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fruits, vegetables, nuts and seeds, whole grains, fish, and dietary fibre on systolic blood pressure and LDL cholesterol, based on all randomised controlled feeding studies (six treatment groups from three studies for blood pressure and six treatment groups from two studies for cholesterol). When translated into an effect using the RRs of blood pressure and cholesterol for ischaemic heart disease, the average ratio of the estimated to measured RR reduction was 1.07 for all components and 0.85 when excluding fish, which has mechanisms additional to lowering blood pressure and cholesterol.¹⁵¹ These two supplementary analyses suggest that the RRs estimated in the meta-analyses of single dietary risk factors are unlikely to be significantly biased because of residual confounding due to other diet components.

Pooled epidemiological studies of cardiovascular disease risks show that the RR decreases with age, and that the inverse age association is roughly log-linear. Based on a pooled analysis of several risk factors (high blood pressure, high fasting plasma glucose, high total cholesterol, and tobacco smoking), the age at which the RR reaches 1 is often between 100 and 120 years. We therefore estimated age-specific RRs for all cardiovascular risk factors by meta-regression of available data with logRR as the dependent variable and median age at event

as the independent variable with an age intercept (RR=1) at age 110 years. Uncertainty in the RR was generated by simulation analyses.¹⁵²

The causal association between a risk factor and a disease outcome is often informed by a wider body of evidence than epidemiological studies of RRs for specific measures of exposure, especially when disease-specific and age-specific RRs are needed. For example, although smoking is an established cause of cardiovascular diseases, when cohorts are analysed in fine age groups, the 95% CI for the effect of smoking on stroke spans 1.0 in several age groups.³⁸ Similarly, randomised trials of zinc supplementation were designed to detect effects on total mortality.^{36,153} Re-analysis of the same trials for disease-specific outcomes, which is necessary to extrapolate effects to populations with different causes of death, reduced their statistical power and gave 95% CIs that spanned 1.0. To use the broad evidence while accounting for the uncertainty of the subgroup RRs, we included in the uncertainty analysis all draws of the RR distribution, including those that show a protective effect as long as the overall relation for the risk factor across all ages is significant. In other cases, if there are different degrees of exposure for a risk factor, in some exposure categories the RR might not be significant. We have included draws from these posterior distributions if the mean values show a dose-response relation. To fairly represent the extent of our epidemiological knowledge, we have included in the uncertainty analysis draws from the posterior distribution for those exposure categories that show a protective effect.

Theoretical-minimum-risk exposure distributions for counterfactual comparison

In the comparative risk assessment framework, disease burden attributable to risk factors is calculated with reference to an alternative (counterfactual) distribution of exposure; in GBD 2010, we used an optimal exposure distribution (in terms of effect on population health), termed the theoretical-minimum-risk exposure distribution. For several risk factors, such as tobacco smoking, the choice of theoretical-minimum-risk exposure distribution is clear—ie, 100% of the population being lifelong non-smokers. However, for many of the other risk factors zero exposure is not possible (eg, blood pressure), or the lowest amount of exposure that is still beneficial is not yet established. In these cases the theoretical-minimum-risk exposure distribution was informed by two considerations: the availability of convincing evidence from epidemiological studies that support a continuous reduction in risk of disease to the chosen distribution; and a distribution that is theoretically possible at the population level (table 1).

For some risk factors, new evidence has resulted in a revision of the theoretical-minimum-risk exposure distribution compared to the previous comparative risk assessment. For example, the previous distribution for systolic blood pressure was a mean of 115 mm Hg (SD 6).⁶ However, subsequent randomised trials¹⁵⁴ of blood

	Disability-adjusted life-years (%)
Physiological risk factors	
High blood pressure	53%
High total cholesterol	29%
High body-mass index	23%
High fasting plasma glucose	16%
Alcohol use	5%
Tobacco smoking, including second-hand smoke	31%
Dietary risk factors and physical inactivity	
Diet low in nuts and seeds	40%
Physical inactivity and low physical activity	31%
Diet low in fruits	30%
Diet low in seafood omega-3 fatty acids	22%
Diet low in whole grains	17%
Diet high in sodium	17%
Diet high in processed meat	13%
Diet low in vegetables	12%
Diet low in fibre	11%
Diet low in polyunsaturated fatty acids	9%
Diet high in trans fatty acids	9%
Diet high in sugar-sweetened beverages	2%
Air pollution	
Ambient particulate matter pollution	22%
Household air pollution from solid fuels	18%
Other environmental risks	
Lead exposure	4%

Table 2: Proportion of ischaemic heart disease disability-adjusted life-years attributable to individual risk factors, worldwide, 2010

pressure-lowering medication suggest that the benefits of lowering blood pressure could continue to 110 mm Hg or lower. On this basis, we changed the theoretical-minimum-risk exposure distribution to a mean of 110–115 mm Hg (SD 6). For other exposures, the distribution was increased because of data from new epidemiological studies⁷⁵—eg, for mean body-mass index we used 21–23 kg/m², compared with 21 kg/m² used previously.

For ambient particulate matter pollution, we did a sensitivity analysis with an alternative theoretical-minimum-risk exposure distribution that included the effect of regional dust particulate matter. We did so because although particulate exposure from dust could theoretically be reduced, it would probably be prohibitively expensive and could only be done over a very long period. This factor is particularly relevant in areas with high amounts of dust—eg, deserts. Dusty grid cells were identified as those with an ambient air concentration of PM_{2.5} of 36 µg/m³ or more and where the dust fraction from the TM5 chemical transport model was 50% or more.

Mortality and disease burden attributable to individual and clusters of risk factors

We calculated the burden attributable to risk factors with continuous exposure by comparing the present distribution of exposure to the theoretical-minimum-risk exposure distribution for each age group, sex, year (1990 and 2010), and cause according to the following formula:

$$PAF = \frac{\int_{x=0}^m RR(x)P1(x)dx - \int_{x=0}^m RR(x)P2(x)dx}{\int_{x=0}^m RR(x)P1(x)dx}$$

Where PAF is the population attributable fraction (burden attributable to risk factor), RR(x) is the RR at exposure level x, P1(x) is the (measured or estimated) population distribution of exposure, P2(x) is the counterfactual distribution of exposure (ie, the theoretical-minimum-risk exposure distribution), and m the maximum exposure level.⁴

Burden attributable to categorical exposures was calculated by comparing exposure categories to a reference category for each age, sex, year, and cause according to the following formula:

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

Where RR_i is the RR for exposure category i, P_i is the fraction of the population in exposure category i, and n is the number of exposure categories.⁴

We calculated the burden attributable to clusters of risk factors by computing the combined population

attributable fraction for risk factors for each age, sex, year, and cause according to the following formula:

$$PAF = 1 - \prod_{r=1}^R (1 - PAF_r)$$

Where r is each individual risk factor, and R is the number of risk factors. This approach assumes that risk factors are independent—ie, it does not account for mediation, exposure correlation, or effect size modification that might exist between risk factors in a cluster.¹⁵⁵

To represent uncertainty in the estimates we used simulation analysis to take 1000 draws from the posterior distribution of exposure, RR, and each relevant outcome for each age, sex, country, year. We accounted for the correlation structure of uncertainty (ie, whether exposure in a country, age group, and sex is high or low might be related to whether it is high or low in other subgroups) by use of the same draw of exposure across different outcomes and the same draw of RR across country, age, and sex subgroups when the RR does not vary by country, age, or sex. We otherwise assumed that the uncertainties in exposure, RR, and underlying burden attributable to the outcome were independent.

