## **Supplements**

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eFigure 1. Subgroup analysis, association between laxative use and the risk of all-cause dementia

Subgroup	No of participants		Hazard Ratio (95% CI) P intera	
Baseline age	_		0.1	7
< 65	386 609		1.54 (1.21 to 1.96)	
≥ 65	89 610	_ <del>-</del>	1.51 (1.25 to 1.82)	
Gender			0.3	4
Women	259 480		1.33 (1.08 to 1.63)	
Men	216 739		1.75 (1.41 to 2.17)	
SES			0.7	8
Above median	233 554		1.58 (1.30 to 1.91)	•
Below median	242 665	_	1.42 (1.12 to 1.80)	
Ethnicity	242 005		0.3	
Non-white	22 474		1.98 (1.10 to 3.59)	
White		-		
	453 745		1.48 (1.27 to 1.72)	
Education level			0.2	4
University or higher	228 553	_	1.65 (1.26 to 2.16	
Others	247 666		1.47 (1.23 to 1.75)	
Alcohol consumption			0.0	3
Never or occasionally	89 307	-	1.80 (1.44 to 2.25)	
Monthly or weekly ≤ 14 units	169 387	<del>-</del>	1.00 (0.74 to 1.37)	
Weekly > 14 units	217 525	-	1.71 (1.31 to 2.23)	
Processed meat consumption			0.8	9
≤ once a week	328 620		1.53 (1.27 to 1.84)	
> once a week	147 599		1.51 (1.18 to 1.94)	
Stroke			0.0	ā
Yes	6797		0.91 (0.51 to 1.63)	
No	469 422		1.59 (1.36 to 1.85)	
High blood pressure	409 422		1.59 (1.36 to 1.65)	
Yes	100.077			.5
	126 977	_	1.44 (1.15 to 1.80)	
No	349 242		1.57 (1.29 to 1.92)	
Depression			0.3	8
Yes	14 220	•	1.68 (0.98 to 2.88)	
No	461 999	<u>-</u>	1.52 (1.30 to 1.77)	
Overall health rating			0.7	1
Excellent or good	358 378		1.64 (1.28 to 2.09)	
Fair	97 854		1.36 (1.06 to 1.75)	
Poor	19 987	<del>-</del>	1.79 (1.35 to 2.37)	
Long-standing illness, disability or infirmit			0.9	1
Yes	148 716		1.56 (1.31 to 1.85)	
No	327 503	_ <del>-</del> _	1.41 (1.05 to 1.89)	
Anticholinergic drugs			0.0	1
Yes	19 816	<b></b>	1.20 (0.86 to 1.67)	
No	456 403		1.64 (1.39 to 1.93)	
NO Calcium channel blocker drugs	400 400		1.64 (1.39 to 1.93)	
	28 646			
Yes			1.78 (1.24 to 2.56)	
No	447 573	<del></del>	1.48 (1.26 to 1.75)	
Opioid			0.0	13
Yes	13 700	-	1.02 (0.65 to 1.60)	
No	462 519	L- <del></del>	1.60 (1.37 to 1.87)	
Statin			0.4	2
Yes	73 924	-	1.71 (1.36 to 2.14)	
No	402 295		1.39 (1.14 to 1.69)	
Steroids			0.7	9
Yes	17 986	-	1.55 (1.01 to 2.38)	-
No	458 233		1.53 (1.30 to 1.79)	
110	700 £00		1.00 (1.00 to 1.70)	

Note: The model is fully adjusted for sociodemographic variables, lifestyle factors, medical conditions and status of regular medication use. The Bonferroni-corrected significance level is 0.003 (original  $\alpha = 0.05$ , number of tests = 17). Difference between subgroups is statistically significant only when the P-interaction is lower than 0.003.

eFigure 2. Subgroup analysis, association between laxative use and the risk of vascular dementia

