Appendix 1: Supplementary tables [posted as supplied by author]

Table S1. Search strategy in PubMed and Embase

1. fruits
2. vegetables
3. fruit
4. vegetable
5. berry
6. berries
7. citrus
8. “citrus fruits”
9. cruciferae
10. “cruciferous vegetables”
11. cabbages
12. “allium vegetables”
13. strawberry
14. strawberries
15. tomato
16. tomatoes
17. cereal
18. cereals
19. “breakfast cereal”
20. grain
21. grains
22. “whole grain”
23. “whole grains”
24. rice
25. bread
26. nut
27. seed
28. peanut
29. peanuts
30. legumes
31. soy
32. soya
33. chickpeas
34. chickpea
35. bean
36. beans
37. lentil
38. legume
39. legumes
40. fiber
41. “dietary fiber”
42. “fruit fiber”
43. “vegetable fiber”
44. “legume fiber”
45. “cereal fiber”
46. fibre
47. “dietary fibre”

48. “fruit fibre”
49. “vegetable fibre”
50. “cereal fibre”
51. “DASH diet”
52. diet
53. foods
54. “dietary patterns”
55. “dietary pattern”
56. “dietary score”
57. “diet score”
58. “diet index”
59. “food index”
60. “nutrient index”
61. “Mediterranean diet”
62. “vitamin C”
63 “ascorbic acid”
64. “vitamin E”
65. carotenoids
66. carotenoid
67. flavonoid
68. flavonoids
69. (1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34 OR 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58 OR 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66 OR 67 OR 68)
70. “coronary heart disease”
71. “heart disease”
72. “ischemic heart disease”
73. “ischaemic heart disease”
74. CHD
75. “coronary artery disease”
76. “myocardial infarction”
77. stroke
78. “ischemic stroke”
79. “haemorrhagic stroke”
80. “cardiovascular disease”
81. CVD
82. cancer
83. “total cancer”
84. mortality
85. “all-cause mortality”
86. “total mortality”
87. survival
88. (70 OR 71 OR 72 OR 73 OR 74 OR 75 OR 76 OR 77 OR 78 OR 79 OR 80 OR 81 OR 82 OR 83 OR 84 OR 85 OR 86 OR 87)
89. “case-control”
90. cohort

91. cohorts
92. prospective
93. longitudinal
94. retrospective
95. “follow-up”
96. “cross-sectional”
97. “population-based”
98. “relative risk
99. “odds ratio”
100 “hazard ratio”
101 “incidence rate ratio”
102 (89 OR 90 OR 91 OR 92 OR 93 OR 94 OR 95 OR 96 OR 97 OR 98 OR 99 OR 100 OR 101)
103. 69 AND 88 AND 102

Table S2. List of excluded studies and reason for exclusion

Exclusion reason	Reference number
Abstract only publication	(1-10)
Case-control study	(11-24)
Cross-sectional study	(25)
Crude dietary assessment	(26)
Diabetes patient population	(27;28)
Duplicates	(29-34)
Ecological study	(35)
Meta-analysis	(36-44)
No confidence intervals	(45;46)
No risk estimates	(47)
Not original data	(48)
Not usable result	(49)
Not relevant exposure	(50;51)
Not relevant outcome	(52-58)
Patients with heart disease	(59)
Qualitative assessment (whole grain vs. refined grains)	(60;61)
Quantity not provided	(62)
Review	(63-80)
Total disease mortality as outcome (not all-cause mortality), quantity not provided	(81)
Unadjusted risk estimates	(82)

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Table S3. Whole grains and refined grains and coronary heart disease

Author, publication year, country	Study name	Study period	Number of participants, gender, age, number of cases/deaths	CHD incidence or mortality	Dietary assessment	Exposure and subgroup	Whole grain consumption frequency or amount	Relative risks (95% confidence intervals)	Adjustment for confounding factors
Pietinen P et al, 1996, Finland	Alpha-Tocopherol Beta-Carotene Cancer Prevention Study	1986-1987 -1993, 6.1 years follow-up	21930 smoking men, age 50-69 years: 635 CHD deaths	Mortality	Validated FFQ, 276 food items	Rye products	16 g/day	1.00	Age, treatment group, smoking, BMI, blood pressure, intake of energy, alcohol, SFA, education, physical activity
							54.9	0.87 (0.68-1.10)	
							82.0	0.86 (0.68-1.10)	
							115.0	0.79 (0.61-1.01)	
							172.2	0.75 (0.58-0.98)	
						Other cereal products	47.0	1.00	
							83.3	0.94 (0.73-1.21)	
							114.8	0.93 (0.72-1.21)	
							150.6	1.03 (0.79-1.34)	
							214.5	1.05 (0.79-1.40)	
Gartside PS et al, 1998, USA	National Health and Nutrition Examination Follow-up Study 1	1971-1987, 16 years follow-up	5811 men and women, age 40-74 years: 1976 CHD cases	Incidence	NA	Bread	H vs l	1.16, p=0.05	Age, sex, race, geographic region, serum cholesterol, education, physical exercise, physical activity, smoking, BMI, alcohol, fish, dessert, cheese
Jacobs DR Jr et al, 1998, USA	Iowa Women's Health Study	1986-1995, 8.64 years of follow-up	34492 women, age 55-69 years: 438 ischemic heart disease cases	Incidence	FFQ, 127 food items	Dark bread	0-0.5 serv/wk	1.00	Age, total energy, education, marital status, high blood pressure, diabetes, BMI, waist-to-hip ratio, physical activity, pack-years, alcohol, use of vitamin supplements, oral contraceptive use, HRT, Keys score, fruit and vegetable intake (except juice), red meat, fish and seafood, sucrose
							1.0-3.0	0.81 (0.62-1.06)	
							5.5-7.0	0.62 (0.46-0.82)	
							17.5-42.0	0.67 (0.49-0.91)	
						Whole-grain breakfast cereal	0 serv/wk	1.00	
							0.5-1.0	0.82 (0.62-1.08)	
							3.0	0.78 (0.58-1.06)	
							5.5-7.0	0.77 (0.56-1.04)	
						Other whole grains	0 serv/wk	1.00	
							0.5-1.0	1.43 (1.01-2.02)	
							1.5-5.0	1.17 (0.81-1.68)	
							5.5-91.0	1.26 (0.81-1.95)	
						White bread	0 serv/wk	1.00	
							0.5-1.0	0.90 (0.64-1.27)	
							3.0-5.5	1.43 (1.08-1.89)	
							7.0-42.0	1.24 (0.94-1.64)	

						Refined-grain breakfast cereal	0 serv/wk	1.00	
							0.5-1.0	1.11 (0.81-1.53)	
							3.0	0.82 (0.52-1.28)	
							5.5-7.0	1.45 (0.99-2.13)	
						Sweets or desserts	0-2.0 serv/wk	1.00	
							2.5-5.0	0.94 (0.70-1.26)	
							5.5-7.0	1.13 (0.78-1.64)	
							7.5-11.0	1.17 (0.81-1.67)	
							11.5-143.0	0.86 (0.56-1.31)	
						Other refined grains	0-1.5 serv/wk	1.00	
							2.0-3.0	0.94 (0.74-1.20)	
							3.5-5.0	0.90 (0.65-1.25)	
							5.5-50.0	0.79 (0.52-1.21)	
						Crackers	0 serv/wk	1.00	
							0.5	0.91 (0.66-1.25)	
							1.0	0.99 (0.71-1.40)	
							3.0	0.87 (0.63-1.22)	
							5.5-42.0	0.81 (0.57-1.14)	

Liu S et al, 1999, USA	Nurses' Health Study	1984-1994, 10 years follow-up	75521 women, age 38-63 years: 761 CHD cases	Incidence	Validated FFQ, 126 food items	Whole grain	0.13 serv/day	1.00	Age, BMI, cigarette smoking, alcohol, parental or family history of myocardial infarction before age 60, hypertension, hypercholesterolemia, menopausal status, HRT, protein intake, aspirin use, multiple/vitamin E use, vigorous activity, total energy, SFA, PUFA, MUFA, trans-FA
							0.43	0.92 (0.75-1.14)	
							0.85	0.93 (0.75-1.15)	
							1.31	0.83 (0.66-1.05)	
							2.70	0.75 (0.59-0.95)	
						Dark bread	0 serv/day	1.00	
							0.07	1.13 (0.89-1.43)	
							0.43	0.92 (0.72-1.18)	
							0.71	0.97 (0.74-1.29)	
							1.30	0.98 (0.77-1.25)	
						Whole-grain breakfast cereal	0 serv/day	1.00	
							0.07	0.89 (0.72-1.10)	
							0.22	0.72 (0.56-0.92)	
							0.43	0.82 (0.66-1.02)	
							0.93	0.76 (0.57-1.00)	
						Popcorn	0 serv/day	1.00	
							0.07	0.86 (0.74-1.01)	
							0.33	0.88 (0.66-1.18)	
							0.62	0.42 (0.18-0.92)	
							1.00	0.92 (0.45-1.87)	
						Cooked oatmeal	0 serv/day	1.00	
							0.07	0.92 (0.79-1.08)	
							0.33	0.70 (0.49-0.98)	
							0.67	1.41 (0.75-2.26)	
							1.00	1.10 (0.45-2.68)	
						Brown rice	0 serv/day	1.00	
							0.07	0.86 (0.72-1.02)	
							0.31	0.77 (0.45-1.32)	
							0.79	0.45 (0.06-3.20)	
						Wheat germ	0 serv/day	1.00	
							0.07	0.55 (0.37-0.81)	
							0.36	1.11 (0.64-1.93)	
							0.93	0.41 (0.15-1.10)	
						Bran	0 serv/day	1.00	
							0.07	0.76 (0.59-0.98)	
							0.36	0.68 (0.44-1.03)	
							1.00	0.63 (0.42-0.95)	
						Other grains	0 serv/day	1.00	
							0.07	0.79 (0.57-1.08)	

Jacobs DR et al, 2001, Norway	Norwegian County Study	1977-1983 – 1994, 14.4 years follow-up	33848 men and women, age 35-56 years: 553 CHD deaths	Mortality	FFQ, 66 food items	Whole grain bread score	0.05-0.60 0.83-0.83 0.90-1.13 1.35-1.80 2.25-5.40	1.00 0.99 (0.75-1.31) 0.94 (0.73-1.22) 0.88 (0.67-1.16) 0.76 (0.56-1.02)	Age, energy intake, sex, smoking status, physical activity during leisure, physical activity during work, cod liver oil, multivitamin use, SFA, SBP, serum total cholesterol, BMI
Appleby PN et al, 2002, UK	The Health Food Shoppers Study	1973-1979 – 1997, 19.8 years follow-up	10741 men and women, age 16-89 years: 605 ischemic heart disease deaths	Mortality	FFQ	Wholemeal bread Bran cereals	Daily vs less Daily vs less	0.86 (0.72-1.03) 1.13 (0.94-1.35)	Age at recruitment, sex, smoking, fresh fruit, nuts/dried fruit, raw vegetables salads, mutual adjustment: wholemeal bread and bran cereals
Liu S et al, 2003, USA	Physicians' Health Study	1982-1988, 5.5 years follow-up	86190 men, age 40-84 years: 488 MI cases	Incidence	Validated FFQ	Whole grain breakfast cereals Refined grain breakfast cereals Total breakfast cereals	Rarely 1 serv/wk 2-6/wk ≥1/day Rarely 1 serv/wk 2-6/wk ≥1/day Rarely 1 serv/wk 2-6/wk ≥1/day	1.00 0.83 (0.56-1.23) 0.79 (0.56-1.10) 0.71 (0.51-0.98) 1.00 1.08 (0.81-144) 1.05 (0.76-1.44) 0.96 (0.68-1.36) 1.00 0.87 (0.67-1.14) 0.84 (0.62-1.07) 0.76 (0.54-0.94)	Age, cigarette smoking, alcohol intake, physical activity, BMI, history of type 2 diabetes, high cholesterol, hypertension, use of multivitamins
Steffen LM et al, 2003, USA	Atherosclerosis Risk in Communities Study	1987-1989 - 1999, 11 years follow-up	11940 men and women, age 45-64 years: 535 fatal or nonfatal coronary artery disease cases	Incidence	Validated FFQ, 61 food items	Whole grain Refined grain	0.1 serv/day 0.5 1.0 1.5 3.0 0.5 serv/day 1.5 2.0 3.0 5.0	1.00 0.76 (0.58-0.99) 0.93 (0.72-1.21) 0.73 (0.55-0.98) 0.72 (0.53-0.97) 1.00 0.91 (0.65-1.27) 1.14 (0.83-1.56) 1.28 (0.93-1.75) 1.17 (0.82-1.66)	Age, race, sex, time-dependent energy intake, education, smoking status, pack-years of smoking, physical activity, alcohol intake, HRT (women), BMI, waist-to-hip ratio, SBP, antihypertensive medication use, HDL-cholesterol, LDL-cholesterol
Jensen MK et al, 2004, USA	Health Professionals Follow-up Study	1986-2000, 14 years follow-up	42850 men, age 40-75 years: 1818 CHD cases	Incidence	Validated FFQ, 131 food items	Whole grains Added bran	3.5 g/d 9.6 16.0 24.7 42.4 0 g/d	1.00 0.96 (0.83-1.10) 0.94 (0.81-1.09) 0.86 (0.74-1.01) 0.84 (0.71-0.98) 1.00	Age, energy, smoking, alcohol, physical activity, family history of MI, use of vitamin E supplements, SFA, PUFA, trans FA, fruit, vegetables, fish, BMI, mutual adjustment between

						Germ	0.30 1.40 4.23 11.10 0 g/d 0.20 0.83	0.81 (0.70-0.95) 0.79 (0.67-0.92) 0.80 (0.68-0.93) 0.72 (0.61-0.84) 1.00 0.93 (0.81-1.07) 0.98 (0.85-1.12)	whole grains, added bran, and added germ
Mink PJ et al, 2007, USA	Iowa Women's Health Study	1986-2002, 16 years follow-up	34489 women, age 55-69 years: 1329 CHD deaths	Mortality	FFQ, 127 food items	Bran, added to food	0 serv/wk ・0	1.00 0.91 (0.78-1.06)	Age, energy intake, marital status, education, blood pressure, diabetes, BMI, waist-to-hip ratio, physical activity, smoking, HRT
Jacobs DR, 2007, USA	Iowa Women's Health Study	1986 – 2003, 17 years follow-up	27312 women, age 55-69 years: 1034 CHD deaths	Mortality	FFQ, 127 food items	Whole grains Refined grains	1.8 serv/wk 5.6 8.8 14.5 25.6 0-5.75 serv/wk 6-9.5 9.6-13.5 14-22 ≥22.5	1.00 1.01 (0.84-1.22) 0.85 (0.70-1.04) 0.79 (0.64-0.97) 0.72 (0.57-0.90) 1.00 0.96 (0.79-1.16) 0.90 (0.74-1.11) 0.80 (0.64-0.99) 0.89 (0.70-1.14)	Age, energy intake, BMI, waist-to-hip ratio, smoking, education, physical activity, estrogen use, multivitamin supplement use, intake of alcohol, alcohol^2, coffee, red meat, fish and seafood, total fruit and vegetables, mutual adjustment between whole grains and refined grains
Buckland G et al, 2009, Spain	European Prospective Investigation into Cancer and Nutrition – Spain	1992-1996 – 2004, 10.4 years follow-up	41078 men and women, age 29-69 years: 609 CHD cases	Incidence	Dietary history interview, validated FFQ, ~600 foods	Cereals	0-72.5 g/d >72.5-102.6 >102.6-501.3	1.00 1.01 (0.83-1.24) 1.12 (0.92-1.38)	Age, sex, center, education, physical activity, BMI, smoking status, diabetes, hypertension, hyperlipidemia, total calories
Eshak ES et al, 2011, Japan	Japan Collaborative Cohort Study	1988-1990 – 2003, 14.1 years follow-up	83752 men and women, age 40-79 years: 707 CHD deaths	Mortality	Validated FFQ, 40 food items	Rice, men Rice, women	280 g/d 420 449 583 711 279 g/d 359 420 453 560	1.00 1.04 (0.79-1.37) 0.73 (0.51-1.05) 0.85 (0.60-1.19) 0.70 (0.49-0.99) 1.00 1.01 (0.64-1.59) 0.83 (0.57-1.21) 1.25 (0.74-2.10) 1.08 (0.66-1.77)	Age, history of hypertension, history of diabetes, BMI, alcohol, smoking status, exercise, walking, education, perceived mental stress, sleep duration, fish, meat, fruit, dairy products, soy, total energy, sodium, Key's dietary score

Rautiainen S et al, 2012, Sweden	Swedish Mammmography Cohort	1997-2007, 9.9 years follow-up	32561 women, age 49-83 years: 1114 MI cases	Incidence	Validated FFQ, 96 food items	Whole grains	≤2.3 serv/d 2.4-3.4 3.4-4.7 ≥4.7	1.00 0.95 (0.81-1.13) 0.88 (0.74-1.04) 0.89 (0.74-1.07)	Age, education, smoking, BMI, physical activity, hypertension, hypercholesterolemia, family history – MI, aspirin use, HRT, dietary supplement use, total energy, alcohol
Simila ME et al, 2013, Finland	Alpha-Tocopherol Beta-Carotene Cancer Prevention Study	1985-1988 – 2004, 19 years follow-up	21995 male smokers, age 50-69 years: 4379 CHD cases	Incidence	Validated FFQ, 276 food items	Rye	Per 100 g/d	0.99 (0.94-1.03)	Age, intervention group
Yu D et al, 2013, China	Shanghai Women's Health Study	1997-2000 – 2009, 9.8 years follow-up	64854 women, age 40-70 years: 120 CHD cases	Incidence	Validated FFQ, 77 food items	White rice and refined wheat products	250 g/d 274 290 311	1.00 0.97 (0.49-1.93) 1.41 (0.69-2.90) 1.53 (0.64-3.68)	Age, birth cohort, education, income, smoking status, alcohol, physical activity, waist-to-hip ratio, hypertension, total energy, SFA, protein
Yu D et al, 2013, China	Shanghai Men's Health Study	2002-2006 – 2009, 5.4 years follow-up	52512 men, age 40-74 years: 189 CHD cases	Incidence	Validated FFQ, 81 food items	White rice and refined wheat products	253 g/d 290 327 367	1.00 1.15 (0.69-1.90) 1.38 (0.76-2.51) 2.01 (0.96-4.23)	Age, birth cohort, education, income, smoking status, alcohol, physical activity, waist-to-hip ratio, hypertension, total energy, SFA, protein
Eshak ES et al, 2014, Japan	Japan Public Health Center-based Prospective Study	1990/1993 – 2007/2009, 15.2 years follow-up	91223 men and women, age 40-69 years: 1088 IHD cases 605 IHD deaths	Incidence and mortality	Validated FFQ, 44/52 food items	Rice, CHD incidence Rice, CHD mortality	251 g/d 326 377 430 542 251 g/d 326 377 430 542	1.00 0.93 (0.76-1.14) 0.99 (0.80-1.22) 0.95 (0.77-1.19) 1.08 (0.84-1.38) 1.00 0.81 (0.61-1.06) 0.93 (0.70-1.23) 0.85 (0.64-1.12) 0.93 (0.68-1.27)	Age, sex, public health center area, hypertension, diabetes, use of lipid-lowering drugs, BMI, smoking status, ethanol intake, leisure-time sports activity, occupation, seafood, meat, fruit, vegetables, soy, SFAs, sodium, total energy, women: HRT, menopausal status
Rebello SA et al, 2014, Singapore	Singapore Chinese Health Study	1993-1998 – 2011, 15 years follow-up	53469 men and women, age 45-74 years: 1660 IHD deaths	Mortality	Validated FFQ, 165 food items	Whole-wheat bread, men Whole-wheat bread, women White bread, men	0.00 slices/d 0.33 1.00 Per serv/d 0.00 slices/d 0.33 1.00 Per serv/d 0.00 slices/d	1.00 0.93 (0.77-1.12) 0.94 (0.66-1.33) 0.99 (0.78-1.27) 1.00 0.93 (0.74-1.17) 0.51 (0.30-0.89) 0.58 (0.38-0.89) 1.00	Age, year of interview, father's dialect, total energy intake, cigarette smoking, alcohol, physical activity, sleep duration, education, BMI, hypertension, PUFA/SFA ratio, rice, noodles, vegetables, fruit, fish, red meat, poultry, eggs, legumes, soy protein, white bread and whole-