We computed the mean deaths and DALYs attributable to each risk factor and risk factor cluster from the 1000 draws. The 95% uncertainty intervals (95% UI) were calculated as the 2·5th and 97·5th percentiles of the 1000 draws. We also computed the mean rank and 95% UI for the 43 risk factors included in the ranking list. The mean of the ranks for a risk factor was not necessarily equivalent to the rank of the mean deaths or mean DALYs attributable to the risk factor.

Role of the funding source

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

Results

Quantification of risk factors in this analysis represents the effects of each individual risk factor, holding all other independent factors constant. The effects of multiple risk factors are not a simple addition of the individual effects and are often smaller than their sums,¹⁵⁶ especially for cardiovascular diseases, which are affected by several risk factors (eg, table 2). The sum of the individual effects of just the metabolic risk factors at the global level is 121% and the summation of all the risks is greater than 400%.

We estimated global attributable mortality and DALYs with uncertainty for 1990, and 2010, for each of the 67 risk factors and clusters of risk factors (table 3, 4). The appendix shows full results by region, year, age, and sex for attributable deaths and DALYs. Because of the interest in

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	Men		Women		Both sexes	
	1990	2010	1990	2010	1990	2010
Unimproved water and sanitation	365 244 (18 940-662 551)	171 097 (68 41-326 262)	350 629 (17 531-638 433)	166 379 (66 90-326 989)	715 873 (36 817-1 279 220)	337 476 (13 150-648 205)
Unimproved water source	147 857 (10 566-282 890)	59 463 (38 80-120 264)	140 150 (10 042-271 546)	56 663 (36 04-115 704)	288 007 (20 641-553 293)	116 126 (75 18-233 136)
Unimproved sanitation	252 779 (80 32-480 822)	123 255 (29 24-242 588)	244 207 (73 48-460 913)	120 851 (31 04-242 452)	496 986 (15 380-927 845)	244 106 (60 27-478 186)
Air pollution
Ambient particulate matter pollution	1 549 448 (1 345 894-1 752 880)	1 850 428 (1 614 010-2 082 474)	1 360 712 (1 166 992-1 559 747)	1 373 113 (1 187 639-1 563 793)	2 910 161 (2 546 184-3 286 508)	3 223 540 (2 828 854-3 619 148)
Household air pollution from solid fuels	2 251 932 (1 677 785-2 743 681)	1 867 043 (1 359 090-2 452 588)	2 221 558 (1 862 975-2 581 337)	1 611 730 (1 243 516-2 027 067)	4 473 490 (3 651 253-5 206 632)	3 478 773 (2 638 548-4 386 590)
Ambient ozone pollution	77 087 (25 256-134 021)	86 335 (30 551-153 776)	66 274 (22 424-116 663)	66 100 (21 362-115 225)	143 362 (47 539-251 885)	152 434 (52 272-267 431)
Other environmental risks	109 224 (91 805-131 511)	426 280 (341 744-541 465)	100 699 (82 720-119 745)	346 751 (281 555-413 370)	209 923 (177 673-243 565)	773 030 (640 893-929 935)
Residential radon	..	70 014 (9 140-154 460)	..	28 978 (4 098-64 387)	..	98 992 (13 133-215 237)
Lead exposure	109 224 (91 805-131 511)	356 266 (292 587-435 046)	100 699 (82 720-119 745)	317 772 (265 722-376 431)	209 923 (177 673-243 565)	674 038 (575 858-779 314)
Child and maternal undernutrition	1 805 224 (1 479 043-2 219 888)	739 863 (570 560-909 248)	1 668 365 (1 396 689-1 986 532)	698 442 (569 013-832 012)	3 473 589 (2 906 896-4 175 138)	1 438 305 (1 175 257-1 713 103)
Suboptimal breastfeeding	693 103 (427 028-972 440)	293 449 (175 623-429 772)	581 921 (370 598-814 551)	251 368 (155 884-359 651)	1 275 024 (802 142-1 772 745)	544 817 (338 453-775 077)
Non-exclusive breastfeeding	612 059 (354 236-875 230)	257 771 (143 116-382 459)	505 849 (302 585-720 858)	218 117 (126 383-319 470)	1 117 908 (663 274-1 576 633)	475 888 (272 493-684 422)
Discontinued breastfeeding	81 044 (86 43-178 237)	35 678 (34 75-79 940)	76 073 (78 09-165 395)	33 251 (30 91-73 804)	157 117 (16 188-341 702)	68 929 (6 445-153 290)
Childhood underweight	1 198 178 (997 627-1 484 105)	458 639 (366 866-561 352)	1 065 774 (898 859-1 299 715)	401 478 (325 516-484 452)	2 263 952 (1 927 356-2 735 821)	860 117 (715 742-1 033 573)
Iron deficiency	39 409 (30 677-47 108)	32 287 (21 925-37 449)	128 675 (92 036-156 884)	87 321 (62 505-107 021)	168 084 (130 444-197 085)	119 608 (93 261-139 985)
Vitamin A deficiency	181 151 (85 775-341 439)	63 291 (32 070-104 030)	168 203 (80 696-298 163)	56 472 (28 192-91 464)	349 354 (170 504-632 149)	119 762 (61 723-191 846)
Zinc deficiency	143 518 (27 797-276 850)	52 390 (93 82-105 728)	132 071 (23 716-253 841)	44 940 (76 96-87 711)	275 590 (51 274-529 451)	97 330 (17 575-190 527)
Tobacco smoking (including second-hand smoke)	3 680 571 (3 213 427-4 229 530)	4 507 059 (3 757 779-5 092 460)	1 649 238 (1 380 504-2 144 408)	1 790 228 (1 278 666-2 094 260)	5 329 808 (4 778 526-6 049 296)	6 297 287 (5 395 769-7 006 942)
Tobacco smoking	3 332 192 (2 871 957-3 840 033)	4 251 424 (3 503 674-4 850 554)	1 244 106 (961 356-1 781 819)	1 443 924 (920 763-1 743 849)	4 576 298 (4 068 753-5 312 438)	5 695 349 (4 755 779-6 421 611)
Second-hand smoke	348 378 (273 555-425 310)	255 634 (191 587-314 541)	405 132 (310 224-500 100)	346 304 (252 702-439 439)	753 510 (585 131-912 313)	601 938 (447 705-745 328)
Alcohol and drug use	1 345 743 (1 196 535-1 513 476)	1 925 525 (1 712 465-2 132 787)	702 071 (570 285-844 382)	956 819 (793 785-1 121 300)	2 047 814 (1 831 313-2 270 020)	2 882 343 (2 601 098-3 161 618)
Alcohol use	1 305 926 (1 156 571-1 466 638)	1 824 119 (1 613 616-2 029 574)	682 576 (551 702-825 112)	911 393 (748 254-1 076 004)	1 988 502 (1 772 115-2 214 916)	2 735 511 (2 464 575-3 006 459)
Drug use	46 682 (33 063-78 398)	109 420 (82 297-152 421)	21 895 (15 984-31 023)	48 385 (36 780-64 303)	68 577 (50 706-102 395)	157 805 (124 639-209 873)
Physiological risk factors						
High fasting plasma glucose	1 051 401 (865 949-1 250 550)	1 749 058 (1 455 169-2 039 206)	1 052 773 (881 704-1 230 327)	1 607 214 (1 367 465-1 839 764)	2 104 174 (1 797 633-2 401 170)	3 356 271 (2 917 520-3 782 483)
High total cholesterol	936 749 (767 684-1 128 051)	961 614 (714 774-1 236 023)	1 009 172 (829 163-1 218 442)	1 057 196 (793 595-1 350 633)	1 945 920 (1 625 929-2 318 054)	2 018 811 (1 572 853-2 479 097)
High blood pressure	3 412 588 (3 089 548-3 769 223)	4 750 581 (4 272 529-5 273 576)	3 880 598 (3 559 634-4 250 099)	4 645 279 (4 198 029-5 092 003)	7 293 185 (6 701 203-7 859 894)	9 395 860 (8 579 630-10 147 805)
High body-mass index	887 047 (698 599-1 079 235)	1 632 766 (1 328 501-1 941 988)	1 076 502 (878 065-1 286 482)	1 738 466 (1 454 008-2 036 059)	1 963 549 (1 590 282-2 345 133)	3 371 232 (2 817 774-3 951 127)
Low bone mineral density	52 816 (43 822-69 605)	103 440 (67 743-124 596)	50 455 (40 408-62 110)	84 146 (57 863-102 441)	103 270 (90 672-124 230)	187 586 (140 636-219 906)

