among both men and women, but for most of Western Europe, smoking was the leading risk factor only for men while high systolic blood pressure was the leading risk factor for women. A similar pattern emerged in East and Southeast Asia, with smoking ranked as the leading risk factors for men in China, Thailand, Vietnam, and the Philippines while metabolic risk factors – namely high systolic blood pressure – was the leading risk factor for attributable DALYS for women in these countries. Childhood undernutrition ranked as the leading risk factor for early death and disability for both sexes throughout Western and Central sub-Saharan Africa, as well as a few countries outside of sub-Saharan Africa (eg, Laos and Tajikistan).

In terms of the leading 10 risk factors for both sexes, regional and country risk profiles showed both distinct patterns and heterogeneity (Figure 7). High systolic blood pressure was the leading risk for DALYs for 17 high income countries and territories in 2015, high fasting plasma glucose
was the leading risk for three and smoking was the leading risk for 17 such geographies in terms of disease burden. For a subset of geographies, including the US, Canada, Australia, and countries in the UK, drug use was a major risk for early death and disability in 2015.

In 2015, high systolic blood pressure, high BMI, and high fasting plasma glucose were the leading risk factors for almost all geographies in Latin America and the Caribbean; Haiti was the primary exception, with unsafe sex as its leading risk for attributable DALYs in 2015. Across Southeast Asia, East Asia, and Oceania, high systolic blood pressure was the leading risk factor for disease burden in 11 countries and territories, ranging from China to Vanuatu. High BMI was the leading risk for DALYs in eight geographies, while high fasting plasma glucose ranked as the leading risk factor for three geographies, including Taiwan.

High systolic blood pressure was the leading risk factor for all geographies in South Asia, and except for Pakistan, household air pollution remained among the leading four risk factors for attributable DALYs across geographies in this region. Ambient particulate matter pollution ranked as the third-leading risk factor in India and Nepal, while smoking was the second-leading risk factor for attributable burden in Bangladesh.

In Central Europe, Eastern Europe, and Central Asia, 28 out of 29 countries had high systolic blood pressure as their leading risk factor for attributable DALYs in 2015; Tajikistan, where childhood undernutrition was the leading risk factor, was the only exception. Across Central Europe, smoking was the second-leading risk factor for early death and disability, whereas alcohol use was among the leading four risk factors for attributable DALYs in Belarus, Moldova, and Russia.

Throughout North Africa and the Middle East, high systolic blood pressure was among the three leading risk factors for disease burden in 2015, with 11 geographies, including Egypt and Iran, recording this risk as the leading driver of early death and disability in that year. High BMI accounted for the highest attributable DALYs in seven countries, including Jordan and Saudi Arabia, and also was among the leading six risks for all countries in the region. For Afghanistan and Sudan, childhood undernutrition was the leading risk for DALYs in 2015 and the second- and eighth-leading risk for DALYs in Yemen and Egypt, respectively. Unlike most of sub-Saharan Africa, several metabolic risks also emerged as leading drivers of attributable DALYS in Southern sub-Saharan Africa by 2015; high BMI ranked as the second-leading risk factor in South Africa, while high systolic blood pressure became among the leading three risk factors for attributable DALYs in Botswana and Swaziland. In Central sub-Saharan Africa, childhood undernutrition and unsafe sex occupied the first and second ranks for attributable disease burden in all geographies.

High systolic blood pressure ranked among the leading risk factors for attributable DALYs in most geographies (eg, second and third in Gabon and the Congo, respectively) in the region.
Discussion

Drawing from 18,450 data sources, we estimated exposure to 79 metabolic, environmental and occupational, and behavioural risk factors or clusters of risks from 1990 to 2015 in 195 countries and territories, and attributed deaths and overall disease burden to these risks. In 2015, all risks combined contributed to 58.0% (56.9-59.0%) of deaths and 41.3% (40.0-42.9%) of DALYs worldwide. Since 1990, global risk exposure for both sexes combined increased significantly for 27 risks, did not significantly change for seven risks, and declined significantly for 27 risks. At the same time that risk exposure rose for a number of leading risks, particularly metabolic risk factors associated with NCDs, age-standardised risk-attributable deaths and DALYs declined for most risks. Globally, pronounced reductions in risk-deleted or underlying cause-specific DALY rates offset minimal changes in, or increased, risk exposure. These gains in risk-deleted DALY rates may not be large enough in the future to compensate for rising levels of risk exposure, such as high BMI or high FPG.

Rethinking the risk transition

Societal processes of urbanisation, the so-called “Westernisation” of diets and lifestyles, and changes in employment activities, have all been viewed as primary drivers of changes in human health.\textsuperscript{22–25} Such shifts have been thought to lead to deteriorating diets, rising obesity, decreased physical activity, and ultimately to worsening levels of metabolic risks with associated higher rates of cardiovascular diseases and cancers.\textsuperscript{26,27} Results from the present study point to an ongoing risk transition, but with a trajectory that is far more complex and nuanced than originally conceived. The relationship between SEVs for most risks and SDI identified that poor water, poor sanitation, household air pollution and micronutrient deficiencies and undernutrition declined steadily as countries develop. In contrast, some risks become worse as development proceeds, at least through to levels of SDI around 0.8, these include: low physical activity, high BMI, high total cholesterol, low PUFA, partial breastfeeding, alcohol use, high red meat, smoking, and high sugar-sweetened beverages. Some risks that appear to worsen through earlier phases of development improved at the highest levels of SDI such as smoking. As improvements in SDI continue, and behavioural risks grow in dominance, understanding how to change behaviours effectively at both the individual level and for populations becomes increasingly relevant. Many other components of diet, occupational exposures, and some environmental risks do not show a marked relationship with development.

