Supplementary Table 1. Information of genetic variants associated with type 2 diabetes in the UK Biobank study

SNP	Chr	Nearest Gene	EA/NEA	OR (SE)	P
rs3768321	1	MACF1	T/G	1.144 (0.028)	1.72E-06
rs12031920	1	FAF1	T/A	1.004 (0.024)	0.855
rs67156297	1	ATP8B2	A/G	1.041 (0.026)	0.126
rs340874	1	PROX1	C/T	1.092 (0.024)	2.06E-04
rs145819220	2	GCKR	C/G	1.122 (0.173)	0.504
rs6757251	2	THADA	C/T	1.172 (0.04)	6.18E-05
rs9309245	2	ASB3	C/G	1.019 (0.025)	0.438
rs1116357	2	CCDC85A	G/A	1.026 (0.023)	0.264
rs10193447	2	BCL11A	T/C	1.015 (0.024)	0.538
rs6723108	2	TMEM163	T/G	1.008 (0.023)	0.719
rs7560163	2	RBM43/RND3	C/G	1.082 (0.24)	0.743
rs1563575	2	RBMS1	G/A	1.006 (0.026)	0.83
rs28584669	2	GRB14	T/C	1.031 (0.032)	0.343
rs1861612	2	DNER	A/G	1.025 (0.023)	0.287
rs11712037	3	PPARG	C/G	1.108 (0.037)	0.006
rs35352848	3	UBE2E2	T/C	1.14 (0.03)	1.18E-05
rs79819696	3	PSMD6	A/G	1.019 (0.236)	0.938
rs7428936	3	ADAMTS9	T/C	1.064 (0.024)	0.01
rs11708067	3	ADCY5	A/G	1.096 (0.028)	0.001
rs4402960	3	IGF2BP2	T/G	1.225 (0.024)	1.27E-16
rs9820223	3	ST6GAL1	C/T	1.07 (0.024)	0.005
rs6777684	3	LPP	G/A	1.116 (0.024)	7.73E-06
rs1531583	4	MAEA	T/G	1.163 (0.057)	0.008
rs3821943	4	WFS1	T/C	1.067 (0.024)	0.006
rs7660590	4	TMEM154	C/T	1.015 (0.026)	0.561
rs60780116	4	ACSL1	T/C	1.046 (0.033)	0.166
rs173964	5	ANKRD55	G/A	1.077 (0.027)	0.006
rs9687833	5	ANKRD55	A/G	1.088 (0.028)	0.003
rs6453287	5	ZBED3	C/A	1.06 (0.025)	0.021
rs78408340	5	PAM	G/C	1.637 (0.097)	3.60E-07
rs74944275	5	PAM	T/C	1.092 (0.053)	0.098
rs6923241	6	SSR1/RREB1	T/C	1.003 (0.026)	0.909
rs7451008	6	CDKAL1	C/T	1.154 (0.026)	2.84E-08
rs2244020	6	HLA-B	G/A	1.047 (0.025)	0.063
rs143308245	6	ZFAND3	T/A	1.744 (0.613)	0.364
rs11759026	6	CENPW	G/A	1.108 (0.027)	1.74E-04
rs10276674	7	DGKB	C/T	1.114 (0.029)	2.28E-04
rs10238625	7	DGKB	A/G	1.074 (0.024)	0.003
rs1635852	7	JAZF1	T/C	1.087 (0.023)	3.47E-04

