#### Supplementary Online Content

#### Comparisons of Polyexposure, Polygenic, and Clinical Risk Scores Implicate Prominent Roles of Non-Genetic Factors in Risk Prediction and Screening of Type 2 Diabetes

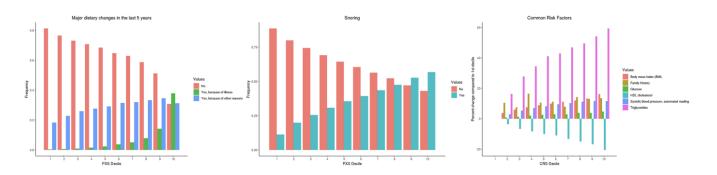
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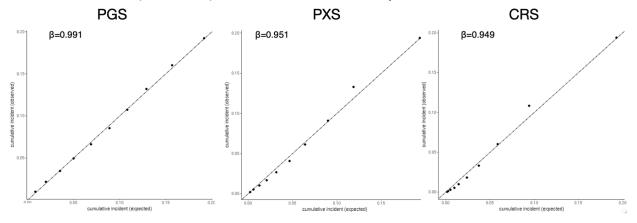
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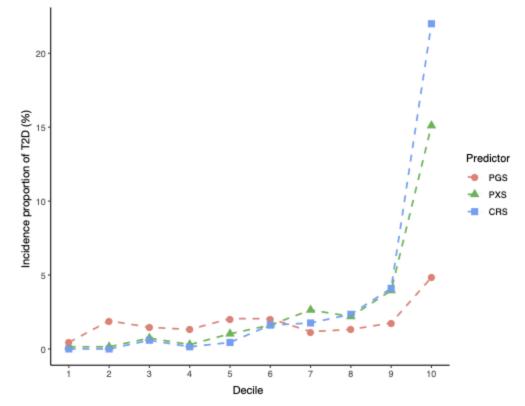
**Supplementary Figure S1. Changes in variable responses over risk gradients.** Left and middle: the frequency of each response was calculated within each PXS decile and plotted for the top two exposure variables. Right: The average value of each clinical risk variable was calculated for each decile, and the percent change compared to the first decile is plotted.



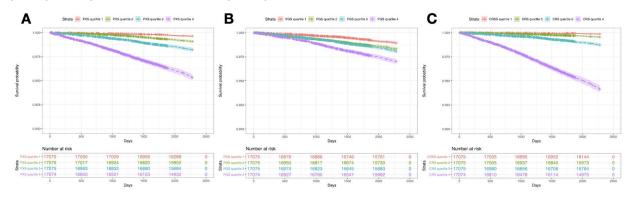
**Supplementary Figure S2. Calibration plots for PGS, PXS, and CRS.** The observed probability (Kaplan-Meier estimates) is plotted against the mean predicted probability within tenths of the predicted probabilities at t=2000 days.



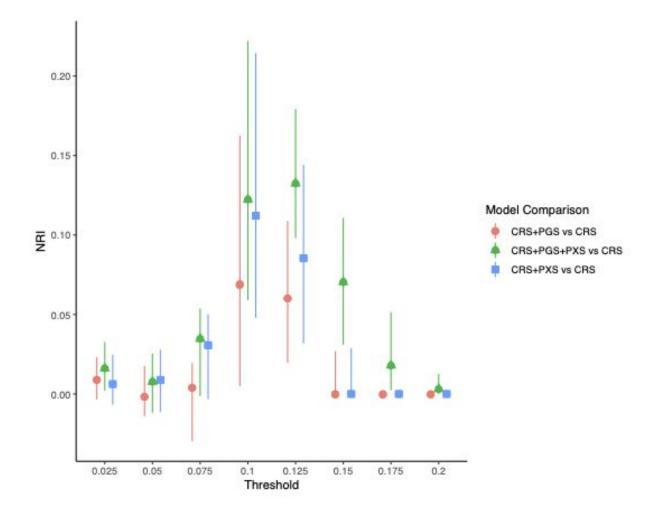
**Supplementary Figure S3: Risk gradient for T2D.** The incidence of T2D in 10 groups binned according to the decile of polygenic risk score (PGS), polyexposure risk score (PXS), or clinical risk score (CRS).



**Supplementary Figure S4: Kaplan Meier (KM) plots of time-to-events for risk scores.** The KM plots illustrate significant differences in time-to-events between different quartiles using A) polygenic risk score (PGS), B) polyexposure risk score (PXS), or C) clinical risk score (CRS).



Supplementary Figure S5: NRI of risk models over a range of risk thresholds. The categorical NRI for different risk models.



# Supplementary Figure S6: Categorical NRI of CRS+PGS model over range of risk thresholds

		CRS	CRS+PGS Model		
	CRS Model	< 0.025	>= 0.025	Total	
ß	< 0.025	259	33	292	
Events	>= 0.025	35	954	989	
ш	Total	294	987	1281	
nts	< 0.025	49197	1053	50250	
Nonevents	>= 0.025	1759	15009	16768	
Nor	Total	50956	16062	67018	

		CRS	CRS+PGS Model		
	CRS Model	< 0.1	>= 0.1	Total	
ß	< 0.1	966	165	1131	y.
Events	>= 0.1	60	90	150	Events
ш	Total	1026	255	1281	ш
nts	< 0.1	65383	1103	66486	nts
Nonevents	>= 0.1	246	286	532	Nonevents
Nor	Total	65629	1389	67018	Nor

		CRS	S+PGS Mode	əl	
	CRS Model	< 0.05	>= 0.05	Total	
ß	< 0.05	482	41	523	
ven	>= 0.05	57	701	758	
ш	Total	539	742	1281	1
ents	< 0.05	57208	1007	58215	
leve	>= 0.05	1725	7078	8803	
Nor	Total	58933	8085	67018	
	Nonevents Events	st = 0.05 >= 0.05 Total	CRS Model < 0.05   \$\$\$ < 0.05	CRS Model < 0.05 >= 0.05   \$\$ < 0.05	s < 0.05 482 41 523   >= 0.05 57 701 758   Total 539 742 1281

		CRS	S+PGS Mode	el	
	CRS Model	< 0.125	>= 0.125	Total	
ß	< 0.125	1198	83	1281	9
Events	>= 0.125	0	0	0	
ш	Total	1198	83	1281	
nts	< 0.125	66703	315	67018	40
Nonevents	>= 0.125	0	0	0	
No	Total	66703	315	67018	No.

		CRS+PGS Model		
	CRS Model	< 0.075	>= 0.075	Total
ß	< 0.075	688	103	791
Events	>= 0.075	96	394	490
ш	Total	784	497	1281
nts	< 0.075	62145	1266	63411
Nonevents	>= 0.075	1163	2444	3607
Nor	Total	63308	3710	67018

		CRS+PGS Model			
	CRS Model	< 0.15	>= 0.15	Total	
ß	< 0.15	1281	0	1281	
Events	>= 0.15	0	0	0	
ш	Total	1281	0	1281	
ints	< 0.15	67018	0	67018	
Nonevents	>= 0.15	0	0	0	
Nor	Total	67018	0	67018	

		CRS	CRS+PGS Model		
	CRS Model	< 0.175	>= 0.175	Total	
s	<17.5%	1281	0	1281	
Events	>=17.5%	0	0	0	
ш	Total	1281	0	1281	
nts	<17.5%	67018	0	67018	
Nonevents	>=17.5%	0	0	0	
Nor	Total	67018	0	67018	

