Supplementary Table 1. Characteristics of genetic variants associated with coronary heart disease in the UK biobank

SNP	Chromosome	Nearest gene	EA/NA	Risk estimate
rs11206510	1	*PCSK9*	T/C	1.08
rs17114036	1	*PPAP2B*	A/G	1.13
rs646776	1	*SORT1*	T/C	1.11
crs4845625	1	*IL6R*	T/C	1.05
rs17464857	1	*MIA3*	T/G	1.06
rs17465637	1	*MIA3*	C/A	1.08
rs16986953	2	*AK097927*	A/G	1.09
rs515135	2	*APOB*	C/T	1.07
rs6544713	2	*ABCG5-ABCG8*	T/C	1.05
rs1561198	2	*VAMP5-VAMP8-GGCX*	T/C	1.06
rs2252641	2	*ZEB2-ACO74093.1*	C/T	1.03
rs6725887	2	*WDR12*	C/T	1.14
rs9818870	3	*MRAS*	T/C	1.07
rs1878406	4	*EDNRA*	T/C	1.06
rs7692387	4	*GUCY1A3*	G/A	1.07
rs17087335	4	*REST-NOA1*	T/G	1.06
rs273909	5	*SLC22A4-SLC22A5*	G/A	1.06
rs6903956	6	*ADTRP-C6orf105*	A/G	1
rs12526453	6	*PHACTR1*	C/G	1.1
rs17609940	6	*ANKS1A*	G/C	1.03
rs10947789	6	*KCNK5*	T/C	1.05
rs12190287	6	*TCF21*	C/G	1.06
rs2048327	6	*SLC22A3-LPAL2-LPA*	C/T	1.06
rs4252120	6	*PLG*	T/C	1.03
rs2023938	7	*HDAC9*	C/T	1.06
rs10953541	7	*7q22*	C/T	1.05
rs11556924	7	*ZC3HC1*	C/T	1.08
rs3918226	7	*NOS3*	T/C	1.14
rs264	8	*LPL*	G/A	1.06
rs2954029	8	*TRIB1*	A/T	1.04
rs3217992	9	*9p21*	T/C	1.14
rs4977574	9	*9p21*	G/A	1.21
rs579459	9	*ABO*	C/T	1.08
rs2505083	10	*KIAA1462*	C/T	1.06
rs2047009	10	*CXCL12*	G/T	1.06
rs501120	10	*CXCL12*	T/C	1.08
rs11203042	10	*LIPA*	T/C	1.04
rs1412444	10	*LIPA*	T/C	1.07
rs12413409	10	*CYP17A1-CNNM2-NT5C2*	G/A	1.08

rs974819	11	*PDGFD*	T/C	1.07
rs964184	11	*ZNF259-APOA5-APOA1*	G/C	1.05
rs10840293	11	*SWAP70*	A/G	1.06
rs7136259	12	*ATP2B1*	T/C	1.04
rs3184504	12	*SH2B3*	T/C	1.07
rs11830157	12	*KSR2*	G/T	1.04
rs9319428	13	*FLT1*	A/G	1.04
rs4773144	13	*COL4A1/A2*	G/A	1.05
rs9515203	13	*COL4A1/A2*	T/C	1.07
rs2895811	14	*HHIPL1*	C/T	1.04
rs7173743	15	*ADAMTS7*	T/C	1.08
rs17514846	15	*FURIN-FES*	A/C	1.05
rs56062135	15	*SMAD3*	C/T	1.07
rs8042271	15	*MFGE8-ABHD2*	G/A	1.10
rs216172	17	*SMG6*	C/G	1.05
rs12936587	17	*RAI1-PEMT-RASD1*	G/A	1.03
rs46522	17	*UBE2Z*	T/C	1.04
rs663129	18	*PMAIP1-MC4R*	A/G	1.06
rs1122608	19	*LDLR*	G/T	1.08
rs2075650	19	*APOE-APOC1*	G/A	1.07
rs445925	19	*APOE-APOC1*	G/A	1.09
rs12976411	19	*ZNF507-LOC400684*	T/A	0.95
rs9982601	21	*KCNE2*	T/C	1.12
rs180803	22	*POM121L9P-ADORA2A*	G/T	1.20

We did not use rare or low frequency variants with <5 % minor allele frequency

Supplementary Table 2. Characteristics of genetic variants associated with stroke in the UK biobank

