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Metabolic Syndrome in Very Low Birth Weight Young Adults and Controls: The New Zealand 1986 VLBW Study

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Objective To assess the physical well-being and components of the metabolic syndrome in a national cohort of very low birth weight (VLBW) young adults and same age controls.

Study design The New Zealand VLBW Study cohort prospectively included all infants with birth weight <1500 g born in 1986, with 338 (82%) surviving to discharge home. Height and weight were measured at age 7-8 years. The VLBW cohort (n = 229; 71% alive) and term-born controls (n = 100) aged 27-29 years were clinically assessed in a single center over 2 days, including assessment for components of the metabolic syndrome.

Results Compared with controls, both male and female VLBW adults were significantly shorter ($P < .001$), but only females were lighter ($P < .001$) and had lower mean body mass index ($P = .044$), fat mass, and body fat percentage. Males, but not females, had significantly higher systolic blood pressure ($P = .028$), but there were no significant differences in other components of the metabolic syndrome. There was no difference in the prevalence of the metabolic syndrome in VLBW adults compared with controls (males, 22.2% vs 11.1%; $P = .15$: females, 12.8% vs 13.1%; $P = .95$). Examining the VLBW cohort with logistic regression, male sex, gestational age <28 weeks, Māori/Pacific Island ethnicity, and body mass index >90th percentile at age 7-8 years were significant predictors for the metabolic syndrome at age 27-29 years, with ORs of 2-4.

Conclusions Systolic blood pressure in males was the only component of the metabolic syndrome that was significantly elevated in VLBW adults compared with controls. Extreme prematurity (<28 weeks) and body mass index >90th percentile at age 7-8 years were significant predictors of the metabolic syndrome at age 27-29 years. *(J Pediatr 2019;206:128-33).*

Trial registration Registered at the Australian Clinical Trials Registry: ACTRN12612000995875.

In the now-classic studies of Barker et al, smaller size at birth in predominantly term-born infants was reported to be associated with increased of risk of coronary heart disease in adulthood compared with contemporary births with higher birth weight.[1] Many subsequent studies addressing the "developmental origins of adult disease" have identified other adverse health outcomes associated with smaller size at birth, as well as the important contributions to the risk of these outcomes from nutritional, growth, and other factors in early childhood.[2] Both preterm birth and intrauterine growth retardation are associated with smaller size at birth, and both have also been associated with elevated blood pressure (BP) and other features of the metabolic syndrome in early adulthood.[3] However, there is a lack of consensus about the relative impact of small for gestational age status, prematurity, and antenatal corticosteroid use on metabolic and cardiovascular outcomes in adulthood.[3-5] Relatively few studies have focused specifically on very preterm (<32 weeks of gestation) or very low birth weight (VLBW; <1500 g) infants, and fewer still have been population-based.[6-13]

The population-based New Zealand VLBW Study cohort included all VLBW infants born in 1986 and admitted to a neonatal unit and subsequently followed up in childhood and as young adults.[14] The objectives of the present study were to assess growth, BP, and other components of the metabolic syndrome in the VLBW cohort and term-born controls at age 27-29 years. We hypothesized that compared with their same age full-term peers, adults born VLBW will have poorer growth (height), elevated BP, and elevated metabolic risk factors, and that in the VLBW cohort growth measures at age 7-8 years would be predictive for the metabolic syndrome in young adulthood.

Methods

In 1986, all 413 VLBW infants born in New Zealand and admitted to a neonatal unit of any level were prospectively enrolled in an audit of retinopathy of

BMI	Body mass index
BP	Blood pressure
ELBW	Extremely low birth weight
HOMA-IR	Homeostasis model assessment of insulin resistance
VLBW	Very low birth weight

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prematurity, with 338 (82%) surviving to discharge home.[14] At birth, gestational age was recorded, based on menstrual history and antenatal ultrasound before 20 weeks if available and on neonatal examination otherwise. The cohort was followed up at age 7-8 years, when height and weight were obtained,[15] and by questionnaire at age 22-23 years.[14] For the present study, when participants were age 27-29 years, 250 members of the VLBW cohort (77% of 323 known survivors) consented to follow-up, and 229 (71%) were seen in 1 center (Christchurch) for 2 days of assessments over the period February 2013 to June 2016 (**Figure**; available at www.jpeds.com). A control group of 100 subjects born healthy at full term in New Zealand in 1986 was first recruited when the VLBW cohort was age 22-23 years, through a process of peer nomination by a cohort member or via random sampling from the electoral rolls, aiming to ensure balance with respect to sex, ethnicity, and regional distribution.[14] Birth weight (or estimated birth weight) was the only other perinatal or childhood data available from controls.

