



PAPER

Impaired fasting glycaemia in middle-aged women: a prospective study

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OBJECTIVES: To investigate: (i) the incidence of impaired fasting glycaemia (IFG) developed over 5 y in a population-based sample of Australian-born women; (ii) prospectively the factors which are associated with the development of IFG; (iii) the association of the menopausal transition with the onset of IFG and an increase in serum insulin concentrations.

DESIGN AND METHODS: A total of 265 women (110 pre-, 138 peri-, 17 postmenopausal) participants in the longitudinal phase of the Melbourne Women's Midlife Health Project, aged 46–57 and with normal fasting plasma glucose concentrations at the time of the initial measure, were interviewed, had physical measurements and blood taken annually over a 5 y follow-up period.

RESULTS: During the study period 43 women (16%) recorded a fasting glucose concentration of ≥ 6.1 mmol/l (IFG). Women who recorded IFG prospectively had, at the time of the initial measure when fasting glucose concentrations were normal: higher body mass index (BMI), trunk skinfold thicknesses, waist and hip circumferences ($P < 0.005$), lower SHBG, higher free androgen index and serum insulin concentrations ($P < 0.05$), higher systolic blood pressure, serum triglyceride and lower HDL-cholesterol concentrations ($P < 0.05$) than women whose fasting glucose concentrations remained normal. The onset of IFG was not triggered by the menopausal transition or hormone use. Changes in insulin concentration were associated with changes in BMI ($P < 0.05$).

CONCLUSION: Women who developed IFG during the menopausal transition exhibited significantly higher levels of body fatness and dyslipidemia, premenopausally, compared with the women who did not develop IFG. The menopausal transition did not have an effect on the development of IFG, but weight gain during this period was associated with an increase in insulin concentration.

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Introduction

Type 2 diabetes is a strong risk factor for coronary heart disease, ischaemic stroke, and cardiovascular mortality among middle-aged women.¹ Oestrogen deficiency, associated with the menopause, has been reported to have a deleterious effect on plasma lipids and lipoproteins, and to increase the risk of heart disease.² An increase in abdominal fat has also been reported to be associated with a number of

metabolic abnormalities including dyslipidemia and insulin resistance, which lead to an increased risk of heart disease,³ although the importance of visceral obesity as a causal agent remains to be established.⁴ An increase in central body fatness also occurs with the menopause transition,^{5,6} however, the effect of the menopause on insulin sensitivity has not been clearly established. Matthews and colleagues² reported that the natural menopause did not affect fasting plasma glucose or insulin, whereas Poehlman and colleagues⁵ found in an age-matched sample that women who experienced the menopause had a significantly greater increase in insulin compared with women who remained premenopausal.

Further information is needed from prospective population-based studies on the role of the menopausal transition

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in the development of insulin resistance and impaired fasting glycaemia. A fasting plasma glucose concentration of ≥ 6.1 and < 7.0 mmol/l is classified as impaired fasting glycaemia (IFG)⁷ and it is associated with the risk of developing diabetes.

The aims of this study were to investigate: (i) the incidence of IFG developed over 5 y in a population-based sample of Australian-born women; (ii) prospectively the factors, at the initial measure, which were associated with the development of IFG; (iii) the association of the menopausal transition with the onset of IFG and an increase in insulin concentrations.

Subjects and methods

The study was approved by the Human Research Ethics Committee of the University of Melbourne. Details of the sample acquisition and characteristics and questionnaire design of the Melbourne Midlife Health Project have been described previously.^{8,9} In summary, an initial sample of 2001 Melbourne women who were Australian-born and aged between 45 and 55 y were recruited by random digit telephone dialling in 1991. Women were eligible for the longitudinal study if they had menstruated in the previous 3 months, had an intact uterus and at least one ovary and were not currently taking oral contraceptives or hormone therapy (HT). From the original 2001 women, 779 met this criteria, of whom 438 (56%) agreed to be interviewed in the first year of the longitudinal study. Participants were significantly more likely than eligible non-participants to: report better health compared with women of the same age; be in paid employment; have had more than 12 y of education; have had a Pap smear; to exercise once a week; and to have undergone dilatation and curettage.⁹ Fasting plasma glucose was first estimated in the second year of follow-up in the longitudinal study. The content of this paper represents 6 y of data collection, from the second to the seventh year of follow-up. Retention after the seventh year was 390 (89%). The second year of follow-up data is referred to as the initial measure for the purpose of the present paper.

