

**Supplemental Table 1. Mean and median values for all nutrient intakes in per time point in NHS (1984-2010), NHS2 (1991-2015), and HPFS (1986-2014).**

Year	Vitamin B2		Vitamin B6		Vitamin B12		Folate (mcg/d)		Methionine	
	(mg/d)	(mg/d)	(mg/d)	(mg/d)	(mcg/d)	(mcg/d)	(mcg/d)	(mcg/d)	(g/d)	(g/d)
	Mean	Median [IQR]	Mean	Median	Mean	Median	Mean	Median	Mean	Median
	(sd)		(sd)	[IQR]	(sd)	[IQR]	(sd)	[IQR]	(sd)	[IQR]
<b>NHS</b>										
1984	4.2 (7.1)	1.9 [1.5-3.5]	9.6 (28.4)	2.1 [1.6-4.0]	11.5 (20.7)	9.0 [5.0-14.0]	382.7 (230.3)	300.0 [230.0-474.0]	1.7 (0.4)	1.6 [1.4-1.9]
1986	4.4 (7.8)	2.1 [1.5-3.6]	8.9 (26.1)	2.3 [1.7-4.2]	10.3 (17.1)	8.0 [5.0-11.0]	403.2 (221.2)	325.0 [250.0-515.0]	1.8 (0.4)	1.7 [1.5-2.0]
1990	4.0 (8.0)	2.0 [1.5-3.3]	7.4 (23.4)	2.2 [1.7-3.8]	9.8 (14.2)	7.0 [5.0-11.0]	426.9 (222.1)	349.0 [267.0-560.0]	1.8 (0.4)	1.8 [1.5-2.0]
1994	4.3 (8.8)	2.3 [1.6-3.6]	8.5 (24.9)	2.6 [1.9-4.3]	10.4 (12.8)	8.0 [5.0-12.0]	449.5 (229.9)	374.3 [273.1-613.0]	1.7 (0.4)	1.7 [1.5-1.9]
1998	7.6 (16.2)	2.9 [1.8-4.0]	13.8 (34.0)	3.5 [2.0-5.0]	19.4 (32.6)	10.0 [6.0-19.0]	600.1 (270.8)	585.0 [369.0-785.0]	1.6 (0.3)	1.6 [1.4-1.8]
2002	7.7 (15.7)	3.2 [2.1-4.2]	14.0 (33.0)	3.8 [2.1-5.4]	32.4 (67.3)	11.7 [6.6-28.2]	696.3 (326.2)	702.0 [423.0-877.0]	1.6 (0.4)	1.5 [1.3-1.8]
2006	8.1 (16.4)	3.3 [2.1-4.2]	13.7 (30.6)	3.9 [2.2-5.5]	50.7 (129.1)	12.5 [7.0-30.3]	710.0 (333.1)	718.0 [431.0-886.0]	1.6 (0.4)	1.5 [1.3-1.8]
2010	7.7 (16.0)	3.2 [2.0-4.1]	13.5 (32.1)	3.8 [2.1-5.3]	74.3 (202.8)	12.1 [6.7-30.7]	680.8 (325.2)	690.0 [404.0-861.0]	1.6 (0.4)	1.5 [1.3-1.8]
<b>NHS2</b>										
1991	4.0 (8.3)	2.3 [1.7-3.6]	8.2 (25.1)	2.5 [2.0-4.2]	9.8 (12.6)	7.0 [5.0-11.0]	479.8 (292.5)	373.0 [280.0-611.0]	2.0 (0.4)	2.0 [1.8-2.3]
1995	4.4 (9.7)	2.4 [1.7-3.6]	8.9 (26.9)	2.5 [2.0-4.2]	10.1 (15.2)	7.0 [5.0-11.0]	460.2 (276.2)	365.6 [265.0-602.2]	2.0 (0.4)	2.0 [1.7-2.2]
1999	8.5 (18.2)	2.7 [1.9-4.0]	14.1 (36.8)	3.0 [2.0-4.6]	16.8 (27.5)	8.6 [5.3-13.6]	611.5 (285.1)	554.9 [388.4-788.8]	1.8 (0.4)	1.8 [1.6-2.1]

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2003	8.0 (16.1)	3.1 [2.2-4.3]	13.1 (31.4)	3.3 [2.1-4.9]	25.8 (59.0)	9.6 [5.7-16.5]	690.8 (322.8)	650.0 [434.0-870.0]	1.8 (0.4)	1.8 [1.5-2.0]
2007	8.7 (17.3)	3.2 [2.2-4.6]	13.6 (30.7)	3.5 [2.2-5.5]	41.3 (117.5)	10.3 [6.2-20.4]	714.3 (337.6)	673.0 [447.0-896.0]	1.8 (0.4)	1.8 [1.6-2.1]
2011	9.0 (18.5)	3.1 [2.1-4.2]	15.6 (37.6)	3.3 [2.1-5.1]	73.4 (214.6)	9.7 [5.6-20.2]	697.2 (343.0)	649.0 [422.0-889.0]	1.8 (0.4)	1.8 [1.6-2.1]
2015	8.8 (18.1)	2.6 [2.0-3.9]	15.9 (37.2)	3.1 [2.1-6.5]	95.4 (239.8)	10.5 [6.0-42.8]	660.7 (336.8)	587.0 [401.0-843.0]	1.8 (0.5)	1.8 [1.5-2.0]
<b>HPFS</b>										
1986	5.1 (9.8)	2.3 [1.8-4.0]	8.4 (24.2)	2.6 [2.0-4.5]	12.5 (17.8)	9.0 [7.0-14.0]	478.2 (274.5)	387.0 [301.0-573.0]	2.2 (0.4)	2.1 [1.9-2.4]
1990	4.7 (10.2)	2.3 [1.8-3.7]	7.1 (20.8)	2.7 [2.1-4.3]	12.2 (17.8)	9.0 [6.0-14.0]	499.2 (262.2)	410.0 [317.0-633.0]	2.1 (0.4)	2.1 [1.8-2.4]
1994	5.0 (11.1)	2.6 [1.8-4.0]	8.4 (24.2)	2.9 [2.1-4.7]	12.2 (16.8)	8.8 [5.8-13.5]	518.7 (278.7)	427.3 [312.0-688.9]	2.0 (0.4)	2.0 [1.8-2.3]
1998	8.3 (17.8)	3.1 [2.0-4.4]	13.8 (33.6)	3.7 [2.3-5.6]	22.0 (41.9)	11.1 [7.0-20.4]	672.5 (324.6)	613.0 [414.0-865.0]	2.0 (0.4)	2.0 [1.7-2.3]
2002	8.4 (16.8)	3.4 [2.2-4.7]	15.0 (34.7)	4.1 [2.4-6.1]	36.1 (75.9)	12.9 [7.4-28.8]	767.5 (379.2)	737.0 [462.0-962.0]	1.9 (0.4)	1.9 [1.6-2.2]
2006	8.5 (16.8)	3.5 [2.3-4.6]	14.8 (33.2)	4.2 [2.5-6.0]	51.3 (129.6)	13.6 [7.9-30.8]	770.7 (378.1)	747.0 [463.0-965.0]	1.9 (0.4)	1.9 [1.6-2.2]
2010	8.2 (17.1)	3.3 [2.2-4.4]	14.7 (34.9)	4.1 [2.4-5.9]	67.1 (189.0)	13.2 [7.5-30.8]	743.2 (363.7)	718.0 [448.0-934.0]	1.9 (0.4)	1.9 [1.7-2.2]
2014	8.3 (17.3)	3.2 [2.2-4.3]	14.9 (34.4)	4.0 [2.4-7.2]	82.7 (201.3)	13.1 [7.5-40.2]	705.0 (358.2)	647.0 [429.0-887.0]	1.9 (0.5)	1.9 [1.6-2.2]

*HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study; NHS2, Nurses' Health Study 2*

**Supplemental Table 2. Hazard ratios (95% CIs) for type 2 diabetes according to quintiles of vitamin B12 intake adjusted for red meat intake in meta-analysis of NHS, NHS2, and HPFS cohorts**

	<b>Q1</b>	<b>Q2</b>	<b>Q3</b>	<b>Q4</b>	<b>Q5</b>	<b>P-trend</b>
Total vitamin B12 intake	1	0.99 (0.95, 1.04)	1.02 (0.98, 1.07)	1.04 (0.99, 1.09)	1.00 (0.96, 1.05)	0.91
Vitamin B12 intake from food	1	0.96 (0.92, 1.01)	1.00 (0.96, 1.06)	1.05 (1.00, 1.11)	1.04 (0.99, 1.10)	0.004

*Models are adjusted for age (continuously), race (white, black, or other), smoking (never, past, current: 1-14, 15-24, or ≥25 cigarettes/day), marital status (currently married, widowed, divorced or separated, or never married), family history of type 2 diabetes (yes/no), hypertension(yes/no), hypercholesterolemia (yes/no), postmenopausal status and hormone use(premenopausal, or if postmenopausal, never, current, or past postmenopausal hormone use), total energy intake (quintiles), level of physical activity (<3, 3-9, 9-18, 18-27, 27-42 or ≥42 MET-h/week), alcohol consumption (0, 0.1-5, 5-10, 10-15, or ≥15 g/day), and BMI (<21, 21-23, 23-25, 25-27, 27-30, 30-33, 33-35, 35-40, or ≥40 kg/m<sup>2</sup>), intake of cereal fiber (quintiles), animal protein (quintiles), and PUFA:SFA ratio (quintiles).*

*BMI, body mass index; HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study; NHS2, Nurses' Health Study 2; PUFA:SFA, polyunsaturated fatty acid to saturated fatty acid ratio.*

**Supplemental Table 3. Hazard ratios (95% CIs) for type 2 diabetes according to quintiles of methionine, choline, and betaine in meta-analysis of NHS, NHS2, and HPFS cohorts**

	Q1	Q2	Q3	Q4	Q5	P-trend
<b>Total methionine (g/d)</b>						
Cases	3089	3319	3706	4157	5204	
Person-years	976955	982611	986357	975178	979079	
Model 1	1	1.07 (1.02, 1.13)	1.19 (1.14, 1.25)	1.34 (1.28, 1.41)	1.66 (1.59, 1.74)*	<.0001*
Model 2	1	0.98 (0.93, 1.02)	0.99 (0.94, 1.04)	1.02 (0.97, 1.06)	1.05 (1.00, 1.10)	0.001
Model 3	1	0.95 (0.89, 1.02)	0.94 (0.86, 1.03)	0.96 (0.86, 1.06)	0.95 (0.84, 1.07)	0.44
<b>Total choline (mg/d)</b>						
Cases	3433	3506	3748	4023	4765	
Person-years	980289	980637	980333	980048	817589	
Model 1	1	1.0 (0.96, 1.05)	1.1 (1.02, 1.12)	1.1 (1.08, 1.18)	1.3 (1.26, 1.37)	<.0001
Model 2	1	1.0 (0.94, 1.04)	1.0 (0.95, 1.04)	1.0 (0.94, 1.03)	1.0 (0.98, 1.08)	0.1438
Model 3	1	1.0 (0.93, 1.03)	1.0 (0.92, 1.02)	0.9 (0.89, 0.99)	1.0 (0.91, 1.02)	0.1372
<b>Total betaine (mg/d)</b>						
Cases	4881	93471	3962	3486	2929	
Person-years	979231	980045	980404	980595	979903	
Model 1	1	0.9 (0.83, 0.90)	0.8 (0.78, 0.85)	0.7 (0.69, 0.75)	0.6 (0.57, 0.63)	<.0001
Model 2	1	0.9 (0.90, 0.98)	0.9 (0.90, 0.98)	0.9 (0.85, 0.92)	0.8 (0.79, 0.86)	<.0001
Model 3	1	1.0 (0.93, 1.02)	1.0 (0.96, 1.05)	1.0 (0.93, 1.03)	1.0 (0.91, 1.02)	0.3682