Subgroup	No of participants		Hazard Ratio (95% CI)	P interaction
Baseline age				0.67
< 65	386 609	-	1.61 (0.93 to 2.80)	
≥ 65	89 610	L	1.68 (1.14 to 2.47)	
Gender				0.85
Women	259 480	_ <del>-</del> _	1.57 (0.97 to 2.52)	
Men	216 739	_ <b>-</b>	1.69 (1.10 to 2.58)	
SES				0.26
Above median	233 554		1.94 (1.33 to 2.83)	
Below median	242 665		1.16 (0.64 to 2.12)	
Ethnicity			1.10 (0.04 to 2.12)	0.61
Non-white	22 474	_	1.86 (0.58 to 5.91)	0.01
White				
	453 745		1.60 (1.15 to 2.23)	
Education level				0.13
University or higher	228 553	_ <del>-</del>	2.04 (1.18 to 3.53)	
Others	247 666	L	1.53 (1.04 to 2.26)	
Alcohol consumption				0.68
Never or occasionally	89 307	_ <del>-</del>	1.91 (1.20 to 3.06)	
Monthly or weekly ≤ 14 units	169 387	+	1.29 (0.68 to 2.43)	
Weekly > 14 units	217 525	-	1.76 (0.97 to 3.19)	
Processed meat consumption				0.24
≤ once a week	328 620		1.79 (1.23 to 2.61)	
> once a week	147 599	_ <del>-</del>	1.40 (0.78 to 2.53)	
Stroke	147 555		1.40 (0.70 to 2.53)	0.34
Yes	6 797		1.23 (0.54 to 2.81)	0.34
No				
	469 422	<del></del>	1.74 (1.23 to 2.45)	
High blood pressure				0.6
Yes	126 977	-	1.59 (1.05 to 2.39)	
No	349 242	<del></del>	1.73 (1.05 to 2.85)	
Depression				0.93
Yes	14 220	· ·	1.65 (0.49 to 5.59)	
No	461 999	<del>-</del>	1.64 (1.18 to 2.28)	
Overall health rating				0.28
Excellent or good	358 378	<b>-</b>	2.26 (1.34 to 3.80)	
Fair	97 854		1.26 (0.73 to 2.18)	
Poor	19 987		1.71 (0.96 to 3.04)	
Long-standing illness, disability or infirmity				0.77
Yes	148 716	_ <b>-</b> _	1.63 (1.14 to 2.34)	
No	327 503		1.64 (0.85 to 3.17)	
Anticholinergic drugs	321 303	<del></del>	1.04 (0.00 to 3.17)	0.91
Anticholinergic drugs Yes	19 816	_	4 70 (0 00 +- 2 00)	0.91
			1.72 (0.88 to 3.33)	
No	456 403	<del></del>	1.62 (1.13 to 2.33)	
Calcium channel blocker drugs				0.04
Yes	28 646	<del>-</del>	2.84 (1.59 to 5.07)	
No	447 573	L <del></del>	1.37 (0.94 to 2.01)	
Opioid				0.43
Yes	13 700	-	1.20 (0.43 to 3.32)	
No	462 519	_ <b></b>	1.72 (1.23 to 2.39)	
Statin		rr		0.34
Yes	73 924		1.93 (1.28 to 2.91)	
No	402 295		1.34 (0.81 to 2.21)	
Steroids		<del>-</del>	1.34 (0.81 to 2.21)	0.65
	47.000	_	4 40 (0 00 4- 0 00)	0.05
Yes	17 986		1.49 (0.69 to 3.22)	
No	458 233	-	1.64 (1.15 to 2.33)	

Note: The model is fully adjusted for sociodemographic variables, lifestyle factors, medical conditions and status of regular medication use. The Bonferroni-corrected significance level is 0.003 (original  $\alpha = 0.05$ , number of tests = 17). Difference between subgroups is statistically significant only when the P-interaction is lower than 0.003.

eTable 1. Description of covariates used in the present study.

