

Supplementary Table 1. Baseline demographic characteristics of UK Biobank and NHS/HPFS participants by sex.

Characteristic	UK Biobank (Women)		UK Biobank (Men)		NHS (Women)		HPFS (Men)	
	Full Cohort (n=217,146)	Glioma Cases (n=188)	Full Cohort (n=188,117)	Glioma Cases (n=302)	Cases (n=52)	Controls (n=104)	Cases (n=32)	Controls (n=64)
Age (median, IQR)	57 (49-62)	61 (56-64)	57 (49-63)	61 (56-65)	59 (53-63)	59 (53-63)	64 (56-72)	64 (56-72)
Year of blood collection	2006-2010				1989-1990		1993-1995	
Time from blood collection to glioma diagnosis (median, range)		3.9 (0.1-9.0)		3.8 (0.02-8.5)	9.3 (1.1-16.7)		6.3 (0.3-20.6)	
BMI (median, IQR)	26.1 (23.4-29.7)	26.4 (23.8-29.5)	27.3 (25.0-30.1)	26.9 (24.7-30.1)	23.6 (21.0-27.2)	25.7 (22.6-29.2)	25.0 (23.5-27.0)	25.2 (22.8-27.4)
Race (n, %)*								
White	203,584 (93.8)	185 (98.4)	176,084 (93.6)	291 (96.4)	8 (15.4)	93 (89.4)	30 (93.8)	60 (93.8)
Non-white	12,930 (6.0)	2 (1.1)	11,232 (6.0)	6 (2.0)	0	0	2 (6.3)	0
Missing	632 (0.3)	1 (0.5)	801 (0.1)	5 (1.7)	44 (84.6)	11 (10.6)	0	4 (6.3)
Education (n, %)^								
Secondary school	62,142 (28.6)	50 (26.6)	45,987 (24.4)	60 (19.9)	0	0	0	0
Vocational training	12,230 (5.6)	10 (5.3)	8,000 (4.3)	12 (4.0)	0	0	0	0
Some college	35,567 (16.4)	25 (13.3)	36,256 (19.3)	53 (17.5)	52 (100)	104 (100)	32 (100)	64 (100)
Completed college	68,588 (31.6)	66 (35.1)	64,183 (34.1)	98 (32.5)	0	0	0	0
None of the above	34,866 (16.1)	32 (17.0)	30,301 (16.1)	69 (22.8)	0	0	0	0
Missing	3,783 (1.7)	5 (2.7)	3,390 (1.8)	10 (3.3)	0	0	0	0
TC (median, IQR)	224.2 (196.3-253.9)	229.2 (199.9-256.5)	211.7 (183.1-241.0)	214.0 (178.6-241.8)	198.7 (173.4-220.4)	195.3 (181.4-219.5)	186.2 (168.0-210.6)	196.4 (164.6-220.5)
HDL-C (median, IQR)	60.1 (51.2-70.3)	58.4 (51.1-67.3)	47.8 (41.1-56.0)	49.3 (43.0-58.9)	55.4 (46.3-63.0)	56.2 (47.5-65.3)	41.8 (35.8-47.1)	40.6 (36.1-51.1)
LDL-C (median, IQR)	137.5 (116.0-161.0)	142.5 (122.5-164.9)	134.4 (111.9-157.0)	133.6 (110.2-155.9)	128.3 (96.5-144.9)	118.1 (96.4-139.9)	119.9 (109.4-138.0)	128.9 (102.0-149.3)
TG (median, IQR)	116.6 (84.3-165.8)	126.1 (94.1-177.1)	149.9 (104.2-217.4)	144.3 (101.4-214.5)	87.6 (63.9-137.2)	91.5 (74.4-120.8)	108.7 (78.6-153.7)	109.8 (67.9-148.8)
History of hypertension (n, %)								
Yes	50781 (23.4)	46 (24.5)	54866 (29.2)	105 (34.8)	14 (26.9)	24 (23.1)	8 (25.0)	11 (17.2)
No	165936 (76.4)	141 (0.75)	132876 (70.6)	195 (64.6)	38 (73.1)	80 (76.9)	24 (75.0)	53 (82.8)
Missing	429 (0.2)	1 (0.5)	375 (0.2)	2 (0.7)	0	0	0	0
History of diabetes (n, %)								
Yes	7909 (3.6)	5 (2.7)	12669 (6.7)	23 (7.6)	2 (3.9)	2 (1.9)	0	4 (6.3)
No	208809 (96.2)	183 (97.3)	174884 (93.0)	277 (91.7)	50 (96.2)	102 (98.1)	32 (100.0)	60 (93.8)
Missing	428 (0.2)	0	564 (0.3)	2 (0.7)	0	0	0	0
Statin use (n, %) [†]								
Current statin use	22994 (10.6)	28 (14.9)	36713 (19.5)	73 (24.2)	-	-	3 (9.4)	4 (6.3)
No current statin use	193973 (89.3)	160 (85.1)	151198 (80.4)	229 (75.9)	-	-	29 (90.6)	60 (93.8)
Missing	179 (0.1)	0	206 (0.1)	0	-	-	0	0