*Model 1: adjusted for age (continuously).*

*Model 2: model 1 + race (white, black, or other), smoking (never, past, current: 1-14, 15-24, or ≥25 cigarettes/day), marital status (currently married, widowed, divorced or separated, or never married), family history of type 2 diabetes (yes/no), hypertension(yes/no), hypercholesterolemia (yes/no), postmenopausal status and hormone use(premenopausal, or if postmenopausal, never, current, or past postmenopausal hormone use), total energy intake (quintiles), level of physical activity (<3, 3-9, 9-18, 18-27, 27-42, or ≥42 MET-h/week), alcohol consumption (0, 0.1-5, 5-10, 10-15, or ≥15 g/day), and BMI (<21, 21-23, 23-25, 25-27, 27-30, 30-33, 33-35, 35-40, or ≥40 kg/m<sup>2</sup>).*

*Model 3: model 2 + intake of cereal fiber (quintiles), animal protein (quintiles), and PUFA:SFA ratio (quintiles).*

*Model 4: model 2 + multivitamin use (yes/no).*

*Model 5: model 3 + multivitamin use (yes/no).*

*Model 6: model 2 + AHEI index: (quintiles).*

*Model 7: model 3 + AHEI index: (quintiles).*

*\* p-Value for Q-statistic <0.05, indicating statistically significant heterogeneity among the three cohorts.*

*AHEI, Alternative Healthy Eating Index; BMI, body mass index; HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study; NHS2, Nurses' Health Study 2; PUFA:SFA, polyunsaturated fatty acid to saturated fatty acid ratio.*

**Supplemental Table 4. Cohort-specific hazard ratios (95% CIs) for type 2 diabetes according to quintiles of vitamin B2 in NHS (n=75,430), NHS2 (n=87,953), and HPFS (n=40,261)**

		Q1	Q2	Q3	Q4	Q5	P-trend
<b>Total vitamin B2(mg/d)</b>							
NHS	<i>Person-years</i>	384542	393435	388156	388614	389070	
	<i>Cases</i>	1881	1886	1820	1724	1599	
	<i>Median intake</i>	1.4	1.9	2.5	3.9	11.3	
	Model 1	1	0.98 (0.92, 1.05)	0.95 (0.89, 1.01)	0.90 (0.84, 0.96)	0.82 (0.77, 0.88)	<.0001
	Model 2	1	0.94 (0.88, 1.01)	0.94 (0.88, 1.00)	0.92 (0.86, 0.98)	0.88 (0.83, 0.95)	0.003
	Model 3	1	0.97 (0.90, 1.03)	0.96 (0.90, 1.03)	0.95 (0.89, 1.02)	0.92 (0.86, 0.98)	0.03
	NHS2	<i>Person-years</i>	409782	411298	413394	411793	412759
<i>Cases</i>		1575	1311	1240	1164	1273	
<i>Median intake</i>		1.6	2.2	2.8	3.8	13.0	
Model 1		1	0.85 (0.79, 0.91)	0.81 (0.75, 0.87)	0.76 (0.71, 0.82)	0.79 (0.73, 0.85)	0.0002
Model 2		1	0.92 (0.85, 0.99)	0.92 (0.85, 0.99)	0.90 (0.83, 0.97)	0.93 (0.87, 1.01)	0.59
Model 3		1	0.94 (0.87, 1.02)	0.95 (0.88, 1.02)	0.93 (0.86, 1.01)	0.96 (0.89, 1.04)	0.94
HPFS		<i>Person-years</i>	179279	179089	179434	179685	179853
	<i>Cases</i>	856	877	756	793	720	
	<i>Median intake</i>	1.6	2.1	2.7	4.2	13.3	
	Model 1	1	1.01 (0.92, 1.11)	0.86 (0.78, 0.95)	0.90 (0.81, 0.99)	0.81 (0.73, 0.89)	<.0001
	Model 2	1	1.03 (0.93, 1.13)	0.90 (0.81, 0.99)	0.95 (0.86, 1.05)	0.89 (0.80, 0.98)	0.02
	Model 3	1	1.05 (0.95, 1.15)	0.92 (0.83, 1.01)	0.97 (0.88, 1.08)	0.91 (0.82, 1.01)	0.04
	<b>Vitamin B2 from food (mg/d)</b>						
NHS	<i>Person-years</i>	384007	390985	388459	393185	387180	
	<i>Cases</i>	1717	1732	1816	1872	1773	
	<i>Median intake</i>	1.3	1.5	1.6	1.8	2.2	
	Model 4	1	0.92 (0.86, 0.99)	0.93 (0.87, 1.00)	0.93 (0.87, 0.99)	0.87 (0.81, 0.93)	0.0003
	Model 5	1	0.93 (0.87, 1.00)	0.95 (0.88, 1.02)	0.95 (0.88, 1.02)	0.89 (0.82, 0.96)	0.01
	NHS2	<i>Person-years</i>	409797	413925	409568	413268	412466
<i>Cases</i>		1658	1404	1330	1194	977	
<i>Median intake</i>		1.5	1.7	1.9	2.2	2.5	
Model 4		1	0.92 (0.85, 0.98)	0.91 (0.84, 0.97)	0.85 (0.79, 0.91)	0.77 (0.71, 0.83)	<.0001
Model 5		1	0.93 (0.86, 1.00)	0.92 (0.85, 1.00)	0.86 (0.79, 0.94)	0.78 (0.71, 0.85)	<.0001
HPFS		<i>Person-years</i>	178669	180026	179742	179294	179609
	<i>Cases</i>	854	751	813	800	784	
	<i>Median intake</i>	1.5	1.7	2.0	2.2	2.6	
	Model 4	1	0.87 (0.78, 0.96)	0.94 (0.85, 1.03)	0.90 (0.82, 0.99)	0.87 (0.78, 0.96)	0.03
	Model 5	1	0.87 (0.79, 0.96)	0.95 (0.86, 1.05)	0.91 (0.82, 1.01)	0.86 (0.77, 0.96)	0.03
	<b>Vitamin B2from supplements (mg/d)</b>						

