

Supplementary Table 1. Characteristics of participants in the fat-soluble vitamins and risk of Glioma analysis by sex in the UK Biobank, Nurses' Health Study, and Health Professionals Follow-up Study.

Characteristics	UKB				NHS and HPFS			
	Women		Men		Women		Men	
	Cases	Cohort	Cases	Cohort	Cases	Controls	Cases	Controls
N	168	182972	276	163813	52	104	32	64
Age, years	59.8 (6.9)	55.6 (8.1)	59.8 (7.0)	55.8 (8.2)	57.8 (6.1)	58.0 (6.1)	63.8 (9.2)	63.9 (9.1)
Follow-up, years	4.1 (2.2)	/	3.9 (2.2)	/	9.4 (4.3)	/	7.3 (4.0)	/
Body mass index, kg/m ²	27.0 (4.7)	27.0 (5.2)	27.6 (4.2)	27.8 (4.3)	24.5 (4.9)	26.6 (5.2)	25.7 (4.8)	25.3 (3.4)
Current multivitamin use, %	/	/	/	/	32.7	31.7	43.8	48.4
Current smoker, %	7.1	8.4	11.6	12.3	13.5	10.6	3.1	1.6
Past smoker, %	36.9	30.5	40.6	37.2	48.1	44.2	56.3	34.4
25(OH)D, nmol/L	48.2 (20.5)	48.5 (20.9)	48.6 (19.0)	48.0 (21.1)	72.5 (22.2)	67.5 (24.0)	70.2 (16.4)	67.5 (16.9)
Retinol, µmol/L	/	/	/	/	2.3 (0.7)	2.2 (0.5)	2.3 (0.4)	2.3 (0.4)
α-tocopherol, µmol/L	/	/	/	/	47.2 (22.3)	46.3 (20.4)	38.7 (11.5)	42.8 (17.5)
γ-tocopherol, µmol/L	/	/	/	/	7.0 (3.9)	6.3 (3.0)	5.1 (2.9)	5.0 (2.9)
Cholesterol, mg/dL	226 (38)	221 (38)	212 (40)	210 (40)	201 (36)	199 (32)	186 (27)	194 (33)
Season of blood draw, %								
Spring	29.8	29.5	25.4	28.4	28.9	32.7	15.6	21.9
Summer	20.8	26.9	22.8	26.1	38.5	30.8	34.4	37.5
Fall	28.0	24.6	28.3	24.0	11.5	14.4	34.4	26.6
Winter	21.4	19.0	23.6	21.5	21.2	22.1	15.6	14.1

Abbreviations: HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study; UKB, United Kingdom Biobank.

/ denotes not applicable or data not available

Continuous variables presented as mean (SD) and categorical variables as percentage (%).

Supplementary Table 2. Associations between circulating 25(OH)D and glioma risk by sex in the UK Biobank, Nurses' Health Study, and Health Professionals Follow-up Study.

Study specific tertiles ³	UKB				HPFS and NHS			
	Women		Men		Women		Men	
	Number of glioma cases	HR (95% CI) ¹	Number of glioma cases	HR (95% CI) ¹	Number of glioma cases	RR (95% CI) ²	Number of glioma cases	RR (95% CI) ²
1	54	1 (ref)	89	1 (ref)	14	1 (ref)	11	1 (ref)
2	55	0.92 (0.63-1.136)	95	0.92 (0.68-1.24)	16	1.17 (0.47-2.91)	12	0.94 (0.33-2.73)
3	59	0.94 (0.64-1.39)	92	0.83 (0.61-1.13)	22	1.42 (0.61-3.32)	9	0.66 (0.20-2.18)
P _{trend} ⁴		0.77		0.23		0.41		0.51
IOM guidelines for bone health, nmol/L								
<50(deficiency/insufficiency)	62	0.96 (0.69-1.34)	108	0.91 (0.70-1.18)	8	1.11 (0.40-3.06)	4	0.54 (0.14-2.04)
50-<75(sufficiency)	91	1 (ref)	143	1 (ref)	20	1 (ref)	17	1 (ref)
≥75 (above sufficiency)	15	0.74 (0.42-1.30)	25	0.71 (0.46-1.10)	24	1.24 (0.59-2.60)	11	0.52 (0.17-1.60)
P _{trend} ⁴		0.55		0.61		0.70		0.77
Continuous ^{5,6}	168	0.99 (0.83-1.19)	276	0.93 (0.80-1.07)	52	1.12 (0.76-1.67)	32	1.02 (0.52-2.00)

Abbreviations: CI, confidence interval; HPFS, Health Professionals Follow-up Study; HR, hazard ratio; IOM, Institute of Medicine; NHS, Nurses' Health Study; RR, risk ratio; UKB, United Kingdom Biobank.

¹Adjusted for sex (male vs female), age (continuous), race (non-white vs white), month of blood collection (continuous), BMI (continuous), and smoking status (never, current and previous).

²In addition to conditioning on matching factors in the NHS and HPFS (age, fasting status, month of blood collection, and race), adjusted for BMI (continuous) and smoking status (never, current and previous).