rs878521	7	GCK	A/G	1.075 (0.027)	0.007
rs10229583	7	PAX4	A/G	1.007 (0.027)	0.797
rs73455744	7	GCC1	G/A	1.268 (1.024)	0.817
rs791595	7	MIR129-LEP	G/A	1.051 (0.031)	0.109
rs10954284	7	KLF14	T/A	1.089 (0.023)	2.59E-04
rs1182436	7	MNX1	C/T	1.129 (0.031)	9.97E-05
rs516946	8	ANK1	C/T	1.085 (0.028)	0.003
rs4734285	8	TP53INP1	T/C	1.038 (0.024)	0.125
rs11786613	8	TP53INP1	C/A	1.195 (0.089)	0.046
rs3802177	8	SLC30A8	G/A	1.146 (0.026)	1.15E-07
rs10758593	9	GLIS3	A/G	1.086 (0.024)	4.77E-04
rs10965223	9	CDKN2A/B	A/G	1.049 (0.024)	0.042
rs10965248	9	CDKN2A/B	T/C	1.21 (0.032)	3.14E-09
rs10757282	9	CDKN2A/B	C/T	1.014 (0.024)	0.552
rs1575972	9	DMRTA1	T/A	1.042 (0.067)	0.534
rs13301067	9	TLE4	G/A	1.175 (0.051)	0.002
rs9410573	9	TLE1	T/C	1.123 (0.024)	1.10E-06
rs635634	9	ABO	T/C	1.013 (0.03)	0.656
rs11787792	9	GPSM1	A/G	1.052 (0.025)	0.041
rs10998572	10	VPS26A	C/A	1.056 (0.049)	0.27
rs810517	10	ZMIZ1	C/T	1.118 (0.023)	1.95E-06
rs11187140	10	HHEX/IDE	G/A	1.172 (0.025)	1.94E-10
rs7903146	10	TCF7L2	T/C	1.501 (0.024)	6.55E-63
rs10886471	10	GRK5	T/C	1.014 (0.023)	0.541
rs2292626	10	PLEKHA1	C/T	1.078 (0.023)	0.001
rs2334499	11	DUSP8	T/C	1.041 (0.024)	0.085
rs11564732	11	INS-IGF2	C/T	1.068 (0.089)	0.456
rs7107784	11	MIR4686	G/A	1.062 (0.025)	0.018
rs231360	11	KCNQ1	T/C	1.084 (0.024)	0.001
rs233449	11	KCNQ1	G/A	1.114 (0.027)	4.64E-05
rs2237897	11	KCNQ1	C/T	1.35 (0.066)	4.89E-06
rs441613	11	KCNQ1	C/T	1.009 (0.025)	0.712
rs5219	11	KCNJ11	T/C	1.072 (0.024)	0.004
rs1061810	11	HSD17B12	A/C	1.025 (0.025)	0.329
rs76550717	11	ARAP1 (CENTD2)	A/G	1.12 (0.033)	0.001
rs10830963	11	MTNR1B	G/C	1.119 (0.026)	1.09E-05
rs11063018	12	CCND2	C/T	1.057 (0.03)	0.067
rs188827514	12	CCND2	A/G	1.481 (0.183)	0.032
rs4238013	12	CCND2	C/T	1.108 (0.028)	3.16E-04
rs7953190	12	KLHDC5	T/C	1.125 (0.03)	1.03E-04
rs147538848	12	FAM60A	G/A	1.24 (1.024)	0.834
rs2258238	12	HMGA2	T/A	1.104 (0.037)	0.007
rs6581998	12	TSPAN8/LGR5	C/T	1.028 (0.026)	0.285

rs56348580	12	HNF1A (TCF1)	G/C	1.048 (0.026)	0.069
rs2851437	12	MPHOSPH9	A/C	1.025 (0.028)	0.363
rs9552911	13	SGCG	G/A	1.214 (0.464)	0.676
rs7330796	13	TBC1D4	T/C	1.023 (0.036)	0.535
rs11616380	13	SPRY2	G/T	1.153 (0.027)	9.17E-08
rs10146997	14	NRXN3	G/A	1.005 (0.028)	0.848
rs67839313	15	INAFM2	C/T	1.032 (0.037)	0.4
rs4774420	15	C2CD4A	C/T	1.008 (0.026)	0.761
rs952471	15	HMG20A	G/C	1.065 (0.026)	0.015
rs62006309	15	ZFAND6	A/G	1.03 (0.023)	0.204
rs12595616	15	PRC1	C/T	1.066 (0.024)	0.008
rs1558902	16	FTO	A/T	1.059 (0.023)	0.014
rs8056814	16	BCAR1	G/A	1.225 (0.045)	7.74E-06
rs2925979	16	CMIP	T/C	1.059 (0.025)	0.024
rs9911305	17	SRR	A/G	1.07 (0.026)	0.009
rs7224685	17	ZZEF1	T/G	1.037 (0.025)	0.142
rs13342692	17	SLC16A11/A13	T/C	1.037 (0.127)	0.774
rs78761021	17	GLP2R	G/A	1.039 (0.025)	0.121
rs757209	17	HNF1B (TCF2)	G/A	1.061 (0.024)	0.012
rs7234111	18	LAMA1	C/T	1.083 (0.024)	0.001
rs1942880	18	MC4R	T/C	1.014 (0.025)	0.587
rs79851087	18	MC4R	A/G	1.004 (0.087)	0.962
rs12454712	18	BCL2A	T/C	1.069 (0.024)	0.006
rs58489806	19	CILP2	T/C	1.125 (0.04)	0.003
rs139990642	19	PEPD	A/G	1.229 (0.145)	0.154
rs429358	19	APOE	T/C	1.067 (0.033)	0.051
rs55864746	19	GIPR	A/G	1.11 (0.026)	4.32E-05
rs12625671	20	HNF4A	C/T	1.081 (0.037)	0.035
rs1800961	20	HNF4A	T/C	1.322 (0.06)	2.79E-06
rs2023681	22	MTMR3/HORMAD2	G/A	1.132 (0.042)	0.003

