SUPPLEMENTARY DATA

Supplementary Table S1. UK Biobank participants' characteristics by average lifetime night shift frequency (N=70,480). Characteristics are shown by average frequency of night shift work. Values are indicated in means (±standard deviation, SD), median (±inter-quartile range, IQR) or percentages (%).

	Average Frequency of Night Shifts per Month			
	None	<3/months	3-7/months	≥8/month
N	53,586	2,261	6,969	7,664
Age (yrs)	53.0 (6.8)	52.9 (6.9)	51.8 (6.6)	52.6 (6.8)
Sex (% male)	41	57	49	58
European (%)	97.1	95.0	96.2	96.1
Single (%)	16.1	17.1	15.9	16.4
Townsend Index	-2.4 (-3.8- -0.17)	-2.3 (-3.6-0.04)	-2.3 (-3.8- -0.06)	-2.1 (-3.6- 0.42)
Weekly work hours	34.6 (12.4)	36.2 (12.1)	36.3 (12.1)	37.5 (12.6)
Family history of T2D (%)	19.9	22.3	21.5	23.0
Body Mass Index (kg/m^2)	26.4 (4.5)	27.1 (4.6)	27.1 (4.7)	27.7 (4.7)
Never smoker (%)	62.6	54.6	57.6	52.5
Physical activity (MET-h/week)	25.3 (12.1-43.4)	27.9 (13.3-53.3)	28.9 (14.6-54.8)	29.2(15.6-62.2)
Daily alcohol consumption (%)	22.0	22.0	19.4	19.4
Sleep duration (h)	7.1 (0.9)	7.1 (0.9)	7.1 (0.9)	7.0 (1.0)
Late chronotype (%)	8.4	8.9	9.0	10.5
Hypertension (%)	16.9	19.5	17.1	19.4
Antihypertensive medication use (%)	10.9	12.9	10.8	12.8
Elevated cholesterol levels (%)	6.1	7.6	6.7	7.8
Lipid-lowering medication use (%)	7.3	9.1	8.1	9.7
Statin use (%)	6.4	8.2	7.1	8.7
Corticosteroid use (%)	0.4	0.3	0.3	0.5

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Supplementary Table S2. UK Biobank genetic sample's characteristics by current night shift work exposure (N=180,704). Characteristics are shown by average frequency of night shift work. Values are indicated in means (±standard deviation, SD), median (±inter-quartile range, IQR) or percentages (%).

	Current Work Schedule				
	Day workers	Shift Work, But only rarely, if ever, nights	Irregular or rotating shifts with some nights	Irregular/ rotating shifts with usual nights	Permanent night shifts
N	151,657	14,445	8,292	2,157	4,153
Age (yrs)	52.9 (7.0)	52.5 (7.0)	51.2 (6.8)	50.9 (6.6)	51.4 (6.7)
Sex (% male)	47	48	63	65	63
European (%)	100	100	100	100	100
Single (%)	15	19	19	19	18
Townsend Index	-1.7 (-3.7-0.1)	-0.9 (-3.3-1.0)	-1.0 (-3.4-0.9)	-0.9 (-1.6-1.1)	-0.8 (-3.2-1.25)
Weekly work hours	34.8 (12.4)	35.9 (12.0)	40.7 (12.6)	40.5 (12.3)	40.2 (12.8)
Family history of T2D (%)	20.2	22.2	22.4	21.6	23.2
Body Mass Index (kg/m^2)	27.0 (4.6)	27.7 (4.9)	28.1 (4.8)	28.1 (4.8)	28.5 (4.8)
Never smoker (%)	58.9	53.5	52.9	52.8	50.7
Physical activity (MET-h/week)	43.0 (12.6-48.5)	63.1 (17.4-79.2)	68.1 (20.2-87.6)	67.0 (20.1-86.2)	73.5 (23.3-96.0)
Daily alcohol consumption (%)	21	18	18	16	11
Sleep duration (h)	7.0 (0.92)	7.0 (1.0)	6.9 (1.0)	6.9 (1.1)	6.8 (1.1)
Late chronotype (%)	7.7	7.6	9.5	12.0	16.3
Hypertension (%)	18.8	20.2	19.8	20.2	21.0
Antihypertensive medication use (%)	12.3	13.0	12.8	12.6	13.7

