Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016

GBD 2016 Risk Factors Collaborators*

Summary

Background The Global Burden of Diseases, Injuries, and Risk Factors Study 2016 (GBD 2016) provides a comprehensive assessment of risk factor exposure and attributable burden of disease. By providing estimates over a long time series, this study can monitor risk exposure trends critical to health surveillance and inform policy debates on the importance of addressing risks in context.

Methods We used the comparative risk assessment framework developed for previous iterations of GBD to estimate levels and trends in exposure, attributable deaths, and attributable disability-adjusted life-years (DALYs), by age group, sex, year, and location for 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks from 1990 to 2016. This study included 481 risk-outcome pairs that met the GBD study criteria for convincing or probable evidence of causation. We extracted relative risk (RR) and exposure estimates from 22,717 randomised controlled trials, cohorts, pooled cohorts, household surveys, census data, satellite data, and other sources, according to the GBD 2016 source counting methods. Using the counterfactual scenario of theoretical minimum risk exposure level (TMREL), we estimated the portion of deaths and DALYs that could be attributed to a given risk. Finally, we explored four drivers of trends in attributable burden: population growth, population ageing, trends in risk exposure, and all other factors combined.

Findings Since 1990, exposure increased significantly for 30 risks, did not change significantly for four risks, and decreased significantly for 31 risks. Among risks that are leading causes of burden of disease, child growth failure and household air pollution showed the most significant declines, while metabolic risks, such as body-mass index and high fasting plasma glucose, showed significant increases. In 2016, at Level 3 of the hierarchy, the three leading risk factors in terms of attributable DALYs at the global level for men were smoking (124·1 million DALYs [95% UI 111·2 million to 137·0 million]), high systolic blood pressure (122·2 million DALYs [110·3 million to 133·3 million], and low birthweight and short gestation (83·0 million DALYs [78·3 million to 87·7 million]), and for women, were high systolic blood pressure (89·9 million DALYs [80·9 million to 98·2 million], high body-mass index (64·8 million DALYs [44·4 million to 87·6 million], and high fasting plasma glucose (63·8 million DALYs [53·2 million to 76·3 million]). In 2016 in 113 countries, the leading risk factor in terms of attributable DALYs was a metabolic risk factor. Smoking remained among the leading five risk factors for DALYs for 109 countries, while low birthweight and short gestation was the leading risk factor for DALYs in 38 countries, particularly in sub-Saharan Africa and South Asia. In terms of important drivers of change in trends of burden attributable to risk factors, between 2006 and 2016 exposure to risks explains an 9·3% (6·9–11·6) decline in deaths and a 10·8% (8·3–13·1) decrease in DALYs at the global level, while population ageing accounts for 14·9% (12·7–17·5) of deaths and 6·2% (3·9–8·7) of DALYs, and population growth for 12·4% (10·1–14·9) of deaths and 12·4% (10·1–14·9) of DALYs. The largest contribution of trends in risk exposure to disease burden is seen between ages 1 year and 4 years, where a decline of 27·3% (24·9–29·7) of the change in DALYs between 2006 and 2016 can be attributed to declines in exposure to risks.

Interpretation Increasingly detailed understanding of the trends in risk exposure and the RRs for each risk-outcome pair provide insights into both the magnitude of health loss attributable to risks and how modification of risk exposure has contributed to health trends. Metabolic risks warrant particular policy attention, due to their large contribution to global disease burden, increasing trends, and variable patterns across countries at the same level of development. GBD 2016 findings show that, while it has huge potential to improve health, risk modification has played a relatively small part in the past decade.

Funding The Bill & Melinda Gates Foundation, Bloomberg Philanthropies.

Copyright © The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY 4.0 license.
Global Health Metrics

Research in context

Evidence before this study
The Global Burden of Diseases, Injuries, and Risk Factors Study 2016 (GBD 2016) remains the most comprehensive effort to conduct a population-level comparative risk assessment across countries and risks. Other sources of population-level estimates of risk include WHO and UNICEF reports as well as independent scientific publications. Notable differences in methods and definitions produce variation in results, although in several cases there is general agreement in regional or global patterns. The GBD study remains the only peer-reviewed, comprehensive, and annual assessment of risk factor burden by age, sex, cause, and location for a long time series that complies with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER).

Added value of this study
This study builds upon GBD 2015 and provides several important improvements as well as the quantification of five new risks. The innovations and improvements from last year can be summarised as follows. Across all risk factors, there were 7155 additional data sources, according to the GBD 2016 source counting methods. For diet, we included data for dietary recall, household budget, and food frequency questionnaires. We also incorporated sales data from 170 countries as well as national accounting of food available to populations in a given year. In GBD 2016, we are producing estimates for the following five new risks: smokeless tobacco, low birthweight and short gestation, low birthweight for gestation, short gestation for birthweight, and diet low in legumes. We also extended the high body-mass index (BMI) analysis to include childhood obesity. We have also added 93 new risk-outcome pairs. Major revisions to the estimation of the following risk factors were undertaken for GBD 2016. For second-hand smoke, we changed the estimation method to ensure consistency with the estimates for smoking prevalence. For alcohol, we estimated new relative risks (RRs) for all outcomes, we incorporated more data for exposure and new adjustments for tourism and unrecorded consumption, and we redefined the theoretical minimum risk exposure level (TMREL). For diet, we estimated the disease burden of dietary risks based on the absolute level of intake rather than the intake standardised to 2000 kcal per day. We developed an ensemble model of different parametric distributions to generate better fits to the distributions of continuous risk factors. Mediation evidence was reviewed and updated based on an analysis of ten pooled cohorts. We have expanded the analysis of geographic and temporal trends in risk exposure and burden by development, using the Socio-demographic Index (SDI), and have also explored where countries are in the risk transition. We also improved and modified our decomposition methods so that the results shown are additive and can be aggregated to explain trends in all-cause and cause-specific mortality, as well as trends across age groups. The decomposition analysis has been extended to examine how risk factors have contributed to trends in all-cause mortality by age and sex as well as by cause.

Implications of all the available evidence
Increasingly detailed understanding of the trends in risk exposure and the RRs for each risk-outcome pair provides insights into both the magnitude of health loss attributable to risks and how modification of risk exposure has contributed to health trends. This analysis shows a mismatch between the potential for risk modification to improve health and the relatively modest role that risk modification has played in the past generation in improving global health.

Introduction
A core premise of public health is that prevention can be a powerful instrument for improving human health, one that is often cost-effective and minimises harm to individuals from ill health. The core objectives of prevention include the reduction or modification of exposure to risks including metabolic, behavioural, environmental, and occupational factors. Quantifying risks to health and thus the targets of many public health actions is an essential prerequisite for effective public health. The evidence on the relation between risk exposure and health is constantly evolving: new information about the relative risks (RRs) associated with different risks for different outcomes continues to emerge from cohort studies, randomised trials, and case-control studies. These studies can establish evidence for new risks or risk-outcome pairs or reduce the strength of evidence for existing risks. New data are also regularly collected on the levels of exposure in different populations and in different settings. Regularly updated monitoring of the evidence base on risk factors is crucial for public health and for individual risk modification through primary care and self-management.

Several studies explore risk-attributable burden for individual risks at the global, regional, or national level. Other studies provide assessments of exposure for selected risks. However, the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) comparative risk assessment (CRA) is the only comprehensive and comparable approach to risk factor quantification. The most recent of these assessments was GBD 2015. With each cycle of GBD, scientific discussions have emerged on various dimensions of risk quantification that have led to improvements and modifications of GBD. Many of these are focused on the strength of evidence supporting a causal connection for specific risk-outcome pairs, while others relate to measurement challenges. Further, new risk factors have been added for important health conditions included in GBD, such as neonatal outcomes and Alzheimer’s dementia, which have previously not had associated risk factors. The recent trials on blood pressure control at lower levels of systolic blood pressure, including
the Systolic Blood Pressure Intervention Trial (SPRINT)\textsuperscript{11} and Heart Outcomes Prevention Evaluation-3 (HOPE-3) trial,"\textsuperscript{2} have also brought attention to the difference between risks and the clinical question of risk reversibility. The CRA framework provides an important insight into the role of different risks in contributing to levels of population health but does not necessarily provide all the information necessary to guide individual clinical decision making.

The GBD 2016 CRA includes 84 risk factors and an associated 481 risk-outcome pairs. In addition to new data and updated methods, we have included five new risks in the GBD 2016 CRA. The study was undertaken for 195 countries and territories and provides estimates of exposure and attributable deaths and disability-adjusted life-years (DALYs) for 1990 through to 2016. We explored how risks change with development, measured by the Socio-demographic Index (SDI), and also decomposed changes in deaths and DALYs into the contributions of population ageing, population growth, trends in risk exposure, and all other factors combined. As with previous iterations of GBD, the GBD 2016 CRA results presented here supersede all previously published GBD CRA estimates.

Methods
Overview
The CRA conceptual framework was developed by Murray and Lopez,\textsuperscript{13} who established a causal web of hierarchically organised risks or causes that contribute to health outcomes (method appendix; appendix 1 p 432), which allows quantification of risks or causes at any level in the framework. In GBD 2016, as in previous iterations of GBD, we evaluated a set of behavioural, environmental, and occupational, and metabolic risks, where risk-outcome pairs were included based on evidence rules (appendix 1 p 344). These risks were organised into five hierarchical levels as described in appendix 1 (p 374). At Level 0, the GBD 2016 provides estimates for all risk factors combined, at Level 1 the GBD 2016 provides estimates for three groups: environmental and occupational, metabolic, and behavioral risk factors. At Level 2, there are 17 risks, at Level 3 there are 50 risks, and at Level 4 there are 67 risks, for a total of 84 risks or clusters of risks. To date, we have not quantified the contribution of other classes of risk factors (appendix 1 p 376); however, using an analysis of the relation between risk exposures and socio-demographic development, measured with the use of SDI, we provide some insights into the potential magnitude of distal social, cultural, and economic factors.

Two types of risk assessment are possible within the CRA framework: attributable burden and avoidable burden.\textsuperscript{13} Attributable burden is the 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\textsuperscript{13} identified four types of counterfactual exposure distributions: theoretical, plausible, feasible, and cost-effective minimum risk. In GBD studies, to date and in this study, we focus on attributable burden using the theoretical minimum risk exposure level, which is the distribution of risk comprising the levels of exposure that minimise risk for each individual in the population.

Overall, this analysis follows the CRA methods used in GBD 2015.\textsuperscript{4} The methods described in this study provide a high-level overview of the analytical logic, focusing on areas of notable change from the methods used in GBD 2015, with details provided in appendix 1 (p 10). This study complies with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) statement\textsuperscript{\textsuperscript{a}} (appendix 1 p 377).

Geographical units of analysis and years for estimation
In GBD 2016, locations are 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, we present estimates at the subnational level for five countries with a population greater than 200 million in 2016: Brazil, China, India, Indonesia, and the USA. We produced a complete set of age-specific, sex-specific, cause-specific, and location-specific estimates of risk factor exposure and attributable burden for 1990–2016 for all included risk factors.

Attributable burden estimation
Four key components are included in estimation of the burden attributable to a given risk factor: the metric of burden being assessed (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 multiplied by the population attributable fraction (PAF) for the risk-outcome pair for a given age, sex, location, and year. A similar logic applies for estimation of attributable deaths, YLLs, or YLDs. Risks are categorised on the basis of how exposure was measured: dichotomous, polytomous, or continuous. The PAF represents the proportion of outcome that would be reduced in a given year if the exposure to a risk factor in the past were reduced to the counterfactual level of the theoretical minimum risk exposure level (supplementary results, appendix 2 p 1).

Causal evidence for risk-outcome pairs
In this study, as in GBD 2015, we have included risk-outcome pairs that we have assessed as meeting the World Cancer Research Fund grades of convincing or probable evidence (see appendix 1 p 10 for definitions of
Global Health Metrics

these grades). Table 1 provides a summary of the evidence supporting a causal relation between a risk and an outcome for each pair included in GBD 2016. For each risk-outcome pair, we used recent systematic reviews to identify independent prospective studies (randomised controlled trials, non-randomised interventions, and cohorts) that evaluated the putative relationship. For risk-outcome pairs with fewer than five prospective studies, we evaluated evidence from case-control studies as well (appendix 1 p 344). Table 1 summarises the evidence using multiple dimensions, which supports our assessment that each included risk-outcome pair meets the criteria of convincing or probable evidence (appendix 1 p 10 contains a justification of the criteria presented to support causality). In this summary of evidence, we have focused on randomised controlled trials and prospective observational studies, along with supporting evidence, like dose–response relationships and biologically plausible mechanisms.

Estimation process

Information about the data sources, estimation methods, computational tools, and statistical analysis used in the derivation of our estimates are provided in appendix 1 (p 10). The analytical steps for estimation of burden attributable to single or clusters of risk-outcome pairs are summarised in appendix 1 (p 10). Table 2 provides definitions of exposure for each risk factor, the theoretical minimum risk exposure level (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 GBD 2015 for each quantity for each risk. Some methodological improvements have been implemented and new data sources incorporated. Appendix 1 (p 34) provides details of each step by risk. Citation information for the data sources used for relative risks are provided in searchable form through an online source tool.

All point estimates are reported with 95% uncertainty intervals (UIs). UIs include uncertainty from each relevant component, consisting of exposure, relative risks, TMREL, and burden rates. Where percentage change is reported (with 95% UIs), we computed it on the basis of the point estimates being compared.

In GBD 2015, we produced a summary measure of exposure for each risk, called the summary exposure value (SEV), which is a metric that captures risk-weighted exposure for a population, or risk-weighted prevalence of an exposure. The scale for SEV spans from 0% to 100%, such that an SEV of 0% reflects no risk exposure in a population and 100% indicates that an entire population is exposure to the maximum possible level for that risk. In GBD 2016, we show estimates of SEVs for each risk factor and provide details on how SEVs are computed for categorical and continuous risks in appendix 1 (p 10).

Fitting a distribution to exposure data

The most informative data describing the distribution of risk factors within a population come from individual-level data; additional sources of data include reported means and variances. In cases when a risk factor also defines a disease, such as haemoglobin level and anaemia, the prevalence of disease is also frequently reported. To model the distribution of any particular risk factor, we seek a family of probability density functions (PDFs), a fitting method, and a model selection criterion. To make use of the most data describing most populations, we used the method of moments (MoM); the first two empirical moments from a population, the mean and variance, were used to determine the PDF describing the distribution of risk within any population, where exceptions to this rule are justified by context. We used the Kolmogorov-Smirnov test to measure the goodness of fit (GoF), but in some cases, the GoF was based on the prediction error for the prevalence of disease.

We used an ensemble technique in which a model selection algorithm is used to choose the best model for each risk factor. We drew the initial set of candidate models from commonly used PDF families. We fitted each PDF candidate family to each dataset using the MoM, and used the Kolmogorov-Smirnov test as the measure of GoF. Preliminary analysis showed that the GoF ranking of PDF families varied across datasets for any particular risk factor and that combining the predictions of differently fitted PDF families could dramatically improve the GoF for each dataset. Therefore, we developed a new model for prediction using the ensemble of candidate models, which is a weighted linear combination of all candidate models, \( \{ f \} \), where a set of weights \( \{ w \} \) is chosen such that it is the sum of the weights equals to one and the values of the weights were determined by a second GoF criterion with its own validation process. Because of basic differences among risk factors, their distributions, and the risk attribution process, the model selection process was often slightly different for each risk factor. The details can be summarised by (1) the summary statistics for each dataset; (2) a table showing the Kolmogorov-Smirnov statistic for each candidate model and URD; (3) the criterion used for determining the overall GoF; (4) summary results of the validation process; and (5) the weights defining the final ensemble model for each dataset.

New risks and risks with significant changes in the estimation methods compared with GBD 2015

We took several steps to improve the estimation of alcohol use as a risk factor. First, on the exposure side, we added 26 survey series, which contributed 12195 datapoints in our models. Second, we developed and implemented a method that adjusts total consumption for tourism and unrecorded consumption for each location-year. Third, we calculated the TMREL. We chose TMREL as being the exposure that minimises an individual’s risk of suffering burden from any given cause related to alcohol...
| Risk | Outcome | RCTs (n) | RCTs with significant effect in the opposite direction (%) | Prospective observational studies (n) | Prospective observational studies with significant association in the opposite direction (%) | Case-control studies assessing the risk-outcome pair relationship (n) | Case-control studies that show significant association in the opposite direction (%) | Lower limit of RR >1·5 | Dose-response relationship ‡ | Biological plausibility § | Analogy $ |
|------|---------|----------|------------------------------------------------|--------------------------------------|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------|----------------------|-----------------------------|-----------------------------|-------------------|
| 2    | Unsafe water, sanitation, and handwashing | 3 Unsafe water source– chlorination or solar (point of use treatment) Diarrhoeal diseases | 24 0 42 6 0 -- -- Yes -- Yes No | | | | | | | | |
| | 3 Unsafe water source-piped Diarrhoeal diseases | 1 0 0 9 11 -- -- Yes -- Yes No | | | | | | | | | |
| | 3 Unsafe water source-filter Diarrhoeal diseases | 11 0 45 2 0 -- -- Yes -- Yes No | | | | | | | | | |
| | 3 Unsafe water source– improved water Diarrhoeal diseases | 0 -- -- 5 0 -- -- Yes -- Yes No | | | | | | | | | |
| | 3 Unsafe sanitation– piped Diarrhoeal diseases | 0 -- -- 7 0 -- -- Yes -- Yes No | | | | | | | | | |
| | 3 Unsafe sanitation– improved sanitation Diarrhoeal diseases | 0 -- -- 9 0 -- -- Yes -- Yes No | | | | | | | | | |
| | 3 No access to handwashing facility Diarrhoeal diseases | 19 0 42 0 -- -- No -- Yes No | | | | | | | | | |
| | 3 No access to handwashing facility Lower respiratory infections | 8 0 50 11 0 -- -- No -- Yes No | | | | | | | | | |
| 2 | Air pollution | 3 Ambient particulate matter pollution Lower respiratory infections | 0 -- -- 19 0 -- -- No Yes Yes No | | | | | | | |
| | 3 Ambient particulate matter pollution Tracheal, bronchus, and lung cancer | 0 -- -- 27 0 -- -- No Yes Yes Yes | | | | | | | | | |
| | 3 Ambient particulate matter pollution Ischaemic heart disease | 0 -- -- 16 0 -- -- No Yes Yes Yes | | | | | | | | | |
| | 3 Ambient particulate matter pollution Ischaemic stroke | 0 -- -- 25 0 -- -- No Yes Yes Yes | | | | | | | | | |
| | 3 Ambient particulate matter pollution Haemorrhagic stroke | 0 -- -- 25 0 -- -- No Yes Yes Yes | | | | | | | | | |
| | 3 Ambient particulate matter pollution Chronic obstructive pulmonary disease | 0 -- -- 12 0 -- -- No Yes Yes Yes | | | | | | | | | |
| | 3 Household air pollution from solid fuels Lower respiratory infections | 0 -- -- 0 -- 9 0 -- No Yes Yes No | | | | | | | | | |
| | 3 Household air pollution from solid fuels Tracheal, bronchus, and lung cancer | 0 -- -- 0 -- 20 0 -- No Yes Yes Yes | | | | | | | | | |
| | 3 Household air pollution from solid fuels Ischaemic heart disease | 0 -- -- 16 0 -- -- No Yes Yes Yes | | | | | | | | | |
| | 3 Household air pollution from solid fuels Ischaemic stroke | 0 -- -- 25 0 -- -- No Yes Yes Yes | | | | | | | | | |
| | 3 Household air pollution from solid fuels Haemorrhagic stroke | 0 -- -- 25 0 -- -- No Yes Yes Yes | | | | | | | | | |

(Table 1 continues on next page)
| Risk                                                                 | Outcome                                                                 | RCTs (n) | RCTs with significant effect in the opposite direction (%) | RCTs with null findings (%) | Prospective observational studies (n)† | Prospective observational studies with significant association in the opposite direction (%) | Case-control studies assessing the risk-outcome pair relationship (n)‡ | Case-control studies that show significant association in the opposite direction (%) | Lower limit of RR >1·5 | Dose-response relationship | Biological plausibility ‡ | Analogy§ |
|----------------------------------------------------------------------|-------------------------------------------------------------------------|----------|-------------------------------------------------------------|-----------------------------|--------------------------------------|---------------------------------------------------------------------------------|--------------------------------------------------------------------|---------------------------------------------------------------------|------------------------|-----------------------------|------------------------|----------|
| (Continued from previous page)                                        |                                                                         |          |                                                             |                             |                                      |                                                                                 |                                                                    |                                                                     |                        |                            |                        |          |
| 3 Household air pollution from solid fuels                           | Chronic obstructive pulmonary disease                                  | 0        | 0                                                           | 0                           | 2                                   | 0                                                                               | No                                                                 | Yes                                                                 | Yes                    | Yes                         | Yes                    | Yes      |
| 3 Household air pollution from solid fuels                           | Cataract                                                              | 0        | 0                                                           | 0                           | 11                                  | 0                                                                               | No                                                                 | Yes                                                                 | Yes                    | No                          | No                     | No       |
| 3 Ambient ozone pollution                                            | Chronic obstructive pulmonary disease                                  | 0        | 0                                                           | 0                           | 4                                   | 0                                                                               | 0                                                                  | 0                      | No                        | Yes                    | No       |
| 2 Other environmental risks                                           |                                                                        |          |                                                             |                             |                                      |                                                                                 |                                                                    |                                                                     |                        |                            |                        |          |
| 3 Residential radon                                                   | Tracheal, bronchus, and lung cancer                                    | 0        | 0                                                           | 1                           | 0                                   | 29                                                              | 0                                                                  | No                     | Yes                     | Yes                    | No       |
| 3 Lead exposure                                                       | Idiopathic developmental intellectual disability                      | 0        | 0                                                           | 8                           | 0                                   | 0                                                                               | 0                                                                  | No                     | Yes                     | Yes                    | No       |
| 3 Lead exposure                                                       | Systolic blood pressure                                               | 0        | 0                                                           | 3                           | 0                                   | 1                                                                               | 0                                                                  | No                     | Yes                     | Yes                    | No       |
| 2 Occupational risks                                                 |                                                                        |          |                                                             |                             |                                      |                                                                                 |                                                                    |                                                                     |                        |                            |                        |          |
| 4 Occupational exposure to asbestos                                  | Larynx cancer                                                         | 0        | 0                                                           | 27                          | 0                                   | 0                                                                               | 0                                                                  | No                     | Yes                     | Yes                    | Yes      |
| 4 Occupational exposure to asbestos                                  | Tracheal, bronchus, and lung cancer                                    | 0        | 0                                                           | 18                          | 0                                   | 0                                                                               | 0                                                                  | Yes                    | Yes                     | Yes                    | Yes      |
| 4 Occupational exposure to asbestos                                  | Ovarian cancer                                                        | 0        | 0                                                           | 15                          | 0                                   | 0                                                                               | 0                                                                  | No                     | Yes                     | Yes                    | Yes      |
| 4 Occupational exposure to asbestos                                  | Mesothelioma                                                          | 0        | 0                                                           | 5                           | 0                                   | 0                                                                               | 0                                                                  | Yes                    | Yes                     | Yes                    | Yes      |
| 4 Occupational exposure to arsenic                                   | Tracheal, bronchus, and lung cancer                                    | 0        | 0                                                           | 9                           | 0                                   | 0                                                                               | 0                                                                  | No                     | Yes                     | No                     | No       |
| 4 Occupational exposure to benzene                                   | Leukaemia                                                             | 0        | 0                                                           | 12                          | 0                                   | 0                                                                               | 0                                                                  | Yes                    | Yes                     | No                     | No       |
| 4 Occupational exposure to beryllium                                 | Tracheal, bronchus, and lung cancer                                    | 0        | 0                                                           | 3                           | 0                                   | 2                                                                               | 0                                                                  | No                     | Yes                     | No                     | No       |
| 4 Occupational exposure to cadmium                                   | Tracheal, bronchus, and lung cancer                                    | 0        | 0                                                           | 7                           | 0                                   | 0                                                                               | 0                                                                  | No                     | Yes                     | No                     | No       |
| 4 Occupational exposure to chromium                                 | Tracheal, bronchus, and lung cancer                                    | 0        | 0                                                           | 26                          | 0                                   | 0                                                                               | 0                                                                  | No                     | Yes                     | No                     | No       |
| 4 Occupational exposure to diesel engine exhaust                    | Tracheal, bronchus, and lung cancer                                    | 0        | 0                                                           | 17                          | 0                                   | 0                                                                               | 0                                                                  | No                     | Yes                     | No                     | No       |
| 4 Occupational exposure to second-hand smoke                         | Tracheal, bronchus, and lung cancer                                    | 0        | 0                                                           | 25                          | 0                                   | 0                                                                               | 0                                                                  | No                     | Yes                     | No                     | No       |
| 4 Occupational exposure to formaldehyde                             | Nasopharynx cancer                                                    | 0        | 0                                                           | 2                           | 0                                   | 6                                                                               | 0                                                                  | No                     | Yes                     | Yes                    | Yes      |

(Table 1 continues on next page)
### Global Health Metrics

| Risk                                                                 | Outcome                        | RCTs (n) | RCTs with significant effect in the opposite direction (%) | Prospective observational studies (n)* | Prospective observational studies with significant association in the opposite direction (%) | Case-control studies assessing the risk-outcome pair relationship (n)† | Case-control studies that show significant association in the opposite direction (%) | Lower limit of RR > 1·5 | Dose-response relationship ‡ | Biological plausibility § | Analogy's |
|---------------------------------------------------------------------|--------------------------------|----------|------------------------------------------------------------|----------------------------------------|------------------------------------------------------------------------------------------|------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------|------------------------|--------------------------------|------------------------|-----------|
| 4 Occupational exposure to formaldehyde                            | Leukaemia                      | 0        | ...                                                        | 13                                     | 0                                                                                       | ...                                                                    | No                                                                                                                                  | Yes                    | Yes                                                            | Yes                    | No        |
| 4 Occupational exposure to nickel                                   | Tracheal, bronchus, and lung cancer | 0        | ...                                                        | 6                                      | 0                                                                                       | ...                                                                    | No                                                                                                                                  | Yes                    | No                                                            | No         | No        |
| 4 Occupational exposure to polycyclic aromatic hydrocarbons        | Tracheal, bronchus, and lung cancer | 0        | ...                                                        | 39                                     | 0                                                                                       | ...                                                                    | No                                                                                                                                  | Yes                    | No                                                            | No         | No        |
| 4 Occupational exposure to silica                                  | Tracheal, bronchus, and lung cancer | 0        | ...                                                        | 17                                     | 0                                                                                       | ...                                                                    | No                                                                                                                                  | Yes                    | No                                                            | No         | No        |
| 4 Occupational exposure to sulfuric acid                           | Kidney cancer                   | 0        | ...                                                        | 20                                     | 0                                                                                       | ...                                                                    | No                                                                                                                                  | Yes                    | No                                                            | No         | No        |
| 3 Occupational asthmagens                                          | Asthma                          | 0        | ...                                                        | 16                                     | 0                                                                                       | ...                                                                    | No                                                                                                                                  | Yes                    | No                                                            | No         | No        |
| 3 Occupational particulate matter, gases, and fumes                | Chronic obstructive pulmonary disease | 0        | ...                                                        | 9                                      | 0                                                                                       | ...                                                                    | No                                                                                                                                  | Yes                    | No                                                            | No         | No        |
| 3 Occupational noise                                               | Age-related and other hearing loss | 0        | ...                                                        | 5                                      | 0                                                                                       | ...                                                                    | Yes                                                                                                                                  | Yes                    | No                                                            | No         | No        |
| 3 Occupational ergonomic factors                                   | Low back pain                   | 0        | ...                                                        | 10                                     | 0                                                                                       | ...                                                                    | No                                                                                                                                  | Yes                    | No                                                            | No         | No        |
| 2 Child and maternal malnutrition                                  | Non-exclusive breastfeeding      | 0        | ...                                                        | 5                                      | 0                                                                                       | ...                                                                    | Yes                                                                                                                                  | Yes                    | Yes                                                            | Yes        | No        |
| 2 Child and maternal malnutrition                                  | Non-exclusive breastfeeding      | 0        | ...                                                        | 6                                      | 0                                                                                       | ...                                                                    | Yes                                                                                                                                  | Yes                    | Yes                                                            | Yes        | No        |
| 2 Child and maternal malnutrition                                  | Discontinued breastfeeding       | 0        | ...                                                        | 2                                      | 0                                                                                       | ...                                                                    | No                                                                                                                                  | Yes                    | No                                                            | No         | No        |
| 2 Child and maternal malnutrition                                  | Child underweight               | 0        | ...                                                        | 7                                      | 0                                                                                       | ...                                                                    | Yes                                                                                                                                  | Yes                    | No                                                            | No         | No        |
| 2 Child and maternal malnutrition                                  | Child underweight               | 0        | ...                                                        | 7                                      | 0                                                                                       | ...                                                                    | Yes                                                                                                                                  | Yes                    | No                                                            | No         | No        |
| 2 Child and maternal malnutrition                                  | Discontinued breastfeeding       | 0        | ...                                                        | 7                                      | 0                                                                                       | ...                                                                    | Yes                                                                                                                                  | Yes                    | No                                                            | No         | No        |
| 2 Child and maternal malnutrition                                  | Child wasting                   | 0        | ...                                                        | 7                                      | 0                                                                                       | ...                                                                    | Yes                                                                                                                                  | Yes                    | No                                                            | No         | No        |
| 2 Child and maternal malnutrition                                  | Discontinued breastfeeding       | 0        | ...                                                        | 7                                      | 0                                                                                       | ...                                                                    | Yes                                                                                                                                  | Yes                    | No                                                            | No         | No        |
| 2 Child and maternal malnutrition                                  | Child wasting                   | 0        | ...                                                        | 7                                      | 0                                                                                       | ...                                                                    | Yes                                                                                                                                  | Yes                    | No                                                            | No         | No        |
| 2 Child and maternal malnutrition                                  | Discontinued breastfeeding       | 0        | ...                                                        | 7                                      | 0                                                                                       | ...                                                                    | Yes                                                                                                                                  | Yes                    | No                                                            | No         | No        |

(Continued from previous page)
Global Health Metrics

| Risk                              | Outcome                                      | RCTs (n) | RCTs with significant effect in the opposite direction (%) | RCTs with null findings (%) | Prospective observational studies (n)† | Prospective observational studies with significant association in the opposite direction (%) | Case-control studies assessing the risk-outcome pair relationship (n)‡ | Case-control studies that show significant association in the opposite direction (%) | Lower limit of RR > 1·5 | Dose-response relationship | Biological plausibility ‡ | Analogy§ |
|----------------------------------|----------------------------------------------|----------|------------------------------------------------------------|-----------------------------|---------------------------------------|-------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|---------------------------------------------------------------------------------|--------------------------|--------------------------------|-------------------------------|---------|
| (Continued from previous page)   |                                              |          |                                                            |                             |                                       |                                                                                          |                                                                                   |                                                                                 |                          |                                |                               |         |
| 4 Child stunting                 | Lower respiratory infections                 | 0        | --                                                         | 7                           | 0                                    | --                                                                                       | --                                                                               | No                                                                              | --                       | Yes                                                        | No                                   |         |
| 4 Child stunting                 | Measles                                      | 0        | --                                                         | 7                           | 0                                    | --                                                                                       | No                                                                               | Yes                                                             | No                       | No                                           |                               |         |
| 4 Short gestation for birthweight| Diarrhoeal diseases                          | 0        | --                                                         | 20                          | 0                                    | --                                                                                       | Yes                                                                              | Yes                                                             | Yes                       | Yes                                           | Yes                               |         |
| 4 Short gestation for birthweight| Lower respiratory infections                 | 0        | --                                                         | 20                          | 0                                    | --                                                                                       | Yes                                                                              | Yes                                                             | Yes                       | Yes                                           | Yes                               |         |
| 4 Short gestation for birthweight| Upper respiratory infections                 | 0        | --                                                         | 20                          | 0                                    | --                                                                                       | Yes                                                                              | Yes                                                             | Yes                       | Yes                                           | Yes                               |         |
| 4 Short gestation for birthweight| Otitis media                                 | 0        | --                                                         | 20                          | 0                                    | --                                                                                       | Yes                                                                              | Yes                                                             | Yes                       | Yes                                           | Yes                               |         |
| 4 Short gestation for birthweight| Pneumococcal meningitis                     | 0        | --                                                         | 20                          | 0                                    | --                                                                                       | Yes                                                                              | Yes                                                             | Yes                       | Yes                                           | Yes                               |         |
| 4 Short gestation for birthweight| Haemophilus influenzae type B meningitis      | 0        | --                                                         | 20                          | 0                                    | --                                                                                       | Yes                                                                              | Yes                                                             | Yes                       | Yes                                           | Yes                               |         |
| 4 Short gestation for birthweight| Meningococcal infection                     | 0        | --                                                         | 20                          | 0                                    | --                                                                                       | Yes                                                                              | Yes                                                             | Yes                       | Yes                                           | Yes                               |         |
| 4 Short gestation for birthweight| Other meningitis                             | 0        | --                                                         | 20                          | 0                                    | --                                                                                       | Yes                                                                              | Yes                                                             | Yes                       | Yes                                           | Yes                               |         |
| 4 Short gestation for birthweight| Encephalitis                                 | 0        | --                                                         | 20                          | 0                                    | --                                                                                       | Yes                                                                              | Yes                                                             | Yes                       | Yes                                           | Yes                               |         |
| 4 Short gestation for birthweight| Neonatal preterm birth complications        | 0        | --                                                         | 20                          | 0                                    | --                                                                                       | Yes                                                                              | Yes                                                             | Yes                       | Yes                                           | Yes                               |         |
| 4 Short gestation for birthweight| Neonatal encephalopathy due to birth asphyxia and trauma | 0 | -- | 20 | 0 | -- | -- | Yes | Yes | Yes | Yes |
| 4 Short gestation for birthweight| Neonatal sepsis and other neonatal infections | 0 | -- | 20 | 0 | -- | -- | Yes | Yes | Yes | Yes |
| 4 Short gestation for birthweight| Haemolytic disease and other neonatal jaundice | 0 | -- | 20 | 0 | -- | -- | Yes | Yes | Yes | Yes |
| 4 Short gestation for birthweight| Other neonatal disorders                     | 0        | --                                                         | 20                          | 0                                    | --                                                                                       | Yes                                                                              | Yes                                                             | Yes                       | Yes                                           | Yes                               |         |
| 4 Short gestation for birthweight| Sudden infant death syndrome                 | 0        | --                                                         | 20                          | 0                                    | --                                                                                       | Yes                                                                              | Yes                                                             | Yes                       | Yes                                           | Yes                               |         |
| 4 Low birthweight for gestation  | Diarrhoeal diseases                          | 0        | --                                                         | 20                          | 0                                    | --                                                                                       | Yes                                                                              | Yes                                                             | Yes                       | Yes                                           | Yes                               |         |
| 4 Low birthweight for gestation  | Lower respiratory infections                 | 0        | --                                                         | 20                          | 0                                    | --                                                                                       | Yes                                                                              | Yes                                                             | Yes                       | Yes                                           | Yes                               |         |
| 4 Low birthweight for gestation  | Upper respiratory infections                 | 0        | --                                                         | 20                          | 0                                    | --                                                                                       | Yes                                                                              | Yes                                                             | Yes                       | Yes                                           | Yes                               |         |

(Table 1 continues on next page)
| Risk | Outcome | RCTs (n) | RCTs with null findings (%) | Prospective observational studies (n)* | Prospective observational studies with significant association in the opposite direction (%) | Case-control studies assessing the risk-outcome pair relationship (n)† | Case-control studies that show significant association in the opposite direction (%) | Lower limit of RR >1·5 | Dose-response relationship‡ | Biological plausibility† | Analogy§ |
|------|---------|----------|----------------------------|----------------------------------------|---------------------------------------------------------------------------------|-------------------------------------------------|-------------------------------------------------|---------------------|--------------------------|----------------------|----------|
| 4    | Low birthweight for gestation | Otitis media | 0                           | 20                                     | 0                                                                               | 0                                               | 0                                               | Yes                 | Yes                      | Yes                  | Yes       |
| 4    | Low birthweight for gestation | Pneumococcal meningitis | 0                           | 20                                     | 0                                                                               | 0                                               | 0                                               | Yes                 | Yes                      | Yes                  | Yes       |
| 4    | Low birthweight for gestation | Haemophilus influenzae type B meningitis | 0                           | 20                                     | 0                                                                               | 0                                               | 0                                               | Yes                 | Yes                      | Yes                  | Yes       |
| 4    | Low birthweight for gestation | Meningococcal infection | 0                           | 20                                     | 0                                                                               | 0                                               | 0                                               | Yes                 | Yes                      | Yes                  | Yes       |
| 4    | Low birthweight for gestation | Other meningitis | 0                           | 20                                     | 0                                                                               | 0                                               | 0                                               | Yes                 | Yes                      | Yes                  | Yes       |
| 4    | Low birthweight for gestation | Encephalitis | 0                           | 20                                     | 0                                                                               | 0                                               | 0                                               | Yes                 | Yes                      | Yes                  | Yes       |
| 4    | Low birthweight for gestation | Neonatal preterm birth complications | 0                           | 20                                     | 0                                                                               | 0                                               | 0                                               | Yes                 | Yes                      | Yes                  | Yes       |
| 4    | Low birthweight for gestation | Neonatal encephalopathy due to birth asphyxia and trauma | 0                           | 20                                     | 0                                                                               | 0                                               | 0                                               | Yes                 | Yes                      | Yes                  | Yes       |
| 4    | Low birthweight for gestation | Neonatal sepsis and other neonatal infections | 0                           | 20                                     | 0                                                                               | 0                                               | 0                                               | Yes                 | Yes                      | Yes                  | Yes       |
| 4    | Low birthweight for gestation | Haemolytic disease and other neonatal jaundice | 0                           | 20                                     | 0                                                                               | 0                                               | 0                                               | Yes                 | Yes                      | Yes                  | Yes       |
| 4    | Low birthweight for gestation | Other neonatal disorders | 0                           | 20                                     | 0                                                                               | 0                                               | 0                                               | Yes                 | Yes                      | Yes                  | Yes       |
| 4    | Low birthweight for gestation | Sudden infant death syndrome | 0                           | 20                                     | 0                                                                               | 0                                               | 0                                               | Yes                 | Yes                      | Yes                  | Yes       |
| 3    | Vitamin A deficiency | Diarrhoeal diseases | 19                          | 63                                     | 0                                                                               | 0                                               | 0                                               | No                  | Yes                      | No                   | No        |
| 3    | Vitamin A deficiency | Measles | 12                          | 83                                     | 0                                                                               | 0                                               | 0                                               | Yes                 | ---                      | No                   | No        |
| 3    | Zinc deficiency | Diarrhoeal diseases | 14                          | 29                                     | 0                                                                               | 0                                               | 0                                               | No                  | Yes                      | Yes                  | No        |
| 3    | Zinc deficiency | Lower respiratory infections | 6                           | 17                                     | 0                                                                               | 0                                               | 0                                               | No                  | Yes                      | Yes                  | No        |