		CRS	CRS+PGS Model			
	CRS Model	< 0.2	>= 0.2	Total		
s	< 0.2	1281	0	1281		
Events	>= 0.2	0	0	0		
ш	Total	1281	0	1281		
ents	< 0.2	67018	0	67018		
Nonevents	>= 0.2	0	0	0		
Nor	Total	67018	0	67018		

Incorrectly reclassified

Correctly reclassified

#### Supplementary Figure S7: Categorical NRI of CRS+PXS model over range of risk thresholds

		CR	CRS+PXS Model				
	CRS Model	< 0.025	>= 0.025	Total		CRS Model	
S	< 0.025	248	44	292	s	< 0.05	
Events	>= 0.025	54	935	989	Events	>= 0.05	
ш	Total	302	979	1281	ш	Total	
nts	< 0.025	48730	1520	50250	nts	< 0.05	
Nonevents	>= 0.025	2460	14308	16768	Nonevents	>= 0.05	
Nor	Total	51190	15828	67018	Nor	Total	

CRS+PXS Model

>= 0.1

208

106

314

1259

336

1595

Total

1131

150

1281

66486

532

67018

Events

Nonevents

< 0.1

923

44

967

65227

196

65423

CRS Model

Events

Nonevents

< 0.1

>= 0.1

Total

< 0.1

>= 0.1

Total

			CR	S+PXS Mode	el
Total		CRS Model	< 0.05	>= 0.05	Total
292	ß	< 0.05	455	68	523
989	Events	>= 0.05	71	687	758
1281	ш	Total	526	755	1281
50250	nts	< 0.05	56890	1325	58215
16768	Nonevents	>= 0.05	2072	6731	8803
67018	Nor	Total	58962	8056	67018

Iotai	30902	8030	0/010	
	CR	S+PXS Mode	el	
CRS Model	< 0.125	>= 0.125	Total	
< 0.125	1165	116	1281	ų
>= 0.125	0	0	0	Evente
Total	1165	116	1281	ш
< 0.125	66672	346	67018	nto
>= 0.125	0	0	0	Nonevente
Total	66672	346	67018	No.

Total

1281

0

1281

67018 0

67018

		CRS+PXS Model		
	CRS Model	< 0.075	>= 0.075	Total
s	< 0.075	666	125	791
Events	>= 0.075	80	410	490
ш	Total	746	535	1281
nts	< 0.075	62038	1373	63411
Nonevents	>= 0.075	1075	2532	3607
Nor	Total	63113	3905	67018

		CRS+PXS Model			
	CRS Model	< 0.15	>= 0.15	Total	
s	< 0.15	1281	0	1281	
Events	>= 0.15	0	0	0	
ш	Total	1281	0	1281	
ints	< 0.15	67018	0	67018	
Nonevents	>= 0.15	0	0	0	
Nor	Total	67018	0	67018	

		CR	S+PXS Mode	əl			CR	S+PXS Mode	əl
	CRS Model	< 0.175	>= 0.175	Total		CRS Model	< 0.2	>= 0.2	
Events	<17.5%	1281	0	1281	s	< 0.2	1281	0	
	>=17.5%	0	0	0	Events	>= 0.2	0	0	
	Total	1281	0	1281	ш	Total	1281	0	
Nonevents	<17.5%	67018	0	67018	nts	< 0.2	67018	0	e
	>=17.5%	0	0	0	Nonevents	>= 0.2	0	0	
	Total	67018	0	67018	Nor	Total	67018	0	e

Incorrectly reclassified

Correctly reclassified

## Supplementary Figure S8: Categorical NRI of CRS+PGS+PXS model over range of risk thresholds

		CRS+PGS+PXS Model			
	CRS Model	< 0.025	>= 0.025	Total	
ß	< 0.025	246	46	292	
Events	>= 0.025	53	936	989	
ш	Total	299	982	1281	
ents	< 0.025	48608	1642	50250	
Nonevents	>= 0.025	3089	13679	16768	
Nor	Total	51697	15321	67018	

		CRS+PGS+PXS Model			
	CRS Model	< 0.1	>= 0.1	Total	
S	< 0.1	895	236	1131	ß
Events	>= 0.1	55	95	150	Events
ш	Total	950	331	1281	ш
ints	< 0.1	64963	1523	66486	ints
Nonevents	>= 0.1	252	280	532	Nonevents
Nor	Total	65215	1803	67018	Nor

CRS+PGS+PXS Model   CRS Model < 0.05 >= 0.05 Total    < 0.05 451 72 523   >= 0.05 83 675 758   Total 534 747 1281	
< 0.05 451 72 523   >= 0.05 83 675 758   Total 534 747 1281	
>= 0.05 83 675 758   Total 534 747 1281	
Total 534 747 1281	
Total 534 747 1281	
	1
0 s < 0.05 56710 1505 58215	-
0 2 < 0.05 56710 1505 58215   8 5 = 0.05 2596 6207 8803   8 70tal 59306 7712 67018	
8 2 Total 59306 7712 67018	-

		CRS+PGS+PXS Model			
	CRS Model	< 0.125	>= 0.125	Total	
Events	< 0.125	1097	184	1281	
	>= 0.125	0	0	0	
	Total	1097	184	1281	
IIIS	< 0.125	66267	751	67018	-
Nonevents	>= 0.125	0	0	0	
LION	Total	66267	751	67018	

		CRS+PGS+PXS Model		
	CRS Model	< 0.075	>= 0.075	Total
Events	< 0.075	648	143	791
	>= 0.075	94	396	490
	Total	742	539	1281
Nonevents	< 0.075	61761	1650	63411
	>= 0.075	1415	2192	3607
	Total	63176	3842	67018

	CRS+PGS+PXS Model			odel
	CRS Model	< 0.15	>= 0.15	Total
ß	< 0.15	1186	95	1281
Events	>= 0.15	0	0	0
ш	Total	1186	95	1281
nts	< 0.15	66766	252	67018
Nonevents	>= 0.15	0	0	0
Nor	Total	66766	252	67018

]			CRS+PGS+PXS Model			
		CRS Model	< 0.175	>= 0.175	Total	
	s	<17.5%	1257	24	1281	9
	Events	>=17.5%	0	0	0	
	ш	Total	1257	24	1281	-
	nts	<17.5%	66964	54	67018	40
	Nonevents	>=17.5%	0	0	0	
	Nor	Total	66964	54	67018	

		CRS+PGS+PXS Model			
	CRS Model	< 0.2	>= 0.2	Total	
Events	< 0.2	1277	4	1281	
	>= 0.2	0	0	0	
	Total	1277	4	1281	
Nonevents	< 0.2	67017	1	67018	
	>= 0.2	0	0	0	
	Total	67017	1	67018	

Incorrectly reclassified

Correctly reclassified

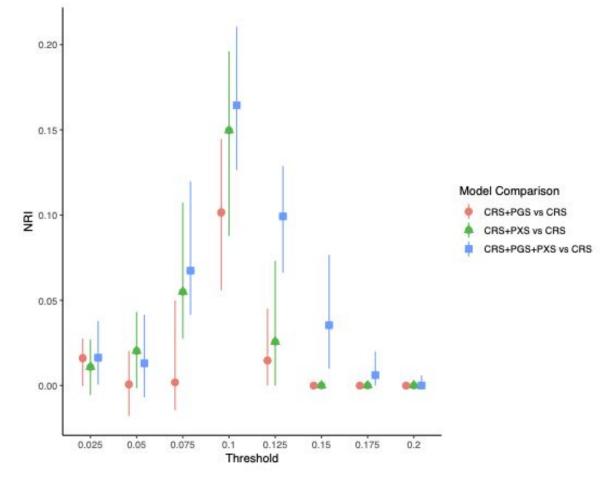
**Supplementary Figure S9: Reclassification of predicted type 2 diabetes risk with glucose removed from CRS.** The reclassified predicted risk with addition of polygenic risk score (PGS) (A), polygenic risk score (PXS) (B), or PGS+PXS (C) to clinical risk score (CRS) model without blood glucose in the continuous case or the categorical case, with a threshold of 12.5% risk.