Elevated cholesterol levels (%)	6.9	7.4	7.3	6.9	8.0
Lipid-lowering medication use (%)	8.4	9.0	9.1	8.8	9.6
Statin use (%)	7.4	8.0	8.0	7.7	8.6
Corticosteroid use (%)	0.4	0.5	0.5	0.4	0.2

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Supplementary Table S3. UK Biobank genetic sample's characteristics by average lifetime night shift frequency (N=44,141). Characteristics are shown by average frequency of night shift work. Values are indicated in means (±standard deviation, SD), median (±inter-quartile range, IQR) or percentages (%).

	Average Frequency of Night Shifts per Month			
	None	<3/months	3-7/months	≥8/month
N	33,714	1,391	4,303	4,733
Age (yrs)	53.0 (6.7)	53.1 (6.7)	51.9 (6.6)	52.6 (6.8)
Sex (% male)	41	56	48	58
European (%)	100	100	100	100
Single (%)	15.9	16.0	15.1	15.8
Townsend Index	-1.8 (-3.8-0.44)	-1.7 (-3.8-0.37)	-1.8 (-3.8-0.33)	-1.5 (-3.7-0.15)
Weekly work hours	34.5 (12.3)	36.2 (11.8)	36.1 (12.0)	37.4 (12.8)
Family history of T2D	19.4	20.3	20.1	22.9
Body Mass Index (kg/m^2)	26.4 (4.4)	27.2 (4.5)	27.2 (4.8)	27.7 (4.7)
Never smoker (%)	63.0	55.1	57.7	51.7
Physical activity (MET-h/week)	36.6 (12.0-43.6)	46.7 (13.1-55.1)	47.1 (14.6- 55.1)	52.8 (15.4- 63.0)
Daily alcohol consumption (%)	22.4	21.7	19.3	19.8
Sleep duration (h)	7.1 (0.8)	7.1 (0.9)	7.1 (0.9)	7.0 (1.0)
Late chronotype (%)	8.9	10.3	9.9	11.3
Hypertension (%)	17.0	21.0	17.3	19.2
Antihypertensive medication use (%)	11.0	13.4	10.8	12.5
Elevated cholesterol levels (%)	6.0	7.9	6.4	7.8
Lipid-lowering medication use (%)	7.3	9.6	7.9	9.7
Statin use (%)	6.4	8.7	6.9	8.6
Corticosteroid use (%)	0.4	0.2	0.4	0.5

SUPPLEMENTARY DATA

Supplementary Table S4. **Association of current shift work and type 2 diabetes odds by sex**. OR=odds ratio, 95%CI= 95% confidence interval.

Shift Work Status	OR[g] 95%CI	P for interaction
Men *(N=129,117, 4,557 cases)*		
No current shift work (N=100,631, 3,463 cases)	1.00 (Ref)	
Shift work, but never, rarely night shift work (N=10,459, 470 cases)	1.10 (0.98-1.24)	0.34
Sometimes night shift work (N=8,078, 336 cases)	1.06 (0.93-1.21)	
Usually night shift work (N=2,259, 126 cases)	1.35 (1.08-1.67)	
Always night shift work (N=3,997, 162 cases)	1.02 (0.84-1.23)	
Women *(N=142,233, 2,213 cases)*		
No current shift work (N=119,124, 1,710 cases)	1.00 (Ref)	
Shift work, but never, rarely night shift work (N=11,983, 260 cases)	1.13 (0.97-1.32)	
Sometimes night shift work (N=5,020, 125 cases)	1.33 (1.06-1.65)	
Usually night shift work (N=1,326, 43 cases)	1.42 (0.97-2.05)	
Always night shift work (N=2,567, 75 cases)	1.27 (0.95-1.66)	

Supplementary Table S5. **Association of current shift work and type 2 diabetes odds by ethnicity-specific obesity status**. OR=odds ratio, 95%CI= 95% confidence interval.