							0.33	1.09 (0.92-1.29)	wheat bread mutually adjusted, women: menopausal status, HRT use
							1.00	1.12 (0.90-1.39)	
							Per serv/d	0.91 (0.79-1.05)	
						White bread, women	0.00 slices/d	1.00	
							0.33	0.91 (0.74-1.11)	
							1.00	0.79 (0.60-1.04)	
							Per serv/d	0.84 (0.68-1.04)	
						Rice, men	2.35 serv/d	1.00	
							3.40	0.96 (0.76-1.20)	
							4.10	0.95 (0.75-1.20)	
							4.80	0.98 (0.77-1.25)	
							6.74	1.02 (0.79-1.31)	
							Per serv/d	1.00 (0.95-1.06)	
						Rice, women	2.40 serv/d	1.00	
							3.39	1.07 (0.79-1.45)	
							4.08	1.20 (0.88-1.63)	
							4.80	1.07 (0.77-1.48)	
							5.77	1.10 (0.77-1.58)	
							Per serv/d	1.00 (0.92-1.08)	
						Noodles, men	0.11 serv/d	1.00	
							0.31	0.96 (0.79-1.18)	
							0.47	1.07 (0.87-1.31)	
							0.66	1.19 (0.96-1.46)	
							1.08	1.32 (1.07-1.62)	
							Per serv/d	1.30 (1.11-1.53)	
						Noodles, women	0.15 serv/d	1.00	
							0.32	1.01 (0.77-1.33)	
							0.46	0.95 (0.71-1.27)	
							0.65	1.14 (0.86-1.53)	
							1.07	1.38 (1.02-1.85)	
							Per serv/d	1.38 (1.09-1.75)	
Muraki I et al, 2014, USA	Nurses' Health Study	1984-2010, 26 years follow-up	73228 women, age 38-63 years: 3060 CAD cases	Incidence	Validated FFQ, 118-166 food items	White rice	<1 serv/wk	1.00	Age, sex, cohort, ethnicity, BMI, smoking status, cigarettes per day, alcohol, physical activity, family history – MI, multivitamin use, current aspirin use, prevalent hypertension, prevalent hypercholesterolemia, prevalent diabetes, total energy
							1	1.04 (0.98-1.09)	
							2-4	1.05 (0.98-1.12)	
							≥5	0.84 (0.69-1.02)	
							Per 3 serv/wk	1.01 (0.94-1.07)	
	Nurses' Health Study 2	1991-2011, 20 years	92158 women, age 27-44 years: 534 CAD cases			Brown rice	<1 serv/wk	1.00	
							1	0.99 (0.92-1.06)	
							2-4	1.05 (0.95-1.16)	

	Health Professionals Follow-up Study	follow-up 1986-2010, 24 years follow-up	42170 men, age 40-75 years: 4125 CAD cases			Total rice	≥5 Per 3 serv/wk <1 serv/wk 1 2-4 ≥5 Per 3 serv/wk	0.80 (0.57-1.12) 1.00 (0.91-1.11) 1.00 1.03 (0.98-1.09) 1.03 (0.97-1.09) 0.97 (0.86-1.08) 0.99 (0.94-1.05)	intake, modified alternate Healthy Eating Index score, women: menopausal status, oral contraceptive use (NHS2), postmenopausal hormone use
Tognon G et al, 2014, Denmark	The 1982-83 Danish Monitoring trends and determinants of Cardiovascular disease study (MONICA)	1982-1983 – 2007, 14 years follow-up	948 women and 901 men, age NA: 161 MI cases 64 MI deaths	Incidence and mortality	Validated 7 day food record, 100 food items	Cereals, MI incidence Cereals, MI death	>median vs. <median >median vs. <median	0.90 (0.66-1.24) 0.69 (0.41-1.16)	Age, sex, BMI, education, physical activity, cigarette smoking
Atkins JL et al, 2014, United Kingdom	British Regional Heart Study	1998-2000 – 2010, 11.3 years follow-up	3328 men, age 60-79 years: 307 CHD cases	Incidence	Validated FFQ, 86 food items	Cereals Bread	Daily vs. <1 day/wk Whole grain vs. none	1.19 (0.73-1.93) 0.76 (0.18-3.15)	Age, smoking, alcohol, physical activity, social class, BMI, energy intake, diet score without respective components
Johnsen NF et al, 2015, Norway, Sweden, Denmark	HELGA Cohort (Norwegian Women and Cancer Study, Northern Sweden Health and Disease Study, Danish Diet, Cancer and Health Study – part of the EPIC study)	1992-1998 – 2008-2009, 11.1 (Norway), 14.2 (Sweden), 11.9 years (Denmark) follow-up	120010 men and women, age 30-64 years: 858/298 CHD deaths	Mortality	Validated FFQ, 88 food items (Norway), 98 food items (Sweden) 173 food items (Denmark)	Whole grain breakfast cereals, women Non-white bread Crisp bread Total whole grain products Oat	0 g/d 0.8 12 50 25 g/d 80 113 180 0.6 g/d 2 6 31 56 g/d 100 131 201 0 g/d 0.4 4 19 8 g/d	1.00 0.71 (0.43-1.16) 0.64 (0.47-0.87) 0.53 (0.37-0.77) 1.00 0.72 (0.52-0.99) 0.54 (0.37-0.79) 0.72 (0.47-1.09) 1.00 0.81 (0.56-1.18) 0.95 (0.68-1.33) 0.94 (0.66-1.34) 1.00 0.72 (0.54-0.97) 0.64 (0.46-0.89) 0.56 (0.40-0.78) 1.00 0.74 (0.52-1.05) 0.85 (0.59-1.21) 0.66 (0.45-0.96) 1.00	Age, follow-up time, education, smoking status/years since quit/ cigarettes per day, alcohol, BMI, total energy

						Rye	18	0.79 (0.57-1.11)	
							22	1.02 (0.75-1.38)	
							41	0.69 (0.46-1.05)	
							0.4 g/d	1.00	
						Wheat	3	0.83 (0.57-1.21)	
							10	0.87 (0.60-1.27)	
							37	0.67 (0.45-1.00)	
							20 g/d	1.00	
						Total whole grain	33	0.83 (0.60-1.14)	
						types	49	0.59 (0.42-0.82)	
							74	0.65 (0.46-0.91)	
							0 g/d	1.00	
							0.8	0.88 (0.69-1.11)	
						Whole grain	7	0.87 (0.72-1.05)	
						breakfast cereals,	50	0.75 (0.61-0.91)	
						men	13 g/d	1.00	
							66	1.13 (0.89-1.42)	
							118	0.95 (0.74-1.22)	
						Non-white bread	201	0.87 (0.65-1.17)	
							1 g/d	1.00	
							2	0.98 (0.81-1.19)	
							4	0.95 (0.78-1.16)	
						Crisp bread	34	1.23 (0.88-1.71)	
							64 g/d	1.00	
							107	0.94 (0.78-1.15)	
							156	0.80 (0.66-0.97)	
						Total whole grain	222	0.85 (0.70-1.04)	
						products	0 g/d	1.00	
							0.4	1.01 (0.83-1.23)	
							3	1.01 (0.80-1.28)	
						Oat	30	0.82 (0.65-1.03)	
							7 g/d	1.00	
							21	0.77 (0.62-0.95)	
							38	0.81 (0.67-0.97)	
						Rye	56	0.88 (0.73-1.07)	
							0.1 g/d	1.00	
							1	0.80 (0.66-0.97)	
							5	0.70 (0.55-0.88)	
						Wheat	10	0.84 (0.65-1.08)	

						Total whole grain types	21 g/d 37 54 80	1.00 0.79 (0.65-0.96) 0.80 (0.66-0.97) 0.74 (0.61-0.91)	
Helnæs A et al, 2016, Denmark	Danish Diet, Cancer and Health Cohort	1993-1997 - 2009, 13.6 years follow-up	54871 men and women, age 50-64 years: 2329 MI cases	Incidence	Validated FFQ, 192 food items	Total whole grain products, men	66 g/d 116 163 224 Per 50 g/d	1.00 0.83 (0.73-0.95) 0.81 (0.71-0.93) 0.77 (0.67-0.89) 0.94 (0.91-0.97)	Age, education, smoking status, pack-years, alcohol from beer and spirits, alcohol from wine, sports, menopausal status, HRT, fruit, vegetables, fish, red meat, processed meat
						Total whole grains	22 g/d 38 52 74 Per 25 g/d	1.00 0.84 (0.73-0.95) 0.86 (0.76-0.99) 0.75 (0.65-0.86) 0.88 (0.83-0.93)	
						Total whole grain products, women	63 g/d 103 135 201 Per 50 g/d	1.00 0.83 (0.67-1.02) 0.78 (0.63-0.96) 0.71 (0.56-0.89) 0.90 (0.84-0.97)	
						Total whole grains	20 g/d 29 42 63 Per 25 g/d	1.00 0.86 (0.70-1.06) 0.77 (0.62-0.95) 0.73 (0.58-0.91) 0.87 (0.78-0.96)	
						Rye bread, men	Per 25 g/d	0.96 (0.94-0.99)	+ BMI, waist circumference, SBP, hypertension, serum cholesterol, hypercholesterolemia
						Whole grain bread	Per 25 g/d	0.99 (0.97-1.02)	
						Oatmeal	Per 25 g/d	0.84 (0.78-0.91)	
						Crispbread	Per 25 g/d	0.97 (0.81-1.17)	
						Wheat	Per 10 g/d	0.96 (0.84-1.09)	
						Rye	Per 10 g/d	0.96 (0.93-0.99)	
						Oats	Per 10 g/d	0.93 (0.88-0.97)	
						Rye bread, women	Per 25 g/d	0.93 (0.88-0.98)	
						Whole grain bread	Per 25 g/d	0.98 (0.93-1.03)	
						Oatmeal	Per 25 g/d	0.89 (0.77-1.02)	
						Crispbread	Per 25 g/d	1.12 (0.92-1.36)	

						Wheat	Per 10 g/d	0.89 (0.70-1.13)	
						Rye	Per 10 g/d	0.96 (0.90-1.01)	
						Oats	Per 10 g/d	0.94 (0.86-1.02)	
						Total whole grain	66 g/d	1.00	
						products, men	116	0.85 (0.75-0.98)	
							163	0.85 (0.74-0.98)	
							224	0.89 (0.77-1.02)	
							Per 50 g/d	0.97 (0.94-1.01)	
						Total whole grains	22 g/d	1.00	
							38	0.87 (0.76-0.99)	
							52	0.93 (0.82-1.07)	
							74	0.88 (0.76-1.02)	
							Per 25 g/d	0.94 (0.88-0.99)	
						Total whole grain	63 g/d	1.00	
						products, women	103	0.82 (0.66-1.02)	
							135	0.80 (0.64-0.98)	
							201	0.72 (0.57-0.91)	
							Per 50 g/d	0.91 (0.85-0.98)	
						Total whole grains	20 g/d	1.00	
							29	0.84 (0.68-1.04)	
							42	0.79 (0.64-0.98)	
							63	0.76 (0.61-0.96)	
							Per 25 g/d	0.89 (0.80-0.99)	
						Rye bread, men	Per 25 g/d	0.98 (0.96-1.01)	
						Whole grain bread	Per 25 g/d	1.01 (0.98-1.03)	
						Oatmeal	Per 25 g/d	0.89 (0.82-0.96)	
						Crispbread	Per 25 g/d	0.93 (0.77-1.11)	
						Wheat	Per 10 g/d	1.03 (0.90-1.17)	
						Rye	Per 10 g/d	0.98 (0.95-1.00)	
						Oats	Per 10 g/d	0.96 (0.91-1.00)	
						Rye bread, women	Per 25 g/d	0.93 (0.88-0.98)	
						Whole grain bread	Per 25 g/d	0.98 (0.93-1.02)	
						Oatmeal	Per 25 g/d	0.92 (0.80-1.05)	
						Crispbread	Per 25 g/d	1.12 (0.92-1.36)	
						Wheat	Per 10 g/d	0.90 (0.71-1.14)	
						Rye	Per 10 g/d	0.96 (0.91-1.01)	
						Oats	Per 10 g/d	0.96 (0.88-1.05)	
Wang JB et al, 2016, China	Linxian Nutrition Intervention Trial	1984-1991 - 2010, 19-	2445 men and women, age 40-	Mortality	FFQ, 64 food items	All grains Non-whole grains	Per 1 time/day Per 1 time/day	1.00 (0.92-1.09) 1.05 (0.94-1.16)	Age, sex, commune, smoking, drinking, season, BMI

	cohort	26 years follow-up	69 years: 355 heart disease deaths			Whole grains	Per 1 time/day	0.94 (0.83-1.07)	

BMI; body mass index, CHD; coronary heart disease, FFQ; food frequency questionnaire, H vs l; High vs low, HDL-cholesterol; high-density lipoprotein cholesterol, HRT; hormone replacement therapy, IHD; ischemic heart disease, LDL; low density lipoprotein cholesterol, MI; myocardial infarction, MUFA; monounsaturated fatty acids, NHS2; Nurses' Health Study 2, PUFA; polyunsaturated fatty acids, SBP; systolic blood pressure, SFA; saturated fatty acids, trans-FA: trans fatty acids

Table S4. Whole grains and refined grains and stroke

Author, publication year, country	Study name	Study period	Number of participants, gender, age, number of cases/deaths	Stroke incidence or mortality	Dietary assessment	Exposure and subgroup	Whole grain consumption frequency or amount	Relative risks (95% confidence intervals)	Adjustment for confounding factors
Liu S et al, 2000, USA	Nurses' Health Study	1984-1996, 12 years follow-up	75521 women, age 38-63 years: 352 ischemic stroke cases	Incidence	Validated FFQ, 126 food items	Whole grains	0.13 serv/day	1.00	Age, BMI, physical activity, cigarette smoking, alcohol, parental history of MI before age 60 years, aspirin use, menopausal status, HRT, hypertension, high blood cholesterol, use of multivitamins and vitamin E supplements, SFA, Trans FA, total energy
							0.43	0.72 (0.53-1.00)	
							0.85	0.78 (0.58-1.08)	
							1.31	0.60 (0.43-0.86)	
							2.70	0.69 (0.50-0.98)	
						Refined grains	1	1.00	
							2	1.11 (0.81-1.52)	
							3	1.18 (0.85-1.64)	
							4	0.94 (0.66-1.35)	
							5	0.97 (0.67-1.42)	
						Total grains	1	1.00	
							2	0.83 (0.60-1.15)	
							3	0.82 (0.59-1.16)	
							4	0.62 (0.43-0.92)	
							5	0.79 (0.54-1.18)	
Appleby PN et al, 2002, UK	The Health Food Shoppers Study	1973-1979 – 1997, 19.8 years follow-up	10741 men and women, age 16-89 years: 356 cerebro-vascular disease deaths	Mortality	FFQ	Wholemeal bread	Daily vs less	0.89 (0.70-1.13)	Age, sex, smoking, fresh fruit, nuts/dried fruit, raw vegetables salads, mutual adjustment between wholemeal bread and bran cereals
						Bran cereals	Daily vs less	0.92 (0.73-1.17)	
Liu S et al, 2003, USA	Physicians' Health Study	1982-1988, 5.5 years follow-up	86190 men, age 40-84 years: 146 stroke cases	Incidence	Validated FFQ	Whole grain breakfast cereals	Rarely	1.00	Age, cigarette smoking, alcohol intake, physical activity, BMI, history of type 2 diabetes mellitus, high cholesterol, hypertension, use of multivitamins
							1 serv/wk	0.92 (0.42-1.99)	
							2-6/wk	1.68 (1.00-2.80)	
							≥1/day	1.41 (0.85-2.34)	
						Refined-grain breakfast cereals	Rarely	1.00	
							1 serv/wk	0.79 (0.43-1.45)	
							2-6/wk	0.79 (0.42-1.49)	
							≥1/day	1.22 (0.71-2.11)	
						Total breakfast cereals	Rarely	1.00	
							1 serv/wk	0.98 (0.56-1.74)	
							2-6/wk	1.40 (0.84-2.32)	
							≥1/day	1.54 (0.94-2.52)	

Steffen LM et al, 2003, USA	Atherosclerosis Risk in Communities Study	1987-1989 - 1999, 11 years follow-up	15792 men and women, age 45-64 years: 214 fatal or incident ischemic stroke	Incidence	Validated FFQ, 61 food items	Whole grain Refined grain 	0.1 serv/day 0.5 1.0 1.5 3.0 0.5 serv/day 1.5 2.0 3.0 5.0	1.00 1.11 (0.75-1.64) 0.79 (0.50-1.21) 0.89 (0.57-1.39) 0.75 (0.46-1.22) 1.00 1.10 (0.71-1.73) 1.00 (0.63-1.58) 0.68 (0.41-1.13) 0.82 (0.48-1.40)	Age at baseline, race, sex, time-dependent energy intake, education, smoking status, pack-years of smoking, physical activity, alcohol intake, HRT (women), BMI, waist-to-hip ratio, SBP, antihypertensive medication use
Jacobs DR, 2007, USA	Iowa Women's Health Study	1986 – 2003, 17 years follow-up	27312 women, age 55-69 years: 414 stroke deaths 113 intracranial hemorrhagic stroke deaths 251 non-hemorrhagic stroke deaths	Mortality	Validated FFQ, 127 food items	Whole grains, all Whole grains, hemorrhagic strokes Whole grains, non-hemorrhagic strokes Refined grains, all Refined grains, hemorrhagic strokes Refined grains, non-hemorrhagic strokes 	1.8 serv/wk 5.6 8.8 14.5 25.6 1.8 serv/wk 5.6 8.8 14.5 25.6 1.8 serv/wk 5.6 8.8 14.5 25.6 0-5.75 serv/wk 6-9.5 9.6-13.5 14-22 ≥22.5 0-5.75 serv/wk 6-9.5 9.6-13.5 14-22 ≥22.5 0-5.75 serv/wk 6-9.5 9.6-13.5 14-22	1.00 0.91 (0.67-1.24) 0.84 (0.61-1.15) 0.88 (0.64-1.22) 0.85 (0.60-1.21) 1.00 1.28 (0.68-2.42) 1.33 (0.71-2.49) 1.01 (0.51-1.99) 1.28 (0.64-2.56) 1.00 0.79 (0.53-1.18) 0.74 (0.49-1.11) 0.87 (0.58-1.31) 0.88 (0.57-1.36) 1.00 1.15 (0.85-1.56) 1.09 (0.78-1.51) 0.86 (0.60-1.22) 1.30 (0.88-1.91) 1.00 0.84 (0.48-1.47) 0.82 (0.45-1.50) 0.61 (0.31-1.20) 1.10 (0.54-2.23) 1.00 1.22 (0.82-1.80) 1.16 (0.76-1.76) 0.87 (0.55-1.38)	Age, energy intake, BMI, waist-to-hip ratio, smoking, education, physical activity, HRT, multivitamin supplement use, intake of alcohol, alcohol^2, coffee, red meat, fish and seafood, total fruit and vegetables, mutual adjustment between whole grains and refined grains

							≥22.5	1.19 (0.72-1.97)	
Mizrahi A et al, 2009, Finland	Finnish Mobile Clinic Health Examination Survey	1968-1972 - 1994, 24 years follow-up	3932 men and women, age 40-74 years: 625 stroke cases	Incidence	Dietary history interview	Cereals, cerebrovascular disease	10-223/20-156 g/d	1.00	Age, sex, BMI, smoking, physical activity, serum cholesterol, blood pressure, energy
							224-295/157-210	1.09 (0.87-1.36)	
							296-390/211-285	1.09 (0.86-1.39)	
							391-1535/286-1092	1.09 (0.82-1.45)	
						Whole grains	0-139/0-89 g/d	1.00	
							140-201/90-134	0.98 (0.78-1.23)	
							202-279/135-194	1.18 (0.93-1.48)	
							280-1321/195-963	1.12 (0.87-1.45)	
						Refined grains	0-50/0-43 g/d	1.00	
							51-82/44-68	0.93 (0.74-1.15)	
							83-124/69-99	0.88 (0.70-1.10)	
							125-567/100-457	0.88 (0.69-1.14)	
						Cereals, ischemic stroke	10-223/20-156 g/d	1.00	
							224-295/157-210	0.96 (0.71-1.31)	
							296-390/211-285	1.12 (0.81-1.53)	
							391-1535/286-1092	0.97 (0.66-1.43)	
						Whole grains	0-139/0-89 g/d	1.00	
							140-201/90-134	0.95 (0.70-1.29)	
							202-279/135-194	1.11 (0.81-1.51)	
							280-1321/195-963	1.06 (0.75-1.50)	
						Refined grains	0-50/0-43 g/d	1.00	
							51-82/44-68	0.81 (0.60-1.10)	
							83-124/69-99	0.95 (0.71-1.28)	
							125-567/100-457	0.85 (0.61-1.19)	
						Cereals, intracerebral stroke	10-223/20-156 g/d	1.00	
							224-295/157-210	1.72 (0.88-3.36)	
							296-390/211-285	0.64 (0.27-1.53)	
							391-1535/286-1092	1.14 (0.47-2.78)	
						Whole grains	0-139/0-89 g/d	1.00	
							140-201/90-134	1.01 (0.49-2.08)	
							202-279/135-194	1.31 (0.64-2.68)	
							280-1321/195-963	1.19 (0.53-2.67)	
						Refined grains	0-50/0-43 g/d	1.00	
							51-82/44-68	0.70 (0.36-1.36)	
							83-124/69-99	0.66 (0.33-1.33)	
							125-567/100-457	0.66 (0.31-1.42)	