NHS	<i>Person-years</i>	415103	363545	386698	389229	389242	
	<i>Cases</i>	1944	1835	1828	1718	1585	
	<i>Median intake</i>	0	0.1	0.7	2.1	9.6	
	Model 6	1	0.95 (0.89, 1.02)	0.98 (0.92, 1.05)	0.97 (0.90, 1.03)	0.93 (0.87, 1.00)	0.10
	Model 7	1	0.96 (0.90, 1.03)	1.00 (0.93, 1.06)	0.98 (0.92, 1.05)	0.95 (0.88, 1.01)	0.15
NHS2	<i>Person-years</i>	456498	365981	412096	411887	412563	
	<i>Cases</i>	1489	1228	1313	1239	1294	
	<i>Median intake</i>	0	0.3	0.8	1.7	11.0	
	Model 6	1	0.90 (0.83, 0.98)	0.97 (0.89, 1.04)	0.97 (0.89, 1.04)	1.00 (0.92, 1.08)	0.23
	Model 7	1	0.91 (0.84, 0.98)	0.97 (0.90, 1.05)	0.98 (0.90, 1.05)	1.00 (0.93, 1.08)	0.22
HPFS	<i>Person-years</i>	204825	153225	179732	179709	179849	
	<i>Cases</i>	931	766	812	774	719	
	<i>Median intake</i>	0	0.1	0.6	2.0	11.2	
	Model 6	1	1.03 (0.92, 1.14)	1.01 (0.91, 1.11)	0.97 (0.87, 1.07)	0.94 (0.85, 1.04)	0.10
	Model 7	1	1.04 (0.93, 1.15)	1.03 (0.93, 1.14)	0.98 (0.89, 1.09)	0.95 (0.86, 1.05)	0.11

*Model 1: adjusted for age (continuously).*

*Model 2: model 1 + race (white, black, or other), smoking (never, past, current: 1-14, 15-24, or  $\geq 25$  cigarettes/day), marital status (currently married, widowed, divorced or separated, or never married), family history of type 2 diabetes (yes/no), hypertension(yes/no), hypercholesterolemia (yes/no), postmenopausal status and hormone use(premenopausal, or if postmenopausal, never, current, or past postmenopausal hormone use), total energy intake (quintiles), level of physical activity (<3, 3-9, 9-18, 18-27, 27-42, or  $\geq 42$  MET-h/week), alcohol consumption (0, 0.1-5, 5-10, 10-15, or  $\geq 15$  g/day), and BMI (<21, 21-23, 23-25, 25-27, 27-30, 30-33, 33-35, 35-40, or  $\geq 40$  kg/m<sup>2</sup>).*

*Model 3: model 2 + intake of cereal fiber (quintiles), animal protein (quintiles), and PUFA:SFA ratio (quintiles).*

*Model 4: model 2 + multivitamin use (yes/no).*

*Model 5: model 3 + multivitamin use (yes/no).*

*Model 6: model 2 + AHEI index: (quintiles).*

*Model 7: model 3 + AHEI index: (quintiles).*

*AHEI, Alternative Healthy Eating Index; BMI, body mass index; HPFS, Health Professionals Follow-up Study; NHS, Nurses'*

*Health Study; NHS2, Nurses' Health Study 2; PUFA:SFA, polyunsaturated fatty acid to saturated fatty acid ratio.*

**Supplemental Table 5. Cohort-specific hazard ratios (95% CIs) for type 2 diabetes according to quintiles of vitamin B6 in NHS (n=75,430), NHS2 (n=87,953), and HPFS (n=40,261)**

		Q1	Q2	Q3	Q4	Q5	P-trend
<b>Total vitamin B6(mg/d)</b>							
NHS	<i>Person-years</i>	393121	385549	386303	389693	389151	
	<i>Cases</i>	1942	1848	1820	1664	1636	
	<i>Median intake</i>	1.6	2.1	2.8	4.4	24.9	
	Model 1	1	0.94 (0.88, 1.00)	0.92 (0.87, 0.98)	0.84 (0.78, 0.89)	0.82 (0.77, 0.88)	<.0001
	Model 2	1	0.93 (0.87, 0.99)	0.95 (0.89, 1.02)	0.90 (0.84, 0.96)	0.88 (0.82, 0.94)	0.004
	Model 3	1	0.95 (0.89, 1.01)	0.98 (0.92, 1.05)	0.93 (0.87, 1.00)	0.91 (0.85, 0.98)	0.03
	NHS2	<i>Person-years</i>	404931	415850	416522	408330	413393
<i>Cases</i>		1466	1300	1300	1199	1298	
<i>Median intake</i>		1.8	2.4	3.2	4.7	25.5	
Model 1		1	0.88 (0.82, 0.95)	0.87 (0.81, 0.94)	0.83 (0.76, 0.89)	0.85 (0.79, 0.92)	0.03
Model 2		1	0.93 (0.86, 1.00)	0.95 (0.88, 1.03)	0.93 (0.86, 1.01)	0.97 (0.90, 1.04)	0.78
Model 3		1	0.95 (0.88, 1.02)	0.98 (0.90, 1.05)	0.96 (0.88, 1.04)	0.99 (0.92, 1.07)	0.51
HPFS		<i>Person-years</i>	176285	182765	177638	180968	179684
	<i>Cases</i>	903	789	791	811	708	
	<i>Median intake</i>	1.8	2.4	3.1	4.7	20.7	
	Model 1	1	0.84 (0.77, 0.93)	0.84 (0.77, 0.93)	0.85 (0.77, 0.93)	0.74 (0.67, 0.82)	<.0001
	Model 2	1	0.88 (0.79, 0.96)	0.90 (0.82, 0.99)	0.93 (0.85, 1.03)	0.84 (0.76, 0.93)	0.01
	Model 3	1	0.89 (0.80, 0.98)	0.93 (0.84, 1.02)	0.96 (0.87, 1.06)	0.87 (0.78, 0.96)	0.05
	<b>Vitamin B6 from food (mg/d)</b>						
NHS	<i>Person-years</i>	384614	387326	389948	392773	389156	
	<i>Cases</i>	1736	1759	1810	1854	1751	
	<i>Median intake</i>	1.4	1.6	1.8	2.0	2.3	
	Model 4	1	0.98 (0.92, 1.05)	0.98 (0.92, 1.05)	0.99 (0.92, 1.06)	0.94 (0.87, 1.00)	0.10
	Model 5	1	0.99 (0.92, 1.06)	1.00 (0.93, 1.07)	1.02 (0.95, 1.10)	0.99 (0.91, 1.07)	0.9976
	NHS2	<i>Person-years</i>	412104	410867	411449	412325	412280
<i>Cases</i>		1453	1281	1319	1261	1249	
<i>Median intake</i>		1.6	1.9	2.1	2.3	2.6	
Model 4		1	0.93 (0.86, 1.00)	0.99 (0.92, 1.07)	0.91 (0.84, 0.98)	0.95 (0.88, 1.03)	0.19
Model 5		1	0.94 (0.87, 1.01)	1.00 (0.92, 1.08)	0.92 (0.85, 1.01)	0.98 (0.89, 1.07)	0.64
HPFS		<i>Person-years</i>	179030	178809	179939	180158	179404
	<i>Cases</i>	870	846	791	734	761	
	<i>Median intake</i>	1.7	2.0	2.2	2.5	2.9	
	Model 4	1	0.98 (0.89, 1.08)	0.92 (0.84, 1.02)	0.88 (0.80, 0.98)	0.95 (0.86, 1.05)	0.13
	Model 5	1	0.98 (0.89, 1.08)	0.93 (0.84, 1.03)	0.90 (0.80, 1.00)	0.98 (0.88, 1.10)	0.52
	<b>Vitamin B6 from supplements (mg/d)</b>						