Measure	Description	Reference group
Sociodemographic variables		
Sex	Female vs. male (Field 31)	Male
Ethnicity	White vs. non-white (Field 21000)	White
Education	University degree or higher vs. degree lower than university (Field 6138)	Degree lower than university
	Townsend deprivation score, based on the preceding national census output areas.	
Socio-economic status	Each participant is assigned a score corresponding to the output area in which their postcode is located. It combines information on social class, employment, car availability and housing: categorized as quintiles 1 (Low), 2 to 4 (Intermediate), and 5(High) (Field 189)	Low
Lifestyle factors		
Smoking status	Touchscreen question: self-reported as never, ex-smoker, or current smoker (Field 20116)	Never
Alcohol consumption	Touchscreen question: categorized as never or occasionally, monthly or weekly lower than 14 units, weekly and more than 14 units (Fields in category 100051)	Never or occasionally
Living alone	Touchscreen question: Including yourself, how many people are living together in your household? (Include those who usually live in the house such as students living away from home during term, partners in the armed forces or professions such as pilots) (Field 709)	Not living alone

Vegetable consumption (servings)	Touchscreen question: total servings of cooked and raw vegetable intake (Field 1289, 1299). One serving of vegetable is defined as 1 cup of raw leafy vegetables; ½ cup of cut-up raw vegetables, cooked vegetables, or 100% vegetable juice.	
Fruit consumption (servings)	Touchscreen question: total servings of fresh and dried fruit intake (Field 1309, 1319). One serving of fruit consumption is defined as 1 medium-sized fruit; ½ cup of fresh, frozen, or unsweetened canned fruit; ½ cup of dried fruit; ½ cup of 100% juice.	
Fish consumption	Touchscreen question: frequency of oily and non-oily fish intake (Field 1329, 1339)	Less than twice a week
Processed meat consumption	Touchscreen question: frequency of processed meat intake (Field 1349)	More than once a week
Unprocessed red meat consumption	Touchscreen question: frequency of beef, lamb and pork intake (Field 1369, 1379, 1389)	More than once a week
Physical activities	Touchscreen question: duration of moderate, vigorous activities and number of days/week of moderate or vigorous physical activity 10+ minutes. (Field 894, 914, 884, 904), activity strength was categorized according to World Health Organization recommendations: low = activity less than moderate; moderate activity = 2.5 hr/week moderate or 75 minutes/week vigorous, or > once per week, or equivalent; high activity (for additional health benefits) = 300 minutes/week moderate or 150 minutes/week vigorous, or equivalent.	High

Body mass index	Physical measures: BMI value was constructed from height and weight measured in the initial Assessment Centre visit. (Field 21001)	
Medical conditions		
Cognitive function (reaction time)	The mean duration to first press of snap-button summed over rounds in which both cards matched. It gives a crude measure of the raw processing and reaction speed of a participant. (Field 20023)	
Diabetes	Touchscreen question and verbal interview: self-reported regular use of insulin, or at nurse interview, reported diagnosis or taking of a diabetes-related medication (Field 6177, 6153, 20002, 20003)	No diabetes
Heart attack		No heart attack
Stroke	Touchscreen question: has a doctor ever told you that you have had any of the following conditions (heart attack, stroke, high blood pressure, etc.) at baseline	No stroke
High blood pressure	assessment (Field 6150)	No high blood pressure
Parkinson's disease	Whether one had records in Parkinson's disease at baseline, using UK Biobank algorithmically-defined outcome. (Field 42030)	No Parkinson's disease
Inflammatory bowel disease	Verbal interview: self-reported non-cancer illness at baseline. (Field 20002)	No inflammatory bowel disease

Depression	Touchscreen question: A combined score of .3 on the first two items of the Patient Health Questionnaire (PHQ-2) that assess the two core criteria of depression experienced in the previous two weeks, or whether participant ever visited a GP for depression or anxiety. (Field 2050, 2060, 2090)	No depression
Family history of dementia	Touchscreen question: self-reported father/mother/sibling with dementia diagnosis Alzheimer's disease/dementia. (Field 20107, 20110, 20111)	No family history of dementia
Overall health rating	Touchscreen question: in general, how would you rate your overall health, with options of poor, fair, good and excellent. (Field 2178)	Excellent
Long-standing illness, disability or infirmity	Touchscreen question: do you have any long-standing illness, disability or infirmity. (Field 2188)	No long-standing illness, disability nor infirmities
Status of regular medication use		
Anticholinergic drugs		No regular use
Calcium channel blocker drugs	Verbal interview: among participants who reported regularly taking other	No regular use
Opioid	prescription medications (Field 2492), whether one has reported anticholinergic,	No regular use
Statin	calcium channel blocker, opioid, statin, antidiarrhoeal or steroids in verbal interview	No regular use
Antidiarrhoeal	(Field 20003). Medications were categorized according to British National Formula.	No regular use
Steroids		No regular use

eTable 2. Baseline characteristics of data used for primary analysis and data excluded.