2 Tobacco

| Risk | Outcome | RCTs (n) | RCTs with null findings (%) | Prospective observational studies (n)* | Prospective observational studies with significant association in the opposite direction (%) | Case-control studies assessing the risk-outcome pair relationship (n)† | Case-control studies that show significant association in the opposite direction (%) | Lower limit of RR >1·5 | Dose-response relationship‡ | Biological plausibility† | Analogy§ |
|------|---------|----------|----------------------------|----------------------------------------|---------------------------------------------------------------------------------|-------------------------------------------------|-------------------------------------------------|---------------------|--------------------------|----------------------|----------|
| 3    | Smoking | Tuberculosis | 0                           | 4                                      | 0                                                                               | 0                                               | 0                                               | No                  | ---                      | Yes                  | Yes       |
| 3    | Smoking | Lip and oral cavity cancer | 0                           | 5                                      | 0                                                                               | 0                                               | 0                                               | Yes                 | ---                      | Yes                  | Yes       |
| 3    | Smoking | Nasopharynx cancer | 0                           | 4                                      | 0                                                                               | 28                                              | 0                                               | Yes                 | ---                      | Yes                  | Yes       |
| 3    | Smoking | Oesophageal cancer | 0                           | 5                                      | 0                                                                               | 0                                               | 0                                               | Yes                 | ---                      | Yes                  | Yes       |
| 3    | Smoking | Colon and rectum cancer | 0                           | 19                                     | 0                                                                               | 0                                               | 0                                               | No                  | Yes                      | Yes                  | Yes       |
| 3    | Smoking | Liver cancer | 0                           | 54                                     | 0                                                                               | 0                                               | 0                                               | Yes                 | ---                      | Yes                  | Yes       |
| 3    | Smoking | Gastric cancer | 0                           | 19                                     | 0                                                                               | 0                                               | 0                                               | No                  | ---                      | Yes                  | Yes       |

(Continued from previous page)
| Risk                                                                 | Outcome                                             | RCTs (n) | RCTs with significant effect in the opposite direction (%) | RCTs with null findings (%) | Prospective observational studies (n)* | Prospective observational studies with significant association in the opposite direction (%) | Case-control studies assessing the risk-outcome pair relationship (n)† | Case-control studies that show significant association in the opposite direction (%) | Lower limit of RR >1·5 | Dose-response relationship ‡ | Biological plausibility § | Analogy§ |
|---------------------------------------------------------------------|-----------------------------------------------------|----------|------------------------------------------------------------|---------------------------|----------------------------------------|------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|---------------------------------------------------------------------|---------------------------------|-----------------------------|---------------------------|----------|
| 3 Smoking                                                           | Pancreatic cancer                                   | 0 -      | -                                                          | 19                        | 0                                      | -                                                                                                   | -                                                                        | Yes                                 | -                              | Yes                          | Yes                       | No        |
| 3 Smoking                                                           | Larynx cancer                                       | 0 -      | -                                                          | 5                         | 0                                      | -                                                                                                   | -                                                                        | Yes                                 | -                              | Yes                          | Yes                       | No        |
| 3 Smoking                                                           | Tracheal, bronchus, and lung cancer                 | 0 -      | -                                                          | 38                        | 0                                      | -                                                                                                   | -                                                                        | Yes                                 | -                              | Yes                          | Yes                       | No        |
| 3 Smoking                                                           | Breast cancer                                       | 0 -      | -                                                          | 19                        | 0                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Cervical cancer                                     | 0 -      | -                                                          | 15                        | 0                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Prostate cancer                                     | 0 -      | -                                                          | 19                        | 0                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Kidney cancer                                       | 0 -      | -                                                          | 8                         | 0                                      | -                                                                                                   | -                                                                        | Yes                                 | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Bladder cancer                                      | 0 -      | -                                                          | 37                        | 0                                      | -                                                                                                   | -                                                                        | Yes                                 | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Leukaemia                                           | 0 -      | -                                                          | 22                        | 0                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Ischaemic heart disease                             | 0 -      | -                                                          | 86                        | -                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Ischaemic stroke                                    | 0 -      | -                                                          | 60                        | -                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Haemorrhagic stroke                                 | 0 -      | -                                                          | 60                        | -                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Atrial fibrillation and flutter                     | 0 -      | -                                                          | 16                        | 0                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Peripheral vascular disease                         | 0 -      | -                                                          | 10                        | 0                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Other cardiovascular and circulatory diseases       | 0 -      | -                                                          | 5                         | 0                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Chronic obstructive pulmonary disease               | 0 -      | -                                                          | 42                        | 0                                      | -                                                                                                   | -                                                                        | Yes                                 | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Asthma                                              | 0 -      | -                                                          | 8                         | 12                                     | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Other chronic respiratory diseases                  | 0 -      | -                                                          | 5                         | 0                                      | -                                                                                                   | -                                                                        | Yes                                 | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Peptic ulcer disease                                | 0 -      | -                                                          | 7                         | 0                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | No        |
| 3 Smoking                                                           | Gallbladder and biliary diseases                    | 0 -      | -                                                          | 10                        | 0                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Alzheimer’s disease and other dementias             | 0 -      | -                                                          | 13                        | 8                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Parkinson’s disease                                 | 0 -      | -                                                          | 8                         | 0                                      | -                                                                                                   | -                                                                        | Yes                                 | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Multiple sclerosis                                  | 0 -      | -                                                          | 6                         | 0                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | No        |
| 3 Smoking                                                           | Diabetes mellitus                                   | 0 -      | -                                                          | 88                        | 0                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | No                       | No        |
| 3 Smoking                                                           | Rheumatoid arthritis                                | 0 -      | -                                                          | 5                         | 0                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | No                       | No        |
| 3 Smoking                                                           | Low back pain                                       | 0 -      | -                                                          | 13                        | 0                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | Yes       |
| 3 Smoking                                                           | Cataract                                            | 0 -      | -                                                          | 13                        | 0                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | No        |
| 3 Smoking                                                           | Macular degeneration                                | 0 -      | -                                                          | 5                         | 0                                      | -                                                                                                   | -                                                                        | No                                  | -                              | Yes                          | Yes                       | No        |

(Table 1 continues on next page)
### Table 1

| Risk | Outcome | RCTs (n) | RCTs with significant effect in the opposite direction (%) | Prospective observational studies (n)* | Prospective observational studies with significant association in the opposite direction (%) | Case-control studies assessing the risk-outcome pair relationship (n)† | Case-control studies that show significant association in the opposite direction (%) | Lower limit of RR > 1.5 | Dose-response relationship | Biological plausibility ‡ | Analogy§ |
|------|---------|---------|-----------------------------------------------------------|--------------------------------------|---------------------------------------------------------------------|----------------------------------------------------------------|-------------------------------------------------|-----------------|----------------------|---------------------|----------|
| 3 Smoking | Low bone mass-related fractures | 14 | 14 | No | Yes | Yes |
| 3 Smoking | Hip fracture | 15 | 20 | No | Yes | Yes |
| 3 Smoking | Abdominal aortic aneurism | 10 | 0 | No | Yes | Yes |
| 3 Smokeless tobacco | Oral cancer | 4 | 0 | 21 | 5 | Yes | Yes | Yes | Yes |
| 3 Smokeless tobacco | Oesophageal cancer | 2 | 0 | 10 | 0 | Yes | Yes | Yes | Yes |
| 3 Second-hand smoke | Lower respiratory infections | 18 | 0 | No | Yes | Yes | Yes |
| 3 Second-hand smoke | Otitis media | 1 | 0 | 4 | 0 | No | Yes | Yes | Yes |
| 3 Second-hand smoke | Tracheal, bronchus, and lung cancer | 13 | 0 | No | Yes | Yes | Yes |
| 3 Second-hand smoke | Breast cancer | 21 | 0 | No | Yes | Yes | Yes |
| 3 Second-hand smoke | Ischaemic heart disease | 5 | 0 | No | Yes | Yes | Yes |
| 3 Second-hand smoke | Ischaemic stroke | 4 | 0 | 3 | No | Yes | Yes | Yes |
| 3 Second-hand smoke | Haemorrhagic stroke | 4 | 0 | 3 | No | Yes | Yes | Yes |
| 3 Second-hand smoke | Chronic obstructive pulmonary disease | 2 | 0 | 1 | 0 | No | Yes | Yes | Yes |
| 3 Second-hand smoke | Diabetes mellitus | 5 | 0 | No | Yes | Yes | Yes |
| 2 Alcohol and drug use | Tuberculosis | 3 | 0 | 18 | 11 | Yes | Yes | Yes | Yes |
| 2 Alcohol and drug use | Lower respiratory infections | 2 | 0 | 2 | 0 | Yes | Yes | Yes | Yes |
| 2 Alcohol and drug use | Lip and oral cavity cancer | 6 | 0 | No | Yes | Yes | Yes |
| 2 Alcohol and drug use | Nasopharynx cancer | 6 | 0 | No | Yes | Yes | Yes |
| 2 Alcohol and drug use | Other pharynx cancer | 6 | 0 | No | Yes | Yes | Yes |
| 2 Alcohol and drug use | Oesophageal cancer | 10 | 0 | No | Yes | Yes | Yes |
| 2 Alcohol and drug use | Colon and rectum cancer | 15 | 13 | No | Yes | Yes | Yes |
| 2 Alcohol and drug use | Liver cancer | 9 | 0 | No | Yes | Yes | Yes |
| 2 Alcohol and drug use | Larynx cancer | 7 | 0 | No | Yes | Yes | Yes |
| 2 Alcohol and drug use | Breast cancer | 13 | 23 | No | Yes | Yes | Yes |
| 2 Alcohol and drug use | Ischaemic heart disease | 63 | 0 | No | Yes | Yes | Yes |
| 2 Alcohol and drug use | Ischaemic stroke | 20 | 0 | No | Yes | Yes | Yes |
| 2 Alcohol and drug use | Haemorrhagic stroke | 16 | 0 | No | Yes | Yes | Yes |
| 2 Alcohol and drug use | Hypertensive heart disease | 12 | 0 | No | Yes | Yes | Yes |

(Continued from previous page)

3 Smoking
3 Smoking
3 Smoking
3 Smokeless tobacco
3 Smokeless tobacco
3 Second-hand smoke
3 Second-hand smoke
3 Second-hand smoke
3 Second-hand smoke
3 Second-hand smoke
3 Second-hand smoke
3 Second-hand smoke
3 Second-hand smoke
3 Second-hand smoke
3 Second-hand smoke
3 Second-hand smoke
3 Second-hand smoke
3 Second-hand smoke
3 Second-hand smoke
3 Second-hand smoke
2 Alcohol and drug use
2 Alcohol and drug use
2 Alcohol and drug use
2 Alcohol and drug use
2 Alcohol and drug use
2 Alcohol and drug use
2 Alcohol and drug use
2 Alcohol and drug use
## Global Health Metrics

### Risk Outcome RCTs

| Risk                           | Outcome                          | RCTs (n) | RCTs with significant effect in the opposite direction (%) | RCTs with null findings (%) | Prospective observational studies (n)* | Prospective observational studies with significant association in the opposite direction (%) | Case-control studies assessing the risk-outcome pair relationship (n)? | Case-control studies that show significant association in the opposite direction (%) | Lower limit of RR >1-5 | Dose-response relationship | Biological plausibility ‡ | Analogy§ |
|--------------------------------|----------------------------------|----------|----------------------------------------------------------|----------------------------|----------------------------------------|------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------|--------------------------------------------------------------------------------|------------------------|-----------------------------|--------------------------|----------|
| Alcohol use                    | Atrial fibrillation and flutter  | 0        |                                                          |                            | 10                                    | 10                                                                                  | Yes                                                                             | Yes                                                                       | Yes                    | Yes                         | Yes                      | Yes      |
| Alcohol use                    | Cirrhosis                        | 0        |                                                          |                            | 14                                    | 0                                                                                   | Yes                                                                             | Yes                         | Yes                      | Yes                         | Yes      |
| Alcohol use                    | Pancreatitis                     | 0        |                                                          |                            | 4                                     | 50                                                                                  | Yes                                                                             | Yes                         | Yes                      | Yes                         | No       |
| Alcohol use                    | Epilepsy                         | 0        |                                                          |                            | 1                                     | 0                                                                                   | 2                                                                               | 0                           | No                       | Yes                         | No       |
| Alcohol use                    | Diabetes mellitus                | 0        |                                                          |                            | 37                                    | 32                                                                                  | Yes                                                                             | Yes                         | Yes                      | Yes                         | No       |
| Alcohol use                    | Motor vehicle road injuries      | 0        |                                                          |                            | 3                                     | 0                                                                                   | Yes                                                                             | Yes                         | Yes                      | Yes                         | Yes      |
| Alcohol use                    | Unintentional injuries           | 0        |                                                          |                            | 4                                     | 0                                                                                   | 4                                                                               | 0                           | Yes                       | Yes                         | Yes      |
| Alcohol use                    | Self-harm                        | 0        |                                                          |                            | 0                                     | 0                                                                                  | Yes                                                                             | Yes                         | Yes                      | Yes                         | Yes      |
| Alcohol use                    | Interpersonal violence           | 0        |                                                          |                            | 2                                     | 0                                                                                   | 1                                                                               | 0                           | Yes                       | Yes                         | Yes      |
| Drug use                       | Hepatitis B                      | 0        |                                                          |                            | 6                                     | 0                                                                                   | Yes                                                                             | Yes                         | Yes                      | Yes                         | Yes      |
| Drug use                       | Hepatitis C                      | 0        |                                                          |                            | 16                                    | 0                                                                                   | Yes                                                                             | Yes                         | Yes                      | Yes                         | Yes      |
| Drug use                       | Self-harm                        | 0        |                                                          |                            | 1                                     | 0                                                                                   | 0                                                                               | 0                           | No                        | Yes                         | No       |

(Continued from previous page)

### 2 Dietary risks

| Risk                           | Outcome                          | RCTs (n) | RCTs with significant effect in the opposite direction (%) | RCTs with null findings (%) | Prospective observational studies (n)* | Prospective observational studies with significant association in the opposite direction (%) | Case-control studies assessing the risk-outcome pair relationship (n)? | Case-control studies that show significant association in the opposite direction (%) | Lower limit of RR >1-5 | Dose-response relationship | Biological plausibility ‡ | Analogy§ |
|--------------------------------|----------------------------------|----------|----------------------------------------------------------|----------------------------|----------------------------------------|------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------|--------------------------------------------------------------------------------|------------------------|-----------------------------|--------------------------|----------|
| Diet low in fruits             | Lip and oral cavity cancer       | 0        |                                                          |                            | 2                                     | 0                                                                                   | 15                                                                             | 0                           | No                        | Yes                       | Yes      |
| Diet low in fruits             | Nasopharynx cancer               | 0        |                                                          |                            | 2                                     | 0                                                                                   | 15                                                                             | 0                           | No                        | Yes                         | Yes      |
| Diet low in fruits             | Other pharynx cancer             | 0        |                                                          |                            | 2                                     | 0                                                                                   | 15                                                                             | 0                           | No                        | Yes                         | Yes      |
| Diet low in fruits             | Oesophageal cancer               | 0        |                                                          |                            | 5                                     | 0                                                                                   | Yes                                                                             | Yes                         | Yes                      | Yes                         | Yes      |
| Diet low in fruits             | Larynx cancer                    | 0        |                                                          |                            | 2                                     | 0                                                                                   | 15                                                                             | 0                           | Yes                       | Yes                         | Yes      |
| Diet low in fruits             | Tracheal, bronchus, and lung cancer | 0        |                                                          |                            | 22                                    | 0                                                                                   | Yes                                                                             | Yes                         | Yes                      | Yes                         | Yes      |
| Diet low in fruits             | Ischaemic heart disease          | 0        |                                                          |                            | 9                                     | 0                                                                                   | Yes                                                                             | Yes                         | Yes                      | Yes                         | Yes      |
| Diet low in fruits             | Ischaemic stroke                 | 0        |                                                          |                            | 9                                     | 0                                                                                   | No                                                                            | Yes                         | Yes                      | Yes                         | Yes      |
| Diet low in fruits             | Haemorrhagic stroke              | 0        |                                                          |                            | 5                                     | 0                                                                                   | No                                                                            | Yes                         | Yes                      | Yes                         | Yes      |
| Diet low in fruits             | Diabetes mellitus                | 0        |                                                          |                            | 9                                     | 0                                                                                   | Yes                                                                            | Yes                         | No                       | Yes                         | No       |
| Diet low in vegetables         | Oesophageal cancer               | 0        |                                                          |                            | 5                                     | 0                                                                                   | Yes                                                                            | Yes                         | No                       | Yes                         | No       |
| Diet low in vegetables         | Ischaemic heart disease          | 0        |                                                          |                            | 9                                     | 0                                                                                   | Yes                                                                            | Yes                         | Yes                      | Yes                         | Yes      |
| Diet low in vegetables         | Ischaemic stroke                 | 0        |                                                          |                            | 8                                     | 0                                                                                   | Yes                                                                            | Yes                         | Yes                      | Yes                         | Yes      |
| Diet low in vegetables         | Haemorrhagic stroke              | 0        |                                                          |                            | 5                                     | 0                                                                                   | Yes                                                                            | Yes                         | Yes                      | Yes                         | Yes      |
| Diet low in legumes            | Ischaemic heart disease          | 0        |                                                          |                            | 5                                     | 0                                                                                   | Yes                                                                            | Yes                         | Yes                      | Yes                         | No       |
| Diet low in whole grains       | Ischaemic heart disease          | 0        |                                                          |                            | 7                                     | 0                                                                                   | Yes                                                                            | Yes                         | Yes                      | Yes                         | Yes      |
| Diet low in whole grains       | Ischaemic stroke                 | 0        |                                                          |                            | 6                                     | 0                                                                                   | Yes                                                                            | Yes                         | Yes                      | Yes                         | Yes      |

(Continued from previous page)
### Global Health Metrics

**Risk** | **Outcome** | **RCTs (n)** | **RCTs with significant effect in the opposite direction (%)** | **Prospective observational studies (n)** | **Prospective observational studies with significant association in the opposite direction (%)** | **Case-control studies assessing the risk-outcome pair relationship (n)** | **Case-control studies that show significant association in the opposite direction (%)** | **Lower limit of RR >1.5** | **Dose-response relationship** | **Biological plausibility** | **Analogy**
--- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | ---
3 Diet low in whole grains | Haemorrhagic stroke | 0 -- -- 6 | 0 -- -- -- | No | Yes | Yes | Yes | 3 | 0 | No | .. | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet low in whole grains | Diabetes mellitus | 0 -- -- 10 | 0 -- -- -- | No | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet low in nuts and seeds | Ischaemic heart disease | 100 6 0 | 0 -- -- -- | No | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet low in nuts and seeds | Diabetes mellitus | 0 -- -- 5 | 0 -- -- -- | No | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet low in milk | Colon and rectum cancer | 0 -- -- 7 | 0 -- -- -- | No | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet high in red meat | Colon and rectum cancer | 0 -- -- 8 | 0 -- -- -- | No | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet high in red meat | Diabetes mellitus | 0 -- -- 9 | 11 -- -- -- | No | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet high in processed meat | Colon and rectum cancer | 0 -- -- 9 | 11 -- -- -- | No | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet high in processed meat | Ischaemic heart disease | 0 -- -- 5 | 0 -- -- -- | No | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet high in processed meat | Diabetes mellitus | 0 -- -- 8 | 0 -- -- -- | No | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet high in sugar-sweetened beverages | Body-mass index | 10 60 0 22 | 0 -- -- -- | Yes | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet low in fibre | Colon and rectum cancer | 0 -- -- 15 | 0 -- -- -- | No | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet low in fibre | Ischaemic heart disease | 0 -- -- 12 | 0 -- -- -- | No | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet low in calcium | Colon and rectum cancer | 0 -- -- 13 | 0 -- -- -- | No | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet low in seafood omega 3 fatty acids | Ischaemic heart disease | 17 94 0 16 | 0 -- -- -- | No | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet low in polyunsaturated fatty acids | Ischaemic heart disease | 8 75 0 11 | 0 -- -- -- | No | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet high in trans fatty acids | Ischaemic heart disease | 0 -- -- 13 | 0 -- -- -- | No | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet high in sodium | Stomach cancer | 0 -- -- 10 | 0 -- -- -- | No | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Diet high in sodium | Systolic blood pressure | 45 73 0 | 0 -- -- -- | No | Yes | Yes | No | No | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
2 Sexual abuse and violence
--- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
3 Childhood sexual abuse | Alcohol use disorders | 0 -- -- 2 | 0 -- -- -- | No | .. | Yes | Yes | 3 | 0 | No | .. | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Childhood sexual abuse | Depressive disorders | 0 -- -- 7 | 0 -- -- -- | No | .. | Yes | Yes | 0 | 0 | 0 | 0 | No | .. | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Intimate partner violence | HIV/AIDS | 0 -- -- 2 | 0 0 0 0 | No | .. | Yes | No | 0 | 0 | 0 | 0 | No | .. | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Intimate partner violence | Maternal abortion, miscarriage, and ectopic pregnancy | 0 -- -- 1 | 0 3 0 0 | Yes | .. | Yes | No | 0 | 0 | 0 | 0 | No | .. | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
3 Intimate partner violence | Depressive disorders | 0 -- -- 4 | 0 0 0 0 | No | .. | Yes | Yes | 0 | 0 | 0 | 0 | No | .. | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |

(Table 1 continues on next page)
## Risk Outcome

| Risk | Outcome                          | RCTs (n) | RCTs with significant effect in the opposite direction (%) | RCTs with null findings (%) | Prospective observational studies (n)* | Prospective observational studies with significant association in the opposite direction (%) | Case-control studies assessing the risk-outcome pair relationship (n)† | Case-control studies that show significant association in the opposite direction (%) | Lower limit of RR >1.5 | Dose-response relationship | Biological plausibility ‡ | Analogy§ |
|------|----------------------------------|----------|-------------------------------------------------------------|-----------------------------|----------------------------------------|---------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|------------------------|-----------------------------|-----------------------------|---------|
| 2    | Low physical activity           | Colon and rectum cancer 0 | 20 | 15 | No | Yes | Yes | Yes |
| 2    | Low physical activity           | Breast cancer 0 | 35 | 0 | No | Yes | Yes | Yes |
| 2    | Low physical activity           | Ischaemic heart disease 0 | 45 | 9 | No | Yes | Yes | Yes |
| 2    | Low physical activity           | Ischaemic stroke 0 | 27 | 11 | No | Yes | Yes | Yes |
| 2    | Low physical activity           | Diabetes mellitus 0 | 57 | 7 | No | Yes | Yes | No |
| 2    | High fasting plasma glucose     | Tuberculosis 0 | 18 | 0 | Yes | Yes | Yes | No |
| 2    | High fasting plasma glucose     | Colon and rectum cancer 0 | 21 | 0 | No | ... | Yes | Yes |
| 2    | High fasting plasma glucose     | Liver cancer 0 | 28 | 0 | Yes | ... | No | ... |
| 2    | High fasting plasma glucose     | Pancreatic cancer 0 | 35 | 0 | Yes | ... | Yes | ... |
| 2    | High fasting plasma glucose     | Lung cancer 0 | 16 | 6 | No | ... | Yes | ... |
| 2    | High fasting plasma glucose     | Breast cancer 0 | 39 | 0 | No | ... | Yes | ... |
| 2    | High fasting plasma glucose     | Ovarian cancer 0 | 11 | 0 | No | ... | Yes | ... |
| 2    | High fasting plasma glucose     | Bladder cancer 0 | 14 | 0 | No | ... | Yes | ... |
| 2    | High fasting plasma glucose     | Ischaemic heart disease 8 | 100 | 150 | ... | Yes | Yes | Yes |
| 2    | High fasting plasma glucose     | Ischaemic stroke disease 9 | 100 | 150 | ... | Yes | Yes | Yes |
| 2    | High fasting plasma glucose     | Haemorrhagic stroke disease 9 | 100 | 150 | ... | Yes | Yes | Yes |
| 2    | High fasting plasma glucose     | Alzheimer’s disease and other dementias 0 | 17 | 0 | No | ... | No | ... |
| 2    | High fasting plasma glucose     | Peripheral vascular disease 14 | 4 | 0 | Yes | Yes | Yes | Yes |
| 2    | High fasting plasma glucose     | Chronic kidney disease 5 | 32 | ... | Yes | Yes | Yes | No |
| 2    | High fasting plasma glucose     | Glaucoma 0 | 5 | 0 | No | ... | Yes | ... |
| 2    | High fasting plasma glucose     | Cataract 0 | 1 | 0 | No | ... | Yes | ... |
| 2    | High total cholesterol          | Ischaemic heart disease 21 | 57 | 88 | Yes | Yes | Yes | Yes |
| 2    | High total cholesterol          | Ischaemic stroke disease 21 | 57 | 88 | Yes | Yes | Yes | Yes |
| 2    | High systolic blood pressure    | Rheumatic heart disease 0 | 62 | ... | Yes | Yes | Yes | Yes |
| 2    | High systolic blood pressure    | Ischaemic heart disease 56 | 88 | ... | Yes | Yes | Yes | Yes |
| 2    | High systolic blood pressure    | Ischaemic stroke disease 54 | 150 | ... | Yes | Yes | Yes | Yes |

*(Table 1 continues on next page)*
| Risk                                      | Outcome                        | RCTs (n) | RCTs with significant effect in the opposite direction (%) | Prospective observational studies (n)* | Prospective observational studies with significant association in the opposite direction (%) | Case-control studies assessing the risk-outcome pair relationship (n)† | Case-control studies that show significant association in the opposite direction (%) | Lower limit of RR >1·5 | Dose-response relationship | Biological plausibility‡ | Analogy§ |
|------------------------------------------|--------------------------------|----------|--------------------------------------------------------------|----------------------------------------|---------------------------------------------------------------------------------------------|-----------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------|---------------------------------------------------------------|------------------------------------------|-----------|
| 2 High systolic blood pressure           | Haemorrhagic stroke            | 54       | 0                                                            | 150                                    | ...                                                                                         | ...                                                                  | ...                                                                                                                                 | ...                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High systolic blood pressure           | Cardiomyopathy and myocarditis| 0        | 0                                                            | 62                                     | ...                                                                                         | ...                                                                  | ...                                                                                                                                 | ...                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High systolic blood pressure           | Other cardiomyopathy           | 0        | 0                                                            | 62                                     | ...                                                                                         | ...                                                                  | ...                                                                                                                                 | ...                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High systolic blood pressure           | Atrial fibrillation and flutter| 20       | 5                                                            | 60                                     | 88                                                                                         | ...                                                                  | ...                                                                                                                                 | ...                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High systolic blood pressure           | Aortic aneurysm                | 0        | 0                                                            | 62                                     | ...                                                                                         | ...                                                                  | ...                                                                                                                                 | ...                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High systolic blood pressure           | Peripheral vascular disease    | 0        | 0                                                            | 88                                     | ...                                                                                         | ...                                                                  | ...                                                                                                                                 | ...                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High systolic blood pressure           | Endocarditis                   | 0        | 0                                                            | 62                                     | ...                                                                                         | ...                                                                  | ...                                                                                                                                 | ...                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High systolic blood pressure           | Other cardiovascular and circulatory diseases | 0        | 0                                                            | 88                                     | ...                                                                                         | ...                                                                  | ...                                                                                                                                 | ...                                                                  | No                                                             | Yes                                                      | Yes        | Yes        |
| 2 High systolic blood pressure           | Chronic kidney disease         | 8        | 8                                                            | 88                                     | ...                                                                                         | ...                                                                  | ...                                                                                                                                 | ...                                                                  | Yes                                                            | Yes                                                      | Yes        | No         |
| 2 High body-mass index (adult)           | Non-Hodgkin lymphoma           | 0        | 0                                                            | 8                                      | 0                                                                                          | ...                                                                  | ...                                                                                                                                 | No                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High body-mass index (adult)           | Oesophageal cancer              | 0        | 0                                                            | 16                                     | 0                                                                                          | ...                                                                  | ...                                                                                                                                 | ...                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High body-mass index (adult)           | Colon and rectum cancer        | 0        | 0                                                            | 38                                     | 0                                                                                          | ...                                                                  | ...                                                                                                                                 | No                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High body-mass index (adult)           | Liver cancer                    | 0        | 0                                                            | 34                                     | 0                                                                                          | ...                                                                  | ...                                                                                                                                 | No                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High body-mass index (adult)           | Gallbladder and biliary tract cancer | 0       | 0                                                            | 10                                     | 0                                                                                          | ...                                                                  | ...                                                                                                                                 | No                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High body-mass index (adult)           | Pancreatic cancer               | 0        | 0                                                            | 20                                     | 0                                                                                          | ...                                                                  | ...                                                                                                                                 | No                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High body-mass index (adult)           | Breast cancer (post menopause)  | 0        | 0                                                            | 44                                     | 2                                                                                          | ...                                                                  | ...                                                                                                                                 | No                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High body-mass index (adult)           | Breast cancer (pre-menopause)   | 0        | 0                                                            | 25                                     | 8                                                                                          | ...                                                                  | ...                                                                                                                                 | No                                                                  | Yes                                                            | Yes                                                      | No         | No         |
| 2 High body-mass index (adult)           | Uterine cancer                  | 0        | 0                                                            | 37                                     | 0                                                                                          | ...                                                                  | ...                                                                                                                                 | No                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High body-mass index (adult)           | Ovarian cancer                  | 0        | 0                                                            | 31                                     | 3                                                                                          | ...                                                                  | ...                                                                                                                                 | No                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High body-mass index (adult)           | Kidney cancer                   | 0        | 0                                                            | 28                                     | 0                                                                                          | ...                                                                  | ...                                                                                                                                 | No                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High body-mass index (adult)           | Thyroid cancer                  | 0        | 0                                                            | 16                                     | 0                                                                                          | ...                                                                  | ...                                                                                                                                 | No                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High body-mass index (adult)           | Multiple myeloma                | 0        | 0                                                            | 20                                     | ...                                                                                         | ...                                                                  | ...                                                                                                                                 | Yes                                                                 | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High body-mass index (adult)           | Leukaemia                       | 0        | 0                                                            | 17                                     | 0                                                                                          | ...                                                                  | ...                                                                                                                                 | No                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |
| 2 High body-mass index (adult)           | Ischaemic heart disease         | 0        | 0                                                            | 129                                    | ...                                                                                         | ...                                                                  | ...                                                                                                                                 | No                                                                  | Yes                                                            | Yes                                                      | Yes        | Yes        |

(Table 1 continues on next page)
Table 1: Descriptive cataloguing of the epidemiological evidence used to assess whether each risk-outcome paper meets the causal criteria for inclusion in the Global Burden of Disease Study 2016 by risk level

| Risk (Continued from previous page) | Outcome | RCTs (n) | RCTs with significant effect in the opposite direction (%) | RCTs with null findings (n) | Prospective observational studies (n)* | Prospective observational studies with significant association in the opposite direction (%) | Case-control studies assessing the risk-outcome pair relationship (n)† | Case-control studies that show significant association in the opposite direction (%) | Lower limit of RR > 1.5 | Dose-response relationship Biological plausibility ‡ | Analogy§ |
|-----------------------------------|---------|---------|----------------------------------------------------------|-----------------------------|----------------------------------------|---------------------------------------------------------------------------------------------|-----------------------------------------------------------------|-----------------------------------------------------------------|-----------------|------------------------------------------------------|---------|
| 2 High body-mass index (adult)    | Ischaemic stroke | 0        | ...                                                      | 102                         | ...                                    | ...                                                                                           | No                                                              | Yes                                                             | Yes             | Yes                                                  | Yes      |
| 2 High body-mass index (adult)    | Haemorrhagic stroke | 0        | ...                                                      | 129                         | ...                                    | ...                                                                                           | No                                                              | Yes                                                             | Yes             | Yes                                                  | Yes      |
| 2 High body-mass index (adult)    | Hypertensive heart disease | 0        | ...                                                      | 85                          | ...                                    | ...                                                                                           | No                                                              | Yes                                                             | Yes             | Yes                                                  | Yes      |
| 2 High body-mass index (adult)    | Atrial fibrillation and flutter | 0        | ...                                                      | 5                           | 0                                      | ...                                                                                           | No                                                              | Yes                                                             | No               | No                                                   | No       |
| 2 High body-mass index (adult)    | Asthma | 0        | ...                                                      | 7                           | 0                                      | ...                                                                                           | Yes                                                             | Yes                                                             | No               | No                                                   | No       |
| 2 High body-mass index (adult)    | Alzheimer’s disease and other dementias | 0        | ...                                                      | 6                           | 0                                      | ...                                                                                           | No                                                              | Yes                                                             | No               | No                                                   | No       |
| 2 High body-mass index (adult)    | Gallbladder disease | 0        | ...                                                      | 16                          | 0                                      | ...                                                                                           | Yes                                                             | Yes                                                             | Yes             | Yes                                                  | Yes      |
| 2 High body-mass index (adult)    | Diabetes mellitus | 0        | ...                                                      | 85                          | ...                                    | ...                                                                                           | Yes                                                             | Yes                                                             | Yes             | No                                                   | No       |
| 2 High body-mass index (adult)    | Chronic kidney disease | 0        | ...                                                      | 57                          | ...                                    | ...                                                                                           | No                                                              | Yes                                                             | Yes             | No                                                   | No       |
| 2 High body-mass index (adult)    | Osteoarthritis | 0        | ...                                                      | 32                          | 0                                      | ...                                                                                           | No                                                              | Yes                                                             | Yes             | Yes                                                  | Yes      |
| 2 High body-mass index (adult)    | Low back pain | 0        | ...                                                      | 5                           | 0                                      | ...                                                                                           | No                                                              | Yes                                                             | Yes             | Yes                                                  | Yes      |
| 2 High body-mass index (adult)    | Gout | 0        | ...                                                      | 10                          | 0                                      | ...                                                                                           | Yes                                                             | Yes                                                             | No               | No                                                   | No       |
| 2 High body-mass index (adult)    | Cataract | 0        | ...                                                      | 17                          | 0                                      | ...                                                                                           | Yes                                                             | Yes                                                             | No               | No                                                   | No       |
| 2 High body-mass index (adult)    | Asthma | 0        | ...                                                      | 5                           | 0                                      | ...                                                                                           | No                                                              | Yes                                                             | No               | No                                                   | No       |
| 2 Low bone mineral density        | Injuries | 0        | ...                                                      | 12                          | ...                                    | ...                                                                                           | No                                                              | Yes                                                             | Yes             | Yes                                                  | Yes      |
| 2 Impaired kidney function        | Ischaemic heart disease | 0        | ...                                                      | 6                           | 0                                      | ...                                                                                           | Yes                                                             | Yes                                                             | No               | Yes                                                  | Yes      |
| 2 Impaired kidney function        | Ischaemic stroke | 0        | ...                                                      | 6                           | 0                                      | ...                                                                                           | Yes                                                             | Yes                                                             | No               | Yes                                                  | Yes      |
| 2 Impaired kidney function        | Haemorrhagic stroke | 0        | ...                                                      | 8                           | 0                                      | ...                                                                                           | Yes                                                             | Yes                                                             | No               | Yes                                                  | Yes      |
| 2 Impaired kidney function        | Peripheral vascular disease | 0        | ...                                                      | 5                           | 0                                      | ...                                                                                           | Yes                                                             | Yes                                                             | Yes             | Yes                                                  | Yes      |
| 2 Impaired kidney function        | Gout | 0        | ...                                                      | 3                           | 0                                      | ...                                                                                           | Yes                                                             | Yes                                                             | No               | Yes                                                  | No       |

If multiple reports existed from the same study, we counted them as one study. We only assessed the dose-response relationship for continuous risks. To evaluate the magnitude of the effect size for continuous risks, we evaluated the relative risk comparing the 75th percentile with the 25th percentile of the exposure distribution at the global level. RCT=randomised controlled trial. RR=relative risk. *Prospective cohort studies or non-randomised interventions. †Case-control studies were included for those risk-outcome pairs where the sum of RCT and prospective observational studies included was less than five (where applicable). ‡Whether or not any biological or mechanistic pathway exists that could potentially explain the relationship of the risk-outcome pair. §Whether or not the risk is associated with another outcome from the same category and whether or not any evidence exists that it can cause the current outcome through the same pathway.