NHS	<i>Person-years</i>	408591	365859	391187	388947	389232	
	<i>Cases</i>	1939	1831	1858	1645	1637	
	<i>Median intake</i>	0	0.2	1.0	2.4	23.0	
	Model 6	1	0.96 (0.90, 1.03)	1.01 (0.95, 1.08)	0.94 (0.88, 1.01)	0.95 (0.88, 1.01)	0.17
	Model 7	1	0.97 (0.90, 1.04)	1.03 (0.96, 1.10)	0.96 (0.89, 1.02)	0.96 (0.89, 1.02)	0.22
NHS2	<i>Person-years</i>	452299	366380	415387	412053	412906	
	<i>Cases</i>	1485	1227	1363	1199	1289	
	<i>Median intake</i>	0	0.4	1.1	2.5	23.4	
	Model 6	1	0.89 (0.83, 0.96)	0.97 (0.90, 1.05)	0.94 (0.87, 1.01)	0.98 (0.91, 1.06)	0.34
	Model 7	1	0.89 (0.83, 0.97)	0.98 (0.91, 1.06)	0.94 (0.87, 1.02)	0.99 (0.92, 1.07)	0.30
HPFS	<i>Person-years</i>	201685	156368	179746	179722	179819	
	<i>Cases</i>	923	788	781	797	713	
	<i>Median intake</i>	0	0.1	0.7	2.3	18.3	
	Model 6	1	1.04 (0.93, 1.15)	0.97 (0.87, 1.07)	0.99 (0.89, 1.09)	0.93 (0.84, 1.03)	0.11
	Model 7	1	1.05 (0.94, 1.16)	0.98 (0.89, 1.09)	1.00 (0.91, 1.11)	0.95 (0.85, 1.05)	0.12

*Model 1: adjusted for age (continuously).*

*Model 2: model 1 + race (white, black, or other), smoking (never, past, current: 1-14, 15-24, or  $\geq 25$  cigarettes/day), marital status (currently married, widowed, divorced or separated, or never married), family history of type 2 diabetes (yes/no), hypertension(yes/no), hypercholesterolemia (yes/no), postmenopausal status and hormone use(premenopausal, or if postmenopausal, never, current, or past postmenopausal hormone use), total energy intake (quintiles), level of physical activity (<3, 3-9, 9-18, 18-27, 27-42, or  $\geq 42$  MET-h/week), alcohol consumption (0, 0.1-5, 5-10, 10-15, or  $\geq 15$  g/day), and BMI (<21, 21-23, 23-25, 25-27, 27-30, 30-33, 33-35, 35-40, or  $\geq 40$  kg/m<sup>2</sup>).*

*Model 3: model 2 + intake of cereal fiber (quintiles), animal protein (quintiles), and PUFA:SFA ratio (quintiles).*

*Model 4: model 2 + multivitamin use (yes/no).*

*Model 5: model 3 + multivitamin use (yes/no).*

*Model 6: model 2 + AHEI index: (quintiles).*

*Model 7: model 3 + AHEI index: (quintiles).*

*AHEI, Alternative Healthy Eating Index; BMI, body mass index; HPFS, Health Professionals Follow-up Study; NHS, Nurses'*

*Health Study; NHS2, Nurses' Health Study 2; PUFA:SFA, polyunsaturated fatty acid to saturated fatty acid ratio.*

**Supplemental Table 6. Cohort-specific hazard ratios (95% CIs) for type 2 diabetes according to quintiles of vitamin B12 in NHS (n=75,430), NHS2 (n=87,953), and HPFS (n=40,261)**