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	Men		Women		Both sexes	
	1990	2010	1990	2010	1990	2010
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Dietary risk factors and physical inactivity	4 473 276 (4 110 262-4 852 556)	6 687 621 (6 172 230-7 206 283)	4 057 558 (3 704 325-4 431 571)	5 815 748 (5 380 274-6 261 225)	8 530 835 (7 907 898-9 150 862)	12 503 370 (11 710 741-13 324 770)
Diet low in fruits	2 013 415 (1 570 347-2 435 112)	2 837 481 (2 203 651-3 414 649)	1 653 787 (1 269 335-2 006 693)	2 064 761 (1 593 495-2 507 876)	3 667 202 (2 870 267-4 394 152)	4 902 242 (3 818 356-5 881 561)
Diet low in vegetables	779 747 (535 472-1 041 517)	1 017 500 (687 787-1 378 721)	674 309 (441 649-910 150)	779 754 (521 285-1 040 304)	1 454 057 (978 665-1 924 334)	1 797 254 (1 205 059-2 394 366)
Diet low in whole grains	649 676 (503 984-787 057)	963 640 (748 116-1 162 721)	580 600 (447 140-706 303)	762 171 (592 879-919 709)	1 230 276 (958 136-1 489 812)	1 725 812 (1 342 896-2 067 224)
Diet low in nuts and seeds	1 041 726 (667 481-1 349 266)	1 389 433 (890 869-1 817 734)	872 483 (541 757-1 147 258)	1 082 390 (663 158-1 441 054)	1 914 209 (1 216 363-2 487 874)	2 471 823 (1 559 603-3 226 994)
Diet low in milk	34 838 (10 464-58 211)	54 093 (16 106-91 527)	33 312 (9745-57 799)	46 858 (13 085-80 413)	68 150 (20 479-114 435)	100 951 (29 728-171 340)
Diet high in red meat	13 888 (3859-23 763)	21 330 (6175-37 340)	12 551 (3425-22 054)	16 762 (4306-29 007)	26 439 (7374-45 232)	38 092 (10 749-65 727)
Diet high in processed meat	397 198 (85 536-688 905)	473 562 (103 608-842 923)	334 476 (71 692-584 050)	367 296 (83 446-637 120)	731 675 (158 044-1 257 423)	840 857 (188 952-1 460 279)
Diet high in sugar-sweetened beverages	100 250 (69 485-134 139)	161 042 (111 700-219 563)	83 548 (53 949-117 567)	138 480 (91 257-203 236)	183 799 (127 938-240 028)	299 521 (212 310-403 716)
Diet low in fibre	333 603 (149 007-521 712)	441 895 (201 062-693 234)	250 541 (111 867-394 088)	300 994 (134 201-470 634)	584 144 (260 065-914 729)	742 888 (334 379-1 166 933)
Diet low in calcium	48 975 (32 814-66 562)	76 413 (51 653-103 188)	33 330 (23 008-43 904)	49 181 (34 016-63 592)	82 305 (57 324-108 535)	125 594 (88 323-164 800)
Diet low in seafood omega-3 fatty acids	576 646 (418 376-735 746)	793 650 (574 241-1 010 930)	466 440 (337 205-601 988)	596 246 (437 287-764 762)	1 043 085 (757 418-1 327 627)	1 389 896 (1 010 300-1 781 401)
Diet low in polyunsaturated fatty acids	248 677 (117 929-381 787)	306 296 (140 873-473 149)	199 388 (95 418-305 733)	227 307 (108 675-350 194)	448 065 (213 262-687 396)	533 603 (245 096-820 854)
Diet high in trans fatty acids	202 725 (144 395-260 843)	293 087 (209 155-371 284)	164 736 (117 395-211 588)	222 173 (160 511-283 740)	367 461 (265 936-467 609)	515 260 (371 081-649 451)
Diet high in sodium	1 197 713 (776 962-1 589 448)	1 732 870 (1 122 107-2 301 781)	1 047 642 (666 779-1 397 486)	1 371 438 (878 780-1 834 541)	2 245 355 (1 459 900-2 966 107)	3 104 308 (2 016 734-4 105 019)
Physical inactivity and low physical activity	..	1 547 833 (1 264 464-1 835 192)	..	1 636 107 (1 369 722-1 899 182)	..	3 183 940 (2 657 204-3 718 963)
Occupational risk factors	694 403 (541 113-858 435)	749 857 (580 954-941 322)	116 743 (74 642-164 679)	102 250 (68 744-140 097)	811 146 (623 674-1 010 107)	852 107 (659 652-1 062 443)
Occupational carcinogens	55 306 (37 867-80 887)	92 154 (57 261-127 678)	16 766 (11 866-24 842)	25 943 (15 498-37 074)	72 073 (50 753-101 233)	118 097 (77 249-160 431)
Occupational exposure to asbestos	17 024 (11 044-26 605)	26 563 (14 454-36 593)	6 033 (4 012-9 397)	7 047 (3 312-9 681)	23 057 (16 939-33 009)	33 610 (20 317-43 647)
Occupational exposure to arsenic	1155 (446-2210)	1915 (717-3496)	463 (176-915)	747 (275-1402)	1 618 (622-3039)	2 662 (1 011-4 860)
Occupational exposure to benzene	993 (426-1757)	1 542 (618-2706)	770 (292-1422)	1 189 (434-2156)	1 764 (741-3085)	2 731 (1 111-4 811)
Occupational exposure to beryllium	61 (24-110)	114 (44-192)	26 (10-47)	49 (19-86)	87 (35-152)	163 (65-276)
Occupational exposure to cadmium	214 (97-370)	410 (179-670)	74 (33-130)	145 (62-245)	288 (131-494)	555 (249-901)
Occupational exposure to chromium	729 (431-1133)	1 361 (720-2014)	293 (171-490)	570 (295-858)	1 022 (618-1578)	1 931 (1 140-2 799)
Occupational exposure to diesel engine exhaust	10 979 (6 241-17 555)	18 773 (9 641-28 714)	2 060 (1 180-3 422)	3 413 (1 709-5 262)	13 040 (7 494-20 486)	22 187 (12 180-33 213)
Occupational exposure to second-hand smoke	10 171 (6 878-15 272)	17 189 (10 127-23 037)	3 854 (2 637-6 207)	7 046 (3 935-9 630)	14 025 (10 058-19 715)	24 235 (16 094-31 803)
Occupational exposure to formaldehyde	299 (117-584)	486 (185-939)	179 (77-325)	245 (97-456)	478 (202-877)	731 (301-1 361)
Occupational exposure to nickel	3578 (935-7585)	6 443 (1 616-13 317)	1 425 (369-3 031)	2 702 (743-5 679)	5 004 (1 331-10 489)	9 145 (2 449-18 834)