(appendix 1 p 22 for more detail). Fourth, we performed a systematic review of all cohort and case-control studies reporting a RR, hazard ratio, or odds ratio for any risk-outcome pairs studied in GBD 2016 and then modelled a dose-response relationship using DisMod ordinary differential equations (ODE). Fifth, we estimated injury PAFs from cohort studies and adjusted them to account for victims.
| Risk factors                                      | Exposure definition                                                                 | Theoretical minimum risk exposure level | Data representativeness index |
|--------------------------------------------------|--------------------------------------------------------------------------------------|----------------------------------------|------------------------------|
| 0 All                                             | ···                                                                                  | ···                                    | 100·0% 100·0% 100·0%        |
| 1 Environmental and occupational risks           | ···                                                                                  | ···                                    | 100·0% 100·0% 100·0%        |
| 2 Unsafe water, sanitation, and handwashing      | ···                                                                                  | ···                                    | 58·0% 75·4% 70·0%          |
| 3 Unsafe water source                            | Proportion of households with access to different water sources (unimproved, improved except piped, piped water supply) and reported use of household water treatment methods (boiling or filtering, chlorinating or solar filtering, no treatment) | All households have access to water from a piped water supply that is also boiled or filtered before drinking | 70·1% 88·4% 83·5%   |
| 3 Unsafe sanitation                               | Proportion of households with access to different sanitation facilities (unimproved, improved except sewer, sewer connection) | All households have access to toilets with sewer connection | 69·5% 88·4% 83·5%   |
| 3 No access to handwashing facility              | Proportion of households with access to handwashing facility with soap, water, and wash station | All households have access to handwashing facility with soap, water, and wash station | 10·3% 33·3% 35·4%   |
| 2 Air pollution                                  | ···                                                                                  | ···                                    | 100·0% 100·0% 100·0%        |
| 3 Ambient particulate matter pollution           | Annual average daily exposure to outdoor air concentrations of PM$_{10}$              | Uniform distribution between 2·4 µg/m$^3$ and 5·9 µg/m$^3$ | 23·1% 56·9% 78·0% |
| 3 Household air pollution from solid fuels       | Individual exposure to PM$_{10}$, due to use of solid cooking fuels                 | No households are exposed to excess indoor concentration of particles from solid fuel use (assuming PM$_{10}$ in no fuel use is consistent with a TMREL of 2·4–5·9) | 72·8% 59·5% 76·4% |
| 3 Ambient ozone pollution                        | Seasonal (3 month) hourly maximum ozone concentrations, measured in ppb              | Uniform distribution between 33·3 µg/m$^3$ and 41·9 µg/m$^3$, according to minimum/5th percent concentrations | 100·0% 100·0% 100·0%  |
| 2 Other environmental risks                      | ···                                                                                  | ···                                    | 48·7% 26·2% 51·8%          |
| 3 Residential radon                              | Average daily exposure to indoor air radon levels measured in becquerels (radon disintegrations per second) per cubic metre (Bq/m$^3$) | 10 Bq/m$^3$, corresponding to the outdoor concentration of radon | 39·0% 0·0% 39·0%     |
| 3 Lead exposure                                  | Blood lead levels in µg/dL of blood, bone lead levels in µg/g of bone                | 2 ug/dL, corresponding to lead levels in pre-industrial humans as natural sources of lead prevent the feasibility of zero exposure | 37·4% 26·2% 43·6% |
| 2 Occupational risks                            | ···                                                                                  | ···                                    | 92·3% 90·8% 100·0%        |
| 3 Occupational carcinogens                       | ···                                                                                  | ···                                    | 86·7% 85·6% 92·8%         |
| 4 Occupational exposure to asbestos              | Proportion of the population with cumulative exposure to asbestos                    | No occupational exposure to asbestos  | 82·6% 74·9% 87·2%        |
| 4 Occupational exposure to arsenic               | Proportion of the population ever exposed to arsenic at work or through their occupation | No occupational exposure to arsenic | 82·6% 74·9% 87·2%        |
| 4 Occupational exposure to benzene               | Proportion of the population ever exposed to benzene at work or through their occupation | No occupational exposure to benzene | 82·6% 74·9% 87·2%        |
| 4 Occupational exposure to beryllium             | Proportion of the population ever exposed to beryllium at work or through their occupation | No occupational exposure to beryllium | 82·6% 74·9% 87·2%        |
| 4 Occupational exposure to cadmium               | Proportion of the population ever exposed to cadmium at work or through their occupation | No occupational exposure to cadmium | 82·6% 74·9% 87·2%        |
| 4 Occupational exposure to chromium             | Proportion of the population ever exposed to chromium at work or through their occupation | No occupational exposure to chromium | 82·6% 74·9% 87·2%        |
| 4 Occupational exposure to diesel engine exhaust | Proportion of the population ever exposed to diesel engine exhaust at work or through their occupation | No occupational exposure to diesel engine exhaust | 82·6% 74·9% 87·2%        |
| 4 Occupational exposure to second-hand smoke     | Proportion of the population ever exposed to second-hand smoke at work or through their occupation | No occupational exposure to second-hand smoke | 82·6% 74·9% 87·2%        |
| 4 Occupational exposure to formaldehyde          | Proportion of the population ever exposed to formaldehyde at work or through their occupation | No occupational exposure to formaldehyde | 82·6% 74·9% 87·2%        |
| 4 Occupational exposure to nickel                | Proportion of the population ever exposed to nickel at work or through their occupation | No occupational exposure to nickel | 82·6% 74·9% 87·2%        |
| 4 Occupational exposure to polycyclic aromatic hydrocarbons | Proportion of the population ever exposed to polycyclic aromatic hydrocarbons at work or through their occupation | No occupational exposure to polycyclic aromatic hydrocarbons | 82·6% 74·9% 87·2%        |

(Table 2 continues on next page)
| Risk factors | Exposure definition | Theoretical minimum risk exposure level | Data representativeness index |
|--------------|---------------------|----------------------------------------|-----------------------------|
|              |                     |                                        | 2006 | 2006-16 | Total |
| 4            | Occupational exposure to silica | Proportion of the population ever exposed to silica at work or through their occupation | No occupational exposure to silica | 82.6% | 74.9% | 87.2% |
| 4            | Occupational exposure to sulfuric acid | Proportion of the population ever exposed to sulfuric acid at work or through their occupation | No occupational exposure to sulfuric acid | 80.5% | 73.3% | 85.1% |
| 4            | Occupational exposure to trichloroethylene | Proportion of the population ever exposed to trichloroethylene at work or through their occupation | No occupational exposure to trichloroethylene | 80.5% | 73.3% | 85.1% |
| 3            | Occupational asthmagens | Proportion of the population currently exposed to asthmagens at work or through their occupation | Background asthmagen exposures | 82.6% | 74.9% | 87.2% |
| 3            | Occupational particulate matter, gases, and fumes | Proportion of the population ever exposed to particulates, gases, or fumes at work or through their occupation | No occupational exposure to particulates, gases, or fumes | 83.6% | 75.9% | 88.2% |
| 3            | Occupational noise | Proportion of the population ever exposed to noise greater than 85 dB at work or through their occupation | Background noise exposure | 83.6% | 75.9% | 88.2% |
| 3            | Occupational injuries | Proportion of the population at risk to injuries related to work or through their occupation | The rate of injury deaths per 100 000 person-years is zero | 82.6% | 75.4% | 87.2% |
| 3            | Occupational ergonomic factors | Proportion of the population who are exposed to ergonomic risk factors for low back pain at work or through their occupation | All individuals have the ergonomic factors of clerical and related workers | 82.6% | 74.9% | 87.2% |

| Risk factors  | Exposure definition | Theoretical minimum risk exposure level | Data representativeness index |
|---------------|---------------------|----------------------------------------|-----------------------------|
| 1            | Behavioural risks | Proportion of the population ever exposed to silica at work or through their occupation | No occupational exposure to silica | 82.6% | 74.9% | 87.2% |
| 2            | Child and maternal malnutrition | Proportion of the population ever exposed to silica at work or through their occupation | No occupational exposure to silica | 82.6% | 74.9% | 87.2% |
| 3            | Suboptimal breastfeeding | Proportion of children younger than 6 months who receive predominant, partial, or no breastfeeding | All children are exclusively breastfed for first 6 months of life | 67.1% | 54.6% | 73.9% |
| 4            | Non-exclusive breastfeeding | Proportion of children aged 6-23 months who do not receive any breastmilk | All children continue to receive breastmilk until 2 years of age | 68.1% | 65.3% | 79.2% |
| 3            | Child growth failure | Proportion of children less than –3 SD, –3 to –2 SD, and –2 to –1 SD of the WHO 2006 standard weight-for-age curve | All children are above –1 SD of WHO 2006 standard weight-for-age curve | 77.4% | 65.1% | 81.0% |
| 4            | Child wasting | Proportion of children less than –3 SD, –3 to –2 SDs, and –2 to –1 SD of the WHO 2006 standard weight-for-length curve | All children are above –1 SD of WHO 2006 standard weight-for-height curve | 78.0% | 66.2% | 82.1% |
| 4            | Child stunting | Proportion of children less than –3 SD, –3 to –2 SD, and –2 to –1 SD of the WHO 2006 standard height-for-age curve | All children are above –1 SD of WHO 2006 standard height-for-age curve | 78.0% | 66.2% | 82.1% |
| 3            | Low birthweight and short gestation | Proportion of births occurring in 2 week bands starting from <24 weeks to 39–40 weeks | 40-41 weeks gestation | 36.0% | 16.4% | 18.0% |
| 4            | Short gestation for birthweight | Proportion of births occurring in 500 g categories starting from <500 g to 4000–4499 g | 4500–4999 g birthweight | 36.0% | 16.4% | 18.0% |
| 3            | Iron deficiency | Peripheral blood haemoglobin concentration in g/L | Countertactual haemoglobin concentration in the absence of iron deficiency in g/L | 81.5% | 44.1% | 85.1% |
| 3            | Vitamin A deficiency | Proportion of children aged 0-5 years with serum retinol concentration <0.7 µmol/L | No childhood vitamin A deficiency | 59.4% | 44.1% | 56.4% |
| 3            | Zinc deficiency | Proportion of the population with inadequate zinc intake versus loss | No inadequate zinc intake | 94.9% | 93.3% | 94.9% |
| 2            | Tobacco | Tobacco use in the past year | All individuals are lifelong non-smokers | 92.8% | 96.9% | 99.0% |
| 3            | Smoking | Smoking Impact Ratio method: cumulative exposure to smoked tobacco products, proxied by excess lung cancer mortality; direct smoking: 5 year lagged proportion of the population who currently smoke daily | All individuals are lifelong non-smokers | 34.4% | 70.8% | 73.3% |
| 3            | Smokeless tobacco | Current use of any smokeless tobacco product | All individuals are lifelong non-users of smokeless tobacco products | 73.9% | 67.7% | 90.8% |
| 3            | Second-hand smoke | Average daily exposure to air particulate matter in the home from second-hand smoke with an aerodynamic diameter smaller than 0.5 µg, measured in µg/m³, among non-smokers living with a current daily smoker | No second-hand smoke exposure | 54.9% | 62.6% | 79.0% |

(Table 2 continues on next page)
### Risk factors

| Risk factors         | Exposure definition                                                                 | Theoretical minimum risk exposure level | Data representativeness index |
|----------------------|--------------------------------------------------------------------------------------|----------------------------------------|------------------------------|
|                      |                                                                                      |                                         | <2006 | 2006–16 | Total |
| 2 Dietary risks      |                                                                                      |                                         |     |         |       |
| 3 Alcohol use        | Average daily alcohol consumption of pure alcohol (measured in g per day) in current drinkers who had consumed alcohol during the past 12 months; binge drinking: proportion of the population reporting binge consumption of at least 60 g for males and 48 g for females of pure alcohol on a single occasion | No alcohol consumption                  | 52.3% | 45.6%   | 69.7% |
| 3 Drug use           | Proportion of the population dependent upon opioids, cannabis, cocaine, or amphetamines; proportion of the population who have ever injected drugs | No drug use                             | 20.5% | 37.4%   | 43.1% |
| 3 Diet low in fruits | Average daily consumption of fruits (fresh, frozen, cooked, canned, or dried fruits, excluding fruit juices and salted or pickled fruit) | Consumption of fruit between 200 g and 300 g per day | 94.9% | 94.9%   | 94.9% |
| 3 Diet low in vegetables | Average daily consumption of vegetables (fresh, frozen, cooked, canned, or dried vegetables, excluding legumes and salted or pickled vegetables, juices, nuts, and seeds, and starchy vegetables such as potatoes or corn) | Consumption of vegetables between 290 g and 430 g per day | 100.0% | 100.0% | 100.0% |
| 3 Diet low in legumes | Average daily consumption of legumes (fresh, frozen, cooked, canned, or dried legumes) | Consumption of legumes between 50 g and 70 g per day | 100.0% | 100.0% | 100.0% |
| 3 Diet low in whole grains | Average daily consumption of whole grains (bran, germ, and endosperm in their natural proportion) from breakfast cereals, bread, rice, pasta, biscuits, muffins, tortillas, pancakes, and other sources | Consumption of whole grains between 100 g and 250 g per day | 15.9%  | 13.9%   | 20.0% |
| 3 Diet low in nuts and seeds | Average daily consumption of nut and seed foods                                      | Consumption of nuts and seeds between 16 g and 25 g per day | 100.0% | 100.0% | 100.0% |
| 3 Diet low in milk    | Average daily consumption of milk including non-fat, low-fat, and full-fat milk, excluding soy milk and other plant derivatives | Consumption of milk between 350 g and 520 g per day | 100.0% | 100.0% | 100.0% |
| 3 Diet high in red meat | Average daily consumption of red meat (beef, pork, lamb, and goat but excluding poultry, fish, eggs, and all processed meats) | Consumption of red meat between 18 g and 27 g per day | 100.0% | 100.0% | 100.0% |
| 3 Diet high in processed meat | Average daily consumption of meat preserved by smoking, curing, salting, or addition of chemical preservatives | Consumption of processed meat between 0 g and 4 g per day | 100.0% | 100.0% | 100.0% |
| 3 Diet high in sugar-sweetened beverages | Average daily consumption of beverages with ≥50 kcal per 226·8 g serving, including carbonated beverages, sodas, energy drinks, fruit drinks, but excluding 100% fruit and vegetable juices | Consumption of sugar-sweetened beverages between 0 g and 5 g per day | 34.9%  | 30.3%   | 36.9% |
| 3 Diet in fibre      | Average daily intake of fibre from all sources including fruits, vegetables, grains, legumes, and pulses | Consumption of fibre between 19 g and 28 g per day | 100.0% | 100.0% | 100.0% |
| 3 Diet in calcium    | Average daily intake of calcium from all sources, including milk, yogurt, and cheese | Consumption of calcium between 1·00 g and 1·50 g per day | 100.0% | 100.0% | 100.0% |
| 3 Diet in seafood omega 3 fatty acids | Average daily intake of eicosapentaenoic acid and docosahexaenoic acid | Consumption of seafood omega 3 fatty acids between 200 mg and 300 mg per day | 96.9%  | 94.9%   | 96.9% |
| 3 Diet in polyunsaturated fatty acids | Average daily intake of omega 6 fatty acids from all sources, mainly liquid vegetable oils, including soybean oil, corn oil, and safflower oil | Consumption of polyunsaturated fatty acids between 9% and 13% of total daily energy | 37.4%  | 38.5%   | 38.5% |
| 3 Diet high in transfatty acids | Average daily intake of transfatty acids from all sources, mainly partially hydrogenated vegetable oils and ruminant products | Consumption of transfatty acids between 0% and 1% of total daily energy | 15.9%  | 21.5%   | 26.2% |
| 3 Diet high in sodium | 24 h urinary sodium measured in μmol per day | 24 h urinary sodium between 1 g and 5 g per day | 100.0% | 100.0% | 100.0% |

### Sexual abuse and violence

| Risk factors         | Exposure definition                                                                 | Theoretical minimum risk exposure level | Data representativeness index |
|----------------------|--------------------------------------------------------------------------------------|----------------------------------------|------------------------------|
|                      |                                                                                      |                                         |     |         |       |
| 2 Sexual abuse and violence |                                                                                      |                                         |     |         |       |
| 3 Childhood sexual abuse | Proportion of the population ever having had the experience of intercourse or other contact abuse (ie, fondling and other sexual touching) when aged 15 years or younger, and the perpetrator or partner was more than 5 years older than the victim | No childhood sexual abuse              | 31.8% | 18.5%   | 38.0% |
| 3 Intimate partner violence | Proportion of the population who have ever experienced one or more acts of physical or sexual violence by a present or former intimate partner since age 15 years | No intimate partner violence           | 67.2% | 76.4%   | 86.2% |
| 3 Unsafe sex          | Proportion of the population with exposure to sexual encounters that convey the risk of disease | No exposure to a disease agent through sex | 14.9% | 51.3%   | 51.8% |
| 2 Low physical activity | Average weekly physical activity at work, home, transport-related, and recreational measured by MET min per week | All adults experience 3000–4500 MET min per week | 52.3% | 35.9%   | 67.2% |

(Table 2 continues on next page)
Global Health Metrics

We made several improvements in the process of estimating the burden of disease attributable to dietary risks. To improve the quality and coverage of our dietary estimates, we systematically searched literature for nationally or subnationally representative studies providing information on consumption of each dietary factor. We also made a systematic effort to obtain individual-level data for consumption of dietary factors; re-extracted data from all available sources; and standardised the definition of dietary factors across different sources. To capture recent trends in consumption, we used data on sales of different fresh and packaged foods to inform our estimates. To address the concerns over within-person variation in intake, we estimated usual intake of each dietary factor and used that to estimate the attributable disease burden. To make the current and optimal levels of intake more comparable, we used absolute intake of each dietary factor (rather than intake standardised to 2000 kcal per day). For more detail, see appendix 1 (p 117).

There were two substantial changes in the estimation of second-hand smoke compared with GBD 2015. First, we estimated the proportion of a population exposed to second-hand smoke using information about household composition and smoking status from household surveys and censuses, rather than using questions that ask directly about exposure to second-hand smoke in surveys. Second, we modelled exposure using spatiotemporal Gaussian process regression (ST-GPR), borrowing strength across sex and age, whereas in GBD 2015 we ran a DisMod model separately by sex and age. Further, we found significant evidence of associations between second-hand smoke exposure and two additional outcomes: breast cancer and diabetes, which were added to the list of risk-outcome pairs for second-hand smoke. More details on the estimation approach are presented in appendix 1 (p 98).

For the first time in the GBD study, we estimated exposure to and burden attributable to smokeless tobacco, defined as current use of any smokeless tobacco product. RR estimates were derived from prospective cohort studies and case-control studies and vary depending on the type of product used. Based on available evidence, for chewing tobacco RRs were significantly higher than one for oral cancer and oesophageal cancer, while for snus or snuff we did not find sufficient evidence of a RR greater than one for any health outcome. Additional details on the estimation methods and RRs are presented in appendix 1 (p 11, p 181).

Low birthweight for gestation and short gestation for birthweight are included as new risk factors for GBD 2016. The estimation has been parameterised to be polynomials by 500 g and 2 week categories. Low birthweight and gestational age are highly correlated risks and they are estimated in a completely interdependent manner. For each univariate analysis, identification of TMREL and calculation of PAFs is contingent on the other dimension. In other words, we found the lowest risk birthweight category for each 2 week gestational age band and, correspondingly, the lowest risk gestational age for each 500 g birthweight band. RRs were then estimated for each 500 g per 2 week bin. Exposure for each bin was estimated in three steps. First, we estimated by generating ensemble distribution estimates using modelled mean and categorical prevalence estimates for each of birthweight (mean, %<2500 g) and gestational age (mean, %<37 weeks, %<28 weeks) for each location, year, and sex. Second, we evaluated all microdata where both gestational age and birthweight were available and found a high degree of consistency in the correlation between them. Third, we took the pooled correlation coefficient from step 2 combined with univariate ensemble distributions from step 1 and used a copula linking function to simulate the joint distribution which was then summarised into each 500 g per 2 week category. Joint PAF calculation used a TMREL defined as the lowest overall risk of the entire matrix of birthweight and gestational age (see appendix 1 p 77 for more details).
Mediation
In GBD 2016, we updated our approach for estimation of the joint effects of combinations of risk factors (appendix 1 p 23). Using individual-level data from prospective cohort studies, we estimated the proportion of the effect of behavioural risks on cardiometabolic outcomes mediated through metabolic risk factors. We also estimated the proportion of the effect of each metabolic risk factor on cardiometabolic outcomes mediated through other metabolic risks. For each mediation pathway, we only included the mediators for which sufficient evidence existed for their causal relationship with the disease endpoint.

Explaining the drivers of trends in deaths and DALYs
As in GBD 2015, we undertook a decomposition analysis of changes in DALYs over the time period into four main components, namely, changes in DALYs due to changes in: (1) population growth; (2) population age structure; (3) exposure to all risks for a disease; and (4) all other factors combined, approximated as the risk-deleted death and DALY rates. Risk-deleted rates refers to death and DALY rates that would be observed if we removed all risk factors included in GBD 2016, estimated as DALY rates multiplied by one minus the PAF for the set of risks. We used methods developed by Das Gupta,19 but as the methods presented there do not result in the decomposition results being linear aggregates over time or risk, we adapted these methods further in GBD 2016. Our decomposition analysis was undertaken for each 5 year time period, at the all-risk level, taking into account risk mediation at the most detailed cause level. The contribution of changes in exposure for the individual risk mediation at the most detailed cause level. The 5 year time period, at the all-risk level, taking into account or risk, we adapted these methods further in GBD 2016.

Risk transition with development
We explored how exposure to risks varies across levels of development using the SDI, a composite indicator of development status constructed for GBD 2015 whose components are strongly correlated with health outcomes. It is the geometric mean of 0 to 1 for indices of total fertility rate, mean education for those aged 15 years and older, and lag-distributed income per capita. More details on the estimation of SDI can be found in appendix 1 (p 32).

Role of the funding source
The funders of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The authors had full access to all data in the study and had final responsibility for the decision to submit for publication.

Results
Global exposure to risks
From 1990 to 2016, trends in SEVs varied across the set of risk factors included in GBD 2016. Of note, SEVs decreased by more than 40% for three risks: diet high in transfatty acids (51·3% [95% UI 34·1–70·1]), household air pollution from solid fuels (3·1% [40·7–45·6]), and unsafe sanitation (3·5% [35·5–44·7]; table 3, appendix 2 p 1399). During the same period, SEVs increased by more than 40% for high body-mass index (BMI; 60·2% [45·1–79·1]), diet high in sugar-sweetened beverages (44·7% [36·1–52·7]), occupational exposure to diesel engine exhaust (41·8% [41·3–42·2]), and occupational exposure to trichloroethylene (40·6% [40·2–41·1]).

Across countries there is substantial variation in risk exposure by level of SDI. Some risk factors, such as high fasting plasma glucose (FPG) and high systolic blood pressure, show similar SEVs across levels of SDI, while others, including household air pollution and unsafe water source, show marked trends with sociodemographic development. Figure 1 shows the relationship between SEVs and SDI for the leading three metabolic, behavioural, and environmental and occupational risk factors and how that changed between 1990 and 2016. Within leading metabolic risks (high BMI, high FPG, and high systolic blood pressure [SBP]), risk-weighted exposure shows an increasing trend with increasing SDI for only high BMI. Overall, the SEV for high BMI has increased during the time period. Looking at the leading three environmental risk factors (ambient air pollution, household air pollution, and unsafe water), figure 2 shows an inverse relationship with SDI for household air pollution and unsafe water, with SEVs approaching zero at high levels of SDI, while the relationship is less consistent with ambient air pollution. Finally, the relationship between SDI and the leading behavioural risk factors is more heterogeneous, with smoking and alcohol use having a positive correlation with SDI, and short gestation for birthweight having a negative correlation with SDI.

Global attributable burden for all risk factors combined and their overlap
Globally, 59·9% (58·4–61·3) of deaths and 45·2% (43·2–47·3) of DALYs could be attributed to the risk factors assessed in GBD 2016. For deaths, non-communicable diseases (NCDs) show the largest proportion attributable to measured risk factors, at 64·4% (62·6–66·2), with communicable, maternal, neonatal, and nutritional (CMNN) causes at 57·9% (55·4–61·0), and injuries at 25·8% (23·7–27·8). The picture was different for DALYs, however, where we observed that 58·2% (56·4–60·3) of DALYs in CMNN causes are attributable to risk factors, compared with 43·5% (40·7–46·7) in NCDs and 21·0% (19·3–22·7) for injuries. Leading causes of DALYs in CMNN causes, such as diarrhoea and lower respiratory infections (LRI), also showed more than 80% of DALYs can be attributed to risk factors (appendix 2 p 1).
### Global Health Metrics

#### 1. Environmental and occupational risks

| Risk | Male | Female | Combined percent change 1990–2016 |
|------|------|--------|-----------------------------------|
| 3 Unsafe water, sanitation, and handwashing | 24.11 | 11.61 | –7.83 |
| 4 Ambient particulate matter pollution | 34.42 | 29.39 | –10.28 |
| 3 Household air pollution from solid fuels | 28.48 | 23.54 | –6.94 |
| 3 Ambient ozone pollution | 38.49 | 38.49 | 0.00 |

#### 2. Air pollution

| Risk | Male | Female | Combined percent change 1990–2016 |
|------|------|--------|-----------------------------------|
| 3 Residential radon | 26.12 | 26.12 | 0.00 |
| 3 Lead exposure | 20.01 | 20.01 | 0.00 |

#### 2. Occupational risks

| Risk | Male | Female | Combined percent change 1990–2016 |
|------|------|--------|-----------------------------------|
| 4 Occupational exposure to asbestos | 4.11 | 4.11 | –18.98 |
| 4 Occupational exposure to anesthetic | 4.44 | 4.44 | –5.07 |

### Table continues on next page
| Risk                          | Male         | Female        | Combined percentage change 1990–2016 |
|------------------------------|--------------|---------------|-------------------------------------|
|                              | Percent 1990| Percent 2006 | Percent 2016                        |
|                              | 1990–2006    | 1990–2016     |                                     |
| Occupational exposure to smoke | (5.66 to 21.95) | (6.00 to 24.44) | (6.25 to 11.25)*                    |
| Occupational exposure to formaldehyde | (0.77 to 0.81) | (0.95 to 1.01) | (0.97 to 15.39)*                    |
| Occupational exposure to nickel | (0.00 to 7.78) | (0.00 to 8.79) | (0.00 to 14.13)*                    |
| Occupational exposure to polycyclic aromatic hydrocarbons | (0.79 to 0.81) | (0.92 to 1.06) | (0.97 to 31.40)*                    |

(Continued from previous page)

| Risk                          | Percent 1990| Percent 2006 | Percent 2016                        |
|------------------------------|--------------|---------------|-------------------------------------|
|                              | 1990–2006    | 1990–2016     |                                     |
| Exposure to cigarette smoke  | 12.58        | 13.77         | 13.02                               |
| Child growth failure         | 4.19         | 4.21          | 0.00                                |
| Child wasting                | 8.46         | 8.39          | 0.00                                |

(Percent change 1990–2016: 0.00 to 8.33)
Global Health Metrics

| Risk | Male | Female | Combined percent change 1990-2016 |
|------|------|--------|----------------------------------|
|      | 1990 | 2006   | 2016   | Percent change 1990-2006 | Percent change 2006-16 | Percent change 1990-2016 | 1990 | 2006   | 2016   | Percent change 1990-2006 | Percent change 2006-16 | Percent change 1990-2016 |
|      |      |        |        | Percent change 1990-2006 | Percent change 2006-16 | Percent change 1990-2016 |      |        |        | Percent change 1990-2006 | Percent change 2006-16 | Percent change 1990-2016 |
| 1. Uptake of health-promoting behaviors |      |        |        | Percent change 1990-2006 | Percent change 2006-16 | Percent change 1990-2016 |      |        |        | Percent change 1990-2006 | Percent change 2006-16 | Percent change 1990-2016 |
| 1. Tobacco |      |        |        | Percent change 1990-2006 | Percent change 2006-16 | Percent change 1990-2016 |      |        |        | Percent change 1990-2006 | Percent change 2006-16 | Percent change 1990-2016 |
| 2. Alcohol and drug use |      |        |        | Percent change 1990-2006 | Percent change 2006-16 | Percent change 1990-2016 |      |        |        | Percent change 1990-2006 | Percent change 2006-16 | Percent change 1990-2016 |
| 3. Dietary risks |      |        |        | Percent change 1990-2006 | Percent change 2006-16 | Percent change 1990-2016 |      |        |        | Percent change 1990-2006 | Percent change 2006-16 | Percent change 1990-2016 |

(Continued from previous page)
### Global Health Metrics

#### Risk

|                  | Male          | Female        | Combined          | 1990  | 2006  | 2016  | Percent change 1990–2006 | Percent change 1990–2016 | Percent change 1990–2006 | Percent change 1990–2016 |
|------------------|---------------|---------------|-------------------|-------|-------|-------|--------------------------|--------------------------|--------------------------|--------------------------|
| **3 Diet low in nuts and seeds** | 88.83         | 87.83         | 83.75             | 31.93 | 37.93 | 41.37 | -5.72 (-13.72 to 2.24)   | -8.38 (-22.95 to 5.87)  | -5.72 (-13.72 to 2.24)   | -8.38 (-22.95 to 5.87)  |
| **3 Diet low in milk** | 81.31         | 81.31         | 83.48             | 18.69 | 21.69 | 24.69 | 0.24 (0.94 to -1.43)     | 0.30 (-1.64 to -1.23)  | 0.24 (0.94 to -1.43)     | 0.30 (-1.64 to -1.23)  |
| **3 Diet low in processed meat** | 78.40         | 78.40         | 79.68             | 21.51 | 24.51 | 27.51 | 0.22 (-1.43 to -1.07)    | 0.37 (-1.95 to -1.58)  | 0.22 (-1.43 to -1.07)    | 0.37 (-1.95 to -1.58)  |
| **3 Diet high in sugar-sweetened beverages** | 69.09         | 69.09         | 73.11             | 30.91 | 33.91 | 36.91 | 0.10 (0.55 to -1.07)     | 0.15 (-1.57 to -1.42)  | 0.10 (0.55 to -1.07)     | 0.15 (-1.57 to -1.42)  |
| **3 Diet high in seafood omega 3 fatty acids** | 78.05         | 78.05         | 81.05             | 21.95 | 24.95 | 27.95 | 0.10 (0.55 to -1.07)     | 0.15 (-1.57 to -1.42)  | 0.10 (0.55 to -1.07)     | 0.15 (-1.57 to -1.42)  |
| **3 Diet high in polyunsaturated fatty acids** | 46.41         | 46.41         | 49.41             | 53.59 | 56.59 | 59.59 | 0.10 (0.55 to -1.07)     | 0.15 (-1.57 to -1.42)  | 0.10 (0.55 to -1.07)     | 0.15 (-1.57 to -1.42)  |
| **3 Diet high in trans fatty acids** | 7.64          | 7.64          | 7.64              | 92.36 | 92.36 | 92.36 | 0.10 (0.55 to -1.07)     | 0.15 (-1.57 to -1.42)  | 0.10 (0.55 to -1.07)     | 0.15 (-1.57 to -1.42)  |
| **3 Intimate partner violence** | 11.80         | 11.80         | 11.80             | 88.60 | 88.60 | 88.60 | 0.10 (0.55 to -1.07)     | 0.15 (-1.57 to -1.42)  | 0.10 (0.55 to -1.07)     | 0.15 (-1.57 to -1.42)  |
| **2 Low physical activity** | 18.02         | 18.02         | 18.02             | 81.98 | 81.98 | 81.98 | 0.10 (0.55 to -1.07)     | 0.15 (-1.57 to -1.42)  | 0.10 (0.55 to -1.07)     | 0.15 (-1.57 to -1.42)  |

(Continued from previous page)
Within NCDs, three of the leading causes of deaths and DALYs, ischaemic heart disease (IHD; 93·3% [90·3–95·7] of deaths and 94·4% [92·6–95·8] of DALYs), haemorrhagic stroke (88·2% [84·3–91·8] of deaths and 89·5% [87·1–91·6] of DALYS), and chronic obstructive pulmonary disorder (COPD; 76·6% [69·9–82·9] of deaths and 73·8% [67·4–80·2] DALYS) all have high proportions attributable to measured risk factors. Lung cancer, a leading cause of death but not DALYs, also has a large proportion of total deaths and DALYs attributed to measured risk factors (84·1% [78·9–88·3] and 83·2% [78·0–87·6] respectively), while for Alzheimer’s disease only 21·4% (11·2–34·0) of deaths attributable to risk factors. However, age-standardised DALY rates for all three Level 1 risk factors, including detail on attributable deaths and DALYs by cause-outcome pair (appendix 2 p 1865) contains results not only for all risk factors considered here from 2006 to 2016, but also for several cancers at nearly zero, such as brain cancer.

## Levels and trends in the burden attributable to risk factors

Table 4 reports all-cause deaths and DALYs attributable to all risk factors, including detail on attributable deaths and DALYs by risk-outcome pair (appendix 2 p 1865) contains results for every location. Globally, 32·8 million (31·9 million to 33·7 million) deaths were attributable to all risk factors in 2016, a significant increase since 2006 of 2·9% (1·1–4·8); however, age-standardised attributable death rate declined from 2006 to 2016 by 18·7% (17·3–20·0). By contrast, total DALYs attributable to all risks decreased by 8·6% (6·6–10·7) since 2006, and age-standardised DALY rate attributable to all risks decreased by 21·7% (20·0–23·3). Among Level 1 risks, the largest decreases in age-standardised death rates were observed for environmental and occupational risks (24·3% [22·5–26·0]), followed by behavioural risks (21·5% [19·8–23·3]), and metabolic risks (11·9% [9·9–13·5]). Similarly, there were significant decreases in age-standardised DALY rates for all three Level 1 risk factors, although the magnitude of decrease was larger for DALY rates than death rates. In the year 2016, behavioural risk factors accounted for the largest number of deaths (21·8 million [20·5 million to 23·3 million]) and DALYs (781·1 million [737·1 million to 830·1 million]). While there were decreases in both deaths and DALYs attributable to behavioural risk factors since 2006, these decreases were significant for deaths (2·5% [0·1–4·9])

| Risk | Male | Female | Combined |
|------|------|--------|----------|
|      | 1990 | 2006 | 2016 | Percent change | 1990–2006 | 2006–2016 | 1990–2016 | Percent change | 1990–2006 | 2006–2016 | 1990–2016 |
| 2 High systolic blood pressure | 25·23 | 25·37 | 25·69 | 0·54 | 1·29 | 1·83 | 26·03 | 25·03 | 24·69 | −3·82 | −1·35 | −5·12 | −9·51 |
| | (23·60 to 27·13) | (23·68 to 27·32) | (23·99 to 27·69) | (0·18 to 0·91)* | (0·96 to 1·62)* | (1·40 to 2·31)* | (24·45 to 27·80) | (23·53 to 26·77) | (23·20 to 26·38) | (−4·22 to −3·47)* | (−1·70 to −0·98)* | (−5·55 to −4·68)* | (−2·28 to −1·61)* |
| 2 High body-mass index | 5·91 | 7·93 | 9·50 | 34·16 | 19·82 | 60·75 | 6·62 | 8·89 | 10·64 | 34·22 | 19·69 | 60·65 | 60·25 |
| | (3·95 to 8·57) | (5·41 to 11·27) | (6·52 to 13·51) | (25·41 to 45·26) | (25·02 to 45·26) | (10·42 to 13·51) | (6·21 to 9·52) | (6·21 to 9·52) | (45·26 to 44·41)* | (45·26 to 44·41)* | (16·07 to 16·07) | (45·14 to 45·14) |
| 2 Low bone mineral density | 11·49 | 11·40 | 11·33 | −0·25 | −0·06 | −0·34 | 12·59 | 12·59 | 12·65 | 0·06 | 0·41 | 0·46 | −0·51 |
| | (10·42 to 12·67) | (10·34 to 12·58) | (10·29 to 12·51) | (−1·08 to −0·46)* | (−0·84 to −0·36)* | (−0·79 to −0·91)* | (11·47 to 13·76) | (11·48 to 13·78) | (11·51 to 13·82) | (−0·16 to 0·27) | (0·16 to 0·46) | (−0·17 to −0·26)* | |
| 2 Impaired kidney function | 4·78 | 4·84 | 4·90 | 1·16 | 1·23 | 2·41 | 5·46 | 5·48 | 5·54 | 0·35 | 1·06 | 1·41 | 1·63 |
| | (2·94 to 9·45) | (2·98 to 9·27) | (3·01 to 9·36) | (0·41 to 1·83)* | (0·61 to 1·76)* | (1·11 to 3·34)* | (3·42 to 10·22) | (3·41 to 10·27) | (3·44 to 10·37) | (−0·80 to 1·78) | (0·47 to 1·73)* | (−0·05 to 0·33) | (2·27 to 3·05)* |

Data in parentheses are 95% uncertainty intervals. SEVs = summary exposure values. *Statistically significant increase or decrease.
and DALYs (14·3% [11·8–16·6]). There was a significant, 17·9% (15·7–20·6), increase in number of deaths attributable to metabolic risk factors, from 14·8 million deaths (14·0 million to 15·7 million) in 2006 to 17·5 million deaths (16·4 million to 18·5 million) in 2016, with similar increases observed for DALYs. Environmental and occupational risk factors accounted for the fewest number of deaths and DALYs, and there was a significant decline in both measures since 2006.

Figure 2 shows that in 2016, the leading Level 2 risk factors in terms of attributable DALYs at the global level for both sexes combined were malnutrition (11·5% [10·8–12·3] of DALYs), diet (9·6% [8·2–11·1] of DALYs), high blood pressure (8·9% [7·9–9·9] of DALYs), tobacco (7·4% [6·7–8·3] of DALYs), and air pollution (6·8% [6·1–7·6] of DALYs). The list at this level of aggregation is similar for

Global patterns of burden attributable to risk factors across quintiles of SDI

Figure 2 shows that in 2016, the leading Level 2 risk factors in terms of attributable DALYs at the global level for both sexes combined were malnutrition (11·5% [10·8–12·3] of DALYs), diet (9·6% [8·2–11·1] of DALYs), high blood pressure (8·9% [7·9–9·9] of DALYs), tobacco (7·4% [6·7–8·3] of DALYs), and air pollution (6·8% [6·1–7·6] of DALYs). The list at this level of aggregation is similar for
Global Health Metrics

- Child and maternal malnutrition
- High systolic blood pressure
- Tobacco
- Air pollution
- High fasting plasma glucose
- High body-mass index
- Alcohol and drug use
- High total cholesterol
- Occupational risks
- Unsafe water, sanitation, and handwashing
- Impaired kidney function
- Unsafe sex
- Low physical activity
- Other environmental risks
- Low bone mineral density
- Sexual abuse and violence

A Global

B Low SDI countries

C Low-middle SDI countries

D Middle SDI countries

E Middle-high SDI countries

F High SDI countries

DALY (%)

- HIV/AIDS and tuberculosis
- Diarrhoea, lower respiratory infections, and other common infectious diseases
- Maternal disorders
- Neonatal disorders
- Nutritional deficiencies
- Other communicable, maternal, neonatal, and nutritional diseases
- Neoplasms
- Cardiovascular diseases
- Chronic respiratory diseases
- Cirrhosis and other chronic liver diseases
- Digestive diseases
- Neurological disorders
- Mental and substance use disorders
- Diabetes, urogenital, blood, and endocrine diseases
- Musculoskeletal disorders
- Other non-communicable diseases
- Transport injuries
- Unintentional injuries
- Self-harm and interpersonal violence

www.thelancet.com Vol 390 September 16, 2017
both sexes combined, with a notable difference being that alcohol and drug use is the fifth-leading risk factor for men, with 7.9% (7.2–8.6) of DALYs, but is at eleventh place for women (2.6% [2.3–2.9] of DALYs). More detail can be found in appendix 2 (p 1399). The patterns of risks vary by development, as seen across the panels of figure 3. At the lowest level of SDI, the leading risk is malnutrition with 25.0% (23.2–26.6) of DALYs, followed by air pollution (8.0% [7.1–9.0] of DALYs), unsafe water, sanitation, and handwashing (7.8% [6.6–9.4] of DALYs), and unsafe sex (4.7% [4.3–5.2] of DALYs). While malnutrition remains the leading risk factor at the low-middle level of SDI, diet (7.8% [6.8–9.0] of DALYs), high systolic blood pressure (7.2% [6.8–8.1] of DALYs), and tobacco use (5.9% [5.3–6.6] of DALYs) get included among the leading five causes as well. At the middle SDI level, diet is among the leading five risks with 12.5% (10.6–14.6) of DALYs while high systolic blood pressure and tobacco follow in importance. At the top three levels of SDI, high BMI increases in importance and makes it to the leading five risks, with 7.2% (4.7–10.0) of DALYs in middle SDI locations, with 9.8% (6.5–13.2) of DALYs in high-middle SDI locations, and 8.7% (5.9–11.7) of DALYs in high SDI locations. The panels in figure 3 clearly show the transition across levels of development.

Changes in leading risk factors in 1990, 2006, and 2016

Figure 3 shows the leading 30 risk factors at Level 3 of the hierarchy and the median change in DALYs between 1990, 2006, and 2016. In terms of rates, among the top ten leading risks in 1990, child growth failure, unsafe sanitation, and unsafe water have experienced the largest declines over the period of 1990–2016. While these three risks have remained in the top 30 in 2016 for men, their ranks have fallen by several places to 9th (child growth failure), 21st (unsafe sanitation), and 16th (unsafe water). For women, their ranks have fallen to 5th (child growth failure), 16th (unsafe sanitation), and 13th (unsafe water). Between 1990 and 2006, median age-standardised DALY rates decreased by 46.7% (42.1–51.1) for men and 49.0% (45.0–53.0) for women, and in the most recent period child growth failure demonstrated further declines by 43.8% (36.9–49.8) for men and 48.7% (42.3–54.6) for women.

The risk factor of low birthweight for gestation and short gestation for birthweight remains among the leading risks (second position in 1990 for both sexes; third position in 2016 for men and fourth position for women), despite declines in both the number of DALYs and the age-standardised DALY rates since 1990. Smoking is another risk where there has been a consistent decline since 1990 in both SEVs and age-standardised DALY rates, yet it has consistently been ranked among the leading three risk factors for men in DALYs since 1990.

The trend in unsafe sex coincides with the HIV/AIDS epidemic. Figure 3 shows that unsafe sex experienced large increases between 1990 and 2006, by 198.8% (170.4–228.2) for men and 204.0% (170.0–236.4) for women, resulting in a higher rank in 2006, followed by declines of 43.8% (41.7–45.7) for men and 46.7% (44.1–49.0) for women since 2006 resulting in a lower rank in 2016. On the other hand, drug use follows a different trend, and increased for men by 17.6% (13.0–25.5) between 1990 and 2006 and resulted in a higher rank in 2006, and decreased 5.7% (2.2–9.0) since 2006. Despite declines, drug use rose from the 25th leading risk to the 18th leading risk for men between 1990 and 2016.

Air pollution, both household air pollution and ambient particulate matter, were among the leading ten risk factors for men and women in 1990 and have remained important in 2016. The median percent change in age-standardised DALY rates showed important declines in both time periods for men and women. Specifically, in the most recent time period household air pollution declined by 38.3% (35.3–41.4) for men and 41.1% (37.8–44.2) for women, and ambient air pollution decreased by 14.2% (11.5–17.1) for men and 21.3% (17.8–24.5) for women, in terms of median age-standardised DALY rates.

The metabolic risk factors have increased in both rank and in the absolute number of DALYs between 1990 and 2016 for both men and women. High blood pressure was the fourth-leading risk factor for both men and women in 1990 and had risen to be the second leading risk factor for men and the leading risk factor for women by 2016. In terms of the number of DALYs, men showed an increase of 16.6% (13.1–19.4) since 2006, while for women the increase was less steep at 7.7% (4.5–11.7). In terms of the median change in age-standardised DALY rates since 2006, both sexes showed a decline, 10.5% (8.2–12.7) for men and 16.8% (13.7–19.3) for women. Other leading metabolic risk factors, including high BMI, high FPG, and high total cholesterol, exhibited similar trends to high blood pressure over this time period. All four of these metabolic risk factors are within the leading ten risk factors globally for men and women in 2016.

