nature research

https://doi.org/10.1038/s41591-020-1116-9

Supplementary information

Pathophysiology-based subphenotyping of individuals at elevated risk for type 2 diabetes

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Supplementary Tables

Supplementary Table 1.

Post-hoc tests for comparison of cluster means in the **TUEF/TULIP** study. Numbers denote p-values for all pairwise comparisons computed with Tukey's test (n=899 individuals).

variable	2-1	3-1	3-2	4-1	4-2	4-3	5-1	5-2	5-3	5-4	6-1	6-2	6-3	6-4	6-5
age	0.37	$<1\times10^{-14}$	8.63×10^{-12}	0.97	0.87	$<1\times10^{-14}$	8.57×10^{-10}	2.11×10^{-05}	0.65	1.19×10^{-07}	6.82×10^{-09}	5.64×10^{-04}	0.0058	2.14×10^{-06}	0.68
BMI (kg/m2)	1.27×10^{-12}	5.12×10^{-06}	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	5.13×10^{-06}	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	9.36×10^{-07}	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	3.80×10^{-13}	0.93
waist circumference (cm)	3.15×10^{-09}	8.18×10^{-11}	3.23×10^{-13}	3.74×10^{-13}	3.23×10^{-13}	0.6	3.23×10^{-13}	3.23×10^{-13}	2.45×10^{-12}	1.39×10^{-08}	3.23×10^{-13}	3.23×10^{-13}	3.75×10^{-13}	1.78×10^{-11}	1
hip circumference (cm)	1.44×10^{-06}	0.003	3.75×10^{-13}	3.79×10^{-13}	3.23×10^{-13}	7.89×10^{-08}	3.78×10^{-13}	3.23×10^{-13}	6.37×10^{-11}	0.38	3.23×10^{-13}	3.23×10^{-13}	3.80×10^{-13}	7.48×10^{-04}	0.68
total adipose tissue MRI (liter)	1.67×10^{-09}	5.00×10^{-06}	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	0.031	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	3.73×10^{-07}	0.54
sq adipose tissue MRI (liter)	4.35×10^{-06}	0.0011	8.92×10^{-14}	4.22×10^{-14}	3.83×10^{-14}	2.38×10^{-11}	3.83×10^{-14}	3.83×10^{-14}	9.04×10^{-14}	0.088	3.83×10^{-14}	3.83×10^{-14}	3.83×10^{-14}	1.39×10^{-07}	0.21
visceral adipose tissue MRI (liter)	0.036	$<1\times10^{-14}$	$<1\times10^{-14}$	6.16×10^{-09}	$<1\times10^{-14}$	0.43	$<1\times10^{-14}$	$<1\times10^{-14}$	2.15×10^{-08}	1.40×10^{-13}	$<1\times10^{-14}$	$<1\times10^{-14}$	1.47×10^{-10}	$<1\times10^{-14}$	1
sq to visceral adipose ratio	0.49	9.11×10^{-08}	0.0011	0.98	0.15	4.16×10^{-09}	2.41×10^{-06}	0.0039	1	1.66×10^{-07}	2.30×10^{-05}	0.051	0.77	1.25×10^{-06}	0.79
visceral adipose % of total	1	3.03×10^{-09}	9.51×10^{-10}	1	0.96	1.47×10^{-07}	8.74×10^{-06}	3.00×10^{-06}	0.99	1.03×10^{-04}	1.18×10^{-05}	3.73×10^{-06}	0.49	2.43×10^{-04}	0.93
liver fat content	0.11	0.0024	2.05×10^{-08}	0.99	0.029	0.024	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$
renal sinus fat (mean of r&l, %)	0.98	6.53×10^{-04}	0.0067	0.18	0.58	0.24	3.70×10^{-08}	3.79×10^{-06}	0.99	0.005	2.07×10^{-10}	2.07×10^{-10}	0.05	3.42×10^{-10}	0.023
diastolic blood pressure (mmHg)	0.76	0.0042	2.74×10^{-05}	0.98	0.34	0.054	2.14×10^{-13}	2.02×10^{-13}	1.17×10^{-05}	2.82×10^{-12}	7.29×10^{-08}	4.93×10^{-11}	0.35	1.09×10^{-05}	0.0075
systolic blood pressure (mmHg)	0.62	6.68×10^{-06}	3.10×10^{-09}	1	0.63	1.67×10^{-05}	2.36×10^{-13}	2.00×10^{-13}	0.0049	3.33×10^{-13}	1.12×10^{-09}	2.91×10^{-13}	0.86	5.52×10^{-09}	0.072
heart rate (BPM)	0.64	1	0.71	0.91	1	0.94	1.79×10^{-04}	5.76×10^{-07}	2.95×10^{-04}	4.89×10^{-06}	0.11	9.97×10^{-04}	0.13	0.0064	0.19
fasting glucose (mmol/l)	0.7	$<1\times10^{-14}$	$<1\times10^{-14}$	1	0.57	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	9.31×10^{-05}	$<1\times10^{-14}$	3.54×10^{-10}	$<1\times10^{-14}$	0.038	7.07×10^{-09}	1.13×10^{-11}
post-challenge glucose (mmol/l)	0.94	$<1\times10^{-14}$	$<1\times10^{-14}$	0.046	0.4	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	0.087	$<1\times10^{-14}$	3.63×10^{-12}	$<1\times10^{-14}$	8.23×10^{-07}	$<1\times10^{-14}$	2.19×10^{-12}
glycated hemoglobin (mmol/mol)	0.26	3.78×10^{-09}	6.54×10^{-04}	1	0.42	4.09×10^{-08}	2.52×10^{-12}	9.33×10^{-07}	0.43	2.84×10^{-11}	2.06×10^{-06}	0.044	0.71	1.57×10^{-05}	0.019
triglycerides (mmol/l)	1.98×10^{-04}	0.0032	1.47×10^{-13}	0.88	0.019	5.78×10^{-05}	1.15×10^{-12}	$<1\times10^{-14}$	3.55×10^{-04}	$<1\times10^{-14}$	0.0024	$<1\times10^{-14}$	1	3.36×10^{-05}	9.77×10^{-05}
insulin sensitivity (Matsuda) (AU)	$<1\times10^{-14}$	2.43×10^{-04}	$<1\times10^{-14}$	1.13×10^{-04}	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	6.41×10^{-10}	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	7.87×10^{-08}	$<1\times10^{-14}$	0.44
fasting insulin (pmol/l)	6.49×10^{-06}	0.98	4.08×10^{-07}	0.95	7.00×10^{-04}	0.62	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	0.02
insulinogenic index (AU)	3.96×10^{-05}	4.55×10^{-09}	0.55	0.52	0.044	9.95×10^{-05}	0.05	0.86	0.1	0.76	1	4.03×10^{-06}	2.21×10^{-10}	0.27	0.016
disposition index (AU)	0.97	3.65×10^{-06}	2.82×10^{-04}	0.96	1	3.31×10^{-04}	6.57×10^{-05}	0.0018	1	0.002	9.13×10^{-04}	0.026	0.71	0.029	0.76
cholesterol (mmol/l)	1	0.011	0.0058	0.95	0.99	7.25×10^{-04}	0.0073	0.0039	0.99	6.06×10^{-04}	0.24	0.15	0.8	0.033	0.55
C-reactive protein (mg/dl)	0.38	1	0.25	0.17	4.65×10^{-04}	0.37	2.96×10^{-09}	4.84×10^{-13}	4.98×10^{-08}	2.48×10^{-04}	3.32×10^{-06}	6.39×10^{-11}	5.14×10^{-05}	0.082	0.25
LDL (mmol/l)	0.011	0.33	4.18×10^{-06}	0.98	0.1	0.092	0.0072	1.29×10^{-08}	0.56	0.0011	0.79	5.77×10^{-05}	0.97	0.37	0.15
HDL (mmol/l)	$<1\times10^{-14}$	1	$<1\times10^{-14}$	0.37	$<1\times10^{-14}$	0.74	4.94×10^{-04}	$<1\times10^{-14}$	0.0045	0.15	0.51	$<1\times10^{-14}$	0.87	1	0.065
aspartate-aminotransferase (U/l)	1	1	1	1	0.99	1	3.38×10^{-14}	3.75×10^{-14}	3.12×10^{-14}	3.44×10^{-14}	0.036	0.14	0.075	0.023	7.41×10^{-10}
alanine-aminotransferase (U/l)	0.77	1	0.66	0.98	0.36	1	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	7.76×10^{-06}	1.08×10^{-08}	7.30×10^{-05}	5.34×10^{-04}	3.99×10^{-09}
gamma-glutamyl transferase (U/l)	0.46	0.23	0.0015	1	0.81	0.085	1.64×10^{-07}	2.33×10^{-11}	0.0028	2.57×10^{-08}	7.62×10^{-05}	7.87×10^{-09}	0.27	1.18×10^{-05}	0.33
serum creatinine (mg/dl)	0.95	1	1	1	1	1	0.26	0.75	0.5	0.52	0.36	0.91	0.68	0.7	0.99
urinary albumin-creatinine ratio (mg/g)	1	1	0.99	1	1	1	0.6	0.78	0.44	0.66	1	0.99	1	1	0.47
carotid intima media thickness	1	1.61×10^{-07}	1.42×10^{-05}	0.95	0.99	6.99×10^{-06}	1.36×10^{-06}	3.11×10^{-05}	1	2.99×10^{-05}	4.06×10^{-05}	0.0016	0.6	0.0013	0.44
polygenic risk score	0.2	0.022	0.96	0.97	0.034	0.0022	0.59	1	0.9	0.22	1	0.28	0.038	0.92	0.7