Larsson SC et al, 2009, Finland	Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study	1985-1988 - 2004, 13.6 years follow-up	26556 male smokers, age 50-69 years: 2702 cerebral infarctions 383 intracerebral hemorrhages 196 subarachnoid hemorrhages	Incidence	Validated FFQ, 276 food items	Cereals, cerebral infarction Cereals, intracerebral hemorrhage Cereals, subarachnoid hemorrhage	116.4 g/d 165.6 205.2 249.9 327.4 116.4 g/d 165.6 205.2 249.9 327.4 116.4 g/d 165.6 205.2 249.9 327.4	1.00 0.98 (0.87-1.10) 0.97 (0.85-1.10) 0.93 (0.81-1.07) 0.87 (0.74-1.03) 1.00 0.85 (0.63-1.16) 0.88 (0.64-1.22) 0.70 (0.48-1.01) 0.64 (0.41-1.01) 1.00 1.12 (0.69-1.81) 0.84 (0.50-1.42) 1.24 (0.74-2.07) 1.00 (0.54-1.84)	Age, supplementation group, cigarettes per day, BMI, SBP, DBP, serum total cholesterol, serum HDL-cholesterol, diabetes, coronary heart disease, leisure-time physical activity, alcohol, total energy
Oba S et al, 2010, Japan	Takayama Study	1992 – 1999, 7 years follow-up	12561 men and 15301 women, age ≥35 years: 247 stroke deaths 126 ischemic stroke deaths 94 hemorrhagic stroke deaths	Mortality	Validated FFQ, 169 food items	Rice, men, total stroke Rice, women Rice, men, ischemic stroke Rice, women Rice, men, hemorrhagic stroke Rice, women	2.3 serv/d (67.6 g) 3.2 3.7 4.0 1.9 serv/d 2.3 2.7 3.2 2.3 serv/d (67.6 g) 3.2 3.7 4.0 1.9 serv/d 2.3 2.7 3.2 2.3 serv/d (67.6 g) 3.2 3.7 4.0 1.9 serv/d 2.3 2.7 3.2	1.00 0.95 (0.59-1.52) 0.53 (0.26-1.04) 0.84 (0.43-1.62) 1.00 1.47 (0.78-2.79) 1.22 (0.62-2.37) 1.37 (0.64-2.94) 1.00 0.97 (0.51-1.82) 0.52 (0.19-1.41) 1.21 (0.61-2.37) 1.00 1.53 (0.64-3.68) 1.14 (0.49-2.67) 1.67 (0.69-4.07) 1.00 0.73 (0.35-1.50) 0.39 (0.15-1.00) 0.71 (0.34-1.49) 1.00 0.98 (0.33-2.91) 1.81 (0.71-4.66) 2.36 (0.92-6.03)	Age, BMI, smoking status, physical activity, hypertension, education, total energy, alcohol, dietary fiber, salt, total fat

Eshak ES et al, 2011, Japan	Japan Collaborative Cohort Study	1988-1990 – 2003, 14.1 years follow-up	83752 men and women, age 40-79 years: 1640 stroke deaths	Mortality	Validated FFQ, 40 food items	Rice, men Rice, women	280 g/d 420 449 583 711 279 g/d 359 420 453 560	1.00 0.96 (0.79-1.17) 0.96 (0.76-1.22) 0.78 (0.61-1.00) 1.02 (0.82-1.31) 1.00 0.85 (0.64-1.12) 0.89 (0.72-1.11) 0.89 (0.64-1.26) 0.99 (0.75-1.31)	Age, history of hypertension, history of diabetes, BMI, alcohol, smoking status, exercise, walking, education, perceived mental stress, sleep duration, fish, meat, fruit, dairy products, soy, total energy
Misirili G et al, 2012, Greece	European Prospective Investigation into Cancer and Nutrition - Greece	1994-1999 – 2009, 10.6 years follow-up	23601 men and women, age 25-67 years: 395 incidence cases 196 deaths cerebro-vascular disease	Incidence and mortality	FFQ, 150 food items	Cereals, incidence Cereals, mortality	Per 70 g/d Per 70 g/d	1.02 (0.89-1.16) 0.97 (0.79-1.19)	Age, education, smoking status, BMI, physical activity, hypertension, diabetes, total energy intake
Eshak E et al, 2014, Japan	Japan Public Health Center-based Prospective Study	1990/1993 – 2007/2009, 15.2 years follow-up	91223 men and women, age 40-69 years: 4395 total strokes 1777 hemorrhagic strokes 2590 ischemic strokes 1153 stroke deaths	Incidence	Validated FFQ, 44/52 food items	Rice, stroke incidence Rice, hemorrhagic stroke incidence Rice, ischemic stroke incidence Rice, stroke mortality	251 g/d 326 377 430 542 251 g/d 326 377 430 542 251 g/d 326 377 430 542 251 g/d 326 377 430 542	1.00 1.07 (0.93-1.17) 0.94 (0.85-1.08) 0.93 (0.84-1.13) 1.01 (0.90-1.14) 1.00 1.05 (0.90-1.22) 0.95 (0.81-1.12) 0.95 (0.81-1.11) 0.96 (0.79-1.15) 1.00 1.07 (0.92-1.23) 0.99 (0.81-1.07)? 0.99 (0.81-1.16) 1.05 (0.90-1.22) 1.00 1.07 (0.88-1.30) 1.07 (0.88-1.32) 1.00 (0.82-1.23) 1.03 (0.82-1.30)	Age, sex, public health center area, hypertension, diabetes, use of lipid-lowering drugs, BMI, smoking status, ethanol intake, leisure-time sports activity, occupation, seafood, meat, fruit, vegetables, soy, SFA, sodium, total energy, menopausal status, HRT

Muraki I et al, 2014, USA	Nurses' Health Study Nurses' Health Study 2 Health Professionals Follow-up Study	1984-2010, 26 years follow-up 1991-2011, 20 years follow-up 1986-2010, 24 years follow-up	73228 women, age 38-63 years: 2703 stroke cases 92158 women, age 27-44 years: 494 stroke cases 42170 men, age 40-75 years: 1475 stroke cases	Incidence	Validated FFQ, 118-166 food items	White rice Brown rice Total rice	<1 serv/wk 1 2-4 ≥5 Per 3 serv/wk <1 serv/wk 1 2-4 ≥5 Per 3 serv/wk <1 serv/wk 1 2-4 ≥5 Per 3 serv/wk	1.00 0.97 (0.90-1.03) 0.97 (0.89-1.05) 1.25 (0.99-1.57) 1.02 (0.94-1.11) 1.00 1.03 (0.94-1.14) 1.05 (0.92-1.19) 1.39 (0.99-1.96) 1.11 (0.98-1.26) 1.00 0.94 (0.87-1.01) 0.98 (0.91-1.06) 1.04 (0.89-1.21) 1.02 (0.95-1.10)	Age, ethnicity, BMI, smoking status, alcohol, physical activity, family history of MI, menopausal status, OC use (NHS2), HRT, multivitamin use, current aspirin use, prevalent hypertension, prevalent hypercholesterolemia, prevalent diabetes, total energy intake, alternate Healthy Eating Index score
Tognon G et al, 2014, Denmark	The 1982-83 Danish Monitoring trends and determinants of Cardiovascular disease study (MONICA)	1982-1983 – 2007, 14 years follow-up	948 women and 901 men, age NA: 167 stroke cases 40 stroke deaths	Incidence and mortality	7 day food record	Cereals, incidence Cereals, mortality	>median vs. <median >median vs. <median	0.82 (0.60-1.11) 1.00 (0.53-1.89)	Age, sex, BMI, education, physical activity, cigarette smoking
Johnsen NF et al, 2015, Norway, Sweden, Denmark	HELGA Cohort (Norwegian Women and Cancer Study, Northern Sweden Health and Disease Study, Danish Diet, Cancer and Health Study – part of the EPIC study)	1992-1998 – 2008-2009, 11.1 (Norway), 14.2 (Sweden), 11.9 years (Denmark) follow-up	120010 men and women, age 30-64 years: 137/143 stroke deaths	Mortality	Validated FFQ, 88 food items (Norway), 98 food items (Sweden) 173 food items (Denmark)	Whole grain breakfast cereals, women Non-white bread Crisp bread Total whole grain products	0 g/d 0.8 12 50 25 g/d 80 113 180 0.6 g/d 2 6 31 56 g/d 100 131 201	1.00 0.70 (0.33-1.47) 0.73 (0.43-1.23) 0.66 (0.43-1.02) 1.00 0.86 (0.48-1.54) 1.02 (0.55-1.87) 0.75 (0.41-1.37) 1.00 1.03 (0.62-1.74) 0.91 (0.54-1.56) 1.22 (0.68-2.18) 1.00 0.78 (0.50-1.22) 0.57 (0.35-0.94) 0.85 (0.53-1.37)	Age, follow-up time, education, smoking status/years since quit/ cigarettes per day, alcohol, BMI, total energy

						Oat	0 g/d	1.00	
							0.4	1.03 (0.64-1.67)	
							4	0.66 (0.38-1.16)	
							19	0.63 (0.34-1.15)	
						Rye	8 g/d	1.00	
							18	0.71 (0.41-1.22)	
							22	0.81 (0.47-1.37)	
							41	0.91 (0.53-1.57)	
						Wheat	0.4 g/d	1.00	
							3	0.72 (0.44-1.18)	
							10	0.83 (0.50-1.38)	
							37	0.55 (0.23-1.30)	
						Total whole grain types	20 g/d	1.00	
							33	0.55 (0.34-0.88)	
							49	0.50 (0.31-0.82)	
							74	0.80 (0.48-1.33)	
						Whole grain breakfast cereals, men	0 g/d	1.00	
							0.8	0.92 (0.59-1.45)	
							7	0.86 (0.56-1.32)	
							50	0.87 (0.47-1.28)	
						Non-white bread	13 g/d	1.00	
							66	0.74 (0.44-1.22)	
							118	0.56 (0.35-0.91)	
							201	0.86 (0.50-1.46)	
						Crisp bread	1 g/d	1.00	
							2	1.10 (0.67-1.79)	
							4	0.97 (0.60-1.57)	
							34	1.30 (0.71-2.39)	
						Total whole grain products	64 g/d	1.00	
							107	1.01 (0.66-1.56)	
							156	0.55 (0.35-0.87)	
							222	0.86 (0.54-1.37)	
						Oat	0 g/d	1.00	
							0.4	0.67 (0.42-1.07)	
							3	1.03 (0.60-1.76)	
							30	0.71 (0.41-1.21)	
						Rye	7 g/d	1.00	
							21	0.77 (0.48-1.23)	
							38	0.72 (0.39-1.31)	

						Wheat Total whole grain types	56 0.1 g/d 1 5 10 21 g/d 37 54 80	0.61 (0.36-1.05) 1.00 0.59 (0.35-0.99) 0.72 (0.41-1.27) 0.74 (0.41-1.32) 1.00 0.70 (0.44-1.10) 0.69 (0.43-1.11) 0.71 (0.44-1.15)	
Wang JB et al, 2016, China	Linxian Nutrition Intervention Trial cohort	1984-1991 - 2010, 19-26 years follow-up	2445 men and women, age 40-69 years: 452 stroke deaths	Mortality	FFQ, 64 food items	All grains Non-whole grains Whole grains	Per 1 time/day Per 1 time/day Per 1 time/day	0.90 (0.83-0.97) 0.90 (0.82-0.98) 0.93 (0.83-1.04)	Age, sex, commune, smoking, drinking, season, BMI

BMI; body mass index, DBP; diastolic blood pressure, FFQ; food frequency questionnaire, HDL-cholesterol; high-density lipoprotein cholesterol, HRT; hormone replacement therapy, MI; myocardial infarction, SBP; systolic blood pressure, SFA; saturated fatty acids, trans-FA: trans fatty acids

Table S5. Whole grains and refined grains and cardiovascular disease

Author, publication year, country	Study name	Study period	Number of participants, gender, age, number of cases/deaths	CVD incidence or mortality	Dietary assessment	Exposure and subgroup	Whole grain consumption frequency or amount	Relative risks (95% confidence intervals)	Adjustment for confounding factors
Jacobs DR et al, 2001, Norway	Norwegian County Study	1977-1983 – 1994, 14.4 years follow-up	33848 men and women, age 35-56 years: 758 CVD deaths	Mortality	FFQ, 66 food items	Whole grain bread score	0.05-0.60 0.83-0.83 0.90-1.13 1.35-1.80 2.25-5.40	1.00 0.93 (0.73-1.18) 0.84 (0.68-1.05) 0.84 (0.66-1.05) 0.77 (0.60-0.98)	Age, energy intake, sex, smoking status, physical activity during leisure, physical activity during work, cod liver oil, multivitamin use, SFA, SBP, serum total cholesterol, BMI
Appleby PN et al, 2002, UK	The Health Food Shoppers Study	1973-1979 – 1997, 19.8 years follow-up	10741 men and women, age 16-89 years: 1202 circulatory disease deaths	Mortality	FFQ	Wholemeal bread Bran cereals	Daily vs less Daily vs less	0.86 (0.76-0.98) 1.04 (0.92-1.18)	Age at recruitment, sex, smoking, fresh fruit, nuts/dried fruit, raw vegetables salads, mutual adjustment between wholemeal bread and bran cereals
Liu S et al, 2003, USA	Physicians' Health Study	1982-1988, 5.5 years follow-up	86190 men, mean age 40-84 years: 1381 CVD deaths	Mortality	Validated FFQ	Whole grain breakfast cereals Refined-grain breakfast cereals Total breakfast cereals	Rarely 1 serv/wk 2-6/wk ≥1/day Rarely 1 serv/wk 2-6/wk ≥1/day Rarely 1 serv/wk 2-6/wk ≥1/day	1.00 0.93 (0.75-1.17) 0.82 (0.68-0.98) 0.80 (0.66-0.97) 1.00 1.18 (0.99-1.40) 1.08 (0.89-1.31) 1.04 (0.84-1.27) 1.00 1.04 (0.89-1.22) 0.93 (0.79-1.10) 0.87 (0.74-1.03)	Age, cigarette smoking, alcohol intake, physical activity, BMI, type 2 diabetes, high cholesterol, hypertension, use of multivitamins
Sahyoun NR et al, 2006, USA	NA	1981-1984 – 1995, 12-15 years follow-up	535 men and women, age ≥60 years: 89 CVD deaths	Mortality	3-day food record	Whole grain	0.31 serv/d 0.86 1.49 2.90	1.00 0.77 (0.41-1.43) 0.76 (0.41-1.41) 0.48 (0.25-0.96)	Age, sex, race, education, marital status, smoking, alcohol intake, exercise, BMI, energy intake, SFA, antihypertensive or lipid-lowering therapy
Mink PJ et al, 2007, USA	Iowa Women's Health Study	1986-2002, 16 years follow-up	34489 women, age 55-69 years: 2316 CVD	Mortality	Validated FFQ, 127 food items	Bran, added to food	0 serv/wk ・0	1.00 0.86 (0.76-0.97)	Age, energy intake, marital status, education, blood pressure, diabetes, BMI, waist-

			deaths						to-hip ratio, physical activity, smoking, HRT
Jacobs DR, 2007, USA	Iowa Women's Health Study	1986-2003, 17 years follow-up	27312 women, age 55-69 years: 1900 CVD deaths	Mortality	Validated FFQ, 127 food items	Whole grains Refined grains	1.8 serv/wk 5.6 8.8 14.5 25.6 0-5.75 serv/wk 6-9.5 9.6-13.5 14-22 ≥22.5	1.00 0.96 (0.84-1.10) 0.83 (0.72-0.96) 0.83 (0.71-0.96) 0.73 (0.62-0.86) 1.00 0.94 (0.82-1.08) 0.89 (0.76-1.03) 0.75 (0.64-0.88) 0.94 (0.78-1.12)	Age, energy intake, BMI, waist-to-hip ratio, smoking, education, physical activity, HRT, multivitamin supplement use, intake of alcohol, coffee, red meat, fish and seafood, total fruit and vegetables, mutual adjustment between whole grains and refined grains
Gardener H et al, 2011, USA	The Northern Manhattan Study	NA – NA, 9 years follow-up	2568 men and women, age >40 years: 314 vascular deaths	Mortality	FFQ	Cereals	≥61 vs. <61 g/d	0.98 (0.79-1.23)	Age, sex, race-ethnicity, education, moderate to heavy physical activity, energy, cigarette smoking
Eshak ES et al, 2011, Japan	Japan Collaborative Cohort Study	1988-1990 – 2003, 14.1 years follow-up	83752 men and women, age 40-79 years: 3514 CVD deaths	Mortality	Validated FFQ, 40 food items	Rice, men Rice, women	280 g/d 420 449 583 711 279 g/d 359 420 453 560	1.00 0.90 (0.79-1.03) 0.87 (0.74-1.02) 0.79 (0.67-0.93) 0.82 (0.70-0.97) 1.00 0.94 (0.78-1.14) 0.90 (0.77-1.05) 1.20 (0.94-1.51) 1.07 (0.88-1.34)	Age, history of hypertension, history of diabetes, BMI, alcohol, smoking status, exercise, walking, education, perceived mental stress, sleep duration, fish, meat, fruit, dairy products, soy, total energy
Fitzgerald KC et al, 2012, USA	Women's Health Study	1992-1994 – 2004, 14.6 years follow-up	34827 women, age ≥45 years: 1094 CVD cases	Incidence	Validated FFQ, 133 food items	Whole grains	<0.50 serv/d 0.50-0.93 0.94-1.36 1.40-2.20 ≥2.21	1.00 1.01 (0.84-1.21) 1.03 (0.86-1.24) 0.86 (0.71-1.05) 0.96 (0.79-1.17)	Age, randomization status, smoking, postmenopausal status, HRT, alcohol intake, energy, physical activity, cigarettes per day, highest education level
Von Ruesten A et al, 2013, Germany	European Prospective Investigation into Cancer and Nutrition–Potsdam study	1994/1998–NA, 8 years follow-up	23531 men and women, age 35–65 years: 363 CVD cases	Incidence	Validated FFQ, 148 food items	Whole grain bread Other bread Grain flakes, muesli Cornflakes, crisps Pasta, rice	Per 50 g/d Per 50 g/d Per 50 g/d Per 50 g/d Per 100 g/d	0.96 (0.81-1.14) 0.99 (0.85-1.16) 0.54 (0.28-1.01) 1.89 (0.79-4.51) 1.01 (0.44-2.34)	Age, sex, smoking status, pack-years of smoking, alcohol, leisure-time physical activity, BMI, waist-to-hip ratio, prevalent hypertension, high blood lipid levels, education, vitamin supplementation, total

									energy, non-consumption of the food group, other food groups
Eshak E et al, 2014, Japan	Japan Public Health Center-based Prospective Study	1990/1993 – 2007/2009, 15.2 years follow-up	91223 men and women, age 40-69 years: 2705 CVD deaths	Mortality	Validated FFQ, 44/52 food items	Rice	251 g/d 326 377 430 542	1.00 0.96 (0.85-1.09) 1.00 (0.88-1.15) 0.81 (0.80-1.11) 0.97 (0.84-1.13)	Age, sex, public health center area, hypertension, diabetes, use of lipid-lowering drugs, BMI, smoking status, ethanol intake, leisure-time sports activity, occupation, seafood, meat, fruit, vegetables, soy, SFAs, sodium, total energy, and for women: menopausal status, HRT
Buil-Cosiales P et al, 2014, Spain	Prevencion con DietaMediterranea (PREDIMED) study	2003-2009 – 2012, 5.9 years follow-up	7216 men and women, age 55-75 years: 103 CVD deaths	Mortality	Validated FFQ, 137 food items	Whole grains	0 g/d 1 7 33 89	1.00 0.79 (0.39-1.59) 0.76 (0.33-1.76) 0.81 (0.35-1.90) 0.73 (0.34-1.58)	Age, sex, smoking status, diabetes, BMI, SBP, DBP, recruitment center, statins, alcohol, education, physical activity, total energy, vegetables, fruits
Atkins JL et al, 2014, United Kingdom	British Regional Heart Study	1998-2000 – 2010, 11.3 years follow-up	3328 men, age 60-79 years: 582 CVD cases 327 CVD deaths	Incidence and mortality	Validated FFQ, 86 food items	Cereals, incidence Bread Cereals, mortality Bread	Daily vs. <1 day/wk Whole grain vs. none Daily vs. <1 day/wk Whole grain vs. none	1.13 (0.79-1.62) 0.60 (0.22-1.65) 1.37 (0.83-2.25) 0.57 (0.14-2.40)	Age, smoking, alcohol, physical activity, social class, BMI, energy intake, diet score without respective components
Muraki I et al, 2014, USA	Nurses' Health Study Nurses' Health Study 2 Health Professionals Follow-up Study	1984-2010, 26 years follow-up 1991-2011, 20 years follow-up 1986-2010, 24 years follow-up	73228 women, age 38-63 years: 5763 CVD cases 92158 women, age 27-44 years: 1028 CVD cases 42170 men, age 40-75 years: 5600 CVD cases	Incidence	Validated FFQ, 118-166 food items	White rice Brown rice Total rice	<1 serv/wk 1 2-4 ≥5 Per 3 serv/wk <1 serv/wk 1 2-4 ≥5 Per 3 serv/wk <1 serv/wk 1 2-4 ≥5 Per 3 serv/wk	1.00 1.01 (0.97-1.05) 1.02 (0.97-1.07) 0.98 (0.84-1.14) 1.01 (0.96-1.06) 1.00 1.01 (0.95-1.07) 1.05 (0.97-1.13) 1.01 (0.79-1.28) 1.04 (0.96-1.13) 1.00 1.00 (0.95-1.04) 1.01 (0.96-1.06) 0.99 (0.90-1.08) 1.00 (0.96-1.05)	Age, ethnicity, BMI, smoking status, alcohol, physical activity, family history of MI, menopausal status, oral contraceptive use (NHS2), HRT, multivitamin use, current aspirin use, prevalent hypertension, prevalent hypercholesterolemia, prevalent diabetes, total energy intake, alternate Healthy Eating Index score