Menopausal status

Menopausal status was determined by menstrual history reported at the time of the interview, and date of final menstrual period (FMP) was verified with the aid of menstrual diaries that had been kept prospectively. Women were classified as premenopausal if they reported no change in frequency of menses, early perimenopausal if there were changes in frequency of their menses, late perimenopausal if they reported amenorrhoea of at least 3, but less than 12 months, and naturally postmenopausal if there was amenorrhoea for 12 or more consecutive months.¹⁰ Women who had experienced a hysterectomy, with or without oophorectomy, or an endometrial ablation were classified as having

a surgical menopause. Hormone therapy use was recorded at the time of each interview.

Laboratory assays and measurements

Women had fasted overnight for at least 10 h prior to blood collection. For women with regular menstrual cycles, the morning blood sample for hormone analysis was taken between days 4 and 8 of the menstrual cycle. For women who were not having regular menses the date of their last menstrual period was noted at the time the blood was taken. Plasma glucose was measured using the hexokinase method and performed on Dimension clinical chemistry systems (Dade International Inc. Newark, USA). Insulin was measured by radioimmunoassay using Linco Human Insulin Specific kits (Linco, Missouri, USA). Total cholesterol and HDL cholesterol and triglycerides were measured according to standard enzymatic methods on routine automated chemistry systems. LDL cholesterol was calculated using the Friedwald formula adapted for SI units. Serum concentrations of FSH, oestradiol (E2), and testosterone (T), were measured as described previously.⁹ Sex hormone binding globulin (SHBG) and dehydroepiandrosterone sulphate (DHEAS) were measured by automated enzyme immunoassay using the Immulite system purchased from Diagnostic Products Corporation, California, USA. Free androgen index (FAI) was calculated as the ratio of measured T to measured SHBG $\times 100$. Systolic (SBP) and diastolic (DBP) blood pressure were measured twice, 5 min apart, with the subject seated, and the mean of the two measures calculated.

Physical and lifestyle measures/family history

The following measures were recorded annually: body height, measured to the nearest 0.1 cm with subjects in the erect position without shoes; body weight, measured to the nearest 0.1 kg with subjects wearing indoor clothes but no shoes; body mass index (BMI), calculated as weight (kg)/height (m^2); waist circumference, measured at the narrowest part of the trunk; hip, measured at the widest circumference over the great trochanters; four skin-fold thicknesses, triceps, biceps, subscapular and supra-iliac, measured using Harpenden skin-fold callipers, two readings taken at each site (recorded to the nearest mm) and if the differences were large, a third measurement taken and the mean of the closest pair recorded.

Three measures of lifestyle-related behaviours were included: (i) exercise, recorded as frequency of engaging in exercise for fitness or recreational purposes, with seven answer options (every day; 4–6 times per week; 2–3 times per week; once a week; a few times a month; less than once a month; never); (ii) current smoking (yes/no); and (iii) alcohol intake, recorded as number of alcoholic drinks consumed in the previous week. Participants were asked if any family members had been diagnosed with diabetes and if so their age at diagnosis and their relationship was recorded.

Statistical analysis

Because of skewed distributions, the BMI, waist, hip, triglyceride, insulin and hormone values were log-transformed before analysis. Chi-square and *t*-tests were used to assess differences between women who recorded IFG and those that did not. Where women were taking blood pressure or cholesterol-lowering drugs their values for blood pressure and lipids were excluded from the analyses. Paired *t*-tests were used to assess differences between initial and follow-up measures and *t*-tests for independent samples were used to assess change. Logistic regression analysis was used to examine the influence of variables on case status using quintiles calculated from the distribution of the data. Multiple linear regression was used to assess the effects of the independent variables (initial age and BMI, change in BMI, menopausal change group) on change in insulin levels. SPSS software was used for all analyses.¹¹

Results

Sample

Excluded from the analysis were: six women who had previously been diagnosed with diabetes; four women who recorded IFG at the time of the initial measure; 61 women who were taking hormone therapy at the time of the initial glucose measurement, as hormone therapy may effect serum lipids or insulin sensitivity;¹² 25 women who had had a surgical menopause during the study period and 29 women who did not provide a blood sample every year. This left a cohort of 265 women with a mean age (s.d.) of 50.5 (2.5) y, range 46–57 y at the time of the initial glucose measurement and normal fasting glucose concentrations. At this stage 110 (42%) women were premenopausal, 89 (34%) were early perimenopausal, 49 (18%) were late perimenopausal and 17 (6%) were postmenopausal.