Supplementary Table 2

Cohort characteristics of the **Whitehall II** cohort after stratification using the cluster medians established in the TUEF/TULIP cohort (n=6810). P-values were computed with one-way ANOVA for continuous variables and two-sided chi-squared tests for categorical variables.

	1	2	3	4	5	6	p
n	1362	4228	322	509	123	266	
sex = male (%)	1052 (77.2)	2979 (70.5)	220 (68.3)	355 (69.7)	76 (61.8)	178 (66.9)	1.57×10^{-06}
BMI (kg/m^2, mean (SD))	25.96 (2.03)	23.72 (2.50)	27.39 (2.58)	30.17 (2.57)	31.58 (3.68)	32.84 (3.68)	$<2.23\times10^{-308}$
age (years, mean (SD))	50.96 (6.51)	50.63 (6.73)	53.73 (6.68)	51.40 (6.40)	54.15 (7.65)	52.16 (7.12)	1.52×10^{-20}
Waist circumference (cm, mean (SD))	89.43 (7.46)	81.95 (9.60)	92.62 (8.56)	100.15 (7.61)	103.25 (9.67)	106.05 (8.78)	$<2.23\times10^{-308}$
Hip circumference (cm, mean (SD))	97.89 (4.48)	94.90 (5.60)	100.75 (5.63)	107.00 (5.41)	106.19 (6.77)	109.69 (7.03)	$<2.23\times10^{-308}$
Systolic blood pressure (mmHg) (mean (SD))	122.99 (13.25)	118.39 (13.25)	129.51 (14.90)	123.67 (13.00)	132.59 (12.86)	129.23 (14.18)	2.94×10^{-109}
Diastolic blood pressure (mmHg) (mean (SD))	81.35 (9.06)	77.17 (9.32)	83.73 (10.51)	81.86 (9.55)	85.16 (9.51)	85.04 (9.43)	3.98×10^{-110}
Glucose (fasting, mmol/l) (mean (SD))	5.28 (0.42)	5.13 (0.45)	5.59 (0.53)	5.19 (0.41)	5.61 (0.54)	5.39 (0.49)	7.49×10^{-109}
Glucose (post-challenge, mmol/l) (mean (SD))	5.74 (1.16)	5.17 (1.40)	8.56 (1.17)	5.01 (1.11)	8.33 (1.41)	5.86 (1.22)	$<2.23\times10^{-308}$
AUC glucose (mmol 2h l-1) (mean (SD))	661.52 (70.94)	618.03 (90.47)	848.98 (67.83)	611.81 (69.17)	836.33 (90.90)	675.38 (73.66)	$<2.23\times10^{-308}$
Insulin (fasting, pmol/l) (mean (SD))	62.90 (28.16)	30.81 (15.91)	58.77 (26.53)	50.99 (20.49)	119.60 (41.87)	122.35 (39.48)	$<2.23\times10^{-308}$
Insulin (post-challenge, pmol/l) (mean (SD))	441.42 (236.65)	219.27 (153.28)	595.78 (268.04)	248.24 (148.82)	884.65 (411.76)	583.18 (288.61)	$<2.23\times10^{-308}$
Insulin secretion (Stumvoll) (AU, mean (SD))	1055.35 (319.60)	752.75 (236.45)	729.55 (348.63)	915.20 (239.87)	1422.77 (504.31)	1528.23 (397.45)	$<2.23\times10^{-308}$
insulin sensitivity (Matsuda) (AU, mean (SD))	17.25 (5.80)	41.43 (21.41)	13.36 (4.74)	26.17 (9.09)	7.50 (2.67)	9.76 (2.81)	$<2.23\times10^{-308}$
Triglycerides (mmol/l) (mean (SD))	1.88 (0.93)	1.08 (0.53)	1.78 (0.81)	1.68 (0.84)	2.93 (1.22)	2.00 (0.92)	$<2.23\times10^{-308}$
HDL chol (mean (SD))	1.18 (0.27)	1.60 (0.40)	1.33 (0.33)	1.18 (0.28)	1.05 (0.26)	1.23 (0.33)	$<2.23\times10^{-308}$
glycaemic category (%)							$<2.23\times10^{-308}$
NGT	968 (71.1)	3393 (80.3)	24 (7.5)	411 (80.7)	20 (16.3)	159 (59.8)	
IFG	333 (24.4)	617 (14.6)	66 (20.5)	93 (18.3)	24 (19.5)	94 (35.3)	
IGT	56 (4.1)	183 (4.3)	141 (43.8)	5 (1.0)	42 (34.1)	10 (3.8)	
IFG+IGT	5 (0.4)	35 (0.8)	91 (28.3)	0 (0.0)	37 (30.1)	3 (1.1)	
Smoking (%)							1.50×10^{-04}
never	580 (42.6)	1909 (45.2)	143 (44.4)	184 (36.1)	60 (48.8)	105 (39.5)	
ex	538 (39.5)	1567 (37.1)	145 (45.0)	213 (41.8)	46 (37.4)	119 (44.7)	
current	177 (13.0)	534 (12.6)	20 (6.2)	86 (16.9)	11 (8.9)	34 (12.8)	
missing	67 (4.9)	218 (5.2)	14 (4.3)	26 (5.1)	6 (4.9)	8 (3.0)	
Antihypertensive medication = yes (%)	113 (8.3)	199 (4.7)	49 (15.2)	51 (10.0)	29 (23.6)	45 (16.9)	3.02×10^{-34}
Lipid lowering medication = yes (%)	9 (0.7)	28 (0.7)	6 (1.9)	6 (1.2)	5 (4.1)	8 (3.0)	2.37×10^{-06}

