

SUPPLEMENTARY DATA

**Supplementary Table 1:** Comparison of lipids, adipokines and C-reactive protein (CRP) between non-decliners and decliners at 3-months postpartum

	<b>Non-decliners</b>	<b>Decliners</b>	
	<b>n=74</b>	<b>N=92</b>	<b>p</b>
<b>At 3-months postpartum</b>			
LDL (mmol/L)	3.68 [2.97-4.34]	3.85 [3.22-4.66]	0.1262
HDL (mmol/L)	1.29 [1.07-1.51]	1.35 [1.18-1.59]	0.1963
Triglycerides (mmol/L)	0.96 [0.73-1.53]	1.12 [0.75-1.63]	0.2645
ApoB (g/L)	0.93 [0.78-1.07]	0.96 [0.78-1.13]	0.2639
ApoB:apoA1	0.62 [0.48-0.76]	0.62 [0.51-0.73]	0.8533
CRP (mg/L)	2.21 [0.98-5.09]	2.74 [1.58-4.61]	0.1213
Leptin (ng/ml)	22.4 [11.7-38.8]	27.2 [14.5-36.9]	0.2977
Adiponectin (ug/ml)	7.7 [5.8-10.8]	8.1 [6.1-9.8]	0.9624

Data are shown as median followed by interquartile range in parentheses.

P-values refer to differences between the two groups as determined by Kruskal-Wallis test

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**Supplementary Table 2: Spearman univariate correlations with the baseline-adjusted change in ISSI-2 between 3- and 12-months postpartum**

					<b>r</b>	<b>p</b>
<b>Measures at 3-months postpartum</b>						
Sport index					0.08	0.35
Leisure-time index					0.01	0.91
Waist circumference					<b>-0.17</b>	<b>0.04</b>
Weight					<b>-0.19</b>	<b>0.02</b>
BMI					<b>-0.21</b>	<b>0.01</b>
LDL					-0.11	0.19
HDL					-0.06	0.45
Triglycerides					-0.12	0.14
ApoB					-0.10	0.23
ApoB:apoA1					0	0.98
CRP					<b>-0.24</b>	<b>0.0031</b>
Leptin					<b>-0.21</b>	<b>0.01</b>
Adiponectin					0.08	0.35
Matsuda index					0.11	0.21
1/HOMA-IR					-0.03	0.68
Fasting C-peptide:insulin					-0.04	0.62
<b>Changes between 3- and 12-months postpartum</b>						
Change in sport index					0	0.98
Change in leisure-time index					0.04	0.63
Change in waist					-0.09	0.30
Change in weight					-0.15	0.08
Change in BMI					-0.15	0.08
Change in Matsuda index					0.15	0.08
Change in 1/HOMA-IR					<b>0.45</b>	<b>&lt;0.0001</b>
Change in fasting C-peptide:insulin					<b>0.22</b>	<b>0.0082</b>

Bold indicates p<0.05

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**Supplementary Table 3: Multiple linear regression analyses of (dependent variable) change in ISSI-2 between 3- and 12-months postpartum**

Model	Predictor					Estimate	SE	t	p
A	CRP at 3-months postpartum					-3.17730	7.03	-0.45	0.6522
B	Leptin at 3-months postpartum					-0.03131	2.14	-0.01	0.9883
C	Change in weight between 3- and 12-months					-8.22970	5.19	-1.58	0.1150
D	Change in Matsuda index between 3- and 12-months					0.21063	4.017	0.05	0.9582
E	Change in 1/HOMA-IR between 3- and 12-months					227.77	41.45	5.5	<0.0001
F	Change in fasting C-peptide:insulin between 3- and 12-months					6.38085	1.968	3.24	0.0015

Each model shows the regression of the indicated variable on (dependent variable) change in ISSI-2 between 3- and 12-months postpartum, after adjustment for age, ethnicity, family history of diabetes, breastfeeding, BMI, and ISSI-2 at 3-months postpartum.

*Sensitivity Analysis:*

To attenuate any effect of extreme observations comprising the upper tail of the distribution of ISSI-2 in the decliners group at 3-months postpartum, we also repeated the multiple linear regression analyses after winsorization, a statistical technique wherein outliers are moved to the 95<sup>th</sup> percentile to limit any excessive effect that they may impose on the results. With the winsorized data, the only significant independent predictors of the change in beta-cell function were again the changes in 1/HOMA-IR (beta=254, t=6.23, p<0.0001) and fasting C-peptide:insulin (beta=7.33, t=3.76, p=0.0002), respectively.

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**Supplementary Table 4: Logistic regression analyses of (dependent variable) decline in ISSI-2 between 3- and 12-months postpartum**

Model	Predictor					Odds Ratio		95% CI		p
A	Change in waist between 3- and 12-months					1.02		[0.97 - 1.06]		0.5326
B	Change in weight between 3- and 12-months					1.07		[0.99 - 1.15]		0.0764
C	Change in Matsuda index between 3- and 12-months					0.98		[0.93 - 1.03]		0.3476
D	Change in 1/HOMA-IR between 3- and 12-months					0.13		[0.06 - 0.29]		<0.0001
E	Change in fasting C-peptide:insulin between 3- and 12-months					0.95		[0.91 - 0.98]		0.0018

Each model shows the regression of the indicated variable on (dependent variable) decline in ISSI-2 between 3- and 12-months postpartum, after adjustment for age, ethnicity, family history of diabetes, breastfeeding, and BMI at 3-months postpartum.

*Sensitivity Analysis:*

A series of sensitivity analyses were performed to evaluate the robustness of these findings:

- (i) First, to eliminate the effect of small changes in ISSI-2 between 3- and 12-months postpartum that may not reflect true physiologic decline or increase, we repeated the logistic regression analyses after limiting the dataset to the 133 women in whom ISSI-2 either decreased or increased by >10%. In this subgroup, the changes in 1/HOMA-IR (OR=0.10, 95%CI 0.04-0.26, p<0.0001) and fasting C-peptide:insulin (OR=0.95, 95%CI 0.92-0.99, p=0.0057) remained as significant independent predictors of declining beta-cell function.
- (ii) Second, when the logistic regression analyses were restricted to the 100 women with GDM, these two measures again emerged as the only significant independent predictors (1/HOMA-IR: OR=0.14, 95%CI 0.05-0.37, p<0.0001; fasting C-peptide:insulin: OR=0.93, 95%CI 0.89-0.97, p=0.0024).
- (iii) Third, the analyses were repeated in only the 124 women with normal glucose tolerance at 3-months postpartum. Once again, the significant independent predictors of declining beta-cell function were the changes in 1/HOMA-IR (OR=0.09, 95%CI 0.03-0.26, p<0.0001) and fasting C-peptide:insulin (OR=0.94, 95%CI 0.90-0.98, p=0.0044), respectively.

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**Supplementary Figure 1: Flow chart describing study population**

