

ESM: Tables and Figures

ESM Table1. Relationships between glucagon measures and glycaemic markers by ethnicity

	Fasting glucose (mmol/l)			2h OGTT glucose (mmol/l)			AUC glucose (mmol/l x h)			HbA _{1c} (mmol/mol)		
	South Asian	Nordic	Total	South Asian	Nordic	Total	South Asian	Nordic	Total	South Asian	Nordic	Total
Fasting glucagon (pmol/l)	0.164*	0.096	0.160**	0.311***	0.204*	0.308***	0.381***	0.199*	0.357***	0.054	0.053	0.126*
Glucagon AUC (pmol/l x h)	0.356***	0.259**	0.344***	0.389***	0.364***	0.402***	0.503***	0.356***	0.480***	0.238**	0.203*	0.297***
Early glucagon suppression (%)	-0.194*	-0.289**	-0.250***	-0.093	-0.326***	-0.191**	-0.126	-0.337***	-0.232***	-0.162*	-0.218*	-0.231***
Late glucagon suppression (%)	-0.232**	0.100	-0.080	0.148	0.382***	0.260***	-0.002	0.355***	0.173**	-0.192*	0.028	-0.051
Total glucagon suppression (%)	-0.342***	-0.157	-0.269***	0.064	0.114	0.090	-0.095	0.104	-0.020	-0.335***	-0.193*	-0.274***

Spearman's rho correlation * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

ESM Table 2. Between-group comparisons of hyperbolic curve constants

Measure	Comparison	Ratio	95% CI	<i>p</i>
HOMA-2S	Nordic normal glucose tolerance vs Nordic prediabetes or diabetes	1.26	0.99–1.60	0.058
HOMA-2S	Nordic normal glucose tolerance vs South Asian normal glucose tolerance	1.26	1.01–1.57	0.042
HOMA-2S	Nordic normal glucose tolerance vs South Asian prediabetes or diabetes	1.33	1.10–1.61	0.004
Matsuda ISI	Nordic normal glucose tolerance vs Nordic prediabetes or diabetes	1.37	1.09–1.73	0.007
Matsuda ISI	Nordic normal glucose tolerance vs South Asian normal glucose tolerance	1.34	1.07–1.68	0.010
Matsuda ISI	Nordic normal glucose tolerance vs South Asian prediabetes or diabetes	1.49	1.24–1.79	<0.001

Data are ratios of the hyperbolic constant (fasting glucagon $\times$ insulin sensitivity) between the indicated groups. Products were log-transformed and compared using Welch's t-test; estimates and 95% CIs were back-transformed.

HOMA-2S: homeostatic model assessment2-sensitivity. Matsuda ISI: Matsuda insulin sensitivity index

For all analyses *p*-values <0.05 were considered significant

ESM Table 3. Patient characteristics across ethnicity by normal glucose tolerance, IFG, IGT, combined IFG/IGT and type 2 diabetes

