

# Increases in Waist Circumference and Weight As Predictors of Type 2 Diabetes in Individuals With Impaired Fasting Glucose: Influence of Baseline BMI

Data from the DESIR study

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**OBJECTIVE** — To evaluate in impaired fasting glucose (IFG) the relative importance of increases in waist circumference and weight on progression to type 2 diabetes.

**RESEARCH DESIGN AND METHODS** — The 9-year incidence of diabetes was studied in 979 men and women with baseline IFG, from the Data from an Epidemiological Study on the Insulin Resistance Syndrome (DESIR) cohort.

**RESULTS** — Increases in both waist circumference and weight were significantly associated with diabetes incidence. Standardized odds ratios (95% CI) were 1.79 (1.45–2.21) and 1.86 (1.51–2.30), respectively, after controlling for baseline risk factors. The impact of waist circumference increase was greater for BMI <25 kg/m<sup>2</sup> (2.40 [1.63–3.52]) than for BMI ≥25 kg/m<sup>2</sup> (1.66 [1.28–2.16]) and persisted after adjusting for concurrent changes in either insulinemia or the homeostasis model assessment of insulin resistance index. Weight change had a similar impact in both BMI groups.

**CONCLUSIONS** — In individuals with IFG, it is important to monitor and prevent increases in waist circumference, in particular for those with BMI <25 kg/m<sup>2</sup>.

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Individuals with impaired fasting glucose (IFG) are at high risk for type 2 diabetes (1,2). Although visceral adiposity and waist circumference are strong risk factors for type 2 diabetes (3), the consequence of an increase in waist circumference among individuals with IFG at baseline has not been fully investigated, in particular in those who are not overweight or obese at

baseline (4,5). This report investigates the relative importance of increases in waist circumference and weight on progression to diabetes in individuals with baseline IFG, according to baseline BMI strata.

## RESEARCH DESIGN AND

**METHODS** — We studied men and women aged 30–64 years, who partici-

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pated in the Data from an Epidemiological Study on the Insulin Resistance Syndrome (DESIR) cohort and who had IFG at baseline (fasting plasma glucose 5.6–6.9 mmol/l). DESIR is a 9-year follow-up study that aimed to clarify the development of the insulin resistance syndrome and type 2 diabetes (6). All participants signed an informed consent, and the protocol was approved by an ethics committee.

Incident cases of diabetes had fasting plasma glucose ≥7.0 mmol/l or treated diabetes at one of the three yearly follow-up examinations. The average variation per year in waist circumference and weight was defined as the difference between the visit when diabetes was screened and the baseline visit divided by the number of years of follow-up. A total of 674 men and 305 women were studied.

All analyses used R version 2.10.0 (Free Software Foundation, Boston, MA), and a two-sided  $P < 0.05$  was considered statistically significant. Homeostasis model assessment of insulin resistance (HOMA2-IR) was computed using software downloaded at <http://www.dtu.ox.ac.uk>. Insulin, glucose, and HOMA2-IR values were log transformed before analysis. We used logistic models for incident diabetes to evaluate standardized odds ratios with Wald 95% CIs, conditioned on baseline BMI < and ≥25 kg/m<sup>2</sup>, adjusted for sex, family history of diabetes, baseline age, current smoking, physical activity, fasting glucose, and hypertension (systolic/diastolic blood pressures ≥140/90 mmHg or treated for hypertension). We tested for interactions between baseline BMI categories with increases in waist circumference and weight on incident diabetes.

**RESULTS** — There were 142 cases of incident diabetes after 9 years of follow-up. Individuals who became diabetic had a greater increase over follow-up in both

Table 1—Odds ratios (95% CI) for 9-year incident diabetes, per 1 SD change in waist circumference and weight in IFG: the DESIR study

	All IFG participants		BMI <25 kg/m <sup>2</sup>		BMI ≥25 kg/m <sup>2</sup>	
	n = 979		n = 433		n = 546	
	Odds ratio (95% CI)	P	Odds ratio (95% CI)*	P	Odds ratio (95% CI)	P
Univariate						
Change in waist circumference	1.69 (1.41–2.03)	<0.0001	2.48 (1.73–3.55)	<0.0001	1.48 (1.20–1.84)	0.0003
Change in weight	1.83 (1.53–2.19)	<0.0001	1.86 (1.35–2.55)	<0.0001	1.85 (1.48–2.32)	<0.0001
Model 1						
Change in waist circumference	1.79 (1.45–2.21)	<0.0001	2.40 (1.63–3.52)	<0.0001	1.66 (1.28–2.16)	0.0002
Change in weight	1.86 (1.51–2.30)	<0.0001	1.92 (1.32–2.79)	0.0006	1.96 (1.50–2.55)	<0.0001
Model 2						
Change in waist circumference	1.65 (1.30–2.09)	<0.0001	1.82 (1.21–2.75)	0.004	1.66 (1.22–2.24)	0.001
Change in weight	1.67 (1.30–2.15)	<0.0001	1.20 (0.77–1.88)	0.4	1.97 (1.44–2.69)	<0.0001
Model 3						
Change in waist circumference	1.52 (1.18–1.96)	0.001	1.82 (1.18–2.80)	0.007	1.49 (1.08–2.06)	0.01
Change in weight	1.48 (1.13–1.95)	0.005	1.04 (0.64–1.70)	0.9	1.79 (1.29–2.50)	0.0006