Incidence of impaired fasting glycaemia (IFG)

Of the 265 women, 43 (16%) recorded a fasting glucose concentration of ≥ 6.1 mmol/l (range 6.1–9.4 mmol/l) on at least one occasion over the 5-y follow-up period. Nineteen women (7%) recorded IFG on more than one occasion. Ten women recorded concentrations of > 7.0 mmol/l and of these two reported a diagnosis of type 2 diabetes by their doctor.

Variables associated with IFG

Table 1 shows that women who prospectively developed IFG had at the time of the initial normal glucose measures, higher BMI, trunk skinfold thicknesses, and waist and hip circumferences ($P < 0.005$) than women whose fasting glucose remained normal during the 5 y follow-up period. They had lower serum SHBG, and higher FAI and serum insulin concentrations ($P < 0.05$). Table 2 shows that mean serum triglyceride concentrations and systolic blood pressure were

Table 1 Initial variables: a comparison of women who developed impaired fasting glycaemia (IFG) ($n=43$) during the 5 y study period with women who continued to have normal fasting glycaemia ($n=222$) (NFG). Geometric means are given and their 95% confidence intervals in parentheses

Variable	Impaired fasting glycaemia	Normal fasting glycaemia
Age (y)	50.0 (49.2–50.8)	50.6 (50.2–51.0)
Glucose (mM)	5.2 (5.0–5.3)	4.7 (4.6–4.8)***
<i>Measures of obesity</i>		
BMI (kg/m^2)	28.2 (26.7–29.8)	25.0 (24.4–25.5)***
Suprailiac skinfold (mm)	25.0 (22.3–27.6)	20.5 (19.3–21.6)**
Subscapular skinfold (mm)	24.7 (22.2–27.3)	19.4 (18.3–20.5)***
Waist (cm)	85.7 (82.2–89.4)	77.8 (76.4–79.2)***
Hip (cm)	108.9 (106.1–111.7)	101.7 (100.5–102.9)***
Waist/hip ratio	0.79 (0.77–0.81)	0.77 (0.76–0.78)*
<i>Hormonal measures</i>		
FSH (IU/L)	16.1 (11.7–22.2)	22.0 (19.2–25.2)
Oestradiol (pM)	210.9 (151.0–294.6)	163.6 (139.9–191.3)
SHBG (nM)	44.0 (38.6–50.1)	58.2 (54.2–62.4)**
Testosterone (nM)	1.2 (1.0–1.3)	1.2 (1.1–1.2)
Free androgen index	2.6 (2.3–3.1)	2.0 (1.8–2.2)*
DHEAS ($\mu\text{g}/\text{ml}$)	2.2 (1.9–2.6)	2.1 (2.0–2.3)
Insulin ($\mu\text{U}/\text{ml}$)	10.8 (9.1–12.9)	8.8 (8.2–9.4)*
Glucose/insulin ratio	0.55 (0.45–0.65)	0.58 (0.53–0.63)

*** $P < 0.0005$; ** $P < 0.005$; * $P < 0.05$ for the comparison of IFG and NFG groups.

higher and HDL cholesterol levels were lower in the women who prospectively developed IFG ($P < 0.05$). There was also a trend for diastolic blood pressure to be higher in the IFG group ($P = 0.07$).

Figure 1 illustrates the relationship between the development of IFG and BMI. BMI was divided into quintiles and the reported log odds ratios (95% confidence intervals) are relative to the middle category.