Supplementary Table 3

Post-hoc tests for comparison of cluster means in the **Whitehall II** study. Numbers denote p-values for all pairwise comparisons computed with Tukey's test (n=6810).

	2-1	3-1	3-2	4-1	4-2	4-3	5-1	5-2	5-3	5-4	6-1	6-2	6-3	6-4	6-5
age	0.64	3.48×10^{-10}	5.79×10^{-13}	0.79	0.14	1.55×10^{-05}	5.98×10^{-06}	1.43×10^{-07}	0.99	6.30×10^{-04}	0.078	0.0043	0.052	0.67	0.07
BMI	4.79×10^{-13}	5.43×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	2.99×10^{-07}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	6.48×10^{-05}
Hip circumference	4.79×10^{-13}	5.38×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	5.35×10^{-13}	0.68	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	1.34×10^{-09}	7.28×10^{-08}
Waist circumference	4.79×10^{-13}	1.61×10^{-07}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	5.01×10^{-13}	0.008	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	5.29×10^{-13}	0.048
Systolic blood pressure (mmHg)	$<1\times10^{-14}$	$<1\times10^{-14}$	$<1\times10^{-14}$	0.92	$<1\times10^{-14}$	1.36×10^{-08}	$<1\times10^{-14}$	$<1\times10^{-14}$	0.25	4.56×10^{-10}	4.83×10^{-11}	$<1\times10^{-14}$	1	5.59×10^{-07}	0.19
Diastolic blood pressure (mmHg)	1.55×10^{-12}	6.05×10^{-04}	1.55×10^{-12}	0.9	1.61×10^{-12}	0.057	2.14×10^{-04}	1.61×10^{-12}	0.7	0.0058	6.09×10^{-08}	1.55×10^{-12}	0.54	1.03×10^{-04}	1
Glucose (fasting, mmol/l)	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.80×10^{-13}	0.61	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	0.71	4.79×10^{-13}	0.13	5.35×10^{-13}	4.79×10^{-13}	5.35×10^{-13}	4.79×10^{-13}
Glucose (post-challenge, mmol/l)	5.34×10^{-13}	5.28×10^{-13}	4.79×10^{-13}	3.77×10^{-04}	0.11	4.79×10^{-13}	9.52×10^{-13}	4.79×10^{-13}	1	5.40×10^{-13}	0.0045	5.48×10^{-13}	2.00×10^{-06}	2.02×10^{-08}	1.82×10^{-04}
Insulin (fasting, pmol/l)	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	5.35×10^{-13}	0.11	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	0.57	4.79×10^{-13}	0.73	5.42×10^{-13}	4.79×10^{-13}	5.33×10^{-13}	4.79×10^{-13}
insulin sensitivity (Matsuda)	4.79×10^{-13}	0.027	4.79×10^{-13}	5.36×10^{-13}	4.79×10^{-13}	7.61×10^{-06}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	0.86
Insulin (post-challenge, pmol/l)	4.79×10^{-13}	0.004	4.79×10^{-13}	5.34×10^{-13}	4.79×10^{-13}	5.36×10^{-13}	3.45×10^{-08}	4.79×10^{-13}	0.018	5.36×10^{-13}	1.70×10^{-09}	4.79×10^{-13}	0.12	4.79×10^{-13}	0.84
Insulin secretion (Stumvoll)	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	0.017	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	5.24×10^{-13}	4.79×10^{-13}	0.97	4.79×10^{-13}	4.79×10^{-13}
Triglycerides (mmol/l)	4.79×10^{-13}	4.79×10^{-13}	0.69	5.41×10^{-13}	4.79×10^{-13}	5.32×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	0.006
HDL cholesterol	4.79×10^{-13}	0.23	4.79×10^{-13}	5.02×10^{-07}	4.79×10^{-13}	0.29	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	4.79×10^{-13}	0.12	4.79×10^{-13}	0.0029	2.45×10^{-08}	4.79×10^{-13}

Supplementary Table 4

Association of clusters with genotype for every tested variant. Tested top diabetes-related variants that were genotyped in TUEF/TULIP were taken from Mahajan et al 2018. Results show one-way ANOVA for each variant between cluster as factor variable and genotype as continuous outcome. P-value adjustment for multiple testing was performed with Benjamini-Hochberg correction.

