

Disorders of Glucose Regulation in Adults and Birth Weight

Results from the Australian Diabetes, Obesity and Lifestyle (AusDiab) Study

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OBJECTIVE — The purpose of this study was to examine the association of birth weight with indexes of glycemia in a population-based survey.

RESEARCH DESIGN AND METHODS — A total of 10,788 participants in the Australian Diabetes, Obesity and Lifestyle (AusDiab) Study were asked to complete a birth weight questionnaire. Fasting plasma glucose (FPG), postload glucose (PLG), and A1C were modeled against birth weight. World Health Organization criteria were used to define impaired fasting glucose (IFG), impaired glucose tolerance (IGT), and diabetes.

RESULTS — Among 7,157 participants who responded to the questionnaire, 4,502 reported their birth weights, with a mean \pm SD of 3.4 ± 0.7 kg. FPG, PLG, and A1C were strongly and inversely correlated with birth weight. The odds ratios (95% CI) for high (>90th sex-specific percentile) FPG, PLG, and A1C were 0.83 (0.71–0.96), 0.74 (0.65–0.84), and 0.81 (0.70–0.94), respectively, for a 1-kg increase in birth weight after adjustment for age and sex. In those with low birth weight (LBW), the risks for having IFG, IGT, and diabetes and for all abnormalities combined were increased by 1.75, 2.22, 2.76, and 2.28, respectively, for women and by 1.40, 1.32, 1.98, and 1.49 for men compared with risks for those with normal birth weight. These trends applied across categories of age and BMI.

CONCLUSIONS — In an affluent Western country with a good adult health profile, birth weight has an inverse relationship with indexes of glycemia, and individuals with LBW were predisposed to higher rates of glycemic dysregulation in adult life. These associations were independent of BMI and of other factors significantly correlated with glycemic dysregulation.

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Type 2 diabetes is increasing worldwide, and it is becoming more common at younger ages. The Australian Diabetes, Obesity and Lifestyle (AusDiab) Study during 1999–2000 reported that

the prevalence of diabetes in the Australian population aged ≥ 25 years was 7.4% (8.0% for men and 6.8% for women) (1). Rates rose from 2.4% in individuals aged 35–44 years to 23.0% in those aged > 75

years (1). The prevalence of abnormal glucose metabolism (impaired glucose tolerance [IGT] or impaired fasting glycaemia [IFG]) in the population was 16.4% (17.3% for men and 15.3% for women) (1).

In recent decades, researchers have reported an association between low birth weight (LBW) and increased risk of type 2 diabetes and earlier onset of type 1 diabetes during adulthood. It is proposed that inadequate nutrition programs the fetus to develop resistance to insulin-stimulated uptake of glucose in later life (2–5). These studies, however, were performed in selected populations, based on geographical location, ethnicity, and/or professional status. None have looked at the phenomenon in a general adult population.

Some researchers had criticized the fetal origin hypothesis on the grounds that many study findings may chiefly reflect the impact of random error, selective emphasis of particular results, and inappropriate adjustment for current weight and for confounding factors (6). In addition, some results were not reported separately for women and men (2). Taking these factors into consideration, we evaluated the relationship between birth weight and indexes of glycemia in the general population of Australia.

RESEARCH DESIGN AND METHODS

The AusDiab Study is a population-based study in which baseline data on 11,247 participants were collected in 1999–2000 (7). Participants were recruited from a stratified sample of Australians aged ≥ 25 years, residing in 42 randomly selected urban and nonurban areas (Census Collector Districts) of the six states of Australia and the Northern Territory (7). In 2004–2005 a 5-year follow-up survey was conducted. All eligible participants ($n = 10,788$) who had been included in the baseline survey were invited back for retesting. Those who were ineligible for invitation ($n = 459$) included individuals who either requested no further contact, were known to be deceased, or were too ill or had

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Abbreviations: AusDiab, Australian Diabetes, Obesity and Lifestyle; FPG, fasting plasma glucose; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; LBW, low birth weight; NBW, normal birth weight; PAR%, population-attributable risk percentage; PLG, postload glucose.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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moved into a nursing facility classified as high care. The study was approved by the ethics committee of the International Diabetes Institute. Informed consent for the study was obtained from all participants.