SNP	Chromosome	Nearest gene	EA/NA	Risk estimate
rs880315	1	*CASZ1*	C/T	1.05
rs12037987	1	*WNT2B*	C/T	1.07
rs12124533	1	*TSPAN2*	T/C	1.17
rs1052053	1	*PMF1–SEMA4A*	G/A	1.06
rs17612742	4	*EDNRA*	C/T	1.19
rs6825454	4	*FGA*	C/T	1.06
rs13143308	4	*PITX2*	T/G	1.32
rs11957829	5	*LOC100505841*	A/G	1.07
rs6891174	5	*NKX2-5*	A/G	1.11
rs16896398	6	*SLC22A7–ZNF318*	T/A	1.05
rs4959130	6	*FOXF2*	A/G	1.08
rs42039	7	*CDK6*	C/T	1.07
rs2107595	7	*HDAC9–TWIST1*	A/G	1.21
rs7859727	9	*Chr9p21*	T/C	1.05
rs10820405	9	*LINC01492*	G/A	1.2
rs635634	9	*ABO*	T/C	1.08
rs2295786	10	*SH3PXD2A*	A/T	1.05
rs7304841	12	*PDE3A*	A/C	1.05
rs35436	12	*TBX3*	C/T	1.05
rs3184504	12	*SH2B3*	T/C	1.08
rs9526212	13	*LRCH1*	G/A	1.06
rs4932370	15	*FURIN–FES*	A/G	1.05
rs12932445	16	*ZFHX3*	C/T	1.2
rs12445022	16	*ZCCHC14*	A/G	1.06
rs11867415	17	*PRPF8*	G/A	1.09
rs2229383	19	*ILF3–SLC44A2*	T/G	1.05
rs8103309	19	*SMARCA4–LDLR*	T/C	1.05

We did not use rare or low frequency variants with <5 % minor allele frequency.

Supplementary Table 3. Adjusted HR (95% CI) for the Use of Glucosamine Supplements and Risk of Cardiovascular Disease (CVD), CVD-mortality and Mortality [a]

	Non-user case, n (%)	User case, n (%)	Age-adjusted HRs	*P*-value	Multivariate-Adjusted HRs [b]	*P*-value
CVD event [c]	5,081 (2.2)	311 (1.9)	0.69 (0.61 to 0.77)	<0.001	0.81 (0.72 to 0.91)	<0.001
CVD death	1,523 (0.7)	84 (0.5)	0.59 (0.47 to 0.73)	<0.001	0.76 (0.61 to 0.95)	0.01
CHD	2,954 (1.3)	164 (1.0)	0.64 (0.54 to 0.74)	<0.001	0.77 (0.65 to 0.90)	0.001
Non-fatal	2,342 (1.0)	136 (0.8)	0.68 (0.57 to 0.80)	<0.001	0.79 (0.69 to 0.94)	0.01
Fatal	612 (0.3)	28 (0.2)	0.49 (0.34 to 0.72)	<0.001	0.69 (0.47 to 1.01)	0.06
Stroke	1,544 (0.7)	108 (0.7)	0.77 (0.63 to 0.94)	0.009	0.87 (0.72 to 1.07)	0.18
Non-fatal	1,348 (0.6)	96 (0.6)	0.79 (0.64 to 0.97)	0.023	0.89 (0.72 to 1.09)	0.26
Fatal	196 (0.1)	12 (0.1)	0.66 (0.37 to 1.19)	0.168	0.79 (0.44 to 1.42)	0.43
Ischemic stroke	1,091 (0.5)	80 (0.5)	0.79 (0.63 to 0.99)	0.044	0.92 (0.73 to 1.15)	0.45
Hemorrhagic stroke	399 (0.2)	27 (0.2)	0.79 (0.53 to 1.16)	0.226	0.84 (0.57 to 1.25)	0.39

[a] After excluding participants who use any other supplements, remaining 244,207 participants.

[b] Results were adjusted for age, sex, race (White European, Mixed, South Asian, Black, Others), average total annual household income (less than £18,000, £18,000 to £ 30,999, £ 31,000 to £ 51,999, £ 52,000 to £ 100,000, greater than £ 100,000 and "do not know" or missing), BMI, smoking (never, past, current, missing), alcohol intake, physical activity (<150min/week, >=150min/week), diabetes (yes, no or missing), hypertension (yes or no), high cholesterol, arthritis (yes or no), antihypertensive medication (yes or no), lipid treatment (yes or no), insulin medication (yes or no), aspirin use (yes or no), non-aspirin NASIDs use (yes or no) and healthy diet (yes or no)

[c] CVD event were a composite end point of first major cardiovascular event (coronary heart disease, stroke, or cardiovascular death)

Supplementary Table 4. Adjusted HR (95% CI) for the Use of Glucosamine Supplements and Risk of Cardiovascular Disease (CVD), CVD-mortality and Mortality (after excluding cardiovascular events or death from CVD within 2 follow-up year)

