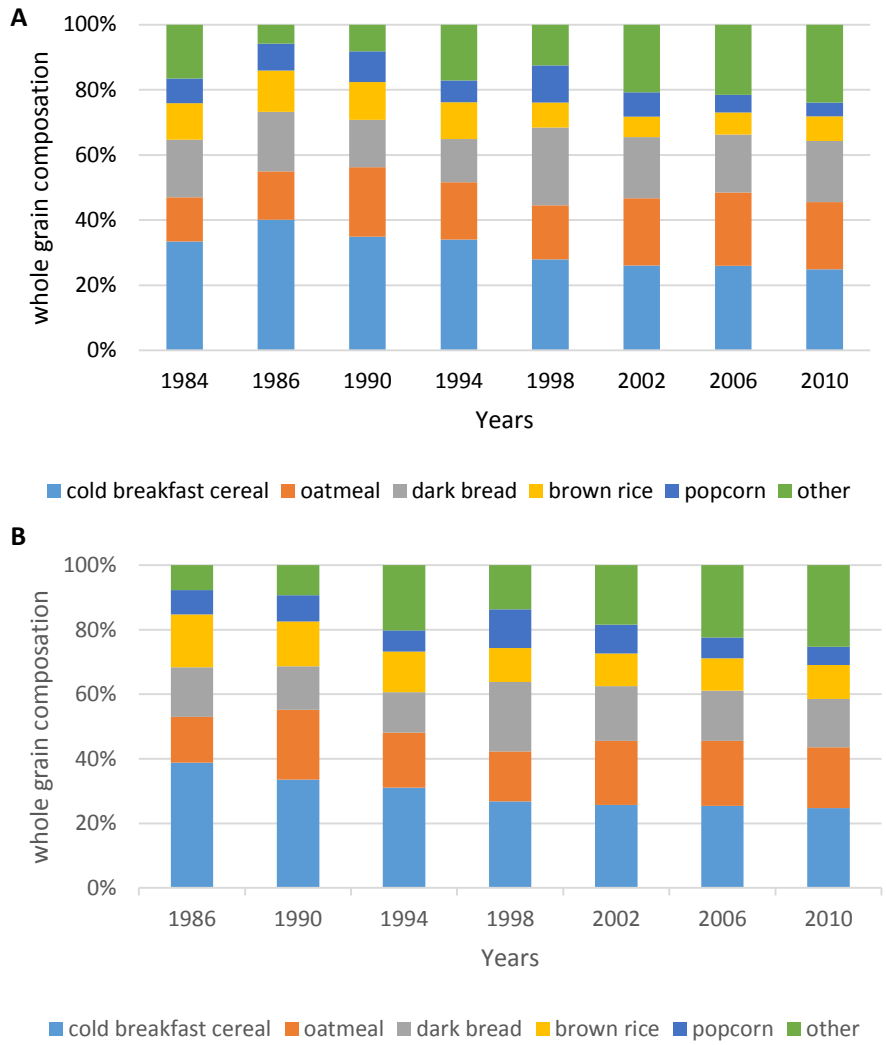
ONLINE SUPPLEMENT

Supplemental Methods

In both cohorts of the Nurses' Health Study (NHS) and Health Professionals Follow-up Study (HPFS), information on body height and weight, medical history, lifestyle characteristics (e.g., cigarette smoking and physical activity), disease diagnoses (e.g., diabetes, hypertension, and hypercholesterolemia), family history, menopausal status and postmenopausal hormone use (NHS only), and other characteristics were collected at baseline and updated at each biennial follow-up cycle using validated questionnaires. Through 2010, a response rate exceeding 90% has been achieved in each follow-up period of both cohorts. Detailed descriptions on the validity and reproducibility of self-reported body weight, physical activity, and alcohol consumption have been published elsewhere[1-3]. Body mass index (BMI) was calculated as weight divided by squared height (kg/m^2). Physical activity was expressed as metabolic equivalent (MET) hours per week by summing the product of moderate or vigorous exercise duration with MET value specific to each activity. Alcohol intake was assessed and updated by the semi-quantitative food frequency questionnaires (sFFQs) every four years. Total energy intake was calculated by summing up energy intakes from all foods. An alternative healthy eating index (aHEI) score was calculated by summarizing consumption of 11 foods and nutrients predictive of chronic disease risk, including fruits, vegetables, whole grains, nuts and legumes, red and processed meat, sugar-sweetened beverages and fruit juice, alcohol, sodium, *trans* fat, long-chain n-3 fat and polyunsaturated fat as an indicator of adherence to healthy eating behavior[4]. In the current study, we modified the aHEI score by excluding whole grain consumption.