During the 2004–2005 follow-up AusDiab Study survey, questions about birth weight were included. Participants were asked to state their birth weight, the likely accuracy of their stated birth weight, and the source of their stated birth weight.

Detailed methodology of the 1999–2000 AusDiab Study was discussed in a previous article (7). In brief, blood was collected by venipuncture after an overnight fast of at least 10 h. Specimens were collected into a fluoride/oxalate tube for plasma glucose and an EDTA tube for A1C.

All participants, except those who were pregnant, those who failed to fast, or those with known diabetes who were taking oral hypoglycemic medication and/or insulin, were given a 300-ml drink of 75 g glucose (Bicorp Australia, Victoria, Australia) to be consumed within 5 min. A second blood sample was taken by venipuncture to determine plasma glucose 2 h after the glucose load. Plasma glucose was determined enzymatically (Olympus AU600; Olympus Optical, Tokyo, Japan). Total A1C analysis was performed by high-performance liquid chromatography (Bio-Rad Variant Hemoglobin Testing System; Bio-Rad, Hercules, CA) with standardized conversion to A1C values (normal 4.2–6.3%). Fasting insulin was measured in participants aged ≥ 35 years because there is a lower risk of insulin resistance in those aged < 35 years.

World Health Organization criteria were used to define IFG, IGT, and diabetes. Fasting plasma glucose (FPG), post-load glucose (PLG), and A1C levels were considered to be “high” if they were greater than the sex-specific 90th percentile. For women, the values were > 6.0 mmol/l, > 8.3 mmol/l, and $> 5.6\%$ for FPG, PLG, and A1C, respectively. For men, values were > 6.4 mmol/l, > 8.4 mmol/l, and $> 5.5\%$ for FPG, PLG, and A1C, respectively.

Birth weights were recorded in pounds and ounces or in kilograms and grams. All values were converted to kilograms for analyses. LBW was defined as birth weight < 2.5 kg. Participants were also divided into sex-specific birth weight quintiles for further categorical analyses. BMI groups were classified according to World Health Organization criteria (8) as

follows: normal < 25.0 kg/m², overweight 25–29.9 kg/m², and obese ≥ 30.0 kg/m².

An interviewer-administered questionnaire was used to determine family history of diabetes, smoking (current, ex-smoker, or nonsmoker), alcohol consumption (kilojoules per day) (9), leisure-time physical activity, and television viewing (10). Assessment of socioeconomic status was based on education (11), type of dwelling (house owners versus not house owners), and income (11).

Statistical analysis

Student's *t* test was used to assess unadjusted associations between LBW and variables that were normally distributed. For variables that were not normally distributed, logarithmic transformations were made, and geometric means and their 95% CIs were calculated. Associations of birth weight with continuous outcome variables were assessed using multivariate regression analyses. Outcome variables were also categorized as high if they were > 90 th sex-specific percentile. The strength of the relationship between birth weight and those dichotomous outcome variables was assessed through logistic regression. Risk factors for diabetes such as age, BMI, physical activity, smoking status, alcohol intake, family history of diabetes (mother/father), and socioeconomic status (education, income, and dwelling type) were adjusted for in the evaluation of the relationship between birth weight and indexes of glycemia. For the population-attributable risk percentage (PAR%) calculations, those with birth weight < 2.5 kg were regarded as exposed. The PAR% represents the proportion of outcomes (IFG, IGT, and diabetes) in the whole population that might be preventable if all individuals in the population had a birth weight ≥ 2.5 kg. Stata for Windows (version 9) was used for statistical analyses. Significance was considered at $P < 0.05$.