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	Men		Women		Both sexes	
	1990	2010	1990	2010	1990	2010
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Occupational exposure to polycyclic aromatic hydrocarbons	1638 (772–2817)	3092 (1394–5028)	492 (230–864)	993 (441–1661)	2130 (1018–3613)	4086 (1909–6567)
Occupational exposure to silica	7870 (5154–11902)	14205 (8244–19702)	1185 (797–1975)	2072 (1102–2948)	9056 (6140–13213)	16277 (9875–22272)
Occupational exposure to sulphuric acid	1964 (531–4383)	2606 (718–5761)	193 (55–452)	239 (74–509)	2157 (626–4707)	2845 (833–6109)
Occupational asthmagens	31666 (15305–62856)	25364 (15642–48748)	10485 (5116–19129)	8352 (4854–13425)	42151 (24425–76872)	33716 (22844–58659)
Occupational particulate matter, gases, and fumes	207366 (92516–320244)	171553 (79656–270369)	68281 (29408–112504)	47311 (20330–77499)	275647 (121774–429427)	218864 (100403–344633)
Occupational noise	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Occupational risk factors for injuries	400064 (308482–507787)	460785 (343904–618319)	21211 (16479–27705)	20644 (15628–27414)	421275 (329209–529004)	481429 (363778–639590)
Occupational low back pain	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Sexual abuse and violence	..	37429 (21366–56607)	..	200930 (113070–292802)	..	238359 (143200–325690)
Childhood sexual abuse	..	37429 (21366–56607)	..	27009 (14290–43424)	..	64438 (37339–94174)
Intimate partner violence	186365 (92028–280059)	..	186365 (92028–280059)

No data indicates that attributable deaths were not quantified.

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

Africa (Prof S Seedat PhD); National Center for Injury Prevention and Control (D A Sleet PhD), Centers for Disease Control and Prevention, Baltimore, MD, USA (ST Wiersma MD); Department of Neuroscience, Norwegian University of Science and Technology, Trondheim, Norway (Prof L J Stovner PhD); New York University, New York City, NY, USA (Prof G D Thurston ScD); Voluntary Health Services, Sneha, Chennai, India (Prof L Vijayakumar MBBS); Royal Children's Hospital and Critical Care and Neurosciences Theme, Murdoch Children's Research Institute, Melbourne, VIC, Australia (R Weintraub); University of Nottingham, Nottingham, UK (Prof H C Williams PhD); National Acoustic Laboratories, Sydney, NSW, Australia (W Williams PhD); Royal Cornwall Hospital, Truro, UK (Prof A D Woolf MBBS); and Centre for Suicide Research and Prevention, The University of Hong Kong, Hong Kong, China (Prof P Yip PhD)

the combined effects of multiple risk factors, we have approximated the joint effects of clusters of risk factors assuming that risk factors included in each cluster are independent. However, risk factors included in a cluster are not necessarily independent; for example, a substantial part of the burden attributable to high body-mass index is mediated through high blood pressure and high fasting plasma glucose. Others act together and risk factor exposures might be correlated at the individual level,¹⁵⁵ especially household air pollution and ambient particulate matter pollution, which might have common sources.

For these reasons we have not computed the joint effects for physiological risk factors or air pollution. However, the combined effects of physiological risk factors are probably large, with high blood pressure the leading single risk factor globally, accounting for 9.4 million (95% UI 8.6 million to 10.1 million) deaths and 7.0% (6.2–7.7) of global DALYs in 2010, followed by high body-mass index (3.4 million [2.8 million to 4.0 million deaths] and 3.8% [3.1–4.4] of global DALYs in 2010), high fasting plasma glucose (3.4 million [2.9 million to 3.7 million] deaths and 3.6% [3.1–4.0] of DALYs), high total cholesterol (2.0 million [1.6 million to 2.5 million] deaths and 1.6% [1.3–2.0] of DALYs), and low bone mineral density (0.2 million [0.1 million to 0.2 million] deaths and 0.21% [0.17–0.25] of DALYs).