Abbreviations: NHS: Nurses' Health Study, HPFS: Health Professionals Follow-Up Study, BMI: body mass index, HDL: high-density lipoprotein, IQR: interquartile range, LDL: low-density lipoprotein, TG: triglycerides

*Race was not assessed in NHS until the 2004 questionnaire, and is presented here for all participants who survived to complete the 2004 questionnaire.

^Although not assessed explicitly in NHS and HPFS, all participants in the cohorts had at least some college education, and are indicated as such in the table.

†Variable was not assessed in the NHS.

Supplementary Table 2. Risk of glioma in the UK Biobank and Nurses' Health Study/Health Professionals Follow-Up Study by baseline cholesterol concentrations by sex.

	Quartile	Range (mg/dL)*	UK Biobank (Women, n=188)			UK Biobank (Men, n=302)			NHS (Women, n=52)			HPFS (Men, n=32)		
			Cases^	MV HR^	95%CI	Cases^	MV HR†	95%CI	Cases	MV OR‡**	95%CI	Cases	MV OR**%	95%CI
TC	Q1	<190	27	Ref.		86	Ref.		20	Ref.		18	Ref.	
	Q2	≥190-218	47	1.39	0.85-2.29	63	0.99	0.70-1.41	17	1.02	0.44-2.33	11	0.93	0.33-2.57
	Q3	≥218-248	48	1.16	0.70-1.95	71	1.24	0.87-1.78	15	1.02	0.42-2.46	3	0.22	0.04-1.23
	Q4	≥248	58	1.15	0.68-1.93	61	1.25	0.86-1.82						
	P-trend			180		0.97	281		0.15	52		0.97	32	
HDL-C	Q1	<45	16	Ref.		91	Ref.		12	Ref.		21	Ref.	
	Q2	≥45-54	41	1.18	0.66-2.12	67	0.98	0.71-1.35	12	0.78	0.25-2.42	10	0.85	0.33-2.15
	Q3	≥54-65	56	1.10	0.62-1.94	53	1.08	0.76-1.54						
	Q4	≥65	51	0.71	0.40-1.29	37	1.44	0.96-2.16	28	0.61	0.23-1.64	1	-	-
	P-trend			164		0.03	248		0.11	52		0.31	32	
LDL-C	Q1	<114	32	Ref.		82	Ref.		22	Ref.		15	Ref.	
	Q2	≥114-136	40	1.17	0.72-1.90	66	1.00	0.70-1.42	10	0.97	0.37-2.58	8	0.86	0.27-2.71
	Q3	≥136-159	50	1.24	0.76-2.03	70	1.09	0.75-1.56						
	Q4	≥159	58	1.33	0.81-2.18	62	1.03	0.70-1.51	20	1.09	0.47-2.51	9	0.45	0.13-1.59
	P-trend			180		0.27	280		0.81	52		0.85	32	
TG	Q1	<92	42	Ref.		54	Ref.		27	Ref.		13	Ref.	
	Q2	≥92-131	51	1.05	0.69-1.60	72	1.08	0.76-1.55	10	0.61	0.22-1.68	7	1.39	0.39-4.99
	Q3	≥131-190	52	1.28	0.84-1.96	63	0.79	0.54-1.15						
	Q4	≥190	35	1.15	0.72-1.86	92	0.99	0.70-1.42	15	1.58	0.66-3.82	12	1.58	0.45-5.51
	P-trend			180		0.46	281		0.85	52		0.37	32	

*Quartiles for each cholesterol measure were computed using the distribution of values among participants in the UK Biobank.

^Cases may not sum to total due to missing cholesterol values.