RESULTS — Of the 10,788 individuals eligible to participate in the 2004–2005 follow-up AusDiab Study who were requested to respond to the birth weight questionnaire, 7,157 (66.3%) responded. Of these, 4,502 reported a value for their birth weight, with the others unable to give a value. These birth weights were linked to the findings of the 1999–2000 study.

More than 90% of respondents who reported a birth weight considered it to be

“accurate”, and only 6% mentioned that their birth weight was based on a “guess.” Among those who reported their birth weight, 80% obtained their birth weight from a family member (67% of participants had a living natural mother, and 46% had a living natural father) and 10% obtained their birth weight from medical records. Reported birth weights ranged from 0.4 to 7.0 kg with a mean \pm SD of 3.37 ± 0.7 kg, which was similar whether birth weight was obtained from family members or from medical records (3.35 ± 0.6 vs. 3.37 ± 0.7 kg; after adjustment for age and sex, $P = 0.36$). Mean birth weight was lower for women (3.3 ± 0.7 kg) than for men (3.5 ± 0.7 kg). The prevalence of LBW (< 2.5 kg) was 8.0% (9.1% in women and 6.1% in men); 1% had a birth weight < 1.5 kg and $< 1\%$ had a birth weight ≥ 5 kg.

Birth weight, A1C, and BMI were approximately normally distributed, whereas logarithmic transformation was used for analysis of FPG and PLG. These data were available for 2,603 and 1,745 women and men, respectively. Participants who did not have these sets of factors were excluded from the analysis with adjustments, but all were included in the crude analysis.

Supplementary Table 1 (available in an online appendix at <http://dx.doi.org/10.2337/dc07-1170>) shows a comparison of those who reported their birth weight and those who did not. Women were more likely to report their birth weight. Women and men who reported their birth weight were younger, taller, and less likely to have glycemic dysregulation and diabetes than those who did not report their birth weight.

Table 1 shows the distribution of birth weight by quintiles for both women and men. Women and men in the lowest birth weight quintile had higher mean FPG, PLG, and A1C levels than those in higher birth weight quintiles. These differences persisted even when participants were stratified by BMI or by age-group (data not shown). Neither J-shaped nor U-shaped relationships were observed. However, when the upper quintile was divided into more categories, as shown in supplementary Fig. 1, there was a reversed J-shaped relationship that was more obvious for women. Table 1 shows that in women, the proportions with IGT and diabetes and the proportion for all abnormalities combined (including IFG, IGT, and diabetes) were significantly higher in the lowest birth weight quintile

Table 1—FPG, PLG, and A1C and the proportion of IFG, IGT, and diabetes by birth weight quintiles

	Women birth weight quintile					P
	<2.81 kg	2.81–3.18 kg	3.19–3.40 kg	3.41–3.72 kg	>3.72 kg	
n	546	637	526	466	536	
FPG	5.44 (5.37–5.51)	5.34 (5.27–5.42)	5.28 (5.20–5.36)	5.28 (5.19–5.36)	5.28 (5.19–5.37)	0.004
PLG	6.41 (6.25–6.57)	6.10 (5.94–6.27)	5.93 (5.75–6.11)	5.87 (5.68–6.06)	5.97 (5.77–6.17)	<0.001
A1C	5.21 (5.17–5.24)	5.09 (5.05–5.13)	5.07 (5.03–5.12)	5.07 (5.02–5.11)	5.07 (5.02–5.11)	<0.001
IFG	0.05 (0.03–0.07)	0.04 (0.02–0.06)	0.04 (0.02–0.06)	0.03 (0.02–0.05)	0.03 (0.02–0.05)	0.165
IGT	0.16 (0.13–0.20)	0.13 (0.10–0.15)	0.09 (0.07–0.12)	0.10 (0.08–0.14)	0.10 (0.08–0.13)	0.004
Diabetes	0.09 (0.06–0.12)	0.07 (0.05–0.09)	0.04 (0.02–0.06)	0.05 (0.03–0.07)	0.04 (0.03–0.07)	0.006
All*	0.25 (0.21–0.29)	0.20 (0.17–0.24)	0.15 (0.12–0.18)	0.17 (0.13–0.20)	0.15 (0.13–0.18)	<0.010