The effects of the risk transition, at least globally, are often mitigated by trends in risk-deleted death or DALY rates. In the present study, we begin to identify likely candidates for specific drivers of improvements. It is possible that unmeasured risk factors may be driving these trends. Unlike cardiovascular diseases and some neoplasms, for other causes such as mental disorders or neurological disorders, the set of risks included in this study account for comparatively little of
the observed burden; these causes make up an increasing share of the burden for geographies at high SDI. To date we have not identified risk factors that meet our criteria of convincing or probable evidence, suggesting research on unquantified risks is needed. In accompanying GBD 2015 analyses, we documented widespread improvements in overall development as measured by SDI. Gains in SDI are likely to operate through many pathways, including improved access to health care, public health programmes, and social and welfare policy. Advances in treatment are well-documented for a number of causes, including HIV/AIDS, ischaemic heart disease, and a number of cancers including breast, testicular, and Hodgkins; yet for other causes, such as oesophageal cancer and interpersonal violence, the policies, programmes and interventions responsible for declining risk-deleted death and DALY rates are less clear. Improving our understanding of the risk-deleted rates in cause-specific mortality and disease burden will strengthen the evidence base for intervention effectiveness, the role of medical care access in addressing disease burden and the importance of other social and welfare policies.

A global risk typology

Our decomposition of drivers of attributable burden can be used to identify four distinct groups of risks at the global level. First, for ten risks, attributable burden is declining as is the exposure to the risk factor. This set of risks is dominated by the environmental risks that are particularly common at lower levels of SDI, and include: vitamin A deficiency, undernutrition, zinc deficiency, sub-optimal breast feeding, poor sanitation, no handwashing, poor water, second-hand smoke, household air pollution, and occupational asthmagens. For these risks as a group, not only has exposure been declining but risk-deleted DALY rates also declined, such as for diarrhoeal diseases. Further, global shifts in population age structure contributed to decreases in both cause-specific and attributable burdens for risks that predominantly affect children. A second group of risks was characterized by declines in exposure exceeding 10% from 1990 to 2015, but increasing attributable burden, due in most cases to large increases driven by population growth and ageing. This group includes smoking, high systolic blood pressure, occupational ergonomic factors, childhood sexual abuse, and iron deficiency; in the latter case, the increase in attributable burden was quite small over the period 1990 to 2015. Smoking and high systolic blood pressure are discussed in greater detail below as both representative of this risk type and because these risks are of high importance in many parts of the world. For a third group, attributable burden is increasing and trends in exposure account for less than a 10% increase or decrease in attributable burden. This larger group of risks includes all components of diet except low PUFA intake and high sugar-sweetened beverages, some occupational exposures, residential radon, low glomerular filtration rate, alcohol use, high total cholesterol, intimate partner violence, lead exposure, low bone mineral density, and low physical activity. For these risks, attributable burden is increasing due to population growth and population ageing. The degree of increase is driven by the extent to which declines in risk-deleted DALY rates compensate for the
increases due to population growth and ageing. The final category are the risks that are perhaps the most concerning: those with increasing attributable burden and exposure contributing to an increase of at least 10% over the last quarter century. This list includes occupational injuries, ambient ozone pollution, occupational carcinogens, diet low in PUFA, sugar-sweetened beverages, drug use, high fasting plasma glucose, and high BMI. For these risks, declines in underlying rates were likely responsible for preventing additional increases in attributable burden. Any risk for which attributable deaths and DALYs are increasing is a threat to both health systems and societies, but the risks that fall within the fourth group – risk factors with rising exposure and associated health loss – require immediate attention from policymakers and other stakeholders.

Unsafe water, sanitation, and hand washing

The conventional approach to assessing the contribution of unsafe water to health is to evaluate access to improved water sources as defined in the Millennium Development Goals (MDGs). The WHO estimated that, in 2015, 91% of populations living in low- and middle-income countries had access to improved water and 68% to improved sanitation. Implicit in the focus on “improved” is the idea that the most important reductions in diarrhoea come from moving from an unimproved to an improved source of water or sanitation. However, meta-analyses of intervention studies and retrospective cohorts show a wide variation of relative risks of diarrhoea within the category of improved water and improved sanitation. We found that the SEV for poor water was only 55.8% (50.3-61.9%) for both men and women in 2015, a small improvement of just 9.4% (5.3-13.0%) since 1990. In contrast, for unsafe sanitation the SEV decreased dramatically from 54.6% (53.3-56.1%) in 1990 to 33.7% (32.2-35.0%) in 2015. Our assessment of SEV for water demonstrated that a substantial agenda is still needed across the world to achieve the overall goal of safe water and sanitation. The sixth Sustainable Development Goal (SDG6) includes targets for achieving both universal and equitable access to safe drinking water (SDG6.1) and adequate and equitable sanitation for all (SDG6.2) by 2030. Given SEVs in many of these areas of the world, a large gap remains between current levels of safe water and sanitation and universal access. Moreover, our analyses show that progress on providing safe water lags behind progress on providing safe sanitation. This shift in focus to the lowest risk categories raises the bar considerably for what is needed for investment to reduce the risk of diarrhoea in all regions of the world.