	Normal glucose tolerance			Isolated IFG			Isolated IGT			Combined IFG/IGT			Type 2 diabetes		
	South Asian	Nordic	<i>p</i>	South Asian	Nordic	<i>p</i>	South Asian	Nordic	<i>p</i>	South Asian	Nordic	<i>p</i>	South Asian	Nordic	<i>p</i>
Number (<i>n</i>) of women	63 (35)	57 (53)	0.004	12 (7)	5 [5]	0.609	57 (32)	23 (21)	0.058	14 (8)	7 (7)	0.816	32 (18)	15 (14)	0.414
Age (years)	34.4±3.87	36.7±4.9	0.006	36.8±9	40.0±9	0.232	34.0±4.1	34.5±4.2	0.609	35.1±5.2	37.1±5.8	0.434	34.7±4.1	37.3±4.8	0.077
Time since index pregnancy (months)	14.9 (12.5-24.6)	16.8 (15.1-25.5)	0.015	14.7 (12.3-21.4)	22.6 (18.7-28.7)	0.082	18.0 (13.4-25.5)	15.6 (13.1-25.3)	0.410	13.4 (12.2-16.2)	19.4 (12.6-29.0)	0.197	16.7 (13.8-26.1)	23.1 (14.7-28.6)	0.380
BMI (kg/m ²)	27.6 (24.3-29.7)	25.5 (22.1-30.8)	0.129	30.5 (28.3-34.3)	30.2 (26.5-32.2)	0.721	27.5 (24.5-30.7)	32.4 (29.0-34.6)	0.002	29.1 (26.8-37.4)	26.7 (22.8-29.7)	0.360	30.2 (26.9-31.6)	33.6 (29.6-37.4)	0.040
Waist-to-height ratio	0.59±0.07	0.55±0.09	0.004	0.64±0.10	0.57±0.12	0.074	0.60±0.07	0.61±0.08	0.345	0.64±0.09	0.58±0.08	0.115	0.63±0.06	0.63±0.08	0.762
HbA _{1c} (mmol/mol)	37.4±3.9	35.0±2.5	<0.001	39.6±2.9	38.2±2.2	0.360	38.1±3.4	35.8±3.6	0.013	40.8±2.5	38.3±1.8	0.018	43.9±6.4	41.5±5.6	0.216
HbA _{1c} [%]	5.6±2.5	5.4±2.4	<0.001	5.8±2.4	5.6±2.2	0.360	5.6±2.5	5.4±2.5	0.013	5.9±2.4	5.7±2.3	0.018	6.2±2.7	5.9±2.7	0.216
Total cholesterol (mmol/l)	4.24±0.8	4.24±0.82	0.980	4.50±0.66	5.16±1.36	0.190	4.37±0.79	4.17±0.62	0.304	4.32±0.47	4.30±0.72	0.935	4.60±0.74	4.37±0.77	0.327
Triglycerides (mmol/l)	1.00 (0.78-1.33)	0.80 (0.60-1.00)	<0.001	1.40 (1.10-1.90)	0.90 (0.85-3.05)	0.799	1.10 (0.85-1.50)	1.00 (0.80-1.50)	0.705	1.35 (0.88-2.03)	1.20 (0.90-1.50)	0.360	1.30 (1.00-1.90)	1.10 (0.80-1.50)	0.121
HDL cholesterol (mmol/l)	1.20±0.28	1.37±0.33	0.003	1.15±0.19	1.12±0.15	0.761	1.12±0.25	1.14±0.26	0.807	1.13±0.27	1.24±0.31	0.391	1.04±0.21	1.29±0.31	0.013
LDL cholesterol (mmol/l)	2.85± 0.57	2.84±0.81	0.962	3.13±0.52	3.68±1.20	0.200	3.03±0.73	2.77±0.66	0.151	2.86±0.51	2.79±0.62	0.781	3.08±0.63	3.02±0.69	0.764
Fasting NEFA (mmol/l)	0.52±0.16	0.49±0.16	0.383	0.53±0.16	0.37±0.10	0.022	0.55±0.15	0.59± 0.15	0.351	0.57±0.21	0.54±0.17	0.694	0.57±0.18	0.61±0.13	0.460
eGFR (mL/min/1.73m ²)	116±11	111±9	0.013	113±13	107±10	0.391	117±8	111±13	0.030	114±17	110±13	0.537	119±9	112±12	0.054

Data are presented as mean ±SD or median (IQR) or n (% of ethnic groups). Prediabetes by WHO-Committee criteria: fasting plasma glucose

6.1-6.9 mmol/L and/or 2-h OGTT: 7.8-11.0 mmol/l.

IFG: impaired fasting glucose, IGT: impaired glucose tolerance. NEFA: non-esterified fatty acids.