The joint effects of air pollution are also likely to be large. Household air pollution from solid fuels accounted for 3.5 million (2.6 million to 4.4 million) deaths and 4.3% (3.4–5.3) of global DALYs in 2010 and

ambient particulate matter pollution accounted for 3.1 million (2.7 million to 3.5 million) deaths and 3.1% (2.7–3.4) of global DALYs. For ambient particulate matter pollution, we also did a post-hoc sensitivity analysis excluding the effects of dust, which had a small effect worldwide—attributable global DALYs decreased by 2%—but large effects in north Africa and Middle East. Household air pollution is an important contributor to ambient particulate matter pollution; we estimate that it accounted for 16% of the worldwide burden from ambient particulate matter pollution in 2010. The effects of ambient ozone pollution, which increases the risk of chronic obstructive pulmonary disease, were smaller than those of household air pollution from solid fuels or ambient particulate matter pollution (0.2 million [0.1 million to 0.3 million] deaths and 0.1% [0.03–0.2] of global DALYs in 2010).

For other clusters of risk factors for which we approximated the joint effects assuming independence, dietary risk factors and physical inactivity were responsible for the largest disease burden: 10.0% (9.2–10.8) of global DALYs in 2010. Of the individual dietary risk factors, the largest attributable burden in 2010 was associated with diets low in fruits (4.9 million [3.8 million to 5.9 million] deaths and 4.2% [3.3–5.0] of global DALYs), followed by diets high in sodium (4.0 million [3.4 million to 4.6 million]; 2.5% [1.7–3.3]), low in nuts and seeds (2.5 million [1.6 million to 3.2 million]; 2.1% [1.3–2.7]), low in whole grains (1.7 million [1.3 million to 2.1 million]; 1.6% [1.3–1.9]), low in vegetables (1.8 million [1.2 million to

	Men		Women		Both sexes	
	1990	2010	1990	2010	1990	2010
Unimproved water and sanitation	27 045 (1409-49 439)	11 022 (458-21 162)	25 123 (1262-45 792)	10 165 (428-19 650)	52 169 (2700-93 073)	21 187 (866-40 957)
Unimproved water source	11 075 (792-21 250)	4080 (266-8172)	10 097 (722-19 424)	3694 (242-7511)	21 172 (1517-40 491)	7775 (514-15 705)
Unimproved sanitation	18 610 (593-35 486)	7735 (190-15 338)	17 441 (522-32 889)	7192 (187-14 099)	36 050 (1115-66 871)	14 927 (377-29 705)
Air pollution
Ambient particulate matter pollution	46 667 (40 185-53 381)	46 732 (41 393-52 602)	35 032 (29 974-40 402)	29 431 (25 722-33 273)	81 699 (71 012-92 859)	76 163 (68 086-85 171)
Household air pollution from solid fuels	91 432 (71 850-109 298)	60 170 (45 087-75 153)	79 261 (64 684-93 004)	47 914 (37 929-58 289)	170 693 (139 087-199 504)	108 084 (84 891-132 983)
Ambient ozone pollution	1409 (460-2456)	1440 (506-2563)	1125 (375-1990)	1016 (331-1758)	2534 (851-4426)	2456 (837-4299)
Other environmental risks	2876 (2406-3459)	9434 (7476-12 045)	2489 (1974-3015)	6617 (5322-7938)	5365 (4534-6279)	16 051 (13 212-19 503)
Residential radon	..	1514 (191-3383)	..	600 (84-1355)	..	2114 (273-4660)
Lead exposure	2876 (2406-3459)	7920 (6491-9683)	2489 (1974-3015)	6017 (4915-7231)	5365 (4534-6279)	13 936 (11 750-16 327)
Child and maternal undernutrition	175 366 (146 049-211 406)	83 202 (67 963-99 704)	164 599 (139 926-192 077)	82 894 (69 171-98 757)	339 965 (289 845-402 489)	166 095 (139 685-193 981)
Suboptimal breastfeeding	59 902 (36 953-84 059)	25 572 (15 540-37 260)	50 359 (32 186-70 526)	21 965 (13 717-31 340)	110 261 (69 615-153 539)	47 537 (29 868-67 518)
Non-exclusive breastfeeding	52 729 (30 540-75 288)	22 258 (12 464-32 936)	43 601 (26 173-62 072)	18 850 (10 926-27 569)	96 330 (57 274-135 861)	41 108 (23 668-58 913)
Discontinued breastfeeding	7173 (767-15 819)	3314 (324-7377)	6758 (696-14 710)	3114 (296-6915)	13 931 (1443-30 062)	6429 (605-14 426)
Childhood underweight	104 713 (87 668-128 697)	41 270 (33 478-50 007)	93 028 (78 656-112 766)	36 045 (29 430-43 394)	197 741 (169 224-238 276)	77 316 (64 497-91 943)
Iron deficiency	21 451 (14 947-30 321)	19 974 (13 595-28 289)	30 390 (22 473-40 703)	28 251 (20 195-39 063)	51 841 (37 477-71 202)	48 225 (33 769-67 592)
Vitamin A deficiency	15 689 (7475-29 165)	5672 (2904-9348)	14 598 (7068-25 637)	5098 (2566-8168)	30 288 (14 884-54 488)	10 770 (5625-17 149)
Zinc deficiency	12 666 (2938-23 883)	4880 (1203-9316)	11 709 (2640-22 049)	4256 (1131-7821)	24 375 (5385-45 685)	9136 (2458-16 903)
Tobacco smoking (including second-hand smoke)	104 840 (91 849-119 255)	115 496 (98 595-130 090)	46 926 (39 634-58 092)	41 342 (30 473-48 563)	151 766 (136 367-169 522)	156 838 (136 543-173 057)
Tobacco smoking	84 956 (73 038-97 937)	105 635 (88 332-120 347)	28 784 (21 829-40 090)	31 272 (19 859-38 467)	113 740 (100 454-131 675)	136 907 (117 201-153 778)
Second-hand smoke	19 884 (14 493-25 591)	9861 (7669-12 312)	18 142 (13 748-22 355)	10 070 (7931-12 429)	38 026 (28 832-47 544)	19 931 (15 707-24 223)
Alcohol and drug use	65 660 (57 545-73 925)	90 578 (79 476-101 772)	22 851 (19 812-26 197)	30 033 (26 232-34 432)	88 510 (78 717-98 794)	120 611 (107 670-134 693)
Alcohol use	55 770 (49 280-62 723)	74 662 (65 764-83 831)	17 945 (15 470-20 768)	22 575 (19 542-25 693)	73 715 (66 090-82 089)	97 237 (87 087-107 658)
Drug use	10 178 (7787-13 073)	16 248 (12 679-20 132)	4993 (3811-6417)	7562 (5922-9471)	15 171 (11 714-19 369)	23 810 (18 780-29 246)
Physiological risk factors
High fasting plasma glucose	30 177 (25 148-34 980)	49 148 (41 619-57 197)	26 181 (22 243-30 349)	39 864 (34 103-45 972)	56 358 (48 720-65 030)	89 012 (77 743-101 390)
High total cholesterol	22 519 (18 230-27 029)	23 179 (17 148-29 650)	17 006 (13 940-20 640)	17 721 (13 153-22 508)	39 526 (32 704-47 202)	40 900 (31 662-50 484)
High blood pressure	73 120 (65 538-81 302)	99 566 (88 193-110 943)	63 897 (57 903-70 789)	73 991 (66 161-81 931)	137 017 (124 360-149 366)	173 556 (155 939-189 025)
High body-mass index	25 391 (19 752-31 108)	48 310 (39 429-57 750)	26 174 (20 911-31 642)	45 300 (37 218-54 219)	51 565 (40 786-62 557)	93 609 (77 107-110 600)
Low bone mineral density	1764 (1448-2208)	3105 (2295-3831)	1361 (1102-1686)	2111 (1627-2618)	3125 (2589-3811)	5216 (4133-6418)