Tognon G et al, 2014, Denmark	The 1982-83 Danish Monitoring trends and determinants of Cardiovascular disease study (MONICA)	1982-1983 – 2007, 14 years follow-up	948 women and 901 men, age NA: 755 CVD cases 223 CVD deaths	Incidence and mortality	Validated 7 day food record	Cereals, incidence Cereals, mortality	>median vs. <median >median vs. <median	0.90 (0.78-1.04) 0.76 (0.58-1.00)	Age, sex, BMI, education, physical activity, cigarette smoking
Wu H et al, 2015, USA	Nurses' Health Study	1984-2010, 26 years follow-up	74341 women, age 38-63 years: 2989 CVD deaths	Mortality	Validated FFQ, 126 food items	Whole grains Total bran Total germ 	4.2 g/d 9.7 14.7 21.1 33.0 0.7 g/d 2.0 3.5 5.7 10.4 0.2 g/d 0.4 0.6 0.9 1.6	1.00 0.97 (0.87-1.08) 0.96 (0.86-1.08) 0.82 (0.73-0.92) 0.86 (0.76-0.96) 1.00 0.89 (0.79-0.99) 0.94 (0.83-1.07) 0.80 (0.70-0.92) 0.80 (0.70-0.91) 1.00 1.07 (0.95-1.20) 1.01 (0.89-1.15) 1.04 (0.91-1.19) 1.11 (0.97-1.27)	Age, ethnicity, BMI, smoking status, cigarettes per day, pack-years smoked, years since quitting smoking, alcohol, physical activity, family history of diabetes, cancer and heart disease, multivitamin use, aspirin use, hypertension, high cholesterol, diabetes, total energy, healthy eating index (excluding whole grains), postmenopausal status, HRT
Wu H et al, 2015, USA	Health Professionals Follow-up Study	1986-2010, 24 years follow-up	43744 men, age 32-87 years: 3621 CVD deaths	Mortality	Validated FFQ, 131 food items	Whole grains Total bran Total germ 	5.9 g/d 14.4 22.1 31.3 47.8 0.7 g/d 2.6 5.0 8.2 15.0 0.2 g/d 0.6 0.9 1.3 2.3	1.00 0.92 (0.84-1.02) 0.92 (0.83-1.02) 0.91 (0.82-1.01) 0.84 (0.75-0.93) 1.00 0.93 (0.84-1.04) 0.93 (0.83-1.05) 0.86 (0.77-0.97) 0.80 (0.71-0.90) 1.00 1.03 (0.93-1.14) 0.94 (0.84-1.05) 1.03 (0.92-1.16) 1.03 (0.92-1.16)	Age, ethnicity, BMI, smoking status, cigarettes per day, pack-years smoked, years since quitting smoking, alcohol, physical activity, family history of diabetes, cancer and heart disease, multivitamin use, aspirin use, hypertension, high cholesterol, diabetes, total energy, healthy eating index (excluding whole grains)

Wu H et al, 2015, USA	Nurses' Health Study & Health Professionals Follow-up Study	1984-2010, 26 years follow-up 1986-2010, 24 years follow-up	74341 women, age 38-63 years: 2989 CVD deaths 43744 men, age 32-87 years: 3621 CVD deaths	Mortality	Validated FFQ, 126/131 food items	Naturally occurring bran Added bran Refined grains	0-0.4/0-0.4 g/d 0.5-1.4/0.5-1.9 1.5-2.99/2.0-3.9 ≥3.0/≥4.0 0-0.4/0-0.4 g/d 0.5-1.4/0.5-1.9 1.5-2.9/2.0-3.9 3.0-5.9/4.0-9.9 ≥6.0/≥10.0 Per 28 g/d	1.00 0.98 (0.90-1.07) 0.92 (0.84-1.01) 0.89 (0.81-0.98) 1.00 0.85 (0.78-0.91) 0.83 (0.77-0.90) 0.82 (0.76-0.88) 0.76 (0.70-0.83) 0.99 (0.97-1.01)	Age, ethnicity, BMI, smoking status, cigarettes per day, pack-years smoked, years since quitting smoking, alcohol, physical activity, family history of diabetes, cancer and heart disease, multivitamin use, aspirin use, hypertension, high cholesterol, diabetes, total energy, healthy eating index (excluding whole grains), women: postmenopausal status, HRT
Huang T et al, 2015, USA	NIH-AARP Diet and Health Study	1995-1996 – 2008, 14 years follow-up	367442 men and women, age 50-71 years: 11283 CVD deaths	Mortality	Validated FFQ, 124 food items	Whole grains	0.13 oz/1000 kcal/d[1] 0.30 0.47 0.69 1.20	1.00 0.93 (0.88-0.98) 0.88 (0.83-0.93) 0.81 (0.77-0.86) 0.83 (0.78-0.88)	Age, sex, number of cigarettes per day, time of smoking cessation, race/ ethnicity, alcohol, education, marital status, health status, BMI, physical activity, red meat, total fruit and vegetables, total energy, HRT (women)
Sonestedt E et al, 2015, Sweden	Malmö Diet and Cancer Study	1991-1996 – 2009, 14 years follow-up	26445 men and women, age 44-74 years: 2921 ischemic CVD events	Incidence	Validated FFQ, 168 food items, diet history interview	Whole grains Refined grains	0.0 portions/d 0.3 0.7 1.2 2.5 1.2 portions/d 2.0 2.5 3.1 4.3	1.00 0.89 (0.80-1.00) 0.92 (0.82-1.02) 0.80 (0.72-0.90) 0.87 (0.77-0.97) 1.00 1.03 (0.92-1.16) 1.05 (0.94-1.18) 1.05 (0.94-1.18) 1.06 (0.95-1.20)	Age, sex, season, diet method version, energy intake, BMI, smoking, alcohol, leisure-time physical activity, education
Xu M et al, 2015, USA	NIH-AARP Diet and Health Study	1995-1996 – 2008, 14 years follow-up	367442 men and women, age 50-71 years: 11283 CVD deaths	Mortality	Validated FFQ, 124 food items	Ready-to-eat cereals	0.00 g/d 0.67 3.48 9.33 22.48	1.00 0.90 (0.85-0.95) 0.90 (0.85-0.95) 0.86 (0.81-0.91) 0.76 (0.71-0.81)	Age, sex, smoking status, smoking dose, time since quitting smoking, race/ethnicity, education, marital status, self-rated health status, BMI, physical activity, menopausal hormone therapy, alcohol, red meat, fruits, vegetables, total

									energy
Wang JB et al, 2016, China[2]	Linxian Nutrition Intervention Trial cohort	1984-1991 - 2010, 19-26 years follow-up	2445 men and women, age 40-69 years: 807 CVD deaths	Mortality	FFQ, 64 food items	All grains Non-whole grains Whole grains	Per 1 time/day Per 1 time/day Per 1 time/day	0.94 (0.89-1.00) 0.96 (0.90-1.03) 0.93 (0.86-1.02)	Age, sex, commune, smoking, drinking, season, BMI

BMI; body mass index, CVD; cardiovascular disease, DBP; diastolic blood pressure, FFQ; food frequency questionnaire, HRT; hormone replacement therapy, SBP; systolic blood pressure, SFA; saturated fatty acids

[1] The original paper reports in ounces/d, after contact with the authors it was confirmed that ounces/1000 kcal/d is correct.

[2] Data for heart disease and stroke deaths were pooled using a fixed effects model.

Table S6. Whole grains and refined grains and total cancer

Author, publication year, country	Study name	Study period	Number of participants, gender, age, number of cases/deaths	Total cancer incidence or mortality	Dietary assessment	Exposure and subgroup	Whole grain consumption frequency or amount	Relative risks (95% confidence intervals)	Adjustment for confounding factors
Jacobs DR et al, 2001, Norway	Norwegian County Study	1977-1983 – 1994, 14.4 years follow-up	33848 men and women, age 35-56 years: 870 cancer deaths	Mortality	FFQ, 66 food items	Whole grain bread score	0.05-0.60 0.83-0.83 0.90-1.13 1.35-1.80 2.25-5.40	1.00 0.96 (0.76-1.20) 0.89 (0.73-1.08) 0.90 (0.73-1.11) 0.79 (0.62-1.02)	Age, energy, sex, smoking status, leisure-time physical activity, occupational physical activity, cod liver oil use, multivitamins, SFA, SBP, serum total cholesterol, BMI
Appleby PN et al, 2002, UK	The Health Food Shoppers Study	1973-1979 – 1997, 19.8 years follow-up	11000 men and women, age 16-89 years: 680 cancer deaths	Mortality	FFQ	Wholemeal bread Bran cereals	Daily vs less Daily vs less	1.01 (0.85-1.20) 0.93 (0.78-1.11)	Age at recruitment, sex, smoking, fresh fruit, nuts/dried fruit, raw vegetables salads, mutual adjustment wholemeal bread bran cereals
Khan MMH et al, 2004, Japan	The Hokkaido Study	1984-1985 – 2002, 14.3 years follow-up	1524 men and 1634 women, age ≥40 years: 155/89 cancer deaths	Mortality	FFQ, 37 food items	Bread, men Instant noodles Noodles Bread, women Instant noodles Noodles	・2/wk vs ・1mo ・2/wk vs ・1mo ・2/wk vs ・1mo ・2/wk vs ・1mo ・2/wk vs ・1mo ・2/wk vs ・1mo	0.8 (0.5-1.2) 0.9 (0.6-1.5) 1.0 (0.7-1.3) 0.9 (0.5-1.5) 0.6 (0.2-1.4) 1.2 (0.8-1.8)	Age, smoking Age, health status, health education, health screening, smoking
Jacobs DR, 2007, USA	Iowa Women's Health Study	1986-2003, 17 years follow-up	27312 women, age 55-69 years: 2099 cancer deaths	Mortality	Validated FFQ, 127 food items	Whole grains Refined grains	1.8 serv/wk 5.6 8.8 14.5 25.6 0-5.75 serv/wk 6-9.5 9.6-13.5 14-22 ≥22.5	1.00 0.86 (0.75-0.99) 0.95 (0.83-1.09) 0.83 (0.72-0.96) 0.89 (0.77-1.04) 1.00 1.00 (0.88-1.15) 0.96 (0.83-1.11) 0.98 (0.85-1.14) 0.98 (0.82-1.16)	Age, energy intake, BMI, waist-to-hip ratio, smoking, education, physical activity, HRT, multivitamin supplement use, intake of alcohol, coffee, red meat, fish and seafood, total fruit and vegetables, mutual adjustment between whole grains and refined grains

Iso H et al, 2007, Japan	Japan Collaborative Cohort Study	1988-1990-2003, ~12.8 years follow-up	42513 men and 57777 women, age 40-79 years: 3579/ 2138 cancer deaths	Mortality	FFQ	Rice, men Rice, women	<3/d 3-4 ≥5 <3/d 3-4 ≥5	1.00 0.99 (0.91-1.07) 0.87 (0.80-0.96) 1.00 0.95 (0.86-1.05) 1.04 (0.91-1.18)	Age, area of study
Couto E et al, 2011, Europe	European Prospective Investigation into Cancer and Nutrition	1992-2000 – 2002-2005, 8.7 years follow-up	142605 men and 335873 women, age 25-70 years: 9669/21062 cancer cases	Incidence	Validated FFQs, 7-day or 14-day record diaries, diet history	Cereals	Per 110 g/d	0.97 (0.95-0.98)	Age, sex, centre, duration of smoking, smoking status, education, height, BMI, total energy intake, physical activity, women: age at menarche, parity, menopausal status, oral contraceptive use, HRT
Von Ruesten A et al, 2013, Germany	European Prospective Investigation into Cancer and Nutrition–Potsdam study	1994/1998–NA, 8 years follow-up	23,531 m & w, age 35–65 years: 844 cancer cases	Incidence	Validated FFQ, 148 food items	Whole grain bread Other bread Grain flakes, muesli Cornflakes, crisps Pasta, rice	Per 50 g/d Per 50 g/d Per 50 g/d Per 50 g/d Per 100 g/d	0.94 (0.84-1.05) 0.98 (0.88-1.09) 0.98 (0.73-1.30) 1.10 (0.57-2.11) 0.84 (0.48-1.48)	Age, sex, smoking status, pack-years of smoking, alcohol, leisure-time physical activity, BMI, waist-to-hip ratio, prevalent hypertension, high blood lipid levels, education, vitamin supplementation, total energy, non-consumption of the food group, other food groups

Sharma S et al, 2013, USA	Multiethnic Cohort Study	1993-1996 – 2001, NA	146389 men and women, age 45-75 years: 2028/1464 cancer deaths	Mortality	Validated FFQ, 180 food items	Grains, men, all	≤5.6 serv/(d	NA (significant heterogeneity by ethnicity)	Age, time on study, years of education, energy intake, smoking status, pack-years, BMI, physical activity, diabetes, alcohol, women: HRT, oophorectomy
							5.7-7.8		
							7.9-10.8		
							>10.8		
						Grains, African American	≤5.6 serv/(d	1.00	
							5.7-7.8	0.88 (0.66-1.17)	
							7.9-10.8	1.18 (0.85-1.65)	
							>10.8	1.24 (0.83-1.85)	
						Grains, Native Hawaiian	≤5.6 serv/(d	1.00	
							5.7-7.8	1.37 (0.76-2.47)	
							7.9-10.8	0.78 (0.40-1.53)	
							>10.8	1.27 (0.62-2.58)	
						Grains, Japanese American	≤5.6 serv/(d	1.00	
							5.7-7.8	0.84 (0.64-1.10)	
							7.9-10.8	0.63 (0.47-0.84)	
							>10.8	0.49 (0.35-0.69)	
						Grains, Latinos	≤5.6 serv/(d	1.00	
							5.7-7.8	1.10 (0.82-1.45)	
							7.9-10.8	0.92 (0.66-1.30)	
							>10.8	0.95 (0.63-1.42)	
						Grains, Caucasian	≤5.6 serv/(d	1.00	
							5.7-7.8	0.86 (0.68-1.10)	
							7.9-10.8	0.82 (0.61-1.10)	
							>10.8	1.17 (0.81-1.68)	
						Grains, women, all	≤4.5 serv/(d	1.00	
							4.6-6.4	0.87 (0.75-1.02)	
							6.5-8.9	0.89 (0.74-1.06)	
							>8.9	0.97 (0.78-1.22)	
						Grains, African American	≤4.5 serv/(d	1.00	
							4.6-6.4	0.98 (0.75-1.28)	
							6.5-8.9	0.82 (0.59-1.13)	
							>8.9	0.91 (0.62-1.34)	
						Grains, Native Hawaiian	≤4.5 serv/(d	1.00	
							4.6-6.4	0.92 (0.47-1.82)	
							6.5-8.9	1.07 (0.51-2.23)	
							>8.9	1.31 (0.54-3.15)	

						Grains, Japanes5 American Grains, Latinos Grains, Caucasian	≤4.5 serv/(d 4.6-6.4 6.5-8.9 >8.9 ≤4.5 serv/(d 4.6-6.4 6.5-8.9 >8.9 ≤4.5 serv/(d 4.6-6.4 6.5-8.9 >8.9	1.00 0.62 (0.41-0.92) 0.86 (0.56-1.32) 1.03 (0.60-1.77) 1.00 1.02 (0.68-1.52) 1.17 (0.74-1.84) 1.33 (0.77-2.28) 1.00 0.84 (0.63-1.12) 0.79 (0.56-1.12) 0.92 (0.59-1.43)	
Buil-Cosiales P et al, 2014, Spain	Prevencion con DietaMediterranea (PREDIMED) study	2003-2009 – 2012, 5.9 years follow-up	7216 men and women, age 55-75 years: 169 cancer deaths	Mortality	Validated FFQ, 137 food items	Whole grains	0 g/d 1 7 33 89	1.00 0.94 (0.55-1.62) 0.91 (0.48-1.73) 0.83 (0.40-1.69) 0.75 (0.40-1.41)	Age, sex, smoking status, diabetes, BMI, SBP, DBP, recruitment center, statins, alcohol, education, physical activity, total energy, vegetables, fruits
Wu H et al, 2015, USA	Nurses' Health Study	1984-2010, 26 years follow-up	74341 women, age 38-63 years: 5964 cancer deaths	Mortality	Validated FFQ, 126 food items	Whole grains	4.2 g/d 9.7 14.7 21.1 33.0	1.00 1.02 (0.94-1.10) 1.10 (1.02-1.19) 1.06 (0.98-1.15) 0.99 (0.91-1.07)	Age, ethnicity, BMI, smoking status, cigarettes per day, pack-years smoked, years since quitting smoking, alcohol, physical activity, family history of diabetes, cancer and heart disease, multivitamin use, aspirin use, hypertension, high cholesterol, diabetes, total energy, healthy eating index (excluding whole grains): women: postmenopausal status, HRT

Wu H et al, 2015, USA	Health Professionals Follow-up Study	1986-2010, 24 years follow-up	43744 men, age 32-87 years: 3921 cancer deaths	Mortality	Validated FFQ, 131 food items	Whole grains	5.9 g/d 14.4 22.1 31.3 47.8	1.00 1.01 (0.92-1.11) 0.98 (0.88-1.08) 1.01 (0.91-1.12) 0.95 (0.86-1.05)	Age, ethnicity, BMI, smoking status, cigarettes per day, pack-years smoked, years since quitting smoking, alcohol, physical activity, family history of diabetes, cancer and heart disease, multivitamin use, aspirin use, hypertension, high cholesterol, diabetes, total energy, healthy eating index (excluding whole grains)
Wu H et al, 2015, USA	Nurses' Health Study & Health Professionals Follow-up Study	1984-2010, 26 years follow-up 1986-2010, 24 years follow-up	74341 women, age 38-63 years: 5964 cancer deaths 43744 men, age 32-87 years: 3921 cancer deaths	Mortality	Validated FFQ, 126/131 food items	Total bran Total germ Naturally occurring bran Added bran Refined grains	1 2 3 4 5 1 2 3 4 5 0-0.4/0-0.4 g/d 0.5-1.4/0.5-1.9 1.5-2.99/2.0-3.9 ≥3.0/≥4.0 0-0.4/0-0.4 g/d 0.5-1.4/0.5-1.9 1.5-2.9/2.0-3.9 3.0-5.9/4.0-9.9 ≥6.0/≥10.0 Per 28 g/d	1.00 1.06 (0.99-1.13) 1.07 (1.00-1.15) 1.11 (1.03-1.20) 1.04 (0.97-1.13) 1.00 1.04 (0.98-1.11) 1.01 (0.95-1.08) 0.96 (0.89-1.03) 0.98 (0.91-1.06) 1.00 1.02 (0.94-1.10) 1.06 (0.98-1.14) 1.02 (0.94-1.10) 1.00 1.09 (1.03-1.16) 1.09 (1.03-1.17) 1.12 (1.06-1.20) 1.04 (0.97-1.12) 0.98 (0.97-1.00)	Age, ethnicity, BMI, smoking status, cigarettes per day, pack-years smoked, years since quitting smoking, alcohol, physical activity, family history of diabetes, cancer and heart disease, multivitamin use, aspirin use, hypertension, high cholesterol, diabetes, total energy, healthy eating index (excluding whole grains), women: postmenopausal status, HRT
Huang T et al, 2015, USA	NIH-AARP Diet and Health Study	1995-1996 – 2009, 14 years follow-up	367442 men and women, age 50-71 years: 19043 cancer deaths	Mortality	Validated FFQ, 124 food items	Whole grains	0.13 oz/1000 kcal/d[1] 0.30 0.47 0.69 1.20	1.00 0.94 (0.90-0.98) 0.91 (0.87-0.95) 0.88 (0.84-0.92) 0.85 (0.81-0.89)	Age, sex, number of cigarettes per day, time of smoking cessation, race/ ethnicity, alcohol, education, marital status, health status, BMI, physical activity, red meat, total fruit and vegetables, total energy, HRT (women)

Xu M et al, 2015, USA	NIH-AARP Diet and Health Study	1995-1996 – 2008, 14 years follow-up	367442 men and women, age 50-71 years: 19043 cancer deaths	Mortality	Validated FFQ, 124 food items	Ready-to-eat cereals	0.00 g/d 0.67 3.48 9.33 22.48	1.00 0.98 (0.94-1.03) 0.95 (0.90-0.99) 0.92 (0.88-0.97) 0.90 (0.86-0.95)	Age, sex, smoking status, smoking dose, time since quitting smoking, race/ethnicity, education, marital status, self-rated health status, BMI, physical activity, menopausal hormone therapy, alcohol, red meat, fruits, vegetables, total energy

Johnsen NF et al, 2015, Norway, Sweden, Denmark	HELGA Cohort (Norwegian Women and Cancer Study, Northern Sweden Health and Disease Study, Danish Diet, Cancer and Health Study – part of the EPIC study)	1992-1998 – 2008-2009, 11.1 (Norway), 14.2 (Sweden), 11.9 years (Denmark) follow-up	120010 men and women, age 30-64 years: 1375/1775 cancer deaths	Mortality	Validated FFQ, 88 food items (Norway), 98 food items (Sweden) 173 food items (Denmark)	Whole grain breakfast cereals, women	0 g/d 0.8 12 50	1.00 0.98 (0.83-1.15) 0.84 (0.74-0.95) 0.85 (0.74-0.98)	Age, follow-up time, education, smoking status/years since quit/ cigarettes per day, alcohol, BMI, total energy
						Non-white bread	25 g/d 80 113 180	1.00 1.01 (0.86-1.18) 0.93 (0.79-1.08) 0.89 (0.75-1.05)	
						Crisp bread	0.6 g/d 2 6 31	1.00 0.89 (0.77-1.03) 0.84 (0.75-0.95) 0.87 (0.74-1.02)	
						Total whole grain products	56 g/d 100 131 201	1.00 0.86 (0.76-0.98) 0.85 (0.75-0.97) 0.86 (0.74-0.99)	
						Oat	0 g/d 0.4 4 19	1.00 0.89 (0.78-1.01) 0.77 (0.67-0.90) 0.84 (0.71-0.99)	
						Rye	8 g/d 18 22 41	1.00 0.98 (0.87-1.11) 1.00 (0.86-1.17) 0.99 (0.79-1.25)	
						Wheat	0.4 g/d 3 10 37	1.00 0.76 (0.65-0.88) 0.74 (0.63-0.87) 0.74 (0.61-0.89)	
						Total whole grain types	20 g/d 33 49 74	1.00 0.99 (0.87-1.13) 0.94 (0.82-1.07) 0.88 (0.77-1.02)	