		F	P-VALUE	ADJUSTED P
1	MTNR1B_rs10830963_G	4.806	0.00024	0.02
2	TCF7L2_rs7903146_T	3.442	0.004	0.1
3	KCNQ1_rs2237892_T	2.953	0.01	0.2
4	PNPLA3_rs738409_C	2.355	0.04	0.6
5	TM6SF2_rs58542926_T	2.281	0.04	0.6
6	CDKAL1_rs7756992_G	2.016	0.07	0.7
7	JAZF1_rs864745_G	1.987	0.08	0.7
8	HNF1B_rs7501939_T	1.909	0.09	0.7
9	VEGFA_rs6905288_G	1.884	0.09	0.7
10	TFAP2B_rs2206277_A	1.69	0.1	0.8
11	ZMIZ1_rs12571751_G	1.669	0.1	0.8
12	BCL11A_rs243021_T	1.558	0.2	0.8
13	C2CD4A-B_rs4502156_C	1.545	0.2	0.8
14	HNF1A_rs1169288_G	1.501	0.2	0.8
15	SLC30A8_rs13266634_T	1.498	0.2	0.8
16	WFS1_rs4689388_G	1.439	0.2	0.8
17	GIPR_GSA-rs8108269_G	1.35	0.2	0.8
18	ABO_exm-rs505922_C	1.317	0.3	0.8
19	CENPW_rs1361108_T	1.253	0.3	0.8
20	IRS1_rs2943641_T	1.179	0.3	0.8
21	ANK1_rs516946_A	1.178	0.3	0.8
22	MC4R_rs17782313_C	1.174	0.3	0.8
23	DGKB_rs2191349_G	1.114	0.4	0.8
24	PRC1_rs8042680_A	1.109	0.4	0.8
25	PAM_GSA-rs35658696_G	1.108	0.4	0.8
26	TMEM258_rs102275_G	1.087	0.4	0.8
27	HMG20A_GSA-rs7177055_G	1.053	0.4	0.8
28	NFAT5_rs1364063_C	1.049	0.4	0.8
29	FTO_rs1558902_A	1.046	0.4	0.8
30	PAX4_rs2233580_A	0.837	0.5	1
31	RREB1_rs9379084_A	0.83	0.5	1
32	POC5_rs2307111_G	0.82	0.5	1
33	CENTD2_rs11603334_A	0.804	0.5	1
34	CCND2_rs11063069_G	0.774	0.6	1
35	GIPR_rs1800437_C	0.767	0.6	1
36	CEP68_rs7572857_A	0.749	0.6	1
37	GRB14_rs13389219_T	0.74	0.6	1
38	CMIP_rs2925979_A	0.725	0.6	1
39	HNF4A_rs1800961_T	0.718	0.6	1
40	ZBED3_rs4457053_G	0.701	0.6	1
41	MRAS_rs2306374_C	0.668	0.6	1
42	ARL15_rs6450176_A	0.66	0.7	1

43	PPARG_rs1801282_G	0.649	0.7	1
44	TOMM40-APOE_rs769449_A	0.595	0.7	1
45	ZHX3_rs17265513_C	0.565	0.7	1
46	MPHOSPH9_GSA-rs1727307_A	0.529	0.8	1
47	BCAR1_rs7202877_G	0.526	0.8	1
48	ADAMTS9_rs4607103_T	0.511	0.8	1
49	CDKN2A-B_rs10965250_A	0.494	0.8	1
50	NRXN3_rs10146997_G	0.485	0.8	1
51	KLF14_rs972283_A	0.431	0.8	1
52	KCNQ1_rs2237895_C	0.398	0.9	1
53	PEPD_rs731839_C	0.388	0.9	1
54	HHEX-IDE_rs5015480_T	0.357	0.9	1
55	SPRY2_rs1359790_T	0.312	0.9	1
56	HMGA2_rs1531343_C	0.272	0.9	1
57	PROX1_rs340874_A	0.268	0.9	1
58	ADCY5_rs11708067_G	0.253	0.9	1
59	CDC123/CAMK1D_rs10906115_G	0.197	1	1
60	HNF1A_GSA-rs1800574_T	0.193	1	1
61	ANKRD55_rs459193_T	0.173	1	1
62	KCNJ11_rs5219_T	0.063	1	1
63	TSPAN8_rs7961581_C	0.043	1	1

Supplementary Table 5

Cluster-wise hazard ratios for different outcomes in the Whitehall II cohort. Clusters and the denoted adjustment covariates were applied in proportional hazards models. Values show point estimates as hazard ratios with 95% confidence intervals.