Among the leading risk factors in terms of DALYs, high BMI and high FPG have the fastest increases in SEVs with annualised rates of change of 1.7% (1.5–1.9) and 0.9% (0.6–1.3), respectively, since 1990 (figure 4). On the other hand, other leading risk factors in 2016 such as smoking and household air pollution exhibited significant and fast declines in SEVs, with a −1.3% (−1.6 to −1.1) annualised rate of change for smoking and −2.3% (−2.5 to −2.2) for household air pollution between 1990 and 2016 (figure 4).

Drivers of changes in risk-attributable deaths and DALYs

Figure 5 shows the relative contributions to changes in deaths and DALYs of important drivers grouped into four

Figure 2: DALYs attributable to all Level 2 risk factors apportioned by Level 2 cause for each risk, both sexes combined, 2016, at the global level (A); for low SDI countries (B); for low-middle SDI countries (C); for middle SDI countries (D); for middle-high SDI countries (E); and for high SDI countries (F). DALYs from causes attributable to each risk factor are shown in different colours. Cutoffs on the SDI scale for the quintiles were selected based on examining the entire distribution of locations between 1980 and 2016. DALYs=disability-adjusted life-years. SDI=Socio-demographic Index.
| Risk                                      | 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of age-standardised DALYs rate 2006–16 |
|-------------------------------------------|----------------------------|-----------------------------|--------------------------------------|----------------------------|-----------------------------|-----------------------------------------------------|
| All risk factors: all causes              | 31,848.45                  | 32,576.24                   | 2.85 (1.2 to 4.76)                   | 118,211.16                 | 10,810.152                  | -8.64 (-6.6 to -10.66)                                       |
| Environmental and occupational risks: all causes | 975.57                     | 9293.43                     | -4.70 (-7.0 to -2.37)                | 367,198.64                 | 335,402.97                 | -12.10 (-10.8 to -14.6)                                        |
| Unsafe water, sanitation, and handwashing: all causes | 2231.21                    | 1660.77                     | -25.57 (-32.8 to -16.3)              | 118,178.24                 | 75,796.04                   | -35.86 (-41.6 to -29.70)                                       |
| Unsafe water source: all causes           | 1570.53                    | 1160.16                     | -26.33 (-34.6 to -18.0)              | 82,040.06                  | 52,440.65                   | -36.08 (-42.6 to -29.4)                                        |
| Diarrheal diseases                        | 1570.53                    | 1160.16                     | -26.33 (-34.6 to -18.0)              | 82,040.06                  | 52,440.65                   | -36.08 (-42.6 to -29.4)                                        |
| Unsafe sanitation: all causes             | 1323.65                    | 898.24                      | -32.44 (-42.7 to -23.2)              | 68,961.68                  | 40,746.60                   | -40.91 (-46.8 to -33.2)                                        |
| Diarrheal diseases                        | 1323.65                    | 898.24                      | -32.44 (-42.7 to -23.2)              | 68,961.68                  | 40,746.60                   | -40.91 (-46.8 to -33.2)                                        |
| No access to handwashing facility: all causes | 1015.06                   | 750.30                      | -36.78 (-41.7 to -30.8)              | 55,096.20                  | 35,254.90                   | -36.01 (-41.2 to -30.5)                                        |
| Diarrheal diseases                        | 972.95                     | 705.85                      | -28.01 (-35.5 to -13.3)              | 41,827.94                  | 26,252.35                   | -29.93 (-37.0 to -21.6)                                        |
| Lower respiratory infections              | 222.11                     | 179.49                      | -28.58 (-35.0 to -22.0)              | 12,628.26                  | 8,882.59                    | -31.45 (-38.7 to -24.1)                                        |
| Air pollution: all causes                 | 6219.85                    | 6161.40                     | -1.66 (-4.1 to 0.7)                  | 186,446.12                 | 162,795.90                  | -12.68 (-15.7 to -9.6)                                         |
| Ambient particulate matter pollution: all causes | 3687.20                    | 4092.69                     | 11.00 (8.0 to 14.9)                  | 105,732.08                 | 105,674.02                  | -0.05 (-3.2 to 3.79)                                           |
| Lower respiratory infections              | 689.26                     | 653.41                      | -5.20 (-10.3 to 0.2)                 | 37,842.21                  | 28,517.03                   | -24.92 (-32.8 to -16.0)                                        |
| Tracheal, bronchus, and lung cancer       | 2232.57                    | 2172.79                     | -12.01 (20.6 to 29.8)                | 51,449.29                  | 60,000.23                   | -51.25 (58.5 to 35.9)                                          |
| Ischaemic heart disease                   | 1291.11                    | 1576.10                     | -7.08 (18.5 to 25.6)                 | 29,250.10                  | 34,916.18                   | 18.34 (14.8 to 21.0)                                           |
| Ischaemic stroke                          | 309.39                     | 348.33                      | -12.50 (8.4 to 17.6)                 | 6437.02                    | 7389.59                     | 14.75 (10.5 to 19.2)                                           |
| Haemorrhagic stroke                       | 535.48                     | 448.19                      | 2.92 (0.0 to 6.1)                    | 11,171.69                  | 11,840.35                   | 7.24 (-0.9 to 5.9)                                             |
| Chronic obstructive pulmonary disease      | 378.38                     | 786.94                      | 6.58 (2.9 to 11.3)                   | 15,614.77                  | 17,155.66                   | 9.87 (6.3 to 14.6)                                             |
| Household air pollution from solid fuels: all causes | 3266.73                    | 3576.36                     | -20.99 (-23.9 to -18.1)              | 108,733.32                 | 77,161.35                   | -29.04 (-32.8 to -25.6)                                        |
| 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYS 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|---------------------------|---------------------------|--------------------------------------|-------------------------------------------------|---------------------------|---------------------------|--------------------------------------|--------------------------------------|
| Lower respiratory infections | 883.96 | 626.13 | -29.17 | -37.62 | 52,410.01 | 30,860.63 | -41.12 | -44.24 |
| Tracheal, bronchus, and lung cancer | 189.07 | 158.38 | -16.23 | -35.50 | 45,153.18 | 36,644.00 | -18.90 | -13.66 |
| Ischaemic heart disease | 813.36 | 738.11 | -9.25 | -30.16 | 20,255.31 | 17,906.39 | -11.51 | -30.11 |
| Ischaemic stroke | 229.91 | 185.00 | -19.10 | -28.70 | 50,445.48 | 45,975.91 | -12.57 | -36.61 |
| Haemorrhagic stroke | 392.09 | 289.08 | -26.27 | -43.44 | 10,360.06 | 7,735.95 | -25.35 | -41.23 |
| Chronic obstructive pulmonary disease | 752.34 | 578.68 | -23.08 | -42.31 | 15,181.60 | 11,804.50 | -22.24 | -40.36 |
| Cataract | 987.74 | - | - | - | 1033.91 | 510.50 | -19.66 | -21.81 |
| Ambient ozone pollution: all causes | 187.61 | 233.64 | 24.53 | -6.98 | 3,159.44 | 3,768.76 | 20.17 | -7.97 |
| Chronic obstructive pulmonary disease | 187.61 | 233.64 | 24.53 | -6.98 | 3,159.44 | 3,768.76 | 20.17 | -7.97 |
| Other environmental risks: all causes | 518.27 | 597.74 | 15.33 | -12.38 | 14,319.52 | 15,128.92 | -5.65 | -15.31 |
| Residential radon: all causes | -49.87 | -57.69 | 15.68 | -11.27 | -1126.44 | 1255.37 | -11.45 | -13.56 |
| Tracheal, bronchus, and lung cancer | -49.87 | -57.69 | 15.68 | -11.27 | -1126.44 | 1255.37 | -11.45 | -13.56 |
| Lead exposure: all causes | 468.39 | 540.04 | 15.30 | -12.50 | 13,191.09 | 13,873.55 | 5.16 | -18.17 |
| Rheumatic heart disease | 3.54 | -3.05 | -13.92 | -31.70 | 108.53 | 81.79 | -24.64 | -38.40 |
| Ischaemic heart disease | 227.95 | 276.33 | 21.23 | -8.33 | 4766.44 | 5298.38 | 11.30 | -13.26 |
| Ischaemic stroke | 60.00 | 66.73 | 11.21 | -15.93 | 1285.87 | 1412.53 | 9.85 | -15.71 |
| Haemorrhagic stroke | 49.90 | 59.67 | -3.26 | -25.84 | 2372.00 | 2182.12 | -7.94 | -28.02 |
| Hypertensive heart disease | 43.68 | 56.00 | 28.21 | -4.14 | 868.54 | 992.22 | 14.24 | -11.18 |
| Other cardiomyopathy | 1.48 | 1.54 | 3.73 | -20.52 | 35.62 | 33.18 | -6.84 | -25.95 |

(Continued from previous page)
| Disease                        | 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006-16 | Percentage change of age-standardised deaths rate 2006-16 |
|--------------------------------|----------------------------|----------------------------|-------------------------------------|--------------------------------------------------------|
| Atrial fibrillation and flutter | 1.76                      | 2.45                      | 39.22                               | 0.69                                                   |
|                                | (0.45 to 3.49)             | (0.88 to 4.91)            | (29.86 to 46.04)*                   | (26.40 to 74.79)*                                      |
| Acute ischaemic stroke         | 1.52                      | 1.62                      | 22.65                               | 3.07                                                   |
|                                | (0.54 to 2.93)             | (0.55 to 3.75)            | (14.92 to 31.03)                     | (22.91 to 62.83)*                                      |
| Peripheral vascular disease    | 0.16                      | 0.20                      | 19.84                               | 11.54                                                  |
|                                | (0.03 to 0.41)             | (0.03 to 0.53)            | (12.64 to 35.45)                     | (15.21 to 12.98)*                                      |
| Endocarditis                   | 0.83                      | 0.97                      | 16.60                               | 20.65                                                  |
|                                | (0.29 to 1.74)             | (0.32 to 2.09)            | (11.24 to 36.89)                     | (1.62 to 15.16)*                                      |
| Other cardiovascular and       | 5.41                      | 5.94                      | 9.71                                | 16.12                                                  |
| circulatory diseases           | (1.95 to 10.17)            | (1.95 to 11.38)           | (1.04 to 16.74)                      | (5.62 to 31.64)*                                      |
| Idiopathic developmental       |                            |                            | 2916.48                             | 2920.47                                                |
| kidney disease due to diabetes |                            |                            | (12.38 to 40.91)                     | (12.38 to 51.51)*                                      |
| Chronic kidney disease due to  |                          |                            | 1216.25                             | 1216.25                                                |
| glomerulonephritis             | (4.15 to 18.35)            | (5.09 to 20.20)           | (19.04 to 29.44)*                    | (102.04 to 495.81)                                     |
| Chronic kidney disease due to  |                          |                            | 260.59                              | 302.16                                                 |
| 2006 DALYs (in thousands)      |                            |                            | (113.45 to 584.15)                   | (9.37 to 20.09)*                                      |
| Occupational risks: all causes | 1409.60                   | 1528.02                   | 68,543.89                           | 75,975.43                                              |
| 2006 DALYs (in thousands)      | (1288.25 to 1597.63)       | (1383.55 to 1680.97)      | (60,461.38 to 77,147.09)             | (66,060.97 to 86,257.10)                               |
| 3 Occupational carcinogens: all |                            |                            | 10.77                               | 8.98                                                   |
| causes                        | (1288.25 to 1597.63)       | (1383.55 to 1680.97)      | (8.84 to 12.62)                      | (–0.61 to –7.49)                                       |
| 4 Occupational exposure        |                            |                            | 14.39                               | 12.97                                                  |
| to asbestos: all causes        | (1288.25 to 1597.63)       | (1383.55 to 1680.97)      | (8.84 to 12.62)                      | (–0.61 to –7.49)                                       |
| Larynx cancer                  | 3.25                      | 3.74                      | 15.08                               | 13.01                                                  |
|                                | (1.02 to 4.92)             | (2.02 to 5.53)            | (11.70 to 18.64)                     | (15.58 to –10.35)*                                    |
| Tracheal, bronchus, and lung    | 155.24                    | 181.45                    | 16.88                               | 11.40                                                  |
| cancer                        | (111.10 to 204.17)         | (128.29 to 236.62)        | (13.29 to 20.48)                     | (14.19 to –8.74)*                                     |
| Ovarian cancer                 | 5.16                      | 6.02                      | 18.67                               | 3.75                                                   |
|                                | (2.58 to 7.94)             | (2.98 to 9.40)            | (9.65 to 23.13)                      | (40.54 to 128.84)                                     |
| Mesothelioma                   | 21.29                     | 27.61                     | 23.73                               | 15.76                                                  |
|                                | (19.16 to 22.57)           | (25.56 to 29.34)          | (5.59 to 23.79)                      | (41.32 to 481.26)                                     |
| Asthma                        | 2.89                      | 3.49                      | 21.00                               | 7.91                                                   |
|                                | (1.92 to 3.56)             | (2.43 to 4.06)            | (13.33 to 30.87)                     | (5.24 to 86.90)                                       |
| Occupational exposure to       | 6.55                      | 8.07                      | 22.67                               | 4.27                                                   |
| arsenic: all causes            | (1.52 to 11.97)            | (2.05 to 14.63)           | (13.28 to 35.03)                     | (15.21 to 35.43)                                      |
| Tracheal, bronchus, and lung    | 6.55                      | 8.07                      | 22.67                               | 4.27                                                   |
| cancer                        | (1.52 to 11.97)            | (2.05 to 14.63)           | (13.28 to 35.03)                     | (15.21 to 35.43)                                      |
| Occupational exposure to       | 1.63                      | 1.90                      | 16.21                               | 1.47                                                   |
| benzene: all causes            | (0.52 to 2.67)             | (0.60 to 12.10)           | (6.03 to 3.50)                       | (14.72 to 131.81)                                     |
| Leukaemia                      | 1.63                      | 1.90                      | 16.21                               | 1.47                                                   |
|                                | (0.52 to 2.67)             | (0.60 to 12.10)           | (6.03 to 3.50)                       | (14.72 to 131.81)                                     |
| Acute lymphoid leukaemia       | 0.28                      | 0.37                      | 32.70                               | 14.39                                                  |
|                                | (0.09 to 0.46)             | (0.11 to 0.62)            | (19.53 to 41.21)                     | (5.39 to 29.97)                                       |

(Continued from previous page)
### Global Health Metrics

| Disease                        | 2006 Deaths (in thousands) | 2016 Deaths (in thousands) | Percentage change of deaths 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|--------------------------------|-----------------------------|-----------------------------|-------------------------------------|---------------------------|---------------------------|----------------------------------|--------------------------------------------------------|
| Chronic lymphoid leukaemia     | 0.09                        | 0.11                        | 24·21                               | 0.43                      | 3.30                      | 4.07                             | 23·32                                                  | 1·98                                                   |
| Acute myeloid leukaemia        | 0.41                        | 0.54                        | 22·16                               | 11·07                     | 17·90                     | 23·24                            | 29·82                                                  | 11·51                                                  |
| Chronic myeloid leukaemia      | 0.15                        | 0.15                        | 4·79                                | -11·79                    | 6·60                      | 6·86                             | 4·04                                                   | -10·84                                                 |
| Other leukaemia                | 0.70                        | 0.71                        | 1·61                                | -13·30                    | 32·49                     | 31·62                            | -2·70                                                  | -15·49                                                 |
| Occupational exposure to beryllium: all causes | 0.20                        | 0.26                        | 28·93                               | -8·08                     | 5·76                      | 7·22                             | 25·48                                                  | -2·63                                                  |
| Tracheal, bronchus, and lung cancer | 0.20                        | 0.26                        | 28·93                               | -8·08                     | 5·76                      | 7·22                             | 25·48                                                  | -2·63                                                  |
| Occupational exposure to cadmium: all causes | 0.46                        | 0.61                        | 31·38                               | -1·00                     | 13·15                     | 16·83                            | 28·00                                                  | -0·75                                                  |
| Tracheal, bronchus, and lung cancer | 0.46                        | 0.61                        | 31·38                               | -1·00                     | 13·15                     | 16·83                            | 28·00                                                  | -0·75                                                  |
| Occupational exposure to chromium: all causes | 0.96                        | 1·28                        | 33·02                               | 2·28                      | 27·33                     | 35·45                            | 29·71                                                  | 0·57                                                   |
| Tracheal, bronchus, and lung cancer | 0.96                        | 1·28                        | 33·02                               | 2·28                      | 27·33                     | 35·45                            | 29·71                                                  | 0·57                                                   |
| Occupational exposure to diesel engine exhaust: all causes | 13·41                      | 17·50                        | 30·45                               | 0·26                      | 381·69                    | 485·69                           | 27·25                                                  | -1·40                                                  |
| Tracheal, bronchus, and lung cancer | 13·41                      | 17·50                        | 30·45                               | 0·26                      | 381·69                    | 485·69                           | 27·25                                                  | -1·40                                                  |
| Lower respiratory infections   | 25·22                       | 31·03                       | 27·03                               | -3·05                     | 75·30                     | 100·93                           | 19·56                                                  | -4·55                                                  |
| Otitis media                   | 0·00                        | 0·00                        | 0·00                                | -2·69                     | 0·00                      | 0·00                             | 0·00                                                   | -2·69                                                  |
| Tracheal, bronchus, and lung cancer | 36·79                      | 44·38                       | 20·63                               | -7·23                     | 1009·34                   | 1385·42                          | 17·45                                                  | -9·21                                                  |
| Breast cancer                  | 3·93                        | 4·86                        | 23·68                               | -3·23                     | 131·38                    | 160·49                           | 22·16                                                  | -3·10                                                  |
| Ischaemic heart disease        | 145·11                      | 172·73                      | 22·33                               | -4·86                     | 4427·58                   | 5337·92                          | 20·56                                                  | -4·76                                                  |
| Ischaemic stroke               | 24·76                       | 28·32                       | 16·84                               | -4·90                     | 3270·63                   | 3665·16                          | 892·52                                                  | -8·13                                                  |
| Haemorrhagic stroke            | 52·28                       | 58·76                       | 8·39                                | -19·19                    | 1579·51                   | 1787·34                          | 17·17                                                  | -14·80                                                 |
| Chronic obstructive pulmonary disease | 48·15                      | 51·90                       | 7·78                                | -17·01                    | 1570·14                   | 1819·99                          | 15·91                                                  | -10·63                                                 |
| Diabetes mellitus              | 27·71                       | 38·64                       | 39·45                               | 7·38                      | 1738·30                   | 2376·30                          | 36·70                                                  | 7·55                                                   |

(Continued from previous page)
### Global Health Metrics

(Continued from previous page)

| 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of age-standardised DALYs rate 2006–16 |
|----------------------------|-----------------------------|------------------------------------|--------------------------------------------------------|-----------------------------|-----------------------------|--------------------------------------------------------|
| 4 Occupational exposure to formaldehyde: all causes | 0.95 | 1.09 | 13.89 | (-4.03) | 42.70 | 46.93 | (9.90) | (1.78 to 18.05)* | (-5.67) | (-12.09 to 0.77) |
| Nasopharynx cancer | 0.42 | 0.48 | 13.08 | (-6.37) | 17.57 | 19.02 | 8.25 | (-5.73 to 24.38) | -8.78 | (-19.03 to 3.13) |
| Acute lymphoid leukaemia | 0.09 | 0.13 | 34.88 | 16.60 | 4.72 | 6.21 | 31.43 | 15.52 |
| Chronic lymphoid leukaemia | 0.02 | 0.03 | 30.39 | 7.25 | 0.95 | 1.22 | 27.96 | 7.86 |
| Acute myeloid leukaemia | 0.11 | 0.15 | 35.38 | 15.11 | 5.06 | 6.70 | 32.57 | 14.91 |
| Chronic myeloid leukaemia | 0.04 | 0.05 | 6.23 | -8.99 | 2.05 | 2.15 | 4.77 | (-9.72) |
| Other leukaemia | 0.26 | 0.26 | -1.61 | -15.54 | 12.35 | 11.64 | -5.80 | (-17.95) |
| Occupational exposure to nickel: all causes | 6.68 | 8.10 | 31.63 | (-6.73) | 187.01 | 221.35 | 18.37 | (-8.40) |
| Trachea, bronchus, and lung cancer | 6.68 | 7.54 | 31.63 | (-6.73) | 187.01 | 221.35 | 18.37 | (-8.40) |
| 4 Occupational exposure to polycyclic aromatic hydrocarbons: all causes | 3.41 | 4.58 | 32.92 | 2.21 | 97.03 | 125.78 | 29.86 | 5.51 |
| Trachea, bronchus, and lung cancer | 3.41 | 4.58 | 32.92 | 2.21 | 97.03 | 125.78 | 29.86 | 5.51 |
| 4 Occupational exposure to silica: all causes | 50.95 | 58.40 | 14.63 | (-16.90 to -8.34)* | (82.37 to 111.83) | (105.37 to 145.87) | (22.76 to 35.89)* | (-4.95 to 4.55) |
| Trachea, bronchus, and lung cancer | 40.38 | 48.00 | 18.88 | (-8.64) | 112.37 | 130.95 | 16.61 | (-10.26) |
| Silicosis | 10.57 | 10.40 | -1.60 | -24.35 | 273.19 | 270.62 | -0.94 | -22.15 |
| 4 Occupational exposure to sulfuric acid: all causes | 2.96 | 3.54 | 19.47 | -12.96 | 89.85 | 89.85 | 105.23 | 17.12 |
| Larynx cancer | 2.96 | 3.54 | 19.47 | -12.96 | 89.85 | 89.85 | 105.23 | 17.12 |
| 4 Occupational exposure to trichloroethylene: all causes | 0.04 | 0.06 | 48.91 | 14.75 | 1.17 | 1.72 | 47.21 | 14.65 |
| Kidney cancer | 0.04 | 0.06 | 48.91 | 14.75 | 1.17 | 1.72 | 47.21 | 14.65 |
| Occupational asthma: all causes | 36.83 | 37.57 | 2.02 | -19.40 | 212.64 | 239.48 | 20.22 | -8.91 |
| Asthma | 36.83 | 37.57 | 2.02 | -19.40 | 212.64 | 239.48 | 20.22 | -8.91 |
| Occupational particulate matter, gases, and fumes: all causes | 407.53 | 424.27 | 4.11 | -21.37 | 877.11 | 937.10 | 6.91 | -17.84 |
| Chronic obstructive pulmonary disease | 399.93 | 416.88 | 4.19 | -21.32 | 855.06 | 915.45 | 6.98 | -17.82 |
| (Table 4 continues on next page)
### Global Health Metrics

| 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|---------------------------|---------------------------|-------------------------------------|---------------------------------------------------------|---------------------------|---------------------------|------------------------------------|---------------------------------------------------------|
| **3 Occupational injuries: all causes** | | | | | | | | |
| Coal workers pneumocionosis | 3.03 | 2.68 | -11.29 | -13.16 | 87.45 | 89.05 | 1.83 | -16.65 |
| Other pneununocionosis | 4.57 | 4.91 | -7.72 | -13.16 | 126.59 | 122.51 | 3.48 | -16.65 |
| **3 Occupational noise: all causes** | | | | | | | | |
| Pedestrian road injuries | 6.71 | 6.97 | -4.53 | -15.16 | 343.81 | 327.98 | -4.54 | -16.52 |
| Cyclist road injuries | 9.32 | 9.99 | -6.16 | -20.16 | 673.49 | 701.70 | -4.04 | -21.66 |
| **Motorcyclist road injuries** | | | | | | | | |
| Other transport injuries | 14.25 | 13.71 | -3.74 | -15.70 | 87.90 | 96.99 | -10.19 | -12.66 |
| **Falls** | | | | | | | | |
| Falls | 38.58 | 39.52 | -2.62 | -16.00 | 339.45 | 321.95 | -5.95 | -16.00 |
| **Drowning** | | | | | | | | |
| Drowning | 29.91 | 26.74 | -10.60 | -20.34 | 155.83 | 136.45 | -12.41 | -21.39 |
| **Poisonings** | | | | | | | | |
| Poisonings | 6.69 | 5.85 | -12.57 | -16.00 | 351.08 | 313.70 | -10.65 | -20.53 |
| Unintentional firearm injuries | 4.19 | 3.83 | -8.61 | -16.00 | 253.51 | 240.12 | -5.28 | -15.61 |
| Unintentional suffocation | 0.77 | 0.92 | -19.08 | -16.00 | 4.58 | 6.06 | 20.23 | 2.43 |
| Other exposure to mechanical forces | 17.58 | 15.29 | -12.04 | -16.00 | 129.58 | 129.07 | -0.91 | -12.26 |
| Venounous animal contact | 6.92 | 5.66 | -18.20 | -16.00 | 446.07 | 389.47 | -12.69 | -23.84 |
| Non-venounous animal contact | 1.47 | 1.32 | -11.77 | -16.00 | 122.37 | 116.27 | -5.44 | -17.63 |
| Pulmonary aspiration and foreign body in airway | 5.70 | 6.15 | -8.00 | -16.00 | 368.29 | 400.80 | 8.82 | -11.16 |

(Continued from previous page)

(2006 deaths in thousands, 2016 deaths in thousands, Percentage change of deaths 2006–16, Percentage change of age-standardised deaths rate 2006–16, 2006 DALYs in thousands, 2016 DALYs in thousands, Percentage change of DALYs 2006–16, Percentage change of age-standardised DALYs rate 2006–16, Global Health Metrics, www.thelancet.com, Vol 390 September 16, 2017)
| 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006-16 | 2006 DALYS (in thousands) | 2016 DALYS (in thousands) | Percentage change of age-standardised deaths rate 2006-16 | Percentage change of age-standardised DALYS rate 2006-16 |
|-----------------------------|-----------------------------|-------------------------------------|---------------------------|---------------------------|-----------------------------------------------------|-----------------------------------------------------|
| 3 Child growth failure: all causes | 22339.17 (21227.31 to 23419.19) | 21830.19 (20450.24 to 23141.22) | -2.51 (-4.89 to -0.33)* | 910996.12 (869499.72 to 933010.97) | 781105.69 (737913.69 to 830667.54) | -14.26 (-16.59 to -11.83)* |
| 2 Child and maternal malnutrition: all causes | 4104.09 (4107.68 to 4499.13) | 2775.96 (2573.81 to 2904.34) | -36.37 (-39.81 to -32.52)* | 405715.03 (385444.16 to 429424.87) | 275068.98 (255317.96 to 296600.82) | -32.37 (-36.04 to -28.67)* |
| 3 Suboptimal breastfeeding: all causes | 278.09 (122.03 to 532.55) | 152.48 (124.06 to 183.65) | -45.17 (-50.75 to -38.89)* | 24214.14 (19400.12 to 28498.90) | 13733.25 (10878.18 to 16807.13) | -44.77 (-50.34 to -38.57)* |
| 4 Non-exclusive breastfeeding: all causes | 264.29 (114.11 to 318.37) | 144.11 (116.23 to 173.92) | -45.45 (-51.08 to -39.34)* | 29727.14 (18284.60 to 76714.42) | 15798.41 (10160.91 to 51944.04) | -45.16 (-50.76 to -39.06)* |
| 1 Behavioural risks: all causes | 180.62 (122.18 to 260.77) | 88.76 (68.74 to 111.24) | -47.67 (-54.86 to -39.28)* | 14810.81 (11518.55 to 18077.32) | 7821.54 (6057.18 to 9801.86) | -47.19 (-54.37 to -38.91)* |
| 2 Child and maternal malnutrition: all causes | 126.16 (112.18 to 200.77) | 75.66 (65.96 to 111.24) | -35.45 (-38.81 to -32.52)* | 11233.51 (9491.35 to 14725.33) | 6528.56 (5276.50 to 8901.86) | -35.45 (-38.81 to -32.52)* |
| 4 Discontinued breastfeeding: all causes | 167.00 (104.00 to 299.00) | 104.00 (64.66 to 146.66) | -39.90 (-48.41 to -29.27)* | 14906.69 (9343.34 to 20619.99) | 9249.24 (3325.52 to 16649.99) | -37.99 (-46.40 to -27.87)* |
| 3 Child growth failure: all causes | 107.00 (107.00 to 119.00) | 107.00 (107.00 to 119.00) | -46.10 (-51.03 to -40.34)* | 146740.87 (146740.87 to 146740.87) | 146740.87 (146740.87 to 146740.87) | -46.10 (-51.03 to -40.34)* |
| 4 Child and maternal malnutrition: all causes | 815.18 (535.40 to 776.56) | 312.61 (266.20 to 389.00) | -49.18 (-55.81 to -39.28)* | 55627.11 (46807.75 to 69301.37) | 30088.73 (25246.30 to 36312.38) | -45.05 (-54.35 to -38.98)* |
| 3 Child growth failure: all causes | 815.18 (535.40 to 776.56) | 312.61 (266.20 to 389.00) | -49.18 (-55.81 to -39.28)* | 55627.11 (46807.75 to 69301.37) | 30088.73 (25246.30 to 36312.38) | -45.05 (-54.35 to -38.98)* |
| 3 Child growth failure: all causes | 127.09 (100.36 to 161.58) | 52.67 (40.79 to 66.71) | -58.56 (-64.86 to -51.39)* | 11105.27 (8743.61 to 14996.57) | 4690.97 (9642.28 to 5935.54) | -57.90 (-64.06 to -50.68)* |
| 3 Child growth failure: all causes | 161.67 (110.46 to 282.27) | 74.94 (59.68 to 134.75) | -54.21 (-59.84 to -48.26)* | 14088.04 (9492.95 to 24135.07) | 4622.64 (2442.77 to 11542.06) | -59.01 (-64.06 to -50.68)* |
| 3 Child growth failure: all causes | 90.51 (19.16 to 218.56) | 18.86 (3.38 to 55.99) | -50.91 (-58.30 to -47.26)* | 7707.17 (1631.01 to 18583.17) | 1607.04 (-38.52 to -85.96) | -79.14 (-85.23 to -79.99) |
| 3 Child growth failure: all causes | 233.90 (206.48 to 265.01) | 106.14 (114.84 to 197.87) | -54.35 (-61.11 to -47.59)* | 22818.80 (20913.26 to 25430.39) | 17289.10 (18450.20 to 20449.29) | -24.20 (-30.00 to -18.97) |
| 3 Child growth failure: all causes | 1734.23 (1516.43 to 1927.79) | 952.40 (813.72 to 1078.99) | -45.08 (-51.43 to -39.05)* | 158212.32 (134415.84 to 169500.58) | 86155.42 (74499.95 to 97423.29) | -45.17 (-51.05 to -39.64)* |

(Continued from previous page)
Global Health Metrics

| 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|---------------------------|---------------------------|-------------------------------------|--------------------------------------------------------|---------------------------|---------------------------|-----------------------------------|-----------------------------------------------|
| **Lower respiratory infections** | **Lower respiratory infections** | **Measles** | **Protein-energy malnutrition** | **Child stunting: all causes** | **Diarrhoeal diseases** | **Diarrhoeal diseases** | **Measles** | **Lower respiratory infections** | **Short gestation for birth: all causes** | **Diarrhoeal diseases** | **Diarrhoeal diseases** | **Lower respiratory infections** | **Upper respiratory infections** | **Otitis media** | **Pneumococcal meningitis** | **H influenzae type B meningitis** | **Meningococcal infection** | **Other meningitis** | **Encephalitis** | **Neonatal preterm birth complications** |
| (548.14 to 830.75) | (298.47 to 479.06) | (–17·41) | (–65·74) | 710·19 | 713·89 | 608·42 | (46·98 to 71·153) | (–93·20 to –70·99) | (22·88 to 295·48) | (166·14 to 197·87) | (–46·97) | (–57·58) | 213·89 | (78·31 to 91·30) | (–54·83) | (–66·01 to 90·01) | (–57·20 to –39·05) | (120·26 to 152·82) | (–76·87) | (–77·76) | (324·80) | (–14·40) | 206·41 | (148·61 to 217·84) | (–57·57) | (–64·00 to –14·21) | (–55·51) | (–72·90 to –21·75) | (–15·86) | (–15·93) | (–65·69) | (–71·40) | (–57·43) | (–64·00 to –14·21) | 0·03 | (0·08 to 0·14) | (–65·69) | (–71·40) | (–57·43) | (–64·00 to –14·21) | 0·03 | (0·08 to 0·14) | (–65·69) | (–71·40) | (–57·43) | (–64·00 to –14·21) |
| (775·51) | (415·43) | (–38·82)* | (–66·01) | 701·19 | 710·19 | 608·42 | (46·98 to 71·153) | (–93·20 to –70·99) | (22·88 to 295·48) | (166·14 to 197·87) | (–46·97) | (–57·58) | 213·89 | (78·31 to 91·30) | (–54·83) | (–66·01 to 90·01) | (–57·20 to –39·05) | (120·26 to 152·82) | (–76·87) | (–77·76) | (324·80) | (–14·40) | 206·41 | (148·61 to 217·84) | (–57·57) | (–64·00 to –14·21) | (–55·51) | (–72·90 to –21·75) | (–15·86) | (–15·93) | (–65·69) | (–71·40) | (–57·43) | (–64·00 to –14·21) | 0·03 | (0·08 to 0·14) | (–65·69) | (–71·40) | (–57·43) | (–64·00 to –14·21) | 0·03 | (0·08 to 0·14) | (–65·69) | (–71·40) | (–57·43) | (–64·00 to –14·21) |
| (562·68 to 775·51) | (291·19 to 415·43) | (–54·62) | (–66·01) | 701·19 | 710·19 | 608·42 | (46·98 to 71·153) | (–93·20 to –70·99) | (22·88 to 295·48) | (166·14 to 197·87) | (–46·97) | (–57·58) | 213·89 | (78·31 to 91·30) | (–54·83) | (–66·01 to 90·01) | (–57·20 to –39·05) | (120·26 to 152·82) | (–76·87) | (–77·76) | (324·80) | (–14·40) | 206·41 | (148·61 to 217·84) | (–57·57) | (–64·00 to –14·21) | (–55·51) | (–72·90 to –21·75) | (–15·86) | (–15·93) | (–65·69) | (–71·40) | (–57·43) | (–64·00 to –14·21) | 0·03 | (0·08 to 0·14) | (–65·69) | (–71·40) | (–57·43) | (–64·00 to –14·21) | 0·03 | (0·08 to 0·14) | (–65·69) | (–71·40) | (–57·43) | (–64·00 to –14·21) |
| 681·26 | 335·50 | (–47·38) | (–66·01) | 701·19 | 710·19 | 608·42 | (46·98 to 71·153) | (–93·20 to –70·99) | (22·88 to 295·48) | (166·14 to 197·87) | (–46·97) | (–57·58) | 213·89 | (78·31 to 91·30) | (–54·83) | (–66·01 to 90·01) | (–57·20 to –39·05) | (120·26 to 152·82) | (–76·87) | (–77·76) | (324·80) | (–14·40) | 206·41 | (148·61 to 217·84) | (–57·57) | (–64·00 to –14·21) | (–55·51) | (–72·90 to –21·75) | (–15·86) | (–15·93) | (–65·69) | (–71·40) | (–57·43) | (–64·00 to –14·21) | 0·03 | (0·08 to 0·14) | (–65·69) | (–71·40) | (–57·43) | (–64·00 to –14·21) | 0·03 | (0·08 to 0·14) | (–65·69) | (–71·40) | (–57·43) | (–64·00 to –14·21) |

(Continued from previous page)
Global Health Metrics

| 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|---------------------------|---------------------------|------------------------------------|--------------------------------------------------------|---------------------------|---------------------------|---------------------------------|--------------------------------------------------------|
| Neonatal encephalopathy due to birth asphyxia and trauma | 477.77 (426.69 to 529.03) | 370.94 (322.96 to 419.15) | -22.36 (-29.79 to -14.93)* | -21.97 (-29.43 to -13.93)* | 413.71 (36.91 to 454.08) | 421.20 (37.96 to 435.29) | -22.36 (-29.79 to -14.93)* | -21.97 (-29.43 to -13.93)* |
| Neonatal sepsis and other neonatal infections | 170.34 (138.61 to 217.43) | 151.23 (126.64 to 206.06) | -11.22 (-21.77 to 2.78) | -10.86 (-21.43 to 3.20) | 147.94 (12.00 to 18.826) | 139.04 (10.964 to 17.842) | -11.22 (-21.77 to 2.78) | -10.86 (-21.43 to 3.20) |
| Haemolytic disease and other neonatal jaundice | 55.72 (48.90 to 64.54) | 32.45 (27.90 to 38.04) | -41.77 (-49.82 to -32.96)* | -41.52 (-49.61 to -32.68)* | 482.42 (423.44 to 557.98) | 280.49 (246.02 to 329.80) | -41.77 (-49.82 to -32.96)* | -41.52 (-49.61 to -32.68)* |
| Other neonatal disorders | 282.16 (250.52 to 317.48) | 197.44 (173.31 to 220.92) | -30.03 (-37.01 to -21.36)* | -29.69 (24.423.57 to 17.094) | 242.37 (15.006 to 19.130) | 21.73* (17.74 to 21.36)* | -30.03 (-37.01 to -21.36)* | -29.69 (24.423.57 to 17.094) |
| Sudden infant death syndrome | 1.98 (1.47 to 2.54) | 1.52 (1.16 to 1.87) | -23.02 (-39.72 to -8.37)* | -22.88 (-39.61 to -8.20)* | 171.26 (127.36 to 219.51) | 131.83 (100.77 to 161.72) | -23.02 (-39.72 to -8.37)* | -22.88 (-39.61 to -8.20)* |

4 Low birthweight for gestation: all causes

| Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | Percentage change of DALYs 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|------------------------------------|--------------------------------------------------------|---------------------------------|--------------------------------------------------------|
| -29.04 (-37.70 to -21.41)* | -28.69 (-33.28 to -23.94)* | -28.69 (304.96 to 178.73) | -28.69 (47.64 to 24.30)* |
| -60.94 (-66.12 to -55.24)* | -60.78 (-65.99 to -55.07)* | -60.78 (537.68 to 101.417) | -60.78 (65.99 to -55.24)* |
| -46.30 (-52.21 to -39.99)* | -46.06 (-51.39 to -39.72)* | -46.06 (216.54 to 418.61) | -46.06 (59.79 to -39.99)* |
| -44.27 (-44.75 to -11.69)* | -44.00 (-45.17 to -11.28)* | -44.00 (1.05 to 2.67) | -44.00 (64.57 to -11.27)* |
| -55.15 (-71.45 to -26.78)* | -55.00 (-71.80 to -26.52)* | -55.00 (0.09 to 0.25) | -55.00 (-71.80 to -26.52)* |
| -19.39 (-35.79 to 2.80)* | -19.04 (-35.49 to 3.25)* | -19.04 (6.55 to 11.749) | -19.04 (-35.49 to 3.25)* |
| -49.97 (-51.99 to 39.72)* | -49.71 (-51.89 to 27.21)* | -49.71 (29.05 to 45.47) | -49.71 (-51.89 to 27.21)* |
| -38.84 (-40.93 to -22.23)* | -38.58 (-40.72 to -22.88)* | -38.58 (69.35 to 161.06) | -38.58 (50.72 to -22.88)* |
| -5.58 (-23.60 to 18.81) | -5.19 (-23.30 to 19.32) | -5.19 (6.37 to 12.98) | -5.19 (-23.30 to 19.32) |
| -29.88 (-45.21 to 31.08)* | -29.59 (-44.57 to -10.70)* | -29.59 (11.22 to 24.41) | -29.59 (-44.57 to -10.70)* |
| -27.95 (-33.72 to -21.78)* | -27.60 (-33.41 to -21.78)* | -27.60 (66.730.52 to 78.805) | -27.60 (-33.41 to -21.78)* |
| -117.60 (-146.31 to 122.15)* | -117.60 (-146.31 to 122.15)* | -117.60 (55.713 to 179.32) | -117.60 (-146.31 to 122.15)* |
| -27.99 (-35.44 to -20.42)* | -27.62 (-35.10 to -20.01)* | -27.62 (10.183 to 1531) | -27.62 (-35.10 to -20.01)* |
| -35.49 (-39.12 to -25.00)* | -35.40 (-40.31 to -25.00)* | -35.40 (50.566 to 10.049) | -35.40 (-40.31 to -25.00)* |
| -132.69 (-157.43 to 112.15)* | -132.69 (-157.43 to 112.15)* | -132.69 (1531 to 4071) | -132.69 (-157.43 to 112.15)* |
| -17.74 (-24.13 to 8.87)* | -17.34 (-25.17 to 11.85)* | -17.34 (8.87 to 24.13) | -17.34 (-25.17 to 11.85)* |
| -257.90 (27.96 to 26.95)* | -257.90 (27.96 to 26.95)* | -257.90 (379.8 to 379.8) | -257.90 (27.96 to 26.95)* |
| -16.34 (-28.32 to -2.51)* | -16.34 (-28.32 to -2.51)* | -16.34 (2400 to 2400) | -16.34 (-28.32 to -2.51)* |
| -29.67 (-53.03 to -34.47)* | -29.67 (-53.03 to -34.47)* | -29.67 (3378.49) | -29.67 (-53.03 to -34.47)* |