	Kept in pr		
Total	Yes	No	SMD*
502 229	476 219 (94.8)	26 010 (5.2)	
56.5 (8.1)	56.5 (8.1)	57.4 (8.3)	0.11
273 251 (54.4)	259 480 (54.5)	13 771 (52.9)	0.03
27 017 (5.4)	22 474 (4.7)	4543 (17.5)	0.42
234 905 (46.8)	228 553 (48.0)	6352 (24.4)	0.51
			0.45
100 607 (20.1)	97 781 (20.5)	2826 (11.1)	
300 702 (59.9)	287 875 (60.5)	12 827 (50.5)	
100 297 (20.0)	90 563 (19.0)	9734 (38.3)	
			0.18
273 384 (54.8)	261 141 (54.8)	12 243 (53.1)	
172 949 (34.6)	166 056 (34.9)	6893 (29.9)	
52 951 (10.6)	49 022 (10.3)	3929 (17.0)	
			0.42
98 565 (19.7)	89 307 (18.8)	9258 (38.0)	
176 809 (35.3)	169 387 (35.6)	7422 (30.5)	
225 209 (45.0)	217 525 (45.7)	7684 (31.5)	
92 858 (18.5)	87 033 (18.3)	5825 (22.4)	0.10
4.9 (3.4)	4.9 (3.3)	5.0 (4.3)	0.02
3.1 (2.6)	3.1 (2.6)	3.1 (3.3)	0.01
259 955 (51.8)	248 273 (52.1)	11 682 (44.9)	0.15
345 012 (68.7)	328 620 (69.0)	16 392 (63.0)	0.13
341 201 (67.9)	324 820 (68.2)	16 381 (63.0)	0.11
	502 229 56.5 (8.1) 273 251 (54.4) 27 017 (5.4) 234 905 (46.8) 100 607 (20.1) 300 702 (59.9) 100 297 (20.0) 273 384 (54.8) 172 949 (34.6) 52 951 (10.6) 98 565 (19.7) 176 809 (35.3) 225 209 (45.0) 92 858 (18.5) 4.9 (3.4) 3.1 (2.6) 259 955 (51.8) 345 012 (68.7)	Total         Yes           502 229         476 219 (94.8)           56.5 (8.1)         56.5 (8.1)           273 251 (54.4)         259 480 (54.5)           27 017 (5.4)         22 474 (4.7)           234 905 (46.8)         228 553 (48.0)           100 607 (20.1)         97 781 (20.5)           300 702 (59.9)         287 875 (60.5)           100 297 (20.0)         90 563 (19.0)           273 384 (54.8)         261 141 (54.8)           172 949 (34.6)         166 056 (34.9)           52 951 (10.6)         49 022 (10.3)           98 565 (19.7)         89 307 (18.8)           176 809 (35.3)         169 387 (35.6)           225 209 (45.0)         217 525 (45.7)           92 858 (18.5)         87 033 (18.3)           4.9 (3.4)         4.9 (3.3)           3.1 (2.6)         3.1 (2.6)           259 955 (51.8)         248 273 (52.1)           345 012 (68.7)         328 620 (69.0)	502 229       476 219 (94.8)       26 010 (5.2)         56.5 (8.1)       56.5 (8.1)       57.4 (8.3)         273 251 (54.4)       259 480 (54.5)       13 771 (52.9)         27 017 (5.4)       22 474 (4.7)       4543 (17.5)         234 905 (46.8)       228 553 (48.0)       6352 (24.4)         100 607 (20.1)       97 781 (20.5)       2826 (11.1)         300 702 (59.9)       287 875 (60.5)       12 827 (50.5)         100 297 (20.0)       90 563 (19.0)       9734 (38.3)         273 384 (54.8)       261 141 (54.8)       12 243 (53.1)         172 949 (34.6)       166 056 (34.9)       6893 (29.9)         52 951 (10.6)       49 022 (10.3)       3929 (17.0)         98 565 (19.7)       89 307 (18.8)       9258 (38.0)         176 809 (35.3)       169 387 (35.6)       7422 (30.5)         225 209 (45.0)       217 525 (45.7)       7684 (31.5)         92 858 (18.5)       87 033 (18.3)       5825 (22.4)         4.9 (3.4)       4.9 (3.3)       5.0 (4.3)         3.1 (2.6)       3.1 (3.3)         259 955 (51.8)       248 273 (52.1)       11 682 (44.9)         345 012 (68.7)       328 620 (69.0)       16 392 (63.0)