Α	CRS+PGS Model			
CRS Model	# Participants	Continuous NRI	Categorical NRI	
Cases	1281	0.157 (0.118 to 0.296)	0.016 (0.000 to 0.049)	
Noncases	67018	0.084 (0.066 to 0.102)	-0.002 (-0.004, 0.00)	
Full population	68299	0.241 (0.186 to 0.296)	0.015 (0.000 to 0.045)	

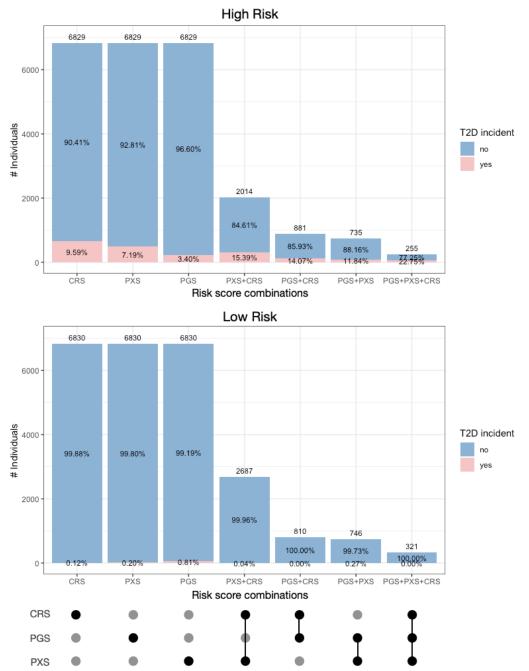
В		CRS+PXS Model			
	CRS Model	# Participants	Continuous NRI	Categorical NRI	
	Cases	1281	0.315 (0.276 to 0.351)	0.027 (0.000 to 0.078)	
	Noncases	67018	0.179 (0.156 to 0.202)	-0.001 (-0.005 to 0.000)	
	Full population	68299	0.494 (0.440 to 0.548)	0.026 (0.00 to 0.073)	

С		CRS+PGS+PXS Model					
	CRS Model	# Participants	Continuous NRI	Categorical NRI			
	Cases	1281	0.258 (0.214 to 0.305)	0.107 (0.071 to 0.140)			
	Noncases	67018	0.235 (0.207 to 0.256)	-0.008 (-0.012 to -0.005)			
	Full population	68299	0.493 (0.430 to 0.552)	0.099 (0.066 to 0.129)			

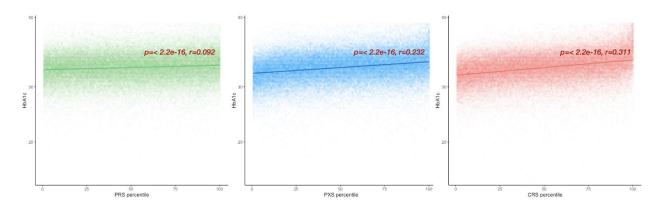
### Supplementary Figure S10: NRI of risk models over a range of risk thresholds with blood glucose removed from CRS. The categorical NRI for different risk models.



Supplementary Figure S11: T2D incidence in Individuals with high (top) and low (bottom) risk CRS, PGS, and/or PXS. Individuals with scores in the top 10 percentiles were classified as high risk (top). Those with scores in the bottom 10 percentiles were classified as low risk (bottom). The total number of individuals within each risk score group is indicated at the top of each bar. Within each high risk group, the percent of individuals who received a formal diagnosis is shaded in pink. A black circle denotes the group that consists of that high risk group; a greyed circle denotes the group that does not consist of that high risk group.



Supplementary Figure S12: Correlation between HbA1c and risk scores in the test set. P values and pearson correlation coefficients are shown above the linear regression lines.



**Supplementary Table S1: eXposure wide association study.** Summary statistics of univariate XWAS. (see attached .xlsx).

**Supplementary Table S2**: **All exposures extracted from UK Biobank.** (see attached .xlsx)

**Supplementary Table S3: T2D polyexposure risk score (PXS).** The PXS was composed of 12 variables that were indicators of alcohol, diet, early life factors, household information, sleep, smoking. The hazard ratio and p values are shown. Hazard ratio of categorical responses are in comparison to the reference responses. Variables are colored by indicator category.