(Continued from previous page)
### Global Health Metrics

| 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|---------------------------|-----------------------------|--------------------------------------|-----------------------------------------------------------|---------------------------|-----------------------------|----------------------------------|----------------------------------------------------------|
| **Global Health Indicators** |                             |                                      |                                                            |                           |                             |                                   |                                                          |
| **Lower respiratory infections** |                             |                                      |                                                            |                           |                             |                                   |                                                          |
| Other neonatal disorders | 65.24                       | 42.37                                | -35.06                                                     | -34.73                    | 56.49                       | 31.69                             | -35.06                                    | -34.73                                                     |
| Sudden infant death syndrome | 0.19                        | 0.14                                 | 28.09                                                      | -27.96                    | 16.64                       | 11.97                             | -27.96                                    | -28.38                                                     |
| Vitamin A deficiency |                                     |                                      |                                                            |                           |                             |                                   |                                                          |
| Iron deficiency | 22.01                        | 14.10                                | -35.97                                                     | -35.34                    | 32.54                       | 22.72                             | -35.34                                    | -35.05                                                     |
| Maternal haemorrhage | 7.33                          | 5.33                                 | -28.00                                                     | -28.60                    | 7.99                        | 9.40                              | -28.60                                    | -28.14                                                     |
| Maternal and other pregnancy-related infections | 5.04                          | 3.89                                 | -29.86                                                     | -39.85                    | 32.54                       | 22.72                             | -39.85                                    | -39.35                                                     |
| Vitamin A deficiency |                                     |                                      |                                                            |                           |                             |                                   |                                                          |
| Zinc deficiency | 5.32                          | 2.59                                 | -52.95                                                     | -52.45                    | 5.53                        | 4.65                              | -52.45                                    | -52.05                                                     |
| Diarrhoeal diseases | 64.17                         | 30.04                                | -53.18                                                     | -53.52                    | 52.80                       | 26.50                             | -53.52                                    | -53.05                                                     |
| Measles | 44.23                         | 12.14                                | -72.55                                                     | -73.85                    | 375.95                      | 103.71                            | -73.85                                    | -73.38                                                     |
| Vitamin A deficiency |                                     |                                      |                                                            |                           |                             |                                   |                                                          |
| Tobacco: all causes | 6853.45                       | 7131.38                               | -20.37                                                      | -20.68                    | 152.265                     | 152.065                           | -20.68                                    | -20.43                                                     |
| Smoking: all causes | 6081.95                       | 5673.66                               | -20.68                                                     | -22.82                    | 138.408                     | 167.888                           | -22.82                                    | -22.45                                                     |
| Drug-susceptible tuberculosis | 129.07                     | 90.24                                | -29.60                                                     | -30.20                    | 420.53                      | 57.38                             | -30.20                                    | -30.01                                                     |
| Multidrug-resistant tuberculosis | 14.07                      | 8.19                                 | -41.90                                                     | -53.46                    | 458.79                      | 257.57                            | -53.46                                    | -53.05                                                     |
| Extensively drug-resistant tuberculosis | 0.92                        | 0.33                                 | -62.00                                                     | -62.75                    | 5.53                        | 2.15                              | -62.75                                    | -62.36                                                     |
| Lower respiratory infections | 326.00                       | 345.94                                | -5.12                                                      | -9.55                     | 700.64                       | 702.96                            | -9.55                                     | -9.33                                                      |

(Continued from previous page)
| Cancer Type                          | 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|-------------------------------------|-----------------------------|-----------------------------|-------------------------------------|--------------------------------------------------------|-----------------------------|-----------------------------|-----------------------------------|-----------------------------------|
| Lip and oral cavity cancer          | 51·72                       | 64·11                       | 23·95                               | -4·81                                                  | 1339·05                     | 1698·72                     | -19·07                            | -6·71                                      |
| Nasopharynx cancer                  | 21·46                       | 22·33                       | 4·05                                | -18·25                                                 | 635·38                      | 618·24                     | -2·70                             | -22·14                                      |
| Oesophageal cancer                  | 144·04                      | 144·40                      | 0·25                                | -23·33                                                 | 1249·88                     | 3104·99                     | -44·6                           | -25·91                                      |
| Stomach cancer                      | 86·47                       | 78·50                       | -9·21                               | -30·05                                                 | 2072·43                     | 1668·26                     | -19·96                            | -34·01                                      |
| Colon and rectum cancer             | 46·29                       | 49·01                       | 5·88                                | -19·96                                                 | 973·58                      | 963·00                      | -1·00                            | -21·19                                      |
| Liver cancer due to hepatitis B     | 41·56                       | 43·39                       | -1·77                               | -24·42                                                 | 2256·72                     | 2164·10                     | -4·76                             | -28·84                                      |
| Liver cancer due to hepatitis C     | 19·24                       | 22·01                       | 14·35                               | -12·81                                                 | 414·97                      | 448·80                      | 8·15                             | -16·20                                      |
| Liver cancer due to alcohol use      | 14·69                       | 16·71                       | 13·74                               | -12·48                                                 | 343·61                      | 377·43                      | 9·84                             | -14·44                                      |
| Liver cancer due to other causes     | 24·71                       | 26·42                       | 6·90                                | -15·62                                                 | 683·22                      | 662·38                      | -3·05                            | -21·80                                      |
| Pancreatic cancer                   | 61·47                       | 70·90                       | 15·34                               | -12·20                                                 | 1315·34                     | 1431·38                     | 8·86                             | -15·66                                      |
| Larynx cancer                       | 60·04                       | 64·92                       | 8·14                                | -17·06                                                 | 1524·37                     | 1596·46                     | 4·73                             | -18·86                                      |
| Trachea, bronchus, and lung cancer  | 1014·39                     | 1144·75                     | 12·85                               | -13·53                                                 | 22049·05                    | 2370·41                     | 7·28                             | -18·15                                      |
| Breast cancer                       | 16·88                       | 17·91                       | 6·11                                | -18·14                                                 | 457·80                      | 452·41                      | -1·18                            | -21·43                                      |
| Cervical cancer                     | 11·03                       | 10·85                       | -1·66                               | -22·54                                                 | 331·91                      | 306·32                      | -7·18                            | -25·19                                      |
| Prostate cancer                     | 15·29                       | 16·68                       | 9·09                                | -19·29                                                 | 257·95                      | 268·27                      | -4·00                            | -25·25                                      |
| Kidney cancer                       | 20·10                       | 22·07                       | 9·79                                | -16·07                                                 | 464·77                      | 480·06                      | 3·29                             | -19·84                                      |
| Bladder cancer                      | 44·33                       | 49·84                       | 12·42                               | -15·76                                                 | 820·50                      | 867·04                      | 5·67                             | -19·01                                      |
| Acute lymphoid leukaemia            | 2·45                        | 2·66                        | 8·51                                | -14·18                                                 | 74·37                       | 77·25                       | 3·87                             | -16·04                                      |
| Chronic lymphoid leukaemia          | 4·32                        | 4·69                        | -3·63                               | -21·24                                                 | 81·77                       | 81·18                       | -0·73                            | -21·72                                      |
| Acute myeloid leukaemia             | 7·27                        | 8·00                        | 10·07                               | -14·79                                                 | 174·17                      | 182·46                      | 4·76                             | -17·20                                      |

(Continued from previous page)
| Condition                          | 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of age-standardised DALYs rate 2006–16 |
|-----------------------------------|----------------------------|----------------------------|--------------------------------------|---------------------------|---------------------------|---------------------------------------------|
| - Chronic myeloid leukaemia       | 2.27                       | 1.92                       | -15.62 (-22.48 to -8.89)*             | 56.81                     | 45.30                     | -20.26 (-27.97 to -13.34)*                |
| - Other leukaemia                 | 8.73                       | 8.74                       | 0.00 (-21.85 to -21.85)               | 220.47                    | 198.49                    | -8.97 (-21.62 to 13.39)                  |
| - Ischaemic heart disease         | 13.64                      | 13.91                      | 2.07 (-12.96 to -17.24)*              | 36.051                    | 36.302                    | -0.70 (-2.92 to 4.82)                     |
| - Ischaemic stroke                | 350.47                     | 347.05                     | -0.98 (-15.13 to 3.31)                | 8972.51                   | 9235.11                   | 2.93 (1.37 to 6.94)                      |
| - Haemorrhagic stroke             | 574.87                     | 535.26                     | -6.93 (-30.41 to -25.36)*             | 16.024.57                 | 14.873.84                 | -7.18 (-10.27 to -4.08)                  |
| - Hypertensive heart disease      | 92.58                      | 104.36                     | 12.72 (-23.84 to -4.65)*              | 2418.95                   | 2611.14                   | 7.95 (-2.72 to 17.63)                     |
| - Attnal fibrillation and flutter | 11.78                      | 14.23                      | 20.80 (16.34 to 24.92)*               | 616.54                    | 710.44                    | 15.23 (12.91 to 17.40)*                  |
| - Aortic aneurysy                 | 22.06                      | 22.71                      | 2.92 (-2.08 to 9.42)                  | 554.61                    | 560.44                    | 1.05 (-4.19 to 8.10)                     |
| - Peripheral vascular disease     | 4.59                       | 5.12                       | 11.65 (-50.30 to 26.59)               | 148.14                    | 163.17                    | 10.14 (0.93 to 20.74)*                   |
| - Other cardiovascular and       | 53.33                      | 55.64                      | 4.33 (-19.55 to -19.55)               | 1998.90                   | 2084.86                   | 4.60 (0.52 to 8.39)*                     |
| - Chronic obstructive pulmonary  | 1190.52                     | 1253.30                    | 5.27 (-26.38 to -15.51)*              | 23697.75                  | 25095.91                   | 5.83 (-0.06 to 13.85)                    |
| - Asthma                          | 65.36                      | 56.81                      | -13.08 (-38.71 to -26.92)*            | 2444.85                   | 2291.51                   | -6.27 (-12.71 to -0.11)                  |
| - Other chronic respiratory       | 3.07                       | 3.77                       | 22.95 (-12.82 to 1.88)                | 1031.00                   | 126.04                    | 22.36 (12.41 to 32.01)*                  |
| - Peptic ulcer disease            | 43.27                      | 36.14                      | -16.48 (-35.23 to -5.24)*             | 882.23.13                 | 1539.63                   | -16.15 (-20.61 to -11.83)*               |
| - Gallbladder and biliary         | 2.22                       | 2.32                       | 4.66 (-30.43 to -5.24)*               | 54.26                     | 55.54                     | 2.36 (-2.84 to 7.48)                     |
| - Alzheimer's disease and         | 67.57                      | 82.08                      | 15.52 (-15.11 to -15.45)              | 1020.60                   | 1265.05                   | 18.19 (12.39 to 22.10)*                  |
| - Parkinson's disease             | -20.15                     | -23.16                     | 14.93 (-16.05 to -9.98)*              | -402.98                   | -461.19                   | 14.16 (-10.52 to 17.80)*                 |
| - Multiple sclerosis              | 1.70                       | 1.68                       | -0.89 (-21.16 to 21.16)               | 98.79                     | 99.08                     | 0.29 (-5.43 to 4.75)                     |
| - Diabetes mellitus               | 56.47                      | 66.30                      | 17.40 (-9.87 to 21.43)*               | 2881.41                   | 3192.65                   | 10.80 (-12.37)                           |
| - Rheumatoid arthritis           | 1.45                       | 1.37                       | -6.01 (-33.59 to -24.03)*             | 224.49                     | 241.06                   | -7.38 (4.34 to 9.34)                     |

(Continued from previous page)
| Category (Continued from previous page) | 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|----------------------------------------|-----------------------------|-----------------------------|------------------------------------|-----------------------------------|-----------------------------|-----------------------------|---------------------------------|----------------------------------|
| Low back pain                          | 2459 39                     | (1047 30 to 4016 91)        | -4.41                              | (1.74 to 7.02)*                  | 2567 74                      | (1082 41 to 4200 46)         | -14.98                          | (-17.00 to -13.33)*             |
| Cataract                               | 404 92                      | (261 96 to 595 50)          | 13.05                              | (9.89 to 16.35)*                 | 457 74                       | (295 38 to 678 21)           | -12.81                          | (-15.31 to -10.33)*             |
| Macular degeneration                   | 35 10                       | (10 74 to 63 30)            | 43.59                              | (13.27 to 79.98)                 | 241 13                       | (140 13 to 285 42)           | -6.46                           | (-10.16 to -3.27)*              |
| Smokeless tobacco: all                 | 4.26                        | (3.12 to 5.55)              | -22.32                             | (-27.66 to -18.89)*              | 192 70                       | (132 72 to 266 50)           | -10.61                          | (-19.72 to -12.60)*             |
| Cyclist road injuries                  | 0.66                        | (0.46 to 0.87)              | -21.59                             | (-27.08 to -15.18)*              | 88 95                        | (56 29 to 134 78)            | -13.26                          | (-10.82 to -6.20)*              |
| Motorcyclist road injuries             | 1.42                        | (0.98 to 1.92)              | -26.20                             | (-25.42 to -15.61)*              | 146 73                       | (93 33 to 217 75)            | 5.58                            | (2.29 to 8.25)*                 |
| Motor vehicle road injuries            | 3.42                        | (2.40 to 4.58)              | -24.68                             | (-28.27 to -18.07)*              | 220 30                       | (149 90 to 322 87)           | -18.53                          | (-21.35 to -15.12)*             |
| Other road injuries                    | 0.11                        | (0.08 to 0.15)              | -22.45                             | (-30.44 to -11.01)*              | 24 54                        | (20.60 to 54.65)             | 33.98                           | (26.47 to 42.74)*               |
| Other transport injuries               | 0.96                        | (0.69 to 1.23)              | -22.86                             | (-27.55 to -15.90)*              | 98 02                        | (63.60 to 141 42)            | -19.19                          | (-21.61 to -16.77)              |
| Falls                                  | 14.00                       | (11.19 to 20.28)            | -17.04                             | (-20.83 to -11.46)*              | 834 32                       | (556 29 to 1207 21)          | 11.15                           | (8.56 to 13.31)*                |
| Other exposure to mechanical forces    | 0.72                        | (0.50 to 0.93)              | -25.28                             | (-34.05 to -20.84)*              | 141 72                       | (85 67 to 229 57)            | -25.96                          | (-32.09 to -15.85)*             |
| Non-venomous animal contact            | 0.07                        | (0.04 to 0.08)              | -33.55                             | (-40.10 to -26.00)*              | 7 11                         | (3.79 to 10.64)              | -45.45                          | (-52.78 to -24.44)*             |
| Assault by other means                 | 0.49                        | (0.27 to 0.61)              | -32.36                             | (-42.05 to -16.11)*              | 79 58                        | (48.44 to 125 25)            | -25.52                          | (-23.97 to -17.23)*             |
| Forces of nature, conflict and terrorism, and state actor violence | 0.05 | (0.01 to 0.03) | -68.62 | (-74.92 to -58.85)* | 73.22 | (289 36 to 522 28) | -33.80 | (-17.96 to -30.60)* |
| 3 Smokeless tobacco: all causes        | 39.05                       | (20 22 to 48.82)            | -4.58                              | (-11.36 to 1.82)                 | 1063 08                      | (872 62 to 1258 43)          | -6.49                           | (-12.92 to -0.38)*              |
| Lip and oral cavity cancer             | 25.14                       | (19.77 to 30.36)            | -2.15                              | (-3.99 to 6.14)                  | 697 47                       | (540 47 to 849 10)           | -24.66                          | (-12.41 to 31.49)*              |
| Oesophageal cancer                     | 13.91                       | (10.12 to 17.58)            | -10.58                             | (-16.11 to -4.51)*               | 306 61                       | (264 21 to 464 10)           | -10.64                          | (-17.96 to -6.30)*              |
| 3 Second-hand smoke: all causes        | 8.68                        | (6.64 to 10.47)             | 4.45                               | (0.25 to 8.62)*                  | 202 46                       | (121 77 to 343 69)           | -10.49                          | (-28.47 to -20.00)*             |
| Lower respiratory infections           | 1.28                        | (0.92 to 1.75)              | -31.09                             | (-34.53 to -27.75)*              | 10 893.99                    | (553 74 to 16 883.74)        | -43.39                          | (-47.17 to -39.63)*             |
| Otitis media                           | -0.09                       | (0.05 to 0.14)              | -58.53                             | (-73.68 to -36.05)*              | 215 81                       | (122 39 to 368 54)           | -10.69                          | (-13.55 to -8.35)*              |

(Table 4 continues on next page)
(Continued from previous page)

| Disease/Condition                        | 2016 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | 2006 DALYs (in thousands) | 2016 DALYS (in thousands) | Percentage change of DALYS 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|------------------------------------------|----------------------------|----------------------------|-------------------------------------|----------------------------------------------------------|---------------------------|---------------------------|-----------------------------------|----------------------------------------------------------|
| - Tracheal, bronchus, and lung cancer    | 22.02                      | 27.35                      | 24.20                               | -8.85                                                    | 508.53                    | 615.93                    | 21.12                             | -5.79                                                    |
| - Breast cancer                          | 9.27                       | 10.30                      | 11.10                               | -13.39                                                   | 287.48                    | 313.04                    | 8.89                              | -12.87                                                   |
| - Ischaemic heart disease                | 280.21                     | 327.35                     | 16.82                               | -6.76                                                    | 572.26                    | 675.01                    | 13.54                             | -8.44                                                    |
| - Ischaemic stroke                       | 73.09                      | 75.15                      | 2.82                                | -13.72                                                   | 1420.64                   | 1493.54                   | 5.13                              | -19.63                                                   |
| - Haemorrhagic stroke                    | 95.38                      | 90.24                      | -5.29                               | -14.18                                                   | 2278.60                   | 2144.62                   | -5.88                             | -26.29                                                   |
| - Chronic obstructive pulmonary disease  | 117.45                     | 119.62                     | 1.85                                | -25.95                                                   | 2373.48                   | 2496.53                   | 5.18                              | -19.35                                                   |
| - Diabetes mellitus                      | 72.64                      | 95.33                      | 31.27                               | -5.07                                                    | 2809.38                   | 2851.43                   | 22.91                             | -2.47                                                    |
| - Extensively drug-resistant tuberculosis| 2.44                       | 3.98                       | 63.02                               | -28.98                                                   | 91.46                     | 140.71                    | 52.84                             | -28.98                                                   |
| - Lower respiratory infections           | 97.10                      | 113.58                     | 16.97                               | -3.81                                                    | 921.70                    | 1196.09                   | 31.13                             | -15.00                                                   |
| - Lip and oral cavity cancer             | 49.44                      | 66.24                      | 33.98                               | -1.95                                                    | 1217.72                   | 820.14                    | -32.65                             | -43.80                                                   |
| - Nasopharynx cancer                     | 24.19                      | 28.38                      | 17.33                               | -7.62                                                    | 758.75                    | 843.69                    | 11.19                             | -10.61                                                   |
| - Other pharynx cancer                   | 33.86                      | 46.29                      | 36.70                               | -13.49                                                   | 970.39                    | 1285.14                   | 32.43                             | -3.89                                                    |
| - Oesophageal cancer                     | 116.52                     | 120.56                     | 12.08                               | -4.03                                                    | 283.24                    | 305.59                    | 7.56                              | -16.61                                                   |
| - Colon and rectum cancer                | 97.08                      | 116.81                     | 20.33                               | -8.33                                                    | 2172.68                   | 2544.90                   | 17.13                             | -9.24                                                    |
| - Liver cancer due to alcohol use        | 99.05                      | 129.18                     | 30.41                               | -0.01                                                    | 281.36                    | 2924.48                   | 28.19                             | -0.56                                                    |

2 Alcohol and drug use: all causes

| Alcohol use: all causes                  | 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | 2006 DALYs (in thousands) | 2016 DALYS (in thousands) | Percentage change of DALYS 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|------------------------------------------|----------------------------|----------------------------|-------------------------------------|----------------------------------------------------------|---------------------------|---------------------------|-----------------------------------|----------------------------------------------------------|
| - 2605.72                                | 281.64                     | 281.64                     | -0.01                               | -18.64                                                   | 9619.07                   | 9920.89                   | 3.13                              | -15.00                                                   |
| - Drug-susceptible tuberculosis          | 705.97                     | 752.60                     | -6.37                               | -3.96                                                    | 1028.96                   | 1027.85                   | -0.91                             | -3.92                                                    |
| - Chronic obstructive pulmonary disease  | 75.32                      | 75.45                      | -0.00                               | -28.64                                                   | 1126.98                   | 1126.90                   | -0.00                             | -28.64                                                   |
| - Multidrug-resistant tuberculosis       | 11.12                      | 11.12                      | -0.00                               | -28.64                                                   | 1126.98                   | 1126.90                   | -0.00                             | -28.64                                                   |
| - Extensively drug-resistant tuberculosis| 2.44                       | 3.98                       | 63.02                               | -28.98                                                   | 91.46                     | 140.71                    | 52.84                             | -28.98                                                   |

3 Alcohol use: all causes

| Alcohol use: all causes                  | 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | 2006 DALYs (in thousands) | 2016 DALYS (in thousands) | Percentage change of DALYS 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|------------------------------------------|----------------------------|----------------------------|-------------------------------------|----------------------------------------------------------|---------------------------|---------------------------|-----------------------------------|----------------------------------------------------------|
| - 2605.72                                | 281.64                     | 281.64                     | -0.01                               | -18.64                                                   | 9619.07                   | 9920.89                   | 3.13                              | -15.00                                                   |
| - Drug-susceptible tuberculosis          | 705.97                     | 752.60                     | -6.37                               | -3.96                                                    | 1028.96                   | 1027.85                   | -0.91                             | -3.92                                                    |
| - Chronic obstructive pulmonary disease  | 75.32                      | 75.45                      | -0.00                               | -28.64                                                   | 1126.98                   | 1126.90                   | -0.00                             | -28.64                                                   |
| - Multidrug-resistant tuberculosis       | 11.12                      | 11.12                      | -0.00                               | -28.64                                                   | 1126.98                   | 1126.90                   | -0.00                             | -28.64                                                   |
| - Extensively drug-resistant tuberculosis| 2.44                       | 3.98                       | 63.02                               | -28.98                                                   | 91.46                     | 140.71                    | 52.84                             | -28.98                                                   |

(Continued from previous page)
Global Health Metrics

(Continued from previous page)

| Disease                        | 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|-------------------------------|-----------------------------|-----------------------------|-------------------------------------|----------------------------------------------------------|---------------------------|---------------------------|-------------------------------------|----------------------------------------------------------|
| Larynx cancer                 | 29.80                       | 11.58                       | -14.18                              | (-18.81 to -9.19)*                                      | 709.81                    | 764.38                    | 7.69                                | (-16.32)                                                 |
| Breast cancer                 | 32.22                       | 12.31                       | -14.02                              | (-18.98 to -8.03)*                                     | 1443.76                   | 1565.91                   | 8.46                                | (-14.40)                                                 |
| Ischaemic heart disease       | -24.32                      | -14.97                      | -14.97                              | (-25.08 to -8.03)*                                     | 767.37                    | 1084.03                   | 41.27                               | (-19.77 to -8.23)*                                      |
| Ischaemic stroke              | 31.24                       | -11.74                      | -22.99                              | (-19.40 to -13.60)                                     | 2588.68                   | 2930.95                   | 16.83                               | (-10.07)                                                 |
| Haemorrhagic stroke           | 41.79                       | 24.93                       | -36.44                              | (-32.48 to -28.96)*                                    | 10194.7                    | 997.29                     | 5.71                                | (-16.87)                                                 |
| Hypertensive heart disease    | 14.84                       | 1.92                        | -12.14                              | (-12.24 to 12.00)                                      | 1987.17                    | 2547.33                   | 28.19                               | (-0.64)                                                  |
| Alcoholic cardiomyopathy      | 63.48                       | 47.06                       | -28.74                              | (-36.79 to -7.35)*                                     | 2877.83                    | 2590.34                   | 9.99                                | (-26.31)                                                 |
| Atrial fibrillation and flutter| 32.14                       | 22.02                       | -30.50                              | (-37.75 to 7.02)*                                      | 542.25                     | 722.89                     | 33.31                               | (-9.64)                                                  |
| Cirrhosis and other chronic liver diseases due to alcohol use | 30.42                       | 28.76                       | -5.44                               | (-11.73 to 3.63)                                       | 1073.26                    | 1196.59                   | 11.28                               | (-8.13)                                                  |
| Pancreatitis                  | 31.98                       | 16.51                       | -46.59                              | (-59.09 to 29.89)*                                     | 507.26                     | 1196.59                   | 11.28                               | (-8.13)                                                  |
| Epilepsy                      | 22.02                       | 5.48                        | -74.92                              | (-66.54 to -13.11)                                     | 1810.40                    | 1903.17                   | 5.12                                | (-9.55)                                                  |
| Alcohol use disorders         | 317.82                      | 16.51                       | -15.35                              | (-16.62 to -4.66)*                                     | 1316.06                    | 1373.15                   | 5.12                                | (-17.15 to -16.0)                                      |
| Diabetes mellitus             | 28.01                       | 23.65                       | -16.52                              | (-24.30 to -9.70)                                      | 529.10                     | 712.23                     | 36.01                               | (-9.02)                                                  |
| Pedestrian road injuries      | 18.41                       | 9.02                        | -50.00                              | (-57.05 to 19.96)                                      | 2844.80                    | 2791.74                   | -3.87                               | (-16.21)                                                 |
| Cyclist road injuries         | 9.71                        | 10.09                       | -21.62                              | (-25.98 to 14.63)                                      | 559.27                     | 647.09                     | 8.71                                | (-8.96)                                                  |
| Motorcycle road injuries      | 32.74                       | 32.45                       | -13.90                              | (-18.65 to 8.24)                                       | 1872.33                    | 1857.69                   | -7.60                               | (-13.07)                                                 |
| Motor vehicle road injuries   | 36.76                       | 30.64                       | -18.04                              | (-20.50 to 3.86)                                       | 3200.16                    | 3210.49                   | -5.56                               | (-17.65)                                                 |
| Other road injuries           | 1.65                        | 1.61                        | -2.42                               | (-9.91 to 8.37)                                        | 131.94                     | 160.16                     | 21.40                               | (-2.40)                                                  |
| Other transport injuries      | 11.79                       | 11.88                       | -0.76                               | (-6.67 to 10.60)                                       | 696.53                     | 717.10                     | 2.95                                | (-11.88)                                                 |

(10 columns)
|                                | 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|--------------------------------|-----------------------------|-----------------------------|-------------------------------------|----------------------------------------------------------|-----------------------------|-----------------------------|-----------------------------------|----------------------------------------------------------|
| **Global Health Metrics**      |                             |                             |                                     |                                                          |                             |                             |                                    |                                                          |
|                                |                             |                             |                                     |                                                          |                             |                             |                                    |                                                          |
| **Multidrug-resistant HIV/AIDS - Tuberculosis** |                             |                             |                                     |                                                          |                             |                             |                                    |                                                          |
| Extensively drug-resistant HIV/AIDS - Tuberculosis | 0.20 (0.12 to 0.32) | 0.44 (0.16 to 0.74) | +65.6% (37.3% to 85.3%) | +31.1% (25.5% to 39.5%) | 815.71 (537.96 to 1,178.82) | 1,042.60 (713.16 to 1,537.55) | +31.1% (25.5% to 39.5%) | +25.6% (20.3% to 32.2%) |
| HIV/AIDS resulting in other diseases | 26.53 (7.08 to 47.66) | 0.20 (−6.36 to −12.35) | −65.6% (−56.4% to −65.9%) | +31.1% (−53.9% to 56.9%) | 845.64 (545.52 to 1,167.74) | 1,042.60 (713.16 to 1,537.55) | +31.1% (−53.9% to 56.9%) | +18.8% (−50.7% to 81.2%) |
| Hepatitis B | 0.32 (0.25 to 0.41) | 0.31 (−6.36 to −12.35) | −65.6% (−56.4% to −65.9%) | +31.1% (−53.9% to 56.9%) | 356.17 (287.81 to 458.05) | 367.50 (294.88 to 452.00) | +18.8% (−50.7% to 81.2%) | +18.8% (−50.7% to 81.2%) |
| Hepatitis C | 0.42 (0.32 to 0.54) | 0.48 (−6.36 to −12.35) | −65.6% (−56.4% to −65.9%) | +31.1% (−53.9% to 56.9%) | 48.42 (19.37 to 157.20) | 58.03 (26.07 to 108.62) | +18.8% (−50.7% to 81.2%) | +18.8% (−50.7% to 81.2%) |
| Liver cancer due to hepatitis B | 1.52 (1.16 to 1.93) | 1.26 (5.87 to 7.99) | +22.4% (12.3% to 37.3%) | +22.4% (12.3% to 37.3%) | 78.10 (59.50 to 101.47) | 83.54 (59.50 to 137.54) | +22.4% (12.3% to 37.3%) | +22.4% (12.3% to 37.3%) |
| Liver cancer due to hepatitis C | 37.35 (31.94 to 43.13) | 62.46 (54.75 to 70.85) | −45.6% (−59.3% to −34.0%) | −45.6% (−59.3% to −34.0%) | 558.54 (353.25 to 918.69) | 567.17 (456.27 to 883.72) | −45.6% (−59.3% to −34.0%) | −45.6% (−59.3% to −34.0%) |

(Continued from previous page)

www.thelancet.com Vol 390 September 16, 2017 1389
Global Health Metrics

|                           | 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006-16 | Percentage change of age-standardised deaths rate 2006-16 | 2006 DALYs (in thousands) | 2015 DALYs (in thousands) | Percentage change of DALYs 2006-16 | Percentage change of age-standardised DALYs rate 2006-16 |
|---------------------------|----------------------------|-----------------------------|--------------------------------------|----------------------------------------------------------|---------------------------|-------------------------------|-----------------------------------|----------------------------------------------------------|
| - Circulatory diseases    |                            |                             |                                      |                                                          |                           |                               |                                    |                                                          |
| - CHD                      | 154 (1.17 to 2.00)         | 2.44                        | 58.98                                | (49.73 to 70.92)*                                       | 27.20                     | (20.44 to 36.57)*             | 53.65                             | (40.20 to 71.54)*                           |
| - Stroke                  |                            |                             |                                      |                                                          |                            |                               |                                    |                                                          |
| - Ischaemic heart disease | 106.76                    | 138.75                      | 29.96                                | (23.69 to 37.62)*                                       | 4.48                      | (–0.44 to 10.18)              | 3778.13                           | (3302.73 to 4435.35)                     |
| - Diabetes                |                            |                             |                                      |                                                          |                            |                               |                                    |                                                          |
| - Cancer                  |                            |                             |                                      |                                                          |                            |                               |                                    |                                                          |
| - Bladder cancer          | 4.17                       | 8.08                        | 8.82                                 | (–1.13 to 16.93)*                                       | –1.06                     | (–17.12 to –1.95)*            | 2060.25                           | (779.98 to 3175.09)                      |
| - Lung cancer             | 4.91                       | 10.05                       | 5.52                                 | (6.86 to 25.65)*                                        | –3.22                     | (–11.47 to 3.81)              | 2671.45                           | (2234.42 to 3175.76)                     |
| - Oral cancer             |                            |                             |                                      |                                                          |                            |                               |                                    |                                                          |
| - Suicide                 |                            |                             |                                      |                                                          |                            |                               |                                    |                                                          |
| - Self-harm by firearm    | 4.91                       | 5.40                        | 10.05                                | (2.38 to 17.43)*                                        | 4.90                      | (–11.27 to 1.34)             | 240.29                            | (162.77 to 343.62)                      |
| - Self-harm by other      |                            |                             |                                      |                                                          |                            |                               |                                    |                                                          |
| - Specified means         |                            |                             |                                      |                                                          |                            |                               |                                    |                                                          |
| - Cancer deaths           | 4.17                       | 8.08                        | 5.52                                 | (6.86 to 25.65)*                                        | –3.22                     | (–11.47 to 3.81)              | 2671.45                           | (2234.42 to 3175.76)                     |
| - Other drug use disorders| 37.94                     | 43.52                       | 16.89                                | (6.86 to 25.65)*                                        | –3.22                     | (–11.47 to 3.81)              | 2671.45                           | (2234.42 to 3175.76)                     |
| - Amphetamine use         |                            |                             |                                      |                                                          |                            |                               |                                    |                                                          |
| - Sudden deaths           | 4.47                       | 5.22                        | 16.67                                | (5.26 to 32.32)*                                        | –1.15                     | (–10.71 to 12.39)            | 831.85                            | (566.91 to 1189.89)                     |
| - Cannabis use disorders  |                            |                             |                                      |                                                          |                            |                               |                                    |                                                          |
| - CHD                     |                            |                             |                                      |                                                          |                            |                               |                                    |                                                          |
| - Stroke                  |                            |                             |                                      |                                                          |                            |                               |                                    |                                                          |
| - Ischaemic heart disease |                            |                             |                                      |                                                          |                            |                               |                                    |                                                          |
| - Ischaemic stroke        |                            |                             |                                      |                                                          |                            |                               |                                    |                                                          |
| - Haemorrhagic stroke     |                            |                             |                                      |                                                          |                            |                               |                                    |                                                          |

(Continued from previous page)
| Year | Deaths (in thousands) | DALYs (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | DALYs rate 2006–16 | Percentage change of DALYs rate 2006–16 |
|------|-----------------------|----------------------|-------------------------------------|--------------------------------------------------------|--------------------|----------------------------------------|
| 2006 | 3 Diet low in vegetables: all causes | 1473.57 | 1519.65 | 3.13 | -21.93 | 23.71 | 34.189 | 2171.59 | -17.79 |
|      | Ischaemic heart disease | 1040.01 | 1121.42 | 7.83 | -18.99 | 23.37 | 9330.74 | 2965.36 | 4.91 |
|      | Haemorrhagic stroke | 267.49 | 229.58 | -10.43 | -30.59 | 757.98 | 794.05 | 16.06 |
| 2006 | 3 Diet low in legumes: all causes | 594.09 | 562.47 | 13.19 | -15.35 | 13.3169 | 14.2145 | 6.75 |
|      | Ischaemic heart disease | 594.09 | 562.47 | 13.19 | -15.35 | 13.3169 | 14.2145 | 6.75 |
|      | Haemorrhagic stroke | 253.17 | 249.68 | -10.90 | -16.06 | 57.3021 | 415.55 |
| 2006 | 3 Diet low in whole grains: all causes | 2171.59 | 2006.87 | 113.67 | 15.35 | 27341.40 | 23571.09 | 6.75 |
|      | Ischaemic heart disease | 538.35 | 542.17 | 9.19 | -17.86 | 9316.91 | 6724.48 | -16.05 |
|      | Haemorrhagic stroke | 500.51 | 505.42 | -0.98 | -21.76 | 13827.83 | 13827.83 | -20.32 |
| 2006 | 3 Diabetes mellitus | 148.55 | 186.92 | 25.39 | -9.83 | 7517.29 | 7396.70 | -14.53 |
|      | 1391 | 288.47 | 25.39 | -9.83 | 7517.29 | 7396.70 | -14.53 |
| 2006 | 3 Ischaemic heart disease: all causes | 1879.32 | 2155.04 | 14.67 | -16.64 | 34280.23 | 49492.97 | -10.43 |
|      | Diabetes mellitus | 114.84 | 143.63 | 25.08 | -4.23 | 5864.75 | 7043.18 | -9.24 |
| 2006 | 3 Diet low in milk: all causes | 100.32 | 123.21 | 123.21 | -7.13 | 2168.24 | 2581.50 | 19.06 |
|      | Colon and rectum cancer | 100.32 | 123.21 | 123.21 | -7.13 | 2168.24 | 2581.50 | 19.06 |
| 2006 | 3 Diet high in red meat: all causes | 22.59 | 31.88 | 41.16 | 7.35 | 893.25 | 1247.33 | 39.64 |
|      | Colon and rectum cancer | 12.29 | 17.88 | 45.48 | 9.72 | 268.60 | 377.78 | 40.65 |