outcome	adjustment	n	cluster2	cluster3	cluster4	cluster5	cluster6
diabetes		6643	0.40*** (0.33-0.47)	3.45*** (2.76-4.31)	0.80 (0.61-1.06)	6.62*** (5.06-8.67)	2.22*** (1.70-2.89)
diabetes	sex, age, age2, BMI	6643	0.45*** (0.38-0.55)	3.02*** (2.41-3.79)	0.67* (0.50-0.90)	5.07*** (3.77-6.82)	1.66** (1.21-2.27)
diabetes	sex, age, age2, BMI, baseline glucose AUC	6643	0.56*** (0.46-0.67)	1.50** (1.15-1.95)	0.79 (0.58-1.07)	2.67*** (1.93-3.69)	1.49* (1.09-2.05)
renal (CKD)		5182	1.11 (0.96-1.27)	1.47** (1.13-1.91)	1.11 (0.88-1.40)	1.60* (1.07-2.37)	1.63*** (1.25-2.12)
renal (CKD)	sex, age, age2, BMI	5182	1.03 (0.88-1.19)	1.49** (1.14-1.94)	1.14 (0.89-1.46)	1.61* (1.06-2.43)	1.61** (1.20-2.15)
renal (CKD)	sex, age, age2, BMI, fasting glucose, systolic BP, diastolic BP	5174	1.01 (0.87-1.18)	1.45* (1.11-1.90)	1.13 (0.88-1.45)	1.55* (1.02-2.35)	1.63** (1.22-2.19)
coronary heart disease		6537	0.64*** (0.54-0.76)	1.38* (1.03-1.86)	1.24 (0.96-1.61)	1.65* (1.08-2.53)	1.22 (0.87-1.70)
coronary heart disease	sex, age, age2, BMI	6537	0.72*** (0.60-0.87)	1.19 (0.88-1.61)	1.13 (0.85-1.49)	1.38 (0.88-2.15)	1.05 (0.72-1.52)
coronary heart disease	sex, age, age2, BMI, fasting glucose, systolic BP, diastolic BP	6523	0.73** (0.61-0.88)	1.21 (0.89-1.64)	1.12 (0.85-1.48)	1.40 (0.89-2.20)	1.04 (0.72-1.52)
CHD + stroke incidence		6704	0.64*** (0.55-0.75)	1.12 (0.85-1.47)	1.25* (1.00-1.56)	1.52* (1.05-2.19)	1.03 (0.76-1.40)
CHD + stroke incidence	sex, age, age2, BMI	6704	0.70*** (0.60-0.83)	0.97 (0.74-1.28)	1.16 (0.91-1.48)	1.27 (0.86-1.87)	0.89 (0.64-1.25)
CHD + stroke incidence	sex, age, age2, BMI, fasting glucose, systolic BP, diastolic BP	6690	0.73*** (0.62-0.85)	0.99 (0.75-1.31)	1.17 (0.92-1.49)	1.31 (0.88-1.94)	0.90 (0.64-1.25)
all-cause mortality		6803	0.66*** (0.56-0.78)	1.00 (0.73-1.38)	0.84 (0.63-1.11)	1.66* (1.11-2.48)	1.47* (1.09-1.99)
all-cause mortality	sex, age, age2, BMI	6803	0.68*** (0.57-0.81)	0.80 (0.58-1.10)	0.85 (0.63-1.15)	1.43 (0.94-2.19)	1.45* (1.03-2.05)
all-cause mortality	sex, age, age2, BMI, fasting glucose, systolic BP, diastolic BP	6789	0.68*** (0.57-0.82)	0.78 (0.56-1.09)	0.85 (0.63-1.15)	1.42 (0.93-2.18)	1.45* (1.02-2.04)

Legend: Hazard ratios with 95% confidence intervals compared to cluster 1. Corresponding p-values are shown with: *** for a p.value < 0.0005, ** for a p.value < 0.005 and * for a p.value <0.05. CKD: chronic kidney disease Stage 3 or worse (eGFR<60 ml/min/1.73m^2), CHD: coronary heart disease

Supplementary Table 6

Cox multivariable proportional hazards model for diabetes as outcome in Whitehall II. Estimate indicates adjusted hazard ratio (exp(β)) with 95% confidence interval, n=6643 individuals with follow-up.

	Diabetes		
Predictors	*Estimates*	*CI*	*p*
cluster [2]	0.631	0.509 – 0.782	2.59×10^{-05}
cluster [3]	2.68	2.12 – 3.38	1.12×10^{-16}
cluster [4]	0.687	0.508 – 0.929	0.015
cluster [5]	2.99	2.16 – 4.13	3.72×10^{-11}
cluster [6]	1.4	1.01 – 1.94	0.043
sex: female	1.11	0.926 – 1.34	0.26
age [1st degree]	90108345	247024 – 3.29×10^{10}	1.16×10^{-09}
age [2nd degree]	57124	134 – 24355955	3.92×10^{-04}
BMI	1.05	1.02 – 1.07	6.22×10^{-04}
Fasting glucose baseline	2.23	1.92 – 2.6	3.87×10^{-25}
Smoking [ex]	1.14	0.975 – 1.33	0.1
Smoking [current]	2.01	1.64 – 2.46	1.25×10^{-11}
Smoking [missing information]	1.38	0.996 – 1.9	0.053
Triglycerides baseline	1.14	1.04 – 1.24	0.006
Cholesterol_baseline	1.04	0.976 – 1.12	0.21
HDL baseline	0.7	0.535 – 0.916	0.0093

Supplementary Table 7

Cluster transitions to Ahqlvist-diabetes classes (N=201)

Pre-diabetic cluster	**Total eligible for Ahlqvist-classification**	**2/SIDD**	**3/SIRD**	**4/MOD**	**5/MARD**
1	817	6 (12%)	8 (17%)	11 (23%)	23 (48%)
2	2552	2 (3%)	1 (2%)	15 (24%)	44 (71%)
3	191	5 (12%)	4 (10%)	13 (31%)	20 (48%)
4	314	0 (0%)	2 (14%)	8 (57%)	4 (29%)
5	65	2 (17%)	4 (33%)	2 (17%)	4 (33%)
6	153	2 (9%)	13 (57%)	8 (35%)	0 (0%)

Supplementary Table 8

Cox multivariable proportional hazards model for stage 3 chronic kidney disease as outcome in Whitehall II. Estimate indicates adjusted hazard ratio (exp(β)) with 95% confidence interval and two-sided p-value, n=5126 individuals with follow-up.