Own or rent accommodation lived in Own or rent accommodation lived in Own outright (by you or someone in your household) 1.25 0.00 1.24 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.24 0.00 1.25 <t< th=""><th></th><th colspan="3">PXS</th><th></th><th colspan="2">+ CRS</th><th colspan="2">+ PGS</th><th colspan="2">+CRS+ PGS</th><th>1</th></t<>		PXS				+ CRS		+ PGS		+CRS+ PGS		1
Vest of birth 0.00 0.94 0.00 0.94 0.00 0.94 0.00 0.94 0.00 0.93 0.00   Own or rest accommodation lived in Own or rest accommodation lived in Pay stret and part motizal autority, to you or someone in your household 1.35 0.00 1.24 0.00 1.24 0.00 1.25 0.00 0.25 0.00 0.25 0.00 0.26	Field	Response	Reference	HR	Р	HR	Р	HR	Р	HR	Р	
Own or rest accommodation lined in Own or rest accommodation lined in Use in accommodation lined in Use in accommodation lined in Use in accommodation lined in Own or rest accommodation lined in Use in a 3,000 0.33 0.06 0.07 0.01 0.05 0.00 0.05 0.01 0.05 0.02 0.05 0.01 0.05 0.02 0.05 0.02 0.05 0.02 0.05 0.02 0.05 0.02 0.05 0.02 0.05 0.02 0.05 0.02 0.05	Sex	Male	Female	1.63	0.00	1.32	0.00	1.64	0.00	1.35	0.00	
Own or rest accommodation lived in Own or rest accommodation lived in Own or rest accommodation lived in the string private standard or letting agency own or rest accommodation lived in the string private standard or letting agency own outright (ty you or someone in your household) 1.25 0.00 1.24 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.24 1.36 0.00 1.25 0.01 2.05 0.01 <td>Year of birth</td> <td></td> <td></td> <td>0.94</td> <td>0.00</td> <td>0.94</td> <td>0.00</td> <td>0.94</td> <td>0.00</td> <td>0.93</td> <td>0.00</td> <td></td>	Year of birth			0.94	0.00	0.94	0.00	0.94	0.00	0.93	0.00	
Own or rest accommodation lived in Own or rest accommodation lived in Ear - from priorit authority, local council, husing associal own ouright (by you or someone in your household) 1.38 0.00 1.19 0.14 1.36 0.00 1.18 0.10   Own or rest accommodation lived in Own or rest accommodation lived in Own or rest accommodation lived in Use in accommodation restrice Non outright (by you or someone in your household) 0.00 0.00 1.66 0.00 1.66 0.00 1.68 0.00 1.68 0.00 1.68 0.00 2.55 0.01 2.05 0.01 2.05 0.01 0.00 0.67 0.51 1.04 0.00 0.68 0.00 0.68 0.00 0.68 0.00 0.68 0.00 0.68 0.00 0.68 0.00 0.03 0.00 0.68 0.00 0.03 0.06 0.03 0.06 0.03 0.06 0.05 0.00 0.025 0.00 0.025 0.06 0.02 0.06 0.02 0.04 0.025 0.04 0.28 0.05 0.04 0.28 0.05 0.04 0.28 <td< td=""><td>Own or rent accommodation lived in</td><td>None of the above</td><td>Own outright (by you or someone in your household)</td><td>1.21</td><td>0.68</td><td>0.91</td><td>0.87</td><td>1.25</td><td>0.62</td><td>0.93</td><td>0.90</td><td>household</td></td<>	Own or rent accommodation lived in	None of the above	Own outright (by you or someone in your household)	1.21	0.68	0.91	0.87	1.25	0.62	0.93	0.90	household
Own or rest accommodation lived in private landing of letting agency Own outright (tyry our someone in your household) 2.10 0.00 1.66 0.00 2.55 0.00 1.65 0.00   Own or rest accommodation lived in unor rest accommodation interd in a commodation interd free 0.00 unoright (tyry our someone in your household) 0.98 0.96 0.76 0.51 1.04 0.90 0.78 0.53   Average table household income before tax 31,000 to 30,993 Liss than 13,000 0.83 0.02 0.68 0.22 0.44 0.40 0.88 0.84 0.20 0.44 0.40 0.88 0.60 0.40 0.88 0.40 0.48 0.40 0.43 0.40 0.43 0.40 0.43 0.40 0.43 0.40 0.43 0.40 0.43 0.40 0.43 0.40 0.43 0.40 0.43 0.40 0.43 0.40 0.43 0.40 0.43 0.40 0.43 0.40 0.43 0.40 0.43 0.40 0.45 0.40 0.45 0.40 0.43 0.40 <td>Own or rent accommodation lived in</td> <td>Own with a mortgage</td> <td>Own outright (by you or someone in your household)</td> <td>1.25</td> <td>0.00</td> <td>1.24</td> <td>0.00</td> <td>1.25</td> <td>0.00</td> <td>1.25</td> <td>0.00</td> <td>sleep</td>	Own or rent accommodation lived in	Own with a mortgage	Own outright (by you or someone in your household)	1.25	0.00	1.24	0.00	1.25	0.00	1.25	0.00	sleep
Own or reft accommodation livel in accommodation reft refere Own outright (tyy our osneene in your household) 2.24 0.02 2.55 0.01 2.09 0.04 2.56 0.01   Warrage tabl household income before tax 13,000 to 30,399 Less than 18,000 0.53 0.00 0.67 0.01 0.54 0.00 0.68 0.01   Average tabl household income before tax 31,000 to 51,599 Less than 18,000 0.87 0.98 0.56 0.22 0.84 0.66 0.22 0.84 0.00 0.88 0.00 0.87 0.98 0.65 0.20 0.44 0.00 0.88 0.00 0.88 0.05 0.00 0.88 0.00 0.38 0.06 0.53 0.00 0.38 0.05 0.06 0.32 0.06 0.32 0.06 0.32 0.06 0.32 0.06 0.32 0.06 0.32 0.00 0.32 0.00 0.32 0.00 0.32 0.00 0.32 0.00 0.32 0.00 0.32 0.00 0.32 0.00<	Own or rent accommodation lived in	Rent - from local authority, local council, housing association	Own outright (by you or someone in your household)	1.38	0.00	1.19	0.14	1.36	0.00	1.18	0.16	smoking
Own or rent accommodation interd in Use in accommodation interd in Own outright (by you or someone in your household) 0.95 0.76 0.51 1.04 0.90 0.78 0.55   Average total household income before tax 31,000 to 33,999 Less than 18,000 0.83 0.09 0.67 0.01 0.54 0.00 0.68 0.01 0.54 0.00 0.68 0.01   Average tab household income before tax 31,000 to 53,999 Less than 18,000 0.81 0.08 0.02 0.86 0.01 0.84 0.00 0.88 0.00 0.28 0.86 0.01 0.88 0.00 0.28 0.08 0.02 0.86 0.60 0.85 0.60 0.85 0.60 0.85 0.60 0.85 0.60 0.85 0.60 0.85 0.60 0.85 0.60 0.85 0.60 0.85 0.60 0.85 0.60 0.85 0.60 0.85 0.60 0.85 0.60 0.85 0.60 0.85 0.60 0.85 0.60 0.85 0.	Own or rent accommodation lived in	Rent - from private landlord or letting agency	Own outright (by you or someone in your household)	2.10	0.00	1.66	0.00	2.05	0.00	1.65	0.00	diet
Average total household income before tax Average total household income before tax 31,000 to 51,999 Deste tas than 18,000 0.53 0.07 0.54 0.00 0.64 0.01   Average total household income before tax S2,000 to 100,000 111 0.88 0.66 0.21 0.84 0.86 0.01 0.84 0.86 0.01 0.84 0.86 0.01 0.84 0.86 0.01 0.84 0.86 0.01 0.84 0.86 0.01 0.84 0.86 0.01 0.84 0.86 0.01 0.84 0.86 0.01 0.84 0.86 0.02 0.84 0.86 0.02 0.84 0.86 0.07 0.88 0.06 0.87 0.86 0.21 0.86 0.67 0.88 0.09 0.81 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.25 0.00 0.27 0.00 0.27 0.00	Own or rent accommodation lived in	Pay part rent and part mortgage (shared ownership)	Own outright (by you or someone in your household)	2.24	0.02	2.65	0.01	2.09	0.04	2.56	0.01	alcohol
Average tabla household income before tax 31,000 to 51,999 Less than 18,000 0.83 0.09 0.66 0.22 0.84 0.11 0.88 0.00   Average tabla household income before tax 52,000 to 100,000 Less than 18,000 0.94 0.31 0.88 0.05 0.95 0.40 0.89 0.07 0.89 0.07   Steeplesness / insomnia Sometimes Newer/rately 1.24 0.00 1.33 0.00 1.32 0.00 1.32 0.00 1.33 0.00 1.32 0.00 1.33 0.00 0.77 0.00 0.77 0.00 0.77 0.00 0.72 0.00 0.73 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25	Own or rent accommodation lived in	Live in accommodation rent free	Own outright (by you or someone in your household)	0.98	0.96	0.76	0.51	1.04	0.90	0.78	0.55	early life
Average table household income before tax 52,000 to 100,000 Less than 18,000 0.87 0.07 0.18 0.06 0.07 0.08 0.06 0.07 0.08 0.06 0.07 0.08 0.06 0.05 0.00 0.03 0.08 0.06 0.05 0.00 0.03 0.08 0.06 0.05 0.04 0.08 0.06   Steplessness / Insomnia Screetimes Newer/rarity 104 0.00 1.33 0.00 1.33 0.00 1.33 0.00 0.32 0.00 0.03 0.06 0.02 0.03 0.06 0.02 0.03 0.06 0.02 0.03 0.06 0.03 0.06 0.03 0.06 0.03 0.06 0.03 0.06 0.03 0.06 0.03 0.06 0.03 0.06 0.03 0.06 0.03 0.03 0.06 0.03 0.06 0.03 0.03 0.03 0.03 0.03 0.03 0.03 0.03 0.03 0.03 0.03 0.03	Average total household income before tax	18,000 to 30,999	Less than 18,000	0.53	0.00	0.67	0.01	0.54	0.00	0.68	0.01	
Average tatal household income before tax Greater than 100,000 Less than 18,000 0.94 0.31 0.88 0.06 0.95 0.40 0.09   Siegepissness / insomnia Sometimes Newer/rarely 1.04 0.09 0.33 0.00 1.33 0.00 0.01	Average total household income before tax	31,000 to 51,999	Less than 18,000	0.83	0.09	0.86	0.22	0.84	0.11	0.88	0.30	