Table 3 shows the change in variables over the 5 y study period. There was a significant increase in mean BMI, trunk skinfold measures and waist circumference in both groups; the increase in BMI, after adjusting for initial measures, was greater ($P < 0.05$) in women who developed IFG. Mean SHBG concentrations fell and insulin and FAI concentrations increased in both groups with the changes only being

Table 2 Initial cardiovascular risk: a comparison of women who developed IFG with those who continued to have normal fasting glycaemia (NFG). Geometric means are given and their 95% confidence intervals in parentheses

Variable	Impaired fasting glycaemia	Normal fasting glycaemia
Triglycerides (mM)	1.01 (0.85–1.20)	0.81 (0.75–0.87)*
Total cholesterol (mM)	5.7 (5.4–6.0)	5.8 (5.7–5.9)
HDL-Cholesterol (mM)	1.44 (1.30–1.58)	1.63 (1.57–1.69)*
LDL-Cholesterol (mM)	3.7 (3.5–4.0)	3.7 (3.6–3.9)
Diastolic BP (mmHg)	77.4 (74.5–80.4)	74.6 (73.5–75.9)
Systolic BP (mmHg)	126.5 (122.0–130.7)	120.2 (118.8–122.4)*

* $P < 0.05$ for the comparison of IFG and NFG groups.

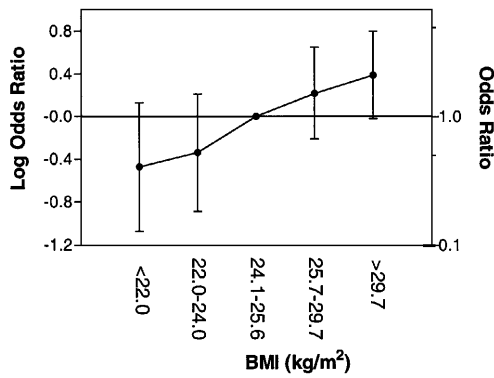


Figure 1 Relationship between the development of impaired fasting glycaemia and body mass index (BMI) (kg/m²). BMI is divided into quintiles. Log odds ratios (95% confidence intervals) are relative to the middle category.

significant in the IFG group. The change in insulin was greater in the IFG group compared with the normal glycaemic group ($P < 0.05$).

In both groups there were increases in serum triglycerides and total and LDL cholesterol over the study period ($P < 0.05$). There was a small decrease in HDL cholesterol in the IFG group, and an increase in HDL cholesterol in the normal glycaemic group (both N.S.). After adjusting for initial measures there was no difference in the changes in the serum lipid concentrations and blood pressure measures between the two groups over the 5 y period. Twenty-three percent of the women who prospectively developed IFG reported having a family history of diabetes compared with 15% of the normal glycaemic group ($P = 0.2$). There was no difference in exercise or smoking behaviours, or alcohol intake between the IFG or normal glycaemic groups.

Menopausal transition and IFG

Table 4 summarizes the percentage distribution of menopausal status for each group at initial measurement and follow-

Table 4 Menopausal status at baseline and after 5 y of follow-up. Number of women (%)

Menopausal status	Impaired fasting glycaemia		Normal fasting glycaemia	
	Initial	5 y follow-up	Initial	5 y follow-up
Premenopausal	20 (47%)	5 (11%)	90 (41%)	14 (6%)
Early perimenopausal	13 (30%)	2 (5%)	76 (34%)	24 (11%)
Late perimenopausal	6 (14%)	3 (7%)	43 (19%)	21 (9%)
Postmenopausal	4 (9%)	27 (63%)	13 (6%)	117 (53%)
Hormone therapy	—	6 (14%)	—	46 (21%)

up. There were no significant differences between the groups with regard to menopausal status or change in menopausal status. There was also no significant difference between the stages of the menopausal transition as regards to the onset of IFG.

Menopausal transition and insulin/glucose concentrations

Women who experienced a natural menopause ($n = 89$), that is changed from pre- or early perimenopausal to postmenopausal, were older at initial measurement ($P < 0.0005$) compared with women who remained pre- or perimenopausal ($n = 45$) over this period. Mean BMI and glucose concentrations increased significantly over the study period in both groups, as did insulin concentrations in women who experienced the natural menopause. There was no significant difference between the two groups for glucose and insulin concentrations or changes in these measures.

Multiple regression analysis found that changes in insulin were independent of age and whether the women remained pre- or early perimenopausal or experienced the natural menopause but were associated with initial BMI ($P = 0.05$) and change in BMI ($P < 0.05$).