		Q1	Q2	Q3	Q4	Q5	P-trend
<b>Total vitamin B12 (mcg/d)</b>							
NHS	<i>Person-years</i>	389818	382130	396784	387132	387952	
	<i>Cases</i>	1686	1744	1821	1859	1800	
	<i>Median intake</i>	4.7	7.0	9.8	13.0	22.3	
	Model 1	1	1.05 (0.98, 1.12)	1.06 (0.99, 1.13)	1.09 (1.02, 1.16)	1.04 (0.97, 1.11)	0.44
	Model 2	1	1.02 (0.95, 1.09)	1.03 (0.96, 1.10)	1.05 (0.98, 1.12)	1.02 (0.95, 1.09)	0.60
	Model 3	1	1.02 (0.95, 1.09)	1.03 (0.96, 1.10)	1.06 (0.99, 1.13)	1.03 (0.96, 1.10)	0.45
	NHS2	<i>Person-years</i>	409673	424133	397396	415457	412366
<i>Cases</i>		1296	1254	1313	1367	1333	
<i>Median intake</i>		4.5	6.5	9.0	12.1	26.3	
Model 1		1	0.99 (0.91, 1.07)	1.04 (0.97, 1.13)	1.03 (0.95, 1.11)	0.98 (0.90, 1.05)	0.38
Model 2		1	0.95 (0.88, 1.02)	1.01 (0.93, 1.09)	0.99 (0.92, 1.07)	0.97 (0.90, 1.05)	0.75
Model 3		1	0.95 (0.88, 1.03)	1.02 (0.94, 1.10)	1.00 (0.93, 1.09)	0.98 (0.91, 1.06)	0.84
HPFS		<i>Person-years</i>	183528	176336	173958	184498	179020
	<i>Cases</i>	731	809	805	882	775	
	<i>Median intake</i>	5.5	8.0	10.8	14.9	27.0	
	Model 1	1	1.12 (1.01, 1.24)	1.10 (0.99, 1.21)	1.15 (1.04, 1.27)	1.02 (0.92, 1.13)	0.55
	Model 2	1	1.05 (0.95, 1.16)	1.03 (0.93, 1.14)	1.08 (0.98, 1.20)	0.97 (0.87, 1.07)	0.28
	Model 3	1	1.03 (0.93, 1.14)	1.02 (0.92, 1.12)	1.06 (0.96, 1.18)	0.95 (0.85, 1.05)	0.16
	<b>Vitamin B12 from food (mcg/d)</b>						
NHS	<i>Person-years</i>	389663	389059	388167	388141	388786	
	<i>Cases</i>	1477	1599	1773	1898	2163	
	<i>Median intake</i>	3.8	4.9	6.1	7.8	11.3	
	Model 4	1	0.98 (0.92, 1.06)	1.05 (0.97, 1.12)	1.08 (1.00, 1.15)	1.13 (1.05, 1.20)	<.0001
	Model 5	1	0.97 (0.91, 1.05)	1.04 (0.96, 1.11)	1.06 (0.99, 1.14)	1.10 (1.03, 1.19)	0.0003
NHS2	<i>Person-years</i>	407120	411064	413202	416069	411570	
	<i>Cases</i>	1137	1181	1308	1450	1487	
	<i>Median intake</i>	3.7	4.8	5.6	6.7	9.1	
	Model 4	1	0.92 (0.85, 1.00)	0.98 (0.90, 1.06)	1.02 (0.95, 1.11)	1.00 (0.93, 1.08)	0.24
	Model 5	1	0.92 (0.85, 1.00)	0.98 (0.90, 1.07)	1.03 (0.94, 1.12)	1.00 (0.91, 1.08)	0.38
HPFS	<i>Person-years</i>	180656	178534	178754	180016	179381	
	<i>Cases</i>	625	731	785	945	916	
	<i>Median intake</i>	4.5	6.0	7.3	9.0	13.5	
	Model 4	1	1.08 (0.97, 1.20)	1.06 (0.95, 1.18)	1.20 (1.08, 1.33)	1.11 (1.0, 1.23)	0.05
	Model 5	1	1.07 (0.96, 1.19)	1.03 (0.92, 1.15)	1.15 (1.03, 1.28)	1.04 (0.93, 1.17)	0.74
<b>Vitamin B12 from supplements (mcg/d)</b>							

NHS	<i>Person-years</i>	400585	375469	389848	388438	389477	
	<i>Cases</i>	1889	1865	1854	1724	1578	
	<i>Median intake</i>	0	0.5	1.9	4.8	13.2	
	Model 6	1	0.99 (0.92, 1.05)	1.01 (0.95, 1.08)	0.99 (0.92, 1.06)	0.94 (0.88, 1.00)	0.04
	Model 7	1	0.99 (0.93, 1.06)	1.02 (0.96, 1.09)	1.00 (0.94, 1.07)	0.95 (0.89, 1.02)	0.08
NHS2	<i>Person-years</i>	455457	358237	420746	410987	413598	
	<i>Cases</i>	1486	1202	1253	1320	1302	
	<i>Median intake</i>	0	0.9	2.5	5.4	18.9	
	Model 6	1	0.92 (0.85, 1.00)	0.96 (0.89, 1.04)	1.00 (0.93, 1.08)	0.98 (0.91, 1.06)	0.62
	Model 7	1	0.93 (0.86, 1.00)	0.97 (0.90, 1.05)	1.01 (0.94, 1.09)	0.99 (0.91, 1.07)	0.60
HPFS	<i>Person-years</i>	198844	158984	179424	179825	180263	
	<i>Cases</i>	927	742	805	806	722	
	<i>Median intake</i>	0	0.3	1.6	5.2	15.7	
	Model 6	1	0.94 (0.85, 1.04)	0.96 (0.87, 1.06)	0.99 (0.90, 1.09)	0.92 (0.83, 1.02)	0.23
	Model 7	1	0.94 (0.85, 1.05)	0.97 (0.88, 1.07)	1.01 (0.91, 1.11)	0.93 (0.84, 1.03)	0.34

*Model 1: adjusted for age (continuously).*

*Model 2: model 1 + race (white, black, or other), smoking (never, past, current: 1-14, 15-24, or  $\geq 25$  cigarettes/day), marital status (currently married, widowed, divorced or separated, or never married), family history of type 2 diabetes (yes/no), hypertension(yes/no), hypercholesterolemia (yes/no), postmenopausal status and hormone use(premenopausal, or if postmenopausal, never, current, or past postmenopausal hormone use), total energy intake (quintiles), level of physical activity (<3, 3-9, 9-18, 18-27, 27-42, or  $\geq 42$  MET-h/week), alcohol consumption (0, 0.1-5, 5-10, 10-15, or  $\geq 15$  g/day), and BMI (<21, 21-23, 23-25, 25-27, 27-30, 30-33, 33-35, 35-40, or  $\geq 40$  kg/m<sup>2</sup>).*