						Whole grain breakfast cereals, men	0 g/d 0.8 7 50	1.00 0.99 (0.81-1.21) 0.73 (0.63-0.85) 0.75 (0.64-0.87)	
						Non-white bread	13 g/d 66 118 201	1.00 0.92 (0.76-1.12) 0.97 (0.79-1.19) 0.79 (0.64-0.97)	
						Crisp bread	1 g/d 2 4 34	1.00 0.99 (0.85-1.15) 0.92 (0.79-1.07) 0.83 (0.67-1.03)	
						Total whole grain products	64 g/d 107 156 222	1.00 0.84 (0.72-0.98) 0.74 (0.64-0.86) 0.70 (0.60-0.81)	
						Oat	0 g/d 0.4 3 30	1.00 0.80 (0.69-0.94) 0.75 (0.64-0.89) 0.75 (0.64-0.89)	
						Rye	7 g/d 21 38 56	1.00 0.97 (0.82-1.14) 0.80 (0.65-0.98) 0.93 (0.78-1.11)	
						Wheat	0.1 g/d 1 5 10	1.00 0.84 (0.72-0.98) 0.69 (0.58-0.82) 0.58 (0.49-0.69)	
						Total whole grain types	21 g/d 37 54 80	1.00 0.85 (0.73-0.99) 0.68 (0.58-0.79) 0.74 (0.63-0.87)	

Zhang R et al, 2016, USA	Nurses' Health Study	1984-2010, 26 years follow-up	70603 women, age 38-63 years: 15673 cancer cases	Incidence	Validated FFQ, 126 food items	Total rice	<1 serv/wk	1.00	Age, ethnicity, BMI, smoking status, cigarettes per day, physical activity, family history of cancer, multivitamin supplement use, total energy intake, alcohol, fruit, vegetables, red meat, fish, nuts, whole grain (except brown rice), sugar-sweetened beverages, HRT
							1	1.01 (0.97-1.05)	
							2-4	1.00 (0.96-1.04)	
							≥5	1.02 (0.93-1.12)	
						White rice	<1 serv/wk	1.00	
							1	1.01 (0.96-1.05)	
							2-4	1.02 (0.97-1.06)	
							≥5	0.96 (0.81-1.14)	
						Brown rice	<1 serv/wk	1.00	
							1	1.02 (0.95-1.10)	
							2-4	1.00 (0.93-1.09)	
							≥5	1.07 (0.84-1.38)	
Zhang R et al, 2016, USA	Nurses' Health Study 2	1991-2009, 18 years follow-up	90264 women, age 27-44 years: 5149 cancer cases	Incidence	Validated FFQ, 133 food items	Total rice	<1 serv/wk	1.00	Age, ethnicity, BMI, smoking status, cigarettes per day, physical activity, family history of cancer, multivitamin supplement use, total energy intake, alcohol, fruit, vegetables, red meat, fish, nuts, whole grain (except brown rice), sugar-sweetened beverages, HRT
							1	0.93 (0.86-1.00)	
							2-4	0.93 (0.86-0.99)	
							≥5	0.83 (0.73-0.94)	
						White rice	<1 serv/wk	1.00	
							1	0.96 (0.89-1.03)	
							2-4	0.96 (0.90-1.03)	
							≥5	0.73 (0.59-0.90)	
						Brown rice	<1 serv/wk	1.00	
							1	1.02 (0.93-1.13)	
							2-4	0.95 (0.85-1.06)	
							≥5	1.28 (0.96-1.70)	
Zhang R et al, 2016, USA	Health Professionals Follow-up Study	1986-2008, 22 years follow-up	45382 men, age 40-75 years: 10833 cancer cases	Incidence	Validated FFQ, 131 food items	Total rice	<1 serv/wk	1.00	Age, ethnicity, BMI, smoking status, cigarettes per day, physical activity, family history of cancer, multivitamin supplement use, total energy intake, alcohol, fruit, vegetables, red meat, fish, nuts, whole grain (except brown rice), sugar-sweetened beverages
							1	0.99 (0.94-1.04)	
							2-4	1.00 (0.95-1.05)	
							≥5	1.00 (0.93-1.10)	
						White rice	<1 serv/wk	1.00	
							1	1.02 (0.97-1.07)	
							2-4	1.03 (0.98-1.08)	
							≥5	0.91 (0.79-1.05)	
						Brown rice	<1 serv/wk	1.00	
							1	1.00 (0.94-1.07)	
							2-4	0.96 (0.91-1.05)	
							≥5	0.95 (0.77-1.17)	

BMI; body mass index, DBP; diastolic blood pressure, FFQ; food frequency questionnaire, HRT; hormone replacement therapy, SBP; systolic blood pressure, SFA; saturated fatty acids

[1] The original paper reports in ounces/d, after contact with the authors it was confirmed that ounces/1000 kcal/d is correct.

Table S7. Whole grains and refined grains and all-cause mortality

Author, publication year, country	Study name	Study period	Number of participants, gender, age, number of deaths	Dietary assessment	Exposure and subgroup	Whole grain consumption frequency or amount	Relative risks (95% confidence intervals)	Adjustment for confounding factors
Kahn HA et al, 1984, USA	Adventist Mortality Study	1960-1980, 21 years follow-up	27530 men and women, age ≥30 years: 5751 deaths	FFQ, 28 food items	Bread, rolls, biscuits Cereal	<1 /wk 1-2 3-4 6-7 <1 /wk 1-2 3-6 7	1.00 0.88 (0.80-0.96) 0.81 (0.69-0.95) 0.82 (0.73-0.92)[1] 1.00 0.80 (0.71-0.90) 0.77 (0.67-0.88) 0.84 (0.75-0.94)[1]	Age, sex, smoking, history of disease, age at initial exposure to the Seventh Day Adventist church
Rotevatn S et al, 1989, Norway	NA	1964-1967 – 1978, 11.5 years follow-up	10187 men, age 35-74 years: 2458 deaths	FFQ	Bread consumption	≥6 vs. <6/d	0.752	Age, physical exercise, cigarette smoking, alcohol
Trichopoulou A, 1995, Greece,	NA	1988-1990 – 1993-1994, ~3-6 years follow-up	182 men and women, >70 years: 53 deaths	Validated FFQ, 198 food items/ beverages	Cereal	20 g/d	1.02 (0.97-1.07)	Age, smoking status, sex
Osler M et al, 1997, Denmark	Euronet SENECA study Denmark	1988-1989 – 1995, NA	202 men and women, mean age 73.4 years: 52 deaths	3-day food record and frequency checklist of foods	Cereals	Per 20 g/d	1.10 (1.03-1.17)	Age, sex, smoking
Fortes C et al, 2000, Italy	NA	1993-1998, 5 years follow-up	162 men and women, age ≥65 years: 53 deaths	FFQ, 114 food items	Pasta	<1/wk 1-4/wk >4/wk	1.00 0.56 (0.26-1.21) 0.61 (0.26-1.45)	Age, sex, education, BMI, smoking, cognitive function, chronic diseases
Jacobs DR et al, 2001, Norway	Norwegian County Study	1977-1983 – 1994, 14.4 years follow-up	33848 men and women, age 35-56 years: 2058 deaths	FFQ, 66 food items	Whole grain bread score	0.05-0.60 0.83-0.83 0.90-1.13 1.35-1.80 2.25-5.40	1.00 0.87 (0.75-1.01) 0.80 (0.71-0.92) 0.85 (0.74-0.98) 0.75 (0.65-0.88)	Age, energy, sex, current smoking, past smoking, leisure-time physical activity, occupational physical activity, cod liver oil use, multivitamins, SFA intake, SBP, serum total cholesterol, BMI

Appleby PN et al, 2002, UK	The Health Food Shoppers Study	1973-1979 – 1997, 19.8 years follow-up	11000 men and women, age 16-89 years: 2529 deaths	FFQ	Wholemeal bread Bran cereals	Daily vs less Daily vs less	0.89 (0.82-0.98) 1.02 (0.94-1.12)	Age at recruitment, sex, smoking, fresh fruit, nuts/dried fruit, raw vegetables salads, mutual adjustment between wholemeal bread and bran cereals
Liu S et al, 2003, USA	Physicians' Health Study	1982-1988, 5.5 years follow-up	86190 men, age 40-84 years: 3114 deaths	Validated FFQ	Whole grain breakfast cereals Refined-grain breakfast cereals Total breakfast cereals	Rarely 1 serv/wk 2-6/wk ≥1/day Rarely 1 serv/wk 2-6/wk ≥1/day Rarely 1 serv/wk 2-6/wk ≥1/day	1.00 0.88 (0.76-1.01) 0.85 (0.74-0.97) 0.83 (0.73-0.94) 1.00 1.15 (1.02-1.29) 1.08 (0.95-1.24) 1.09 (0.95-1.25) 1.00 1.02 (0.92-1.14) 0.94 (0.84-1.05) 0.92 (0.82-1.02)	Age, cigarette smoking, alcohol intake, physical activity, BMI, diabetes mellitus, high cholesterol, hypertension, multivitamin use
Steffen LM et al, 2003, USA	Atherosclerosis Risk in Communities Study	1987-1989 - 1999, 11 years follow-up	11940 men and women, age 45-64 years: 867 deaths	Validated FFQ, 61 food items	Whole grain Refined grain	0.1 serv./day 0.5 1.0 1.5 3.0 0.5 1.0 2.0 3.0 5.0	1.00 0.96 (0.79-1.17) 0.80 (0.65-0.99) 0.87 (0.70-1.08) 0.77 (0.61-0.97) 1.00 0.96 (0.75-1.23) 1.03 (0.81-1.31) 0.97 (0.76-1.23) 1.08 (0.83-1.40)	Age at baseline, race, sex, time-dependent energy intake, education, smoking status, pack-years of smoking, physical activity, alcohol intake, HRT-women, BMI, waist-to-hip ratio, SBP, antihypertensive medication use
Trichopoulou A et al, 2005, Greece	European Prospective Investigation into Cancer and Nutrition – Elderly Study	1992-2000 – 1999-2003, 7.4 years follow-up	74607 men and women, age 60 years: 4047 deaths	Validated FFQs, food records	Cereals	Per 104 g/d	0.94 (0.91-0.98)	Age, sex, country, diabetes, waist-to-hip ratio, BMI, education, smoking status, occupational physical activity, leisure-time physical activity, alcohol, total energy

Hays JC et al, 2005, USA	Established Population for Epidemiologic Studies of the Elderly – Duke University	1992-1993 – 1996, 4 years follow-up	1920 men and women, mean age 76.1 (whites)/ 77.0 (black): 226 deaths	Short interview	Grains, white men Grains, black men Grains, white women Grains, black women	≥2 vs. <2 serv/d ≥2 vs. <2 serv/d ≥2 vs. <2 serv/d ≥2 vs. <2 serv/d	0.34 (0.10-1.19) 0.92 (0.40-2.16) 1.42 (0.56-3.58) 0.92 (0.54-1.60)	Age, lived alone, below poverty threshold, impaired food related activities of daily living, non-dairy protein, dairy, grains, smoking, alcohol, BMI, waist circumference, cognitive status, self-rated health
Knoops KTB et al, 2006, Europe	Healthy Ageing – a Longitudinal Study in Europe (HALE)	1988-1991 - 2000, 10 years follow-up	2068 men and 1049 women, mean age 73.7 years: 1382 deaths	Dietary history	Grains	≥median vs. <median	0.84 (0.77-0.92)	Age, sex, physical activity, smoking, alcohol, education, BMI, chronic disease at baseline, study centre
Sahyoun NR et al, 2006, USA	NA	1981-1984 – 1995, 12-15 years follow-up	535 men and women, age ≥60 years: 186 deaths	3-day food record	Whole grain	0.31 serv/d 0.86 1.49 2.90	1.00 1.08 (0.71-1.66) 1.24 (0.83-1.86) 0.82 (0.52-1.28)	Age, sex, race, education, marital status, smoking, alcohol intake, exercise, BMI, energy intake, SFA, antihypertensive or lipid-lowering therapy
Jacobs DR, 2007, USA	Iowa Women's Health Study	1986 – 2003, 17 years follow-up	27312 women, age 55-69 years: 5552 deaths	Validated FFQ, 127 food items	Whole grains Refined grains	1.8 serv/wk 5.6 8.8 14.5 25.6 0-5.75 serv/wk 6-9.5 9.6-13.5 14-22 ≥22.5	1.00 0.88 (0.81-0.96) 0.88 (0.81-0.96) 0.80 (0.73-0.87) 0.79 (0.72-0.87) 1.00 0.98 (0.90-1.06) 0.95 (0.87-1.04) 0.92 (0.84-1.01) 1.01 (0.91-1.12)	Age, energy intake, BMI, waist-to-hip ratio, smoking, education, physical activity, HRT, multivitamin supplement use, intake of alcohol, coffee, red meat, fish and seafood, total fruit and vegetables, mutual adjustment between whole grains and refined grains
Iso H et al, 2007, Japan	Japan Collaborative Cohort Study	1988-1990-2003, ~12.8 years follow-up	42513 men and 57777 women, age 40-79 years: 9560/6575 deaths	FFQ	Rice, men Rice, women	<3/d 3-4 ≥5 <3/d 3-4 ≥5	1.00 0.92 (0.88-0.97) 0.78 (0.73-0.84) 1.00 0.94 (0.80-0.99) 0.95 (0.88-1.03)	Age, area of study
Trichopoulou A et al, 2009, Greece	European Prospective Investigation into Cancer and Nutrition - Greece	1994-1997 - 2002, 8.5 years follow-up	23349 men and women, age 20-86 years: 1075 deaths	Validated FFQ, 150 food items	Cereals	<median ≥Median	1.00 0.99 (0.86-1.13)	Age, sex, education, smoking status, waist-to-hip ratio, BMI, physical activity, total energy intake

Buckland G et al, 2011, Spain	European Prospective Investigation into Cancer and Nutrition – Spain cohort	1992/1996 - 2008, 13.4 years follow-up	40622 men and women, age 26-69 years: 1855 deaths	Validated DHQ, 600 food items	Cereals	<151.8 g/d 151.8-<214.0 ≥214.0	1.00 0.92 (0.82-1.03) 0.91 (0.81-1.03)	Age, sex, centre, BMI, waist circumference, education level, physical activity, smoking status and intensity, total energy intake
Olsen A et al, 2011, Denmark	Diet, Cancer, and Health Study	1993-1997 – 2008, 12 years follow-up	50290 men and women, age 50-64 years: 4126 deaths	Validated FFQ, 192 food items	Rye bread, men Oatmeal Rye bread, women Oatmeal	<63 g/d ≥63 <21 g/d ≥21 <63 g/d ≥63 <21 g/d ≥21	1.00 0.84 (0.75-0.94) 1.00 0.91 (0.82-1.02) 1.00 0.90 (0.80-1.01) 1.00 0.97 (0.84-1.11)	Age, time under study, smoking status, smoking duration, current tobacco consumption, time since cessation, alcohol, education, participation in sports, time spent in sports per week, BMI, red meat, processed meat, total energy, fish, cabbages, apples and pears, root vegetables
Van den Brandt PA et al, 2011, Netherlands	Netherlands Cohort Study	1986-1996, ~11 years follow-up	120852 men and women, age 55-69 years: 9691 deaths 3576 subcohort members	Validated FFQ, 150 food items	Whole grains, men Whole grains, women	Per 10.6 g/d Per 13.5 g/d	1.01 (0.99-1.02) 1.00 (0.98-1.03)	Age, cigarette smoking, cigarettes per day, years of smoking, BMI, nonoccupational physical activity, hypertension, education, energy intake
Tognon G et al, 2011, Sweden	Gerontological and Geriatric Population Studies in Gothenburg	1971, 1981, 1992, 2000 – 2009, 8.5 years follow-up	1037 men and women, age 70 years: 630 deaths	Dietary history	Whole grains cereals Cereals	H vs. l H vs. l	0.85 (0.73-1.00) 1.01 (0.86-1.19)	Age, sex, baseline BMI, waist circumference, physical activity, marital status, smoking status, birth cohort, education
Martinez-Gonzalez MA et al, 2012, Spain	Seguimiento Universidad de Navarra Project	1999 – 2009, 6.8 years follow-up	15535 men and women, mean age 38 years: 185 deaths	Validated FFQ, 136 food items	Cereals	≥median vs. <median	0.83 (0.54-1.27)	Age, years of university education, BMI, smoking, physical activity, hours spent watching television, history of depression, hypertension, hypercholesterolemia, total energy, egg intake, potato, adoption of special diets, MUFA/SFA ratio, fruits/nuts, vegetables, legumes, fish, meat/meat products, dairy, alcohol

Sluik D et al, 2014, Europe	European Prospective Investigation into Cancer and Nutrition	1992-2000 - NA, 9.9 years follow-up	265295 men and women, age 30-70 years: 830/12135 deaths (diabetes/no diabetes)	Validated FFQs, food records and question-naires	Pasta, diabetes Rice Bread Breakfast cereals Pasta, no diabetes Rice Bread Breakfast cereals	Per 10 g/d Per 10 g/d Per 100 g/d[2] Per 10 g/d Per 10 g/d Per 10 g/d Per 100 g/d[2] Per 10 g/d	0.93 (0.90-0.96) 0.93 (0.86-1.00) 0.87 (0.71-1.07) 1.00 (0.97-1.02) 0.99 (0.98-1.00) 0.96 (0.94-0.98) 0.81 (0.76-0.82) 0.97 (0.97-0.98)	Age, centre, sex, prevalence of heart disease, cancer, stroke, education, diabetes medication use, alcohol, smoking behavior, physical activity, underlying dietary patterns
Li K et al, 2014, Germany	European Prospective Investigation into Cancer and Nutrition - Heidelberg Cohort	1994-1998 – 2009, 11 years follow-up	10235 men and 12234 women, age ≥40 years: 1599 deaths	Validated FFQ, 148 food items	Cereals, men Cereals, women	Low vs. high Low vs. high	1.08 (0.96-1.23) 1.04 (0.86-1.26)	Age, smoking status, duration and cigarettes per day, BMI, alcohol, leisure-time physical activity, red and processed meat, vegetables and fruits, fish, dairy products
Tognon G et al, 2014, Denmark	The 1982-83 Danish Monitoring trends and determinants of Cardiovascular disease study (MONICA)	1982-1983 – 2007, 14 years follow-up	948 women and 901 men, age NA: 553 deaths	7 day food record	Cereals	>median vs. <median	0.97 (0.82-1.15)	Age, sex, BMI, education, physical activity, cigarette smoking
Atkins JL et al, 2014, United Kingdom	British Regional Heart Study	1998-2000 – 2010, 11.3 years follow-up	3328 men, age 60-79 years: 933 deaths	Validated FFQ, 86 food items	Cereals Bread	Daily vs. <1 day/wk Whole grain vs. none	1.15 (0.87-1.52) 0.77 (0.32-1.90)	Age, smoking, alcohol, physical activity, social class, BMI, energy intake, diet score without respective components
Buil-Cosiales P et al, 2014, Spain	Prevencion con DietaMediterranea (PREDIMED) study	2003-2009 – 2012, 5.9 years follow-up	7216 men and women, age 55-75 years: 425 deaths	Validated FFQ, 137 food items	Whole grains, baseline Whole grains, updated 	0 g/d 5 19 84 0 g/d 1 7 33 89	1.00 0.78 (0.52-1.17) 0.67 (0.43-1.04) 0.92 (0.64-1.33) 1.00 0.90 (0.65-1.26) 0.81 (0.55-1.19) 0.90 (0.63-1.30) 0.93 (0.65-1.31)	Age, sex, smoking status, diabetes, BMI, SBP, DBP, intervention group, recruitment center, statins, alcohol, education, physical activity, total energy, vegetables, fruits
Wu H et al, 2015, USA	Nurses' Health Study	1984-2010, 26 years follow-up	74341 women, age 38-63 years: 15106 deaths	Validated FFQ, 126 food items	Whole grains	4.2 g/d 9.7 14.7	1.00 0.98 (0.93-1.03) 1.00 (0.95-1.05)	Age, ethnicity, BMI, smoking status, cigarettes per day, pack-years smoked, years since