	CKD3 or worse		
Predictors	*Estimates*	*CI*	*p*
cluster [2]	0.929	0.781 – 1.1	0.4
cluster [3]	1.37	1.05 – 1.8	0.022
cluster [4]	1.16	0.898 – 1.49	0.26
cluster [5]	1.74	1.11 – 2.72	0.015
cluster [6]	1.63	1.2 – 2.22	0.0016
age [1st degree]	5.57E-10	1.19×10^{-11} – 2.6×10^{-8}	1.65×10^{-27}
age [2nd degree]	7.90E+07	2259923 – 2.76×10^{9}	1.15×10^{-23}
sex: female	1.19	1.03 – 1.36	0.017
Smoking [ex]	1.1	0.985 – 1.23	0.091
Smoking [current]	1.47	1.14 – 1.9	0.0034
Smoking [missing]	0.666	0.494 – 0.897	0.0076
BMI	0.996	0.974 – 1.02	0.68
Systolic blood pressure	1.03	1.02 – 1.03	1.67×10^{-17}
Diastolic blood pressure	0.969	0.961 – 0.977	8.56×10^{-13}
Glucose baseline	0.887	0.784 – 1	0.057
Triglycerides baseline	0.581	0.000818 – 412	0.87
Cholesterol baseline	4.32	2.31×10^{-6} – 8058826	0.84
HDL baseline	0.342	1.84×10^{-7} – 637599	0.88
LDL baseline	0.219	1.18×10^{-7} – 409504	0.84

Supplementary Table 9

Differences in renal sinus fat (RSF, mean of left and right) levels among clusters. Statistical analysis was performed with one-way ANOVA adjusted for sex, age, age^2 (A) or sex, age, age^2 and visceral fat (C). RSF, visceral fat and BMI were log$_e$-transformed. Post-hoc test of pairwise differences between specific clusters was computed with Tukey's HSD test for both models (Table B and D).
Model 1 (n=519 individuals with RSF>0): RSF ~ sex + BMI + Age + Age^2 + cluster
Model 2 (n=519 individuals with RSF>0): RSF ~ sex + BMI + Age + Age^2 + visceral fat + cluster

A. Analysis of variance table for model 1

	TERM	DF	SUMSQ	MEANSQ	STATISTIC	P.VALUE
1	SEX	1	19.72	19.72	51.59	2.44×10^{-12}
2	BMI	1	55.34	55.34	144.76	1.62×10^{-29}
3	poly(AGE, 2)	2	84.82	42.41	110.92	1.04×10^{-40}
4	cluster	5	15.89	3.18	8.31	1.44×10^{-07}
5	Residuals	509	194.6	0.38		

B. Pairwise comparisons of clusters (Tukey) for model 1

	CLUSTER VS	CLUSTER	ESTIMATE	STD.ERROR	DF	STATISTIC	P.VALUE
1	1	2	-0.05	0.11	509	-0.49	1
2	1	3	-0.29	0.13	509	-2.22	0.23
3	1	4	-0.3	0.11	509	-2.81	0.058
4	1	5	-0.33	0.11	509	-3	0.034
5	1	6	-0.6	0.1	509	-5.97	6.7×10^{-08}
6	2	3	-0.23	0.13	509	-1.74	0.5
7	2	4	-0.25	0.12	509	-2.07	0.3
8	2	5	-0.28	0.13	509	-2.23	0.23
9	2	6	-0.55	0.12	509	-4.66	5.8×10^{-05}
10	3	4	-0.01	0.13	509	-0.09	1
11	3	5	-0.05	0.13	509	-0.36	1
12	3	6	-0.32	0.12	509	-2.63	0.093
13	4	5	-0.03	0.1	509	-0.33	1
14	4	6	-0.3	0.09	509	-3.36	0.011
15	5	6	-0.27	0.08	509	-3.36	0.011

C. Analysis of variance table for model 2

	TERM	DF	SUMSQ	MEANSQ	STATISTIC	P.VALUE
1	SEX	1	19.72	19.72	59.64	6.10×10^{-14}
2	BMI	1	55.34	55.34	167.35	2.75×10^{-33}
3	poly(AGE, 2)	2	84.82	42.41	128.23	8.25×10^{-46}
4	VAT	1	37.35	37.35	112.95	5.87×10^{-24}
5	cluster	5	5.14	1.03	3.11	0.009
6	Residuals	508	168	0.33		

D. Pairwise comparisons of clusters (Tukey) for model 2

	CLUSTER VS	CLUSTER	ESTIMATE	STD.ERROR	DF	STATISTIC	P.VALUE
1	1	2	-0.14	0.1	508	-1.38	0.7
2	1	3	-0.05	0.12	508	-0.42	1
3	1	4	-0.07	0.1	508	-0.65	1
4	1	5	0.09	0.11	508	0.82	1
5	1	6	-0.18	0.11	508	-1.7	0.5
6	2	3	0.09	0.13	508	0.66	1
7	2	4	0.07	0.12	508	0.61	1
8	2	5	0.23	0.13	508	1.77	0.5
9	2	6	-0.04	0.12	508	-0.34	1
10	3	4	-0.01	0.12	508	-0.12	1
11	3	5	0.14	0.12	508	1.19	0.8
12	3	6	-0.13	0.11	508	-1.12	0.9
13	4	5	0.16	0.1	508	1.63	0.6
14	4	6	-0.11	0.09	508	-1.3	0.8
15	5	6	-0.27	0.07	508	-3.63	0.004

Supplementary Table 10

Cox multivariable proportional hazards model for all-cause mortality as outcome in Whitehall II. Estimate indicates adjusted hazard ratio (exp(β)) with 95% confidence interval and two-sided p-value, n=6789 individuals with follow-up.

	Death from all causes		
Predictors	*Estimates*	*CI*	*p*
cluster [2]	0.8	0.651 – 0.983	0.034
cluster [3]	0.821	0.59 – 1.14	0.24
cluster [4]	0.823	0.608 – 1.11	0.21
cluster [5]	1.25	0.804 – 1.95	0.32
cluster [6]	1.45	1.02 – 2.08	0.039
age [1st degree]	1.67×10^{26}	1.89×10^{23} – 1.47×10^{29}	3.27×10^{-68}
age [2nd degree]	5.41	0.0146 – 2010	0.58
sex: female	0.911	0.759 – 1.09	0.31
BMI	0.993	0.966 – 1.02	0.63
Systolic blood pressure	1	0.996 – 1.01	0.32
Diastolic blood pressure	1	0.994 – 1.02	0.4
Fasting glucose baseline	0.966	0.826 – 1.13	0.66
Triglycerides baseline	1.09	0.987 – 1.21	0.087
Cholesterol baseline	1.01	0.941 – 1.08	0.86
HDL baseline	0.883	0.692 – 1.13	0.32
Smoking [ex]	1.26	1.07 – 1.48	0.0047
Smoking [current]	2.51	2.07 – 3.04	1.35×10^{-20}
Smoking [missing]	1.28	0.9 – 1.82	0.17

