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

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

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

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

Selection of risk–outcome pairs

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

Distribution of exposure to each risk factor

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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diameter ($PM_{2.5}$) in ambient air: TM5 estimates—based on a nested three-dimensional global atmospheric chemistry transport model—which simulates both particulate matter and ozone at a high spatial resolution;[22,23,121] and satellite-based estimates, which are based on satellite observations of aerosol optical depth, a measure of light extinction by aerosols in the total atmospheric column.[25] TM5 and satellite-based estimates of $PM_{2.5}$, measured in $\mu g/m^3$, were averaged at a $0{\cdot}1° \times 0{\cdot}1°$ grid cell resolution (equivalent to roughly 11 km×11 km at the equator) and linked to available measures of $PM_{2.5}$ from ground-based monitors. We used a regression model with the average of TM5 and satellite-based estimates as the predictor to estimate ground-based $PM_{2.5}$ for all grid cells.[26] For ozone, we relied solely on the TM5 model.

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

Effects of risk factors on disease outcomes

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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