Shift Work Status	OR, 95%CI	$P_{interaction}$
Non-obese *(N=202,449, 2,563 T2D cases)*		
No current shift work	1.00 (Ref)	
Shift work, but never, rarely night shift work	1.19 (1.02-1.37)	0.21
Sometimes night shift work	1.10 (0.91-1.32)	
Usually night shift work	1.72(1.25-2.31)	
Always night shift work	1.12 (0.86-1.44)	
Obese *(N=61,345, 4,147 T2D cases)*		
No current shift work	1.00 (Ref)	
Shift work, but never, rarely night shift work	1.07 (0.95-1.20)	
Sometimes night shift work	1.09 (0.95-1.26)	
Usually night shift work	1.22 (0.96-1.54)	
Always night shift work	1.05 (0.86-1.27)	

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Supplementary Table S6. **Association of current shift work and type 2 diabetes odds by chronotype**. OR=odds ratio, 95%CI= 95% confidence interval.

Shift Work Status	OR[i] 95%CI	$P_{interaction}$[j]
Morning Types (N=61,131, 1,746 cases)		
Day workers	1.00 (Ref)	
Shift work, but never, rarely night shift work	1.15 (0.96-1.37)	0.48
Irregular, rotating shifts with some night shifts	1.07 (0.85-1.33)	
Irregular, rotating shifts with usual night shifts	1.14 (0.74-1.71)	
Permanent night shift work	0.86 (0.59-1.22)	
Intermediate Types (N=152,997, 3,3576 cases)		
Day workers	1.00 (Ref)	
Shift work, but never, rarely night shift work	1.14 (1.00-1.29)	
Irregular, rotating shifts with some night shifts	1.07 (0.91-1.26)	
Irregular, rotating shifts with usual night shifts	1.40 (1.07-1.82)	
Permanent night shift work	1.21 (0.95-1.51)	
Evening Types (N=21,879, 676 cases)		
Day workers	1.00 (Ref)	
Shift work, but never, rarely night shift work	1.11 (0.81-1.51)	
Irregular, rotating shifts with some night shifts	1.55 (1.08- 2.19)	
Irregular, rotating shifts with usual night shifts	1.53 (0.87-2.55)	
Permanent night shift work	0.99 (0.67-1.42)	

Supplementary Table S7. **Association of current shift work and type 2 diabetes odds by physical activity.** Stratification by median-split, cut-off of 26.57MET-hrs/week); OR=odds ratio, 95%CI= 95% confidence interval.

Shift Work Status	OR, 95%CI	$P_{interaction}$
Low physical activity levels *(N=132,464, 3,676 cases)*		
No current shift work	1.00 (Ref)	
Shift work, but never, rarely night shift work	1.10 (0.96-1.26)	0.03
Sometimes night shift work	1.35 (1.14-1.59)	
Usually night shift work	1.37(1.03-1.82)	
Always night shift work	1.33 (1.05-1.66)	
High physical activity levels *(N=132,980, 3,094 cases)*		
No current shift work	1.00 (Ref)	
Shift work, but never, rarely night shift work	1.13 (0.99-1.28)	
Sometimes night shift work	0.98 (0.84-1.15)	
Usually night shift work	1.36 (1.05-1.75)	
Always night shift work	0.94 (0.75-1.16)	

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Supplementary Table S8. Individual type 2 diabetes SNP association with type 2 diabetes odds in the UK Biobank (*N* =180,704). * SNPs included in the GRS_{10}.