To better represent long-term or habitual dietary pattern, and to minimize within-person variation, we calculated and applied the cumulative average of dietary intake based on the repeated valid sFFQ assessments. We replaced missing values in each sFFQ with cumulative averages based on prior valid assessments. To minimize reverse causation bias, we stopped updating information on diet after participants reported a diagnosis of diabetes, cardiovascular disease (CVD), or cancer during follow-up, because diagnosis of these conditions might lead to altered eating habits by consuming healthier foods including those rich in whole grains and therefore may confound the associations between whole grain consumption and risk of ischemic stroke. We then carried forward the cumulative averages of dietary variables prior to the development of these diseases to represent diet for later follow-up.

Supplemental Figure I. Intake of whole grain composition over the years in NHS and HPFS.



Intake of whole grain composition over the years in NHS (A) and HPFS (B). The areas of different colors represent the percent of total whole grains of each specific individual whole grain foods.

Abbreviations: NHS, Nurses' Health Study; HPFS, Health Professionals Follow-up Study.

Supplemental Table I. Baseline Characteristics of Participants according to Intake Levels of Total Whole Grain, the Nurses' Health Study (NHS, 1984) and Health Professionals Follow-up Study (HPFS, 1986).*

	Quintiles in NHS			Quintiles in HPFS		
	Q1	Q3	Q5	Q1	Q3	Q5
Participants, n	14307	14481	14371	8559	8492	8570
Age, years	50.1(7.1)	50.1(7.1)	50.2(7.2)	53.2(9.5)	53.2(9.6)	53.2(9.5)
Caucasian, %	97	98	98	92	96	95
BMI, kg/m^2	25.1(4.8)	25.1(4.5)	24.3(4.0)	25.2(5.2)	25.1(5.0)	24.3(4.7)
Alcohol intake, g/day	9.5(14.7)	7.0(10.8)	4.7(7.8)	14.6(18.9)	11.7(15.3)	8.2(11.4)
Physical activity, MET-hours/week	11.7(17.5)	14.2(21.6)	16.6(22.8)	18.1(29.0)	20.8(28.3)	26.2(33.8)
Total energy intake, kcal/day	1,712(553)	1,785(541)	1,654(477)	1,986(652)	2,061(640)	1,879(557)
Modified aHEI score†	42.8(9.9)	45.6(9.7)	49.5(10.6)	46.0(10.6)	49.8(10.3)	54.6(10.3)
Smoking status, %						
Never smoker	36	45	51	42	51	57
Past smoker	27	32	35	41	41	39
Current smoker	36	23	14	17	8	4
Family history of MI, %	39	39	38	31	31	33
Hypertension, %	22	20	18	23	19	18
High cholesterol, %	7	7	8	9	10	13
Multivitamin use, %	30	37	44	35	41	50
Ever menopausal hormone use, %	19	21	24	-	-	-
Total fruit intake, servings/day	1.79(1.12)	2.13(1.11)	2.31(1.12)	1.90(1.52)	2.37(1.52)	2.71(1.69)
Total vegetable intake, servings/day	2.33(1.04)	2.55(1.08)	2.61(1.14)	2.69(1.58)	3.08(1.65)	3.32(1.87)
Red meat intake, servings/day	0.95(0.59)	0.86(0.52)	0.64(0.45)	0.96(0.66)	0.83(0.58)	0.52(0.46)
Whole grains, g/day	2.23(1.16)	10.37(1.48)	34.03(14.20)	3.16(1.96)	16.84(2.31)	51.48(20.88)

Abbreviations: BMI, body mass index; MET, metabolic equivalent task; aHEI, alternative healthy eating index; MI, myocardial infarction.
*Values are means (SD) for continuous variables or % for categorical variables. All variables are age-standardized, except for age per se.
†Whole grains are excluded when calculating the alternative healthy eating index.