Discussion

The 43 women (16%) who prospectively developed IFG were significantly different at the time of the initial normal glucose measurement in a number of variables to those

Table 3 Change in body composition measures and hormones after 5 y of follow-up: a comparison of women who developed impaired fasting glycaemia with those who continued to have normal fasting glycaemia. Geometric means are given and their 95% confidence intervals in parentheses

Variable	Impaired fasting glycaemia	P ^a	Normal fasting glycaemia	P ^a	Between-group difference p ^b
	Mean change (95% CI)		Mean change (95% CI)		
BMI (kg/m ²)	1.8 (1.1–2.6)	< 0.0005	0.9 (0.6–1.1)	< 0.0005	< 0.05
Suprailiac (mm)	3.8 (1.6–3.0)	< 0.005	4.1 (3.0–5.1)	< 0.0005	0.3
Subscapular (mm)	2.1 (0.2–3.9)	< 0.05	2.4 (1.5–3.3)	< 0.0005	0.5
Waist (cm)	4.5 (2.9–6.1)	< 0.0005	2.4 (1.6–3.2)	< 0.0005	0.08
Hip (cm)	1.0 (–0.5–2.6)	0.2	0.2 (–0.5–2.6)	0.8	0.5
SHBG (nM)	–9.6 (–14.6 to –4.6)	< 0.005	–4.5 (–8.4 to –0.6)	0.06	0.3
FAI	1.0 (0.3–1.7)	< 0.05	0.2 (–0.04–0.4)	0.3	0.2
Insulin (μU/ml)	2.5 (0.6–4.4)	< 0.05	0.5 (–0.1–1.1)	0.1	< 0.05

CI = confidence interval. BMI = body mass index. SHBG = sex hormone binding globulin.

^aP-value for initial vs follow-up (paired t-tests).

^bP-value for comparison of changes between groups adjusted for baseline measures.

who did not develop IFG. The women who developed IFG tended to exhibit the cluster of risk factors referred to as Syndrome X, that is a high level of body fatness, central adiposity, high insulin concentrations and dyslipidemia (high triglycerides and low HDL-cholesterol),¹³ factors that also put them at increased risk of cardiovascular disease.

Elevated triglyceride concentrations, low HDL-cholesterol and hypertension are associated with an increased risk of developing type 2 diabetes.¹⁴ Our women who developed IFG exhibited higher triglyceride, lower HDL-cholesterol concentrations and higher blood pressure than the women who remained normal glycaemic, although their actual mean values were not abnormal at this stage. However, mean BMI, one measure of body fatness, was in the overweight category in the IFG group and has been reported to be strongly associated with serum lipid levels and blood pressure.¹⁵ A high BMI is probably driving the development of other risk factors in this complex metabolic syndrome which precedes type 2 diabetes.

It is debatable as to whether a single fasting blood glucose concentration is useful as a screening tool for diabetes. Larsson *et al*¹⁶ reported that in a large homogeneous population of Swedish women a single fasting blood glucose was not a useful tool for the measurement of diabetes prevalence. One of the aims of our study was to identify Australian-born women with raised fasting glucose, which is a risk factor for the development of diabetes. We were not using fasting glucose as a diagnostic indicator of clinical diabetes. Stern and colleagues have reported that conventional cardiovascular risk factors can predict future diabetes at least as well as, and probably better than, impaired glucose tolerance tests.¹⁷

At initial measurement the women who prospectively developed IFG had lower SHBG concentrations and a higher free androgen index than women with NFG. This increased androgenicity probably predisposed them to increased triglyceride and lower HDL-cholesterol concentrations. The majority of women were either pre- or early perimenopausal at initial measurement, so the hormone findings were not related to menopausal status. SHBG levels have been reported to decline following the menopause^{18,19} and did so over the 5 y follow-up period in both IFG and NFG groups, the women with IFG experiencing a greater decrease over this period. Other studies have shown that low SHBG concentrations are a predictor of the development of type 2 diabetes in both pre- and postmenopausal women independent of other risk factors,^{20,21} perhaps via its relationship to insulin and weight.¹⁸

The increased insulin concentrations in the IFG group may be responsible for the decrease in the SHBG secretion and the resultant increased FAI. This is similar to the findings in women with polycystic ovary syndrome who are hyperinsulinaemic and it is hypothesized that this contributes to their increased androgenicity by insulin decreasing SHBG secretion from hepatocytes and therefore increasing the free fraction of androgens available for biological activity.²²

Oestrogen therapy has been reported to improve glucose metabolism in women with type 2 diabetes and this improvement was accompanied by an increase in SHBG, a decrease in free testosterone but no change in body weight or body fat.²³ The exact role of sex hormones and binding proteins in impaired glucose metabolism is still unclear. In our study there was no significant effect on IFG onset by hormone therapy commenced after the start of the study.