(Continued from previous page)
| 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006-16 | Percentage change of age-standardised deaths rate 2006-16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006-16 | Percentage change of age-standardised DALYs rate 2006-16 |
|-----------------------------|-----------------------------|-------------------------------------|-----------------------------------------------|-----------------------------|-------------------------------|---------------------------------|----------------------------------|
| - Diabetes mellitus         | 10·29                       | (1·45 to 18·98)                     | (1·98 to 25·60)                               | 36·00                       | (29·34 to 43·64)*             | 4·40                            | (0·81 to 10·51)                  |
| - Diet high in processed meat: all causes | 16·67                       | (29·93 to 269·63)                   | (29·84 to 271·40)                             | 36·00                       | (29·34 to 43·64)*             | 4·40                            | (0·81 to 10·51)                  |
|   - Colon and rectum cancer | 9·84                        | (5·09 to 15·48)                     | (5·24 to 16·68)                               | 10·28                       | 4·45                          | (3·10 to 11·58)                 | (0·00 to 10·51)                  |
| - Ischaemic heart disease  | 121·78                      | (5·27 to 240·19)                    | (4·50 to 238·06)                              | 121·78                      | 4·45                          | (3·10 to 11·58)                 | (0·00 to 10·51)                  |
| - Diabetes mellitus         | 15·09                       | (7·05 to 24·10)                     | (6·45 to 25·75)                               | 15·09                       | 1·19                          | (1·12 to 10·00)                 | (1·11 to 10·61)                  |
| - Diet high in sugar-sweetened beverages: all causes | 17·80                       | (11·49 to 29·29)                    | (15·33 to 33·36)                              | 26·77                       | 6·05                          | (0·00 to 10·51)                 | (1·11 to 10·61)                  |
|   - Oesophageal cancer      | 0·29                        | (0·09 to 0·55)                      | (0·11 to 0·70)                                | 28·96                       | 6·05                          | (0·00 to 10·51)                 | (1·11 to 10·61)                  |
|   - Colon and rectum cancer | 0·36                        | (0·27 to 0·65)                      | (0·27 to 0·65)                                | 20·23                       | 6·05                          | (0·00 to 10·51)                 | (1·11 to 10·61)                  |
|   - Liver cancer due to hepatitis B | 0·11                       | (0·07 to 0·29)                      | (0·07 to 0·29)                                | 46·97                       | 6·05                          | (0·00 to 10·51)                 | (1·11 to 10·61)                  |
|   - Liver cancer due to hepatitis C | 0·09                       | (0·06 to 0·17)                      | (0·06 to 0·22)                                | 35·33                       | 6·05                          | (0·00 to 10·51)                 | (1·11 to 10·61)                  |
|   - Liver cancer due to alcohol use | 0·07                       | (0·04 to 0·14)                      | (0·04 to 0·15)                                | 38·16                       | 6·05                          | (0·00 to 10·51)                 | (1·11 to 10·61)                  |
|   - Liver cancer due to other causes | 0·07                       | (0·05 to 0·19)                      | (0·05 to 0·19)                                | 11·27                       | 6·05                          | (0·00 to 10·51)                 | (1·11 to 10·61)                  |
|   - Gallbladder and biliary tract cancer | 0·10                       | (0·06 to 0·27)                      | (0·07 to 0·20)                                | 21·19                       | 6·05                          | (0·00 to 10·51)                 | (1·11 to 10·61)                  |
|   - Pancreatic cancer       | 0·12                        | (0·05 to 0·27)                      | (0·05 to 0·27)                                | 20·20                       | 6·05                          | (0·00 to 10·51)                 | (1·11 to 10·61)                  |
|   - Breast cancer           | 0·15                        | (0·08 to 0·38)                      | (0·08 to 0·32)                                | 14·33                       | 6·05                          | (0·00 to 10·51)                 | (1·11 to 10·61)                  |
|   - Uterine cancer          | 0·10                        | (0·07 to 0·16)                      | (0·09 to 0·20)                                | 31·24                       | 6·05                          | (0·00 to 10·51)                 | (1·11 to 10·61)                  |
|   - Ovarian cancer          | 0·03                        | (0·00 to 0·11)                      | (0·00 to 0·07)                                | 5·42                        | 6·05                          | (0·00 to 10·51)                 | (1·11 to 10·61)                  |
|   - Kidney cancer           | 0·13                        | (0·08 to 0·20)                      | (0·11 to 0·26)                                | 34·51                       | 6·05                          | (0·00 to 10·51)                 | (1·11 to 10·61)                  |
|   - Thyroid cancer          | 0·02                        | (0·01 to 0·04)                      | (0·01 to 0·04)                                | 23·74                       | 6·05                          | (0·00 to 10·51)                 | (1·11 to 10·61)                  |
|   - Non-Hodgkin lymphoma    | 0·07                        | (0·01 to 0·08)                      | (0·01 to 0·10)                                | 14·80                       | 6·05                          | (0·00 to 10·51)                 | (1·11 to 10·61)                  |
|   - Multiple myeloma        | 0·04                        | (0·02 to 0·07)                      | (0·02 to 0·08)                                | 20·90                       | 6·05                          | (0·00 to 10·51)                 | (1·11 to 10·61)                  |
|   - Acute lymphoid leukaemia | 0·01                        | (0·01 to 0·03)                      | (0·01 to 0·03)                                | 21·67                       | 6·05                          | (0·00 to 10·51)                 | (1·11 to 10·61)                  |

(continued from previous page)
| Disease Category                      | 2006 Deaths (in thousands) | 2016 Deaths (in thousands) | Percentage change of deaths 2006–16 (%) | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006–16 (%) | Percentage change of age-standardised deaths rate 2006–16 (%) |
|--------------------------------------|-----------------------------|-----------------------------|----------------------------------------|---------------------------|---------------------------|----------------------------------------|----------------------------------------------------------|
| Chronic lymphoid leukaemia           | 0.02                        | 0.02                        | -18.72                                 | 0.31                      | 0.34                      | 9.98                                   | -15.46                                                   | (-47.66 to 65.06)                                         | (-59.32 to 28.08)                                         |
| Acute myeloid leukaemia              | 0.04                        | 0.04                        | -17.80                                 | 0.18                      | 1.27                      | 17.65                                  | -3.94                                                    | (-24.43 to 64.82)                                         | (-45.68 to 33.05)                                         |
| Chronic lymphoid leukaemia           | 0.01                        | 0.01                        | -13.31                                 | 0.26                      | 0.26                      | -15.95                                 | -31.30                                                   | (-62.20 to 24.58)                                         | (-68.51 to 2.27)                                          |
| Other leukaemia                      | 0.04                        | 0.04                        | -13.15                                 | 0.69                      | 1.09                      | -16.02                                 | -16.40                                                   | (-70.91 to 82.39)                                         | (-73.68 to 52.84)                                         |
| Ischaemic heart due to disease       | 5.98                        | 7.03                        | -12.98                                 | 5.07                      | 5.07                      | -12.62                                 | -7.75                                                    | (-23.17 to 43.80)                                         | (-40.83 to 13.00)                                         |
| Ischaemic stroke                     | 1.09                        | 1.17                        | -10.02                                 | 1.26                      | 1.26                      | -10.02                                 | -9.27                                                    | (-40.45 to 59.57)                                         | (-55.99 to 17.68)                                         |
| Haemorrhagic stroke                  | 2.14                        | 2.47                        | -15.27                                 | 3.28                      | 3.69                      | 16.90                                  | -4.88                                                    | (-28.03 to 35.60)                                         | (-42.13 to 11.16)                                         |
| Hypertensive heart disease           | 0.94                        | 1.33                        | -13.13                                 | 3.33                      | 5.33                      | 5.33                                   | -19.13                                                   | (-22.44 to 46.26)                                         | (-20.06 to 18.87)                                         |
| Atrial fibrillation and flutter      | 0.18                        | 0.44                        | -7.09                                  | 0.73                      | 1.38                      | 3.65                                   | 2.11                                                     | (0.67 to 59.99)                                            | (-24.17 to 18.00)                                         |
| Asthma                               | 0.15                        | 0.14                        | -3.48                                  | 1.50                      | 1.50                      | 1.50                                   | -3.65                                                    | (-40.82 to 40.68)                                         | (-40.85 to 18.12)                                         |
| Gallbladder and biliary diseases     | 0.13                        | 0.19                        | 45.16                                  | 7.18                      | 3.01                      | 4.24                                   | 10.74                                                    | (3.82 to 57.89)                                            | (-18.83 to 24.22)                                         |
| Alzheimer’s disease and other dementias | 1.09                    | 1.57                        | 43.79                                  | 1.32                      | 13.62                     | 48.59                                  | 15.65                                                    | (18.51 to 60.36)                                          | (-48.69 to 32.06)                                         |
| Diabetes mellitus                    | 2.68                        | 3.72                        | 38.65                                  | 6.23                      | 16.49                     | 228.01                                 | 14.03                                                    | (18.01 to 235.77)                                         | (24.20 to 52.10)                                          | (-0.94 to 22.21)                                          |
| Chronic kidney disease due to diabetes mellitus | 0.69                  | 1.65                        | 51.91                                  | 14.19                     | 21.91                     | 32.96                                  | 15.99                                                    | (16.36 to 29.45)                                         | (-9.49 to 49.25)                                          |
| Chronic kidney disease due to hypertension | 0.28                | 0.43                        | 52.70                                  | 10.13                     | 6.42                      | 9.82                                   | 5.19                                                     | (2.60 to 73.37)                                            | (-21.34 to 31.55)                                         |
| Chronic kidney disease due to glomerulonephritis | 0.29              | 0.43                        | 46.29                                  | 11.21                     | 9.59                      | 13.85                                  | 13.38                                                    | (18.51 to 60.36)                                          | (-7.28 to 24.40)                                          |
| Chronic kidney disease due to other causes | 0.30            | 0.45                        | 51.23                                  | -13.60                    | -13.60                    | -13.60                                 | 15.55                                                    | (-13.97 to 28.71)                                         | (-15.97 to 28.71)                                         |
| Osteoarthritis                       | -                           | -                           | -                                      | -                         | -                         | -                                      | -                                                        | -                                                        | -                                                        |
| Low back pain                        | -                           | -                           | -                                      | -                         | -                         | -                                      | -                                                        | -                                                        | -                                                        |
| Cataract                             | -                           | -                           | -                                      | -                         | -                         | -                                      | -                                                        | -                                                        | -                                                        |
| Diet low in fibre: all causes        | 7.69                        | 18.75                       | -14.06                                 | 18.52                     | 21.15                     | 14.06                                  | 12.04                                                    | (-10.75 to 77.51)                                         | (-30.98 to 38.72)                                         |
| Colon and rectum cancer              | 7.77                        | 9.25                        | 19.05                                  | 16.58                     | 19.05                     | 14.91                                  | -10.61                                                   | (9.93 to 19.90)                                            | (-15.08 to 6.81)                                          |

(Continued from previous page)
| Global Health Metrics | 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006-16 | Percentage change of age-standardised deaths rate 2006-16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006-16 | Percentage change of age-standardised DALYs rate 2006-16 |
|-----------------------|-----------------------------|-----------------------------|-----------------------------------|-----------------------------------------------|-----------------------------|-----------------------------|-----------------------------------|-----------------------------------------------|
| - Ischaemic heart disease | 692.02 | 785.32 | 13.48 | (9.90 to 16.76)* | -14.36 | (16.86347) | (18.21356) | 8.01 | (4.25 to 11.19)* |
| 3 Diet low in calcium: all causes | 1347.53 | 1539.76 | 14.19 | (11.23 to 17.24)* | -13.43 | (30.24539) | 33.46794 | 10.26 | -13.56 |
| - Ischaemic heart disease | 1373.85 | 1586.24 | 14.19 | (11.23 to 17.24)* | -13.43 | (30.24539) | 33.46794 | 10.26 | -13.56 |
| 3 Diet low in seafood omega 3 fatty acids: all causes | 1347.53 | 1539.76 | 14.19 | (11.23 to 17.24)* | -13.43 | (30.24539) | 33.46794 | 10.26 | -13.56 |

(Continued from previous page)
| Global Health Metrics | 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|-----------------------|---------------------------|--------------------------|-------------------------------------|-------------------------------------------------|--------------------------|--------------------------|-------------------------------|----------------------------------|
| Endocarditis           | (2777)                    | (1034 496)               | 37.7%                               | 15.6%                                           | (11805)                  | (10075)                  | 17.9%                         | 15.9%                                           |
| Other cardiovascular and circulatory diseases | (11016)                   | (5754)                  | 9.3%                                | 15.5%                                           | (6728)                   | (3748)                  | 8.2%                          | 15.5%                                           |
| Chronic kidney disease due to diabetes mellitus | (1235)                   | (82)                   | 95.1%                               | 95.3%                                           | (123)                    | (48)                   | 95.4%                         | 95.3%                                           |
| Chronic kidney disease due to diabetes mellitus | (31)                      | (23)                   | 96.8%                               | 96.8%                                           | (33)                     | (23)                   | 96.8%                         | 96.8%                                           |
| Chronic kidney disease due to hypertension | (23)                      | (13)                   | 96.8%                               | 96.8%                                           | (33)                     | (23)                   | 96.8%                         | 96.8%                                           |
| Chronic kidney disease due to other causes | (14)                      | (10)                   | 96.8%                               | 96.8%                                           | (33)                     | (23)                   | 96.8%                         | 96.8%                                           |
| Intimate partner violence: all causes | (140)                    | (86)                   | 96.8%                               | 96.8%                                           | (123)                    | (82)                   | 96.8%                         | 96.8%                                           |
| Drug-susceptible HIV/AIDS-tuberculosis | (23)                      | (13)                   | 96.8%                               | 96.8%                                           | (33)                     | (23)                   | 96.8%                         | 96.8%                                           |
| Multidrug-resistant HIV/AIDS-tuberculosis without extensive drug resistance | (2)                       | (1)                    | 96.8%                               | 96.8%                                           | (3)                      | (1)                    | 96.8%                         | 96.8%                                           |
| Extensively drug-resistant HIV/AIDS-tuberculosis | (1)                       | (1)                    | 96.8%                               | 96.8%                                           | (3)                      | (1)                    | 96.8%                         | 96.8%                                           |
| HIV/AIDS resulting in other diseases | (123)                    | (86)                   | 96.8%                               | 96.8%                                           | (123)                    | (86)                   | 96.8%                         | 96.8%                                           |
| Maternal abortion, miscarriage, and ectopic pregnancy | (2)                       | (1)                    | 96.8%                               | 96.8%                                           | (3)                      | (1)                    | 96.8%                         | 96.8%                                           |
| Major depressive disorder | (2)                       | (1)                    | 96.8%                               | 96.8%                                           | (3)                      | (1)                    | 96.8%                         | 96.8%                                           |
| Assault by firearm | (123)                    | (86)                   | 96.8%                               | 96.8%                                           | (123)                    | (86)                   | 96.8%                         | 96.8%                                           |
| Assault by sharp object | (2)                       | (1)                    | 96.8%                               | 96.8%                                           | (3)                      | (1)                    | 96.8%                         | 96.8%                                           |
| Sexual violence | (2)                       | (1)                    | 96.8%                               | 96.8%                                           | (3)                      | (1)                    | 96.8%                         | 96.8%                                           |

(Continued from previous page)
| 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|-----------------------------|-----------------------------|-----------------------------------|------------------------------------------|-----------------------------|-----------------------------|---------------------------------|----------------------------------|
| Assault by other means | 11.73 | 10.26 | -12.56 | (-24.54 to 5.66) | -23.23 | (-32.65 to -7.28)* | 713.59 | (558.79 to 866.06) | -11.14 | (-22.12 to 4.98) | -20.79 | (-30.38 to -7.10)* |
| Unsafe sec. all causes | 1799.64 | 1100.90 | -38.83 | (-40.96 to -36.41)* | -47.76 | (-54.54 to -45.78)* | 868.60 | (714.64 to 1048.39) | -54.03 | (-60.94 to -48.00)* | -45.34 | (-52.60 to -36.21)* |
| Drug-susceptible HIV/AIDS-tuberculosis | 361.54 | 177.41 | -51.20 | (-34.00 to -69.04)* | -58.56 | (-65.24 to -51.68)* | 1718.87 | (1156.46 to 2290.59) | -75.93 | (-80.96 to -71.18)* | -51.73 | (-57.35 to -45.53)* |
| Multidrug-resistant HIV/AIDS-tuberculosis | 30.65 | 14.52 | -52.62 | (-65.10 to -42.60)* | -59.80 | (-67.03 to -51.32)* | 1423.49 | (866.21 to 2131.53) | -40.83 | (-48.23 to -34.47)* | -56.42 | (-64.22 to -47.18)* |
| Extensively drug-resistant HIV/AIDS-tuberculosis | 0.52 | 0.77 | 48.49 | (29.74 to 70.40)* | 27.46 | (11.27 to 46.30)* | 24.64 | (35.40 to 37.41) | 36.82 | (22.60 to 56.99) | 49.44 | (30.40 to 72.32)* |
| HIV/AIDS resulting in other diseases | 1165.31 | 652.04 | -44.05 | (-46.83 to -39.95)* | -51.77 | (-54.17 to -49.13)* | 5895.66 | (3131.35 to 6760.36) | -40.92 | (-47.31 to -34.70)* | -48.30 | (-50.71 to -45.70)* |
| Syphilis | 3.31 | 3.02 | -8.89 | (-13.13 to -9.95)* | -24.89 | (-32.80 to -17.97)* | 277.24 | (229.80 to 328.03) | 19.08 | (14.97 to 23.60)* | 15.95 | (11.02 to 21.76)* |
| Chlamydial infection | 1.24 | 1.19 | -4.51 | (-12.73 to -12.18) | -20.70 | (-26.52 to -17.57)* | 519.31 | (341.24 to 781.67) | 562.13 | (370.06 to 850.69) | 8.05 | (5.89 to 10.42)* |
| Gonococcal infection | 3.51 | 3.27 | -7.97 | (-10.11 to -5.51) | -20.87 | (-26.48 to -7.90)* | 581.90 | (421.35 to 823.83) | 674.77 | (465.35 to 94.12) | 15.96 | (10.35 to 21.76)* |
| Trichomoniasis | 3.37 | 3.02 | -8.89 | (-13.13 to -9.95)* | -24.89 | (-32.80 to -17.97)* | 277.24 | (229.80 to 328.03) | 19.08 | (14.97 to 23.60)* | 15.95 | (11.02 to 21.76)* |
| Genital herpes | 1.73 | 1.63 | -5.92 | (-12.96 to 11.16) | -21.03 | (-26.82 to -7.18)* | 858.99 | (589.04 to 1221.09) | 674.92 | (463.29 to 934.57) | 9.71 | (7.38 to 12.17)* |
| Other sexually transmitted diseases | 1.40 | 0.90 | -36.92 | (-42.17 to 8.08) | -21.03 | (-26.82 to -7.18)* | 858.99 | (589.04 to 1221.09) | 674.92 | (463.29 to 934.57) | 9.71 | (7.38 to 12.17)* |
| Cervical cancer | 229.83 | 246.95 | 7.45 | (1.21 to 15.47)* | -15.99 | (-20.69 to -9.78)* | 7034.76 | (5873.55 to 7509.91) | 7384.00 | (6034.77 to 8862.78) | 4.96 | (-1.30 to 13.23) |
| Low physical activity: all causes | 1159.60 | 1377.34 | 18.43 | (-7.89 to 55.46) | -12.88 | (-31.98 to 13.86) | 21078.75 | (11156.78 to 32368.81) | 24315.86 | (12813.32 to 36604.69) | 15.36 | (-12.53 to 55.44) |
| Colon and rectum cancer | 20.87 | 25.51 | 22.21 | (-6.00 to 82.87) | -8.42 | (-59.11 to 13.61) | 411.01 | (2310.99 to 9711.31) | 489.81 | (2682 to 1183.40) | 18.88 | (-48.80 to 205.64) |
| Breast cancer | 6.71 | 7.85 | 16.97 | (-18.88 to 88.93) | -10.88 | (-18.58 to 44.86) | 175.07 | (105.04 to 388.06) | 200.14 | (80.0 to 448.00) | -14.33 | (-24.10 to 97.98) |
| Ischaemic heart disease | 835.44 | 1005.88 | 20.37 | (-6.38 to 58.30) | -11.49 | (-30.93 to 15.93) | 14658.37 | (6114.10 to 23953.87) | 16943.23 | (2620.81 to 72786.10) | 15.69 | (-11.49 to 54.73) |
| Ischaemic stroke | 267.12 | 295.28 | 10.54 | (-39.96 to 49.40) | -18.82 | (-40.33 to 9.53) | 4725.12 | (1026.32 to 9141.81) | 5268.62 | (938.08 to 10066.35) | 11.50 | (-18.88 to 54.06) |
| Diabetes mellitus | 29.46 | 39.12 | 32.80 | (-11.95 to 104.74) | -0.40 | (-33.63 to 52.78) | 1109.18 | (248.01 to 2082.98) | 1415.26 | (312.14 to 2604.08) | 27.59 | (-12.68 to 104.26) |

(Continued from previous page)
| 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006–16 |
|---------------------------|---------------------------|-------------------------------------|---------------------------|---------------------------|----------------------------------|
| **1 Metabolic risks: all causes** | | | | | |
| 14834.47 (216665 to 15690.95) | 17493.53 (16427.65 to 18724.26) | 17.92 (17.73 to 20.58)* |-11.86 (-13.47 to -9.94)* | 348438.17 (223410.78 to 374936.88) | 401812.92 (377407.85 to 434994.06) |
| **2 High fasting plasma glucose: all causes** | | | | | |
| 4700.40 (3722.99 to 5906.04) | 5612.45 (4457.29 to 6975.54) | 19.40 (15.54 to 23.19)* |-10.32 (-13.29 to -7.61)* | 12396.04 (10288.76 to 146690.95) | 144088.58 (119872.60 to 171587.77) |
| - Drug-susceptible tuberculosis | 125.08 (78.55 to 175.35) | 99.60 (62.39 to 140.59) | -20.36 (-24.38 to -16.57)* | -37.14 (-40.10 to -34.46)* | 4031.77 (2381.12 to 5546.25) | 3126.64 (2002.75 to 4288.46) |
| - Multidrug-resistant tuberculosis without extensive drug resistance | 12.50 (7.74 to 18.06) | 8.80 (5.22 to 12.83) | -29.61 (-36.56 to -22.33)* | -44.21 (-49.66 to -38.40)* | 394.88 (251.40 to 552.02) | 266.97 (-38.90 to -25.48)* |
| - Extensively drug-resistant tuberculosis | 0.54 (0.33 to 0.79) | 0.94 (0.58 to 1.39) | 73.66 (50.32 to 101.15)* | 37.94 (20.01 to 59.36)* | 17.18 (10.63 to 24.33) | 28.42 (17.68 to 40.36) |
| - Colon and rectum cancer | 46.54 (31.36 to 61.70) | 56.18 (33.51 to 82.80) | 20.70 (15.48 to 25.34)* | -9.50 (-13.53 to -5.91)* | 884.79 (508.91 to 1926.46) | 1047.94 (242.88 to 2300.07) |
| - Liver cancer due to other causes | 10.01 (2.06 to 23.07) | 11.82 (2.44 to 26.96) | 18.12 (13.22 to 22.67)* | -8.69 (-12.24 to -5.26)* | 247.67 (51.70 to 571.25) | 279.35 (58.20 to 649.12) |
| - Pancreatic cancer | 21.37 (4.71 to 46.72) | 27.75 (6.10 to 60.79) | 29.86 (26.27 to 33.12)* | -2.11 (-4.96 to 0.48) | 406.22 (90.54 to 891.18) | 518.70 (115.69 to 1142.16) |
| - Tracheal, bronchus, and lung cancer | 100.11 (22.74 to 219.56) | 117.06 (26.22 to 256.14) | 16.93 (13.75 to 19.76)* | -10.83 (-13.59 to -8.84)* | 2028.69 (457.34 to 4483.59) | 2304.26 (529.72 to 5093.70) |
| - Breast cancer | 26.09 (4.93 to 59.11) | 31.03 (9.56 to 69.25) | 18.94 (11.73 to 26.02)* | -10.02 (-15.31 to -4.93)* | 637.43 (120.29 to 1460.33) | 749.77 (144.08 to 1694.69) |
| - Ovarian cancer | 8.11 (1.53 to 19.32) | 10.01 (1.88 to 23.94) | 23.40 (18.12 to 28.40)* | -6.84 (-10.75 to -3.13)* | 182.64 (34.17 to 438.11) | 226.27 (41.63 to 545.49) |
| - Bladder cancer | 10.79 (2.22 to 23.92) | 13.47 (2.80 to 29.79) | 24.87 (20.66 to 28.68) | -6.86 (-10.30 to -3.96)* | 185.65 (37.01 to 413.28) | 225.37 (45.96 to 501.26) |
| - Ischaemic heart disease | 1576.70 (935.55 to 2479.20) | 1883.33 (1104.82 to 2942.53) | 19.45 (13.37 to 25.39)* | -11.29 (-15.21 to -7.64)* | 2910.46 (1881.34 to 45481.26) | 33192.53 (21184.53 to 51236.60) |
| - Ischaemic stroke | 449.06 (229.48 to 849.74) | 472.53 (246.23 to 879.04) | 5.23 (-1.90 to 12.75) | -21.44 (-26.20 to -17.05)* | 8810.40 (4539.51 to 14964.85) | 9467.73 (5021.42 to 15876.46) |
| - Haemorrhagic stroke | 484.34 (304.87 to 745.17) | 473.30 (301.08 to 720.04) | -2.28 (-8.77 to 3.28) | -25.71 (-30.75 to -21.17)* | 10796.83 (6676.12 to 15844.21) | 10638.08 (6692.27 to 15631.04) |
| - Peripheral vascular disease | 8.67 (6.23 to 12.26) | 11.73 (8.71 to 17.62) | 35.33 (24.67 to 48.64)* | -2.51 (-9.98 to 6.88) | 213.89 (150.72 to 302.55) | 271.68 (195.01 to 383.83) |
| - Alzheimer’s disease and other dementias | 123.02 (26.35 to 274.89) | 137.45 (37.30 to 388.04) | 41.73 (38.26 to 45.05)* | -2.10 (-3.44 to 1.60) | 1584.88 (330.64 to 3963.61) | 2138.24 (445.48 to 4872.90) |
| - Diabetes mellitus | 1095.53 (1065.39 to 1121.32) | 1436.26 (1401.25 to 1469.57) | 31.10 (28.92 to 33.39)* | -0.87 (-2.52 to 0.84) | 4594.47 (3865.07 to 54662.94) | 54717.75 (47919.49 to 68211.91) |
| - Chronic kidney disease due to diabetes mellitus | 384.78 (349.87 to 418.93) | 500.41 (452.11 to 543.57) | 30.05 (26.18 to 32.84)* | -0.63 (-3.43 to 1.30) | 11732.50 (10608.16 to 12883.26) | 14649.82 (13196.95 to 16191.89) |

(Continued from previous page)
### Global Health Metrics

(Continued from previous page)

| Disease Category | 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|------------------|-----------------------------|-----------------------------|-------------------------------------|---------------------------|---------------------------|-----------------------------------|-----------------------------------------------|
| Chronic kidney disease due to hypertension | 103.23 | 135.31 | 31.08 | -3.63 | 2165.18 | 2744.97 | 25.85 | -4.20 |
| Chronic kidney disease due to glomerulonephritis | 42.94 | 54.38 | 26.63 | -3.72 | 1251.76 | 1519.82 | 21.42 | -4.39 |
| Chronic kidney disease due to other causes | 71.01 | 94.20 | 32.66 | -0.55 | 1866.69 | 2346.66 | 25.71 | -2.03 |
| Glaucoma | ... | ... | ... | ... | ... | ... | ... | ... |
| Cataract | ... | ... | ... | ... | ... | ... | ... | ... |
| 2 High total cholesterol all causes | 3802.10 | 4392.51 | 15.52 | -14.34 | 81976.46 | 93443.05 | 12.75 | -13.29 |
| Ischaemic heart disease | 3343.63 | 3896.10 | 15.82 | -13.22 | 73403.57 | 81287.03 | 11.97 | -12.88 |
| Ischaemic stroke | 458.46 | 496.40 | 8.18 | -20.63 | 10572.88 | 11657.00 | 10.25 | -16.02 |
| 2 High systolic blood pressure all causes | 9083.10 | 10455.86 | 15.11 | -14.05 | 188363.23 | 212105.09 | 12.44 | -13.27 |
| 2 Rheumatic heart disease | 85.51 | 80.86 | ... | ... | 2412.32 | 2234.54 | ... | ... |
| Ischaemic heart disease | 4476.47 | 5263.72 | 17.54 | -12.69 | 85294.47 | 92868.68 | 13.85 | -12.44 |
| Ischaemic stroke | 1283.00 | 1372.51 | 6.98 | -20.42 | 25674.19 | 28119.95 | 10.00 | ... |
| Haemorrhagic stroke | 1636.18 | 1662.64 | 2.23 | -22.45 | 37290.74 | 38611.64 | ... | ... |
| Hypertensive heart disease | 694.18 | 892.14 | 28.66 | -4.39 | 13562.97 | 16233.95 | 20.35 | -6.60 |
| Other cardiomyopathy | 66.04 | 74.91 | 23.56 | -8.74 | 1352.53 | 1595.77 | 18.28 | -7.37 |
| Atrial fibrillation and flutter | 61.68 | 85.31 | 28.31 | -2.78 | 12396.49 | 18653.37 | 24.39 | -5.82 |
| Aortic aneurysm | 51.01 | 60.10 | 17.81 | -11.62 | 961.55 | 1100.81 | 14.48 | -11.71 |
| Peripheral vascular disease | 12.49 | 16.55 | 24.05 | -4.83 | 290.81 | 360.60 | 24.00 | -6.80 |
| Endocarditis | 25.33 | 32.12 | 25.54 | -2.62 | 958.46 | 1248.71 | 96.99 | -7.37 |
| Other cardiovascular and circulatory diseases | 174.04 | 208.84 | 24.05 | -10.49 | 4740.48 | 5577.83 | 17.66 | -8.60 |

(Table 4 continues on next page)
| 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|---------------------------|---------------------------|-------------------------------------|--------------------------|--------------------------|----------------------------------|----------------------------------|
| Chronic kidney disease due to diabetes mellitus | 176.23 | 233.70 | 52.57 | 32.61 | (–0.06) | –2.77 to 1.94 | 475.11 | 615.78 | 29.44 | (–0.01) | –2.10 to 1.78 |
| Chronic kidney disease due to hypertension | 222.32 | 299.48 | 36.07 | 34.71 | (–0.96) | (–3.95 to 1.00) | 516.00 | 660.34 | 27.80 | (–1.02) | (–3.31 to 0.87) |
| Chronic kidney disease due to glomerulonephritis | 47.82 | 60.17 | 33.55 | 25.83 | (–4.69) | (–6.90 to –2.70) | 144.30 | 173.95 | 20.49 | (–4.97) | (–6.98 to –2.95) |
| Chronic kidney disease due to other causes | 76.17 | 102.79 | 34.86 | 34.95 | (0.84) | (–3.83 to 3.10) | 203.46 | 260.39 | 28.16 | (–0.11) | (–2.27 to 1.77) |
| High body-mass index: all causes | 35.39 | 45.10 | 28.59 | 21.97 | (–6.97) | (–7.54 to 3.67) | 105.25 | 125.81 | 28.62 | 0.88 | (15.24 to 3.26) |
| Oesophageal cancer | 57.66 | 70.33 | 23.43 | 19.17 | (–6.97) | (–6.52 to 2.81) | 135.9 | 162.45 | 19.48 | (–7.80) | (9.83 to 33.83) |
| Colon and rectum cancer | 49.63 | 65.11 | 31.19 | 25.23 | (–0.94) | (–5.70 to 4.74) | 107.85 | 121.74 | 29.57 | (–0.04) | (–9.44 to 6.05) |
| Liver cancer due to hepatitis B | 26.37 | 37.72 | 43.05 | 31.19 | (–11.96) | (2.72 to 28.75) | 78.13 | 107.86 | 37.86 | (10.01) | (6.01 to 27.39) |
| Liver cancer due to hepatitis C | 15.00 | 21.21 | 41.40 | 33.58 | (6.97) | (1.14 to 15.12) | 328.28 | 459.82 | 40.07 | 7.44 | (1.26 to 16.40) |
| Liver cancer due to alcohol use | 11.43 | 16.59 | 45.18 | 35.92 | (10.99) | (3.90 to 20.62) | 265.34 | 384.17 | 44.30 | 11.45 | (4.17 to 21.82) |
| Liver cancer due to other causes | 34.98 | 46.12 | 36.21 | 35.51 | (12.85) | (5.45 to 27.54) | 415.44 | 586.63 | 41.21 | 12.10 | (3.36 to 27.26) |
| Gallbladder and biliary tract cancer | 19.19 | 24.23 | 26.31 | 20.46 | (–5.9) | (–9.47 to 0.48) | 398.83 | 501.99 | 25.87 | (3.50) | (–8.43 to 2.52) |
| Pancreatic cancer | 17.09 | 23.80 | 39.31 | 33.12 | (5.04) | (0.00 to 10.77) | 355.53 | 488.30 | 37.34 | (5.41) | (0.50 to 11.10) |
| Breast cancer | 24.50 | 34.14 | 39.33 | 26.71 | (1.49) | (–7.17 to 17.88) | 478.48 | 696.82 | 45.61 | (4.33) | (–6.57 to 30.51) |
| Uterine cancer | 25.33 | 31.98 | 26.29 | 17.00 | (–4.35) | (–11.5 to 5.40) | 616.37 | 776.07 | 26.07 | (–5.10) | (–10.14 to 7.44) |
| Ovarian cancer | 3.96 | 5.16 | 30.26 | 21.79 | (–0.87) | (–7.38 to 6.92) | 100.08 | 130.91 | 30.81 | 1.63 | (22.13 to 41.76) |
| Kidney cancer | 18.46 | 24.80 | 34.35 | 28.83 | (1.72) | (–2.45 to 6.95) | 414.68 | 545.45 | 31.53 | 1.48 | (–7.22 to 6.69) |
| Thyroid cancer | 2.91 | 3.99 | 37.08 | 29.94 | (1.25) | (–1.57 to 12.41) | 75.91 | 104.28 | 37.39 | 7.53 | (13.4 to 15.42) |
| Non-Hodgkin lymphoma | 8.76 | 12.11 | 38.22 | 32.55 | (5.46) | (1.16 to 10.68) | 214.81 | 295.53 | 37.58 | 8.27 | (3.8 to 13.37) |
| Multiple myeloma | 4.86 | 6.66 | 37.06 | 31.41 | (3.30) | (–1.17 to 9.24) | 103.69 | 142.21 | 37.15 | 5.30 | (9.94 to 11.53) |

(continued from previous page)
| Disease                                | 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|----------------------------------------|-----------------------------|----------------------------|-------------------------------------|---------------------------------------------------------|---------------------------|-------------------------------|-----------------------------------|-----------------------------------|
| Acute lymphoid leukaemia               | 1.59                        | 2.22                       | 39.14                               | 10.63                                                   | 53.85                      | 73.29                         | 36.10                             | 12.10                             |
| Chronic lymphoid leukaemia             | 2.36                        | 2.92                       | 23.58                               | -8.23                                                   | 45.52                      | 55.53                         | 21.98                             | -6.69                             |
| Acute myeloid leukaemia                | 4.65                        | (2.33 to 7.66)             | 33.79                               | -10.54                                                  | (59.43 to 197.90)          | (79.64 to 253.37)             | 151.34                            | 4.62                              |
| Chronic myeloid leukaemia              | (0.74 to 2.54)              | (1.50 to 4.80)             | 3.86                                | -8.41                                                   | (18.95 to 66.00)           | (22.44 to 89.89)              | 37.85                             | -11.35                            |
| Other leukaemia                        | 5.65                        | (5.69 to 11.92)            | 22.26                               | -5.29                                                   | 150.74                     | 175.88                        | 16.62                             | -6.03                             |
| Ischaemic heart disease                | 1288.03                     | (949.29 to 1719.37)        | 23.62                               | -6.63                                                   | 70.81                      | 72.49                         | -2.61                             | -19.13                            |
| Haemorrhagic stroke                    | 283.31                      | (179.56 to 446.42)         | 12.38                               | -14.52                                                  | 7636.97                    | 9139.16                       | 19.67                             | -12.19                            |
| Hypertensive heart disease             | 215.62                      | (162.11 to 282.35)         | 39.51                               | -6.93                                                   | 4745.65                    | 11.59                         | 14.90                             | -2.55                             |
| Atrial fibrillation and flutter        | 30.66                       | (23.86 to 37.45)           | 50.50                               | 4.01                                                    | (1434.95)                  | (2008.58)                     | 42.67                             | 6.27                              |
| Asthma                                 | 50.50                       | (36.88 to 727.93)          | 19.33                               | -15.43                                                  | (1685.64 to 5065.91)       | (2214.88 to 6021.97)          | 33.34                             | 3.67                              |
| Gallbladder and biliary diseases       | 22.65                       | (16.31 to 31.11)           | 37.32                               | -1.35                                                   | (411.73 to 7029)           | (295.15 to 7078)              | 32.63                             | -2.70                             |
| Alzheimer’s disease and other dementia | 185.54                      | (105.50 to 359.86)         | 54.38                               | -6.35                                                   | 2571.17                    | 3493.12                       | 48.20                             | 7.68                              |
| Diabetes mellitus                      | 360.47                      | (386.74 to 530.40)         | 41.74                               | 8.24                                                    | (1926.88 to 2915.92)       | (2194.88 to 3287.38)          | 19.16                             | 3.10                              |
| Chronic kidney disease due to diabetes | 98.46                       | (65.81 to 140.34)          | 84.69                               | 12.65                                                   | 3124.61                    | 4656.03                       | 12.04                             | 13.04                             |
| Chronic kidney disease due to hypertension | 47.69                      | (26.3 to 73.45)            | 54.03                               | 12.85                                                   | (501.88 to 2012.81)        | (1785.47 to 2934.09)          | 51.77                             | 15.47                             |
| Chronic kidney disease due to diabetes | 30.93                       | (18.41 to 69.06)           | 34.87                               | 2.81                                                    | (147.03 to 1809.69)        | (1538.82 to 2256.09)          | 31.60                             | 3.51                              |
| Chronic kidney disease due to other causes | 42.14                      | (26.60 to 104.77)          | 47.39                               | 11.26                                                   | (1301.30 to 1215.60)       | (1867.82 to 1805.69)          | 43.54                             | 11.97                             |
| Osteoarthritis                         | -                           | -                           | -                                   | -                                                       | -                          | -                             | -                                 | -                                 |
| Low back pain                          | -                           | -                           | -                                   | -                                                       | -                          | -                             | -                                 | -                                 |

(Continued from previous page)
### Global Health Metrics

**Table 4:**

| 2006 deaths (in thousands) | 2016 deaths (in thousands) | Percentage change of deaths 2006–16 | Percentage change of age-standardised deaths rate 2006–16 | 2006 DALYs (in thousands) | 2016 DALYs (in thousands) | Percentage change of DALYs 2006–16 | Percentage change of age-standardised DALYs rate 2006–16 |
|-----------------------------|-----------------------------|-------------------------------------|------------------------------------------------------|-----------------------------|-----------------------------|-----------------------------------|------------------------------------------------------|
| **2 Impaired kidney function: all causes** | | | | | | | |
| 2100.85 (1943.12 to 2277.00) | 3194.65 (2951.90 to 3437.40) | 81.00% (74.49% to 86.94%) | 45.49% (43.02% to 46.98%) | 21.44 (18.37 to 23.96) | 29.33 (24.32 to 34.47) | -10.88% (9.17% to -12.63%) | -5.32% (5.45% to -7.02%) |
| **Ischaemic heart disease** | | | | | | | |
| 753.35 (627.96 to 868.81) | 1259.37 (1080.12 to 1438.62) | 66.53% (60.31% to 72.52%) | 45.49% (43.02% to 46.98%) | 20.27 (15.84 to 24.87) | 30.23 (23.62 to 37.84) | -14.40% (12.09% to -16.67%) | -9.15% (8.83% to -9.45%) |
| **Ischaemic stroke** | | | | | | | |
| 201.59 (153.59 to 247.89) | 219.00 (164.95 to 274.84) | 9.07% (4.20% to 13.94%) | 45.49% (43.02% to 46.98%) | 8.63 (2.78 to 14.64) | 12.46 (7.79 to 17.12) | -12.40% (7.23% to -17.57%) | -7.79% (3.83% to -11.78%) |
| **Haemorrhagic stroke** | | | | | | | |
| 227.29 (185.54 to 269.78) | 236.16 (191.40 to 283.30) | 4.07% (0.12% to 7.40%) | 45.49% (43.02% to 46.98%) | 3.91 (0.62 to 7.40) | 5.43 (0.72 to 9.40) | -20.50% (18.22% to -22.78%) | -3.88% (2.19% to -6.57%) |
| **Peripheral vascular disease** | | | | | | | |
| 5.64 (3.85 to 8.18) | 7.32 (4.82 to 11.42) | 29.76% (16.19% to 46.98) | 45.49% (43.02% to 46.98%) | 29.76 (16.19 to 46.98) | 32.93 (19.29 to 46.98) | -8.48% (5.43% to -11.48%) | -3.88% (2.19% to -6.57%) |
| **Chronic kidney disease due to diabetes mellitus** | | | | | | | |
| 384.78 (349.87 to 418.93) | 500.41 (452.11 to 543.57) | 30.05% (26.18 to 32.84) | 45.49% (43.02% to 46.98%) | 30.05 (26.18 to 32.84) | 32.16 (28.30 to 36.02) | -6.67% (4.39% to -8.93%) | -3.88% (2.19% to -6.57%) |

*(Table 4 continues on next page)*
mutually exclusive categories: population growth, population ageing, trends in exposure to all risk factors measured in GBD 2016, and all other factors combined. Globally, trends in exposure to all risk factors combined would have led to a decrease of deaths by 9·3% (6·9–11·6) and DALYs by 10·8% (8·3–13·1). Risk factors play a larger part in CMNN causes, where trends in exposure to risks would have resulted in a decrease of deaths by 14·9% (12·4–17·1) and DALYs by 15·0% (12·7–17·6). Overall, population ageing and population growth are both driving deaths and DALYs to increase significantly. At the global level, across all causes, population growth alone would have resulted in 12·4% (10·1–14·9) more deaths and 12·4% (10·1–14·9) more DALYs, while population ageing would have contributed 14·9% (12·7–17·6) more deaths and 12·4% (10·1–14·9) more DALYs. The contribution of population ageing in NCDs is noteworthy as it is the largest driver of trends in NCDs, and accounts for 19·5% (17·3–22·0) more deaths and 14·0% (11·6–16·3) more DALYs. The residual category, which includes improvements in treatment along with changes in risk exposure, would have contributed 14·9% (12·7–17·6) more deaths and 12·4% (10·1–14·9) more DALYs, which includes improvements in treatment along with changes in risk exposure.