†Adjusted for age, race (White vs. non-White), education (secondary school vs. vocational training vs. some college vs. completed college vs. none of the above), history of diabetes (yes vs. no), history of hypertension (yes vs. no), BMI (≤25 kg/m² vs. 25-30 kg/m² vs. ≥30 kg/m²), smoking status (never vs. past vs. current), and statin use (current use vs. no current use).

‡Adjusted for hypertension (yes vs. no), diabetes (yes vs. no), BMI (continuous), and smoking status (never vs. past vs. current).

**Matched on age, cohort, fasting status, month of sample collection, and ethnic background.

%Adjusted for history of hypertension (yes vs. no), history of diabetes (yes vs. no), statin use (current use vs. no current use), BMI (continuous), and smoking status (never vs. past vs. current).

Abbreviations: BMI: body mass index, CI: confidence interval, HDL-C: high-density lipoprotein cholesterol, HR: hazard ratio, LDL-C: low-density lipoprotein cholesterol, MV: multivariable, OR: odds ratio, TC: total cholesterol, TG: triglycerides

Supplementary Table 3. Risk of glioma subtypes in the UK Biobank by baseline cholesterol, age and multivariable adjusted.

	Quartile	Range (mg/dL)*	Cases [^]	HR [†]	95%CI	MV HR [‡]	95%CI	Cases [^]	HR [†]	95%CI	MV HR [‡]	95%CI	
		GBM					Non-GBM						
TC	Q1	<190	86	Ref.		Ref.		27	Ref.		Ref.		
	Q2	≥190-218	83	1.23	0.90-1.67	1.14	0.82-1.58	27	1.06	0.62-1.82	1.09	0.62-1.92	
	Q3	≥218-248	77	1.13	0.83-1.55	1.06	0.75-1.49	42	1.62	1.00-2.64	1.67	0.97-2.87	
	Q4	≥248	96	1.40	1.04-1.90	1.31	0.93-1.84	23	0.87	0.49-1.53	0.89	0.48-1.67	
	P-trend		342		0.04		0.15	119		0.99		0.95	
HDL-C	Q1	<45	85	Ref.		Ref.		22	Ref.		Ref.		
	Q2	≥45-54	80	1.05	0.77-1.42	0.98	0.72-1.35	28	1.37	0.78-2.41	1.28	0.72-2.26	
	Q3	≥54-65	73	1.02	0.74-1.41	0.97	0.70-1.36	36	1.89	1.09-3.27	1.66	0.94-2.94	
	Q4	≥65	67	1.07	0.76-1.52	0.99	0.68-1.44	21	1.18	0.62-2.23	0.98	0.50-1.92	
	P-trend		305		0.74		0.96	107		0.52		0.98	
LDL-C	Q1	<114	89	Ref.		Ref.		25	Ref.		Ref.		
	Q2	≥114-136	71	0.99	0.72-1.36	0.91	0.65-1.27	35	1.47	0.88-2.46	1.54	0.89-2.66	
	Q3	≥136-159	96	1.27	0.95-1.70	1.16	0.84-1.62	24	0.98	0.56-1.72	1.04	0.56-1.93	
	Q4	≥159	86	1.15	0.85-1.56	1.05	0.75-1.49	34	1.36	0.81-2.28	1.46	0.81-2.63	
	P-trend		342		0.20		0.51	118		0.49		0.42	
TG	Q1	<92	66	Ref.		Ref.		30	Ref.		Ref.		
	Q2	≥92-131	90	1.14	0.83-1.57	1.11	0.80-1.54	33	0.98	0.60-1.62	1.00	0.60-1.65	
	Q3	≥131-190	88	1.05	0.76-1.45	1.06	0.76-1.47	27	0.76	0.45-1.29	0.78	0.46-1.34	
	Q4	≥190	98	1.15	0.84-1.58	1.16	0.84-1.62	29	0.80	0.48-1.34	0.84	0.49-1.46	
	P-trend		342		0.54		0.44	119		0.32		0.47	

*Quartiles for each cholesterol measure were computed using the distribution of values among participants in the UK Biobank.

[^]Cases may not sum to total due to missing cholesterol values.

[†]Adjusted for age and sex (male vs. female)

[‡]Additionally adjusted for race (White vs. non-White vs. missing), education (secondary school vs. vocational training vs. some college vs. completed college vs. none of the above vs. missing), diabetes (yes vs. no vs. missing), hypertension (yes vs. no vs. missing), BMI (≤25 kg/m² vs. 25-30 kg/m² vs. ≥30 kg/m² vs. missing), smoking status (never vs. past vs. current vs. missing), and statin use (yes vs. no vs. missing).