For all analyses *p*-values <0.05 were considered significant

ESM Table 4. Ethnic differences in glucagon, incretins, glucose and insulin levels during OGTT by normal glucose tolerance, IFG, IGT, combined IFG/IGT and type 2 diabetes

	Normal glucose tolerance			Isolated IFG			Isolated IGT			Combined IFG/IGT			Type 2 diabetes		
Number (<i>n</i>) of women	South Asian 63 [35]	Nordic 57 [53]	<i>p</i> 0.004	South Asian 12 [7]	Nordic 5 [5]	<i>p</i> 0.609	South Asian 57 [32]	Nordic 23 [21]	<i>p</i> 0.058	South Asian 14 [8]	Nordic 7 [7]	<i>p</i> 0.816	South Asian 32 [18]	Nordic 15 [14]	<i>p</i> 0.414
Fasting glucagon (pmol/l)	4.76 (3.56-6.94)	3.91 (2.74-5.71)	0.091	6.31 (2.82-8.63)	9.01 (6.24-9.41)	0.234	6.40 (5.08-9.17)	4.54 (2.91-7.47)	0.026	7.26 (3.83-13.47)	3.03 (1.90-4.09)	0.016	7.97±2.49	6.69± 1.74	0.052
AUC glucagon (pmol/l x h)	4.64 (3.55-6.80)	3.44 (2.42-4.91)	0.006	5.12 (3.44-9.61)	10.13 (7.93-10.73)	0.160	6.17 (4.20-9.46)	5.53 (3.37-7.39)	0.226	6.25 (4.12-14.41)	3.17 (2.41-3.56)	0.006	9.71 (7.28-13.32)	7.61 (4.93-12.93)	0.193
Glucagon suppression, 0-15 min (%)	12 [-11 to 30]	27 [5-48]	0.001	9 [-18 to 29]	15 [-13 to 29]	0.799	11 [-14 to 33]	5 [-14 to 22]	0.404	10 [-19 to 19]	6 [-18 to 31]	1.000	0 [-13 to 20]	10 [-9 to 42]	0.403
Glucagon suppression, 15-120 min (%)	65 [56-75]	57 [40-66]	0.003	39 [17-61]	56 [34-64]	0.510	71 [59-80]	71 [56-80]	0.940	68 [53-76]	61 [51-79]	0.938	66 [53-75]	64 [50-76]	0.924
Glucagon suppression, 0-120min (%)	73 [55-79]	71 [58-78]	0.705	48 [27-62]	62 [39-69]	0.320	72 [64-80]	71 [62-79]	0.490	73 [57-80]	73 [57-80]	1.000	66 [58-74]	68 [62-82]	0.328
Fasting GIP (pmol/l)	3.32 (2.04-4.80)	2.62 (2.03-4.01)	0.118	4.76 (2.31-8.79)	2.16 (1.81-3.51)	0.130	2.71 (1.84-3.85)	2.71 (2.32-4.20)	0.576	3.10 (2.23-4.13)	3.07 (2.52-3.50)	0.913	2.82 (1.72-4.59)	4.53 (2.76-8.26)	0.022
AUC GIP (pmol/l x h)	52.94 (37.90-73.81)	58.44 (48.17-75.66)	0.253	52.37 (26.05-91.94)	82.39 (60.00-100.40)	0.234	48.69 (35.65-71.93)	58.59 (45.32-70.80)	0.187	47.29 (35.46-70.79)	75.18 (48.47-99.95)	0.067	52.07 (36.13-67.61)	66.74 (37.80-64.50)	0.019
Peak GIP (pmol/l)	35.90 (22.80-50.60)	37.70 (28.75-46.25)	0.340	33.50 (25.68-55.95)	52.40 (38.95-65.75)	0.130	34.50 (22.85-47.00)	36.00 (29.90-43.10)	0.258	29.65 (21.08-47.30)	44.30 (32.20-64.20)	0.149	34.05 (23.33-44.73)	52.50 (37.80-64.50)	0.018
Fasting GLP (pmol/l)	3.47 (2.51-4.56)	3.58 (2.46-4.99)	0.836	5.32 (3.71-6.59)	5.57 (3.10-6.77)	0.959	3.78 (2.98-4.59)	3.71 (2.21-5.45)	0.667	4.11 (3.22-8.13)	3.33 (3.27-4.31)	0.585	5.20 (3.91-7.38)	4.02 (3.73-5.73)	0.178
AUC GLP-1 (pmol/l x h)	18.34 (14.20-22.24)	19.23 (13.70-23.13)	0.817	19.02 (13.30-33.07)	18.47 (15.78-24.28)	1.000	17.78 (14.72-22.94)	16.63 (13.18-19.92)	0.355	21.86 (12.78-27.47)	23.67 (18.87-26.17)	0.743	19.25 (15.88-27.94-)	20.97 (15.10-23.79)	0.553
Peak GLP-1 (pmol/l)	11.60 (10.00-15.70)	12.20 (8.75-16.4)	0.881	13.50 (10.20-22.25)	12.30 (11.50-21.45)	1.000	13.50 (10.35-18.05)	12.40 (8.30-13.40)	0.081	14.05 (8.35-21.58)	16.50 (16.20-19.20)	0.585	14.05 (11.55-18.85)	15.40 (10.50-19.00)	0.648
Fasting plasma glucose (mmol/l)	5.5 (5.2-5.8)	5.4 (5.1-5.7)	0.087	6.3 (6.1-6.6)	6.2 (6.1-6.4)	0.506	5.5 (5.3-5.8)	5.5 (5.2-5.8)	0.835	6.3 (6.2-6.6)	6.2 (6.2-6.5)	0.535	6.7 (6.0-7.4)	6.9 (6.2-7.6)	0.681