*Model 3: model 2 + intake of cereal fiber (quintiles), animal protein (quintiles), and PUFA:SFA ratio (quintiles).*

*Model 4: model 2 + multivitamin use (yes/no).*

*Model 5: model 3 + multivitamin use (yes/no).*

*Model 6: model 2 + AHEI index: (quintiles).*

*Model 7: model 3 + AHEI index: (quintiles).*

*AHEI, Alternative Healthy Eating Index; BMI, body mass index; HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study; NHS2, Nurses' Health Study 2; PUFA:SFA, polyunsaturated fatty acid to saturated fatty acid ratio.*

**Supplemental Table 7. Cohort-specific hazard ratios (95% CIs) for type 2 diabetes according to quintiles of Folate in NHS (n=75,430), NHS2 (n=87,953), and HPFS (n=40,261)**

		Q1	Q2	Q3	Q4	Q5	P-trend
<b>Total Folate (mcg/d)</b>							
NHS	<i>Person-years</i>	387480	388137	389174	389415	389610	
	<i>Cases</i>	1990	1964	1724	1694	1538	
	<i>Median intake</i>	230	312	392	519	718	
	Model 1	1	0.97 (0.91, 1.03)	0.84 (0.79, 0.90)	0.83 (0.77, 0.88)	0.74 (0.70, 0.80)	<.0001
	Model 2	1	1.03 (0.97, 1.10)	0.94 (0.88, 1.00)	0.95 (0.88, 1.01)	0.91 (0.85, 0.98)	0.0006
	Model 3	1	1.06 (1.00, 1.13)	0.98 (0.92, 1.05)	1.00 (0.93, 1.06)	0.97 (0.90, 1.04)	0.08
NHS2	<i>Person-years</i>	409059	411822	412844	412585	412715	
	<i>Cases</i>	1695	1332	1261	1217	1058	
	<i>Median intake</i>	266	389	496	631	843	
	Model 1	1	0.78 (0.73, 0.84)	0.73 (0.68, 0.79)	0.71 (0.66, 0.76)	0.62 (0.58, 0.67)	<.0001
	Model 2	1	0.93 (0.87, 1.00)	0.91 (0.85, 0.98)	0.92 (0.85, 0.99)	0.91 (0.84, 0.98)	0.02
	Model 3	1	0.95 (0.89, 1.03)	0.95 (0.88, 1.02)	0.96 (0.89, 1.04)	0.96 (0.88, 1.04)	0.33
HPFS	<i>Person-years</i>	178900	179249	179466	179953	179772	
	<i>Cases</i>	926	854	776	722	724	
	<i>Median intake</i>	277	369	463	619	872	
	Model 1	1	0.91 (0.83, 1.00)	0.81 (0.74, 0.90)	0.75 (0.68, 0.83)	0.75 (0.68, 0.82)	<.0001
	Model 2	1	0.99 (0.90, 1.08)	0.94 (0.86, 1.04)	0.89 (0.80, 0.98)	0.93 (0.85, 1.03)	0.0576
	Model 3	1	1.03 (0.93, 1.13)	1.00 (0.90, 1.10)	0.95 (0.86, 1.05)	1.01 (0.91, 1.11)	0.6507
<b>Folate from food (mcg/d)</b>							
NHS	<i>Person-years</i>	387276	389174	387937	389835	389594	
	<i>Cases</i>	1932	1925	1810	1705	1538	
	<i>Median intake</i>	208	258	293	334	411	
	Model 4	1	1.01 (0.95, 1.08)	0.98 (0.92, 1.05)	0.97 (0.91, 1.04)	0.93 (0.87, 1.00)	0.02
	Model 5	1	1.04 (0.98, 1.11)	1.03 (0.97, 1.10)	1.04 (0.97, 1.11)	1.01 (0.94, 1.09)	0.86
NHS2	<i>Person-years</i>	409002	411910	412690	412014	413409	
	<i>Cases</i>	1794	1439	1265	1184	881	
	<i>Median intake</i>	236	300	341	386	472	
	Model 4	1	0.95 (0.88, 1.02)	0.94 (0.88, 1.01)	0.97 (0.90, 1.04)	0.87 (0.80, 0.95)	0.003
	Model 5	1	0.98 (0.91, 1.05)	0.99 (0.92, 1.07)	1.03 (0.95, 1.12)	0.95 (0.86, 1.04)	0.49
HPFS	<i>Person-years</i>	178854	179468	179626	179424	179969	
	<i>Cases</i>	945	851	765	794	647	
	<i>Median intake</i>	257	318	363	416	514	
	Model 4	1	0.97 (0.89, 1.07)	0.90 (0.82, 0.99)	0.98 (0.89, 1.08)	0.88 (0.79, 0.98)	0.03
	Model 5	1	1.01 (0.91, 1.10)	0.96 (0.87, 1.06)	1.06 (0.96, 1.17)	0.98 (0.88, 1.09)	0.98
<b>Folate from supplements (mcg/d)</b>							
NHS	<i>Person-years</i>	405578	372528	387790	388626	389295	
	<i>Cases</i>	1929	1899	1826	1652	1604	

	<i>Median intake</i>	0	13	87	204	377	
	Model 6	1	0.98 (0.91, 1.04)	0.97 (0.91, 1.04)	0.92 (0.86, 0.99)	0.95 (0.88, 1.01)	0.05
	Model 7	1	0.99 (0.92, 1.06)	0.99 (0.92, 1.06)	0.94 (0.88, 1.01)	0.96 (0.90, 1.03)	0.13
NHS2	<i>Person-years</i>	464003	361294	408696	412844	412187	
	<i>Cases</i>	1517	1287	1252	1340	1167	
	<i>Median intake</i>	0	46	140	259	448	
	Model 6	1	0.95 (0.88, 1.03)	0.91 (0.84, 0.99)	1.01 (0.94, 1.09)	0.95 (0.87, 1.02)	0.67
	Model 7	1	0.95 (0.88, 1.03)	0.92 (0.85, 0.99)	1.02 (0.95, 1.10)	0.95 (0.88, 1.03)	0.83
HPFS	<i>Person-years</i>	220272	136892	180874	179591	179711	
	<i>Cases</i>	973	712	823	740	754	
	<i>Median intake</i>	0	12	62	226	440	
	Model 6	1	1.04 (0.93, 1.16)	1.04 (0.94, 1.16)	0.98 (0.88, 1.08)	0.99 (0.90, 1.09)	0.37
	Model 7	1	1.05 (0.94, 1.17)	1.06 (0.96, 1.18)	1.00 (0.90, 1.11)	1.01 (0.91, 1.11)	0.54