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For the WHO Global Database on Child Growth and Malnutrition see <http://apps.who.int/nutrition/landscape/search.aspx?dm=52&countries=>

	Men		Women		Both sexes	
	1990	2010	1990	2010	1990	2010
(Continued from previous page)						
Dietary risk factors and physical inactivity	102 663 (94 539-111 011)	149 576 (138 035-160 263)	74 611 (68 196-81 173)	104 757 (97 047-112 535)	177 274 (164 710-190 286)	254 333 (237 748-270 495)
Diet low in fruits	47 979 (37 530-57 842)	65 523 (51 056-78 959)	32 474 (25 061-39 155)	38 573 (29 923-46 512)	80 453 (63 298-95 763)	104 095 (81 833-124 169)
Diet low in vegetables	18 755 (12 859-24 939)	24 169 (16 503-32 480)	12 803 (8 412-17 503)	14 389 (9 434-19 284)	31 558 (21 349-41 921)	38 559 (26 006-51 658)
Diet low in whole grains	17 033 (13 513-20 522)	24 881 (19 486-29 709)	12 370 (9 625-14 895)	15 881 (12 615-18 949)	29 404 (23 097-35 134)	40 762 (32 112-48 486)
Diet low in nuts and seeds	24 918 (16 268-31 946)	32 615 (21 258-41 958)	15 607 (9 915-20 208)	18 674 (11 716-24 404)	40 525 (26 308-51 741)	51 289 (33 482-65 959)
Diet low in milk	818 (248-1366)	1171 (350-1977)	710 (210-1210)	931 (264-1605)	1527 (461-2555)	2101 (619-3544)
Diet high in red meat	642 (306-1014)	1026 (484-1629)	566 (263-903)	827 (374-1362)	1208 (571-1909)	1853 (870-2946)
Diet high in processed meat	10 477 (2801-17 479)	12 901 (4012-21 421)	6882 (2340-11 119)	8038 (2932-12 685)	17 359 (5137-27 949)	20 939 (6982-33 468)
Diet high in sugar-sweetened beverages	3085 (2120-4151)	4858 (3154-6549)	2358 (1586-3484)	3695 (2356-5255)	5443 (3769-7373)	8553 (5823-11 418)
Diet low in fibre	8485 (3787-13 262)	10 893 (4903-17 191)	4862 (2188-7562)	5559 (2500-8639)	13 347 (5970-20 751)	16 452 (7401-25 783)
Diet low in calcium	1083 (752-1406)	1570 (1113-2058)	753 (521-975)	1019 (720-1319)	1836 (1316-2368)	2590 (1873-3322)
Diet low in seafood omega-3 fatty acids	13 620 (9915-17 307)	18 300 (13 267-23 201)	8120 (5900-10 388)	9899 (7241-12 596)	21 740 (15 869-27 537)	28 199 (20 624-35 974)
Diet low in polyunsaturated fatty acids	6185 (2891-9362)	7521 (3455-11 583)	3727 (1788-5709)	4159 (1973-6396)	9912 (4655-14 976)	11 680 (5360-17 798)
Diet high in trans fatty acids	4979 (3571-6413)	7339 (5240-9300)	3085 (2226-3944)	4253 (3106-5416)	8064 (5893-10 305)	11 592 (8395-14 623)
Diet high in sodium	26 807 (17 646-35 273)	37 378 (24 639-49 428)	19 376 (12 521-25 596)	23 852 (15 544-31 682)	46 183 (30 363-60 604)	61 231 (40 124-80 342)
Physical inactivity and low physical activity	..	37 007 (30 583-43 466)	..	32 311 (27 698-37 217)	..	69 318 (58 646-80 182)
Occupational risk factors	42 660 (35 146-50 545)	48 317 (38 407-58 677)	12 754 (9357-16 658)	14 171 (10 344-18 842)	55 414 (45 312-66 718)	62 488 (49 471-76 240)
Occupational carcinogens	1346 (917-1958)	2087 (1315-2928)	412 (284-611)	594 (368-855)	1758 (1220-2477)	2681 (1773-3689)
Occupational exposure to asbestos	362 (236-555)	521 (279-709)	122 (78-189)	132 (61-184)	484 (354-695)	653 (389-840)
Occupational exposure to arsenic	29 (11-56)	45 (17-84)	12 (5-24)	18 (7-33)	41 (16-77)	63 (24-114)
Occupational exposure to benzene	36 (15-64)	52 (21-92)	28 (11-52)	40 (15-72)	65 (27-112)	92 (39-163)
Occupational exposure to beryllium	2 (1-3)	3 (1-5)	1 (0-1)	1 (0-2)	2 (1-4)	4 (2-6)
Occupational exposure to cadmium	5 (2-9)	10 (4-16)	2 (1-3)	3 (1-6)	7 (3-12)	13 (6-21)
Occupational exposure to chromium	18 (11-28)	32 (17-48)	8 (4-13)	13 (7-21)	26 (16-40)	45 (27-66)
Occupational exposure to diesel engine exhaust	278 (158-436)	442 (232-682)	54 (31-88)	81 (42-126)	332 (192-517)	523 (292-789)
Occupational exposure to second-hand smoke	257 (173-383)	405 (244-544)	100 (69-162)	167 (95-228)	358 (255-500)	572 (386-762)
Occupational exposure to formaldehyde	11 (4-20)	17 (6-31)	7 (3-13)	9 (4-16)	18 (8-32)	25 (11-47)
Occupational exposure to nickel	90 (24-191)	151 (38-312)	37 (10-79)	64 (18-132)	128 (34-266)	215 (58-443)

(Continues on next page)