Steeplessness / Insomnia Sometimes Newer/rarely 1.34 0.00 1.32 0.00 1.32 0.00   Steeplessness / Insomnia Usually Newer/rarely 1.02 0.65 0.46 1.02 0.67 0.98 0.66   Storing No Yes 0.07 0.00 0.91 0.00 0.72 0.00 0.72 0.00 0.72 0.00 0.72 0.00 0.72 0.00 0.72 0.00 0.72 0.00 0.72 0.00 0.72 0.00 0.72 0.00 0.72 0.00 0.73 0.00   Past tobacco smoking Just tried once or twice Smoked on mest or all days 1.36 0.00 1.25 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.33 0.00 1.33	Average total household income before tax	52,000 to 100,000	Less than 18,000	0.87	0.09	0.91	0.28	0.86	0.07	0.89	0.20	
Steeplessness / Insomnia Usually Newer/rarely 102 0.95 0.45 1.02 0.67 0.06   Storing No Yer 0.70 0.00 0.72 0.00 0.72 0.00 0.73 0.00 0.73 0.00 0.72 0.00 0.72 0.00 0.73 0.00 0.72 0.00 0.72 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.72 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.73 0.00 0.70 0.00 0.70 0.00 0.70 0.00 0.70 0.00 0.70 0.00 0.70 0.00	Average total household income before tax	Greater than 100,000	Less than 18,000	0.94	0.31	0.88	0.06	0.95	0.40	0.89	0.09	
Storing No Yes 0.75 0.00 0.91 0.03 0.76 0.00 0.92 0.03   Past tobacco smoking Smoked or castorally Smoked or most or all days 0.71 0.00 0.72 0.00 0.72 0.00 0.72 0.00 0.72 0.00 0.72 0.00 0.72 0.00 0.72 0.00 0.72 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.01 0.48 0.25 0.21 0.28 0.21 0.28 0.21 0.28 0.21 0.28 0.21 0.28 0.21 0.28 0.21 0.28 0.21 0.28 0.21 0.28 0.21 0.28 0.21 0.24 0.26	Sleeplessness / insomnia	Sometimes	Never/rarely	1.34	0.00	1.33	0.00	1.32	0.00	1.32	0.00	
Past tobacco-moking Past tobacco-smoking Smoked occasionally Just tried once or twice Smoked on most or all days Smoked on most or all days 0.71 1.8 0.00 0.72 0.00 0.72 0.00 0.72 0.15 0.00 0.00 0.72 1.8 0.00 0.72 0.15 0.00 0.72 0.15 0.00 0.72 0.15 0.00 0.72 0.15 0.00 0.72 0.15 0.00 1.75 0.00 0.27 0.00 0.02 0.15 0.00 1.75 0.00 0.28 0.00 0.23 0.40 0.00   Mik type used Fuil cream Semi-skimmed 0.91 0.42 0.95 0.14 0.98 0.38 0.98 0.87   Mik type used Symmed Semi-skimmed 0.91 0.42 0.95 0.01 0.49 0.00 0.55 0.01 0.49 0.00 0.56 0.01   Mik type used Other type of symmed Semi-skimmed 0.79 0.16 0.70 0.00 0.70 0.09 0.76 0.09 0.70 0.00   Spread type Butter/spreadable butter Other type of spread/margarine 0.65 0.00 0.77<	Sleeplessness / insomnia	Usually	Never/rarely	1.02	0.69	0.96	0.46	1.02	0.67	0.98	0.60	
Past tobacco smoking Past tobacco smoking Just tried once or wide I have never smoked Smoked on most or all days Smoked on most or all days 136 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.25 0.00 1.02 0.03 0.03 0.03 0.00   Milk type used Fild ceam Semi-skimmed 0.91 0.44 0.05 0.11 0.05 1.08 0.24 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.01	Snoring	No	Yes	0.75	0.00	0.91	0.03	0.76	0.00	0.92	0.03	
Past tobacco smoking Have never smoking Have never smoking Smoked on most or all days 0.95 0.44 0.96 0.53 0.94 0.38 0.93 0.00   Milk type used Full cream Semi-skimmed 0.91 0.42 0.95 0.41 0.93 0.53 0.98 0.80   Milk type used Skimmed Semi-skimmed 1.14 0.04 1.07 0.31 1.12 0.055 0.01 0.48 0.00 0.55 0.01 0.48 0.00 0.55 0.01 0.49 0.00 0.56 0.01   Milk type used Other type of milk Semi-skimmed 0.84 0.00 0.55 0.01 0.49 0.00 0.56 0.01   Milk type used Never/rarely use spread Other type of spread/margarine 0.65 0.00 0.07 0.00 0.05 0.00 0.05 0.00 0.05 0.00 0.02 0.00 0.05 0.01 0.04 0.24 0.09   Spread type Bitattr/spseadable butter <td>Past tobacco smoking</td> <td>Smoked occasionally</td> <td>Smoked on most or all days</td> <td>0.71</td> <td>0.00</td> <td>0.72</td> <td>0.00</td> <td>0.72</td> <td>0.00</td> <td>0.73</td> <td>0.00</td> <td></td>	Past tobacco smoking	Smoked occasionally	Smoked on most or all days	0.71	0.00	0.72	0.00	0.72	0.00	0.73	0.00	
Mik type used Full cream Semi-skimmed 0.91 0.42 0.95 0.71 0.93 0.53 0.98 0.87   Mik type used Skimmed Semi-skimmed 1.04 0.04 0.05 0.11 1.12 0.05 1.08 0.24 0.95 0.11 0.05 0.08 0.27   Mik type used Sype Semi-skimmed 0.48 0.00 0.55 0.01 0.40 0.00 0.56 0.01   Mik type used Other type of spread/magarine 0.85 0.00 0.72 0.00 0.85 0.00 0.70 0.00   Spread type Newer/rarely as pread Other type of spread/magarine 0.65 0.00 0.72 0.00 0.55 0.00 0.70 0.00   Spread type Botter/spreadable butter Other type of spread/magarine 0.65 0.00 0.27 0.00 0.55 0.00 0.51 1.50 0.12 0.50   Teal rate Other type of spread/magarine 1.52 0.15 1.50	Past tobacco smoking	Just tried once or twice	Smoked on most or all days	1.36	0.00	1.25	0.00	1.35	0.00	1.25	0.00	
Mik type used Skimmed Skimmed Semi-skimmed 1.14 0.04 1.07 0.31 1.12 0.05 1.08 0.24   Milk type used Soya Semi-skimmed 0.48 0.00 0.55 0.01 0.49 0.00 0.56 0.01   Milk type used Other type of milk Semi-skimmed 0.89 0.81 1.04 0.88 0.91 0.70 1.09 0.75 0.01   Milk type used Never/rarely use spread Other type of spread/margarine 0.65 0.00 0.07 0.00 0.05 0.00 0.05 0.00 0.07 0.00   Spread type Bitter/spreadable butter Other type of spread/margarine 1.04 0.52 1.05 1.06 1.07 1.03 0.07 </td <td>Past tobacco smoking</td> <td>I have never smoked</td> <td>Smoked on most or all days</td> <td>0.95</td> <td>0.44</td> <td>0.96</td> <td>0.58</td> <td>0.94</td> <td>0.38</td> <td>0.93</td> <td>0.40</td> <td></td>	Past tobacco smoking	I have never smoked	Smoked on most or all days	0.95	0.44	0.96	0.58	0.94	0.38	0.93	0.40	
Mik type used Sopa Sopa Sopa Out Out Out Out Out Out Out   Mik type used Other type of nik Semi-skimmed 0.84 0.61 0.48 0.91 0.55 0.01 0.76 0.01   Mik type used Other type of nik Semi-skimmed 0.79 0.16 0.70 0.08 0.90 0.75 0.09   Spread type Newer/rarely use spread Other type of spread/margarine 0.65 0.09 0.75 0.09 0.55 0.09 0.55 0.01 0.00 0.55 0.00 0.55 0.01 0.00 0.55 0.00 0.55 0.01 0.00 0.05 0.00 0.05 0.00 0.05 0.01 0.00 0.05 0.01 0.00 0.05 0.01 0.00 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.05 0.01 0.00 0.05 0.01 0.05 0.01 0.05	Milk type used	Full cream	Semi-skimmed	0.91	0.42	0.95	0.71	0.93	0.53	0.98	0.87	
Mik type used Other type of mik Semi-skimmed 0.89 0.61 1.04 0.88 0.70 1.09 0.76   Milk type used Newer/rarely use synead Semi-skimmed 0.79 0.16 0.70 0.08 0.80 0.17 0.70 0.09   Spread type Newer/rarely use synead Other type of spread/margarine 0.65 0.00 0.72 0.00 0.65 0.00 0.75 0.09   Spread type Butter/ spreadable butter Other type of spread/margarine 1.04 0.52 1.06 0.39 1.04 0.51 1.05 0.42   Spread type Butter/ spreadable butter Other type of spread/margarine 1.02 0.16 1.72 0.09 1.50 0.16 1.72 0.09 1.50 0.16 1.72 0.09 1.50 0.16 1.72 0.09 1.50 0.74 0.39 1.01 0.00 1.62 1.61 1.00 0.77 1.30 0.07 1.30 0.27 1.30 0.27 1.30 0.27	Milk type used	Skimmed	Semi-skimmed	1.14	0.04	1.07	0.31	1.12	0.05	1.08	0.24	
Mik type und Never/rarely have milk Gemi-skimmed 0.79 0.16 0.70 0.08 0.00 0.17 0.09   Spread type Never/rarely use spread Other type of spread/margarine 0.65 0.00 0.72 0.00 0.65 0.00 0.65 0.00 0.65 0.00 0.65 0.00 0.65 0.00 0.65 0.00 0.65 0.00 0.65 0.00 0.65 0.00 0.65 0.00 0.65 0.05 1.72 0.09   Spread type Fina Pro-Active/Benecol Other type of spread/margarine 1.52 0.15 0.15 0.15 0.15 0.15 0.15 0.15 0.15 0.00 0.00 0.00 0.00 0.00 0.01 1.30 0.01 1.31 0.28 0.00 0.02 0.00 0.01 1.31 0.28 0.00 1.32 0.61 0.30 0.31 0.00 1.31 0.32 0.00 1.32 0.28 0.01 1.32 0.28 0.01 <td< td=""><td>Milk type used</td><td>Soya</td><td>Semi-skimmed</td><td>0.48</td><td>0.00</td><td>0.55</td><td>0.01</td><td>0.49</td><td>0.00</td><td>0.56</td><td>0.01</td><td></td></td<>	Milk type used	Soya	Semi-skimmed	0.48	0.00	0.55	0.01	0.49	0.00	0.56	0.01	
Spread type Never/rarely us spread Other type of spread/margarine 0.65 0.00 0.72 0.00 0.65 0.00 0.70 0.00   Spread type Butter/spreadable butter Other type of spread/margarine 1.04 0.52 1.06 0.39 1.04 0.51 1.05 0.42   Spread type Flora Pro-Active/Benecol Other type of spread/margarine 1.52 0.15 1.72 0.09 1.50 0.16 1.72 0.09   Tea intake 0.88 0.00 0.33 0.01 0.88 0.00 0.93 0.01 0.88 0.00 0.92 0.00   Never ext eggs, dain, wheat, sugar Eggs or foods containing eggs I eat all of the above 1.32 0.05 1.35 0.47 0.39 1.34 0.28   Never ext eggs, dain, wheat, sugar Dairy products I eat all of the above 1.97 0.00 1.72 0.09 1.32 0.39 0.96 1.24 0.32   Never ext eggs, dain, wheat, sugar Sugar or foods/drinks containing sugar I eat all o	Milk type used	Other type of milk	Semi-skimmed	0.89	0.61	1.04	0.88	0.91	0.70	1.09	0.76	