SNP	Chr	BP	Nearest Gene	EA/NEA	N	OR (SE)	P
rs3768321	1	40035928	*MACF1*	T/G	180111	1.144 (0.028)	1.72E-06
rs12031920	1	51109269	*FAF1*	T/A	179957	1.004 (0.024)	0.855
rs67156297	1	154336716	*ATP8B2*	A/G	179166	1.041 (0.026)	0.126
rs340874	1	214159256	*PROX1*	C/T	180704	1.092 (0.024)	2.06E-04
rs145819220*	2	27748539	*GCKR*	C/G	179568	1.122 (0.173)	0.504
rs6757251	2	43734847	*THADA*	C/T	180657	1.172 (0.04)	6.18E-05
rs9309245	2	53397048	*ASB3*	C/G	179356	1.019 (0.025)	0.438
rs1116357	2	57287411	*CCDC85A*	G/A	179963	1.026 (0.023)	0.264
rs10193447	2	60552476	*BCL11A*	T/C	177419	1.015 (0.024)	0.538
rs6723108	2	135479980	*TMEM163*	T/G	180704	1.008 (0.023)	0.719
rs7560163	2	151637936	*RBM43/RND3*	C/G	180704	1.082 (0.24)	0.743
rs1563575	2	161131694	*RBMS1*	G/A	179482	1.006 (0.026)	0.830
rs28584669	2	165689720	*GRB14*	T/C	178372	1.031 (0.032)	0.343
rs1861612	2	230522398	*DNER*	A/G	180483	1.025 (0.023)	0.287
rs11712037	3	12344730	*PPARG*	C/G	180149	1.108 (0.037)	0.006
rs35352848	3	23455582	*UBE2E2*	T/C	180495	1.14 (0.03)	1.18E-05
rs79819696*	3	63944174	*PSMD6*	A/G	180538	1.019 (0.236)	0.938
rs7428936	3	64710850	*ADAMTS9*	T/C	180299	1.064 (0.024)	0.010
rs11708067	3	123065778	*ADCY5*	A/G	180704	1.096 (0.028)	0.001
rs4402960	3	185511687	*IGF2BP2*	T/G	180704	1.225 (0.024)	1.27E-16
rs9820223	3	186663868	*ST6GAL1*	C/T	175666	1.07 (0.024)	0.005
rs6777684	3	187741842	*LPP*	G/A	177070	1.116 (0.024)	7.73E-06
rs1531583	4	744972	*MAEA*	T/G	180395	1.163 (0.057)	0.008
rs3821943	4	6299940	*WFS1*	T/C	177630	1.067 (0.024)	0.006
rs7660590	4	153397823	*TMEM154*	C/T	180437	1.015 (0.026)	0.561
rs60780116	4	185708807	*ACSL1*	T/C	179049	1.046 (0.033)	0.166
rs173964	5	55809465	*ANKRD55*	G/A	180594	1.077 (0.027)	0.006
rs9687833	5	55861601	*ANKRD55*	A/G	180537	1.088 (0.028)	0.003
rs6453287	5	76453765	*ZBED3*	C/A	180704	1.06 (0.025)	0.021
rs78408340*	5	102338739	*PAM*	G/C	180704	1.637 (0.097)	3.60E-07
rs74944275	5	102726073	*PAM*	T/C	180704	1.092 (0.053)	0.098
rs6923241	6	7258847	*SSR1/RREB1*	T/C	177057	1.003 (0.026)	0.909
rs7451008	6	20673880	*CDKAL1*	C/T	179644	1.154 (0.026)	2.84E-08
rs2244020	6	31347451	*HLA-B*	G/A	180139	1.047 (0.025)	0.063
rs143308245*	6	38228979	*ZFAND3*	T/A	180582	1.744 (0.613)	0.364
rs11759026	6	126792095	*CENPW*	G/A	179199	1.108 (0.027)	1.74E-04
rs10276674	7	14922007	*DGKB*	C/T	180704	1.114 (0.029)	2.28E-04
rs10238625	7	15054232	*DGKB*	A/G	179545	1.074 (0.024)	0.003
rs1635852	7	28189411	*JAZF1*	T/C	180704	1.087 (0.023)	3.47E-04
rs878521	7	44255643	*GCK*	A/G	179328	1.075 (0.027)	0.007
rs10229583	7	127246903	*PAX4*	A/G	179011	1.007 (0.027)	0.797
rs73455744*	7	127631181	*GCC1*	G/A	180640	1.268 (1.024)	0.817
rs791595	7	127862802	*MIR129-LEP*	G/A	180108	1.051 (0.031)	0.109
rs10954284	7	130463758	*KLF14*	T/A	180329	1.089 (0.023)	2.59E-04
rs1182436	7	157027753	*MNX1*	C/T	180391	1.129 (0.031)	9.97E-05
rs516946	8	41519248	*ANK1*	C/T	180704	1.085 (0.028)	0.003
rs4734285	8	95882365	*TP53INP1*	T/C	179473	1.038 (0.024)	0.125
rs11786613*	8	95957984	*TP53INP1*	C/A	179867	1.195 (0.089)	0.046
rs3802177	8	118185025	*SLC30A8*	G/A	180704	1.146 (0.026)	1.15E-07
rs10758593	9	4292083	*GLIS3*	A/G	180704	1.086 (0.024)	4.77E-04
rs10965223	9	22067004	*CDKN2A/B*	A/G	180523	1.049 (0.024)	0.042