Supplementary Table 2. Hazard ratios of type 2 diabetes incidence according to categories of hours of sedentary behaviors in the UK Biobank after excluding the cases developed in the first 2 years of follow-up.

Sedentary time/day	# cases/# total	Model 1		Model 2	
		HR (95% CI)	p	HR (95% CI)	p
<2	653/37563	1 (reference)		1 (reference)	
2-3	2640/139398	1.08 (1.01, 1.17)	0.02	1.08 (0.99, 1.17)	0.08
4-5	4297/163226	1.46 (1.36, 1.56)	<.001	1.26 (1.16, 1.37)	<.001
≥6	5066/128953	2.08 (1.94, 2.23)	<.001	1.55 (1.43, 1.68)	<.001
Per SD increase		1.30 (1.28, 1.32)	<.001	1.17 (1.16, 1.94)	<.001
		p-trend	<.001	p-trend	<.001

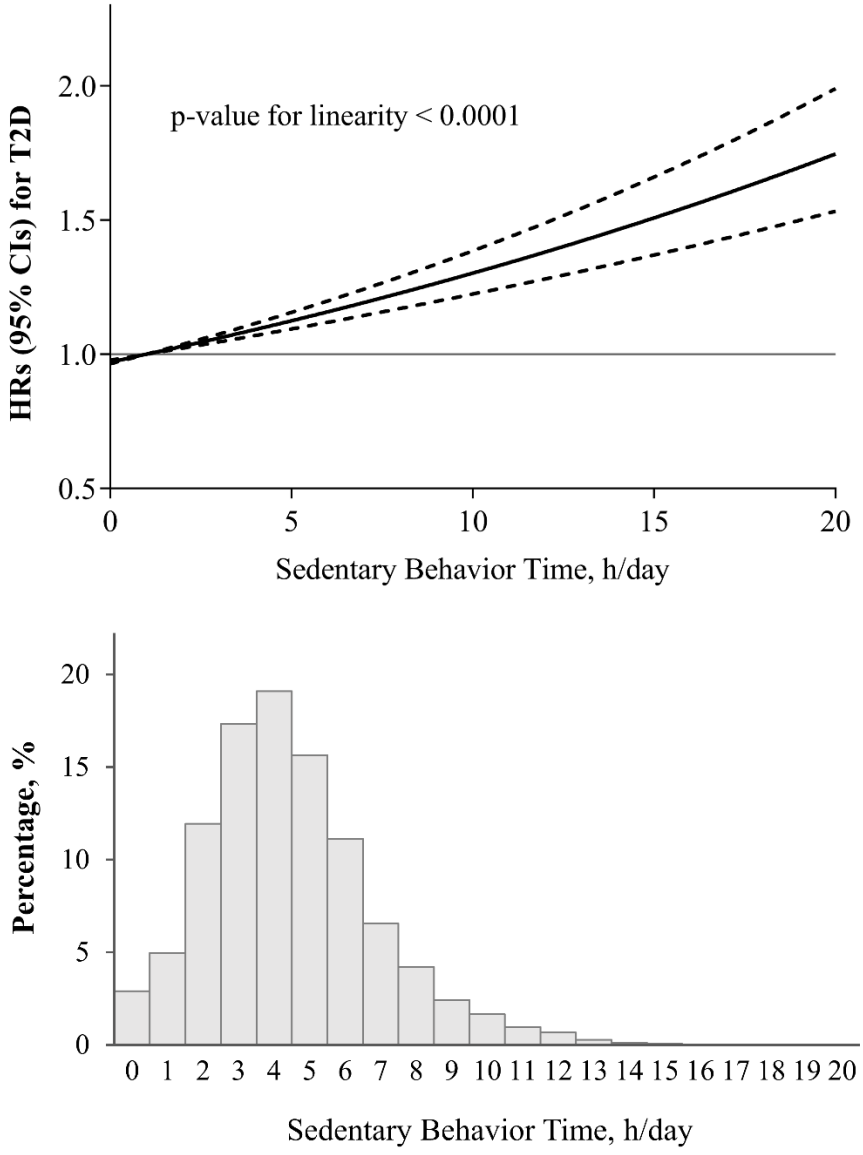
1 SD of sedentary time = 2.4 h/d
Model 1: age, race, gender.
Model 2: Model 1+ smoking status, alcohol intake, healthy diet score, education, average household income, total MET, Townsend deprivation index, assessment center, hypertension, cholesterol-lowering medication, anti-hypertensive medication, T2D-GRS, and the first 10 genetic principal components.