Supplementary Table 11

Cohort characteristics of the TUEF/TULIP showing the full set and the subset the partitioning was performed on. Values denote means (SD).

	all	**clustered**
n	2771	899
sex = male (%)	1058 (38.2)	346 (38.5)
age (mean (SD))	42.14 (14.35)	44.61 (13.36)
BMI (kg/m2) (mean (SD))	27.95 (6.15)	29.84 (5.73)
waist circumference (cm) (mean (SD))	92.85 (15.33)	96.26 (14.76)
total adipose tissue MRI (liter) (mean (SD))	35.64 (13.93)	35.95 (13.95)
subcutaneous adipose tissue MRI (liter) (mean (SD))	12.41 (6.42)	12.44 (6.44)
visceral adipose tissue MRI (liter) (mean (SD))	3.73 (2.40)	3.80 (2.42)
subcutaneous to visceral adipose ratio (mean (SD))	4.49 (2.85)	4.35 (2.72)
visceral adipose % of total (mean (SD))	0.11 (0.06)	0.11 (0.06)
liver fat content (mean (SD))	6.48 (6.78)	7.06 (7.01)
fatty-liver disease (%) = yes (%)	392 (36.9)	341 (37.9)
renal sinus fat (mean of r&l, %) (mean (SD))	10.67 (6.37)	10.76 (6.35)
systolic blood pressure (mmHg, mean (SD))	129.80 (18.31)	131.45 (17.91)
diastolic blood pressure (mmHg, mean (SD))	82.69 (13.87)	83.60 (12.27)
heart rate (BPM, mean (SD))	70.84 (10.92)	70.08 (10.69)
fasting glucose (mmol/l) (mean (SD))	5.17 (0.56)	5.35 (0.57)
post-challenge glucose @ 30 min (mmol/l, mean (SD))	8.44 (1.56)	8.87 (1.54)
post-challenge glucose @ 60 min (mmol/l, mean (SD))	8.20 (2.40)	8.95 (2.37)
post-challenge glucose @ 90 min (mmol/l, mean (SD))	6.95 (2.09)	7.63 (2.14)
post-challenge glucose @ 120 min (mmol/l, mean (SD))	6.23 (1.61)	6.73 (1.54)
glycaemic category (%)		
NGT	1960 (70.7)	529 (58.8)
IFG	360 (13.0)	168 (18.7)
IGT	247 (8.9)	98 (10.9)
IFG+IGT	204 (7.4)	104 (11.6)
GAD antibody = TRUE (%)	36 (4.7)	17 (4.9)
triglycerides (mmol/l) (mean (SD))	1.37 (1.40)	1.37 (0.86)
insulin sensitivity (Matsuda) (AU, mean (SD))	18.87 (12.67)	13.95 (8.66)
fasting insulin (pmol/l) (mean (SD))	53.39 (38.72)	64.46 (44.40)
insulinogenic index (AU, mean (SD))	128.26 (151.49)	141.55 (165.61)
disposition index (AU, mean (SD))	2106.75 (3773.09)	1823.42 (3688.84)
C-reactive protein (mg/dl, mean (SD))	0.27 (0.36)	0.27 (0.38)
LDL cholesterol (mmol/l) (mean (SD))	3.04 (0.87)	3.06 (0.85)
HDL cholesterol (mmol/l) (mean (SD))	1.42 (0.37)	1.36 (0.34)
aspartate-aminotransferase (U/l, mean (SD))	22.25 (9.47)	24.06 (9.33)
alanine-aminotransferase (U/l, mean (SD))	27.71 (17.34)	29.09 (18.83)
gamma-glutamyl transferase (U/l, mean (SD))	25.39 (27.40)	26.69 (23.74)
serum creatinine (mg/dl) (mean (SD))	0.82 (0.17)	0.81 (0.17)
urinary albumin-creatinine ratio (mean (SD))	18.88 (47.13)	17.84 (28.92)
polygenic risk score (mean (SD))	-0.02 (1.01)	0.01 (0.94)
family history of diabetes (%)		
a_no family history	360 (41.0)	168 (39.5)
b_second degree relative	185 (21.1)	94 (22.1)
c_first degree relative	333 (37.9)	163 (38.4)
ever smoked = yes (%)	411 (42.5)	215 (48.0)
current smoking = yes (%)	8 (1.1)	5 (1.3)
cholesterol lowering medication = yes (%)	66 (2.4)	23 (2.6)
antihypertensive medication = yes (%)	219 (7.9)	105 (11.7)

Supplementary Table 12

Cohort characteristics of the analysed set from the Whitehall-II cohort also showing what proportion of subjects was assigned to the clusters in specific study phases (upon first availability of the complete set of variables needed for cluster assignment). Values denote means (SD).

	Overall
n	6810
sex = male (%)	4860 (71.4)
cluster (%)	
1	1362 (20.0)
2	4228 (62.1)
3	322 (4.7)
4	509 (7.5)
5	123 (1.8)
6	266 (3.9)
clustered at (%)	
Phase03	5855 (86.0)
Phase05	478 (7.0)
Phase07	374 (5.5)
Phase09	103 (1.5)
BMI (kg/m^2, mean (SD))	25.32 (3.58)
age (years, mean (SD))	51.03 (6.74)
Waist circumference (cm, mean (SD))	86.64 (11.45)
Hip circumference (mean (SD))	97.46 (6.97)
Systolic blood pressure (mmHg) (mean (SD))	120.91 (13.86)
Diastolic blood pressure (mmHg) (mean (SD))	79.12 (9.71)
Glucose (fasting, mmol/l) (mean (SD))	5.21 (0.47)
Glucose (post-challenge, mmol/l) (mean (SD))	5.52 (1.55)
AUC glucose (mmol 2h l-1) (mean (SD))	643.37 (101.35)
Insulin (fasting, pmol/l) (mean (SD))	45.24 (31.74)
Insulin (post-challenge, pmol/l) (mean (SD))	309.90 (242.27)
Insulin secretion (Stumvoll) (AU, mean (SD))	866.71 (338.79)
insulin sensitivity (Matsuda) (AU, mean (SD))	32.27 (21.14)
Triglycerides (mmol/l) (mean (SD))	1.39 (0.82)
HDL cholesterol (mmol/l) (mean (SD))	1.45 (0.41)
glycaemic category (%)	
NGT	4975 (73.1)
IFG	1227 (18.0)
IGT	437 (6.4)
IFG+IGT	171 (2.5)
Smoking (%)	
never	2981 (43.8)
ex	2628 (38.6)
current	862 (12.7)
missing	339 (5.0)
Antihypertensive medication = yes (%)	486 (7.1)
Lipid lowering medication = yes (%)	62 (0.9)