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rs10965248	9	22132878	*CDKN2A/B*	T/C	179918	1.21 (0.032)	3.14E-09
rs10757282	9	22133984	*CDKN2A/B*	C/T	180011	1.014 (0.024)	0.552
rs1575972	9	22301092	*DMRTA1*	T/A	180602	1.042 (0.067)	0.534
rs13301067	9	81900744	*TLE4*	G/A	180492	1.175 (0.051)	0.002
rs9410573	9	84311800	*TLE1*	T/C	178226	1.123 (0.024)	1.10E-06
rs635634	9	136155000	*ABO*	T/C	180704	1.013 (0.03)	0.656
rs11787792	9	139252148	*GPSM1*	A/G	180704	1.052 (0.025)	0.041
rs10998572	10	70859204	*VPS26A*	C/A	179760	1.056 (0.049)	0.270
rs810517	10	80942620	*ZMIZ1*	C/T	180662	1.118 (0.023)	1.95E-06
rs11187140	10	94466910	*HHEX/IDE*	G/A	177633	1.172 (0.025)	1.94E-10
rs7903146*	10	114758349	*TCF7L2*	T/C	180704	1.501 (0.024)	6.55E-63
rs10886471	10	121149403	*GRK5*	T/C	180704	1.014 (0.023)	0.541
rs2292626	10	124186714	*PLEKHA1*	C/T	180479	1.078 (0.023)	0.001
rs2334499	11	1696849	*DUSP8*	T/C	180704	1.041 (0.024)	0.085
rs11564732	11	2150895	*INS-IGF2*	C/T	179458	1.068 (0.089)	0.456
rs7107784	11	2215089	*MIR4686*	G/A	180216	1.062 (0.025)	0.018
rs231360	11	2692249	*KCNQ1*	T/C	178347	1.084 (0.024)	0.001
rs233449	11	2843803	*KCNQ1*	G/A	180704	1.114 (0.027)	4.64E-05
rs2237897*	11	2858546	*KCNQ1*	C/T	180704	1.35 (0.066)	4.89E-06
rs441613	11	2910191	*KCNQ1*	C/T	176579	1.009 (0.025)	0.712
rs5219	11	17409572	*KCNJ11*	T/C	180704	1.072 (0.024)	0.004
rs1061810	11	43877934	*HSD17B12*	A/C	180704	1.025 (0.025)	0.329
rs76550717	11	72428172	*ARAP1 (CENTD2)*	A/G	178012	1.12 (0.033)	0.001
rs10830963	11	92708710	*MTNR1B*	G/C	180704	1.119 (0.026)	1.09E-05
rs11063018	12	4288001	*CCND2*	C/T	180704	1.057 (0.03)	0.067
rs188827514*	12	4291596	*CCND2*	A/G	180238	1.481 (0.183)	0.032
rs4238013	12	4376089	*CCND2*	C/T	178610	1.108 (0.028)	3.16E-04
rs7953190	12	27962719	*KLHDC5*	T/C	180363	1.125 (0.03)	1.03E-04
rs147538848	12	31466613	*FAM60A*	G/A	180636	1.24 (1.024)	0.834
rs2258238	12	66221060	*HMGA2*	T/A	179459	1.104 (0.037)	0.007