Tobacco

The SEV for smoking has decreased in many countries as well as globally. Global tobacco-attributable deaths and DALYs, however, have continued to rise because of increases in population numbers and ageing, which overwhelm declines both in exposure and risk-deleted rates of related disease burden. Given a known highly effective set of intervention strategies to
reduce tobacco consumption, the challenge for tobacco is one of political priority for tobacco control. Despite the important developments of the Framework Convention on Tobacco Control, in many countries there has been slow progress or even increases in consumption. Continued close monitoring of tobacco consumption and the deaths and DALYs attributable to tobacco remains an essential aid to promoting policies to reduce tobacco consumption.

In the GBD 2015, for long-term effects of smoking on lung cancer and COPD, we used the Peto-Lopez method which estimates the lifetime cumulative effect of cigarette smoking using a transformation of the observed lung cancer death rate. While this method provides robust estimates of the burden of cancers related to tobacco, it is not fully consistent with the GBD approach of estimating exposure independently of the outcomes affected by exposure. With an increased body of evidence on the association between smoking and other cancers, and a good estimate on distribution of smoking, direct estimation of attributable burden is possible.

Modeling the relationship directly between smoking exposure in the past and present to cancers will also allow for the exploration of counterfactual scenarios and other forms of comparative risk assessment such as the estimation of avoidable burden. The set of outcomes that have been related to tobacco in pooled cohort studies includes many outcomes not quantified here such as road traffic accidents, renal failure, and infectious diseases; careful assessment of which of these new outcomes meet the criteria of convincing or probable evidence is needed. Quantifying the full effects of tobacco will also require the inclusion in future GBD studies of smokeless tobacco consumption. Regardless of the estimation method used or the scope of outcomes evaluated, tobacco remains a major global risk factor despite more than 50 years of anti-tobacco efforts.

**Dietary assessment**

Many aspects of dietary assessment remain controversial. Evidence on the effect of diet on NCDs mostly come from prospective cohort studies using food frequency questionnaires (FFQ) with one-year recall to establish diet at baseline. Findings from 24-hour recalls, or multiple-day diary records, show a poor correlation with annual FFQ. Proponents of FFQs argue that the rank order of levels of intake across individuals in the annual FFQ is relatively robust. Some authors have argued that measurement error for each diet component in the statistical analysis of the cohort data will tend to bias the findings toward the null, and thus underestimate the effects of a diet component. However, the direction of bias in settings with measurement error in multiple independent variables is unknown in the presence of correlation between different variables.

At the population level, single 24-hour recall has been used in many nutrition surveys. 24-hour recall likely underestimates as demonstrated in doubly labelled water and urinary sodium studies.

Correlation between diet components is also a critical aspect of diet. Intake of beneficial dietary factors are generally, but not always, positively correlated with each other and inversely
correlated with harmful dietary factors. This correlation could overestimate the relative risk of each dietary factor in cohorts as well as the total effect of dietary risks at the population level. Using dietary pattern as the main exposure could potentially address this problem; however, several challenges exist in adopting this approach for GBD. Concerns remain about the magnitude of the effect size of individual dietary risk factors on chronic diseases. While many prospective cohorts have collected dietary data, published meta-analyses for most diet-disease pairs have included reports from only a fraction of these cohorts, indicating the potential for publication bias. Further, the majority of cohorts evaluating the effect of diet on disease endpoints have adjusted for total energy intake in their statistical models. This practice emerged to address measurement error in dietary assessment tools and remove the effect of energy as a potential confounder. This means diet components are defined as risks in terms of the share of diet and not absolute levels of exposure. Because diet shares are analyzed, increases in any component imply reductions in some other component leading to the notion of replacement. Diet components are often analyzed as pairs where one component replaces another further complicating the analysis of cohort data. Given that many of the cohorts did not include the same dietary components in their analysis, the relative risks of dietary factors across cohorts may not be strictly comparable. This has been one of the main reasons for inconsistent findings in dietary meta-analyses in recent years. Future work to encourage more pooled analyses of diet components for all the major cohorts would be beneficial; the release of more data from the major cohorts would stimulate a range of alternative analyses on diet that would help strengthen the evidence for diet and attributable burden.