*Model 1: adjusted for age (continuously).*

*Model 2: model 1 + race (white, black, or other), smoking (never, past, current: 1-14, 15-24, or  $\geq 25$  cigarettes/day), marital status (currently married, widowed, divorced or separated, or never married), family history of type 2 diabetes (yes/no), hypertension (yes/no), hypercholesterolemia (yes/no), postmenopausal status and hormone use (premenopausal, or if postmenopausal, never, current, or past postmenopausal hormone use), total energy intake (quintiles), level of physical activity (<3, 3-9, 9-18, 18-27, 27-42, or  $\geq 42$  MET-h/week), alcohol consumption (0, 0.1-5, 5-10, 10-15, or  $\geq 15$  g/day), and BMI (<21, 21-23, 23-25, 25-27, 27-30, 30-33, 33-35, 35-40, or  $\geq 40$  kg/m<sup>2</sup>).*

*Model 3: model 2 + intake of cereal fiber (quintiles), animal protein (quintiles), and PUFA:SFA ratio (quintiles).*

*Model 4: model 2 + multivitamin use (yes/no).*

*Model 5: model 3 + multivitamin use (yes/no).*

*Model 6: model 2 + AHEI index: (quintiles).*

*Model 7: model 3 + AHEI index: (quintiles).*

*AHEI, Alternative Healthy Eating Index; BMI, body mass index; HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study; NHS2, Nurses' Health Study 2; PUFA:SFA, polyunsaturated fatty acid to saturated fatty acid ratio.*

**Supplemental Table 8. Cohort-specific hazard ratios (95% CIs) for type 2 diabetes according to quintiles of Methionine in NHS (n=75,430), NHS2 (n=87,953), and HPFS (n=40,261)**

		Q1	Q2	Q3	Q4	Q5	P-trend
<b>Total Methionine (mg/d)</b>							
NHS	<i>Person-years</i>	384426	389963	394927	386026	388474	
	<i>Cases</i>	1399	1571	1717	1947	2276	
	<i>Median intake</i>	1.3	1.5	1.7	1.8	2.1	
	Model 1	1	1.11 (1.03, 1.19)	1.2 (1.12, 1.29)	1.38 (1.28, 1.47)	1.59 (1.49, 1.70)	<.0001
	Model 2	1	1.02 (0.95, 1.10)	1.02 (0.95, 1.10)	1.06 (0.99, 1.14)	1.05 (0.98, 1.12)	0.12
	Model 3	1	1.01 (0.90, 1.12)	0.96 (0.84, 1.10)	1.01 (0.86, 1.17)	0.96 (0.80, 1.16)	0.63
	NHS2	<i>Person-years</i>	413006	412832	411483	409817	411887
<i>Cases</i>		1020	1094	1237	1340	1872	
<i>Median intake</i>		1.5	1.8	1.9	2.1	2.4	
Model 1		1	1.08 (0.99, 1.18)	1.23 (1.13, 1.34)	1.33 (1.22, 1.44)	1.81 (1.68, 1.96)	<.0001
Model 2		1	0.95 (0.87, 1.03)	0.97 (0.89, 1.05)	0.94 (0.87, 1.02)	1.03 (0.95, 1.11)	0.24
Model 3		1	0.93 (0.83, 1.05)	0.95 (0.81, 1.11)	0.90 (0.75, 1.08)	0.96 (0.78, 1.18)	0.91
HPFS		<i>Person-years</i>	179523	179816	179947	179335	178718
	<i>Cases</i>	670	654	752	870	1056	
	<i>Median intake</i>	1.6	1.9	2.1	2.3	2.6	
	Model 1	1	0.98 (0.88, 1.10)	1.12 (1.01, 1.24)	1.30 (1.17, 1.44)	1.57 (1.42, 1.73)	<.0001
	Model 2	1	0.92 (0.82, 1.02)	0.95 (0.85, 1.05)	1.04 (0.93, 1.15)	1.10 (0.99, 1.21)	0.0028
	Model 3	1	0.89 (0.76, 1.03)	0.89 (0.73, 1.07)	0.95 (0.76, 1.19)	0.89 (0.69, 1.16)	0.4319

*Model 1: adjusted for age (continuously).*

*Model 2: model 1 + race (white, black, or other), smoking (never, past, current: 1-14, 15-24, or ≥25 cigarettes/day), marital status (currently married, widowed, divorced or separated, or never married), family history of type 2 diabetes (yes/no), hypertension(yes/no), hypercholesterolemia (yes/no), postmenopausal status and hormone use(premenopausal, or if postmenopausal, never, current, or past postmenopausal hormone use), total energy intake (quintiles), level of physical activity (<3, 3-9, 9-18, 18-27, 27-42, or ≥42 MET-h/week), alcohol consumption (0, 0.1-5, 5-10, 10-15, or ≥15 g/day), and BMI (<21, 21-23, 23-25, 25-27, 27-30, 30-33, 33-35, 35-40, or ≥40 kg/m<sup>2</sup>).*

*Model 3: model 2 + intake of cereal fiber (quintiles), animal protein (quintiles), and PUFA:SFA ratio (quintiles).*

*AHEI, Alternative Healthy Eating Index; BMI, body mass index; HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study; NHS2, Nurses' Health Study 2; PUFA:SFA, polyunsaturated fatty acid to saturated fatty acid ratio.*