2-h OGTT glucose (mmol/l)	6.7 (5.8-7.2)	6.1 (5.4-7.1)	0.132	6.1 (5.4-6.5)	6.9 (6.7-7.1)	0.009	9.3 (8.6-9.9)	8.7 (8.3-9.3)	0.025	8.9 (8.3-9.9)	9.0 (8.2-9.7)	0.856	12.4 (11.6-14.2)	12.2 (11.5-13.8)	0.767
AUC glucose (mmol/l x h)	15.2 (13.7-16.5)	13.9 (12.4-15.4)	0.003	16.7 (14.8-18.4)	17.1 (15.1-18.4)	0.799	18.1 (17.0-19.3)	17.9 (16.5-18.9)	0.323	18.8 (18.1-19.7)	19.1 (17.5-20.4)	0.913	22.8 (21.2-25.6)	23.5 (18.8-25.5)	0.793
Fasting pre-hepatic insulin (pmol/l)	206 (166-261)	172 (125-230)	0.006	313 (228-382)	222 (109-299)	0.037	228 (184-279)	259 (190-324)	0.300	273 (253-295)	209 (186-294)	0.287	294 (231-393)	273 (201-408)	0.802
15-min pre-hepatic insulin (pmol/l)	668 (452-818)	548 (375-642)	0.008	751 (553-827)	793 (431-929)	0.959	646 (447-832)	726 (484-880)	0.392	642 (530-843)	538 (403-780)	0.689	478 (403-642)	481 (347-700)	1.000
AUC pre-hepatic insulin (pmol/l x h)	1645 (1422-2135)	1353 (1124-1718)	<0.001	2087 (1660-2549)	1684 (1310-2230)	0.195	2042 (1561-2386)	2058 (1520-2490)	0.953	1869 (1546-2147)	1755 (1269-2199)	0.636	1824 (1337-2243)	1927 (1365-2291)	0.784
Fasting insulin (pmol/l)	87 (61-129)	52 (39-74)	<0.001	151 (81-176)	71 (62-108)	0.090	97 (61-147)	83 (49-132)	0.385	118 (86-173)	67 (49-92)	0.017	154 (102-196)	95 (59-145)	0.024
AUC insulin (pmol/l x h)	1139 (835-1737)	679 (507-925)	<0.001	1264 (1220-1657)	728 (561-1383)	0.048	1486 (930-1976)	1050 (629-1513)	0.047	1438 (1025-1652)	797 (453-968)	0.031	1362 (797-1872)	913 (607-1214)	0.029

Data are presented as mean $\pm$ SD or median (IQR) or median (%) [IQR] or *n* (% of ethnic groups).