						21.1 33.0	0.94 (0.89-0.99) 0.88 (0.84-0.93)	quitting smoking, alcohol, physical activity, family history of diabetes, cancer and heart disease, multivitamin use, aspirin use, hypertension, high cholesterol, diabetes, total energy, healthy eating index (including fruits, vegetables, nuts and legumes, red or processed meat, sugar-sweetened beverages, alcohol, sodium, trans fat, long-chain n-3 FA, other PUFAs, but excluding whole grains), postmenopausal status, HRT
Wu H et al, 2015, USA	Health Professionals Follow-up Study	1986-2010, 24 years follow-up	43744 men, age 32-87 years: 11814 deaths	Validated FFQ, 133 food items	Whole grains	5.9 g/d 14.4 22.1 31.3 47.8	1.00 1.00 (0.94-1.05) 0.97 (0.91-1.02) 1.01 (0.95-1.07) 0.95 (0.89-1.00)	Age, ethnicity, BMI, smoking status, cigarettes per day, pack-years smoked, years since quitting smoking, alcohol, physical activity, family history of diabetes, cancer and heart disease, multivitamin use, aspirin use, hypertension, high cholesterol, diabetes, total energy, healthy eating index (including fruits, vegetables, nuts and legumes, red or processed meat, sugar-sweetened beverages, alcohol, sodium, trans fat, long-chain n-3 FA, other PUFAs, but excluding whole grains)
Wu H et al, 2015, USA	Nurses' Health Study & Health Professionals Follow-up Study	1984-2010, 26 years follow-up 1986-2010, 24 years follow-up	74341 women, age 38-63 years: 15106 deaths 43744 men, age 32-87 years: 11814 deaths	Validated FFQ,	Total bran Total germ	1 2 3 4 5 1 2	1.00 1.00 (0.96-1.04) 0.99 (0.95-1.04) 1.00 (0.95-1.04) 0.94 (0.90-0.99) 1.00 1.02 (0.98-1.06)	Age, ethnicity, BMI, smoking status, cigarettes per day, pack-years smoked, years since quitting smoking, alcohol, physical activity, family history of diabetes, cancer and heart disease, multivitamin use,

						3 4 5	0.98 (0.94-1.03) 0.97 (0.93-1.02) 1.00 (0.96-1.05)	aspirin use, hypertension, high cholesterol, diabetes, total energy, healthy eating index (including fruits, vegetables, nuts and legumes, red or processed meat, sugar-sweetened beverages, alcohol, sodium, trans fat, long-chain n-3 FA, other PUFAs, but excluding whole grains), women: postmenopausal status, HRT
					Naturally occurring bran	0-0.4/0-0.4 g/d 0.5-1.4/0.5-1.9 1.5-2.99/2.0-3.9 ≥3.0/≥4.0	1.00 0.99 (0.94-1.03) 0.98 (0.93-1.02) 0.93 (0.89-0.98)	
					Added bran	0-0.4/0-0.4 g/d 0.5-1.4/0.5-1.9 1.5-2.9/2.0-3.9 3.0-5.9/4.0-9.9 ≥6.0/≥10.0	1.00 0.99 (0.95-1.02) 0.99 (0.95-1.03) 1.00 (0.97-1.04) 0.93 (0.89-0.97)	
					Refined grains	Per 28 g/d	0.98 (0.97-0.99)	
Boggs DA et al, 2015, USA	Black Women's Health Study	1995-2001 – 2011, 16 years follow-up	37001 women, age 30-69 years: 1678 deaths	Validated FFQ, 68 food items	Whole grains	0.01 serv/d 0.11 0.32 0.62 1.44	1.00 0.96 (0.83-1.12) 0.82 (0.70-0.97) 0.85 (0.73-0.99) 0.75 (0.64-0.89)	Age, total energy intake, education, marital status, vigorous exercise, TV watching, smoking, alcohol, vegetables, fruits, nuts/legumes, low-fat dairy, red or processed meat, sugar-sweetened beverages, sodium
Huang T et al, 2015, USA	NIH-AARP Diet and Health Study	1995-1996 – 2009, 14 years follow-up	367442 men and women, age 50-71 years: 46067 deaths	Validated FFQ, 124 food items	Whole grains	0.13 oz/1000 kcal/d[3] 0.30 0.47 0.69 1.20	1.00 0.93 (0.90-0.95) 0.89 (0.87-0.92) 0.85 (0.82-0.87) 0.83 (0.81-0.86)	Age, sex, number of cigarettes per day, time of smoking cessation, race/ ethnicity, alcohol, education, marital status, health status, BMI, physical activity, red meat, total fruit and vegetables, total energy, HRT (women)
Xu M et al, 2015, USA	NIH-AARP Diet and Health Study	1995-1996 – 2008, 14 years follow-up	367442 men and women, age 50-71 years: 46067 deaths	Validated FFQ, 124 food items	Ready-to-eat cereals	0.00 g/d 0.67 3.48 9.33 22.48	1.00 0.94 (0.92-0.97) 0.92 (0.89-0.95) 0.88 (0.86-0.91) 0.85 (0.83-0.88)	Age, sex, smoking status, smoking dose, time since quitting smoking, race/ethnicity, education, marital status, self-rated health status, BMI, physical activity, menopausal hormone therapy, alcohol, red meat, fruits, vegetables, total energy

Prinelli F et al, 2015, Italy	NA	1991-1995 – 2012, 17.4 years follow-up	974 men and women, age 40-74 years: 193 deaths	FFQ, 158 food items	Cereals	>median vs. ≤median	0.91 (0.66-1.26)	Age, sex, education, BMI, physical activity, smoking status, time spent watching TV, energy intake, vegetables, legumes, fruits, potatoes, fish and seafood, dairy products, red meat and meat products, poultry, olive oil, ethanol
Roswall N et al, 2015, Sweden	Swedish Women's Lifestyle and Health Cohort	1991-1992 - 2012, 21.3 years follow-up	44961 women, age 29-49 years: 1855 deaths	Validated FFQ, ~80 food items	Whole grain bread Oatmeal	<median ≥median <median ≥median	1.00 0.83 (0.76-0.92) 1.00 0.99 (0.90-1.09)	Age, smoking status, duration, current tobacco consumption, time since smoking cessation, education, BMI, alcohol, red meat, processed meat, energy intake
Johnsen NF et al, 2015, Norway, Sweden, Denmark	HELGA Cohort (Norwegian Women and Cancer Study, Northern Sweden Health and Disease Study, Danish Diet, Cancer and Health Study – part of the EPIC study)	1992-1998 – 2008-2009, 11.1 (Norway), 14.2 (Sweden), 11.9 years (Denmark) follow-up	120010 men and women, age 30-64 years: 4181/3658 deaths	Validated FFQ, 88 food items (Norway), 98 food items (Sweden) 173 food items (Denmark)	Whole grain breakfast cereals, women Non-white bread Crisp bread Total whole grain products Oat Rye Wheat	0 g/d 0.8 12 50 25 g/d 80 113 180 0.6 g/d 2 6 31 56 g/d 100 131 201 0 g/d 0.4 4 19 8 g/d 18 22 41 0.4 g/d	1.00 0.77 (0.67-0.89) 0.79 (0.71-0.88) 0.75 (0.69-0.82) 1.00 0.84 (0.76-0.93) 0.74 (0.65-0.84) 0.72 (0.65-0.81) 1.00 0.90 (0.82-0.99) 0.86 (0.78-0.94) 0.91 (0.81-1.01) 1.00 0.78 (0.71-0.86) 0.77 (0.71-0.85) 0.68 (0.62-0.75) 1.00 0.85 (0.78-0.93) 0.74 (0.67-0.82) 0.78 (0.70-0.87) 1.00 0.92 (0.84-1.01) 0.81 (0.73-0.90) 0.93 (0.83-1.03) 1.00	Age, follow-up time, education, smoking status/years since quit/ cigarettes per day, alcohol, BMI, total energy

						3	0.72 (0.65-0.79)	
						10	0.65 (0.58-0.72)	
						37	0.63 (0.53-0.74)	
					Total whole grain types	20 g/d	1.00	
						33	0.80 (0.73-0.87)	
						49	0.74 (0.67-0.81)	
						74	0.74 (0.67-0.81)	
					Whole grain breakfast cereals, men	0 g/d	1.00	
						0.8	0.92 (0.82-1.04)	
						7	0.82 (0.76-0.89)	
						50	0.74 (0.68-0.81)	
					Non-white bread	13 g/d	1.00	
						66	0.92 (0.83-1.03)	
						118	0.85 (0.75-0.95)	
						201	0.78 (0.69-0.88)	
					Crisp bread	1 g/d	1.00	
						2	0.97 (0.89-1.06)	
						4	0.94 (0.86-1.02)	
						34	1.03 (0.90-1.17)	
					Total whole grain products	64 g/d	1.00	
						107	0.87 (0.80-0.95)	
						156	0.74 (0.68-0.81)	
						222	0.75 (0.68-0.81)	
					Oat	0 g/d	1.00	
						0.4	0.87 (0.80-0.95)	
						3	0.85 (0.77-0.94)	
						30	0.76 (0.69-0.85)	
					Rye	7 g/d	1.00	
						21	0.91 (0.83-1.00)	
						38	0.82 (0.74-0.91)	
						56	0.86 (0.78-0.95)	
					Wheat	0.1 g/d	1.00	
						1	0.87 (0.80-0.95)	
						5	0.76 (0.69-0.84)	
						10	0.71 (0.64-0.78)	
					Total whole grain types	21 g/d	1.00	
						37	0.82 (0.75-0.90)	
						54	0.72 (0.66-0.78)	
						80	0.75 (0.68-0.82)	

Shi Z et al, 2015, China	Chinese Longitudinal Health Longevity Survey	1998-1999 - 2011, 4.3 years follow-up	8959 men and women, age ≥80 years: 6626 deaths	FFQ, 10 items	Staple food (total grains: rice, corn, wheat, other)	≤200 g/d 250-300 350-400 ≥450	1.00 0.92 (0.86-0.98) 0.92 (0.85-0.99) 0.91 (0.84-0.98)	Age, sex, job before 60 years age, residence, smoking, alcohol, physical activity, number of chronic diseases, fruit and vegetables
Wang JB et al, 2016, China[2]	Linxian Nutrition Intervention Trial cohort	1984-1991 - 2010, 19-26 years follow-up	2445 men and women, age 40-69 years: 1501 deaths	FFQ, 64 food items	All grains Non-whole grains Whole grains	Per 1 time/day Per 1 time/day Per 1 time/day	0.96 (0.93-1.00) 0.96 (0.92-1.01) 0.98 (0.93-1.05)	Age, sex, commune, smoking, drinking, season, BMI
Bongard V et al, 2016, France	MONitoring of trends and determinants in CArdiovascular disease (MONICA) Project	1995-1997 - 2010, 14.8 years follow-up	960 men, age 45-64 years: 150 deaths	3-day food record	Cereals Bread	<21 g/d 21-<47 47-<78 ≥78 <80 g/d 80-<120 120-<170 ≥170	1.00 0.60 (0.39-0.92) 0.50 (0.31-0.81) 0.76 (0.48-1.19) 1.00 0.69 (0.45-1.07) 0.43 (0.26-0.70) 0.80 (0.51-1.26)	Age, center, payment of income tax, obesity, alcohol, smoking status, physical activity, presence of a serious chronic condition, diet quality score

BMI; body mass index, DBP; diastolic blood pressure, FA; fatty acids, FFQ; food frequency questionnaire, HRT; hormone replacement therapy, MUFA; monounsaturated fatty acids, PUFA; polyunsaturated fatty acids, SBP; systolic blood pressure, SFA; saturated fatty acids, TV; television

[1] The study reported 99% confidence intervals which have been recalculated to 95% confidence intervals.

[2] The original paper reports per 10 g/d for bread, but after contact with authors it was confirmed that 100 g/d is correct.

[3] The original paper reports in ounces/d, after contact with the authors it was confirmed that ounces/1000 kcal/d is correct.

Table S8. Whole grains and refined grains and respiratory disease mortality

Author, publication year, country	Study name	Study period	Number of participants, gender, age, number of cases/deaths	Dietary assessment	Exposure and subgroup	Whole grain consumption frequency or amount	Relative risks (95% confidence intervals)	Adjustment for confounding factors
Jacobs DR, 2007, USA	Iowa Women's Health Study	1986 – 2003, 17 years follow-up	27312 women, age 55-69 years: 569 respiratory disease deaths	Validated FFQ, 127 food items	Whole grains	1.8 serv/wk 5.6 8.8 14.5 25.6	1.00 0.65 (0.51-0.83) 0.65 (0.50-0.84) 0.58 (0.44-0.76) 0.60 (0.46-0.80)	Age, energy intake, BMI, waist-to-hip ratio, smoking, education, physical activity, HRT, multivitamin supplement use, intake of alcohol, coffee, red meat, fish and seafood, total fruit and vegetables, mutual adjustment between whole grains and refined grains
Wu H et al, 2015, USA	Nurses' Health Study & Health Professionals Follow-up Study	1984-2010, 26 years follow-up 1986-2010, 24 years follow-up	74341 women, age 38-63 years and 43744 men, age 32-87 years: 2016 respiratory disease deaths	Validated FFQ, 126/133 food items	Whole grains	4.2/5.9 g/d (w/m) 9.7/14.4 14.7/22.1 21.1/31.1 33.0/47.8	1.00 0.96 (0.84-1.08) 1.00 (0.87-1.14) 0.88 (0.76-1.02) 0.89 (0.77-1.03)	Age, ethnicity, BMI, smoking status, cigarettes per day, pack-years smoked, years since quitting smoking, alcohol, physical activity, family history of diabetes, cancer and heart disease, multivitamin use, aspirin use, hypertension, high cholesterol, diabetes, total energy, healthy eating index (including fruits, vegetables, nuts and legumes, red or processed meat, sugar-sweetened beverages, alcohol, sodium, trans fat, long-chain n-3 FA, other PUFAs, but excluding whole grains), women: postmenopausal status, HRT

Huang T et al, 2015, USA	NIH-AARP Diet and Health Study	1995-1996 – 2009, 14 years follow-up	367442 men and women, age 50-71 years: 3796 respiratory disease deaths	Validated FFQ, 124 food items	Whole grains	0.13 oz/1000 kcal/d[1] 0.30 0.47 0.69 1.20	1.00 0.99 (0.90-1.09) 0.94 (0.85-1.03) 0.91 (0.82-1.01) 0.89 (0.80-0.98)	Age, sex, number of cigarettes per day, time of smoking cessation, race/ ethnicity, alcohol, education, marital status, health status, BMI, physical activity, red meat, total fruit and vegetables, total energy, HRT (women)
Xu M et al, 2015, USA	NIH-AARP Diet and Health Study	1995-1996 – 2008, 14 years follow-up	367442 men and women, age 50-71 years: 3796 respiratory disease deaths	Validated FFQ, 124 food items	Ready-to-eat cereals	0.00 g/d 0.67 3.48 9.33 22.48	1.00 0.95 (0.88-1.03) 0.94 (0.87-1.02) 0.91 (0.84-0.99) 0.91 (0.83-0.99)	Age, sex, smoking status, smoking dose, time since quitting smoking, race/ethnicity, education, marital status, self-rated health status, BMI, physical activity, menopausal hormone therapy, alcohol, red meat, fruits, vegetables, total energy

Johnsen NF et al, 2015, Norway, Sweden, Denmark	HELGA Cohort (Norwegian Women and Cancer Study, Northern Sweden Health and Disease Study, Danish Diet, Cancer and Health Study – part of the EPIC study)	1992-1998 – 2008-2009, 11.1 (Norway), 14.2 (Sweden), 11.9 years (Denmark) follow-up	120010 men and women, age 30-64 years: 111/125 respiratory disease deaths	Validated FFQ, 88 food items (Norway), 98 food items (Sweden) 173 food items (Denmark)	Whole grain breakfast cereals, women	0 g/d 0.8 12 50	1.00 0.28 (0.11-0.69) 0.48 (0.28-0.83) 0.39 (0.23-0.65)	Age, follow-up time, education, smoking status/years since quit/ cigarettes per day, alcohol, BMI, total energy
					Non-white bread	25 g/d 80 113 180	1.00 0.87 (0.50-1.53) 0.47 (0.24-0.93) 0.74 (0.41-1.35)	
					Crisp bread	0.6 g/d 2 6 31	1.00 0.80 (0.51-1.25) 0.59 (0.32-1.07) 1.03 (0.59-1.79)	
					Total whole grain products	56 g/d 100 131 201	1.00 0.56 (0.35-0.89) 0.53 (0.33-0.86) 0.82 (0.49-1.37)	
					Oat	0 g/d 0.4 4 19	1.00 0.56 (0.36-0.88) 0.48 (0.27-0.85) 0.51 (0.28-0.93)	
					Rye	8 g/d 18 22 41	1.00 1.62 (0.86-3.04) 1.12 (0.61-2.05) 1.12 (0.60-2.10)	
					Wheat	0.4 g/d 3 10 37	1.00 0.63 (0.41-0.99) 0.57 (0.34-0.94) 0.44 (0.09-2.05)	
					Total whole grain types	20 g/d 33 49 74	1.00 0.65 (0.40-1.08) 0.64 (0.39-1.04) 0.47 (0.28-0.77)	
					Whole grain breakfast cereals, men	0 g/d 0.8 7 50	1.00 1.50 (0.79-2.82) 1.23 (0.76-1.98) 0.66 (0.37-1.16)	

					Non-white bread	13 g/d	1.00	
						66	1.04 (0.52-2.08)	
						118	0.62 (0.28-1.35)	
						201	0.94 (0.46-1.94)	
					Crisp bread	1 g/d	1.00	
						2	0.77 (0.45-1.32)	
						4	0.98 (0.59-1.62)	
						34	1.00 (0.50-2.01)	
					Total whole grain products	64 g/d	1.00	
						107	1.03 (0.61-1.76)	
						156	1.05 (0.63-1.77)	
						222	0.60 (0.33-1.07)	
					Oat	0 g/d	1.00	
						0.4	0.99 (0.59-1.68)	
						3	0.87 (0.50-1.51)	
						30	0.52 (0.28-0.97)	
					Rye	7 g/d	1.00	
						21	1.16 (0.65-2.10)	
						38	0.70 (0.32-1.57)	
						56	1.02 (0.53-1.97)	
					Wheat	0.1 g/d	1.00	
						1	1.46 (0.83-2.55)	
						5	1.40 (0.76-2.56)	
						10	1.06 (0.57-1.95)	
					Total whole grain types	21 g/d	1.00	
						37	0.96 (0.58-1.61)	
						54	0.65 (0.38-1.11)	
						80	0.74 (0.42-1.30)	

BMI; body mass index, FA; fatty acids, FFQ; food frequency questionnaire, HRT; hormone replacement therapy, PUFA; polyunsaturated fatty acids

[1] The original paper reports in ounces/d, but after contact with the authors it was confirmed that ounces/1000 kcal/d is correct.

Table S9. Whole grains and refined grains and infectious disease mortality

Author, publication year, country	Study name	Study period	Number of participants, gender, age, number of cases/deaths	Dietary assessment	Exposure and subgroup	Whole grain consumption frequency or amount	Relative risks (95% confidence intervals)	Adjustment for confounding factors
Jacobs DR, 2007, USA	Iowa Women's Health Study	1986 – 2003, 17 years follow-up	27312 women, age 55-69 years: 59 infectious disease deaths	Validated FFQ, 127 food items	Whole grains	1.8 serv/wk 5.6 8.8 14.5 25.6	1.00 0.89 (0.39-2.02) 0.92 (0.41-2.09) 1.03 (0.46-2.33) 0.68 (0.26-1.75)	Age, energy intake, BMI, waist-to-hip ratio, smoking, education, physical activity, HRT, multivitamin supplement use, intake of alcohol, coffee, red meat, fish and seafood, total fruit and vegetables, mutual adjustment between whole grains and refined grains
Wu H et al, 2015, USA	Nurses' Health Study & Health Professionals Follow-up Study	1984-2010, 26 years follow-up 1986-2010, 24 years follow-up	74341 women, age 38-63 years and 43744 men, age 32-87 years: 405 infectious disease deaths	Validated FFQ, 126/133 food items	Whole grains	4.2/5.9 g/d (w/m) 9.7/14.4 14.7/22.1 21.1/31.1 33.0/47.8	1.00 0.88 (0.65-1.18) 0.76 (0.55-1.05) 1.01 (0.75-1.38) 0.90 (0.66-1.23)	Age, ethnicity, BMI, smoking status, cigarettes per day, pack-years smoked, years since quitting smoking, alcohol, physical activity, family history of diabetes, cancer and heart disease, multivitamin use, aspirin use, hypertension, high cholesterol, diabetes, total energy, healthy eating index (including fruits, vegetables, nuts and legumes, red or processed meat, sugar-sweetened beverages, alcohol, sodium, trans fat, long-chain n-3 FA, other PUFAs, but excluding whole grains), women: postmenopausal status, HRT

Huang T et al, 2015, USA	NIH-AARP Diet and Health Study	1995-1996 – 2009, 14 years follow-up	367442 men and women, age 50-71 years: 922 infectious disease deaths	Validated FFQ, 124 food items	Whole grains	0.13 oz/1000 kcal/d[1] 0.30 0.47 0.69 1.20	1.00 0.84 (0.70-1.02) 0.78 (0.64-0.96) 0.79 (0.65-0.97) 0.77 (0.62-0.95)	Age, sex, number of cigarettes per day, time of smoking cessation, race/ ethnicity, alcohol, education, marital status, health status, BMI, physical activity, red meat, total fruit and vegetables, total energy, HRT (women)
Xu M et al, 2015, USA	NIH-AARP Diet and Health Study	1995-1996 – 2008, 14 years follow-up	367442 men and women, age 50-71 years: 922 infectious disease deaths	Validated FFQ, 124 food items	Ready-to-eat cereals	0.00 g/d 0.67 3.48 9.33 22.48	1.00 0.97 (0.79-1.20) 0.85 (0.68-1.06) 0.84 (0.68-1.05) 0.97 (0.78-1.21)	Age, sex, smoking status, smoking dose, time since quitting smoking, race/ethnicity, education, marital status, self-rated health status, BMI, physical activity, menopausal hormone therapy, alcohol, red meat, fruits, vegetables, total energy

BMI; body mass index, FA; fatty acids, FFQ; food frequency questionnaire, HRT; hormone replacement therapy, PUFA; polyunsaturated fatty acids

[1] The original paper reports in ounces/d, but after contact with the authors it was confirmed that ounces/1000 kcal/d is correct.