**Sodium Intake**

Age-standardized DALYs attributable to diets high in sodium and exposure (as measured by SEV) for diets high in sodium increased slightly at the global level (6.4% [0.6–16.9%]) for both sexes between 1990 and 2015. Reduction in sodium intake at the population level is one of the WHO’s nine global targets for NCDs. Many countries (eg, UK, Finland, Japan, Brazil) have already implemented or are considering implementation (eg, US) of policies to reduce sodium intake. Reports from countries with high levels of sodium intake (eg, Japan) that have successfully implemented sodium reduction policies have argued for the beneficial effects of lowering sodium intake in these populations. While multiple lines of epidemiologic evidence support the harmful effects of very high levels of sodium intake, there remains no scientific consensus on the optimal level of sodium intake. In GBD 2013, based on the findings of the Prospective Urban Rural Epidemiology (PURE) collaboration on sodium and cardiovascular mortality, and to incorporate the lack of scientific consensus on the optimal intake of sodium, we expanded the uncertainty for the TMREL for sodium to 1-5 grams per day. More recently, PURE collaborators published a further analysis that raised the possibility that, for those without hypertension, there may be an inverse relationship between sodium intake, all-cause mortality,
and cardiovascular events. These findings challenge long-standing beliefs in the public health community on the importance of modulating sodium intake at the population level. Current policy is grounded in the evidence linking sodium intake and systolic blood pressure, which shows increases in systolic blood pressure with increases in sodium above one gram per day. However, we have identified no prospective cohort studies directly linking sodium to disease endpoints that support reductions in the risk of outcomes at levels of intake below three grams per day. Proponents of a lower TMREL for sodium have argued that the cohort studies that generally show rising mortality at levels below 3-5 gm/day may suffer from reverse causation because sick individuals reduce sodium consumption. Given this continued debate, we chose not to change the uncertainty range of the TMREL from the current 1-5 grams per day. We should note that if the findings from PURE and the more recent pooled analysis are correct, there may be increased risk for non-hypertensives consuming less than five grams per day. We have not included that potential increased risk in our quantification of uncertainty. Many studies have been completed or are underway examining the effects of sodium reduction in population groups or whole communities on systolic blood pressure but none to date that report the effects of sodium reduction on disease endpoints. Such studies, when and if they are conducted, may go a long way toward resolving outstanding questions about the TMREL for sodium. Regardless of the debate on the TMREL, we found that sodium accounted for at least 2.0% of global DALYs in 2015. The risk profile of increasing attributable numbers of DALYs, and no global progress in reducing exposure to diets high in sodium, places this risk among those of greater concern for the management of health systems.

Diet and policies

Much of the diet policy debate has focused on the importance of reducing sodium, sugar, and fat. Our assessment of the burden from diseases attributable to 14 dietary factors showed that, at the global scale, six factors each accounted for more than 1% of global DALYs, in order of importance: high sodium, low vegetables, low fruit, low whole grains, low nuts and seeds, and low seafood omega-3s. Our findings suggest that, in addition to a policy focus on sodium, sugar, and fat, there are many important components of diet that should be minimized, and more importantly, many that need to be promoted through education, subsidies, and other evidence-based programs. If our findings are correct, a policy focus on the sugar and fat components of diets may have comparatively smaller effect than promoting increased uptake of the five more important healthy components of diet we evaluated. The disconnect between the diet policy debate and the evidence on which diet factors are most important globally can also be seen for red meat, where the harm of increased diabetes and colorectal cancer is smaller than for all of the other 13 diet components considered under the GBD framework. Consideration of diet policy is made more complicated when cost-effectiveness, political feasibility, intensity of implementation, reactions of various stakeholders (eg, consumers and the food industry), and
environmental impacts, including on climate change, are factored into national diet policy discussions. For example, the promotion of healthy diet components can have more or less deleterious impacts on environmental sustainability. These dimensions of diet policy should be added to the debates on how to transform national diets to be lower risk.

**Cholesterol**

Based on findings from recent studies that showed the benefits from the reduction of LDL and total cholesterol to very low levels, for GBD 2015 we revised the TMREL for total cholesterol downwards from 3.80 to 4.00 mmol/L to 2.78 to 3.38 mmol/L. This increased our estimate of the burden of total cholesterol for the year 2010 from 2.7 million (1.9-3.8 million) deaths in GBD 2013 to 4.0 million (3.1-5.1 million) deaths in GBD 2015, and shifted our placement of cholesterol among leading risks from 10th (GBD 2013 ranking for the year 2010) to 4th (GBD 2015 ranking for the year 2010). Effective intervention options to influence population total cholesterol levels are available, including efforts to increase physical activity, diet, and pharmacological intervention. Although the consumption of dietary cholesterol is not linked to serum cholesterol, diet interventions, such as increased consumption of fruits, vegetables, and fibre, and increased physical activity can influence LDL and total cholesterol and should be encouraged. Statins are highly effective with relatively low rates of side effects, justifying their use in many individuals, either alone or in combination with other medicines. In general, given the existence of proven and effective intervention strategies, the increase in the importance of cholesterol highlights a major opportunity for intervention.