Physical activities:				0.16
Low	207 775 (42.4)	201 789 (42.4)	5986 (43.6)	
Moderate	124 399 (25.4)	120 178 (25.2)	4221 (30.7)	
High	157 778 (32.2)	154 252 (32.4)	3526 (25.7)	
Mean (SD) cognitive function (reaction time)	559.6 (117.9)	557.8 (115.8)	603.4 (154.7)	0.33
Diabetes	26 057 (5.2)	23 456 (4.9)	2601 (10.0)	0.19
Heart attack	11 588 (2.3)	10 592 (2.2)	996 (3.8)	0.09
Stroke	7647 (1.5)	6797 (1.4)	850 (3.3)	0.12
High blood pressure	135 662 (27.0)	126 977 (26.7)	8685 (33.4)	0.15
Parkinson's disease	936 (0.2)	851 (0.2)	85 (0.3)	0.03
Inflammatory bowel disease	4227 (0.8)	4030 (0.8)	197 (0.8)	0.01
Mean (SD) body mass index	27.4 (4.8)	27.4 (4.8)	28.7 (5.4)	0.26
Depression	15 980 (3.2)	14 220 (3.0)	1760 (6.8)	0.18
Family history of dementia	58 308 (11.6)	55 978 (11.8)	2330 (9.0)	0.09
Overall health rating:				0.49
Excellent	81 842 (16.4)	80 099 (16.8)	1743 (7.7)	
Good	288 913 (57.9)	278 279 (58.4)	10 634 (47.2)	
Fair	105 274 (21.1)	97 854 (20.5)	7420 (32.9)	
Poor	22 719 (4.6)	19 987 (4.2)	2732 (12.1)	
Long-standing illness, disability or infirmity	159 704 (31.8)	148 716 (31.2)	10 988 (42.2)	0.23
Anticholinergic drugs	21 846 (4.3)	19 816 (4.2)	2030 (7.8)	0.15
Calcium channel blocker drugs	30 973 (6.2)	28 646 (6.0)	2327 (8.9)	0.11
Opioid	15 355 (3.1)	13 700 (2.9)	1655 (6.4)	0.17
Statin	79 463 (15.8)	73 924 (15.5)	5539 (21.3)	0.15
Antidiarrhoeal	383 (0.1)	358 (0.1)	25 (0.1)	0.01
Steroid	19 044 (3.8)	17 986 (3.8)	1058 (4.1)	0.02

The numbers in the parenthesis are column percentages, unless stated otherwise.

\* SMD is standardized mean differences shown as an absolute value, which indicates meaningful imbalance if its value is greater than 0.1.

eTable 3. Association of regular use of specific types of laxatives with the risk of all-cause dementia (comparison with bulk-forming).

	All-cause dementia					
Laxative class	cases/total	HR (95% CI)				
<b>Bulk-forming</b>	19/2339 (0.8)	1 (ref)				
Softening	6/315 (1.9)	1.57 (0.59 to 4.17)				
Osmotic	44/2051 (2.1)	2.10 (1.20 to 3.69)**				
Stimulant	18/1095 (1.6)	1.25 (0.62 to 2.53)				

This analysis included 5800 participants who reported the use of only one type of laxatives. The model is fully adjusted for sociodemographic variables, lifestyle factors, medical conditions and status of regular medication use.

eTable 4. Association between regular laxative use and risk of all-cause dementia, Alzheimer's disease, and vascular dementia in competing risk analysis.†