Abbreviations: BMI: body mass index, CI: confidence interval, GBM: glioblastoma, HDL-C: high-density lipoprotein cholesterol, HR: hazard ratio, LDL-C: low-density lipoprotein cholesterol, MV: multivariable, TC: total cholesterol, TG: triglycerides

Supplementary Table 4. Risk of glioma in the UK Biobank by baseline cholesterol, age and multivariable adjusted, restricted to non-users of statins at baseline.

	Quartile	Range (mg/dL)*	Cases [^]	HR [†]	95%CI	MV HR [‡]	95%CI
TC	Q1	<190	59	Ref.		Ref.	
	Q2	≥190-218	85	0.99	0.71-1.39	0.99	0.71-1.39
	Q3	≥218-248	114	1.16	0.84-1.59	1.16	0.84-1.60
	Q4	≥248	113	1.09	0.79-1.50	1.09	0.78-1.51
	P-trend		371		0.48		0.47
HDL-C	Q1	<45	79	Ref.		Ref.	
	Q2	≥45-54	86	1.02	0.76-1.40	1.00	0.73-1.36
	Q3	≥54-65	97	1.20	0.88-1.63	1.13	0.83-1.56
	Q4	≥65	70	0.87	0.62-1.24	0.80	0.56-1.16
	P-trend		332		0.55		0.30
LDL-C	Q1	<114	58	Ref.		Ref.	
	Q2	≥114-136	81	0.92	0.66-1.30	0.93	0.66-1.30
	Q3	≥136-159	114	1.05	0.76-1.44	1.06	0.76-1.46
	Q4	≥159	117	1.06	0.77-1.46	1.07	0.78-1.48
	P-trend		370		0.49		0.44
TG	Q1	<92	79	Ref.		Ref.	
	Q2	≥92-131	104	1.06	0.79-1.44	1.08	0.80-1.45
	Q3	≥131-190	95	0.99	0.73-1.34	1.01	0.74-1.37
	Q4	≥190	93	0.95	0.70-1.28	0.98	0.71-1.34
	P-trend		371		0.54		0.70

*Quartiles for each cholesterol measure were computed using the distribution of values among participants in the UK Biobank.

[^]Cases may not sum to total due to missing cholesterol values.

[†]Adjusted for age and sex (male vs. female)

[‡]Additionally adjusted for race (White vs. non-White vs. missing), education (secondary school vs. vocational training vs. some college vs. completed college vs. none of the above vs. missing), diabetes (yes vs. no vs. missing), hypertension (yes vs. no vs. missing), BMI (≤ 25 kg/m² vs. 25-30 kg/m² vs. ≥ 30 kg/m² vs. missing), and smoking status (never vs. past vs. current vs. missing).

Abbreviations: BMI: body mass index, CI, confidence interval, HDL-C: high-density lipoprotein cholesterol, HR: hazard ratio, LDL-C: low-density lipoprotein cholesterol, MV: multivariable, TC: total cholesterol, TG: triglycerides

Supplementary Table 5. Risk of glioma subtypes in the UK Biobank by baseline cholesterol concentrations with a four year lag period.

	Quartile	Range (mg/dL)*	Total			GBM			LGG		
			Cases^	MV HR†	95%CI	Cases^	MV HR†	95%CI	Cases^	MV HR‡	95%CI
TC	Q1	<190	49	Ref.		35	Ref.		14	Ref.	
	Q2	≥190-218	53	1.39	0.91-2.12	41	1.58	0.96-2.61	12	0.96	0.43-2.17
	Q3	≥218-248	56	1.49	0.96-2.31	37	1.47	0.86-2.50	19	1.50	0.69-3.29
	Q4	≥248	71	1.86	1.21-2.88	56	2.20	1.32-3.66	15	1.14	0.49-2.65
	P-trend		229		0.005			0.004			0.60
HDL-C	Q1	<45	45	Ref.		34	Ref.		11	Ref.	
	Q2	≥45-54	54	1.27	0.85-1.92	42	1.36	0.85-2.17	12	1.06	0.46-2.43
	Q3	≥54-65	56	1.46	0.96-2.21	38	1.40	0.86-2.28	18	1.57	0.70-3.50
	Q4	≥65	49	1.49	0.93-2.37	35	1.64	0.95-2.83	14	1.18	0.48-2.91
	P-trend		204		0.09			0.09			0.64
LDL-C	Q1	<114	56	Ref.		41	Ref.		15	Ref.	
	Q2	≥114-136	44	0.94	0.61-1.45	28	0.84	0.50-1.43	16	1.15	0.54-2.44
	Q3	≥136-159	62	1.23	0.81-1.87	51	1.43	0.88-2.32	11	0.77	0.33-1.81
	Q4	≥159	66	1.33	0.87-2.04	49	1.40	0.85-2.31	17	1.15	0.51-2.56
	P-trend		228		0.10			0.07			0.88
TG	Q1	<92	53	Ref.		36	Ref.		17	Ref.	
	Q2	≥92-131	66	0.98	0.67-1.42	49	1.03	0.66-1.61	17	0.87	0.44-1.72
	Q3	≥131-190	48	0.69	0.46-1.04	37	0.77	0.48-1.24	11	0.54	0.25-1.17
	Q4	≥190	62	0.88	0.60-1.31	47	0.95	0.60-1.50	15	0.75	0.35-1.57
	P-trend		229		0.48			0.72			0.42