Key results for new risks, leading risks, and risks with significant changes in GBD 2016

In 2016, for Level 3 risks factors, more DALYs were attributable to increased SBP than any other risk factor. Increased SBP was the second leading risk factor for men and leading risk factor for women globally, accounting for 89·9 million (80·9 million to 98·2 million) DALYs among women and 124·1 million (111·2 million to 138·0 million) DALYs among men. IHD was the largest source of DALYs attributable to increased SBP, followed by haemorrhagic stroke and ischaemic stroke. Since 1990, the SEV for increased SBP rose for men (22·9 [21·5–24·6] in 1990 to 24·6 [23·0–26·6] in 2016, a 7·5% increase [7·0–8·0]), and increased for women (24·2 [22·7–25·8] in 1990 to 24·2 [22·7–25·8] in 2016, a 0·7% increase [0·2–1·2]).

In 2016, 7·1 million (6·5 million to 7·8 million) deaths and 177·3 million (162·3 million to 194·3 million) DALYs...
### Global Health Metrics

#### Leading risks 1990 vs 2006 vs 2016

| Risk Category | Risk Factor | 1990 DALYs | 2006 DALYs | 2016 DALYs |
|---------------|-------------|------------|------------|------------|
| 1 Child growth failure | No access to handwashing facility | 325.1 | -6.0 | -7.6 |
| 2 Low birthweight and short gestation | Zinc deficiency | 384.4 | -19.8 | -26.8 |
| 3 Smoking | Iron deficiency | 323.4 | 2.8 | -14.2 |
| 4 High blood pressure | Workplace injury | 383.9 | -23.0 | -7.7 |
| 5 Household air pollution | 6th highest plasma glucose | 393.1 | -82.2 | -22.2 |
| 6 Ambient particulate matter | Ambient particulate matter | 384.9 | -22.2 | -22.2 |
| 7 Unsafe water | Ambient particulate matter | 347.5 | -39.8 | -27.8 |
| 8 Alcohol use | Industrial ergonomics | 311.5 | -28.5 | -30.0 |
| 9 Unsafe sanitation | 9th highest plasma glucose | 311.5 | 0.6 | -3.0 |
| 10 Low household air pollution | 10th highest plasma glucose | 311.5 | -46.8 | -41.2 |
| 11 No access to handwashing facility | 11th highest plasma glucose | 311.5 | -35.5 | -38.3 |
| 12 High total cholesterol | 12th highest plasma glucose | 311.5 | -9.1 | -15.9 |
| 13 High body mass index | 13th highest plasma glucose | 311.5 | -14.2 | -14.2 |
| 14 Low fruit | 14th highest plasma glucose | 311.5 | -13.0 | -12.6 |
| 15 Low physical activity | 15th highest plasma glucose | 311.5 | -11.6 | -10.4 |
| 16 Low nuts and seeds | 16th highest plasma glucose | 311.5 | -10.9 | -12.4 |
| 17 Low sodium | 17th highest plasma glucose | 311.5 | -9.3 | -12.0 |
| 18 Occupational injuries | 18th highest plasma glucose | 311.5 | -8.0 | -3.9 |
| 19 Impaired kidney function | 19th highest plasma glucose | 311.5 | -5.5 | -8.0 |
| 20 Alcohol use | 20th highest plasma glucose | 311.5 | -5.7 | -5.3 |
| 21 Second-hand smoke | 21st highest plasma glucose | 311.5 | -2.7 | -1.0 |
| 22 Low vegetables | 22nd highest plasma glucose | 311.5 | -2.2 | -1.6 |
| 23 Low omega 3 | 23rd highest plasma glucose | 311.5 | -2.0 | -1.6 |
| 24 Vitamin A deficiency | 24th highest plasma glucose | 311.5 | -1.6 | -1.0 |
| 25 Drug use | 25th highest plasma glucose | 311.5 | -1.0 | 0.0 |
| 26 low accessibility | 26th highest plasma glucose | 311.5 | -0.3 | 0.7 |
| 27 Low physical activity | 27th highest plasma glucose | 311.5 | -0.7 | -0.3 |
| 28 Occupational injuries | 28th highest plasma glucose | 311.5 | -0.7 | -0.3 |
| 29 Low physical activity | 29th highest plasma glucose | 311.5 | -0.7 | -0.3 |
| 30 Low fibre | 30th lead | 311.5 | -0.7 | -0.3 |
| 31 Low vegetables | 31st lead | 311.5 | -0.7 | -0.3 |
| 32 Vitamin A deficiency | 32nd lead | 311.5 | -0.7 | -0.3 |

### Leading risks 2006 vs 2016

| Risk Category | Risk Factor | 2006 DALYs | 2016 DALYs |
|---------------|-------------|------------|------------|
| 1 Child growth failure | No access to handwashing facility | -20.7 | -20.7 |
| 2 Low birthweight and short gestation | Zinc deficiency | -2.5 | -2.5 |
| 3 Smoking | Iron deficiency | -2.5 | -2.5 |
| 4 High blood pressure | Workplace injury | -3.8 | -3.8 |
| 5 Household air pollution | 6th highest plasma glucose | -2.0 | -2.0 |
| 6 Ambient particulate matter | Ambient particulate matter | -2.0 | -2.0 |
| 7 Unsafe water | Ambient particulate matter | -2.0 | -2.0 |
| 8 Alcohol use | Industrial ergonomics | -2.0 | -2.0 |
| 9 Unsafe sanitation | 9th highest plasma glucose | -2.0 | -2.0 |
| 10 Low household air pollution | 10th highest plasma glucose | -2.0 | -2.0 |
| 11 No access to handwashing facility | 11th highest plasma glucose | -2.0 | -2.0 |
| 12 High total cholesterol | 12th highest plasma glucose | -2.0 | -2.0 |
| 13 High body mass index | 13th highest plasma glucose | -2.0 | -2.0 |
| 14 Low fruit | 14th highest plasma glucose | -2.0 | -2.0 |
| 15 Low physical activity | 15th highest plasma glucose | -2.0 | -2.0 |
| 16 Low nuts and seeds | 16th highest plasma glucose | -2.0 | -2.0 |
| 17 Low sodium | 17th highest plasma glucose | -2.0 | -2.0 |
| 18 Occupational injuries | 18th highest plasma glucose | -2.0 | -2.0 |
| 19 Impaired kidney function | 19th highest plasma glucose | -2.0 | -2.0 |
| 20 Alcohol use | 20th highest plasma glucose | -2.0 | -2.0 |
| 21 Second-hand smoke | 21st highest plasma glucose | -2.0 | -2.0 |
| 22 Low vegetables | 22nd highest plasma glucose | -2.0 | -2.0 |
| 23 Low omega 3 | 23rd highest plasma glucose | -2.0 | -2.0 |
| 24 Vitamin A deficiency | 24th highest plasma glucose | -2.0 | -2.0 |
| 25 Drug use | 25th highest plasma glucose | -2.0 | -2.0 |
| 26 low accessibility | 26th highest plasma glucose | -2.0 | -2.0 |
| 27 Low physical activity | 27th highest plasma glucose | -2.0 | -2.0 |
| 28 Occupational injuries | 28th highest plasma glucose | -2.0 | -2.0 |
| 29 Low physical activity | 29th highest plasma glucose | -2.0 | -2.0 |
| 30 Low fibre | 30th lead | -2.0 | -2.0 |
| 31 Low vegetables | 31st lead | -2.0 | -2.0 |
| 32 Vitamin A deficiency | 32nd lead | -2.0 | -2.0 |

### Leading risks 2016

| Risk Category | Risk Factor | 2016 DALYs |
|---------------|-------------|------------|
| 1 Child growth failure | No access to handwashing facility | -20.7 |
| 2 Low birthweight and short gestation | Zinc deficiency | -2.5 |
| 3 Smoking | Iron deficiency | -2.5 |
| 4 High blood pressure | Workplace injury | -3.8 |
| 5 Household air pollution | 6th highest plasma glucose | -2.0 |
| 6 Ambient particulate matter | Ambient particulate matter | -2.0 |
| 7 Unsafe water | Ambient particulate matter | -2.0 |
| 8 Alcohol use | Industrial ergonomics | -2.0 |
| 9 Unsafe sanitation | 9th highest plasma glucose | -2.0 |
| 10 Low household air pollution | 10th highest plasma glucose | -2.0 |
| 11 No access to handwashing facility | 11th highest plasma glucose | -2.0 |
| 12 High total cholesterol | 12th highest plasma glucose | -2.0 |
| 13 High body mass index | 13th highest plasma glucose | -2.0 |
| 14 Low fruit | 14th highest plasma glucose | -2.0 |
| 15 Low physical activity | 15th highest plasma glucose | -2.0 |
| 16 Low nuts and seeds | 16th highest plasma glucose | -2.0 |
| 17 Low sodium | 17th highest plasma glucose | -2.0 |
| 18 Occupational injuries | 18th highest plasma glucose | -2.0 |
| 19 Impaired kidney function | 19th highest plasma glucose | -2.0 |
| 20 Alcohol use | 20th highest plasma glucose | -2.0 |
| 21 Second-hand smoke | 21st highest plasma glucose | -2.0 |
| 22 Low vegetables | 22nd highest plasma glucose | -2.0 |
| 23 Low omega 3 | 23rd highest plasma glucose | -2.0 |
| 24 Vitamin A deficiency | 24th highest plasma glucose | -2.0 |
| 25 Drug use | 25th highest plasma glucose | -2.0 |
| 26 low accessibility | 26th highest plasma glucose | -2.0 |
| 27 Low physical activity | 27th highest plasma glucose | -2.0 |
| 28 Occupational injuries | 28th highest plasma glucose | -2.0 |
| 29 Low physical activity | 29th highest plasma glucose | -2.0 |
| 30 Low fibre | 30th lead | -2.0 |
| 31 Low vegetables | 31st lead | -2.0 |
| 32 Vitamin A deficiency | 32nd lead | -2.0 |
were attributable to tobacco, most of which is attributable to smoking tobacco. Smoking-attributable deaths have increased by 20·1% (15·3–25·2) since 1990, with most deaths occurring in China, India, the USA, and Russia. Smoking is the second-leading risk factor for men for deaths and leading for DALYs, accounting for 16·3% (14·6–17·9) of deaths and 9·5% (8·5–10·7) of DALYs, and the sixth for women for deaths and ninth for DALYs, with 5·8% (5·0–6·7) of deaths and 2·9% (2·5–2·94) of DALYs. In 2016, there were 177·3 million (162·3 million to 194·3 million) smoking-attributable DALYs globally. Overall, in 2016 chronic respiratory diseases (30·3% [25·2–36·0]), neoplasms (19·2% [16·0–22·8]), and cardiovascular diseases (18·0% [16·0–20·0]) were the three leading causes of smoking-attributable age-standardised DALYs across both sexes. For women, the leading cause of DALYs was COPD, whereas the leading cause for men was IHD.

Second-hand smoke exposure is highest in eastern Asia and Oceania and higher among women and children compared with men. The distribution of DALYs attributable...
to second-hand smoke exposure is bimodal, with peaks in the post-neonatal period and again in older age groups. Globally 0·9 million (0·7 million to 1·1 million) deaths were attributable to second-hand smoke exposure, of which 56 540 (28951–89043) occurred among children younger than age 10 years.

In estimating the burden attributable to smokeless tobacco, we found that the risk varies by the toxicity of the type used; there is sufficient evidence that chewing tobacco and other products of similar toxicity cause excess risk of oral and oesophageal cancer while, at this time, existing evidence does not support attributing burden to snus or similar smokeless tobacco products. Globally, smoking tobacco causes far more burden than smokeless tobacco; nonetheless, smokeless tobacco is an important risk factor for oral and oesophageal cancer in India, where more than half of the 32 141 (24 930–39 243) global deaths attributable to smokeless tobacco occur.

Low birthweight and short gestation, new risk factors in GBD 2016, were the third-ranked Level 3 risk factor globally for all-ages DALYs in 2016, which reflects a 61·6% (59·3–64·6%) decrease in all-ages DALY rates from 5112·8 (4934·2–5389·6) DALYs per 100 000 in 1990 to 1960·8 (1862·0–2060·3) DALYs in 2016. In 1990, this risk factor was the second-ranked Level 3 risk factor globally for all-age DALYs; most of the decrease from 1990 to 2016 is due to a lower mortality burden in the causes attributable to low birthweight and short gestation rather than changes in exposure itself. Increasing SDI was associated with decreasing exposure, but the exposure gradient between SDI quintiles was not as large as the differential between high and low SDI in attributable burden. Exposure was highest in South Asia, eastern sub-Saharan Africa, and parts of the western Sahel zone, while attributable burden was highest in South Asia and parts of the western Sahel zone. The trend in exposure to low birthweight for gestation decreased at the global level from 1990 to 2016, reflective of the overall decrease in DALYs burden during the same time period. The biggest improvements were seen in Colombia, Brunei, and Zimbabwe, with broad improvements also seen across much of eastern sub-Saharan Africa.

In 2016, high FPG was the third-leading risk factor for deaths and the fourth-leading risk factor for DALYs globally among Level 3 risk factors, accounting for more than 5·6 million deaths (4·5 million to 7·0 million) and 144·1 million DALYs (119·9 million to 171·6 million). Since 1990, the age-standardised percent of deaths and DALYs attributable to high FPG has increased globally from 7·8% (6·0–10·1%) to 10·5% (8·3–13·1%) and 4·4% (3·7–5·3%) to 6·2% (5·3–7·3%), respectively. Diabetes was the largest source of DALYs attributable to increased FPG, followed by ischaemic heart disease and chronic kidney disease. We re-evaluated epidemiological evidence supporting the causal relationship between high FPG and disease endpoints and found sufficient evidence to include ten new outcomes for high FPG. These new outcomes included glaucoma, cataracts, dementia, liver cancer, lung cancer, ovarian cancer, breast cancer, bladder cancer, colorectal cancer, and pancreatic cancer. The new outcomes together contributed to 174 352 (37 297–388 039) additional deaths and 2·6 million (0·6 million to 5·7 million) additional DALYs beyond the causes that were included in GBD 2015.

In 2016, BMI was the fifth-ranked Level 3 risk factor for death globally, accounting for more than 4·5 million (2·9 million to 6·4 million) deaths and 135·4 million (88·6 million to 187·4 million) DALYs. Among Level 3 risk factors with more than 10 million attributable DALYs, high BMI had the fastest annualised rate of increase in SEV since 1990 (appendix 2 p 1399). Despite this significant increase in risk exposure, increases in attributable burden were attenuated by significant decreases in risk-deleted DALY rates, mainly due to reductions in cardiovascular disease mortality rates. We find that the burden attributable to high BMI increases with increasing development, with the lowest rates of disease attributable to high BMI found in sub-Saharan Africa, yet development is not the only predictor. We conducted a systematic search of health outcomes caused by excess bodyweight and added eight new causes for GBD 2016, which together contributed to 442 750 (191 407–796 350) additional deaths beyond the causes that were included in GBD 2015. Additionally, we included childhood overweight and childhood obesity as new risk factors, allowing us to better capture the health effects of excess bodyweight across the life course. Within
the CRA framework, the only childhood overweight and obesity outcome eligible for inclusion was asthma. We found that 10.4% (3.1–21.2) of asthma can be attributed to childhood excess bodyweight globally, a total of 1128 (311–2354) deaths and 642,532·1 (180,916·3 to 1,456,342·7) DALYs. While childhood burden is much smaller compared with adult burden, estimating exposure for children is crucially important in view of the well described effects of childhood overweight and obesity on adult health outcomes.

Air pollution was ranked sixth in terms of attributable DALYs in 2016. We found that 7.5% (6.6–8.4) of deaths globally were attributable to ambient air pollution in 2016 (4·1 million [3·6 million to 4·6 million] deaths, 1·3 million [1·1 million to 1·5 million] in South Asia). Countries with notably high levels of attributable deaths include China (11·1% [9·7–12·7] of all deaths attributable to ambient particulate matter) and India (10·6% [9·2–11·9] of all deaths). The diseases with the largest proportion of burden attributable to air pollution are LRI and COPD; ambient particulate matter is responsible for 27·5% (21·4–34·4) of all LRI and 26·8% (16·1–38·6) of COPD deaths and 33·3% (26·3–40·5) of LRI deaths in children younger than 5 years. In terms of overall ranking, ambient particulate matter has increased from seventh in 1990 with 115·2 million (99·1 million to 132·9 million) DALYs to sixth in 2016 with 105·7 million (94·2 million to 117·8 million) DALYs. For deaths, it is among the top ten ranked risk factors in 195 countries and territories, including India and China, where it was in third and fourth place, respectively. Also of note is that updated satellite data indicate increased ambient air pollution in 2015–16 in West Africa that is driven by wind-blown dust from the Sahara. This effect has profound effect on disease burden in this region, as intense particulate matter with an aerodynamic diameter smaller than 2·5 µm (PM2·5) events affect Africa’s densest region.

Globally, alcohol is estimated to be the seventh-leading risk factor in 2016 in terms of DALYs. In the same year, alcohol use was estimated to have caused 99·2 million DALYs (88·3 million to 111·2 million), accounting for 4·2% (3·7–4·6) of total DALYs. This is a larger share of total burden than previously reported, driven primarily by changes made to both the exposure and RR models. This burden is distributed unequally among the sexes and regions. When decomposed by sex, alcohol use accounts for 6·2% (5·6–6·9) of total DALYs among men and 1·7% (1·4–2·0) of total DALYs among women. When decomposed by region in 2016, alcohol use accounts for 13·9% (11·5–16·8) of age-standardised DALYs in eastern Europe, 4·0% (3·4–4·6) of age-standardised DALYs in Southeast Asia, but only 0·8% (0·6–1·0) of age-standardised DALYs in the Middle East. Alcohol use attributable DALYs have also increased by more than 25% over the years 1990–2016, driven primarily by increased consumption in South Asia, Southeast Asia, and Central Asia, among both men and women. Globally, alcohol use exposure has increased by 15·2% (8·7–22·6) over that time frame among men and decreased by 3·2% (–9·1 to 3·1) among women. However, the largest increases in exposure have been in countries in the low-middle quintile of SDI. Globally, alcohol use is the leading risk factor in DALYs between the ages of 15 years and 49 years in 2016. However, unlike tobacco or drugs, governments have been discouraged from efforts to limit...
alcohol’s availability by trade agreements and disputes. Given alcohol’s health burden within these age groups, an increased focus on alcohol control policies is needed to effectively address this risk factor.

It is worth noting some key results for dietary risks as well. In 2016, suboptimal diet was the second-leading risk factor for deaths and DALYs globally, accounting for 18·8% (16·0–21·7) of all deaths and 9·6% (8·2–11·1) of all DALYs. Comparing men and women, suboptimal diet accounts for the greatest percentage of total deaths in men (19·0% [16·3–21·8]) and the second largest in women (18·6% [15·7–21·7]). Meanwhile, suboptimal diet accounts for the second-largest percent of total DALYs in both men (10·6% [9·1–12·2]) and women (8·4% [7·0–9·9]). More than 50% of deaths (51·5% [44·2–59·2]) and DALYs (54·1% [47·1–61·5]) attributable to suboptimal diet were due to cardiovascular diseases. Among the individual dietary risks, a diet low in whole grains accounted for the largest number of deaths (4·6% [3·0–6·4]), followed by a diet low in fruits (4·3% [2·7–6·3]) and a diet high in sodium (4·2% [1·2–8·3]). Leading dietary risks for DALYs were low intakes of whole grains (2·6% [1·8–3·6]), fruits (2·6% [1·6–3·7]), and nuts and seeds (2·1% [1·4–2·8]). The greatest increase in attributable deaths and DALYs between 1990 and 2016 occurred for a diet high in red meat, followed by a diet high in sugar-sweetened beverages and a diet low in milk, respectively.

Discussion
General findings

Based on the analysis of 22717 sources, we estimated disease burden attributable to 84 metabolic, environmental, occupational, and behavioural risk factors or clusters of risks from 1990 to 2016 in 195 countries and territories. In 2016, all risks combined contributed to 59·9% (58·4–61·3) of deaths and 45·2% (43·2–47·3) of DALYs worldwide, compared with 60·3% (59·0–61·6) of deaths and 49·6% (47·6–51·7) of DALYs in 1990. The role of changes in risk factors in explaining changes in deaths and DALYs varies considerably across causes and ages, with the largest effects noted in children due to infectious diseases. Since 1990, exposure increased significantly for 30 risks, did not change significantly for four risks, and decreased significantly for 31 risks. The risks with the highest increases in SEVs include high body-mass index, occupational exposure to diesel engine exhaust, and occupational exposure to trichloroethylene, while the risks with the largest decreases in exposure are diet high in transfatty acids, household air pollution from solid fuels, and unsafe sanitation.

We found substantial heterogeneity across countries in the leading risk factors. Some notable patterns are the role of unsafe sexual practices as a driver of the HIV epidemic in Eastern and Southern Africa and the role of alcohol consumption in Eastern Europe and Central Asia. There are also marked spatial patterns for other risks such as high BMI in Central America, North Africa and the Middle East, and Oceania. Interpreting spatial patterns needs to take into account the fact that some risks have a strong relationship with socioeconomic development. Several environmental and behavioural risks, including water, sanitation, handwashing, household air pollution, and childhood growth failure decline profoundly with development. Another cluster of risks tends to increase with socioeconomic development, including high BMI, high SBP, red meat consumption, sugar-sweetened beverages, alcohol, and high FPG.

Cross-cutting themes

Many factors should determine government priorities for action including the size of the problem, inequalities related to the problem, likely future trends, the availability of effective policy options, and the opportunity cost of tackling a particular problem. In this analysis, we provided information about the size of the problem, trends in exposure in the last 27 years, and the range of exposure at given levels of socioeconomic development. Problems that
are large, increasing, and variable across countries at the same level of development likely warrant particular policy attention. Our analysis showed that components of diet, obesity, FPG, and SBP are the most prominent global risks fulfilling these criteria. Because of the strong inter-relationships between these risks, the true driver of this cluster is likely diet, the risk in BMI, or both, with knock-on consequences for FPG and SBP. The rise of obesity and the associated increases in FPG and SBP warrant considerable global policy attention. Other major risks that should continue to receive attention—even intensified attention in some locations—such as smoking, are nevertheless declining at the global level. The unique combination of large current effect and increasing exposure puts obesity in a special category of risks. Obesity is likely to not only influence future population health in many locations, but will have considerable financial implications for health systems, given what we know about treatment costs for the associated diseases. Since important drivers of obesity such as physical activity and diet patterns are adopted in childhood and adolescence, more work is needed to proactively address the adoption of these risks in these younger age groups.

For the first time, we assess the contribution of changes of risk exposures to the overall global trend for deaths and DALYs; for example, in the past 10 years, changes in all risk exposures contributed to an 10.8% (8.3–13.1) decline in DALYs, while other factors contributed to a 16.5% (14.1–18.8) decrease in DALYs. More detailed assessments show large declines in CMNN causes and increases in injuries and non-communicable DALYs. In each case, the contribution of other factors was substantially larger than the contribution of risk reduction. Our findings of the relatively small contribution of risk reduction to the declines in NCDs are not at odds with published studies for the UK and the USA, because we are reporting at the global level; our results at the national level suggest a larger role for risk reduction in some high-SDI locations. These observations lead to two directions for further analysis. First, what is the explanation for the declines driven by other factors? Some of this effect might be social policy working through various causal channels, and some is likely due to improvements in access to high-quality health care. This is particularly true for conditions such as selected cancers, ischaemic heart disease, cerebrovascular disease, chronic kidney diseases, HIV/AIDS, tuberculosis, and maternal mortality, for which health care is known to have large effects. Second, in view of the enormous potential of risk reduction to change health outcomes as documented in this and many other studies, why has progress on many risks been comparatively slow? For example, even though global tobacco consumption is declining in terms of rates, the pace of decline has been remarkably slow on average, despite more than 50 years of good evidence on the harms of tobacco. The relatively poor track record for global risk reduction might in part reflect the low rate of investment in risk reduction compared with curative health care. It might also reflect the continuing challenge of changing many risky behaviours. Relatively little funding for research on changing behaviours compared with new diagnostics and therapeutics might also be part of the explanation of the prevention paradox. Changing behavioural risks could also require more than government action; harnessing the private sector to facilitate behavioural change might also be crucial.

Important changes in GBD 2016 compared with in GBD 2015 (risks ordered by global rank)

**Systolic blood pressure**

Increased SBP remains the leading global risk at Level 3 in the GBD risk hierarchy. Highly effective interventions exist to manage blood pressure at the primary care level, as do a range of public health interventions, so it is quite remarkable that global exposure to increased SBP is increasing. Part of this increase might be tied to the global rise in high BMI, but the increase in SBP represents significant missed opportunity for the world’s health systems. In 54 countries high SBP is actually declining, while its increase in China is now well documented in a series of population-based surveys. Tackling rising SBP is a global concern, but this is particularly important in those locations where rates are increasing. In view of the effect of the risk and the large array of available, effective interventions, health systems and the global health community need to mobilise increased resources and policy attention to tackle this problem. It might be necessary to design a variety of public policies including food reformulation to reduce sodium content and efforts to incentivise primary care providers to give priority to the management of SBP.

**Tobacco**

In moving toward developing a comprehensive picture of tobacco use globally, in GBD 2016, we have for the first time included smokeless tobacco use as a risk factor. While the burden of smokeless tobacco is minimal in the majority of countries, it is of huge importance in south Asia, where the highest risk-weighted exposure is observed in Bangladesh (risk-weighted exposure of 0.75 [0.61–0.87]), Bhutan (0.53 [0.44–0.62]), Myanmar (0.50 [0.42–0.59]), Nepal (0.50 [0.42–0.58]), and India (0.45 [0.43–0.47]). In these countries more women use smokeless tobacco products than smoked tobacco products, and we find that use of any tobacco products, smoked or smokeless, continuously increases with age, a regional age pattern that differs from the global and male regional age pattern. The combination of high exposure and large population results in a majority of global deaths attributable to smokeless tobacco in 2016 occurring in India, where it is also the leading risk factor for oral cancer.

In GBD 2016, we also improved the estimation of burden attributable to second-hand smoke. At the global level, while the burden of second-hand smoke remains substantial, exposure to second-hand smoke has been declining significantly at an annualised rate of change of
Progress combatting the tobacco epidemic has resulted in global declines in prevalence of tobacco use and second-hand smoke exposure, yet the number of deaths and DALYs attributable to tobacco has increased since 1990. Increases in burden were driven by a combination of population growth and population ageing, along with persistently high smoking prevalence in some of the most populous countries of the world. Taken together, we can expect the burden of tobacco to remain high in years to come, unless the rate of progress is significantly accelerated. Many countries with persistently high levels of daily smoking recorded marginal progress in the past decade, and smoking remains a leading risk factor in most countries. The fact that tobacco use patterns diverge by location, level of development, and sex highlights the need for more tailored approaches to change smoking behaviours in the future. Particularly worrisome are the trends among young men and women. For example, in Indonesia, a country that has not yet ratified the FCTC,11 more than half of men aged 20–24 years are daily smokers. Understanding what works—and what does not—for tobacco control across contexts and within subpopulations (ie, men and women, younger and older individuals, various socioeconomic groups) is of growing priority. To significantly and permanently change the toll of tobacco, a renewed and sustained focus is needed on comprehensive tobacco control policies around the world.

**Fasting plasma glucose**

The global increase in FPG is likely tied to the increase in BMI. While exposure is increasing, age-standardised attributable mortality rate is not; a related pattern is that the prevalence of diabetes is increasing, but deaths from diabetes have been declining, likely because clinical management of the macrovascular complications of diabetes has improved in many (but not all) locations. Prevention trials show that with intensive resources devoted to weight loss and physical activity, reductions in FPG can be achieved; however, these interventions have not been implemented at a national scale and adherence in the long run is challenging. Systematic efforts to screen for high FPG implemented in some countries may increase awareness and action in more patients but can be resource-intensive. Clinical interventions to reduce FPG can be effective, although there are more recent debates on the appropriate targets for treatment in some cases. With FPG increasing in many settings, it is difficult to determine the population effect of treatment of blood sugar on population FPG. FPG remains one of the risk factors that is most likely influenced at the primary health-care level, emphasising the role of universal coverage for primary care in a multigroosed response to this increasing problem.

**Body-mass index**

One of the most alarming risks in the analysis is increased BMI, because its burden is large and increasing, and it is prevalent across all levels of SDI.22,23 The potential drivers of this global epidemic include changes in food industries and systems, which increase availability, accessibility, and affordability of energy-dense foods, along with intense marketing of such foods, as well as reduced opportunities for physical activity.24 A range of interventions have been proposed to reduce obesity, including restricting the advertisement of unhealthy foods to children, improving school meals, taxation of sugar-sweetened beverages, and taxation to reduce consumption of other unhealthy foods and subsidies to increase intake of healthy foods, and using supply-chain incentives to increase production of healthy foods.25 However, the evidence base that many of these interventions can affect trends in obesity at scale is currently weak.26 What we know without a doubt is that obesity rates continue to increase in almost all locations. Low-SDI and middle-SDI countries generally have little financial resources for nutrition programs and mostly rely on external donors whose programmes often preferentially target undernutrition.27 The increase in exposure to high BMI is greater than the increase in attributable burden largely because cardiovascular disease death rates continue to decline because of other changes, particularly improvements in treatment and declines in smoking and high cholesterol. Proposed policies, even if fully implemented, are unlikely to rapidly reduce the prevalence of obesity. While not a solution to the rise of overweight and obesity, clinical interventions that control high SBP, cholesterol, and FPG (the major risk factors for cardiovascular disease) can be used to mitigate some of the cardiovascular ill-effects.28 Expanded use of such interventions among obese people could effectively reduce the disease burden of high BMI. Sustained progress, however, will require policies that effectively control weight in childhood and in young and middle-aged adults.

**Diet**

In GBD 2016, poor dietary habits were the second leading risk factor at Level 2 of the hierarchy for mortality globally, accounting for nearly one in every five deaths. The overall burden of dietary risks at the global level was 14·8% (11·7–18·5) lower than in GBD 2015. Additionally, important differences were observed in the attributable burden and the ranking of individual dietary risks. Multiple factors have contributed to these differences, including using more data sources, as well as improving the method of estimation of the mean and distribution of intake for each dietary factor. In GBD 2016, for the first time, we used sales data to inform our estimates of consumption for most dietary factors. Using sales data, in addition to improving our overall data coverage, allowed us to capture recent trends in consumption. This was particularly important for specific dietary factors, such as sugar-sweetened beverages, which have been the target of dietary policies in several
countries. Additionally, to improve the consistency of definitions of dietary risk factors across surveys, we made a systematic effort to obtain and re-extract individual-level data from nutrition surveys. To make the current level of intake and optimal level of intake more comparable, we used the absolute level of intake (rather than the intake standardised to 2000 kcal per day) as the primary exposure in GBD 2016. We also corrected our estimated daily intake of each individual dietary factor for within-person variation and characterised the usual intake at the population level. Finally, given the differences in the health effects and patterns of intake for legumes and vegetables, we estimated the burden of disease attributable to low intake of legumes and low intake of vegetables separately.

The decade of 2016–25 has been declared as the Decade of Action on Nutrition by the United Nations General Assembly. GBD 2016 provides a comprehensive picture of various forms of malnutrition (ie, undernutrition, overweight or obesity, and poor dietary habits) across all countries at the start of the Decade of Action on Nutrition and can inform priorities for evidence-based interventions in each country. GBD also provides an independent avenue to annually monitor the progress of countries toward achieving their nutrition-related goals in a comparable and consistent manner. Our results show that among all forms of malnutrition, poor dietary habits, particularly low intake of healthy foods, is the leading risk factor for mortality. This finding has important implications for national governments and international organisations aiming at ending malnutrition over the next decade, highlighting the need for comprehensive food system interventions to promote the production, distribution, and consumption of healthy foods across nations.

Low birthweight and short gestation

Low birthweight and short gestation have been added for GBD 2016; they are the third-leading global risk at Level 3 in the GBD risk hierarchy. Improvements in burden attributable to low birthweight and short gestation have been largely driven by other factors influencing neonatal death rates, given that exposure to low birthweight and short gestation have not improved much over the past 27 years. Little progress in exposure suggests suboptimal coverage of interventions and programmes that can prevent low birthweight and short gestation. These include women-centred services for optimising nutrition (including minimising obesity), infection control, smoking cessation, and preventive care for pregnant women or those contemplating pregnancy.

Efforts should also focus on maximising the quality of antenatal care services to identify and appropriately manage at-risk and high-risk pregnancies, including avoidance of provider-initiated preterm delivery. If evidence-based interventions are employed, it should be possible even in resource-limited settings to shift the risk curve for those babies who will be born early, small, or both, despite best efforts. Before birth, this includes potentially antenatal steroid administration to promote lung development; at birth, this requires presence of adequately trained and equipped neonatal resuscitation services; post-delivery, it should include physicians with neonatal specialisation and availability of supportive equipment such as continuous positive airway pressure. Facility-based infection control measures are crucial to prevent nosocomial transmission, as such events are highly lethal in low birthweight or short gestation neonates. The inclusion of this risk for a major cause of DALYs—namely, neonatal mortality—also expands the share of overall burden that can be attributed to risks in general. More work remains, however, to understand the relationship between low birthweight and short gestation and childhood growth failure after 1 month. Our analysis to date may actually underestimate the importance of this risk if the share of childhood growth failure that can be traced to low birthweight and gestational age is fully established.

Alcohol

Globally, alcohol is estimated to be the seventh-leading risk factor in 2016 in both DALYs (4·2% [3·7–4·6]) and deaths (5·2% [4·4–6·0]). Previous studies have noted the possibility that the preventive effects of alcohol might have been overstated due to selection bias and choice of the reference population. Our findings lend further credence to these hypotheses; with the exception of IHD, our results show either a minor or non-significant preventive effect for causes previously estimated to have large preventive effects. Further, our analysis noted a much larger risk of neoplasms due to alcohol use than previously reported. Combined with our new data for alcohol use exposure, alcohol use is ranked as one of the leading risk factors, surpassing cholesterol as a share of total DALYs, compared with previous iterations of GBD.

Ensemble distributions

In GBD 2016 we have introduced a more accurate method for developing the distributions of exposure for many risk factors. Our work on distributions and the shift to ensemble distributions shows that the assessment of attributable burden is sensitive to distributional assumptions. Given that a number of risks, such as BMI, SBP, cholesterol, and FPG, rise exponentially as a function of exposure, the estimation of the tail of the distribution has an important effect on the results. The ensemble modelling approach can provide more accurate estimation of the full distribution, including the tails of the distribution. In general, we believe that the assessment of the distribution of the risks deserves more careful attention in future research.

Comparison of GBD 2016 to other estimates

The GBD study is the most comprehensive effort to conduct a population-level CRA across countries and risks. Differences between GBD 2016 estimates and other global estimates are generally related to approaches to data processing, access to data sources, and analysis decisions.
For several risks, including smoking, ambient ozone pollution, household air pollution from solid fuels, lead exposure, intimate partner violence, and breastfeeding, GBD estimates were lower than published WHO estimates. These discrepancies can be attributed to different definitions, methodological decisions, granularity, and input data. For some findings, annual estimates might disagree, but regional patterns were consistent between WHO and GBD. UNICEF produces estimates for child stunting that are lower than GBD estimates with some disagreement where progress has been made globally. There is more consistency in estimates between UNICEF and GBD for child wasting and child underweight. GBD estimates for the prevalence of low birthweight and short gestation are slightly lower when compared with WHO estimates, but show similar geographical patterns. Scientific literature reveals similar results to GBD for impaired kidney function and low birthweight and short gestation. Research published on iron-deficiency anaemia differs from GBD in methods and definitions, resulting in generally higher GBD estimates. GBD estimates were much lower than published research on occupational estimates, largely due to different cause-outcome pairs and GBD’s application of the CRA approach (see appendix 1 p 10).

Future directions

Interpretation of our results and prioritisation at the national level might also need to take into account the variable strength of evidence supporting the causal connection for each risk-outcome pair. In GBD 2016, we have continued to use the World Cancer Research Fund criteria of convincing or probable evidence to select risk-outcome pairs for inclusion. Some aspects of these definitions are subjective. Not all researchers would agree on the interpretation of the available evidence as fulfilling these criteria. For example, there are six studies on non-exclusive breastfeeding and LRI; there are two studies on discontinued breastfeeding and diarrhoeal diseases. We have sought to quantify the number of studies of different kinds that are available to support these judgements in table 1, but not all studies support causality to the same extent. Randomised trials, if well conducted, provide the strongest evidence of causality, because they are likely not affected by confounding. But even randomised trials can have biases when there are missing observations, as is often the case. Randomised trials are also not feasible in many cases, or if feasible, not representative for many risks, including environmental risks. Cohort studies can provide compelling evidence, but many cohorts do not adequately control for socioeconomic confounders and can suffer from many other issues related to the quality of exposure measurement or outcome ascertainment. To go beyond, the quantification of the number of studies of each type we have provided here will necessitate a deeper analysis of the potential limitations of all 2579 studies used across the risk-outcome pairs. In future work, we plan to evaluate the quality of each of these studies with a standardised approach and work toward an overall evidence summary. There is also a more fundamental philosophical question about the presentation of risk information. Should decision makers only pay attention to risk factor quantification for those risks supported by the strongest causal evidence such as randomised trials? Or do notions such as the precautionary principle suggest that we should pay attention to risk quantification even for risk-outcome pairs where the evidence is less definitive. Because the social response to risks, particularly risks that might be emerging, can take considerable time, ignoring risks for which the evidence is less definitive might actually lead to worse outcomes for society. Conversely, in a world of scarce political and financial resources, devoting attention to risks that might turn out not to be causal might lead to less action on more well documented risks.

As part of future iterations of GBD, we plan to quantify the burden attributable to some distal social risks. We have embarked on this work, but it proves to have challenges that are qualitatively different than many of the risks included here. For nearly all risk-outcome pairs, we assume in the absence of other evidence that the RRs by age and sex are generalisable across populations (the exception is for BMI in Asian and non-Asian populations for breast cancer). In principle, if there is evidence of statistically significant RRs for different population groups, we would incorporate these into the CRA. For distal social risks, the pathways to outcomes can be modified in many ways by other risks or by health-system interventions. We expect that the RR due to low education for 40-year-old men would be different in Norway than in Kenya. Given the greater potential for variation in RRs for distal risks, inclusion in GBD will require more local quantification of RRs and then a further modelling step to estimate RRs for these determinants for all locations. Our first planned target for this quantification is educational attainment. Given the global policy focus on the potential health effects of climate change driven by rising levels of greenhouse gases, and consequently temperature, we will add temperature and precipitation as risk factors that are quantified on an annual basis in future iterations of GBD. Even though most of the potential harm that might come from rising temperatures or extreme weather events will occur in the future, in some locations, we might already find significant attributable burden. This analysis will need to examine the relationship between disease and mortality risk and temperature for each relevant outcome. For some outcomes, these relationships are likely to be U shaped, with an optimal temperature for minimum risk. These U-shaped relationships could mean that for some outcomes in some locations, rising temperature might reduce harm, even if in most locations it will increase burden. Likewise, a major issue in understanding the temperature and health outcome relationships is that we
would expect these to be attenuated in high-SDI settings, where many individuals can protect themselves from some of the consequences. In other words, generalising from studies in high-SDI locations to other locations might underestimate the risk relationships.