	Regular laxative users		Cox regression Competing risk analysis		No of
	Yes	No			competing
Outcomes	(n = 16703)	(n = 459516)	HR (95% CI)	HR (95% CI)	(death)
All-cause dementia	218 (1.3)	1969 (0.4)	1.51 (1.30 to 1.75)***	1.52 (1.30 to 1.77)***	25 920
Alzheimer's disease	55 (0.3)	769 (0.2)	1.05 (0.79 to 1.40)	1.04 (0.78 to 1.40)	26 756
Vascular dementia	47 (0.3)	403 (0.1)	1.65 (1.21 to 2.27)**	1.62 (1.17 to 2.24)**	26 954

The model is fully adjusted for sociodemographic variables, lifestyle factors, medical conditions and status of regular medication use. †Modified Fine and Gray competing risk analysis.

eTable 5. Association between regular laxative use and risk of all-cause dementia, Alzheimer's disease, and vascular dementia after excluding 106 participants diagnosed with dementia within first two years of follow-up

	Regular laxativ	ve users		Hazard rat	io (95% CI)	
	Yes	No				
Outcomes	(n = 16683)	$(n = 459 \ 430)$	Model 1†	Model 2‡	Model 3¶	Model 4§
All-cause dementia	198 (1.2)	1883 (0.4)	2.39 (2.06 to 2.77)***	2.24 (1.93 to 2.60)***	1.53 (1.31 to 1.78)***	1.45 (1.24 to 1.69)***
Alzheimer's disease	51 (0.3)	746 (0.2)	1.47 (1.11 to 1.96)**	1.39 (1.05 to 1.85)**	1.06 (0.79 to 1.42)	1.01 (0.75 to 1.35)
Vascular dementia	39 (0.2)	388 (0.1)	2.35 (1.69 to 3.28)***	2.13 (1.52 to 2.97)***	1.50 (1.07 to 2.10)*	1.44 (1.03 to 2.03)*

<sup>†</sup>Adjusted for sociodemographic variables: age (time scale), sex, ethnicity, education, and socio-economic status.

<sup>‡</sup>Additionally adjusted for lifestyle factors: smoking status, alcohol consumption, living alone, dietary consumption of vegetable, fruit, fish, and processed/unprocessed meat, physical activities, and body mass index.

<sup>¶</sup>Additionally adjusted for medical conditions: diabetes, heart attack, stroke, high blood pressure, Parkinson's disease, inflammatory bowel disease, depression, cognitive test, family history of dementia, overall health rating and long-standing illness.

<sup>§</sup>Additionally adjusted for status of regular medication use: opioids, anticholinergic drugs, statins, calcium channel blockers, antidiarrheal agents, and steroids.

eTable 6. Association between regular laxative use and risk of all-cause dementia, Alzheimer's disease, and vascular dementia after excluding 393 participants diagnosed with dementia within first four years of follow-up.

	Regular laxativ	e users	Hazard ratio (95% CI)				
	Yes	No					
Outcomes	(n = 16 655)	(n = 459 171)	Model 1†	Model 2†	Model 3¶	Model 4§	
All-cause dementia	170 (1.0)	1624 (0.4)	2.35 (2.01 to 2.76)***	2.20 (1.88 to 2.59)***	1.53 (1.30 to 1.81)***	1.44 (1.22 to 1.71)***	
Alzheimer's disease	44 (0.3)	642 (0.1)	1.48 (1.09 to 2.01)*	1.39 (1.02 to 1.89)*	1.07 (0.78 to 1.47)	1.01 (0.74 to 1.39)	
Vascular dementia	32 (0.2)	335 (0.1)	2.19 (1.52 to 3.16)***	1.97 (1.36 to 2.84)***	1.42 (0.98 to 2.06)	1.35 (0.93 to 1.97)	

§Additionally adjusted for status of regular medication use: opioids, anticholinergic drugs, statins, calcium channel blockers, antidiarrheal agents, and steroids.

<sup>†</sup>Adjusted for sociodemographic variables: age (time scale), sex, ethnicity, education, and socio-economic status.

<sup>‡</sup>Additionally adjusted for lifestyle factors: smoking status, alcohol consumption, living alone, dietary consumption of vegetable, fruit, fish, and processed/unprocessed meat, physical activities, and body mass index.