*Quartiles for each cholesterol measure were computed using the distribution of values among participants in the UK Biobank.

^Cases may not sum to total due to missing cholesterol values.

†Adjusted for age, sex (male vs. female), race (White vs. non-White), education (secondary school vs. vocational training vs. some college vs. completed college vs. none of the above), history of hypertension (yes vs. no), history of diabetes (yes vs. no), BMI (≤25 kg/m² vs. 25-30 kg/m² vs. ≥30 kg/m²), smoking status (never vs. past vs. current), and statin use (current use vs. no current use).

‡Adjusted for age, sex (male vs. female), race (White vs. non-White), education (secondary school vs. vocational training vs. some college vs. completed college vs. none of the above), history of hypertension (yes vs. no), history of diabetes (yes vs. no), BMI (≤25 kg/m² vs. 25-30 kg/m² vs. ≥30 kg/m²), and smoking status (never vs. past vs. current).

Abbreviations: BMI: body mass index, CI: confidence interval, HDL-C: high-density lipoprotein cholesterol, HR: hazard ratio, LDL-C: low-density lipoprotein cholesterol, MV: multivariable, TC: total cholesterol, TG: triglycerides

Supplementary Table 6. Risk of glioma in the UK Biobank by baseline statin use, age and multivariable adjusted.

	Category	Cases*	HR[^]	95%CI	MV HR[†]	95%CI
Total						
Statin use	No current use	389	Ref.		Ref.	
	Current use	101	1.00	0.79-1.25	1.04	0.81-1.33
Statin use with four year lag	No current use	191	Ref.		Ref.	
	Current use	47	0.96	0.69-1.33	1.05	0.73-1.50
Male						
Statin use	No current use	229	Ref.		Ref.	
	Current use	73	0.98	0.75-1.28	0.97	0.72-1.31
Statin use with four year lag	No current use	112	Ref.		Ref.	
	Current use	34	0.96	0.64-1.42	1.00	0.64-1.54
Female						
Statin use	No current use	160	Ref.		Ref.	
	Current use	28	1.04	0.69-1.57	1.25	0.80-1.95
Statin use with four year lag	No current use	79	Ref.		Ref.	
	Current use	13	0.97	0.53-1.76	1.20	0.63-2.29
GBM						
Statin use	No current use	289	Ref.		Ref.	
	Current use	77	1.01	0.78-1.31	1.03	0.77-1.38
Statin use with four year lag	No current use	143	Ref.		Ref.	
	Current use	35	1.00	0.68-1.47	1.16	0.73-1.83
Non-GBM						
Statin use	No current use	100	Ref.		Ref.	
	Current use	24	1.01	0.64-1.59	0.83	0.49-1.41
Statin use with four year lag	No current use	48	Ref.		Ref.	
	Current use	12	1.02	0.53-1.94	1.02	0.46-2.27

*Cases may not sum to total due to missing statin use values.

[^]Adjusted for age and sex (male vs. female)

[†]Additionally adjusted for race (White vs. non-White), education (secondary school vs. vocational training vs. some college vs. completed college vs. none of the above), diabetes (yes vs. no), hypertension (yes vs. no), BMI (≤ 25 kg/m² vs. 25-30 kg/m² vs. ≥ 30 kg/m²), and smoking status (never vs. past vs. current).

Abbreviations: BMI: body mass index, CI, confidence interval, GBM: glioblastoma, HR: hazard ratio, MV: multivariable