	Men		Women		Both sexes	
	1990	2010	1990	2010	1990	2010
(Continued from previous page)						
Occupational exposure to polycyclic aromatic hydrocarbons	41 (19-71)	73 (33-119)	13 (6-23)	23 (10-39)	54 (26-92)	96 (45-156)
Occupational exposure to silica	199 (129-297)	333 (199-463)	31 (21-52)	49 (26-71)	230 (154-328)	382 (239-526)
Occupational exposure to sulphuric acid	52 (14-114)	66 (19-143)	5 (1-12)	6 (2-13)	57 (16-122)	71 (21-152)
Occupational asthmagens	1467 (874-2439)	1359 (917-2153)	662 (366-1062)	661 (407-994)	2129 (1419-3222)	2020 (1441-2871)
Occupational particulate matter, gases, and fumes	6808 (3162-10 425)	6682 (3293-10 311)	2745 (1216-4406)	2460 (1105-4025)	9552 (4385-14 636)	9142 (4377-14 250)
Occupational noise	1936 (1149-3103)	2284 (1348-3649)	933 (550-1489)	1167 (696-1870)	2869 (1698-4582)	3451 (2072-5574)
Occupational risk factors for injuries	20 175 (15 588-25 639)	22 434 (16 711-29 943)	1090 (836-1437)	1010 (771-1331)	21 265 (16 644-26 702)	23 444 (17 736-30 904)
Occupational low back pain	10 929 (7340-15 116)	13 471 (8968-18 945)	6912 (4487-9835)	8279 (5502-11 602)	17 841 (11 846-24 945)	21 750 (14 492-30 533)
Sexual abuse and violence	..	3588 (2669-4679)	..	19 931 (14 524-26 397)	..	23 519 (17 961-30 322)
Childhood sexual abuse	..	3588 (2669-4679)	..	4244 (3082-5533)	..	7833 (5964-10 005)
Intimate partner violence	16 794 (11 373-23 087)	..	16 794 (11 373-23 087)

No data indicates that attributable disability-adjusted life-years were not quantified. Total disability-adjusted life-years (in 1000s) in 1990 were 1360569 for men, 1142032 for women, and 2502601 for both. In 2010, they were 1370177 for men, 1120208 for women, and 2490385 for both.

Table 4: Disability-adjusted life-years (1000s) attributable to risk factors and risk factor clusters, worldwide

2.3 million]; 1.5% [1.0–2.1]), and low in seafood omega-3 fatty acids (1.4 million [1.0 million to 1.8 million]; 1.1% [0.8–1.5]). Our sensitivity analysis of omega-3 fatty acids using relative risks from randomised trials reduced the attributable burden by more than half, to 0.6 million (–0.6 million to 1.7 million) deaths, and 0.5% (–0.5 to 1.4) of global DALYs in 2010. Physical inactivity and low physical activity accounted for 3.2 million (2.7 million to 3.7 million) deaths, and 2.8% (2.4–3.2) of DALYs in 2010.

Child and maternal undernutrition was responsible for the next largest attributable burden of the risk factor clusters (1.4 million [1.2 million to 1.7 million] deaths; 6.7% [5.7–7.7] of global DALYs in 2010), with childhood underweight the largest individual contributor (0.9 million [0.7 million to 1.0 million]; 3.1% [2.6–3.7]), followed by iron deficiency (0.1 million [0.09 million to 0.14 million]; 1.9% [1.4–2.6]), and suboptimal breastfeeding (0.5 million [0.3 million to 0.8 million]; 1.9% [1.2–2.7]). Vitamin A and zinc deficiencies amongst children accounted for less than 0.8% of the disease burden.

The burdens of disease attributable to tobacco smoking including second-hand smoke (6.3 million [5.4 million to 7.0 million] deaths and 6.3% [5.5–7.0] of DALYs) as well as alcohol and drug use (2.9 million [2.6 million to 3.2 million] deaths and 4.8% [4.3–5.4] of DALYs) were substantial in 2010. These burdens are mainly driven by active smoking, which accounts for 87% of the combined

burden with second-hand smoke, and alcohol use which accounted for 2.7 million (2.5 million to 3.0 million) deaths and 3.9% (3.5–4.3) of global DALYs in 2010. Of the remaining risk factor clusters, occupational risk factors accounted for 0.9 million (0.7 million to 1.1 million) deaths and 2.5% (2.0–3.0) of global DALYs in 2010, followed by sexual abuse and violence (0.2 million [0.1 million to 0.3 million] deaths and 0.9% [0.7–1.2] DALYs), unimproved water and sanitation, (0.3 million [0 to 0.6 million] deaths and 0.9% [0.04–1.6] DALYs), and other environmental risks (0.7 million [0.6 million to 0.9 million] deaths and 0.6% [0.5–0.8] DALYs).

The rest of the results section refers to the 43 risk factors and clusters of risk factors in the rank list. The predominance of non-communicable disease risks in 2010 highlights the global epidemiological transition that has occurred since 1990 (figures 1, 2, 3). In 1990, the leading risks were childhood underweight (7.9% [6.8–9.4] of global DALYs), household air pollution from solid fuels (7.0% [5.6–8.3]), and tobacco smoking including second-hand smoke (6.1% [5.4–6.8]), high blood pressure (5.5% [4.9–6.0]), and suboptimal breastfeeding (4.4% [2.8–6.1]). With the exception of household air pollution, which is a significant contributor to childhood lower respiratory tract infections, the five leading risk factors in 2010 (high