Spread type Butter/sposedable butter Other type of spread/margarine 1.04 0.52 1.06 0.33 1.04 0.51 1.05 0.42   Spread type Flora Pro-Active/Benecol Other type of spread/margarine 1.52 0.15 1.50 0.51 1.72 0.09 1.50 0.51 1.72 0.09   Tea inslaw 0.05 1.50 0.61 1.72 0.09 1.50 0.62   Never exteggs, dair, wheat, sugar Eggs of foods containing eggs 1 eat all of the above 1.82 0.06 1.26 0.17 1.30 0.07 1.33 0.28   Never exteggs, dair, wheat, sugar Wheat products I eat all of the above 1.46 0.77 1.24 0.33 0.99 0.97 1.24 0.33 0.99 0.32 0.00 1.23 0.00 1.24 0.33 0.99 0.37 0.20 1.24 0.33 0.99 0.32 0.00 1.32 0.00 1.24 0.33 0.99 0.32 0.00 1.24 0.00	Milk type used	Never/rarely have milk	Semi-skimmed	0.79	0.16	0.70	0.08	0.80	0.17	0.71	0.09	
Spread type Flora Pro-Active/Benecol Other type of spread/margarine 152 0.15 1.72 0.09 1.00 0.16 1.72 0.09   Tea intake 0.08 0.00 0.03 0.01 0.88 0.00 0.92 0.00   Never ext eggs, dairy, wheat, sugar Eggs or foods containing eggs I eat all of the above 1.32 0.06 1.35 0.27 1.30 0.07 1.34 0.09   Never ext eggs, dairy, wheat, sugar Dairy products I eat all of the above 0.46 0.07 1.35 0.25 1.47 0.07 1.33 0.28   Never ext eggs, dairy, wheat, sugar Wheat products I eat all of the above 0.99 0.97 1.34 0.39 0.96 1.24 0.32   Never ext eggs, dairy, wheat, sugar Sugar or foods/drinks containing sugar I eat all of the above 1.77 0.00 1.74 0.00 1.52 0.00   Major dietary charges in the last 5 years Yes, because of liness No 3.69 0.00 1.32 0.00 1.32 0.00<	Spread type	Never/rarely use spread	Other type of spread/margarine	0.65	0.00	0.72	0.00	0.65	0.00	0.70	0.00	
Tes instale 0.88 0.00 0.93 0.01 0.88 0.00 0.92 0.00   Newer ext eggs, dainy, wheat, sugar Eggs of bods containing eggs leat all of the above 1.32 0.06 1.35 0.25 1.47 0.07 1.33 0.28   Newer ext eggs, dainy, wheat, sugar Dairy products leat all of the above 1.46 0.07 1.35 0.25 1.47 0.07 1.33 0.28   Newer ext eggs, dainy, wheat, sugar Wheat products leat all of the above 0.99 0.97 1.24 0.39 0.96 1.24 0.32   Newer ext eggs, dainy, wheat, sugar Sugar or food/infinis containing sugar leat all of the above 1.77 0.00 1.24 0.00 1.24 0.00 1.24 0.00 1.24 0.00 1.24 0.00 1.24 0.00 1.24 0.00 1.24 0.00 1.24 0.00 1.24 0.00 1.24 0.00 1.24 0.00 1.24 0.00 1.24 0.00 1.24 0.00 <t< td=""><td>Spread type</td><td>Butter/spreadable butter</td><td>Other type of spread/margarine</td><td>1.04</td><td>0.52</td><td>1.06</td><td>0.39</td><td>1.04</td><td>0.51</td><td>1.05</td><td>0.42</td><td></td></t<>	Spread type	Butter/spreadable butter	Other type of spread/margarine	1.04	0.52	1.06	0.39	1.04	0.51	1.05	0.42	
Never eat eggs, dairy, wheat, sugar Eggs or foods containing eggs I eat all of the above 1.32 0.06 1.26 0.17 1.30 0.07 1.24 0.19   Never eat eggs, dairy, wheat, sugar Dairy products I eat all of the above 1.46 0.07 1.35 0.25 1.47 0.07 1.33 0.28   Never eat eggs, dairy, wheat, sugar Wheat products I eat all of the above 0.99 0.97 1.24 0.33 0.99 0.65 1.24 0.32 0.99 0.96 1.24 0.32 0.99 0.97 1.24 0.33 0.99 0.65 1.24 0.32 0.99 0.97 1.24 0.33 0.99 0.96 1.24 0.32 0.99 0.96 1.24 0.32 0.99 0.97 1.30 0.94 0.35 0.00 1.32 0.00 1.32 0.00 1.32 0.00 1.32 0.00 1.32 0.00 1.32 0.00 1.32 0.00 1.32 0.00 1.32 0.00 1.32	Spread type	Flora Pro-Active/Benecol	Other type of spread/margarine	1.52	0.15	1.72	0.09	1.50	0.16	1.72	0.09	
Never est eggs, dain, wheat, sugar Dainy products I eat all of the above 1.46 0.07 1.35 0.25 1.47 0.07 1.33 0.28   Never est eggs, dain, wheat, sugar Wheat products I eat all of the above 0.99 0.97 1.24 0.33 0.99 0.96 1.24 0.32   Never est eggs, dain, wheat, sugar Sugar or food/drinks containing sugar I eat all of the above 1.77 0.00 1.24 0.32 0.00   Major dietary changes in the last 5 years Yes, because of liness No 3.69 0.00 2.79 0.00 1.32 0.00 2.72 0.01   Major dietary changes in the last 5 years Yes, because of ther reasons No 1.33 0.00 1.24 0.32 0.00 1.32 0.00 1.32 0.00 1.32 0.00 1.32 0.00 1.32 0.00 1.32 0.00 1.32 0.01 1.32 0.01 1.32 0.01 1.32 0.01 1.32 0.01 1.32 0.01 1.32 0.01	Tea intake			0.88	0.00	0.93	0.01	0.88	0.00	0.92	0.00	
Never eat-eggs, dairy, wheat, sugar Wheat products I eat all of the above 0.99 0.97 1.24 0.33 0.99 0.96 1.24 0.32   Never eat-eggs, dairy, wheat, sugar Sugar of book/drinks containing sugar I eat all of the above 1.77 0.00 1.51 0.00 1.52 0.00   Major dietary changes in the last 5 years Yes, because of illness No 3.69 0.00 2.79 0.00 1.32 0.00 1.32 0.00 1.32 0.01 1.32 <td>Never eat eggs, dairy, wheat, sugar</td> <td>Eggs or foods containing eggs</td> <td>I eat all of the above</td> <td>1.32</td> <td>0.06</td> <td>1.26</td> <td>0.17</td> <td>1.30</td> <td>0.07</td> <td>1.24</td> <td>0.19</td> <td></td>	Never eat eggs, dairy, wheat, sugar	Eggs or foods containing eggs	I eat all of the above	1.32	0.06	1.26	0.17	1.30	0.07	1.24	0.19	
Never eat eggs, dairy, wheat, sugar Sugar or foods/drinks containing sugar I eat all of the above 1.77 0.00 1.51 0.00 1.74 0.00 1.52 0.00   Major dietary changes in the last Syears Yes, because of liness No 3.69 0.00 2.79 0.00 1.52 0.00   Major dietary changes in the last Syears Yes, because of ther reasons No 1.33 0.00 1.32 0.00 1.32 0.01	Never eat eggs, dairy, wheat, sugar	Dairy products	I eat all of the above	1.46	0.07	1.35	0.25	1.47	0.07	1.33	0.28	
Major dietary changes in the last 5 years Yes, because of illness No 3.69 0.00 2.79 0.00 3.57 0.00 2.72 0.00   Major dietary changes in the last 5 years Yes, because of other reasons No 1.33 0.00 1.23 0.00 1.22 0.01	Never eat eggs, dairy, wheat, sugar	Wheat products	l eat all of the above	0.99	0.97	1.24	0.33	0.99	0.96	1.24	0.32	
Major dietary changes in the last 5 years Yes, because of other reasons No 1.33 0.00 1.23 0.00 1.22 0.01	Never eat eggs, dairy, wheat, sugar	Sugar or foods/drinks containing sugar	l eat all of the above	1.77	0.00	1.51	0.00	1.74	0.00	1.52	0.00	
	Major dietary changes in the last 5 years	Yes, because of illness	No	3.69	0.00	2.79	0.00	3.57	0.00	2.72	0.00	
Alcohol intake frequency Three or four times a week Daily or almost daily 2.05 0.00 1.45 0.00 2.01 0.00 1.46 0.00	Major dietary changes in the last 5 years	Yes, because of other reasons	No	1.33	0.00	1.23	0.00	1.32	0.00	1.22	0.01	
	Alcohol intake frequency	Three or four times a week	Daily or almost daily	2.05	0.00	1.45	0.00	2.01	0.00	1.46	0.00	
Alcohol intake frequency Once or twice a week Daily or almost daily 0.93 0.29 0.99 0.93 0.94 0.40 1.00 0.98	Alcohol intake frequency	Once or twice a week	Daily or almost daily	0.93	0.29	0.99	0.93	0.94	0.40	1.00	0.98	
Alcohol intake frequency One to three times a month Daily or almost daily 0.82 0.00 0.86 0.04 0.82 0.00 0.87 0.05	Alcohol intake frequency	One to three times a month	Daily or almost daily	0.82	0.00	0.86	0.04	0.82	0.00	0.87	0.05	-
Alcohol intake frequency Special ocassions only Daily or almost daily 0.98 0.74 0.99 0.85 0.96 0.57 0.98 0.75	Alcohol intake frequency	Special ocassions only	Daily or almost daily	0.98	0.74	0.99	0.85	0.96	0.57	0.98	0.75	
Alcohol intake frequency Never Daily or almost daily 1.00 0.99 1.03 0.72 0.99 0.85 1.02 0.77	Alcohol intake frequency	Never	Daily or almost daily	1.00	0.99	1.03	0.72	0.99	0.85	1.02	0.77	5
Comparative body size at age 10 Plumper Thinner 0.87 0.00 0.80 0.00 0.87 0.00 0.80 0.00 0.80 0.00	Comparative body size at age 10	Plumper	Thinner	0.87	0.00	0.80	0.00	0.87	0.00	0.80	0.00	
Comparative body size at age 10 About average Thinner 0.85 0.00 1.15 0.03 0.87 0.01 1.16 0.02	Comparative body size at age 10	About average	Thinner	0.85	0.00	1.15	0.03	0.87	0.01	1.16	0.02	5
BMI 1.10 0.00 1.00 0.04	BMI				-	1.10	0.00	-	-	1.00	0.04	
Systolic blood pressure - 0.42 0.00 1.10 0.00	Systolic blood pressure					0.42	0.00	-		1.10	0.00	
Glucose 1.59 0.00 1.58 0.00	Glucose				-	1.59	0.00	-	-	1.58	0.00	
HDL cholesterol 0.42 0.00 0.42 0.00	HDL cholesterol				-	0.42	0.00		-	0.42	0.00	
Triglycerides 1.09 0.00 1.07 0.00	Triglycerides					1.09	0.00	-		1.07	0.00	
Family History of Diabetes 1.90 0.00 1.81 0.00	Family History of Diabetes				-	1.90	0.00	-	-	1.81	0.00	
PXS 24.89 0.00 14.32 0.00	PXS							24.89	0.00	14.32	0.00	