	Men birth weight quintile					P
	<3.06 kg	3.06–3.36 kg	3.37–3.63 kg	3.64–4.04 kg	≥4.05 kg	
n	364	355	408	311	353	
FPG	5.81 (5.75–5.95)	5.71 (5.60–5.82)	5.67 (5.58–5.76)	5.64 (5.53–5.74)	5.62 (5.53–5.71)	0.059
PLG	6.48 (6.20–6.77)	6.04 (5.78–6.30)	6.03 (5.79–6.26)	6.01 (5.75–6.26)	5.83 (5.62–6.04)	0.016
A1C	5.28 (5.21–5.35)	5.23 (5.16–5.29)	5.18 (5.11–5.24)	5.17 (5.11–5.23)	5.19 (5.13–5.23)	0.061
IFG	0.15 (0.11–0.19)	0.10 (0.07–0.14)	0.11 (0.08–0.15)	0.08 (0.06–0.12)	0.09 (0.07–0.13)	0.049
IGT	0.13 (0.09–0.17)	0.11 (0.08–0.15)	0.11 (0.08–0.15)	0.08 (0.05–0.11)	0.12 (0.09–0.16)	0.495
Diabetes	0.14 (0.10–0.19)	0.07 (0.05–0.11)	0.06 (0.04–0.10)	0.07 (0.04–0.11)	0.09 (0.06–0.13)	0.011
All*	0.32 (0.27–0.37)	0.24 (0.20–0.28)	0.24 (0.20–0.29)	0.20 (0.16–0.25)	0.26 (0.21–0.30)	0.010

Data are means (95% CI). *Includes IFG, IGT, and diabetes.

compared with those in the higher birth weight quintiles. In men, the proportions with IFG and diabetes and the proportion for all abnormalities combined were significantly higher in the lowest birth weight quintile compared with those in the higher birth weight quintiles.

When we use the traditional definition of LBW (<2.5 kg), as shown in supplementary Table 2, women and men with LBW had higher mean FPG, higher mean PLG, and higher mean A1C than those with normal birth weight (NBW) (≥2.5 kg). In women, the proportions with IGT and diabetes and the proportion for all abnormalities combined were significantly higher in those with LBW than in those with NBW. In men, the proportions for diabetes were significantly higher in those with LBW than in those with NBW.

Table 2 shows the odds ratios (OR) and 95% CI for high FPG, high PLG, and high A1C among individuals with LBW relative to those with NBW. Individuals with LBW were at higher risk for having high FPG, high PLG, and high A1C compared with those with NBW. In those with LBW, the risks for having IFG, IGT, diabetes, and all abnormalities combined were increased by 1.75, 2.22, 2.76, and 2.28 for women and by 1.40, 1.32, 1.98, and 1.49 for men compared with those with NBW, respectively. The same rela-

Table 2—Sex-specific glycemic indexes and categories of glucose intolerance in individuals with LBW (<2.5 kg) compared with those with NBW (≥2.5 kg)