**Systolic blood pressure**

In this assessment, as in GBD 2013, we found that the most important Level 3 risk factor globally is elevated systolic blood pressure. The TMREL for this estimation, a systolic blood pressure between 110 mmHg and 115 mmHg, is based on evidence from the pooling of prospective cohort studies that showed individuals with a baseline blood pressure at this level have the lowest risk of future cardiovascular death. In addition to this observational evidence, two randomized clinical trials of blood pressure lowering have added substantially to the evidence in this area. The SPRINT trial showed that adults in the US with elevated vascular risk and pre-existing hypertension (mean systolic blood pressure at baseline 139.7 mmHg on 1.8 mean medications) benefited from antihypertensive therapy that targeted a systolic blood pressure of 120 mmHg. The HOPE-3 trial, a multinational study, showed that older adults with elevated vascular risk but without significantly elevated systolic blood pressure (mean systolic blood pressure at baseline 138.2 mmHg) did not have any benefit when they received hydrochlorothiazide 12.5 mg plus candesartan 16 mg daily. However, neither study directly addresses the selection of the GBD TMREL of 110-115 mmHg since observational studies necessarily reflect both the benefits accrued through maintaining a healthy blood pressure
throughout life rather than from the use of blood pressure-lowering medications. The GBD estimate necessarily represents the impact of primary prevention and lifestyle modification as well as the possibility of pharmacotherapy for achieving the TMREL. The large potential gain in global health that we estimate if an optimal blood pressure was to be achieved suggests that further studies of blood pressure at younger ages remains an important area for investigation. A wide array of clinical and population strategies are available to reduce systolic blood pressure, including lowering population salt intake, increasing physical activity, reducing or slowing the rise of high BMI, and providing access to effective antihypertensives which merit considerable attention in many countries.

**Alcohol use**

We report that the global SEV for alcohol decreased 5.2% (2.1-9.4%) from 1990 to 2015. Of note, however, because of the distribution of where alcohol consumption occurs and background disease rates, alcohol consumption contributed to an increase in alcohol attributable DALYs over the same period. The assessment of the burden attributable to alcohol is complicated by potentially elevated risks in former drinkers compared to abstainers, potential protective effects of mild to moderate use of alcohol, and the use of a TMREL of zero consumption for this study. Meta-analyses have shown considerably elevated relative risks in former drinkers, equivalent to 30 grams of pure alcohol per day or more for some outcomes, although this may occur as a result of confounding by misclassification of former drinkers as lifetime abstainers and a sick ex-drinker phenomenon. Future GBD studies should carefully re-evaluate whether the excess risk in former drinkers is overestimated. If the relative risks for former drinkers have been overestimated this will also affect our assessment of the alcohol SEV and the global trend in the SEV. More controversial is the protective effect of mild to moderate alcohol use reported for ischemic heart disease, diabetes in women, and reduced all-cause mortality; some authors argue this consistent finding is due to confounding. However, recent studies on all-cause mortality with certain types of quality exclusions find no overall mortality benefit of mild to moderate use. A number of Mendelian randomization studies – which use genetic variation not associated with typical confounding factors, but with reliable association to putative causal factors – have contradicted previously claimed benefits of moderate alcohol consumption on several outcomes. Marked differences in male and female patterns of relative risk, such as for diabetes, raise many questions about the biological pathways through which these effects may act. Finally, our alcohol analysis uses a TMREL of zero consumption; using a higher TMREL for alcohol use would increase our estimate of the global burden attributed to alcohol. Given the large burden of alcohol and the availability of effective options to reduce consumption at the population level, such as increased alcohol taxes, controls on outlet location and density, establishing or maintaining limits for days or hours of sale, and screening and advice from health care givers, narrowing the uncertainty in the alcohol assessment is important.
High body mass index and fasting plasma glucose

Among the top five Level 3 risk factors, DALYs attributable to high BMI increased the most from 1990 to 2015 while SEV also increased. High BMI is mediated through increases in systolic blood pressure, cholesterol, and fasting plasma glucose (see Appendix pp 23-30). Our decomposition analysis suggests that the increase in risk attributable burden due to high BMI is considerably smaller than it could have been if underlying rates, particularly for cardiovascular diseases, had not declined as much as they did over the past decade. The decline in the underlying rates is likely due to expanded access to preventive treatment and higher quality of care. If obesity continues to increase in the future, the consequences to health trends may be greater if the trend in underlying rates attenuates. While closely linked, we also estimate that the pace of increase in high fasting plasma glucose is slightly higher than for obesity. The combined effect of rising obesity and rising fasting plasma glucose has consequences for a variety of health outcomes and on the costs of delivering health care. For obesity, a wide range of policy options have been proposed, but few if any strategies have proven to work at the population level. Analysis of obesity options needs to be more closely linked to consideration of diet and physical activity. We found, for example, that 1.3% (0.6-2.1%) of the burden of obesity globally is linked to sugar-sweetened beverages, providing one target for policy action. While for most diet components we have reported on the effect of diet composition on health outcomes, there is a strong argument to explore the relationship of specific diet components and overall BMI.

Methods strengths and challenges

Uncertainty in causality

To move the GBD and the CRA field forward, we have reported for the first time details of the evidence that is available to support the causal relationship of each risk-outcome pair (Table 1). The strength of the evidence of causality varies widely across risk factors. For the risk-outcome pairs where evidence from randomized controlled trials or high quality prospective observational studies was not available, we considered the possibility of using other types of evidence including Mendelian randomization to establish causality. While we have not used this approach in GBD 2015, this body of evidence seems to provide useful information that deserves a more detailed evaluation in future iterations of GBD. Likewise, the appropriate use of case-control data to support causality needs to be more clearly defined.