Model 1 = adjusted for sex, family history of diabetes, and baseline age, current smoking, physical activity, fasting glucose, and hypertension. Model 2 = model 1 + change in fasting insulinemia. Model 3 = model 1 + change in HOMA2-IR. \*SDs for the standardization of the odds ratios in all IFG participants, BMI <25 kg/m<sup>2</sup> group, and BMI ≥25 kg/m<sup>2</sup> group were, respectively, 0.78, 0.74, and 0.82 cm/year for change in waist circumference and 0.71, 0.62, and 0.77 kg/year for change in weight.

waist circumference and weight than those who did not progress (online appendix Table 1, available at <http://care.diabetesjournals.org/cgi/content/full/dc10-0368/DC1>).

Changes in waist circumference and weight were significantly associated with incident type 2 diabetes in multivariate analysis, in both BMI categories (Table 1). The significant impact of change in either waist circumference or weight did not vary by age at baseline (aged < or >50 years). There was an interaction between BMI category and the effect of waist increase for progression to diabetes, with a larger impact in participants with BMI <25 kg/m<sup>2</sup> than in those with BMI ≥25 kg/m<sup>2</sup> (*P* for interaction = 0.049).

An increase in waist circumference remained significantly associated with progression to type 2 diabetes after controlling for concurrent changes in either insulinemia or the HOMA2-IR index, irrespective of baseline BMI category (Table 1). In contrast, the effect of weight change was no longer significant after controlling for variations in either insulinemia or the HOMA2-IR index in those with BMI <25 kg/m<sup>2</sup>.

**CONCLUSIONS**— The main finding of this study is that an increase in waist circumference is a major risk factor for type 2 diabetes in individuals with IFG, irrespective of baseline BMI. In those with BMI <25 kg/m<sup>2</sup>, an increase in waist circumference appears to be a stronger risk

marker for progression to type 2 diabetes than weight gain. This is in agreement with a previous report that found greater risk for diabetes in U.S. men who increased their waist circumference (7); however, these authors did not specifically assess risk in IFG (7).

To our knowledge, this study is the first to assess the impact of waist increase for progression to diabetes in the absence of excessive weight at baseline. Previous studies assessing risk factors for diabetes in either the general population or in IFG subjects did not perform analyses according to BMI strata (4,5).

Our findings suggest the potential value of monitoring waist circumference over time in IFG. Waist circumference probably reflects more accurately visceral fat in leaner subjects because of the thinner subcutaneous abdominal depot (8). Another explanation may be that individuals with IFG and prone to develop overt diabetes tend to gain visceral fat more selectively than subcutaneous fat, compared with those who remained nondiabetic. This could be sustained by defects in adipogenesis and/or specificities in adipose tissue morphology, independently of body fat level, as recently suggested (9). However, this hypothesis cannot be demonstrated in the present study. The effect of an increase in waist circumference on the progression to diabetes was independent, at least partly, of concomitant variations in insulinemia or the HOMA2-IR index, suggesting addi-

tional mechanisms linking abdominal adiposity and  $\beta$ -cell function (10).

Impaired  $\beta$ -cell function is considered an important characteristic in individuals with IFG (11), and reduced insulin secretion has been shown to be a prominent mechanism leading to diabetes in lean individuals (12,13). We speculate that an increase in waist circumference may induce further alterations in insulin secretion beyond that inherent in worsening insulin resistance. Potential mechanisms may involve  $\beta$ -cell lipotoxicity through enhanced free fatty acid release from adipose tissue (14).

Limitations of the present study include the absence of gold-standard measures of insulin sensitivity such as the euglycemic–hyperinsulinemic clamp; strengths are the large cohort with a low prevalence of obesity and a long follow-up. In conclusion, our results emphasize the importance of monitoring and preventing increases in waist circumference in individuals with IFG, in particular in those with BMI <25 kg/m<sup>2</sup>.

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