AUC: area under the curve, GIP: glucose-dependent insulintropic polypeptide, GLP-1: glucagon-like peptide-1, IFG: impaired fasting glucose,

IGT: impaired glucose tolerance.

For all analyses *p*-values <0.05 were considered significant

ESM Table 5. Ethnic differences in glucagon, incretins, glucose and insulin levels during OGTT by prediabetes

	Isolated IFG, Isolated IGT and combined IFG/ IGT		<i>p</i>
	South Asian	Nordic	
Number (<i>n</i>) of women	83	35	0.025
Fasting glucagon (pmol/l)	7.15±3.86	5.22±2.96	0.004
AUC glucagon (pmol/l x h)	6.17 (4.13-9.86)	5.53 (3.19-9.76)	0.141
Glucagon suppression, 0-15 min (%)	11 [-14 to 31]	8 [-14 to 22]	0.568
Glucagon suppression, 15-120 min (%)	68 [52-77]	68 [54-79]	0.971
Glucagon suppression, 0-120min (%)	71 [60-79]	69 [61-78]	0.658
Fasting GIP (pmol/l)	2.88 (2.03-4.08)	2.71 (2.31-3.80)	0.897
AUC GIP (pmol/l x h)	48.69 (35.35-70.21)	63.50 (48.47-87.09)	0.012
Peak GIP (pmol/l)	32.20 (22.90-46.50)	38.90 (30.30-59.30)	0.023
Fasting GLP (pmol/l)	3.97 (3.18-5.22)	3.71 (2.63-5.57)	0.453
AUC GLP-1 (pmol/l x h)	18.27 (14.53-23.92)	18.47 (14.14-22.91)	0.821
Peak GLP-1 (pmol/l)	13.50 (10.20-18.80)	12.60 (10.70-16.70)	0.274
Fasting plasma glucose (mmol/l)	5.8 (5.3-6.2)	5.8 (5.3-6.2)	0.967
2-h OGTT glucose (mmol/l)	8.9 (8.2-9.8)	8.4 (8.0-9.3)	0.165
AUC glucose (mmol/l x h)	18.1 (16.9-19.2)	17.8 (16.9-19.1)	0.388
Fasting pre-hepatic insulin (pmol/l)	258 (207-291)	249 (188-303)	0.730
15-min pre-hepatic insulin (pmol/l)	667 (486-830)	726 (484-880)	0.665
AUC pre-hepatic insulin (pmol/l x h)	2006 (1610-2351)	1877 (1502-2446)	0.523
Fasting insulin (pmol/l)	105 (68-154)	79 (59-112)	0.024
AUC insulin (pmol/l x h)	1475 (1027-1762)	797 (571-1469)	0.001

Data are presented as mean ±SD or median (IQR) or median (%) [IQR] or *n* (% of ethnic groups).

AUC: area under the curve, GIP: glucose-dependent insulintropic polypeptide, GLP-1: glucagon-like peptide-1, IFG: impaired fasting glucose, IGT: impaired glucose tolerance

For all analyses *p*-values <0.05 were considered significant

ESM Table 6. Log glucagon AUC_{0-120 min} in unadjusted and adjusted linear regression analyses in women with normal glucose tolerance

	Unadjusted		Model 1		Model 2	
	Crude B	<i>p</i>	Standard B	<i>p</i>	Standard B	<i>p</i>
Ethnicity	0.242	0.010	0.097	0.302	0.068	0.482
Age (years)	-0.101	0.290	0.060	0.538	0.098	0.326
Waist-to-height ratio (per 0.10 cm)	0.339	<0.001	0.093	0.377	0.044	0.673
eGFR (ml/min/1.73m ²)	0.262	0.005	0.151	0.140	0.093	0.369
Fasting plasma glucose (mmol/l)	0.111	0.243	0.036	0.689	-0.059	0.534
Fasting NEFA (mmol/l)	0.014	0.880	-0.059	0.509	0.037	0.680
Prehepatic insulin AUC _{0-120 min} (pmol/l x h)	0.447	<0.001	0.346	0.001		
Matsuda ISI	-0.489	<0.001			-0.458	<0.001