	n	Women		Men	
		OR (95% CI)	P	OR (95% CI)	P
High FPG	392				
Unadjusted		2.15 (1.53–3.02)	<0.001	1.74 (1.06–2.86)	0.030
Adjusted*		2.01 (1.30–3.08)	0.002	1.89 (0.99–3.08)	0.101
High PLG	609				
Unadjusted		2.29 (1.70–3.08)	<0.001	1.64 (1.00–2.69)	0.052
Adjusted*		2.24 (1.54–3.25)	<0.001	1.69 (0.96–3.08)	0.102
High A1C	474				
Unadjusted		2.45 (1.78–3.35)	<0.001	1.59 (0.92–2.35)	0.123
Adjusted*		1.86 (1.24–2.85)	0.005	1.55 (0.90–2.61)	0.104
IFG	239				
Unadjusted		1.75 (0.91–3.37)	0.094	1.40 (0.77–2.63)	0.202
Adjusted*		1.82 (0.82–4.04)	0.114	1.79 (0.87–3.70)	0.113
IGT	447				
Unadjusted		2.22 (1.57–3.14)	<0.001	1.32 (0.94–2.37)	0.236
Adjusted*		1.89 (1.22–2.90)	0.004	1.37 (0.76–3.01)	0.224
Diabetes	254				
Unadjusted		2.76 (1.75–4.35)	<0.001	1.98 (1.07–3.68)	0.031
Adjusted*		2.52 (1.39–4.52)	0.001	2.13 (0.96–4.23)	0.054
All†	940				
Unadjusted		2.28 (1.72–3.01)	<0.001	1.49 (0.99–2.26)	0.058
Adjusted*		2.07 (1.44–2.97)	<0.001	1.70 (1.02–2.82)	0.040

High values represent >90th sex-specific percentile. *Adjusted for age, BMI, physical activity (based on time spent on exercise and watching television), smoking, alcohol intake, socioeconomic status, and family history of diabetes. Because of missing data, multivariate analyses were based on 2,603 of the 2,711 women and 1,745 of the 1,791 men. †Includes IFG, IGT, and diabetes.

Table 3—IFG, IGT, and diabetes by birth weight quintiles

	Women (birth weight quintile)				
	<2.81 kg	2.81–3.18 kg	3.19–3.40 kg	3.41–3.72 kg	>3.72 kg
<i>n</i>	546	637	526	466	536
IFG					
Unadjusted	1.76 (1.01–3.67)	1.27 (0.80–2.69)	1.42 (0.67–3.03)	1.37 (0.69–2.96)	1.0
Adjusted*	2.49 (1.02–5.91)	1.79 (0.72–4.41)	1.94 (0.78–4.63)	1.23 (0.44–3.43)	1.0
IGT					
Unadjusted	1.73 (1.17–2.53)	1.31 (0.87–1.96)	0.86 (0.58–1.33)	1.03 (0.67–1.58)	1.0
Adjusted*	1.86 (1.18–2.94)	1.66 (1.05–2.62)	0.99 (0.60–1.64)	1.04 (0.61–1.76)	1.0
Diabetes					
Unadjusted	2.05 (1.15–3.60)	1.65 (0.94–2.88)	0.82 (0.41–1.57)	1.05 (0.55–2.01)	1.0
Adjusted*	2.70 (1.34–5.44)	2.08 (1.01–4.29)	0.96 (0.42–2.17)	1.30 (0.56–3.04)	1.0

	Men (birth weight quintile)				
	<3.06 kg	3.06–3.36 kg	3.37–3.63 kg	3.64–4.04 kg	≥4.05 kg
<i>n</i>	364	355	408	311	353
IFG					
Unadjusted	1.69 (1.01–2.82)	1.05 (0.61–1.85)	1.23 (0.73–2.06)	0.87 (0.48–1.56)	1.0
Adjusted*	2.17 (1.19–3.96)	1.30 (0.69–2.45)	1.53 (0.84–2.798)	1.12 (0.58–2.17)	1.0
IGT					
Unadjusted	0.95 (0.56–1.52)	0.85 (0.52–1.40)	0.87 (0.54–1.41)	0.62 (0.35–1.06)	1.0
Adjusted*	1.28 (0.86–2.26)	1.13 (0.60–2.12)	0.97 (0.54–1.75)	0.98 (0.52–1.86)	1.0
Diabetes					
Unadjusted	1.63 (0.97–2.74)	0.79 (0.44–1.44)	0.69 (0.38–1.25)	0.74 (0.39–1.38)	1.0
Adjusted*	2.38 (1.30–7.72)	1.09 (0.56–2.14)	0.76 (0.39–1.50)	1.01 (0.50–2.02)	1.0