Supplemental Table II. Hazard Ratio (95% CI) of Ischemic Stroke according to Quintiles of Whole Grain Intake among participants in NHS and HPFS.

	Quintiles of Whole Grain Intake					P_{trend}
	Q1	Q2	Q3	Q4	Q5	
NHS						
Median	4.43	10.10	15.15	21.46	33.23	
No. of cases/ Person-years	328/365029	262/367305	310/368956	282/368999	368/368557	
Age-adjusted model*	1.00	0.77(0.66,0.91)	0.87(0.75,1.02)	0.73(0.62,0.86)	0.84(0.72,0.97)	0.07
HPFS						
Median	5.92	14.47	22.35	31.50	47.90	
No. of cases/ Person-years	188/194616	223/196243	167/196459	147/197139	183/196825	
Age-adjusted model*	1.00	1.25(1.03,1.51)	0.90(0.73,1.11)	0.76(0.61,0.95)	0.92(0.75,1.13)	0.01
Pooled†						
Age-adjusted model*	1.00	0.94(0.83, 1.07)	0.88(0.78, 1.00)	0.74(0.65, 0.84)	0.86(0.77, 0.98)	0.002

Abbreviations: CI, confidence interval; NHS, Nurses' Health Study; HPFS, Health Professionals Follow-up Study.

* Age-adjusted model was adjusted for age (years).

† Pooled hazard ratios were calculated using a fixed-effects meta-analysis.

Supplemental Table III. Hazard Ratio (95% CI) of Ischemic Stroke by Individual Whole Grain Foods Intake among participants in NHS and HPFS.

	Individual Whole Grain Foods			Every 1 serving/day	P_{trend}
	< 1 serving/month	1 serving/month - 1 serving/week	> 1 serving/week		
Whole grain cold breakfast cereal					
NHS					
No. of cases/ Person-years	386/423700	224/263805	940/1151403		
Age-adjusted model *	1.00	0.89(0.76,1.05)	0.81(0.72,0.91)	0.86(0.74,1.00)	<0.001
HPFS					
No. of cases/ Person-years	275/262406	122/134968	511/583908		
Age-adjusted model *	1.00	0.94(0.75,1.16)	0.82(0.70,0.95)	0.80(0.66,0.96)	0.006
Pooled[†]					
Age-adjusted model *	1.00	0.91(0.80, 1.04)	0.81(0.74, 0.89)	0.83(0.74,0.94)	<0.001
Oatmeal					
NHS					
No. of cases/ Person-years	543/674537	603/798228	404/366143		
Age-adjusted model *	1.00	1.04(0.92,1.17)	0.98(0.86,1.11)	0.87(0.65,1.15)	0.55
HPFS					
No. of cases/ Person-years	424/458739	246/274888	238/247655		
Age-adjusted model *	1.00	0.92(0.78,1.07)	0.83(0.70,0.97)	0.79(0.57,1.09)	0.02
Pooled[†]					
Age-adjusted model *	1.00	0.99(0.90, 1.09)	0.91(0.82, 1.01)	0.83(0.67,1.03)	0.06
Dark Bread					
NHS					
No. of cases/ Person-years	103/130512	176/236539	1271/1471857		
Age-adjusted model *	1.00	1.03(0.80,1.31)	0.96(0.78,1.17)	1.00(0.96,1.05)	0.38
HPFS					
No. of cases/ Person-years	130/124924	122/153822	656/702536		
Age-adjusted model *	1.00	0.83(0.65,1.07)	0.87(0.72,1.05)	0.96(0.87,1.05)	0.44