**Supplementary Table S4: Clinical Risk Score (CRS).** Weights of 8 clinical risk factors. \*Sex served as an interactor, not a mediator, in the Framingham Heart Study.

	CRS model						
Field	Class	HR	95% CI	P-val	Field	OR	
Male (versus Female)	Binary	1.30	1.20 - 1.40	2.58E-07	Male (versus Female)	0.66*	
Year of birth	Continuous	0.94	0.93 - 0.94	6.38E-80	Age (years)	1.05	
Systolic blood pressure (mmHg)	Continuous	1.00	1.00 - 1.01	6.80E-03	Systolic blood pressure (mmHg)	1.01	
BMI (kg/m2)	Continuous	1.12	1.12 - 1.13	1.96E-215	BMI (kg/m2)	1.14	
Glucose (mmol/L)	Continuous	1.60	1.57 - 1.63	2.57E-275	Glucose (mg/dL)	1.14	
HDL cholesterol (mmol/L)	Continuous	0.27	0.09 - 0.45	2.48E-47	HDL cholesterol (mg/dL))	0.99	
Triglycerides (mmol/L)	Continuous	1.12	1.08 - 1.15	8.63E-10	Triglycerides ( mg/dL)	1.00	
Family History of Diabetes (versus no history)	Binary	1.99	1.90 - 2.05	8.98E-49	Family History of Diabetes (versus no history)	1.72	