The mid-life period in women is associated with weight gain and a change in the distribution of body fat.⁶ The women who developed raised blood glucose concentrations had a significantly greater increase in their BMI than the normal glycaemic group and this no doubt accentuated the development of insulin resistance in this group. In our cohort the risk of developing IFG was associated positively with BMI, the lowest categories of BMI (<24 kg/m²) being associated with reduced risk compared to higher categories (>25.6 kg/m²), although the results were not significant. An unfavourable body fat distribution has been associated with an increased incidence of type 2 diabetes and waist/hip ratio has been reported to be a better single screening measure for type 2 diabetes risk than BMI, and some researchers suggest that waist measurements alone are best.²⁴ In our cohort waist, waist/hip ratio and skinfolds were so highly correlated with BMI that we cannot make such conclusions.

Type 2 diabetes is associated with a strong genetic predisposition²⁵ but this was not evident in our cohort. The genetics of type 2 diabetes are complex and have not been clearly defined. Sedentary behaviour has previously been reported to be associated with type 2 diabetes,²⁶ but was not demonstrated in our study. The women recruited into our longitudinal study were significantly more likely to exercise at least once per week compared with eligible non-participants of the original population-based sample.⁹ This may have reduced the incidence of IFG in the current cohort and is a limitation of this study.

The development of IFG did not appear to be associated with any particular phase of the menopausal transition or hormone therapy use. This is in agreement with Matthews *et al*,² but not with Poehlman and colleagues.⁵ In Poehlman's study the sample size was small—17 women remaining premenopausal and 18 experiencing the menopause. In our cohort increases in 5 y insulin concentrations were significantly and independently associated with increases in BMI and higher initial BMI levels.

In conclusion the 16% of our population who developed IFG during the menopausal transition exhibited significantly higher levels of body fatness and dyslipidemia, premenopausally, compared with the women who did not develop IFG. The menopause *per se* was not associated with an increase in glucose concentrations and effective interventions in the prevention of IFG are to be encouraged, particularly avoiding the increase in body weight that generally occurs in the mid-life years.