Log glucagon AUC_{0-120 min} (pmol/l x h) adjusted for ethnicity, age, waist-to-height ratio, eGFR, fasting NEFA, fasting plasma glucose and prehepatic insulin AUC_{0-120 min} (Model 1) or insulin sensitivity by Matsuda ISI (insulin sensitivity index) (Model 2) in women with normal glucose tolerance.

eGFR: estimated glomerular filtration rate, NEFA: non-esterified fatty acids.

For all analyses *p*-values <0.05 were considered significant

ESM Table 7. Early glucagon suppression in unadjusted and adjusted linear regression analyses in women with normal glucose tolerance

	Unadjusted		Model 1		Model 2	
	Crude B	<i>p</i>	Standard B	<i>p</i>	Standard B	<i>p</i>
Ethnicity	-0.277	0.012	-0.232	0.048	-0.184	0.117
Age (years)	0.131	0.241	0.095	0.452	0.095	0.461
Waist-to-height ratio (per 0.10 cm)	-0.287	0.009	-0.272	0.045	-0.241	0.063
eGFR (ml/min/1.73m ²)	-0.032	0.777	0.173	0.171	0.216	0.093
Fasting plasma glucose (mmol/l)	-0.202	0.069	-0.191	0.083	-0.202	0.077
Fasting NEFA (mmol/l)	0.013	0.911	0.040	0.713	0.035	0.755
Prehepatic insulin AUC _{0-15 min} (pmol/l x h)	-0.232	0.036	0.002	0.986		
HOMA-2S index	0.284	0.011			0.094	0.504

Cube root-transformed glucagon suppression AUC_{0-15 min} adjusted for ethnicity, age, waist-to-height ratio, eGFR, fasting NEFA, fasting plasma glucose and prehepatic insulin AUC_{0-15 min} (Model 1) or insulin sensitivity by HOMA-2S index (Model 2) in women with normal glucose tolerance.

eGFR: estimated glomerular filtration rate, HOMA-2S: homeostatic model assessment2-sensitivity.

NEFA: non-esterified fatty acids.

For all analyses *p*-values <0.05 were considered significant

ESM Table 8. Fasting glucagon in unadjusted and adjusted linear regression analyses in women with prediabetes or diabetes

	Unadjusted		Model 1		Model 2	
	Crude B	<i>p</i>	Standard B	<i>p</i>	Standard B	<i>p</i>
Ethnicity	0.217	0.004	0.144	0.047	0.071	0.357
Age (years)	-0.110	0.151	-0.013	0.877	-0.023	0.780
Waist-to-height ratio (per 0.10 cm)	0.144	0.061	-0.009	0.915	0.013	0.877
eGFR (ml/min/1.73m ²)	0.178	0.020	0.146	0.064	0.163	0.047
Fasting plasma glucose (mmol/l)	0.120	0.116	-0.005	0.952	-0.003	0.973
Fasting NEFA (mmol/l)	-0.181	0.018	-0.196	0.006	-0.129	0.097
Fasting prehepatic insulin (pmol/l)	0.358	<0.001	0.369	<0.001		
HOMA-2S index	-0.392	<0.001			-0.387	<0.001

Fasting glucagon adjusted for ethnicity, age, waist-to-height ratio, eGFR, fasting NEFA, fasting plasma glucose and fasting prehepatic insulin (Model 1) or insulin sensitivity by HOMA-2S index (Model 2) in women with prediabetes or diabetes.

eGFR: estimated glomerular filtration rate, HOMA-2S: homeostatic model assessment2-sensitivity. NEFA: non-esterified fatty acids

For all analyses *p*-values <0.05 were considered significant

ESM Table 9. GIP AUC_{0-120 min} in unadjusted and adjusted linear regression analyses in women with prediabetes or diabetes