Pooled†					
Age-adjusted model *	1.00	0.93(0.78, 1.10)	0.91(0.79, 1.04)	0.99(0.95,1.03)	0.24
Brown Rice					
NHS					
No. of cases/ Person-years	1029/1248570	399/474292	122/116045		
Age-adjusted model *	1.00	0.95(0.84,1.07)	1.05(0.86,1.28)	1.00(0.93,1.07)	0.82
HPFS					
No. of cases/ Person-years	438/444974	352/387185	118/149123		
Age-adjusted model *	1.00	1.04(0.90,1.19)	1.00(0.81,1.22)	0.93(0.52,1.66)	0.96
Pooled†					
Age-adjusted model *	1.00	0.98(0.90, 1.08)	1.02(0.89, 1.18)	1.00(0.93,1.07)	0.83
Popcorn					
NHS					
No. of cases/ Person-years	473/478234	719/963695	358/396979		
Age-adjusted model *	1.00	1.14(1.01,1.28)	1.19(1.03,1.36)	1.01(0.98,1.03)	0.04
HPFS					
No. of cases/ Person-years	318/279858	316/376635	274/324789		
Age-adjusted model *	1.00	0.94(0.80,1.10)	1.08(0.91,1.27)	1.04(0.83,1.30)	0.22
Pooled†					
Age-adjusted model *	1.00	1.06(0.97, 1.17)	1.14(1.02, 1.27)	1.01(0.98,1.03)	0.02

Abbreviations: CI, confidence interval; NHS, Nurses' Health Study; HPFS, Health Professionals Follow-up Study.

* Age-adjusted model was adjusted for age (years).

† Pooled hazard ratios were calculated using a fixed-effects meta-analysis.

Supplemental Table IV. Hazard Ratio (95% CI) of Ischemic Stroke by Regular and Light/Fat-free Popcorn Intakes among participants in NHS and HPFS (2002-2010).

	Regular Popcorn intake			P_{trend}	Light/Fat-free Popcorn Intake			P_{trend}
	< 1 serving /month	1 serving/month - 1 serving/week	> 1 serving /week		< 1 serving /month	1 serving/month - 1 serving/week	> 1 serving /week	
NHS								
No. of cases	440	120	38		421	127	50	
Person-years	430693	121193	29293		384883	145995	50301	
Model 1*	1.00	1.20(0.98,1.48)	1.58(1.12,2.24)	0.005	1.00	0.99(0.81,1.21)	1.20(0.89,1.63)	0.24
Model 2†	1.00	1.20(0.97,1.47)	1.51(1.06,2.14)	0.01	1.00	1.00(0.81,1.23)	1.17(0.86,1.58)	0.34
Model 3‡	1.00	1.21(0.98,1.49)	1.45(1.01,2.07)	0.02	1.00	1.00(0.81,1.22)	1.11(0.81,1.53)	0.51
HPFS								
No. of cases	90	49	26		118	31	16	
Person-years	97183	60119	25798		118067	44469	20564	
Model 1*	1.00	1.08(0.76,1.54)	1.19(0.77,1.85)	0.42	1.00	0.88(0.58,1.31)	0.93(0.55,1.58)	0.70
Model 2†	1.00	1.03(0.72,1.48)	1.16(0.74,1.81)	0.55	1.00	0.90(0.60,1.35)	0.96(0.57,1.63)	0.80
Model 3‡	1.00	1.06(0.73,1.52)	1.19(0.76,1.86)	0.46	1.00	0.88(0.58,1.33)	0.94(0.55,1.60)	0.73
Pooled§								
Model 1*	1.00	1.17(0.98, 1.40)	1.42(1.08, 1.86)	0.003	1.00	0.97(0.81,1.16)	1.13(0.87,1.47)	0.31
Model 2†	1.00	1.15(0.96, 1.38)	1.36(1.03, 1.80)	0.01	1.00	0.98(0.81,1.17)	1.11(0.85,1.45)	0.40
Model 3‡	1.00	1.17(0.98, 1.40)	1.34(1.01, 1.77)	0.02	1.00	0.97(0.81,1.17)	1.07(0.81,1.40)	0.60

Abbreviations: CI, confidence interval; NHS, Nurses' Health Study; HPFS, Health Professionals Follow-up Study.