Being explicit about the supporting evidence also demonstrates that some risks have a similar body of evidence supporting them, even though in some debates the strength of evidence is thought to be very different. For this study, we focused on evidence mainly from prospective studies of exposure and disease endpoints. In select cases we had to use prospective studies of intermediate outcomes, including trials of the effect of sodium on systolic blood pressure, prospective cohort studies of the effect of lead on systolic blood pressure, and trials and cohort
studies of SSBs’ impact on body mass index. We did not include the strength of evidence uncertainty in our estimation of attributable burden which require more consensus on how different types of evidence can be combined to support a causal connection.

Integrated exposure response curve for particulates less than 2.5 µg

In this study, as for GBD 2013, we have estimated the relative risk of exposure to PM2.5 over a broad range of daily doses by integrating relative risks from diverse sources of PM2.5, including ambient air pollution, household air pollution, secondhand smoke, and tobacco smoking, using a single integrated exposure response (IER) curve. The premise behind this approach is that PM2.5 daily dose is a common indicator of risk from diverse sources of particulate pollution. Although recent assessments support an assumption of the equitoxicity of particulate matter mass from different sources for the purposes of burden estimation, this issue remains an area of active research. We expect that the IER will continue to evolve in response to the latest evidence in the field of air pollution dose-response; in keeping with the iterative nature of the GBD estimates, the inclusion of additional cohort studies at lower levels of PM2.5 led to a revision of the TMREL distribution that is less than half of the level used in GBD 2013. The inclusion of new high quality studies (available through http://ghdx.healthdata.org/) and the nonlinear nature of the IER curve have increased our estimate of global burden. Methodological improvements to the curve-fitting algorithm that better capture the heterogeneity of component studies produces uncertainty intervals that are considerably wider than those estimated in GBD 2013.

Future directions for GBD CRA

To date, attributable burden has been the primary metric that was methodologically and computationally feasible for GBD risk assessments. As burden forecasts become routinely available, quantifying avoidable burden within the GBD analytic framework will become more tractable. Developing avoidable burden estimates will require resolving a range of important issues, such as the degree of reversibility for some risks and the type of counterfactual distribution most relevant to avoidable burden calculation. Arguably, feasible or cost-effective counterfactual distributions of exposure may be more relevant than minimum risk.

In the next iterations of the GBD CRA we plan to incorporate new risks in two areas: distal socioeconomic factors such as educational attainment, and the absence of effective health interventions such as vaccination or seatbelts. We will evaluate the evidence supporting new risk factors for inclusion and expand the scope of the analysis based on both the evidence for causality and the availability of evidence for estimating exposure levels. For behavioural, environmental and occupational, and metabolic risks, other candidate risks have been proposed for inclusion in the GBD, including climate change, smokeless tobacco, added sugar, and access to health care. For existing risks, we will also carefully evaluate the inclusion of new risk-outcome...
pairs. Continued close examination of evidence supporting causality may lead to modifications of the criteria for inclusion. For many distal factors such as educational attainment, there is highly consistent evidence from prospective cohorts for all-cause mortality, but the relationships for cause-specific mortality may well vary by context; for example, where access to treatment may modulate the effects of education on an outcome. For GBD 2015, we have made progress clarifying the evidence base for each risk-outcome pair. This sort of in-depth examination will, we hope, lead to a simpler and more transparent approach to defining which risk-outcome pairs at any level of the causal web should be considered convincing or probable.

Limitations

Since the estimation of the attributable burden of disease includes estimates of deaths, YLLs, YLDs, or DALYs; the limitations described for elsewhere for those also apply to this analysis.\textsuperscript{134,135} We have developed our modeling strategies to quantify uncertainty given the available data. New data – particularly from countries where we currently lack data – might reveal levels of exposure that are outside the uncertainty intervals that we have estimated. We assume that the joint effect for risk factors where we do not correct for mediation can be estimated with the multiplicative risk model. Although plausible, this model might not accurately capture how all risks interact.\textsuperscript{136} Recent analyses of the NHANES-III cohort suggest sub-multiplicative effects for some risks. Shifting from a multiplicative model to a sub-multiplicative model has profound implications for all aspects of risk factor epidemiology, beginning at the estimation of relative risks and extending to the use of relative risks as a generalizable construct.\textsuperscript{137}

As a consequence of the lack of sufficient studies across all risk-outcome pairs we did not systematically correct relative risks for publication bias. We did not correct relative risks for non-masking in studies; however, not all risks can be studied in a masked fashion (eg, tobacco smoking). Comparability would be compromised if we corrected some risks but not others. We generally assumed that relative risks were uniform across countries for a given age-sex group.\textsuperscript{138,139} Differences in relative risks with geography may exist, as has been found for the BMI relative risk curve and TMREL, but with the exception of breast cancer, we find there is insufficient evidence to date to identify statistically significant differences.

It is more difficult to develop robust models to estimate variation in the SD than for estimations of the mean. Because measurement error is necessarily included in SD from studies, they are an overestimate of the true SD. We did not correct SD for measurement error, with the exception of correcting observed systolic blood pressure to usual blood pressure. Measurement error also affects estimation of relative risks through regression dilution bias – the attenuation of the association between the level of risk and the incidence of disease outcomes; due to the lack of detailed data for key cohorts we have not corrected cholesterol or fasting plasma glucose relative risks for regression dilution bias. Our approach of estimating the maximum relative risk
based on the reported cohorts and trials may underestimate burden if risk continues to rise at
the highest levels of exposure beyond those reported. While a log-linear function for relative
risks and levels of exposure is adequate for the observed range of exposure, the available data
on the most extreme values are limited. Given that a very small fraction of the population in any
country is in these extreme exposure levels, the potential bias in our estimates is minimal.