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References

- Manson JE, Colditz GA, Stampfer MJ, Willett WC, Krolewski AS, Rosner B, Arky RA, Speizer FE, Hennekens CH. A prospective study of maturity-onset diabetes mellitus and risk of coronary heart disease and stroke in women. *Arch Intern Med* 1991; **151**: 1141–1147.
- Matthews KA, Meilahn E, Kuller LH, Kelsey SF, Caggiula AW, Wing RR. Menopause and risk factors for coronary heart disease. *New Engl J Med* 1989; **321**: 641–646.
- Kissbah AH, Krakower GR. Regional adiposity and morbidity. *Physiol Rev* 1994; **74**: 761–811.
- Seidell JC, Bouchard C. Visceral fat in relation to health: is it a major culprit or simply an innocent bystander? *Int J Obes Relat Metab Disord* 1997; **21**: 626–631.
- Poehlman ET, Toth MJ, Gardner AW. Changes in energy balance and body composition at menopause: a controlled longitudinal study. *Ann Intern Med* 1995; **123**: 673–675.
- Guthrie JR, Dennerstein L, Dudley EC. Weight gain and the menopause: a 5-year prospective study. *Climacteric* 1999; **2**: 205–211.
- Colman PG, Thomas DW, Zimmet PZ, Welborn TA, Garcia-Webb P, Moore MP. New classification and criteria for diagnosis of diabetes mellitus. *Med J Aust* 1999; **170**: 375–378.
- Dennerstein L, Smith AMA, Morse C, Burger HG, Green A, Hopper J, Ryan M. Menopausal symptoms in Australian women. *Med J Aust* 1993; **159**: 232–236.
- Burger HG, Dudley EC, Hopper JL, Shelley JM, Green A, Smith A, Dennerstein L, Morse C. The endocrinology of the menopausal transition: a cross-sectional study of a population-based sample. *J Clin Endocrinol Metab* 1995; **80**: 3537–3545.
- Dudley EC, Hopper JL, Taffe J, Guthrie JR, Burger HG, Dennerstein L. Using longitudinal data to define the perimenopause by menstrual cycle characteristics. *Climacteric* 1998; **1**: 1–8.
- SPSS for Windows. *Statistical package for social sciences*, Version 8.0. SPSS Inc.: Chicago, IL; 1996.
- Tchernof A, Calles-Escandon J, Sites CK, Poehlman ET. Menopause, central body fatness, and insulin resistance: effects of hormone replacement therapy. *Coron Artery Dis* 1988; **9**: 503–511.
- Haffner SM, Valdez RA, Hazuda HP, Mitchell BD, Morales PA, Stern MP. Prospective analysis of the insulin resistance syndrome (Syndrome X). *Diabetes* 1992; **41**: 715–722.
- Haffner SM, Stern MP, Hazuda HP, Mitchell BD, Patterson JK. Cardiovascular risk factors in confirmed prediabetic individuals: does the clock for coronary heart disease start ticking before the onset of clinical diabetes? *JAMA* 1990; **263**: 2893–2898.
- Do KA, Green A, Guthrie JR, Dudley EC, Burger HG, Dennerstein L. A longitudinal study of risk factors for coronary heart disease across the menopausal transition. *Am J Epidemiol* 2000; **151**: 584–593.
- Larsson H, Ahren B, Lindgarde F, Berglund G. Fasting blood glucose in determining the prevalence of diabetes in a large, homogenous population of caucasian middle-aged women. *J Intern Med* 1995; **237**: 537–541.
- Stern MP, Morales PA, Valdez RA, Monterrosa A, Haffner SM, Mitchell BD, Hazuda HP. Predicting diabetes. Moving beyond impaired glucose tolerance. *Diabetes* 1993; **42**: 706–714.
- Bruschi F, Meschia M, Amicarelli F, Bologna E, Curtarelli M, Crosignani PG. Changes in sex hormone-binding globulin plasma concentrations induced by body weight and estrogen status in perimenopausal years. *Menopause* 1997; **4**: 28–31.
- Burger HG, Dudley EC, Cui J, Dennerstein L, Hopper JL. A prospective longitudinal study of serum testosterone, dyhydroepiandrosterone sulfate, and sex hormone-binding globulin levels through the menopause transition. *J Clin Endocrinol Metab* 2000; **85**: 2832–2838.
- Haffner SM, Valdez RA, Morales PA, Hazuda HP, Stern MP. Decreased sex hormone-binding globulin predicts non-insulin-dependent diabetes mellitus in women but not in men. *J Clin Endocrinol Metab* 1993; **77**: 56–60.
- Lindstedt G, Lundberg GA, Kitabchi AE, Wilmas JA. Low sex-hormone-binding globulin concentration as independent risk factor for the development of NIDDM: 12-year follow-up of population study of women in Gothenburg, Sweden. *Diabetes* 1990; **40**: 123–128.
- Taylor AE. Polycystic ovary syndrome. *Endo Metab Clin N Am* 1998; **27**: 877–901.
- Anderson B, Mattsson L, Hahn L, Marin P, Lapidus L, Holm G, Bengtsson B, Bjorntorp P. Estrogen replacement therapy decreases hyperandrogenicity and improves glucose homeostasis and plasma lipids in postmenopausal women with non insulin-dependent diabetes mellitus. *J Clin Endocrinol Metab* 1997; **82**: 638–643.
- James WP. The epidemiology of obesity. *CIBA Found Symp* 1996; **201**: 1–11.
- Barnett AH, Eff C, Leslie RDG, Pyke DA. Diabetes in identical twins: a study of 200 pairs. *Diabetologia* 1981; **20**: 87–93.
- Manson JE, Rimm EB, Stampfer MJ, Colditz GA, Willett WC, Krolewski AS, Rosner B, Hennekens CH, Speizer FE. Physical activity and incidence of non-insulin-dependent diabetes mellitus in women. *Lancet* 1991; **338**: 774–778.