Table S10. Whole grains and refined grains and diabetes mortality

Author, publication year, country	Study name	Study period	Number of participants, gender, age, number of cases/deaths	Dietary assessment	Exposure and subgroup	Whole grain consumption frequency or amount	Relative risks (95% confidence intervals)	Adjustment for confounding factors
Jacobs DR, 2007, USA	Iowa Women's Health Study	1986 – 2003, 17 years follow-up	27312 women, age 55-69 years: 60 deaths due to endocrine, nutritional and metabolic disorders (mainly diabetes)	Validated FFQ, 127 food items	Whole grains	1.8 serv/wk 5.6 8.8 14.5 25.6	1.00 0.44 (0.19-1.02) 0.65 (0.31-1.37) 0.46 (0.20-1.08) 0.55 (0.24-1.28)	Age, energy intake, BMI, waist-to-hip ratio, smoking, education, physical activity, HRT, multivitamin supplement use, intake of alcohol, coffee, red meat, fish and seafood, total fruit and vegetables, mutual adjustment between whole grains and refined grains
Wu H et al, 2015, USA	Nurses' Health Study & Health Professionals Follow-up Study	1984-2010, 26 years follow-up 1986-2010, 24 years follow-up	74341 women, age 38-63 years and 43744 men, age 32-87 years: 283 diabetes deaths	Validated FFQ	Whole grains	4.2/5.9 g/d (w/m) 9.7/14.4 14.7/22.1 21.1/31.1 33.0/47.8	1.00 0.59 (0.42-0.83) 0.52 (0.35-0.77) 0.52 (0.34-0.79) 0.50 (0.34-0.75)	Age, ethnicity, BMI, smoking status, cigarettes per day, pack-years smoked, years since quitting smoking, alcohol, physical activity, family history of diabetes, cancer and heart disease, multivitamin use, aspirin use, hypertension, high cholesterol, diabetes, total energy, healthy eating index (including fruits, vegetables, nuts and legumes, red or processed meat, sugar-sweetened beverages, alcohol, sodium, trans fat, long-chain n-3 FA, other PUFAs, but excluding whole grains), women: postmenopausal status, HRT

Huang T et al, 2015, USA	NIH-AARP Diet and Health Study	1995-1996 – 2009, 14 years follow-up	367442 men and women, age 50-71 years: 371 diabetes deaths	Validated FFQ, 124 food items	Whole grains	0.13 oz/1000 kcal/d[1] 0.30 0.47 0.69 1.20	1.00 0.71 (0.53-0.96) 0.76 (0.56-1.03) 0.72 (0.53-0.99) 0.52 (0.37-0.75)	Age, sex, number of cigarettes per day, time of smoking cessation, race/ ethnicity, alcohol, education, marital status, health status, BMI, physical activity, red meat, total fruit and vegetables, total energy, HRT (women)
Xu M et al, 2015, USA	NIH-AARP Diet and Health Study	1995-1996 – 2008, 14 years follow-up	367442 men and women, age 50-71 years: 371 diabetes deaths	Validated FFQ, 124 food items	Ready-to-eat cereals	0.00 g/d 0.67 3.48 9.33 22.48	1.00 0.96 (0.68-1.36) 1.22 (0.87-1.69) 1.14 (0.81-1.61) 0.70 (0.47-1.03)	Age, sex, smoking status, smoking dose, time since quitting smoking, race/ethnicity, education, marital status, self-rated health status, BMI, physical activity, menopausal hormone therapy, alcohol, red meat, fruits, vegetables, total energy

Johnsen NF et al, 2015, Norway, Sweden, Denmark	HELGA Cohort (Norwegian Women and Cancer Study, Northern Sweden Health and Disease Study, Danish Diet, Cancer and Health Study – part of the EPIC study)	1992-1998 – 2008-2009, 11.1 (Norway), 14.2 (Sweden), 11.9 years (Denmark) follow-up	120010 men and women, age 30-64 years: 70/24 diabetes deaths	Validated FFQ, 88 food items (Norway), 98 food items (Sweden) 173 food items (Denmark)	Whole grain breakfast cereals, women	0 g/d	1.00	Age, follow-up time, education, smoking status/years since quit/ cigarettes per day, alcohol, BMI, total energy
						0.8	0.80 (0.23-2.77)	
						12	0.45 (0.13-1.59)	
						50	0.28 (0.07-1.04)	
					Non-white bread	25 g/d	1.00	
						80	0.47 (0.15-1.48)	
						113	0.40 (0.11-1.50)	
						180	0.55 (0.17-1.73)	
					Crisp bread	0.6 g/d	1.00	
						2	1.21 (0.41-3.54)	
						6	1.25 (0.36-4.35)	
						31	1.09 (0.27-4.43)	
					Total whole grain products	56 g/d	1.00	
						100	0.41 (0.13-1.29)	
						131	0.41 (0.13-1.29)	
						201	0.90 (0.31-2.62)	
					Oat	0 g/d	1.00	
						0.4	0.88 (0.34-2.27)	
						4	0.36 (0.09-1.51)	
						19	0.25 (0.05-1.31)	
					Rye	8 g/d	1.00	
						18	0.93 (0.28-3.09)	
						22	0.46 (0.14-1.53)	
						41	0.70 (0.22-2.25)	
					Wheat	0.4 g/d	1.00	
						3	0.69 (0.26-1.85)	
						10	0.61 (0.20-1.88)	
						37	3.17 (0.27-37.59)	
					Total whole grain types	20 g/d	1.00	
						33	0.77 (0.25-2.41)	
						49	0.44 (0.14-1.38)	
						74	0.64 (0.20-2.04)	
					Whole grain breakfast cereals, men	0 g/d	1.00	
						0.8	0.59 (0.24-1.50)	
						7	0.31 (0.14-0.68)	
						50	0.45 (0.23-0.90)	

					Non-white bread	13 g/d	1.00	
						66	1.89 (0.66-5.41)	
						118	1.59 (0.52-4.82)	
						201	2.30 (0.79-6.72)	
					Crisp bread	1 g/d	1.00	
						2	1.33 (0.68-2.61)	
						4	1.07 (0.53-2.15)	
						34	2.35 (1.10-5.03)	
					Total whole grain products	64 g/d	1.00	
						107	1.76 (0.83-3.74)	
						156	1.09 (0.49-2.42)	
						222	1.67 (0.79-.3.51)	
					Oat	0 g/d	1.00	
						0.4	0.60 (0.32-1.12)	
						3	0.33 (0.16-0.72)	
						30	0.40 (0.20-0.81)	
					Rye	7 g/d	1.00	
						21	1.14 (0.53-2.48)	
						38	0.40 (0.12-1.34)	
						56	1.80 (0.80-4.05)	
					Wheat	0.1 g/d	1.00	
						1	0.75 (0.37-1.56)	
						5	1.07 (0.51-2.22)	
						10	1.18 (0.60-2.34)	
					Total whole grain types	21 g/d	1.00	
						37	0.92 (0.45-1.87)	
						54	0.95 (0.49-1.86)	
						80	1.18 (0.59-2.38)	

BMI; body mass index, FA; fatty acids, FFQ; food frequency questionnaire, HRT; hormone replacement therapy, PUFA; polyunsaturated fatty acids

[1] The original paper reports in ounces/d, but after contact with the authors it was confirmed that ounces/1000 kcal/d is correct.

Table S11. Whole grains and refined grains and nervous system disease mortality

Author, publication year, country	Study name	Study period	Number of participants, gender, age, number of cases/deaths	Dietary assessment	Exposure and subgroup	Whole grain consumption frequency or amount	Relative risks (95% confidence intervals)	Adjustment for confounding factors
Jacobs DR, 2007, USA	Iowa Women's Health Study	1986 – 2003, 17 years follow-up	27312 women, age 55-69 years: 241 nervous system deaths	Validated FFQ, 127 food items	Whole grains	1.8 serv/wk 5.6 8.8 14.5 25.6	1.00 0.84 (0.53-1.32) 1.33 (0.88-1.99) 0.83 (0.53-1.31) 0.89 (0.55-1.42)	Age, energy intake, BMI, waist-to-hip ratio, smoking, education, physical activity, HRT, multivitamin supplement use, intake of alcohol, coffee, red meat, fish and seafood, total fruit and vegetables, mutual adjustment between whole grains and refined grains
Wu H et al, 2015, USA	Nurses' Health Study & Health Professionals Follow-up Study	1984-2010, 26 years follow-up 1986-2010, 24 years follow-up	74341 women, age 38-63 years and 43744 men, age 32-87 years: 2044 neurodegenerative disease deaths	Validated FFQ	Whole grains	4.2/5.9 g/d (w/m) 9.7/14.4 14.7/22.1 21.1/31.1 33.0/47.8	1.00 1.24 (1.08-1.42) 1.25 (1.09-1.44) 1.35 (1.17-1.55) 1.20 (1.04-1.38)	Age, ethnicity, BMI, smoking status, cigarettes per day, pack-years smoked, years since quitting smoking, alcohol, physical activity, family history of diabetes, cancer and heart disease, multivitamin use, aspirin use, hypertension, high cholesterol, diabetes, total energy, healthy eating index (including fruits, vegetables, nuts and legumes, red or processed meat, sugar-sweetened beverages, alcohol, sodium, trans fat, long-chain n-3 FA, other PUFAs, but excluding whole grains), women: postmenopausal status, HRT

Table S12. Whole grains and refined grains and non-cardiovascular, non-cancer causes of death

Author, publication year, country	Study name	Study period	Number of participants, gender, age, number of cases/deaths	Dietary assessment	Exposure and subgroup	Whole grain consumption frequency or amount	Relative risks (95% confidence intervals)	Adjustment for confounding factors
Jacobs DR, 2007, USA	Iowa Women's Health Study	1986 – 2003, 17 years follow-up	27312 women, age 55-69 years: 1072 non-CVD, non-cancer, inflammatory disease deaths 482 non-CVD, non-cancer, non-inflammatory disease deaths	Validated FFQ, 127 food items	Whole grains, non-CVD, non-cancer, inflammatory diseases Whole grains, non-CVD, non-cancer, non-inflammatory diseases	1.8 serv/wk 5.6 8.8 14.5 25.6 1.8 serv/wk 5.6 8.8 14.5 25.6	1.00 0.69 (0.57-0.83) 0.79 (0.66-0.95) 0.64 (0.53-0.79) 0.66 (0.54-0.81) 1.00 1.25 (0.94-1.67) 1.12 (0.83-1.51) 1.02 (0.74-1.39) 1.02 (0.74-1.42)	Age, energy intake, BMI, waist-to-hip ratio, smoking, education, physical activity, HRT, multivitamin supplement use, intake of alcohol, coffee, red meat, fish and seafood, total fruit and vegetables, mutual adjustment between whole grains and refined grains
Buil-Cosiales P et al, 2014, Spain	Prevencion con DietaMediterranea (PREDIMED) study	2003-2009 – 2012, 5.9 years follow-up	7216 men and women, age 55-75 years: 153 non-CVD, non-cancer deaths	Validated FFQ, 137 food items	Whole grains	0 g/d 1 7 33 89	1.00 0.89 (0.49-1.63) 1.03 (0.52-2.02) 1.03 (0.51-2.10) 0.76 (0.38-1.53)	Age, sex, smoking status, diabetes, BMI, SBP, DBP, recruitment center, statins, alcohol, education, physical activity, total energy, vegetables, fruits

Wu H et al, 2015, USA	Nurses' Health Study & Health Professionals Follow-up Study	1984-2010, 26 years follow-up 1986-2010, 24 years follow-up	74341 women, age 38-63 years and 43744 men, age 32-87 years: 10425 non-CVD, non-cancer deaths[1]	Validated FFQ	Whole grains	4.2/5.9 g/d (w/m) 9.7/14.4 14.7/22.1 21.1/31.1 33.0/47.8	1.00 0.98 (0.93-1.04) 0.95 (0.89-1.01) 0.97 (0.91-1.03) 0.91 (0.86-0.97) [1]	Age, ethnicity, BMI, smoking status, cigarettes per day, pack-years smoked, years since quitting smoking, alcohol, physical activity, family history of diabetes, cancer and heart disease, multivitamin use, aspirin use, hypertension, high cholesterol, diabetes, total energy, healthy eating index (including fruits, vegetables, nuts and legumes, red or processed meat, sugar-sweetened beverages, alcohol, sodium, trans fat, long-chain n-3 FA, other PUFAs, but excluding whole grains), women: postmenopausal status, HRT
Huang T et al, 2015, USA	NIH-AARP Diet and Health Study	1995-1996 – 2009, 14 years follow-up	367442 men and women, age 50-71 years: 10312 non-CVD, non-cancer deaths[1]	Validated FFQ, 124 food items	Whole grains	0.13 oz/1000 kcal/d[2] 0.30 0.47 0.69 1.20	1.00 0.97 (0.88-1.06) 0.97 (0.89-1.06) 0.87 (0.79-0.96) 0.86 (0.78-0.94) [1]	Age, sex, number of cigarettes per day, time of smoking cessation, race/ ethnicity, alcohol, education, marital status, health status, BMI, physical activity, red meat, total fruit and vegetables, total energy, HRT (women)

BMI; body mass index, DBP; diastolic blood pressure, FA; fatty acids, FFQ; food frequency questionnaire, HRT; hormone replacement therapy, PUFA; polyunsaturated fatty acids, SBP; systolic blood pressure

[1] For the Nurses' Health Study, Health Professionals Follow-up Study, and NIH-AARP Diet and Health Study data were pooled for all non-CVD, non-cancer causes of death (NHS&HPFS: deaths from respiratory disease, neurodegenerative disease, infectious disease, kidney disease, diabetes, and other causes, and NIH-AARP Diet and Health Study: deaths from diabetes, respiratory disease, infections and other/unknown causes) using a fixed effects model.

[2] The original paper reports in ounces/d, but after contact with the authors it was confirmed that ounces/1000 kcal/d is correct.

Table S13. Relative risks from nonlinear dose-response analysis of whole grains and coronary heart disease, stroke, cardiovascular disease, total cancer, and all-cause mortality

Coronary heart disease		Stroke		Cardiovascular disease		Total cancer		All-cause mortality	
g/d	**RR (95% CI)**	**g/d**	**RR (95% CI)**	**g/d**	**RR (95% CI)**	**g/d**	**RR (95% CI)**	**g/d**	**RR (95% CI)**
0	1.00	0	1.00	0	1.00	0	1.00	0	1.00
15	0.93 (0.92-0.95)	15	0.94 (0.92-0.95)	15	0.93 (0.91-0.94)	15	0.97 (0.96-0.98)	15	0.95 (0.94-0.96)
30	0.87 (0.85-0.90)	30	0.88 (0.85-0.91)	30	0.87 (0.85-0.89)	30	0.95 (0.93-0.97)	30	0.90 (0.89-0.92)
45	0.82 (0.79-0.85)	45	0.83 (0.78-0.87)	45	0.83 (0.81-0.86)	45	0.93 (0.90-0.95)	45	0.87 (0.85-0.89)
60	0.78 (0.75-0.82)	60	0.78 (0.73-0.84)	60	0.81 (0.79-0.84)	60	0.91 (0.88-0.94)	60	0.85 (0.82-0.87)
75	0.75 (0.71-0.79)	75	0.75 (0.69-0.81)	75	0.80 (0.77-0.82)	75	0.89 (0.86-0.92)	75	0.83 (0.80-0.85)
90	0.72 (0.69-0.76)	90	0.73 (0.66-0.79)	90	0.79 (0.76-0.82)	90	0.87 (0.84-0.91)	90	0.81 (0.79-0.83)
105	0.70 (0.66-0.74)	105	0.71 (0.64-0.78)	105	0.78 (0.75-0.82)	105	0.86 (0.83-0.90)	105	0.80 (0.78-0.82)
120	0.69 (0.65-0.73)	120	0.70 (0.63-0.77)	120	0.78 (0.74-0.82)	120	0.85 (0.81-0.89)	120	0.78 (0.76-0.81)
135	0.67 (0.63-0.71)	135	0.69 (0.62-0.77)	135	0.77 (0.72-0.82)	135	0.83 (0.80-0.87)	135	0.77 (0.75-0.80)
150	0.66 (0.62-0.70)	150	0.69 (0.62-0.77)	150	0.76 (0.71-0.82)	150	0.82 (0.78-0.86)	150	0.76 (0.73-0.79)
165	0.65 (0.61-0.69)	165	0.69 (0.62-0.77)	165	0.75 (0.70-0.82)	165	0.81 (0.77-0.86)	165	0.75 (0.71-0.78)
180	0.64 (0.59-0.68)	180	0.69 (0.62-0.77)	180	0.75 (0.68-0.82)	180	0.80 (0.75-0.85)	180	0.73 (0.70-0.77)
195	0.63 (0.58-0.68)	195	0.69 (0.62-0.77)	195	0.74 (0.67-0.82)	195	0.78 (0.73-0.84)	195	0.72 (0.68-0.76)
210	0.62 (0.57-0.67)	210	0.70 (0.62-0.78)	210	0.73 (0.66-0.82)	210	0.77 (0.72-0.83)	210	0.71 (0.67-0.75)
225	0.61 (0.56-0.66)	225	0.70 (0.63-0.78)	225		225	0.76 (0.71-0.82)	225	0.70 (0.65-0.75)
240		240	0.70 (0.63-0.79)	240		240		240	
$P_{nonlinearity}$	<0.0001		<0.0001		<0.0001		0.15		<0.0001

Table S14. Relative risks from nonlinear dose-response analysis of whole grains and

Respiratory disease mortality		**Diabetes mortality**		**Infectious disease mortality**		**Nervous system disease mortality**		**All noncardiovascular, noncancer causes of death**	
g/d	**RR (95% CI)**	**g/d**	**RR (95% CI)**	**g/d**	**RR (95% CI)**	**g/d**	**RR (95% CI)**	**g/d**	**RR (95% CI)**
4.8	1.00	4.8	1.00	4.8	1.00	4.8	1.00	0	1.00
15	0.93 (0.91-0.96)	15	0.80 (0.77-0.83)	15	0.89 (0.85-0.93)	15	1.14 (1.11-1.18)	15	0.96 (0.95-0.97)
30	0.88 (0.84-0.92)	30	0.65 (0.61-0.70)	30	0.81 (0.75-0.88)	30	1.26 (1.19-1.33)	30	0.92 (0.90-0.94)
45	0.83 (0.78-0.88)	45	0.55 (0.50-0.60)	45	0.78 (0.72-0.85)	45	1.28 (1.20-1.37)	45	0.88 (0.86-0.91)
60	0.79 (0.73-0.85)	60	0.48 (0.43-0.54)	60	0.77 (0.71-0.84)	60	1.23 (1.15-1.33)	60	0.85 (0.83-0.88)
75	0.76 (0.69-0.82)	75	0.44 (0.39-0.50)	75	0.76 (0.70-0.84)	75	1.14 (1.05-1.25)	75	0.82 (0.79-0.85)
90	0.73 (0.67-0.80)	90	0.42 (0.37-0.48)	90	0.76 (0.68-0.85)	90	1.05 (0.93-1.17)	90	0.79 (0.77-0.82)
105	0.71 (0.65-0.78)	105	0.41 (0.35-0.48)	105	0.76 (0.66-0.87)	105	0.95 (0.83-1.10)	105	0.77 (0.74-0.80)
120	0.70 (0.63-0.77)	120	0.41 (0.35-0.48)	120		120		120	0.75 (0.72-0.78)
135	0.68 (0.61-0.76)	135	0.41 (0.35-0.49)	135		135		135	0.72 (0.69-0.75)
150	0.67 (0.60-0.75)	150	0.42 (0.35-0.50)	150		150		150	0.70 (0.67-0.73)
165	0.66 (0.59-0.74)	165	0.43 (0.36-0.52)	165		165		165	0.68 (0.65-0.71)
180	0.65 (0.57-0.73)	180	0.44 (0.36-0.54)	180		180		180	0.66 (0.62-0.69)
195	0.63 (0.56-0.72)	195	0.45 (0.36-0.56)	195		195		195	0.64 (0.60-0.67)
210	0.62 (0.54-0.72)	210	0.46 (0.37-0.58)	210		210		210	0.62 (0.58-0.66)
225	0.62 (0.53-0.71)	225	0.47 (0.37-0.59)	225		225		225	0.60 (0.57-0.64)
240		240		240		240		240	
$P_{nonlinearity}$	0.001		<0.0001		0.003		<0.0001		0.06

Table S15: Subgroup analyses of whole grains and coronary heart disease, stroke, and cardiovascular disease, per 3 servings per day