* Model 1 was adjusted for age (years).

† Model 2 was further adjusted for BMI (<18.5, 18.5-22.9, 23.0-24.9, 25.0-29.9, 30.0-34.9, or ≥35.0 kg/m^2), smoking status (never, past, current [1-14,15-24, or ≥25 cigarettes/day]), alcohol intake (0, 0.1-4.9, 5.0-14.9, ≥15.0 g/day for women and 0, 0.1-4.9, 5.0-29.9 or ≥30.0 g/day for men), physical activity (quintiles), family history of diabetes, cancer and heart disease(yes or no), multivitamin use(yes or no), hypertension, high cholesterol at baseline (yes or no), total energy intake (kcal/day) and modified alternative health eating index score, which did not include whole

grains, as a summary measure of diet quality. For women, menopausal status and postmenopausal hormone use were further adjusted for.
‡ Model 3 was further adjusted for butter (serving/day), high fat dairy (g/day), refined grain (g/day) and saturated fat (g/day).
§ Pooled hazard ratios were calculated using a fixed-effects meta-analysis.

Supplemental Table V. Hazard Ratio (95% CI) of Ischemic Stroke by Individual Whole Grain Ingredients Intake among participants in NHS and HPFS.

	Individual Whole Grain Ingredients			P_{trend}
	T1	T2	T3	
Total Bran‡				
NHS				
Median	1.10	3.64	8.50	
No. of cases/ Person-years	489/610232	516/615654	545/613022	
Age-adjusted model *	1.00	1.00(0.88,1.15)	0.89(0.77,1.03)	0.04
HPFS				
Median	1.30	4.85	11.91	
No. of cases/ Person-years	334/325482	298/328270	276/327530	
Age-adjusted model *	1.00	0.88(0.74,1.05)	0.70(0.58,0.84)	<0.001
Pooled†				
Age-adjusted model *	1.00	0.96(0.86, 1.06)	0.81(0.72, 0.91)	<0.001
Total Germ‡				
NHS				
Median	0.26	0.63	1.26	
No. of cases/ Person-years	549/603767	480/611376	521/623764	
Age-adjusted model *	1.00	0.90(0.79,1.03)	0.94(0.81,1.08)	0.62
HPFS				
Median	0.34	0.90	1.80	
No. of cases/ Person-years	355/333085	272/321337	281/326860	
Age-adjusted model *	1.00	0.94(0.79,1.12)	1.03(0.86,1.24)	0.66
Pooled†				
Age-adjusted model *	1.00	0.92(0.82, 1.02)	0.97(0.87, 1.09)	1.00

Abbreviations: CI, confidence interval; NHS, Nurses' Health Study; HPFS, Health Professionals Follow-up Study.

* Age-adjusted model was adjusted for age (years).

† Pooled hazard ratios were calculated using a fixed-effects meta-analysis.

ǂ Total bran and total germ were mutually adjusted in all models.

Supplemental References

1. Rimm EB, Stampfer MJ, Colditz GA, Chute CG, Litin LB, Willett WC. Validity of self-reported waist and hip circumferences in men and women. *Epidemiology*. 1990;1:466-473
2. Giovannucci E, Colditz G, Stampfer MJ, Rimm EB, Litin L, Sampson L, et al. The assessment of alcohol consumption by a simple self-administered questionnaire. *Am J Epidemiol*. 1991;133:810-817
3. Chasan-Taber S, Rimm EB, Stampfer MJ, Spiegelman D, Colditz GA, Giovannucci E, et al. Reproducibility and validity of a self-administered physical activity questionnaire for male health professionals. *Epidemiology*. 1996;7:81-86
4. Chiuve SE, Fung TT, Rimm EB, Hu FB, McCullough ML, Wang M, et al. Alternative dietary indices both strongly predict risk of chronic disease. *The Journal of nutrition*. 2012;142:1009-1018