Additionally, estimating burden for risks divided into polytomous risks might underestimate their
burden compared with estimating burden with a continuous risk variable.

Although the use of a log-normal distribution is the best of the parametric distributions we have
evaluated for FGP, there are important deviations from the log-normal in survey data such as
NHANES. We have explored different mixtures of distributions, including two log-normal or a
normal and log-normal, some of which provided better overall fit. However, we have so far not
been able to solve the optimization problem of estimating two distributions given only a mean
and SD reported from particular studies.

We did not use the relative risk and exposure PAF calculation for unsafe sex, HIV risk from
injecting drug use, and occupational injuries; we used direct evidence of the attributable
fraction. The comparability of the results derived from these direct or categorical approaches to
the risks estimated with the relative risk and exposure model is not certain.

Too few studies exist to allow estimation of the contribution of household air pollution to
ambient air pollution or vice versa. A consequence is that we may have underestimated the
burden of household air pollution as a single risk factor; we may also have overestimated the
burden of air pollution combined. Further, our analysis of ambient air pollution has focused on
PM2.5, other pollutants including larger particulates and NO₂ may also be important to quantify.

For cholesterol, we determined our estimates of burden using total cholesterol; however,
increasing evidence supporting the effects of LDL cholesterol – and recent improvements in data
availability for serum LDL in different populations – suggest future estimations of risk from high
cholesterol should use LDL cholesterol as the unit of estimation.

Proxies for exposure to some risk factors are coarse; this is particularly the case for zinc
deficiency, for which we estimated the balance between theoretical intake and physiological
requirements from FAO food balance sheets for absorbable zinc. While zinc deficiency can be
estimated from the proportion of people estimated to have inadequate zinc intake, the
individual-level measurement of the exposure truly needed to estimate the number of people at
risk is not available. In a similar fashion, the proportion of the population in coarse occupational
categories was used as a proxy for exposure to specific carcinogens, and fuel type was used as a
proxy for household air pollution. Our ability to capture geographical variation and uncertainty in
converting household solid fuel use to PM2.5 exposure improved the validity of our findings and
uncertainty intervals. It would be preferable to use direct PM2.5 measurement in households to
calibrate the more widely available data for fuel use; however, such data have rarely been collected. As with all previous studies, we assessed the burden attributable to the availability of water and sanitation infrastructure, not the use of the infrastructure. Exposure for these risks has been defined in terms of availability and not use because that is what household surveys have collected. Our estimates are not biased, however, by this limitation, because relative risks were derived from similar exposure definitions. Finally, we have not estimated intimate partner violence for men because of a lack of evidence of the health effects amongst men.

Conclusion

Quantification of the health impacts of a diverse set of largely avoidable risks is an important input into any national or global strategy to improve population health and to make progress with the Sustainable Development Goals. For the first time, we have been able to separately assess and report trends in risk exposure and decompose trends in attributable burden into the contribution of demographic change, risk exposure, and risk-deleted rates. Reductions in some risks strongly associated with low levels of development such as poor water, poor sanitation, household air pollution, and undernutrition have been important contributors to global progress. Some critical risks for NCDs, particularly obesity, high fasting plasma glucose and alcohol are increasing. Deleterious trends have had a smaller impact than expected because of favorable declines in risk-deleted DALY rates for many causes, a component of which may be due to access to effective healthcare. In an era of rapid transition in societies and in levels of health, tracking and responding to key risks will require constant monitoring at the local level. As the set of risk factors expands to encompass access to specific health care interventions in future iterations of the GBD, the GBD CRA will provide an even more comprehensive understanding of the drivers of health improvement, and how they relate to the operation and priorities of health systems.
Figures and Tables


Figure 2. Global DALYs attributable to level 2 risk factors for males (A) and females (B), 2015. DALYs from different causes attributable to each risk factor are shown in different colours. DALYs=disability-adjusted life-years.

Figure 3. Leading 25 level 3 global risk factors for DALYs for both sexes combined, 2005 and 2015, with age-standardised median percentage change. Risks are connected by arrows between time periods. Behavioural risk factors are shown in red, environmental risks in blue and metabolic risks in green. For the time period 1990 to 2005 and for 2005 to 2015, three measures of change are shown: percent change in the number of DALYs, percent change in the all-age DALY rate and percent change in the age-standardised DALY rate. Statistically significant changes are shown in bold. DALYs=disability-adjusted life-years.