Data are ORs (95% CI). *Adjusted for age, BMI, physical activity (based on time spent on exercise and watching television), smoking status, alcohol intake, socioeconomic status, and family history of diabetes. Because of missing data, multivariate analyses were based on 2,603 of the 2,711 women and 1,745 of the 1,791 men.

tionship persisted with examination by birth weight quintiles as shown in Table 3, in which women in the lowest birth weight quintile had ORs of at least 1.76, 1.73, and 2.05 for IFG, IGT, and diabetes, respectively, compared with the referent group, with birth weight ≥3.72 kg. Men in the lowest birth weight quintile had ORs of 1.69 and 1.63 for IFG and diabetes, respectively, compared with the referent group, with birth weight ≥4.05 kg. The risk remained similar when participants were categorized by BMI and age (data not shown). From point estimates, there appear to be reversed J-shaped relationships for diabetes. However, the CIs for the higher birth weight categories overlapped.

FPG, PLG, and A1C were strongly and inversely correlated with birth weight. The ORs (95% CI) for high (>90th sex-specific percentile) FPG, PLG, and A1C were 0.83 (0.71–0.96), 0.74 (0.65–0.84), and 0.81 (0.70–0.94), respectively, for a 1-kg increase in birth weight after adjustment for age and sex. In women, the PAR% values (95% CI) of LBW for IFG, IGT, and diabetes were 7.3% (–5.1 to 18.3), 8.9% (4.2–

13.4), and 13.5% (5.3–21.0), respectively. In men, the PAR% values of LBW for IFG, IGT, and diabetes were 3.5% (–1.7 to 8.0), 1.9% (–2.3 to 6.6), and 4.8% (–0.01 to 10.4), respectively. These values were not significantly changed when adjustments were made for various confounders.

CONCLUSIONS— This is the first report of the influence of birth weight on risk factors for and the prevalence of diabetes and other disorders of glucose regulation in a general population. An inverse association was identified between birth weight and IFG, IGT, and diabetes. This association applied to analyses of unadjusted data and remained with adjustment for age, sex, current body size, and other covariates, including physical activity, smoking, alcohol intake, family history of diabetes, and current socioeconomic status.

To our knowledge, no other study has examined the relationship of birth weight with all indexes of glycemia in a national adult population, describing sex differences and considering various other potentially important factors. We examined

a comprehensive set of markers of glucose regulation, including FPG, PLG, and A1C, as well as categorical definitions of glucose dysregulation, all of which are important in terms of cardiovascular disease.

On a population level, the effect of a birth weight <2.5 kg on the development of IFG, IGT, and diabetes was different for women and men. In women, the PAR% for diabetes was 13.5%, whereas for men it was 4.8%. This discrepancy between sexes might be related to central adiposity in our women with LBW (unpublished data) and the fact that women throughout life are intrinsically more insulin resistant than men (12). PAR% for diabetes was reported to be 5% for the Nurses' Health Study (13), by definition a professional group, which is lower than that reported in our population-based study. In the Male Health Professional Study, the PAR% for diabetes was 4%, which is very similar to our reported rate for men (13).

An inverse relationship between birth weight and glycemic dysregulation has been reported in a number of studies worldwide (2). A few studies

have suggested an association between high birth weight and type 2 diabetes. A reversed J-shaped association between birth weight and diabetes was found in the Nurses' Health Study (4). A longitudinal study in Helsinki of individuals with type 2 diabetes showed that babies with birth weights >3.5 kg who also had slow growth in length between birth and 3 months of age had a significantly increased risk of later development of type 2 diabetes (14). In addition, studies in Pima Indians (5) and Taiwanese school children (15) showed U-shaped associations between birth weight and type 2 diabetes. Our study showed a reversed J-shaped relationship for diabetes when point estimates were considered, as shown in Table 3, and a similar relationship when means (95% CI) were examined for high birth weight (≥ 4.5 kg) (supplementary Fig. 1).

