

# Electronic Supplementary Material (ESM)

**One hour post-load plasma glucose and three-year risk of worsening fasting and 2 hour glucose tolerance in the RISC cohort**

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**ESM Table 1** Anthropometrics and metabolic characteristics of RISC participants who had baseline 1hPG <8.6 mmol/l and progressed over 3 years to isolated IFG, isolated IGT, both.

Low 1hPG < 8.6 mmol/l

	Non progressor  n=505 (81%)	Progressor		<i>P-values</i>		Progressor isolated 2hPH n=26 (4%)	Progressor both FPG & 2hPG high n=8 (1%)	<i>P-values</i>	
		Isolated high FPG n=81 (13%)	<i>comparing isolated high FPG and isolated high 2hPG progressor</i>		<i>comparing four groups</i>				
			univariate	adjusted†				univariate	adjusted†
<b>At baseline</b>									
Men	37%	49%			35%	38%	0.2138	2496	
Age (years)	42 (36;49 )	46 (38;53)	0.1844	0.9976	46 (41;55)	44 (39;54)	0.0003	0.0006	
BMI (kg/m <sup>2</sup> )	23.8 (21.8;26.2)	25.2 (23.4;27.6)	0.2541	0.2840	24.7 (23.2;27.7)	28.2 (24.6;29.8)	0.0006	0.0034	
Diabetes in family	21%	22%			19%	50%	0.3204	0.3456	
Smoker	25%	28%			19%	12%	0.6677	0.5135	
Fasting plasma glucose (mmol/l)	4.9 (4.6;5.1)	5.3 (5.0;5.4)	0.0061	0.0101	5.0 (4.7;5.2)	5.0 (4.9;5.3)	<.0001	<.0001	
2 hour plasma glucose (mmol/l)	5.0 (4.3;5.8)	5.3 (4.6;6.0)	0.0050	0.0068	6.0 (5.7;6.8)	6.5 (6.0;6.9)	<.0001	<.0001	
LDL-cholesterol (mmol/l)	2.8 (2.2;3.3)	2.8 (2.2;3.3)			3.1 (2.8;3.7)	3.0 (2.6;3.0)	0.0630	0.1429	
HDL-cholesterol (mmol/l)	1.5 (1.2;1.7)	1.3 (1.1;1.7)			1.3 (1.1;1.6)	1.3 ( 1.1;1.6)	0.0796	0.0871	
Triglycerides (mmol/l) <sup>a</sup>	0.83 (0.62;1.14)	0.93 (0.68;1.14)			1.00 (0.65;1.32)	0.81 (0.63;1.41)	0.3323	0.6122	
Systolic blood pressure (mmHg)	115 (107;124)	120 (111;128)			116 (109;126)	120 (112;128)	0.0879	0.9839	
Diastolic blood pressure (mmHg)	73 (67;79)	75 (70;79)			74 (70;77)	77 (70;84)	0.2285	0.8246	
Basal insulin secretion (pmol·min <sup>-1</sup> ·m <sup>-2</sup> )*	61 (49;78)	68 (53;92)			71 (58;92)	70 (68;96)	0.0134	0.1289	
Total insulin secretion	36	37	0.0069	0.0057	45	40	0.0015	0.0075	

(nmol·m <sup>-2</sup> )	(28;43)	(33;44)			(37;57)	(32;43)		
Beta cell glucose sensitivity	133	136			119	97	0.4238	0.3212
(pmol·min <sup>-1</sup> ·m <sup>-2</sup> ·mmol/l) <sup>a</sup>	(100;187)	(108;188)			(97;153)	(90;123)		
Clamp insulin sensitivity	143	145	0.0003	<.0001	105	108	0.0002	<.0001
(μmol·min·kg <sub>FFM</sub> ·nmol·l) <sup>a</sup>	(111;194)	(110;197)			(81;123)	(92;150)		
OGIS (ml·min <sup>-1</sup> ·m <sup>2</sup> )*	12.7	11.8	0.1261	0.1973	11.0	11.0	<.0001	<.0001
	(11.1;14.5)	(10.7;12.9)			(9.6;13.0)	(9.9;12.4)		

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#### Percent change over 3 years

BMI	1.0	1.3			2.2	5.0	0.4144	0.2552
	(-2.1;4.9)	(-1.8;4.3)			(-0.5;5.4)	(-0.6;8)		
Basal insulin secretion <sup>a</sup>	-0.5	19.0	0.0075	0.0139	-6.5	10.3	0.0001	0.0001
	(-18;20)	(-1;46)			(-25;25)	(1;17)		
Total insulin secretion <sup>a</sup>	4.8	12.7	0.0089	0.0074	16.6	22.8	0.0017	0.0088
	(-10;24)	(-3.8;39)			(3.3;40)	(1.5;49)		
Beta cell glucose sensitivity <sup>a</sup>	-8.7	-8.7			-33	-22	0.1771	0.1233
	(-37;35)	(-30; 30)			(-41;-4.1)	(-31;0.4)		
OGIS	-2.7	-9.7	0.0097	0.0082	-17.2	-20.8	<.0001	<.0001
	(-12;7)	(-21;-2.4)			(-28;-11)	(-25; -12)		

Data are reported as median values (quartile1; quartile 3) or % of baseline characteristics and of per cent change over 3 years. *p* values used multinomial regression, unadjusted and †adjusted for sex, age and BMI. The isolated high FPG and isolated high 2hPG are compared statistically in the case where the comparison over four groups was statistically significant.

<sup>a</sup> Logarithms, base, were used in the logistic regression analyses

FFM, fat-free mass

Progressors on isolated IFG were participants who presented with FPG ≥ 5.6 mmol/l, but 2hPG <7.8 mmol/l;

Progressors on isolated IGT were participants who presented with FPG < 5.6 mmol/l, but 2hPG ≥ 7.8 mmol/l;

Progressors on both FPG and 2hPG high, had FPG ≥ 5.6 mmol/l and 2hPG ≥7.8 mmol/l.