Supplementary Table 3 Hazard ratios for T2D by iso-temporal substitution of 30 minutes/day of sedentary behavior time with equivalent durations of each different types of physical activity according to tertile categories of T2D-GRS

	HR (95% CI)		
	Low GRS	Intermediate GRS	High GRS
Walking for pleasure	0.81 (0.76, 0.85)	0.84 (0.81, 0.88)	0.87 (0.84, 0.90)
Light DIY	0.92 (0.87, 0.97)	0.93 (0.90, 0.97)	0.96 (0.93, 0.99)
Heavy DIY	0.90 (0.84, 0.96)	0.92 (0.88, 0.97)	0.94 (0.90, 0.98)
Daily life activity*	0.88 (0.85, 0.90)	0.90 (0.88, 0.92)	0.92 (0.91, 0.94)
Strenuous sports	0.65 (0.52, 0.81)	0.63 (0.52, 0.75)	0.74 (0.65, 0.84)
Other exercise	0.75 (0.69, 0.82)	0.74 (0.69, 0.79)	0.77 (0.72, 0.81)
Structured exercise†	0.73 (0.68, 0.79)	0.71 (0.67, 0.76)	0.76 (0.73, 0.80)
Total PA ‡	0.85 (0.83, 0.88)	0.87 (0.85, 0.89)	0.89 (0.88, 0.91)