³Median serum 25(OH)D for each tertile in the UKB 26.91, 46.43, 68.67 nmol/L; median plasma 25(OH)D for each tertile in the NHS and HPFS: 47.55, 68.29, and 87.90 nmol/L.

⁴The p-value for linear trend corresponds to the p-value of the ordinal variable constructed by assigning the median value of each category to all participants in that category.

⁵Results for the continuous analyses are given for a 25 nmol/L increment.

⁶P for interaction by sex: 0.62 for UKB; 0.84 for NHS and HPFS.

Supplementary Table 3. Associations between circulating 25(OH)D and glioma risk among non-smokers and after a 4-year lag in the UK Biobank, Nurses' Health Study, and Health Professionals Follow-up Study.

	Non-smokers				After applying a 4-year lag			
	UKB		NHS and HPFS		UKB		NHS and HPFS	
	Number of glioma cases	HR (95%CI) ¹	Number of glioma cases	RR (95%CI) ²	Number of glioma cases	HR (95%CI) ¹	Number of glioma cases	RR (95%CI) ²
Study specific tertiles³								
1	118	1 (ref)	23	1 (ref)	70	1 (ref)	18	1 (ref)
2	139	0.97 (0.75-1.25)	27	1.07 (0.53-2.16)	76	0.95 (0.68-1.33)	25	1.43 (0.66-3.09)
3	138	0.88 (0.68-1.15)	26	1.01 (0.49-2.07)	75	0.91 (0.65-1.29)	24	1.21 (0.56-2.64)
P _{trend} ⁴		0.34		0.99		0.60		0.74
IOM guidelines for bone health, nmol/L								
<50(deficiency/insufficiency)	158	0.92 (0.74-1.14)	11	0.82 (0.36-1.90)	84	0.90 (0.68-1.21)	12	0.77 (0.35-1.68)
50-<75(sufficiency)	202	1 (ref)	35	1 (ref)	115	1 (ref)	37	1 (ref)
≥75 (beyond sufficiency)	35	0.68 (0.47-0.98)	30	0.91 (0.49-1.71)	22	0.82 (0.51-1.32)	31	0.79 (0.43-1.46)
P _{trend} ⁴		0.38		0.93		1.00		0.87
Continuous ^{5,6}	395	0.94 (0.84-1.07)	76	1.09 (0.55-2.16)	221	0.97 (0.82-1.14)	67	1.08 (0.73-1.58)

Abbreviations: CI, confidence interval; HPFS, Health Professionals Follow-up Study; HR, hazard ratio; IOM, Institute of Medicine; NHS, Nurses' Health Study; RR, risk ratio; UKB, United Kingdom Biobank.

¹Adjusted for sex (male vs female), age (continuous), race (non-white vs white), month of blood collection (continuous), BMI (continuous), and smoking status (never, current and previous).

²In addition to conditioning on matching factors in the NHS and HPFS (age, fasting status, month of blood collection, and race), adjusted for BMI (continuous) and smoking status (never, current and previous).

³Median serum 25(OH)D for each tertile in the UKB 26.91, 46.43, 68.67 nmol/L; median plasma 25(OH)D for each tertile in the NHS and HPFS: 47.55, 68.29, and 87.90 nmol/L.

⁴The p-value for linear trend corresponds to the p-value of the ordinal variable constructed by assigning the median value of each category to all participants in that category.

⁵Results for the continuous analyses are given for a 25 nmol/L increment.

Supplementary Table 4. Spearman correlation coefficients for fat soluble vitamins and cholesterol in the Nurses' Health Study (NHS) and Health Professionals Follow-up Study (HPFS).

	25 (OH)D	Retinol	α -tocopherol	γ -tocopherol	Cholesterol
NHS (Females) <i>n</i> =104					
25(OH)D	1	0.22*	0.30*	-0.21*	0.01
Retinol		1	0.55*	0.02	0.42*
α -tocopherol			1	-0.15	0.55*
γ -tocopherol				1	0.24*
Cholesterol					1
HPFS (Males) <i>n</i> =64					
25(OH)D	1	0.12	0.11	-0.22	-0.04
Retinol		1	0.32*	0.12	0.39*
α -tocopherol			1	-0.27*	0.41*
γ -tocopherol				1	0.31*
Cholesterol					1.0

Abbreviations: HPFS, Health Professionals Follow-up Study; NHS, Nurses' Health Study; *p<0.05

Supplementary Table 5. Associations between circulating retinol, α - and γ -tocopherol and glioma risk by sex in the Nurses' Health Study and Health Professionals Follow-up Study.