	Non-user case, n (%)	User case, n (%)	Age-adjusted HRs	*P*-value	Multivariate-Adjusted HRs [a]	*P*-value
CVD event [b]	6,751 (1.8)	1,417 (1.6)	0.71 (0.67 to 0.76)	<0.001	0.84 (0.79 to 0.90)	<0.001
CVD death	2,127 (0.6)	408 (0.5)	0.63 (0.56 to 0.70)	<0.001	0.79 (0.71 to 0.89)	<0.001
CHD	3,814 (1.0)	724 (0.8)	0.66 (0.61 to 0.71)	<0.001	0.80 (0.74 to 0.87)	<0.001
Non-fatal	3,023 (0.8)	601 (0.7)	0.70 (0.64 to 0.76)	<0.001	0.82 (0.74 to 0.90)	<0.001
Fatal	791 (0.2)	123 (0.1)	0.52 (0.43 to 0.62)	<0.001	0.73 (0.60 to 0.90)	0.003
Stroke	2,063 (0.6)	513 (0.6)	0.84 (0.76 to 0.92)	<0.001	0.91 (0.82 to 1.01)	0.09
Non-fatal	1,772 (0.5)	441(0.5)	0.84 (0.75 to 0.93)	0.001	0.92 (0.82 to 1.03)	0.14
Fatal	289 (0.1)	72 (0.1)	0.81 (0.62 to 1.04)	0.101	0.89 (0.67 to 1.17)	0.40
Ischemic stroke	1,417 (0.4)	349 (0.4)	0.81 (0.72 to 0.91)	<0.001	0.93 (0.82 to 1.06)	0.29
Hemorrhagic stroke	534 (0.1)	130 (0.1)	0.85 (0.70 to 1.03)	0.091	0.84 (0.68 to 1.03)	0.10

[a] Results were adjusted for age, sex, race (White European, Mixed, South Asian, Black, Others), average total annual household income (less than £18,000, £18,000 to £ 30,999, £ 31,000 to £ 51,999, £ 52,000 to £ 100,000, greater than £ 100,000 and "do not know" or missing), BMI, smoking (never, past, current, missing), alcohol intake, physical activity (<150min/week, >=150min/week), diabetes (yes, no or missing), hypertension (yes or no), high cholesterol, arthritis (yes or no), antihypertensive medication (yes or no), lipid treatment (yes or no), insulin medication (yes or no), aspirin use (yes or no), non-aspirin NASIDs use (yes or no), vitamin supplements use (yes or no), other supplements use (yes or no) and healthy diet (yes or no)

[b] CVD event were a composite end point of first major cardiovascular event (coronary heart disease, stroke, or cardiovascular death)

Supplementary Table 5. Adjusted HR (95% CI) for the Use of Glucosamine Supplements and Risk of Cardiovascular Disease (CVD), CVD-mortality and Mortality (after further adjustment for CHD genetic predisposition score or stroke genetic predisposition)

	Non-user case, n (%)	User case, n (%)	Age-adjusted HRs	*P*-value	Multivariate-Adjusted HRs*	*P*-value
CVD event [a, d]	5,282 (2.3)	1,163 (2.0)	0.74 (0.69 to 0.79)	<0.001	0.86 (0.81 to 0.93)	<0.001
CVD death [a, d]	1,659 (0.7)	338 (0.6)	0.66 (0.58 to 0.74)	<0.001	0.84(0.75 to 0.96)	0.008
CHD [b, e]	4,118 (1.3)	792 (1.0)	0.66 (0.61 to 0.71)	<0.001	0.80 (0.74 to 0.87)	<0.001
Non-fatal [b, e]	3,253 (1.0)	659 (0.8)	0.70 (0.65 to 0.76)	<0.001	0.82 (0.75 to 0.90)	<0.001
Fatal [b, e]	865 (0.3)	133 (0.2)	0.51 (0.42 to 0.61)	<0.001	0.72 (0.60 to 0.88)	0.001
Stroke [c, f]	1,827 (0.7)	458 (0.7)	0.83 (0.75 to 0.93)	0.001	0.91 (0.82 to 1.02)	0.10
Non-fatal [c, f]	1,568 (0.6)	398 (0.6)	0.85 (0.76 to 0.95)	0.004	0.92 (0.82 to 1.03)	0.16
Fatal [c, f]	259 (0.1)	60 (0.1)	0.75 (0.57 to 0.99)	0.046	0.86 (0.63 to 1.16)	0.32
Ischemic stroke [c, f]	1,281 (0.5)	319 (0.5)	0.81 (0.72 to 0.92)	0.001	0.91 (0.80 to 1.04)	0.18
Hemorrhagic stroke [c, f]	492 (0.2)	123 (0.2)	0.87 (0.71 to 1.06)	0.157	0.87 (0.71 to 1.08)	0.22

* Results were adjusted for age, sex, race (White European, Mixed, South Asian, Black, Others), average total annual household income (less than £18,000, £18,000 to £ 30,999, £ 31,000 to £ 51,999, £ 52,000 to £ 100,000, greater than £ 100,000 and "do not know" or missing), BMI, smoking (never, past, current, missing), alcohol intake, physical activity (<150min/week, >=150min/week), diabetes (yes, no or missing), hypertension (yes or no), high cholesterol, arthritis (yes or no), antihypertensive medication (yes or no), lipid treatment (yes or no), insulin medication (yes or no), aspirin use (yes or no), non-aspirin NASIDs use (yes or no), vitamin supplements use (yes or no), other supplements use (yes or no) and healthy diet (yes or no)

[a] N=289, 445

[b] N=393, 771

[c] N=330, 419

[d] further adjustment for CHD genetic predisposition score and stroke genetic predisposition score

[e] further adjustment for CHD genetic predisposition score
[f] further adjustment for stroke genetic predisposition score