	Unadjusted		Model 1		Model 2	
	Crude B	<i>p</i>	Standard B	<i>p</i>	Standard B	<i>p</i>
Ethnicity	-0.273	0.001	-0.216	0.003	-0.243	0.002
Age (years)	0.221	0.004	0.059	0.462	0.080	0.342
Waist-to-height ratio (per 0.10 cm)	0.133	0.083	0.035	0.652	0.047	0.582
eGFR (ml/min/1.73m ²)	-0.291	<0.001	-0.202	0.011	-0.217	0.008
Fasting plasma glucose (mmol/l)	0.205	0.007	0.196	0.009	0.104	0.210
Fasting NEFA (mmol/l)	-0.005	0.950	-0.017	0.809	-0.011	0.888
Prehepatic insulin AUC _{0-120 min} (pmol/l x h)	0.184	0.015	0.186	0.015		
Matsuda ISI	-0.144	0.064			-0.162	0.075

GIP AUC_{0-120 min} (pmol/l x h) adjusted for ethnicity, age, waist-to-height ratio, eGFR, fasting NEFA, fasting plasma glucose and prehepatic insulin AUC_{0-120 min} (Model 1) or insulin sensitivity by Matsuda ISI (insulin sensitivity index) (Model 2) in women with prediabetes or diabetes. eGFR: estimated glomerular filtration rate, GIP: glucose-dependent insulintropic polypeptide, NEFA: non-esterified fatty acids.

For all analyses *p*-values <0.05 were considered significant

ESM Table 10. Ethnic differences in insulin secretion, NAFLD liver fat score and insulin sensitivity

	Normal glucose tolerance			Prediabetes or diabetes		
	South Asian	Nordic	<i>p</i>	South Asian	Nordic	<i>p</i>
Number (<i>n</i>) of women	55 (31)	57 (53)		123 (69)	50 (47)	
Prehepatic insulin AUC _{0-30min} (pmol/l x h)	313 (235-391)	245 (182-296)	<0.001	296 (228-381)	300 (210-367)	0.861
NAFLD liver fat score	-0.78 (-1.59 to 0.11)	-2.01 (-2.42 to -1.27)	<0.001	0.64 (-0.97 to 1.96)	-0.26 (-1.04 to 0.91)	0.035
Insulin sensitivity index						
HOMA-2S index	61 (44-87)	102 (70-138)	<0.001	44 (32-69)	63 (46-87)	0.03
Matsuda ISI	3.1 (2.4-4.2)	5.5 (3.5-7.2)	<0.001	2.2 (1.6-3.3)	3.2 (2.1-4.2)	<0.01

Data are presented as median (IQR) for continuous variables, or *n* (% of ethnic group) for

categorical variables (Note that non-alcoholic fatty liver disease (NAFLD) is now referred to as metabolic dysfunction-associated steatotic liver disease [MASLD]).

HOMA-2S: homeostatic model assessment2-sensitivity, ISI: insulin sensitivity index.

For all analyses *p*-values <0.05 were considered significant

ESM Table 11. Predictors of prehepatic insulin in unadjusted and adjusted linear regression analyses in women with normal glucose tolerance

Prehepatic insulin _{0-30 min}	Unadjusted		Adjusted (Model 1)		Adjusted (Model 2)	
	Crude B	<i>p</i>	Standard B	<i>p</i>	Standard B	<i>p</i>
Ethnicity	0.306	0.001	0.195	0.037	0.105	0.185
Age (years)	-0.201	0.033	-0.148	0.135	-0.006	0.941
eGFR (ml/min/1.73m ²)	0.205	0.031	0.046	0.645	-0.069	0.414
Fasting plasma glucose (mmol/l)	0.115	0.227	0.065	0.463	-0.023	0.761
Glucagon AUC _{0-30 min} (pmol/l x h)	0.279	0.003	0.146	0.114	-0.005	0.951
GIP AUC _{0-30 min} (pmol/l x h)	0.312	<0.001	0.305	0.002	0.223	0.008
GLP-1 AUC _{0-30 min} (pmol/l x h)	0.120	0.206	-0.015	0.877	0.031	0.707
HOMA-2S index	-0.660	<0.001			-0.617	<0.001