**Supplementary Table S5:** The C-statistics of the new PXS model when each of the exposure variables were iteratively dropped from the score in subset of the validation set of N=68,299 with complete information for all variables.

Dropped Exposure	C-Statistic (95% CI)
Major dietary changes in the last 5 years	0.737 (0.724, 0.75)
Snoring	0.756 (0.743, 0.769)
Alcohol intake frequency	0.757 (0.744, 0.77)
Own or rent accommodation lived in	0.759 (0.746, 0.772)
Sleeplessness / insomnia	0.760 (0.747, 0.773)
Never eat eggs, dairy, wheat, sugar	0.760 (0.747, 0.773)
Comparative body size at age 10	0.760 (0.747, 0.773)
Average total household income before tax	0.761 (0.748, 0.774)
Past tobacco smoking	0.761 (0.749, 0.773)
Spread type	0.761 (0.749, 0.773)
Tea intake	0.761 (0.749, 0.773)
Milk type used	0.767 (0.755, 0.779)

**Supplementary Table S6: C-Statistics for evaluating performance of risk models in sensitivity analysis.** The performance was evaluated in the full test population as well as stratified by sex and year of birth where blood glucose removed from CRS. \* Denotes models adjusted for all covariates (sex, age, assessment center, and genetic principal components) in the full test population, all covariates except sex in the sex stratified analysis, and all covariates except age in year of birth stratified analysis.

	C-Statistic (95% CI), blood glucose removed from CRS						
	All	Male	Female	Born before 1945	Born between 1945-1950	Born between 1950-1958	Born after 1958
Ν	68299	32657	35642	15032	16529	18547	18191
# of Events	1281	844	437	468	377	291	145
Sex+Age	0.670 (0.656, 0.684)	0.629 (0.612, 0.646)	0.637 (0.612, 0.662)	0.594 (0.569, 0.619)	0.606 (0.579, 0.633)	0.624 (0.593, 0.655)	0.592 (0.548, 0.636)
PGS*	0.709 (0.696, 0.722)	0.680 (0.663, 0.697)	0.705 (0.682, 0.728)	0.658 (0.634, 0.682)	0.674 (0.648, 0.7)	0.713 (0.687, 0.739)	0.719 (0.678, 0.760)
PXS*	0.762 (0.749, 0.775)	0.732 (0.716, 0.748)	0.774 (0.753, 0.795)	0.714 (0.69, 0.738)	0.718 (0.692, 0.744)	0.785 (0.759, 0.811)	0.782 (0.743, 0.821)
CRS*	0.820 (0.810, 0.820)	0.789 (0.775, 0.803	0.842 (0.824, 0.86)	0.774 (0.754, 0.794)	0.791 (0.77, 0.812)	0.838 (0.818, 0.858)	0.845 (0.811, 0.879)
PGS+PXS*	0.776 (0.764, 0.788)	0.749 (0.734, 0.764)	0.786 (0.765, 0.807)	0.729 (0.706, 0.752)	0.730 (0.705, 0.755)	0.803 (0.779, 0.827)	0.802 (0.764, 0.84)
CRS+PGS*	0.826 (0.816, 0.836)	0.797 (0.783, 0.811)	0.848 (0.831, 0.865)	0.781 (0.762, 0.8)	0.796 (0.775, 0.817)	0.849 (0.83, 0.868)	0.856 (0.824, 0.888
CRS+PXS*	0.835 (0.825, 0.845	0.807 (0.793, 0.821)	0.855 (0.838, 0.872)	0.790 (0.771, 0.809)	0.801 (0.708, 0.822)	0.861 (0.842, 0.88)	0.856 (0.822, 0.890)
CRS+PXS+PGS*	0.841 (0.831, 0.851)	0.814 (0.801, 0.827)	0.86 (0.843, 0.877)	0.797 (0.778, 0.816)	0.805 (0.784, 0.826)	0.87 (0.852, 0.888)	0.866 (0.834, 0.898)

**Supplementary Table S7: Hazard ratio (HR) for individuals with highest risk of T2D.** The HR and 95 CI for individuals in the top 1% (versus the bottom 99%), 5% (versus the bottom 95th), 10% (versus the bottom 90th), and 20% (versus the bottom 80th) of using the polygenic risk score (PGS), polyexposure risk score (PXS), or clinical risk score (CRS) models.

	Hazard Ratio (95% CI)							
		PGS	PXS	CRS				
e	1%	2.64 (1.87, 3.73)	9.74 (7.96, 11.91)	15.11 (12.74, 17.92)				
score	5%	2.27 (1.90, 2.71)	6.72 (5.92, 7.63)	10.54 (9.39, 11.83)				
% doj	10%	2.00 (1.73, 2.31)	5.90 (5.28, 6.61)	9.97 (8.94, 11.13)				
Ĕ	20%	1.96 (1.75, 2.21)	4.72 (4.23, 5.27)	9.51 (8.44, 10.71)				

**Supplementary Table S8: Sensitivity of risk scores in participants with undiagnosed T2D.** Undiagnosed individuals (N=3,658) with scores in the top 10th of the reference group were classified as high risk. Those with scores in the bottom 10th of the reference group were classified as low risk.

Score type	High Risk N	Low Risk N	High Risk Incidence	Low Risk Incidence
CRS	2869	34	1572 (54.79%)	5 (14.71%)
PXS	1436	75	878 (61.14%)	18 (24.00%)
PGS	83	132	456 (54.68%)	73 (55.30%)
PXS and CRS	1217	7	755 (62.04%)	0 (0.00%)
PGS and CRS	657	1	375 (57.08%)	0 (0.00%)
PGS and PXS	328	3	216 (65.85%)	1 (33.33%)
PGS and PXS and CRS	274	0	184 (67.15%)	0 (NA)