Figure 4. Global attributable DALYs in 2015 for each level 3 risk factor, versus annualised rate of change in summary exposure value from 1990 to 2015, for both sexes combined. Risks with 100,000 DALYs or more are presented. DALYs are represented in log-scale. DALYs=disability-adjusted life-years. This figure excludes occupational exposure to occupational exposure to benzene, diesel engine exhaust, and occupational exposure to silica which all had SEV increases greater than 50%. Metabolic risk factors are shown in green, occupational risks in violet, environmental risks in red and behavioural risks in blue. DALYs=disability-adjusted life-years. SEV=summary exposure value. Water=Unsafe water. Sanitation =Unsafe sanitation. Handwashing=No handwashing with soap. Ambient PM=Ambient particulate matter pollution. Household air=Household air pollution. Ozone=Ambient ozone pollution. Radon=Residential radon. Lead=Lead exposure. Asbestos=Occupational exposure to asbestos. Arsenic=Occupational exposure to arsenic. Beryllium=Occupational exposure to beryllium. Cadmium=Occupational exposure to cadmium. Chromium=Occupational exposure to chromium. Occ SHS=Occupational exposure to second-


**Figure 5.** Global decomposition of changes in all-cause DALYs attributable to level 3 risk factors from 1990 to 2015 due to population growth, population ageing, risk exposure, and the risk-deleted DALY rate. Risks are reported in order of percent change in the number of attributable DALYs from 1990 to 2015. This figure excludes DALYs attributable to unsafe sex because it is not estimated based on exposure and relative risk. DALYs=disability-adjusted life-years.

**Figure 6.** Co-evolution of summary exposure value and Socio-demographic Index for the top 10 global risks in terms of attributable DALYs in 2015, with comparisons to expected summary exposure value on the basis of Socio-demographic Index. Coloured points show SEVs for GBD regions. Each point represents one year in 5-year intervals from 1990 to 2015. The solid black line represents the expected SEV based on SDI alone. SDI = Socio-demographic Index. DALYs=disability-adjusted life-years. SEV=summary exposure values.

Table 1. Summary of epidemiologic evidence supporting causality between risk-outcome pairs included in GBD 2015. “RCTs (Number)” represents the total number of independent randomized controlled trials evaluating the relationship of each risk-outcome pair. “RCTs with significant effect in the opposite direction (%)” represents the percentage of randomized controlled trials showing a significant effect in the opposite direction. “Prospective observational studies (Number)” shows the total number of independent prospective cohort studies or non-randomized interventions evaluating the relationship of the risk-outcome pair. “Prospective observational studies with significant association in the opposite direction (%)” represents the percentage of prospective cohort studies or non-randomized interventions reporting a significant association in the opposite direction. “Lower limit of RR > 1.5” shows whether the lower limit of the 95% confidence interval for the relative risk of the risk-outcome pair is greater than 1.5. “Dose-response relationship” shows whether there is any evidence of linear or non-linear dose-response relationship between the risk and the outcome. “Biologic plausibility” shows whether there is any biologic or mechanistic pathway that could potentially explain the relationship of the risk-outcome pair. “Analogy” shows whether the risk is associated with another outcome from the same category and there is evidence that it can cause the current outcome through the same pathway. GBD=Global Burden of Disease.

Table 2. GBD 2015 risk factor hierarchy, exposure definitions, theoretical minimum risk exposure level and data representativeness index (DRI) for the entire period 1985-2015, pre-2005, and 2005-2015. The percentage of available data is calculated out of a total of 519 subnational level 2 geographies. GBD=Global Burden of Disease.

Table 3. Global age-standardised summary exposure values (SEVs) for all risk factors 1990, 2005, and 2015 and percentage change in the SEV from 1990 to 2005 and 2005 to 2015. Data in parenthesis are 95% uncertainty intervals. Statistically significant increases or decreases are shown in bold (p < 0.05). Risks are reported in order of percent change for both sexes combined, 1990-2015.

Table 4. Global all-age deaths and DALYs attributable to each risk factor at each level of the risk factor hierarchy and outcome for both sexes combined in 2005 and 2015 and percentage change in the all-age deaths and DALYs from 2005 to 2015 and of age-standardized death PAFs and DALY PAFs from 2005 to 2015. 95% UIs are in parentheses. Statistically significant increases or decreases are shown in bold (p < 0.05). UI = uncertainty interval. DALYs=disability-adjusted life-years.
References


27 Popkin BM. Global nutrition dynamics: the world is shifting rapidly toward a diet linked with noncommunicable diseases. *Am J Clin Nutr* 2006; **84**: 289–98.


http://professional.heart.org/professional/GuidelinesStatements/searchresults.jsp?q=&y=&t=1001.


63 Willett W. Nutritional Epidemiology. OUP USA, 2013.


Pooling Project of Prospective Studies of Diet and Cancer: Cohort Study Participants. https://www.hsph.harvard.edu/pooling-project/cohort-study-participants/.


Trinquart L, Johns DM, Galea S. Why do we think we know what we know? A metaknowledge analysis of the salt controversy. *Int J Epidemiol* 2016; **45**: 251–60.


Frieden TR. Sodium Reduction-Saving Lives by Putting Choice Into Consumers’ Hands. *JAMA* 2016; published online June 1. DOI:10.1001/jama.2016.7992.

He FJ, MacGregor GA. Hypertension: Salt: flawed research should not divert actions to reduce intake. *Nat Rev Nephrol* 2016; published online July 11. DOI:10.1038/nrneph.2016.97.


100 Stockwell T, Greer A, Fillmore K, Chikritzhs T, Zeisser C. How good is the science? *BMJ* 2012; 344: e2276; author reply e2294.