<sup>¶</sup>Additionally adjusted for medical conditions: diabetes, heart attack, stroke, high blood pressure, Parkinson's disease, inflammatory bowel disease, depression, cognitive test, family history of dementia, overall health rating and long-standing illness.

eTable 7. Association between regular laxative use and risk of all-cause dementia, Alzheimer's disease, and vascular dementia after multiple imputation.

	Regular laxativ	ve users				
	Yes	No				
Outcomes	$(n = 18 \ 235)$	(n = 483 994)	Model 1†	Model 2‡	Model 3¶	Model 4§
All-cause dementia	258 (1.4)	2244 (0.5)	2.51 (2.20 to 2.86)***	2.35 (2.06 to 2.68)***	1.60 (1.40 to 1.83)***	1.53 (1.34 to 1.76)***
Alzheimer's disease	65 (0.4)	865 (0.2)	1.56 (1.21 to 2.01)**	1.47 (1.14 to 1.89)**	1.12 (0.87 to 1.45)	1.07 (0.83 to 1.39)
Vascular dementia	59 (0.3)	466 (0.1)	2.82 (2.14 to 3.71)***	2.56 (1.94 to 3.37)***	1.72 (1.30 to 2.28)***	1.66 (1.25 to 2.20)***

§Additionally adjusted for status of regular medication use: opioids, anticholinergic drugs, statins, calcium channel blockers, antidiarrheal agents, and steroids.

<sup>†</sup>Adjusted for sociodemographic variables: age (time scale), sex, ethnicity, education, and socio-economic status.

<sup>‡</sup>Additionally adjusted for lifestyle factors: smoking status, alcohol consumption, living alone, dietary consumption of vegetable, fruit, fish, and processed/unprocessed meat, physical activities, and body mass index.

<sup>¶</sup>Additionally adjusted for medical conditions: diabetes, heart attack, stroke, high blood pressure, Parkinson's disease, inflammatory bowel disease, depression, cognitive test, family history of dementia, overall health rating and long-standing illness.

eTable 8. Association between regular laxative use and early-onset dementia

	Regular	laxative use	Hazard ratio (95% CI)		
Outcome	Yes (n=5150)	No (n=181 593)	Fully adjusted model		
Early-onset dementia	32 (0.6)	261 (0.1)	1.65 (1.09 to 2.50)*		

This analysis included 186 643 participants aged 40-64. The model is fully adjusted for sociodemographic variables, lifestyle factors, medical conditions and status of regular medication use.

eTable 9. Association between regular laxative use and late-onset dementia

	Regular l	axative use	Hazard ratio (95% CI)		
Outcome	Yes (n=16 703)	No (n=459 516)	Fully adjusted model		
Late-onset dementia	186 (1.1)	1708 (0.4)	1.48 (1.26 to 1.73)***		

Note: \*P<0.05, \*\*P<0.01, \*\*\*P<0.001.

The model is fully adjusted for sociodemographic variables, lifestyle factors, medical conditions and status of regular medication use.

eTable 10. Negative control outcome analysis examining the association between regular laxative use and risk of hip fracture

Regular laxative users			Hazard ratio (95% CI)			
Outcome	Yes (n = 16 651)	No $(n = 458 974)$	Model 1†	Model 2‡	Model 3¶	Model 4§
Hip fracture	116 (0.7)	1732 (0.4)	1.42 (1.18 to 1.72)***	1.38 (1.14 to 1.67)**	1.10 (0.91 to 1.34)	1.05 (0.87 to 1.28)

- ¶Additionally adjusted for medical conditions: diabetes, heart attack, stroke, high blood pressure, Parkinson's disease, inflammatory bowel disease, depression, cognitive test, family history of dementia, overall health rating and long-standing illness.
- §Additionally adjusted for status of regular medication use: opioids, anticholinergic drugs, statins, calcium channel blockers, antidiarrheal agents, and steroids.

<sup>†</sup>Adjusted for sociodemographic variables: age (time scale), sex, ethnicity, education, and socio-economic status.

<sup>‡</sup>Additionally adjusted for lifestyle factors: smoking status, alcohol consumption, living alone, dietary consumption of vegetable, fruit, fish, and processed/unprocessed meat, physical activities, and body mass index.