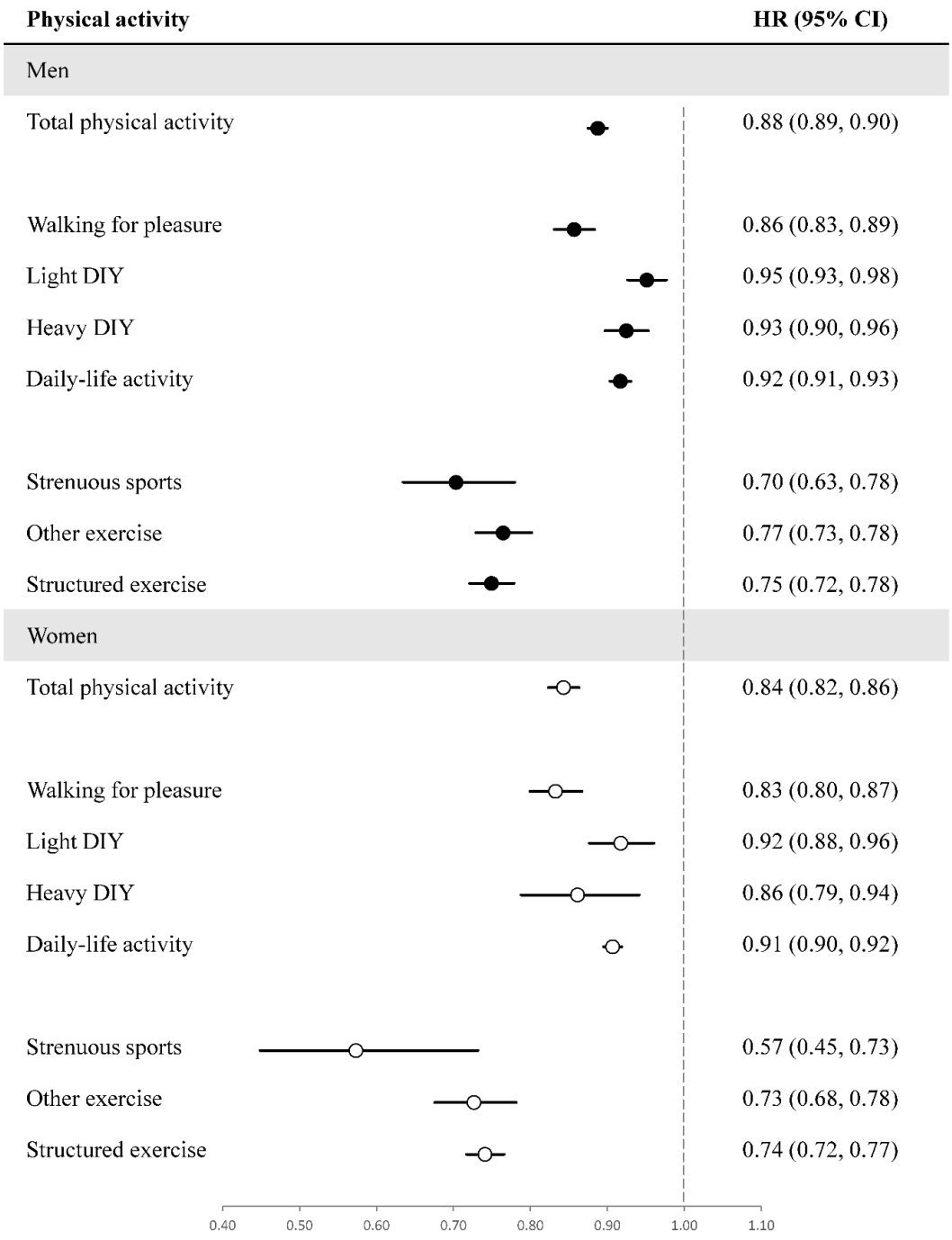
*Daily life activity is the sum of walking for pleasure, light DIY, and heavy DIY.
†Structured exercise is the sum of strenuous sports and other exercise.
‡Total PA includes all the five types of physical activity.
Models have omitted the sedentary behavior component, and adjusted for total discretionary time, time of each type of physical activity, age, gender, race, smoking status, alcohol intake, education, average household income, healthy diet score, Townsend deprivation index, assessment center, hypertension, cholesterol-lowering medication, anti-hypertensive medication, T2D-GRS, and the first 10 genetic principal components.

Supplementary Figure 1. Dose-response relationship between sedentary behavior time and risk of T2D



Dose-response relationship between sedentary behavior time and the risk of T2D. Dashed lines represent the 95% confidence intervals of the HR. The reference was set at the 5th percentile of sedentary behavior time. The model was adjusted for age, race, gender, assessment center, Townsend deprivation index, smoking, alcohol intake, education, average household income, healthy diet score, hypertension, total MET, cholesterol-lowering medication, anti-hypertensive medication, T2D-GRS, and the first 10 genetic principal components. The histogram represents the frequency distribution of sedentary behavior time in the study population.

Supplementary Figure 2. Hazard ratios for T2D according to iso-temporal substitution of 30 minutes/day of sedentary time with equivalent durations of each different types of physical activity in men and women.



Iso-temporal substitution models were performed in men and women separately. Models have omitted the sedentary behavior component, and adjusted for total discretionary time, time of each type of physical activity, age, race, smoking status, alcohol intake, education, average household

income, healthy diet score, Townsend deprivation index, assessment center, hypertension, cholesterol-lowering medication, anti-hypertensive medication, T2D-GRS, and the first 10 genetic principal components.