rs6581998	12	71656723	*TSPAN8/LGR5*	C/T	179581	1.028 (0.026)	0.285
rs56348580	12	121432117	*HNF1A (TCF1)*	G/C	179192	1.048 (0.026)	0.069
rs2851437	12	123653592	*MPHOSPH9*	A/C	174011	1.025 (0.028)	0.363
rs9552911*	13	23864657	*SGCG*	G/A	180659	1.214 (0.464)	0.676
rs7330796	13	75898163	*TBC1D4*	T/C	179730	1.023 (0.036)	0.535
rs11616380	13	80705315	*SPRY2*	G/T	178080	1.153 (0.027)	9.17E-08
rs10146997	14	79945162	*NRXN3*	G/A	180704	1.005 (0.028)	0.848
rs67839313	15	40619724	*INAFM2*	C/T	180136	1.032 (0.037)	0.400
rs4774420	15	62117975	*C2CD4A*	C/T	175008	1.008 (0.026)	0.761
rs952471	15	77776498	*HMG20A*	G/C	180681	1.065 (0.026)	0.015
rs62006309	15	80411245	*ZFAND6*	A/G	178786	1.03 (0.023)	0.204
rs12595616	15	91563513	*PRC1*	C/T	180414	1.066 (0.024)	0.008
rs1558902	16	53803574	*FTO*	A/T	180607	1.059 (0.023)	0.014
rs8056814	16	75252327	*BCAR1*	G/A	180065	1.225 (0.045)	7.74E-06
rs2925979	16	81534790	*CMIP*	T/C	180704	1.059 (0.025)	0.024
rs9911305	17	2309188	*SRR*	A/G	180473	1.07 (0.026)	0.009
rs7224685	17	4014384	*ZZEF1*	T/G	180180	1.037 (0.025)	0.142
rs13342692	17	6946287	*SLC16A11/A13*	T/C	180704	1.037 (0.127)	0.774
rs78761021	17	9780387	*GLP2R*	G/A	177577	1.039 (0.025)	0.121
rs757209	17	36102833	*HNF1B (TCF2)*	G/A	178726	1.061 (0.024)	0.012
rs7234111	18	7067652	*LAMA1*	C/T	180704	1.083 (0.024)	0.001
rs1942880	18	57793209	*MC4R*	T/C	177594	1.014 (0.025)	0.587
rs79851087	18	58034883	*MC4R*	A/G	180545	1.004 (0.087)	0.962
rs12454712	18	60845884	*BCL2A*	T/C	180704	1.069 (0.024)	0.006
rs58489806	19	19456917	*CILP2*	T/C	180138	1.125 (0.04)	0.003
rs139990642*	19	33943994	*PEPD*	A/G	180437	1.229 (0.145)	0.154

SUPPLEMENTARY DATA

rs429358	19	45411941	*APOE*	T/C	180704	1.067 (0.033)	0.051
rs55864746	19	46160246	*GIPR*	A/G	180529	1.11 (0.026)	4.32E-05
rs12625671	20	42994812	*HNF4A*	C/T	180704	1.081 (0.037)	0.035
rs1800961	20	43042364	*HNF4A*	T/C	180704	1.322 (0.06)	2.79E-06
rs2023681	22	30599562	*MTMR3/HORMAD2*	G/A	180655	1.132 (0.042)	0.003