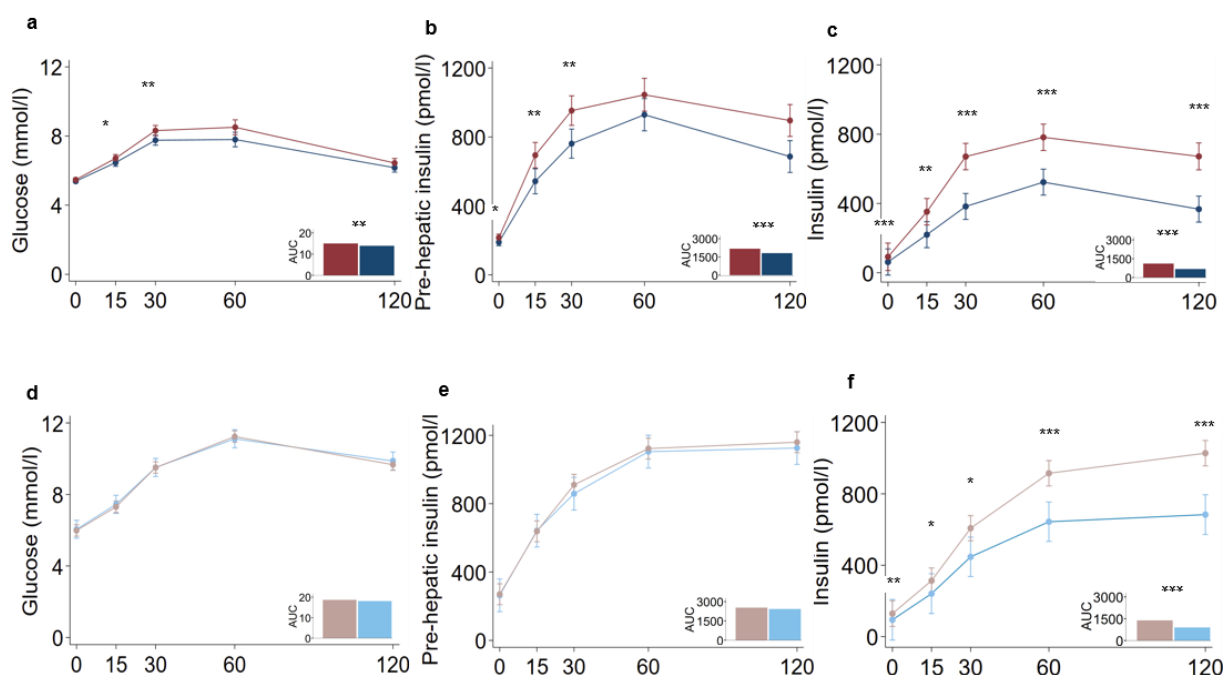
Prehepatic insulin during the first 30 min of the OGTT in women with normal glucose

tolerance in unadjusted and adjusted (Model 1: ethnicity, age, eGFR, fasting plasma glucose, glucagon AUC_{0-30 min}, GIP AUC_{0-30 min} and GLP AUC_{0-30 min}. Model 2: Model 1 + HOMA-2S (homeostatic model assessment2-sensitivity) index) regression analyses.

eGFR: estimated glomerular filtration rate, GIP: glucose-dependent insulinotropic polypeptide, GLP-1: glucagon-like peptide-1.

For all analyses *p*-values <0.05 were considered significant

ESM Figure 1.



ESM Fig 1. Glucose (a, d) estimated prehepatic insulin (b, e), peripheral insulin (c, f) levels in South Asian (red) and Nordic (blue) women with normal glucose tolerance (dark colour) and prediabetes or diabetes (light colour).

Units for AUC is mmol/l x h for glucose vs time, and pmol/l x h for pre-hepatic insulin or insulin vs time.

Data are means $\pm$ 95% CI. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ for South Asian vs. Nordic women.