	Coronary heart disease					**Stroke**					**Cardiovascular disease**				
	n	RR (95% CI)	I^2	P_h[1]	P_h[2]	*n*	RR (95% CI)	I^2	P_h[1]	P_h[2]	*n*	RR (95% CI)	I^2	P_h[1]	P_h[2]
All studies	7	0.81 (0.75-0.87)	8.9	0.36		6	0.88 (0.75-1.03)	56.3	0.04		10	0.78 (0.73-0.85)	40.0	0.09	
Duration of follow-up															
<10 yrs follow-up	1	0.90 (0.78-1.04)			0.24	0				NC	1	0.83 (0.40-1.71)			0.90
≥10 yrs follow-up	6	0.80 (0.74-0.86)	0	0.47		6	0.88 (0.75-1.03)	56.3	0.04		9	0.78 (0.73-0.85)	46.6	0.06	
Outcome															
Incidence	5	0.84 (0.77-0.92)	33.8	0.20	0.61	3	0.84 (0.59-1.20)	74.2	0.02	0.81	2	0.87 (0.78-0.97)	0	0.85	0.15
Mortality	3	0.81 (0.74-0.89)	9.8	0.33		3	0.86 (0.74-0.99)	0	0.90		8	0.71 (0.61-0.82)	72.1	0.001	
Outcome subtype															
Myocardial infarction	2	0.92 (0.87-0.97)	0	0.69	0.05	-				-	-				-
Coronary heart disease	5	0.78 (0.72-0.86)	12.3	0.34		-					-				
Ischemic stroke	-					4	0.89 (0.71-1.11)	50.8	0.11	0.38	-				-
Hemorrhagic stroke	-					2	1.11 (0.82-1.50)	0	0.86		-				
Gender															
Men	2	0.80 (0.60-1.08)	66.1	0.09	0.60/	1	0.84 (0.65-1.07)			0.46/	2	0.82 (0.67-1.00)	65.1	0.09	0.67/
Women	4	0.76 (0.66-0.88)	51.8	0.10	0.58	3	0.84 (0.70-1.00)	0	0.50	NC	4	0.75 (0.65-0.86)	37.6	0.19	0.44
Men and women	2	0.78 (0.62-0.98)	0	0.68		3	0.90 (0.68-1.19)	63.2	0.07		5	0.79 (0.70-0.88)	36.1	0.18	
Geographic location															
Europe	2	0.86 (0.79-0.93)	0	0.51	0.11	2	0.98 (0.78-1.22)	76.2	0.04	0.24	3	0.85 (0.79-0.91)	0	0.97	0.06
America	4	0.72 (0.63-0.81)	0	0.95		3	0.79 (0.64-0.97)	0	0.47		6	0.74 (0.67-0.81)	24.9	0.25	
Asia	1	0.83 (0.57-1.23)				1	0.80 (0.57-1.13)				1	0.82 (0.63-1.05)			
Australia	0					0					0				
Number of cases															
Cases <500	1	0.83 (0.57-1.23)			0.61	5	0.82 (0.72-0.93)	0	0.76	0.04	2	0.62 (0.34-1.13)	25.3	0.25	0.66
Cases 500-<1000	2	0.73 (0.61-0.89)	0	0.85		1	1.08 (0.96-1.22)				1	0.82 (0.63-1.05)			
Cases ≥1000	4	0.81 (0.73-0.90)	42.7	0.16		0					7	0.79 (0.72-0.85)	52.9	0.05	
Validated dietary assessment															
Yes	6	0.80 (0.74-0.87)	24.0	0.25	0.86	4	0.83 (0.72-0.95)	0	0.61	0.11	8	0.79 (0.73-0.85)	45.1	0.08	0.81
No	1	0.83 (0.57-1.23)				2	0.98 (0.74-1.29)	62.1	0.10		2	0.67 (0.39-1.17)	54.1	0.14	
Study quality															
0-3 stars	0				0.86	0				0.71	0				0.81
4-6	1	0.83 (0.57-1.23)				1	0.80 (0.57-1.12)				1	0.82 (0.63-1.05)			
7-9	6	0.80 (0.74-0.87)	24.0	0.25		5	0.88 (0.74-1.05)	61.6	0.03		9	0.78 (0.72-0.85)	46.5	0.06	
Adjustment for confounding factors															

Age	Yes	7	0.81 (0.75-0.87)	8.9	0.36	NC	6	0.88 (0.75-1.03)	56.3	0.04	NC	10	0.78 (0.73-0.85)	40.0	0.09	NC
	No	0					0					0				
Education	Yes	4	0.83 (0.76-0.90)	22.0	0.28	0.23	3	0.85 (0.73-0.99)	0	0.66	0.64	7	0.80 (0.74-0.87)	40.7	0.12	0.25
	No	3	0.73 (0.61-0.87)	0	0.66		3	0.88 (0.66-1.18)	71.7	0.03		3	0.71 (0.59-0.86)	32.6	0.23	
Family history of CHD	Yes	3	0.78 (0.65-0.95)	50.3	0.13	0.95	1	0.69 (0.48-1.00)			0.31	2	0.66 (0.52-0.84)	33.3	0.22	0.13
	No	4	0.81 (0.75-0.88)	0	0.47		5	0.91 (0.78-1.06)	52.3	0.08		8	0.80 (0.75-0.86)	31.0	0.18	
Body mass index	Yes	7	0.81 (0.75-0.87)	8.9	0.36	NC	6	0.88 (0.75-1.03)	56.3	0.04	NC	9	0.78 (0.72-0.84)	43.1	0.08	0.39
	No	0					0					1	0.89 (0.71-1.11)			
Smoking	Yes	7	0.81 (0.75-0.87)	8.9	0.36	NC	6	0.88 (0.75-1.03)	56.3	0.04	NC	10	0.78 (0.73-0.85)	40.0	0.09	NC
	No	0					0					0				
Alcohol	Yes	7	0.81 (0.75-0.87)	8.9	0.36	NC	5	0.82 (0.72-0.93)	0	0.76	0.04	10	0.78 (0.73-0.85)	40.0	0.09	NC
	No	0					1	1.08 (0.96-1.22)				0				
Physical activity	Yes	5	0.77 (0.69-0.87)	28.0	0.24	0.43	4	0.88 (0.69-1.11)	64.5	0.04	0.72	8	0.76 (0.70-0.84)	37.7	0.13	0.26
	No	2	0.84 (0.77-0.93)	0	0.93		2	0.84 (0.72-1.00)	0	0.75		2	0.84 (0.78-0.91)	0	0.78	
Hypertension	Yes	3	0.82 (0.71-0.95)	24.2	0.27	0.70	2	0.69 (0.52-0.93)	0	0.99	0.17	3	0.64 (0.51-0.80)	21.9	0.28	0.08
	No	4	0.79 (0.71-0.88)	20.2	0.29		4	0.94 (0.80-1.09)	52.8	0.10		7	0.81 (0.76-0.86)	23.5	0.25	
Hypercholesterolemia, serum cholesterol	Yes	2	0.83 (0.67-1.01)	51.3	0.15	0.54	2	0.90 (0.58-1.38)	80.4	0.02	0.35	2	0.66 (0.52-0.84)	33.3	0.22	0.13
	No	5	0.80 (0.74-0.87)	0	0.41		4	0.84 (0.73-0.96)	0	0.82		8	0.80 (0.75-0.86)	31.0	0.18	
Coffee, caffeine	Yes	1	0.72 (0.60-0.87)			0.22	1	0.89 (0.67-1.19)			0.90	1	0.75 (0.63-0.89)			0.68
	No	6	0.83 (0.77-0.89)	0	0.46		5	0.86 (0.71-1.04)	64.4	0.02		9	0.79 (0.73-0.86)	45.0	0.07	
Sugar-sweetened beverages	Yes	0				NC	0				NC	2	0.66 (0.52-0.84)	33.3	0.22	0.13
	No	7	0.81 (0.75-0.87)	8.9	0.36		6	0.88 (0.75-1.03)	56.3	0.04		8	0.80 (0.75-0.86)	31.0	0.18	
Red or processed meat	Yes	1	0.72 (0.60-0.87)			0.22	1	0.89 (0.67-1.19)			0.90	4	0.73 (0.68-0.78)	0	0.49	0.02
	No	6	0.83 (0.77-0.89)	0	0.46		5	0.86 (0.71-1.04)	64.4	0.02		6	0.85 (0.80-0.90)	0	0.69	
Fish	Yes	2	0.71 (0.60-0.83)	0	0.62	0.11	1	0.89 (0.67-1.19)			0.90	1	0.75 (0.63-0.89)			0.68
	No	5	0.84 (0.78-0.90)	0	0.62		5	0.86 (0.71-1.04)	64.4	0.02		9	0.79 (0.73-0.86)	45.0	0.07	
Fruits and vegetables	Yes	2	0.71 (0.60-0.83)	0	0.62	0.11	1	0.89 (0.67-1.19)			0.90	5	0.66 (0.57-0.76)	54.2	0.07	0.02
	No	5	0.84 (0.78-0.90)	0	0.62		5	0.86 (0.71-1.04)	64.4	0.02		5	0.85 (0.80-0.91)	0	0.55	
Dairy	Yes	0				NC	0				NC	0				NC
	No	7	0.81 (0.75-0.87)	8.9	0.36		5	0.86 (0.71-1.04)	64.4	0.02		10	0.78 (0.73-0.85)	40.0	0.09	
Energy intake	Yes	6	0.80 (0.74-0.87)	24.0	0.25	0.86	5	0.88 (0.74-1.05)	61.6	0.03	0.71	9	0.78 (0.72-0.85)	46.5	0.06	0.81
	No	1	0.83 (0.57-1.23)				1	0.80 (0.57-1.12)				1	0.82 (0.63-1.05)			

*n*denotes the number of studies.

[1] P for heterogeneity within each subgroup,

[2] P for heterogeneity between subgroups with meta-regression analysis,

[3] P for heterogeneity between men and women (studies with genders mixed were excluded),

NC = not calculable

Table S16: Subgroup analyses of whole grains and total cancer and all-cause mortality, per 3 servings per day

		Total cancer					All-cause mortality				
		n	RR (95% CI)	I^2	P_h[1]	P_h[2]	*n*	RR (95% CI)	I^2	P_h[1]	P_h[2]
All studies		6	0.85 (0.80-0.91)	37.0	0.16		11	0.83 (0.77-0.90)	82.9	<0.0001	
Duration of follow-up											
<10 yrs follow-up		1	0.77 (0.43-1.38)			0.74	1	0.98 (0.67-1.44)			0.55
≥10 yrs follow-up		5	0.86 (0.80-0.92)	49.0	0.10		10	0.82 (0.76-0.89)	84.3	<0.0001	
Outcome											
Incidence		0				NC	-				NC
Mortality		6	0.87 (0.81-0.93)	51.2	0.07		10	0.82 (0.75-0.89)	83.9	<0.0001	
Gender											
Men		2	0.83 (0.77-0.89)	0	0.36	0.63/	3	0.93 (0.80-1.08)	86.2	0.001	0.39/
Women		3	0.92 (0.86-0.98)	0	0.92	0.13	5	0.78 (0.68-0.88)	80.5	<0.0001	0.27
Men and women		2	0.79 (0.74-0.84)	0	0.94		5	0.81 (0.73-0.91)	41.1	0.15	
Geographic location											
Europe		2	0.86 (0.81-0.91)	0	0.72	0.87	3	0.94 (0.76-1.16)	90.7	<0.0001	0.53
America		4	0.87 (0.78-0.97)	58.5	0.07		7	0.77 (0.70-0.85)	72.6	0.001	
Asia		0					1	0.94 (0.80-1.16)			
Australia		0					0				
Number of cases											
Cases <500		1	0.77 (0.43-1.38)			0.74	2	0.91 (0.67-1.23)	0	0.52	0.82
Cases 500-<1000		0					1	0.77 (0.61-0.96)			
Cases ≥1000		5	0.86 (0.80-0.92)	49.0	0.10		8	0.83 (0.76-0.90)	87.8	<0.0001	
Validated dietary assessment											
Yes		6	0.85 (0.80-0.91)	37.0	0.16	NC	9	0.82 (0.75-0.89)	85.7	<0.0001	0.60
No		0					2	0.92 (0.78-1.10)	0	0.55	
Study quality											
0-3 stars		0				NC	0				0.51
4-6		0					1	0.94 (0.80-1.16)			
7-9		6	0.85 (0.80-0.91)	37.0	0.16		10	0.82 (0.76-0.89)	83.9	<0.0001	
Adjustment for confounding factors											
Age	Yes	6	0.85 (0.80-0.91)	37.0	0.16	NC	11	0.83 (0.77-0.90)	82.9	<0.0001	NC
	No	0					0				
Education	Yes	4	0.84 (0.78-0.90)	51.1	0.11	0.36	8	0.83 (0.76-0.91)	84.5	<0.0001	0.97
	No	2	0.93 (0.80-1.08)	0	0.66		3	0.83 (0.67-1.03)	84.4	0.002	
Family history of CHD	Yes	2	0.93 (0.80-1.08)	0	0.66	0.36	2	0.78 (0.57-1.06)	90.6	0.001	0.67

	No	4	0.84 (0.78-0.90)	51.1	0.11		9	0.84 (0.77-0.92)	83.3	<0.0001	
Body mass index	Yes	6	0.85 (0.80-0.91)	37.0	0.16	NC	10	0.84 (0.78-0.91)	82.2	<0.0001	0.02
	No	0					1	0.30 (0.15-0.60)			
Smoking	Yes	6	0.85 (0.80-0.91)	37.0	0.16	NC	11	0.83 (0.77-0.90)	82.9	<0.0001	NC
	No	0					0				
Alcohol	Yes	6	0.85 (0.80-0.91)	37.0	0.16	NC	10	0.80 (0.75-0.86)	71.0	<0.0001	0.07
	No	0					1	1.05 (0.95-1.17)			
Physical activity	Yes	5	0.86 (0.78-0.95)	45.2	0.12	0.95	9	0.81 (0.72-0.91)	85.5	<0.0001	0.67
	No	1	0.86 (0.81-0.91)				2	0.85 (0.76-0.96)	51.9	0.15	
Hypertension	Yes	2	0.93 (0.80-1.08)	0	0.66	0.36	5	0.84 (0.69-1.02)	85.6	<0.0001	0.74
	No	4	0.84 (0.78-0.90)	51.1	0.11		6	0.81 (0.75-0.87)	75.4	0.001	
Hypercholesterolemia	Yes	2	0.93 (0.80-1.08)	0	0.66	0.36	2	0.78 (0.57-1.06)	90.6	0.001	0.67
	No	4	0.84 (0.78-0.90)	51.1	0.11		9	0.84 (0.77-0.92)	83.3	<0.0001	
Coffee	Yes	1	0.92 (0.81-1.04)			0.36	1	0.80 (0.73-0.87)			0.99
	No	5	0.84 (0.79-0.89)	30.2	0.22		10	0.83 (0.76-0.91)	84.6	<0.0001	
Sugar-sweetened beverages	Yes	2	0.93 (0.80-1.08)	0	0.66	0.36	3	0.67 (0.47-0.95)	89.0	<0.0001	0.25
	No	4	0.84 (0.78-0.90)	51.1	0.11		8	0.85 (0.79-0.93)	82.4	<0.0001	
Red or processed meat	Yes	4	0.87 (0.78-0.97)	58.5	0.07	0.87	5	0.77 (0.69-0.86)	81.7	<0.0001	0.17
	No	2	0.86 (0.81-0.91)	0	0.72		6	0.90 (0.78-1.03)	78.9	<0.0001	
Fish	Yes	1	0.92 (0.81-1.04)			0.36	1	0.80 (0.73-0.87)			0.99
	No	5	0.84 (0.79-0.89)	30.2	0.22		10	0.83 (0.76-0.91)	84.6	<0.0001	
Fruit and vegetables	Yes	5	0.86 (0.78-0.95)	45.2	0.12	0.95	6	0.78 (0.70-0.87)	78.6	<0.0001	0.27
	No	1	0.86 (0.81-0.91)				5	0.89 (0.77-1.03)	82.7	<0.0001	
Dairy	Yes	0				NC	1	0.30 (0.15-0.60)			0.02
	No	6	0.85 (0.80-0.91)	37.0	0.16		10	0.84 (0.78-0.91)	82.2	<0.0001	
Energy intake	Yes	6	0.85 (0.80-0.91)	37.0	0.16	NC	10	0.82 (0.76-0.89)	83.9	<0.0001	0.51
	No	0					1	0.94 (0.80-1.16)			

*n*denotes the number of studies.

[1] P for heterogeneity within each subgroup,

[2] P for heterogeneity between subgroups with meta-regression analysis,

[3] P for heterogeneity between men and women (studies with genders mixed were excluded),

NC = not calculable

Table S17: Study quality of studies included in the analysis of whole grains and coronary heart disease

Author, publication year	Represen-tativeness	Selection of non-exposed cohort	Exposure-ascertainment[1]	Demonstration of outcome not present at start	Adjustment for age	Adjustment for any other factor	Assess-ment of outcome	Long enough follow-up	Adequacy of follow-up[2]	Total score
Helnæs, 2016	1	1	1	1	1	1	1	1	1	9
Wang, 2016	0	1	0	0	1	1	1	1	0	5
Johnsen, 2015	1	1	1	0	1	1	1	1	1	8
Rautiainen, 2012	1	1	1	1	1	1	1	1	1	9
Jacobs, 2007	1	1	1	1	1	1	1	1	0	8
Jensen, 2004	0	1	1	1	1	1	1	1	1	8
Steffen, 2003	1	1	1	1	1	1	1	1	1	9
Liu, 1999	0	1	1	1	1	1	1	1	1	8

[1] 1 point for validated self-reported questionnairesor interview
[2] 1 point for loss-to-follow-up less than 10%

Table S18: Study quality of studies included in the analysis of whole grains and stroke

Author, publication year	Represen-tativeness	Selection of non-exposed cohort	Exposure-ascertainment[1]	Demonstration of outcome not present at start	Adjustment for age	Adjustment for any other factor	Assess-ment of outcome	Long enough follow-up	Adequacy of follow-up[2]	Total score
Wang, 2016	0	1	0	0	1	1	1	1	0	5
Johnsen, 2015	1	1	1	0	1	1	1	1	1	8
Mizrahi, 2009	1	1	1	1	1	1	1	1	0	8
Jacobs, 2007	1	1	1	1	1	1	1	1	0	8
Steffen, 2003	1	1	1	1	1	1	1	1	1	9
Liu, 2000	0	1	1	1	1	1	1	1	1	8

[1] 1 point for validated self-reported questionnairesor interview
[2] 1 point for loss-to-follow-up less than 10%

Table S19: Study quality of studies included in the analysis of whole grains and cardiovascular disease

Author, publication year	Represen-tativeness	Selection of non-exposed cohort	Exposure-ascertainment[1]	Demonstration of outcome not present at start	Adjustment for age	Adjustment for any other factor	Assess-ment of outcome	Long enough follow-up	Adequacy of follow-up[2]	Total score
Wang, 2016	0	1	0	0	1	1	1	1	0	5
Huang, 2015	1	1	1	1	1	1	1	1	0	8
Johnsen, 2015	1	1	1	0	1	1	1	1	1	8
Sonestedt, 2015	1	1	1	1	1	1	1	1	0	8
Wu, 2015, HPFS	0	1	1	1	1	1	1	1	1	8
Wu, 2015, NHS	0	1	1	1	1	1	1	1	1	8
Buil-Cosiales, 2014	0	1	1	1	1	1	1	1	0	7
Fitzgerald, 2012	1	1	1	1	1	1	1	1	1	9
Jacobs, 2007	1	1	1	1	1	1	1	1	0	8
Sahyoun, 2006	1	1	1	1	1	1	1	1	0	8

[1] 1 point for validated self-reported questionnairesor interview
[2] 1 point for loss-to-follow-up less than 10%

Table S20: Study quality of studies included in the analysis of whole grains and total cancer

Author, publication year	Represen-tativeness	Selection of non-exposed cohort	Exposure-ascertainment[1]	Demonstration of outcome not present at start	Adjustment for age	Adjustment for any other factor	Assess-ment of outcome	Long enough follow-up	Adequacy of follow-up[2]	Total score
Huang, 2015	1	1	1	1	1	1	1	1	0	8
Johnsen, 2015	1	1	1	0	1	1	1	1	1	8
Wu, 2015, HPFS	0	1	1	1	1	1	1	1	1	8
Wu, 2015, NHS	0	1	1	1	1	1	1	1	1	8
Buil-Cosiales, 2014	0	1	1	1	1	1	1	1	0	7
Jacobs, 2007	1	1	1	1	1	1	1	1	0	8

[1] 1 point for validated self-reported questionnaires or interview
[2] 1 point for loss-to-follow-up less than 10%

Table S21: Study quality of studies included in the analysis of whole grains and all-cause mortality

Author, publication year	Represen-tativeness	Selection of non-exposed cohort	Exposure-ascertainment[1]	Demonstration of outcome not present at start[2]	Adjustment for age	Adjustment for any other factor	Assess-ment of outcome	Long enough follow-up	Adequacy of follow-up[3]	Total score
Wang, 2016	0	1	0	0	1	1	1	1	0	5
Huang, 2015	1	1	1	1	1	1	1	1	0	8
Johnsen, 2015	1	1	1	0	1	1	1	1	1	8
Wu, 2015, HPFS	0	1	1	1	1	1	1	1	1	8
Wu, 2015, NHS	0	1	1	1	1	1	1	1	1	8
Boggs, 2014	1	1	1	1	1	1	1	1	1	9
Buil-Cosiales, 2014	0	1	1	1	1	1	1	1	0	7
van den Brandt, 2011	1	1	1	1	1	1	1	1	1	9
Jacobs, 2007	1	1	1	1	1	1	1	1	0	8
Sahyoun, 2006	1	1	1	1	1	1	1	1	0	8
Steffen, 2003	1	1	1	1	1	1	1	1	1	9

[1] 1 point for validated self-reported questionnaires or interview
[2] 1 point for exclusion of prevalent cardiovascular disease or cancer cases
[3] 1 point for loss-to-follow-up less than 10%