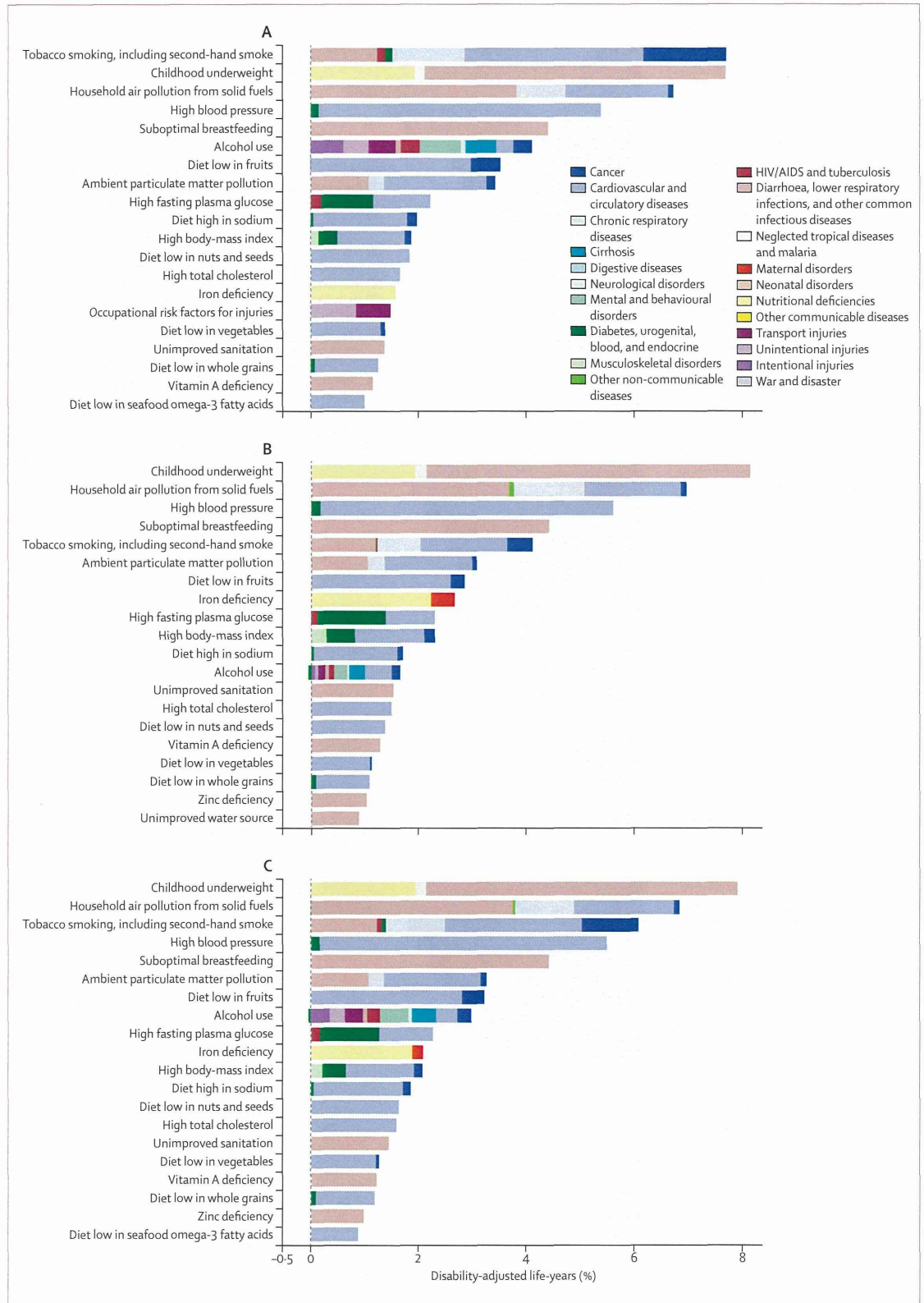


Figure 1: Burden of disease attributable to 20 leading risk factors in 1990, expressed as a percentage of global disability-adjusted life-years For men (A), women (B), and both sexes (C).

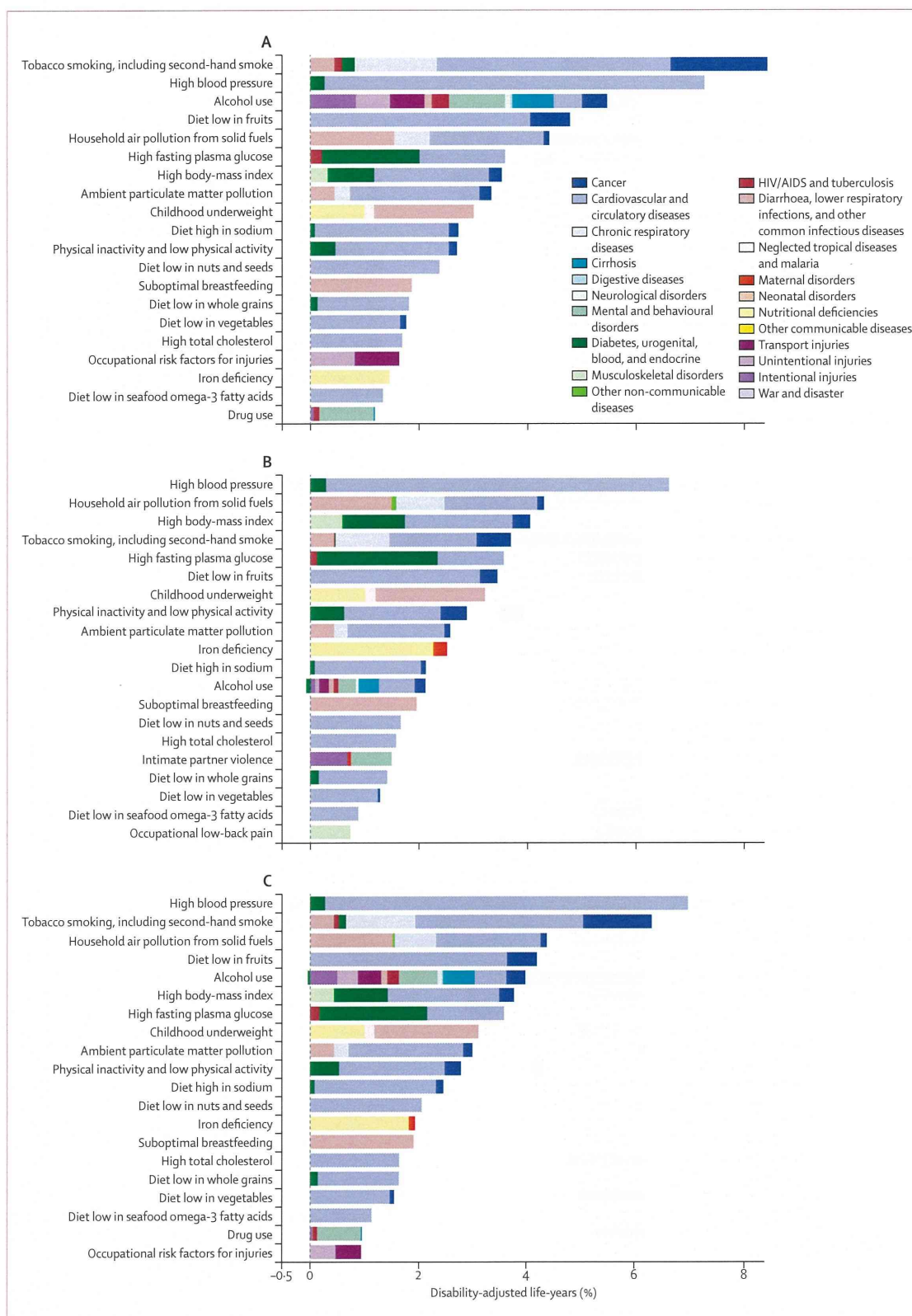


Figure 2: Burden of disease attributable to 20 leading risk factors in 2010, expressed as a percentage of global disability-adjusted life-years for men (A), women (B), and both sexes (C).