**ESM Table 2** Anthropometrics and metabolic characteristics of RISC participants who had baseline 1hPG  $\geq$ 8.6 mmol/l and progressed over 3 years to isolated IFG, isolated IGT, both.

	Non-progressor n=109 (62%)	Progressor	<i>P-values</i>		Progressor	Progressor	<i>P-values</i>	
		isolated high FPG n=36 (20%)	<i>comparing isolated high FPG and isolated high 2hPG progressor</i>		isolated 2hPH n=14 (8%)	both FPG & 2hPG high n=18 (10%)	<i>comparing four groups</i>	
			univariate	adjusted <sup>†</sup>			univariate	adjusted <sup>†</sup>
<b>At baseline</b>								
Men	48%	78%	0.0608	0.0798	50%	61%	0.0223	0.0204
Age (years)	46 (38;51)	46 (43;54)			42 (38;50)	48 (39;55)	0.4735	0.2613
BMI (kg/m <sup>2</sup> )	24.7 (23.2;27.1)	25.8 (23.6;28.0)	0.6579	0.9244	25.2 (21.8;28.1)	28.4 (24.5;31.2)	0.0332	0.0484
Diabetes in family	28%	47%			29%	22%	0.1625	0.1001
Smoker	36%	17%			43%	56%	0.0443	0.0830
Fasting plasma glucose (mmol/l)	5.1 (4.8;5.3)	5.3 (5.1;5.4)			5.2 (4.9;5.3)	5.3 (5.1;5.3)	0.0265	0.1171
2 hour plasma glucose (mmol/l)	6.1 (5.3;6.9)	5.9 (5.3;6.9)	0.0210	0.0504	6.9 (6.1;7.4)	6.7 (5.8;7.0)	0.0357	0.0465
LDL-cholesterol (mmol/l)	2.9 (2.4;3.3)	3.2 (2.5;3.7)			3.1 (2.6;4.0)	2.9 (2.8;3.5)	0.1950	0.2096
HDL-cholesterol (mmol/l)	1.4 (1.1;1.6)	1.3 (1.1;1.5)			1.3 (1.2;1.9)	1.2 (1.0;1.5)	0.2594	0.5388
Triglycerides (mmol/l) <sup>a</sup>	0.91 (0.70;1.15)	1.06 (0.69;1.95)			0.99 (0.87;1.16)	1.29 (0.89;2.27)	0.0144	0.1687
Systolic blood pressure (mmHg)	119 (110;125)	125 (117;130)			118 (112;119)	122 (116;130)	0.0114	0.1120
Diastolic blood pressure (mmHg)	75 (69;80)	78 (74;84)			75 (72;77)	78 (71;82)	0.0712	0.3403
Basal insulin secretion (pmol·min <sup>-1</sup> ·m <sup>-2</sup> )*	65 (48;91)	76 (66;95)	0.6597	0.2730	82 (72;94)	96 (82;128)	0.0019	0.0247
Total insulin secretion (nmol·m <sup>-2</sup> )	44 (34;55)	45 (38;52)			47 (43;53)	49 (42;58)	0.3275	0.6093

Beta cell glucose sensitivity (pmol·min <sup>-1</sup> ·m <sup>-2</sup> ·mmol/l) <sup>a</sup>	90 (66;112)	83 (72;97)			89 (82;103)	86 (56;111)	0.8684	0.8604
Clamp insulin sensitivity (μmol·min·kg <sub>FFM</sub> ·nmol/l) <sup>a</sup>	133 (90;171)	100 (82;134)	0.4695	0.0212	79 (60;153)	89 (80;157)	0.0151	0.0488
OGIS (ml·min <sup>-1</sup> ·m <sup>2</sup> )	10.5 (9.6;11.9)	9.9 (8.8;11.2)			9.4 (8.7;12.0)	10.1 (9.1;11.1)	0.1785	0.6469

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**Percent change over**

**3 years**

BMI	1.5 (-2.3;3.7)	1.1 (-2.6;2.8)	0.1416	0.1945	1.8 (0.4;6.1)	4.6 (2.2;6.6)	0.0596	0.0353
Basal insulin secretion <sup>a</sup>	4.5 (-14;24)	12 (-5.8;34)			-2.3 (-17;26)	18.0 (-4.7;42)	0.2330	0.1780
Total insulin secretion <sup>a</sup>	-5.3 (-22;12)	-0.2 (-18;20)			28 (22;32)	16 (-1.4;34)	0.2818	0.5469
Beta cell glucose sensitivity <sup>a</sup>	24 (-3.7;74)	-9.9 (-20;50)			9.6 (-12;30)	-1.9 (-38;53)	0.1328	0.2147
OGIS	7.7 (-6.9;20)	-5.9 (-16, 4.1)	0.0835	0.0902	-14 (-17;-9.3)	-19 (-23;-13)	<.0001	<.0001

Data are reported as median values (quartile1; quartile 3) or % of baseline characteristics and of per cent change over 3 years.

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Progressors on both FPG and 2hPG high, had FPG ≥ 5.6 mmol/l and 2hPG ≥7.8 mmol/l.

## Supplementary Figure

Percentage of people progressing to incident glucose intolerance (fasting plasma glucose  $\geq 5.6$  mmol/l and/or 2 hour plasma glucose  $\geq 7.8$  mmol/l) over a three year follow-up of 797 people from the EGIR-RISC Study. The thresholds of 1hPG potentially associated with risk of progression to glucose intolerance were 6.2; 7.5; 8.6; 8.95 mmol/l)