Supplementary Table 13

Correlation of clustering variables in the TUEF/TULIP cohort (n=899 individuals). The numbers indicate Spearman correlation coefficients.

variables	AUC glu	genetic risk	HDL chol	insulin secr	insulin sensitivity	liver fat	sq adip	visc adip
AUC glu	1	0.06	-0.08	-0.09	-0.53	0.44	0.12	0.42
genetic risk	0.06	1	-0.04	-0.04	0.01	0.05	-0.04	-0.05
HDL cholesterol	-0.08	-0.04	1	-0.26	0.28	-0.19	-0.27	-0.26
insulin secretion	-0.09	-0.04	-0.26	1	-0.47	0.28	0.31	0.22
insulin sensitivity	-0.53	0.01	0.28	-0.47	1	-0.48	-0.36	-0.52
liver fat	0.44	0.05	-0.19	0.28	-0.48	1	0.32	0.55
sq adipose	0.12	-0.04	-0.27	0.31	-0.36	0.32	1	0.55
visc adipose	0.42	-0.05	-0.26	0.22	-0.52	0.55	0.55	1

Supplementary Table 14

Sex-stratified cohort means in the **TUEF/TULIP** (n=899) and **Whitehall II** (n=6810) dataset for the proxy variables which were available in both cohorts.

		TUEF		WHITEHALL-II	
	SEX	TUEF_mean	TUEF_sd	WH-II_mean	WH-II_sd
AUC_GLUCOSE	female	722.01	107.8	643.48	103.39
BMI	female	29.66	5.98	25.51	4.58
HDL	female	1.46	0.35	1.72	0.43
HIP	female	109.07	12.87	97.73	9.23
INSU_F	female	9.22	6.26	6.16	4.4
MATSUDA	female	14.22	8.42	31.17	19.09
SECR_STUM	female	956.39	552.93	910.11	330.12
TRIG	female	1.23	0.67	1.15	0.6
WAIST	female	92.1	13.97	78.39	12.1
AUC_GLUCOSE	male	729.52	114.2	643.57	100.82
BMI	male	30.12	5.32	25.27	3.17
HDL	male	1.2	0.25	1.34	0.35
HIP	male	105.41	11.89	97.37	5.96
INSU_F	male	9.38	6.61	6.66	4.62
MATSUDA	male	13.53	9.04	32.69	21.9
SECR_STUM	male	917.41	574.45	849.22	339.83
TRIG	male	1.59	1.06	1.49	0.88
WAIST	male	102.84	13.56	89.97	9.37

TRIG: fasting triglycerides in mmol/l; HDL: HDL-cholesterol in mmol/l; INSU_F: fasting insulin in µIU/mL; SECR_STUM: Stumvoll's first phase insulin secretion index computed as 2503+6.476 * fasting insulin in pmol/l - 126.5 * GLUC_2h + 0.954 * 2h-post-challenge insulin in pmol/l - 293.3 * GLUC_F; MATSUDA: insulin sensitivity computed as 10000/sqrt(GLUC_F*fasting insulin in pmol/l*(fasting insulin in pmol/l+2h-post-challenge insulin in pmol/l)/2*(GLUC_F+GLUC_2h)/2); AUC glucose: OGTT 5-point glucose (TUEF) or 2-point glucose area-under-curve computed according to the trapezoid rule; BMI: body mass index in kg/m^2 ; HIP and WAIST circumferences in cm;

Supplementary Table 15

Cluster medians (sex-stratified and Z-score-transformed value for each clustering variable on the population means/sd) in TUEF/TULIP (n=899) and in Whitehall-II (n=6810) for the proxy clustering variables

	CLUSTER 1 TUEF	CLUSTER 1 WH-II	CLUSTER 2 TUEF	CLUSTER 2 WH-II	CLUSTER 3 TUEF	CLUSTER 3 WH-II	CLUSTER 4 TUEF	CLUSTER 4 WH-II	CLUSTER 5 TUEF	CLUSTER 5 WH-II	CLUSTER 6 TUEF	CLUSTER 6 WH-II
AUC_GLU	-0.435	-0.575	-0.59	-1.076	0.699	1.02	-0.667	-1.021	1.25	0.967	0.143	-0.451
BMI	-0.475	-0.761	-1.196	-1.149	-0.244	-0.504	0.165	-0.027	0.692	0.192	0.777	0.373
HDL	-0.14	-0.355	1.08	1.034	-0.101	0.046	-0.396	-0.395	-0.762	-0.877	-0.323	-0.315
HIP	-0.455	-0.666	-1.016	-0.93	-0.161	-0.463	0.344	0.016	0.597	-0.144	0.693	0.195
INSU_F	-0.369	-0.163	-0.806	-0.814	-0.282	-0.245	-0.438	-0.375	0.667	1.152	0.58	1.134
MATSUDA	-0.092	0.317	1	2.551	-0.449	-0.123	0.272	1.241	-0.967	-0.756	-0.861	-0.499
SECR_STUM	-0.164	0.155	-0.525	-0.308	-0.549	-0.38	-0.238	-0.056	0.38	0.702	0.435	1.006
TRIG	-0.278	0.184	-0.699	-0.553	-0.129	0.15	-0.406	0.005	0.489	1.542	0.071	0.33
WAIST	-0.579	-0.785	-1.224	-1.316	-0.007	-0.517	0.136	0.011	0.923	0.292	0.78	0.482

For variable description see previous Supplementary Table