Obesity is the strongest known risk factor for type 2 diabetes. Studies have variously suggested roles for excessive weight gains both in childhood and in adult life (16,17). However, our data indicate a significant role for birth weight as well, with its own independent significance. The Life Course hypothesis provides a conceptual framework for the modulation of risk by interactions between effects of birth weight and patterns of postnatal weight gain, as well as other factors (17,18).

Our study used a self-recall questionnaire to obtain birth weight data. We opted for this method of obtaining birth weight because there are no readily available data banks of birth weights that cover the AusDiab Study population. Many seminal studies that have reported associations of birth weight with adult health have used this technique (3,4,19–21). The British Telecom Study had a 50% response rate, and only 39.4% provided data on birth weight (19); the British Women's Heart and Health Study had a 60% response rate, and 33% reported their birth weight (20,21); and the Health Professional Follow-up Study (HPFS) had a 75% response rate, and 59% of the responders reported their birth weight (3).

In our study, individuals who did not respond to the questionnaire and those who could not recall their birth weight were older and had higher rates of diabetes than those who reported a birth weight. Hence, overstatement of an exacerbating effect of lower birth weights on glycemic dysregulation in our study group is not a major concern. Among birth weight respondents it is reassuring

that the mean birth weight of those who guessed their birth weight was similar to that for those who obtained their birth weights from medical records or from a family member. This was also the case in the British Telecom Study (19). In addition, the mean recalled birth weight in our study (3.37 ± 0.7 kg) is consistent with that reported in those born between 1931 and 1939 in Hertfordshire in the U.K. (22) for the Health Professional Follow-up Study (3) and similar to the recent average Australian birth weight of 3.36 kg (23).

The effects of potential inaccuracies in birth weight recall have been discussed in reports of the Nurses' Health Study (4,17) and the Health Professional Follow-up Study (3). In our study, most sources of bias should not lead to overstatement of the risks associated with lower birth weights. Tendencies of individuals with the highest and lowest birth weights to understate the extremes of their birth weights will lead to underestimates of risk. Biases driven by a known diagnosis of type 2 diabetes will have various effects. More accurate recall of higher birth weights (a heavy baby) will lead to an underestimate of risk, whereas more accurate recall of lower birth weights by those with a diabetes diagnosis might lead to overstatement of risk. The latter scenario, which is conjectural, cannot be defended or refuted further, but, unlike the "heavy baby" scenario, LBW is not generally embedded in public consciousness as an antecedent of diabetes.

Our results indicate that lower birth weights increase risk for glycemic dysregulation later in life, even in a Westernized country with one of the world's healthiest populations. Birth weights in mainstream Australia are now as high as anywhere in the western world; ~6% of infants are LBW (<2.5 kg), ~10% are small for gestational age, and ~6% are premature. Although there is always room to reduce intrauterine growth retardation by improved antenatal care and influencing health behaviors (such as eliminating smoking), the overall public health impact of lower birth weights on adult health is probably not a major concern. Nonetheless, it is important that the pathophysiological principle can be documented in such a context. The fate of the increasing numbers of survivors of very LBW associated with prematurity in all Western countries is, however, potentially of concern. This phenomenon has more potential implications in developing countries and high-risk populations,

where birth weights are lower, compatible with smaller adult stature, where intrauterine growth retardation is often superimposed, and where improving infant mortality is allowing lower birth weight infants to increasingly survive to adult life. In all populations, a secular trend toward higher levels of body fat and BMI potentially compounds the potentiation and expression of glycemic abnormalities associated with lower birth weights. Modest increases in body fat might have a trivial impact on the burden of glycemic abnormalities when acting in isolation but a substantial impact when other risk factors are also operating. In all instances, it would be prudent to adopt policies of intensified whole-of-life surveillance for individuals of lower birth weight, anticipating this risk.

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