In the GBD CRA approach, the TMREL is the level of risk exposure that leads to minimum risk for individuals. In principle, the TMREL could vary by location, age, and sex. To date, the TMREL in the GBD work has been selected to be universal. For more detail on TMREL, see appendix 1 (p 22). The analysis of alcohol, where for IHD there is a protective effect at mild to moderate consumption but a harmful effect for neoplasms and injuries, is a good example of where it would be desirable to vary TMREL by age. In younger ages, injuries will be more important than cardiovascular diseases, pushing the TMREL toward zero consumption of alcohol, whereas at older ages, the TMREL might be higher. Letting the TMREL vary by age and sex and even location will add an extra analytical step to GBD; like all other estimation steps, this can have estimation error. To date, we have thought the estimation error associated with a TMREL that varies may not make the effort worthwhile. As evidence accumulates on some risks like alcohol, we will carefully evaluate this position.

Limitations
A study of this scope has many limitations. Here we discuss the limitations that apply to the overall risk factor analytical framework and limitations in the estimation approach for new risks and risks that have undertaken significant revisions from GBD 2015. More details and limitations of the analytical approach for each risk factor are presented in appendix 1 (p 43). First, we continue to include risk-outcome pairs that meet the World Cancer Research Fund criteria of convincing or probable evidence for causality. While these criteria have proven a useful bar for inclusion, there is an important subjective element to their interpretation. Some risk-outcome pairs included in this study might not meet these criteria or alternative criteria that are developed as new randomised trials, cohort studies, or case-control studies are published. Second, we used published cohort studies to evaluate the degree to which different risks are mediated through other risks. Estimates of pathways of mediation are used to compute the burden attributable to aggregates of risk factors such as all behavioural risks or all risks combined. While we have conducted pooled cohort analyses to strengthen the assessment of mediation, this work was not yet ready for inclusion in this assessment. Pooled cohort studies have the advantage of providing a more standardised framework for assessing mediation across multiple risks. A related issue is the validation of the aggregation of risks in GBD. Pooled cohort studies will allow (in some circumstances) the opportunity to estimate if the aggregation of GBD RRs is as predictive of outcomes as suggested by the risk-by-risk analysis with mediation. Third, we have used the Das Gupta formula applied for each 5-year interval and for GBD Level 3 causes. Aggregations at higher levels of causes and for longer periods of time are based on these more granular analyses to guarantee consistency. Given the non-linear nature of the Das Gupta decomposition formula, however, alternative results are possible using different time periods and causes in the formula. Fourth, we have introduced the use of ensemble distributions to improve the empirical fitting of distributions of risk exposure in settings where only mean and standard deviation are known or where we use models to predict the mean and standard deviation of exposure. Ensemble models provide more accurate fits as assessed out of sample for settings with microdata. The underlying assumption is that the same ensemble weights are applicable across all settings. It is possible that the shape of distributions of risk exposure might vary across locations, for example because of the effects of access to treatment.

Limitations that apply to new risks in GBD 2016 or risks with significant estimation updates are presented here. For low birthweight and short gestation, we have included the effect of low birthweight and short gestation only on neonatal outcomes; we have not found the evidence to meet our inclusion criteria for the link between low birthweight and short gestation and NCDs in adult age groups. Our analysis of RRs has used a very large US-linked birth cohort dataset and much more limited data from middle-SDI and low-SDI populations. Given the large number of observations from the USA, our results are heavily influenced by the pattern of RRs across birthweight and gestational age in that population. The microdata used to develop the ensemble distributions for birthweight and gestational age are largely from middle-SDI and high-SDI locations. The estimation of alcohol use relies heavily on sales data, which are limited and whose quality we cannot easily assess. Also, the estimation of unrecorded consumption of alcohol is based on limited data and has significant uncertainty; nevertheless, we feel it is important to include it and plan to continue to look for additional sources of information to improve the estimation of unrecorded consumption in future iterations of GBD. Lastly, methods for calculating TMREL rely on observed DALYs for a given time rather than on the expected share of DALYs estimated from alcohol use alone. Future iterations of GBD will likely need to test this assumption further and determine if separate TMREL by age and sex should be calculated.

Conclusion
Understanding the levels and trends of major risks for human health is essential to prioritise public health action and evaluate the success of different programmes and policies. This study provides a comprehensive and comparable assessment of 84 metabolic, environmental, occupational, and behavioural risks across locations and time. Our findings show that risk modification has been an important contributor to reductions in communicable, maternal, neonatal, and nutritional causes, but has played a relatively small part in trends in NCDs. Conflicting trends in risks for NCDs at the global level, such as the decline in...
smoking prevalence coupled with the rise in obesity, FPG, and SBP, account for this finding. By contrast with trends in diseases and injuries at the global level and even at the national level, there is much greater heterogeneity of global trends across risks and considerable geographical variation in leading risks as well. Public health action in each country and region needs to focus on the major risks in that community. Our findings reinforce the crucial need for robust monitoring of the exposure to risks to health and assessment of the evidence supporting causal effects for each risk-outcome pair; GBD provides the main global mechanism for this monitoring function.

GBD 2016 Risk Factors Collaborators

Global Health Metrics
Bath, Bath, UK (G Shaddick PhD, M L Thomas MRes); Department of Public Health, An-Najah University, Nablus, Palestine (A Shabeen PhD); Tivff Medical Center, Boston, MA, USA (Prof S Sitnikov PhD); Independent Consultant, Karachi, Pakistan (M A Shaiखी PhD); Department of Medical Surgical Nursing, School of Nursing and Midwifery, Hamadan University of Medical Sciences, Hamadan, Iran (M Mansizadeh MPH); The George Institute for Global Health, Sydney, NSW, Australia (M S Shahid Islam PhD); Ministry of Health, Thimphu, Bhutan (J Sharma MPH); Indian Institute of Technology Ropar, Rupnagar, India (R Sharma MA); Department of Pulmonary Medicine, Zhongshan Hospital, Fudan University, Shanghai, China (J Shen MD); Research Institute at Nationwide Children’s Hospital, Columbus, OH, USA (J Shen PhD); National Institute of Infectious Diseases, Tokyo, Japan (M Shigematsu PhD); Sandia National Laboratories, Albuquerque, NM, USA (M Shimakos PD); Department of Public Health Sciences (Prof M Shin PhD); Department of Preventive Medicine, College of Medicine (S Yooy PhD); Korea University, Seoul, South Korea; Washington State University, Spokane, WA, USA (K Shishish PhD); Harvard Medical School, Boston, MA, USA (M G Shirmer MD); Reykjavik University, Reykjavik, Iceland (I D Sigfusdottir PhD); Federal University of Santa Catarina, Florianopolis, Brazil (D A S Silva PhD); Brasilia University, Brasilia, Brazil (D A G A Silveira MD); Asthma Bhawan, Jaipur, India (V Singh MD); School of Preventive Oncology, Patna, India (D S Singh PhD); WHO ICTC, Delhi, India; Qatar; Shanghai, China (Prof E Smolenski PhD); Taoyuan Central Hospital, Taoyuan, Taiwan (Prof E Smolenski PhD); Dartmouth College, Hanover, NH, USA (S Sonie PhD); Department of Community Medicine, International Medical University, Kuala Lumpur, Malaysia (T C Sreeramareddy MD); University of East Anglia, Norwich, UK (Prof N Steel PhD); Public Health England, London, UK (Prof N Steel PhD); South African Medical Research Council Unit on Anxiety & Stress Disorders, Cape Town, South Africa (Prof D Stein PhD); Department of Dermatology, University Hospital Muenster, Muenster, Germany (S Steinker DrMed); Deakin University, Burwood, VIC, Australia (Prof M A Stokes PhD); Ministry of Health, Kingdom of Saudi Arabia, Riyadh, Saudi Arabia (A A Solakiankathi MD); Indian Council of Medical Research, New Delhi, India (S Swaminathan MD); Departments of Criminology, Law & Society, and Public Health, University of California, Irvine, CA, USA (Prof B L Sykes PhD); University College London, London, UK (Prof B L Sykes PhD); Griffith University, Gold Coast, QLD, Australia (S A Talakadilma PhD); Asbestos Diseases Research Institute, Concord Clinical School (Prof K Takahashi MD); The University of Sydney, Sydney, NSW, Australia (K Alam PhD, J Leigh PhD); WSH Institute, Ministry of Manpower, Singapore, Singapore (J S Dakta DSc); Tampere University of Technology, Tampere, Finland (J S Dakta DSc); Ethiopian Public Health Association, Addis Ababa, Ethiopia (Y L Tarekregn MS); New York Medical Center, Valhalla, NY, USA (M Tavakkoli MD); Department of Anesthesiology, University of Virginia, Charlottesville, VA, USA (A S Terkawi MD); Department of Anesthesiology, King Fahad Medical City, Riyadh, Saudi Arabia (A S Terkawi MD); Outcomes Research Consortium (A T Thakor MD, C P Tupe MD); Cleveland Clinic, Cleveland, OH, USA (Prof E M Tiuco MD); School of Public Health, Post Graduate Institute of Medical Education and Research, Chandigarh, India (Prof J Thakur MD); Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum, Thiruvananthapuram, India (Prof K R Thanikkan MD); Adaptive Knowledge Management, Victoria, BC, Canada (A T Thomson PhD); National Center for Child Health and Development, Tokyo, Japan (R Tobe-Gai PhD); National Institute of Public Health, Bergen, Norway (M C Tollanes PhD); Faculty of Health Sciences, Wroclaw Medical University, Wroclaw, Poland (R Topor-Madry PhD); School of Medicine, University of Valencia, Valencia, Spain (M Tortajada PhD); INSERM (French National Institute for Health and Medical Research), Paris, France (M Touvier PhD); Hanoi Medical University, Hanoi, Vietnam (B X Tran PhD); Department of Neurology, Righshospitalet, University of Copenhagen, Copenhagen, Denmark (T Truelsen DMSc); Parc Sanitari Sant Joan de Deu, Fundacíó Sant Joan de Deu, Universitat de Barcelona, CIBERSAM, Barcelona, Spain (S Tyrovolas PhD); Department of Internal Medicine, Federal Teaching Hospital, Abakaliki, Nigeria (K N Ukwaja MD); Eboony State University, Abakaliki, Nigeria (C J Uneke PhD); Warwick Medical Center, Boston, MA, USA (Prof S Ulbricht PhD); UKK Institute for Health Promotion Research, Tampere, Finland (Prof T Vasankari PhD); Raffles Neuroscience Centre, Raffles Hospital, Singapore, Singapore (N Venketasubramanian MBBS); University of Bologna, Bologna, Italy (Prof F S Volante MD); Federal Research Institute for Health Organization and Informatics, Moscow, Russia (S K Vladimirov PhD); National Research University Higher School of Economics, Moscow, Russia (Prof V V Vlassov MD); Wola Sota University, Wola Sota, Ethiopia (Prof Wadiyo MS); VA Medical Center, Washington, DC, USA (M T Wallin MD); Neurology Department, Georgetown University, Washington, DC, USA (M T Wallin MD); University of São Paulo Medical School, São Paulo, Brazil (Y Wang PhD); McGill University, Ottawa, ON, Canada (Prof C W Weichenthal PhD); Department of Research, Cancer Registry of Norway, Institute of Population-Based Cancer Research, Oslo, Norway (E Weidarpas PhD); Department of Community Medicine, Faculty of Health Sciences, University of Tromsø, The Arctic University of Norway, Tromsø, Norway (E Weidarpas PhD); Genetic Epidemiology Group, Folkhälso Research Center, Helsinki, Finland (E Weidarpas PhD); Royal Children’s Hospital, Melbourne, VIC, Australia (R G Weirinraub MBBS); German National Cohort Consortium, Heidelberg, Germany (R Westerman PhD); South African Medical Research Council, Cochrane South Africa, Cape Town, South Africa (Prof C S Wiysonge PhD); National Institute for Health Research Comprehensive Biomedical Research Centre, Guy’s & St Thomas’ NHS Foundation Trust and King’s College London, London, UK (Prof C D Wolfe MD); Ghana University, Ghana, Belgium (A Workicho MPH); St John’s Medical College and Research Institute, Bangalore, India (Prof D Xavier MD); Department of Neurology, Jinglin Hospital, Nanjing University School of Medicine, Nanjing, China (Prof G Xu PhD); Global Health Research Center, Duke Kunshan University, Kunshan, China (Prof L L Yan PhD); Mizan Tefari University, Mizan Tefari, Ethiopia (H H Yirmiy MPH); Social Work and Social Administration Department (Prof P Yip PhD), The Hong Kong Jockey Club Centre for Suicide Research and Prevention (Prof P Yip PhD), University of Hong Kong, Hong Kong, China; Department of Biostatistics, School of Public Health, Kyotou University, Kyoto, Japan (N Yongomoto MPH); School of Public Health, University of Kinshasa, Kinshasa, Democratic Republic of the Congo (M Yotebieng PhD); Jackson State University, Jackson, MS, USA (Prof M Z Yousif PhD); University Hospital of Setif, Setif, Algeria (Prof Z Zaidi DSc); Faculty of Medicine, Mansoura University, Mansoura, Egypt (Prof M E Zaki PhD); University of Texas School of Public Health, Houston, TX, USA (X Zhang MS); and MD Anderson Cancer Center, Houston, TX, USA (X Zhang MG). Contributors

Please see appendix 1(p i) for more detailed information about individual authors’ contributions to the research, divided into the following categories: managing the estimation process; writing the first draft of the manuscript; providing data or critical feedback on data sources; developing methods or computational machinery; applying analytical methods to produce estimates; providing critical feedback on methods or results; drafting the work or revising it critically for important intellectual content; extracting, cleaning, or cataloguing data; designing or coding figures and tables; and managing the overall research enterprise.

Declaration of interests

Laith J Abu-Raddad acknowledges the support of Qatar National Research Fund (NPRP 9-040-3-008), who provided the main funding for generating the data provided to the GBD-IHME effort. Anurag Agrawal received a Wellcome Trust DTP India Alliance fellowship. Ashish Awasthi received financial support from Department of Science and Technology, Government of India through INSPIRE Faculty award Alaa Badawi acknowledges the Public Health Agency of Canada. Scientific work of Aleksandra Bara is part of the Project No. IIH5001 granted by the Ministry of Education, Science, and Technological Development of the Republic of Serbia. Till Bärnighausen is funded by the Alexander von Humboldt Foundation through the Alexander von Humboldt Professorship endowed by the German Federal Ministry of Education and Research; he is also supported by the Wellcome Trust, the European Commission, the Clinton Global Health Metrics

www.thelancet.com Vol 390 September 16, 2017 1419
Health Access Initiative and NICHD of NIH [R01-HD084233], NIAID of NIH [R01-AI124389 and R01-AI122339] and FIC of NIH [D43-TW009773]. Boris Bikov has received funding from the European Union’s Horizon 2020 research and innovation programme under Marie Skłodowska-Curie grant agreement No. 703226. Boris Bikov acknowledges that work related to this paper has been done on the behalf of the GBD Genitourinary Disease Expert Group. Cyrus Cooper reports personal fees from Alliance for Better Bone Health, Amgen, Eli Lilly, GSK, Medtronic, Merck, Novartis, Pfizer, Roche, Servier, Takeda, and UCB, outside the submitted work. José das Neves was supported in his contribution to this work by a Fellowship from Fundação para a Ciência e a Tecnologia, Portugal (SFRH/BPD/92954/2013). Barbara de Courten is supported by National Heart Foundation Future Leader Fellowship (100864). Rebeka Derbes is funded by a Wellcome Trust Intermediate Fellowship in Public Health and Tropical Medicine [grant number 201900]. Joao Fernandes is supported by FCT - Fundação para a Ciência e a Tecnologia (Grant number UID/Multi/50016/2013). Katharine Gilsey is supported by an NHMRC early career fellowship, Arndon Goodridge acknowledges the Sistema Nacional de Investigación (SNI) de Panamá & Secretaría Nacional de Ciencia, Tecnología e Innovación (SENACYT). Simon I Hay is funded by grants from the Bill & Melinda Gates Foundation (OPPP110602, OPP119467, OPP1093011, and OPP1132415). Mamani Inoue was the beneficiary of a financial contribution from the AXA Research Fund as chair-holder of the AXA Department of Health and Human Security, Graduate School of Medicine, The University of Tokyo. The AXA Research Fund had no role in this work. Shiratul Islam received a postdoctoral research fellowship from the George Institute for Global Health and career transition grants from High Blood Pressure Research Council of Australia, Ministry of Education Science and Technological Development of the Republic of Serbia has co-financed Serbian part of Mihajlo Jakovljevic’s GBD-related contribution through Grant ON 175 014. Publication of results was not contingent upon the Ministry’s censorship or approval. Paramyntamkbul Jeerom reports a clinical and public health intermediate fellowship from the Wellcome Trust and Department of Biotechnology, India Alliance. Nicholas Kassebaum reports personal fees and non-financial support from Vifor Pharmaceuticals, outside the submitted work. S Vittal Katikireddi was funded by a NRS Scottish Senior Clinical Fellowship (SCAF/15/02), the UK Medical Research Council (MC_UU_12071/13 & MC_UU_12071/15) and the Scottish Government Chief Scientist Office (SPHSU13 & SPHSU15/19). Christian Kieling has received support from Brazilian governmental research funding agencies Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (Fapergs), and Hospital de Clínicas de Porto Alegre (FiPE/HC/PA). Al Koyanagi’s work was supported by the Miguel Servet contract financed by the CP13/00150 and PI15/00862 projects, integrated into the National R + D + I and funded by the ISCIII - General Branch Evaluation and Promotion of Health Research - and the European Regional Development Fund (ERDF-FEDER). Katharine J Looker thanks the National Institute for Health Research Health Protection Research Unit (NIHR HPRU) in Evaluation of Interventions at the University of Bristol, in partnership with Public Health England (PHE), for research support. Katharine J Looker received separate funding from WHO and Sexual Health 24 during the course of this study. These funders had no role in the writing of the manuscript nor the decision to submit it for publication. The views expressed are those of the authors and not necessarily those of the National Health Service, the NIHR, the Department of Health or Public Health England. Azeem Majeed and Imperial College London are grateful for support from the NW London NIHR Collaboration for Leadership in Applied Health Research & Care. Francisco Martino-Melo received a postdoctoral fellowship from the CAPES (Brazilian Federal Agency for Support and Evaluation of Graduate Education), outside the submitted work. Kunihito Matsushita reports grants from the US National Kidney Foundation and the US National Institutes of Health during the conduct of the study; grants and personal fees from Kyowa Hakko Kirin, and Pfizer Japan, and personal fees from Daiichi Sankyo, outside the submitted work. Moises Mazidi was supported by the World Academy of Sciences and Chinese Academy of Sciences. John McGrath received John Cade Fellowship APP056929 from the National Health and Medical Research Council, and Niels Bohr Professorship from the Danish National Research Foundation. Tom Meier acknowledges additional institutional support from the Competence Center for Nutrition and Cardiovascular Health (nutriCARD), Jena-Halle-Leipzig. Philip Mitchell’s research is supported by an Australian NHMRC Project Grant (no. 1031796). Ulrich Mueller gratefully acknowledges financial support from the German National Cohort Study (BMBF grant # G01ER151I/D). Olanrewaju Oladimeji is a Senior Research Specialist at the Human Sciences Research Council (HSRC) and Doctoral Candidate at the University of KwaZulu-Natal (UKZN). South Africa acknowledges the institutional support from HSRC and UKZN for him to participate in this study. Alberto Ortiz was supported by Spanish Government (Intensificacion ICSIII FEDER funds and RETIC REDINREN RD06/0019). Mayowa Owohali is supported by the GBD Genitourinary Disease Expert Group. Giuseppe Rennuzzi acknowledges that the work related to this paper has been done on the behalf of the GBD Genitourinary Disease Expert Group. Bart van Oorbeek is supported by the International Society for Nephrology (ISN). Luz Myriam Reyes-Shigematsu acknowledges the Global Adult Tobacco Survey, GATS Mexico 2015, with financial support provided by the CONADIC, Ministry of Health, Mexico and the Bloomberg Initiative to Reduce Tobacco Use through the CDC Foundation with a grant from Bloomberg Philanthropies. Prof Aletta E Schute received support from the South African Medical Research Council and the National Research Foundation’s SARCHI Programme. Mark Shrimne acknowledges the Danone Ruminocillaceae Cancer Research Foundation GE Safe Surgery 2020 Project. Javin Singh reports consultancy fees from Saviert, Takeda, Regeneron, Merz, Iroko, Bionilberica, Crealta/Horizon, Allergen, UBM LLC, WebMD, and the American College of Rheumatology and grants from Saviert and Takeda. JS serves as the principal investigator for an investigator-initiated study funded by Horizon pharmaceuticals through a grant to DINORA Inc, a 501c3 entity; he is also on the steering committee of OMERACT, an international organization that develops measures for clinical trials and receives arms length funding from 36 pharmaceutical companies. Michael Soljak received funding from Public Health England for modelling of NCD prevalence. Cassandra Szeoke reports grants from the Australian National Medical Health Research Council (NHMRC) during the conduct of the study, and grants from Lundbeck and Alzheimer’s Association, outside the submitted work; in addition, Cassandra Szeoke has a patent, PCT/AU2008/001556 issued. Raphael Tahtou received support from the department of Clinical Pharmacy and Clinical Pharmacology, University Medical Center Groningen, University of Groningen, Netherlands. Lijing Yan is partially supported by the National Natural Sciences Foundation of China grants (71233001 and 71490732). Marcel Yotebieng is partially supported by the National Health & Medical Research Council (Australia; 1042600). Stefano Tyrovola’s work was funded by Horizon pharmaceuticals through a grant to DINORA Inc, a 501c3 entity; he is also on the steering committee of OMERACT, an international organization that develops measures for clinical trials and receives arms length funding from 36 pharmaceutical companies. Michael Soljak received funding from Public Health England for modelling of NCD prevalence. Cassandra Szeoke reports grants from the Australian National Medical Health Research Council (NHMRC) during the conduct of the study, and grants from Lundbeck and Alzheimer’s Association, outside the submitted work; in addition, Cassandra Szeoke has a patent, PCT/CA2008/001556 issued. Raphael Tahthou received support from the department of Clinical Pharmacy and Clinical Pharmacology, University Medical Center Groningen, University of Groningen, Netherlands. Lijing Yan is partially supported by the National Natural Sciences Foundation of China grants (71233001 and 71490732). Marcel Yotebieng is partially supported by the NHMRC U01A039629 and the NICHD R01HD087991.

Acknowledgments

The Palestinian Central Bureau of Statistics gratefully acknowledges the researchers access to relevant data in accordance with license no. SLN2014-1-170, after subjecting data to processing aiming to preserve the confidentiality of individual data in accordance with the General Statistics Law—2000. The researchers are solely responsible for the conclusions and inferences drawn upon available data. We thank the Russia Statistical Committee for providing the Russia Longitudinal Monitoring Survey, RLMS-HSE, conducted by the National Research University Higher School of Economics and ZAO “DemoScope” together with Carolina Population Center, University of North Carolina at Chapel Hill and the Institute of Sociology RAS for making these data available. The Panel Study of Income Dynamics is primarily sponsored by the National Science Foundation, the National Institute of Aging, and the National Institute of Child Health and Human Development and is conducted by the University of Michigan. This research used data from the National Health Survey 2003 and the National Health Survey 2009–10. The authors are grateful to the Ministry of Health.
Survey copyright owner, allowing them to have the database. All results of the study are those of the author and no way connected to the Ministry. This research uses data from Add Health, a program project designed by J Richard Udry, Peter S Bearman, and Kathleen Mullan Harris, and funded by a grant P01-HD31921 from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, with cooperative funding from 17 other agencies. Special acknowledgment is due to Ronald R Rindfuss and Barbara Barash for assistance in the original design. Persons interested in obtaining data files from Add Health should contact Add Health, Carolina Population Center, 123 W Franklin Street, Chapel Hill, NC 27516-2524 (addhealth@unc.edu). No direct support was received from grant P01-HD31921 for this analysis. The HRS (Health and Retirement Study) is sponsored by the National Institute on Aging (grant number NIA U01AG099740) and is conducted by the University of Michigan. This paper uses data from SHARE Waves 1, 2, 3 (SHARELIFE), 4, 5 and 6 (DOI: 10.1001/Square.w1.600. 10.1001/Square.w1.600. 10.1001/Square.w1.600. 10.1001/Square.w1.600. 10.1001/Square.w1.600. 10.1001/Square.w1.600. 10.1001/Square.w1.600). Data collection has primarily been funded by the European Commission through FP5 (QLK6-CT-2001-00360), FP6 (SHARE-EU: N°227822, SHARE M4: N°261982). Additional funding to the German Ministry of Education and Research, the Max Planck Society for the Advancement of Science, the US National Institute on Aging (U01 AG07940-1352, P01 AG005842, P01 AG08291, P01 AG12815, R21 AG051169, Y1-AG-4553-01, IAG_BSR06-11, OGA_HA-04-064, HHSN271201100073C) and from various national funding sources is gratefully acknowledged. HBSC is an international study carried out in collaboration with WHO/EURO. The International Coordinator of the 1997/98, 2001/02, 2005/06 and 2009/10 surveys was Candace Currie and the Data Bank Manager for the 1997/98 survey was Bente Wold, whereas for the following survey Prof Oddrun Samdal was the Databank Manager. A list of principal investigators in each country can be found online. This analysis uses data or information from the LASI Pilot micro data and documentation. The development and release of the LASI Pilot Study was funded by the National Institute on Ageing/National Institute of Health (R37AG02572, RO3AG04502, and R01 AG010153). The data used in this paper come from the 2009–10 Ghana Socioeconomic Panel Study Survey which is a nationally representative survey of over 5000 households in Ghana. The survey is a joint effort undertaken by the Institute of Statistical, Social and Economic Research (ISSER) at the University of Ghana, and the Economic Growth Centre (ECG) at Yale University. It was funded by the Economic Growth Center. At the same time, ISSER and the ECG are not responsible for the estimations reported by the analyst(s). The data reported here have been supplied by the United States Repertory Data System (USRDS). The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy or interpretation of the US Government. We thank the Russia Longitudinal Monitoring Survey, RLMS-HSE, conducted by the National Research University Higher School of Economics and ZAO “Demoscope” together with Carolina Population Center, University of North Carolina at Chapel Hill and the Institute of Sociology RAS for making these data available.

References
1 Beem J, Sheikh A. Risk factors for neonatal disorders and the Global Burden of Disease. Lancet 2016; 388: 560–61.
2 Beem J, Bell S. The protective effects of moderate drinking: lies, damned lies, and... selection biases? Addict Abingdon Engl 2017; 112: 218–19.
3 Steenland K. Excess deaths due to occupation. Occup Environ Med 2016; 73: 497–98.
4 Forouzanfar M, Afshin A, Alexander JL, Anderson H, Bhutta Z, Murray CJL, Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016; 388: 1659–724.
5 Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380: 2224–60.
6 Forouzanfar MH, Alexander JL, Anderson HR, et al. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015; 386: 2287–323.
7 Micha R, Khatibzadeh S, Shi P, Andrews KG, Engell RE, Mozaffarian D. Global, regional and national consumption of major food groups in 1990 and 2010: a systematic analysis including 266 country-specific nutrition surveys worldwide. BMJ Open 2015; 5: e008705.
8 Singh GM, Micha R, Khatibzadeh S, et al. Global, regional, and national consumption of sugar-sweetened beverages, fruit juices, and milk: a systematic assessment of beverage intake in 187 countries. PLoS One 2015; 10: e0124845.
9 Singh GM, Micha R, Khatibzadeh S, Lims S, Ezzati M, Mozaffarian D. Estimated Global, Regional, and National Disease Burdens Related to Sugar-Sweetened Beverage Consumption in 2010. Circulation 2015; 132: 639–66.
10 Norton S, Matthews FE, Barnes DE, Yaffe K, Brayne C. Potential for primary prevention of Alzheimer’s disease: an analysis of population-based data. Lancet Neurol 2014; 13: 788–94.
11 SPRINT Research Group, Wright J, Williamson JD, et al. A randomized trial of intensive versus standard blood-pressure control. N Engl J Med 2015; 373: 2103–16.
12 Yusuf S, Bosch J, Dagenais G, et al. Cholesterol Lowering in Intermediate-Risk Persons without Cardiovascular Disease. N Engl J Med 2016; 374: 2021–31.
13 Murray CJ, Lopez AD. On the comparable quantification of health risks: lessons from the Global Burden of Disease Study. Epidemiol Rev 1999; 21: 594–605.
14 Stevens GA, Aliema I, Black RE, et al. Guidelines for Accurate and Transparent Health Estimates Reporting: the GATHER statement. Lancet 2016; 388: e19–23.
15 American Institute for Cancer Research. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. Washington, DC: American Institute for Cancer Research, 2007. http://www.aicr.org/assets/docs/pdf/reports/Second_Expert_Report.pdf (accessed Sept 2, 2017).
16 Dzierski S, Zenko B. Is Combining Classifiers with Stacking Better than Selecting the Best One? Mach Learn 2004; 54: 255–73.
17 Massey FJ. The Kolmogorov-Smirnov Test for Goodness of Fit. J Am Stat Assoc 1951; 46: 68–78.
18 Flaxman AD, Vos T, Murray CJL, eds. An Integrative Metaregression Framework for Descriptive Epidemiology, 1st edn. Seattle: University of Washington Press, 2015.
19 Gupta PD, Standardization and Decomposition of Rates: A User’s Manual. US Department of Commerce, Economics and Statistics Administration, Bureau of the Census, 1993.
20 Ford ES, Ajani UA, Croft JB, et al. Explaining the Decrease in U.S. Deaths from Coronary Disease, 1980–2000. N Engl J Med 2007; 356: 2388–98.
21 Bhattacharya P, Wickramasinghe K, Williams J, Rayner M, Townsend N. The epidemiology of cardiovascular disease in the UK 2014. Heart 2015; 101: 1182–89.
22 Scarborough P, Wickramasinghe K, Bhattacharya P, Rayner M. Trends in coronary heart disease, 1961-2011. London, England: British Heart Foundation, 2011.
23 Cecchini M, Sass F, Lauer JA, Lee YY, Guajardo-Baron V, Chisholm D. Tackling of unhealthy diets, physical inactivity, and obesity: health effects and cost-effectiveness. Lancet 2010; 376: 775–84.
24 Goertzel RZ, Anderson DR, Whitmer RW, et al. The relationship between modifiable health risks and health. J Occup Environ Med 1998; 40: 843–54.
25 Attard SM, Herring AH, Zhang B, Du S, Popkin BM, Gordon-Larsen P. Associations between age, cohort, and urbanization with SRB and DRP in China: a population-based study across 18 years. J Hypertens 2015; 33: 948–56.
26 Song L, Shen L, Li H, et al. Height and prevalence of hyper tension in a middle-aged and older Chinese population. Sci Rep 2016; 6: 39480.
27 Munter P, Gu D, Wu X, et al. Factors associated with hypertension awareness, treatment, and control in a representative sample of the Chinese population. Hypertension 2004; 43: 578–85.
28 Coleman K, Hamblin R. Can pay-for-performance improve quality and reduce health disparities? PLoS Med 2007; 4: e216.
29 Smith PC, York N. Quality Incentives: The Case Of U.K. General Practitioners. Health Aff (Millwood). 2004; 23: 312–38.

30 Morrissey Y, Bedford M, Irving J, Farmer CKT. Older people remain on blood pressure agents despite being hypotensive resulting in increased mortality and hospital admission. Age Ageing 2016; 45: 783–88.

31 WHO. WHO Framework convention on tobacco control. Geneva: World Health Organization, 2003.

32 NCD Risk Factor Collaboration. Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19·2 million participants. Lancet 2016; 387: 1377–96.

33 Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2014; 384: 766–81.

34 Swinburn BA, Sacks G, Hall KD, et al. The global obesity pandemic: shaped by global drivers and local environments. Lancet 2011; 378: 804–14.

35 Hawkes C, Smith TG, Jewell J, et al. Smart food policies for obesity prevention. Lancet 2013; 385: 2410–21.

36 Roberto CA, Swinburn B, Hawkes C, et al. Patchy progress on obesity prevention: emerging examples, entrenched barriers, and new thinking. Lancet 2015; 385: 2400–09.

37 WHO. Global nutrition policy review: What does it take to scale up nutrition action? Geneva: World Health Organization, 2013. http://www.who.int/nutrition/publications/policies/global_nut_policyreview/en/ (accessed May 29, 2017).

38 Colchero MA, Popkin BM, Rivera JA, Ng SW. Beverage purchases from stores in Mexico under the excise tax on sugar sweetened beverages: observational study. BMJ 2016; 352: i6704.

39 Clark SE, Hawkes C, Murphy SME, Hansen-Kuhn KA, Wallinga D. Exporting obesity: US farm and trade policy and the transformation of the Mexican consumer food environment. Int J Occup Environ Health 2012; 18: 53–65.

40 Alvarado M, Kostova D, Suhchrce M, et al. Trends in beverage prices following the introduction of a tax on sugar-sweetened beverages in Barbados. Prr Med 2017; published online July 15. DOI:10.1016/j.prr.2017.07.013.

41 Mazocchi M. The impact of the French soda tax on prices, purchases and tastes: an ex post evaluation. Applied Economics 2016; 48: 976–94.

42 Briggs AD, Mytton OT, Madden D, O’Shea D, Rayner M, Scarbrough P. The potential impact on obesity of a 10% tax on sugar-sweetened beverages in Ireland, an effect assessment modelling study. BMC Public Health 2013; 13: 860.

43 Cabrelle Escolar MA, Veerman JL, Tollman SM, Bertram MY, Hofman KJ. Evidence that a tax on sugar-sweetened beverages reduces the obesity rate: a meta-analysis. BMC Public Health 2013; 13: 1072.

44 United Nations. International Decades, 2017. http://www.un.org/en/sections/observances/international-decades/ (accessed May 29, 2017).

45 Toce LC, Bouckaert KP, Benf KD, et al. Seasonality modifies the effect of a lipid-based nutrient supplement for pregnant rural women on birth length. J Nutr 2015; 145: 634–39.

46 Bhutta ZA, Das JK, Rizvi A, et al. Evidence-based interventions for improvement of maternal and child nutrition: what can be done and at what cost? Lancet 2013; 382: 452–77.

47 Blencowe H, Cousens S, Chou D, et al. Born too soon: The global epidemiology of 15 million preterm births. Lancet 2013; 10: S2.

48 Agrawal V, Hirsch E. Intrauterine infection and preterm labor. Semin Fetal Neonatal Med 2012; 17: 12–19.

49 Gyamlari-Bannerman C, Thom EA, Blackwell SC, et al. Antenatal betamethasone for women at risk for preterm delivery. N Engl J Med 2016; 374: 1311–20.

50 Reisman J, Arlington L, Jensen L, Louis H, Suarez-Rebling D, Nelson BD. newborn resuscitation training in resource-limited settings: a systematic literature review. Pediatrics 2016; 138: e2015490.

51 Arlington L, Kairukzi AK, Isangula KG, et al. Implementation of ‘Helping Babies Breathe’: a 3-year experience in Tanzania. Pediatrics 2017; 139: e20162132.

52 Network SSG of the EKSNR. Early CPAP versus surfactant in extremely preterm infants. N Engl J Med 2010; 362: 1970–79.

53 Zaidi AK, Huskins WC, Thaver D, Blutta ZA, Abbas Z, Goldmann A. Hospital-acquired neonatal infections in developing countries. Lancet 2005; 365: 1175–88.

54 Rehm J, Irving H, Ye Y, Kerr WC, Bond J, Greenfield TK. Are lifetime abstainers the best control group in alcohol epidemiology? On the stability and validity of reported lifetime abstinence. Am J Epidemiol 2016; 183: 866–71.

55 Holmes MV, Dale CE, Zuccolo L, et al. Association between alcohol and cardiovascular disease: Mendelian randomisation analysis based on individual participant data. BMJ 2014; 349: g4164.

56 McCambridge J, Hartwell G. Has industry funding biased studies of the protective effects of alcohol on cardiovascular disease? A preliminary investigation of prospective cohort studies. Drug Alcohol Res 2015; 34: 58–66.

57 Bilano V, Gilmour S, Moffett T, et al. Global trends and projections for tobacco use, 1990–2025: an analysis of smoking indicators from the WHO Comprehensive Information Systems for Tobacco Control. Lancet 2015; 385: 966–76.

58 Fewtrell LJ, Pruess-Ustun A, Landgrigan P, Ayuso-Mateos JL. Estimating the global burden of disease of mild mental retardation and cardiovascular diseases from environmental lead exposure. Environ Res 2004; 94: 120–33.

59 WHO. Global and regional estimates of violence against women: prevalence and health effects of intimate partner violence and non-partner sexual violence. Geneva: World Health Organization, 2013. http://apps.who.int/iris/bitstream/10665/85239/1/9789241564625_eng.pdf (accessed Sept 1, 2017).

60 WHO, UNICEF. Joint Monitoring Programme for Water Supply and Sanitation. Jt. Monit. Programme. https://www.wssinfo.org/ (accessed May 29, 2017).

61 UNICEF, WHO, The World Bank. Joint child malnutrition estimates—Levels and trends (2017 edition). Geneva: World Health Organization, 2017. http://www.who.int/nutgrowthdb/estimates2016/en/ (accessed May 29, 2017).

62 WHO, UNICEF. Low birthweight: Country, regional, and global estimates. Geneva: World Health Organization, 2004. https://www.unicef.org/publications/files/low_birthweight_Infographic_En.pdf (accessed May 28, 2017).

63 Hill NR, Fatoba ST, Oke JI, et al. Global prevalence of chronic kidney diseased—a systematic review and meta-analysis. PLoS One 2016; 11: e0158765.

64 Blencowe H, Cousens S, Oestergaard MZ, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet 2012; 379: 2362–72.

65 Lawn JE, Gravett MG, Nunes TM, Rubens CE, Stanton C, GAPPs Review Group. Global report on preterm birth and stillbirth (I of 7): definitions, description of the burden and opportunities to improve data. BMC Pregnancy Childbirth 2016; 16: S1.

66 Leleved J, Evans JS, Faiya M, Giannadaki D, Pozzer A. The contribution of outdoor air pollution sources to premature mortality on a global scale. Nature 2015; 525: 367–71.

67 Petry N, Olofin I, Hurrell RF, et al. The proportion of anaemia associated with iron deficiency in low, medium, and high human development index countries: a systematic analysis of national surveys. Nutrients 2016; 8: 693.

68 Takala J, Hamiläinen P, Saarela KL, et al. Global estimates of the burden and mortality of alcohol in 2012. J Occup Environ Hyg 2014; 11: 326–37.

69 Rushlow I, Hutchinson SJ, Fortunato L, et al. Occupational cancer burden in Great Britain. Br J Cancer 2012; 107: S1–37.

70 Raffensperger C, Tickner JA. Protecting Public Health and the Environment: Implementing The Precautionary Principle. Washington, DC, USA: Island Press, 1999.

71 Sandin P. Dimensions of the precautionary principle. Hum Ecol Risk Assess Int J 1999; 5: 889–907.

72 Foster KR, Vecchia P, Repacholi MH. Science and the precautionary principle. Science 2000; 288: 979–81.

73 Gasparini A, Guo Y, Hashizume M, et al. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. Lancet 2015; 386: 369–75.