	Women		Men	
	Number of glioma cases	RR (95%CI) ¹	Number of glioma cases	RR (95%CI) ¹
Retinol				
Tertile ²				
1	17	1	7	1
2	15	1.23 (0.49-3.06)	15	1.09 (0.33-3.54)
3	20	1.14 (0.47-2.77)	10	1.31 (0.37-4.60)
p_{trend}^3		0.80		0.66
Continuous ^{4,5}	52	1.00 (0.70-1.45)	32	0.76 (0.37-1.56)
α -tocopherol				
Tertile ⁶				
1	18	1	16	1
2	14	0.48 (0.18-1.27)	11	1.21 (0.44-3.29)
3	20	0.66 (0.23-1.91)	5	0.39 (0.10-1.52)
p_{trend}^3		0.55		0.24
Continuous ^{4,7}	52	1.39 (0.99-1.95)	32	1.18 (0.68-2.04)
γ -tocopherol				
Tertile ⁸				
1	12	1	17	1
2	19	1.23 (0.48-3.14)	7	0.82 (0.28-2.38)
3	21	1.37 (0.51-3.65)	8	1.28 (0.39-4.17)
p_{trend}^3		0.54		0.76
Continuous ^{4,9}	52	1.03 (0.74-1.42)	32	1.50 (0.80-2.81)

Abbreviations: CI, confidence interval; RR, risk ratio.

¹In addition to conditioning on matching factors in the NHS and HPFS (age, fasting status, month of blood collection, and race), adjusted for BMI (continuous), smoking status (never, current and previous), and cholesterol (continuous).

²Median plasma retinol for each tertile in the NHS and HPFS: 1.74, 2.16, and 2.74 $\mu\text{mol/L}$.

³The p-value for linear trend across tertiles was the p-value of the ordinal variable constructed by assigning medians to all participants in the tertiles.

⁴Results for continuous analyses for each standard deviation increment.

⁵P for interaction by sex: 0.29 for retinol.

⁶Median plasma α -tocopherol for each tertile in the NHS and HPFS: 29.66, 41.32, and 57.50 $\mu\text{mol/L}$.

⁷P for interaction by sex: 0.50 for α -tocopherol.

⁸Median plasma γ -tocopherol for each tertile in the NHS and HPFS: 2.94, 5.60, and 8.59 $\mu\text{mol/L}$.

⁹P for interaction by sex: 0.62 for γ -tocopherol.

Supplementary Table 6. Associations between circulating retinol, α - and γ -tocopherol and glioma risk among non-smokers and after a 4-year lag in the Nurses' Health Study, and Health Professionals Follow-up Study.

	Non-smokers		After applying a 4-year lag	
	Number of glioma cases	RR (95%CI)	Number of glioma cases	RR (95%CI)
Retinol				
Tertile ²				
1	22	1 (ref)	18	1 (ref)
2	28	1.05 (0.51-2.19)	26	1.24 (0.57-2.71)
3	26	1.23 (0.56-2.70) 0.59	23	1.17 (0.49-2.80) 0.75
p_{trend}^3	76	1.15 (0.83-1.60)	67	1.06 (0.77-1.46)
α -tocopherol				
Tertile ⁵				
1	33	1 (ref)	29	1
2	23	0.68 (0.34-1.37)	21	0.60 (0.28-1.31)
3	20	0.56 (0.24-1.29) 0.17	17	0.46 (0.19-1.12) 0.09
p_{trend}^3	76	0.97 (0.66-1.41)	67	0.86 (0.60-1.23)
γ -tocopherol				
Tertile ⁶				
1	28	1 (ref)	22	1 (ref)
2	24	1.18 (0.58-2.40)	22	1.12 (0.52-2.41)
3	24	1.20 (0.56, 2.60) 0.65	23	1.42 (0.62-3.21) 0.39
p_{trend}^3	76	1.32 (0.97-1.79)	67	1.30 (0.96-1.77)
Continuous ⁴				

Abbreviations: CI, confidence interval; RR, risk ratio.

¹In addition to conditioning on matching factors in the NHS and HPFS (age, fasting status, month of blood collection, and race), adjusted for BMI (continuous), smoking status (never, current and previous), and cholesterol (continuous).

²Median plasma retinol for each tertile in the NHS and HPFS: 1.74, 2.16, and 2.74 $\mu\text{mol/L}$.

³The p -value for linear trend across tertiles was the p -value of the ordinal variable constructed by assigning medians to all participants in the tertiles.

⁴Results for continuous analyses for each standard deviation increment.

⁵Median plasma α -tocopherol for each tertile in the NHS and HPFS: 29.66, 41.32, and 57.50 $\mu\text{mol/L}$.

⁶Median plasma γ -tocopherol for each tertile in the NHS and HPFS: 2.94, 5.60, and 8.59 $\mu\text{mol/L}$.

Supplementary Table 7. Joint associations between plasma α - and γ -tocopherol and glioma risk in the Nurses' Health Study and Health Professionals Follow-up Study.

	Lower ¹ γ -tocopherol		Higher ² γ -tocopherol	
	Gliomas	RR (95%CI) ³	Gliomas	RR (95%CI) ³
Lower ¹ α -tocopherol	22	1 (ref)	25	1.06 (0.48-2.34)
Higher ² α -tocopherol	18	0.60 (0.26-1.41)	19	0.84 (0.33-2.14)

Abbreviations: CI, confidence interval; RR, risk ratio.

¹ Below median level.

²Above median level.

³In addition to conditioning on matching factors in the NHS and HPFS (age, fasting status, month of blood collection, and race), adjusted for BMI (continuous), smoking status (never, current and previous), and cholesterol (continuous).