At the age 27-29 year assessment, the participant interview included questions on history of tobacco use, previous diagnosis of diabetes or hypertension, and/or use of prescribed medications for these conditions. Investigations relevant to the metabolic syndrome included anthropometric measurements (height with a Harpenden stadiometer, weight, body mass index [BMI], waist-to-hip ratio [waist circumference measured at the narrowest point between the lower costal border and the top of the iliac crest, hip circumference measured at the widest part of buttocks or hip]),[16] BP (third manual reading measured in the nondominant arm while seated), total body fat (estimated by bioelectrical impedance analysis), and, following an overnight fast, standard laboratory tests for plasma glucose and free insulin, lipid screen (cholesterol, triglycerides, high-density lipoprotein cholesterol, total cholesterol), and hemoglobin A1c.

Using fasting insulin and glucose measurements, we calculated estimated insulin resistance from the homeostasis model assessment of insulin resistance (HOMA-IR) using the following formula: fasting glucose (mmol/L) × fasting insulin (μU/mL)/22.5.[17] Internationally accepted criteria were used to identify the metabolic syndrome (**Table I**; available at www.jpeds.com).[18] BMI percentile at age 7-8 years was calculated using the Centers for Disease Control and Prevention's online calculator (https://www.cdc.gov/healthyweight/bmi/calculator.html).

Between-group comparisons were tested for statistical significance using the independent-samples *t* test for comparison of means and the χ^2 test for comparison of percentages. Mean between-group differences in metabolic outcomes were adjusted for sex and ethnicity as appropriate using multiple regression methods. Triglycerides and HOMA-IR data were also analyzed using a log10 transformation to account for nonnormality. The risk of the metabolic syndrome was modeled using logistic regression, with additional checks for sex and ethnicity by risk factor interactions, and effect size was summarized by OR and associated 95% CI. $P < .05$ was taken to indicate statistical significance. With 229 VLBW and 100 controls, the study had 80% power at $\alpha_2 = 0.05$ to detect a mean between-group difference >0.34 SD. For subgroup comparisons (eg, by sex), the corresponding effect size estimates ranged between 0.43 and 0.55 SD. For analysis of the metabolic syndrome within the VLBW cohort, the study had 80% power to detect ORs of 2.7-4.3, depending on the base rate of the risk factor in controls.

The study was approved by the Southern Health and Disability Ethics Committee, and all participants gave written informed consent.

Results

Table II (available at www.jpeds.com) presents demographic and perinatal data for the subjects in the VLBW cohort who were assessed and those who were not assessed, as well as for controls. The mean age of assessment was similar in the VLBW cohort and controls. There were proportionally more males and those identifying as Māori or Pacific Island ethnicity in the VLBW cohort compared with controls, although the differences were not statistically significant. In the VLBW cohort, birth weight was lower in the survivors who were assessed compared with those who were not assessed. Fewer subjects in the cohort with moderate or severe disability at age 7-8 years were assessed than were not assessed at age 27-29 years, but the numbers in each group were small.

Table III shows growth and body composition for the VLBW cohort and controls by sex. The VLBW cohort were significantly shorter than controls (by 4-5 cm), but only females were lighter (by 10 kg), and BMI was significantly lower only in females. Body fat percentage, fat mass, and fat-free mass were all significantly lower in female VLBW participants compared with controls, but only fat-free mass was significantly lower in males. The percentage of VLBW young adults with obesity (BMI >30) was 25.6% in females and 21.8% in males, compared with 34.4% and 25.0%, respectively, in controls. **Table IV** (available at www.jpeds.com) presents the same data adjusted for ethnicity, which produced minor changes in the size of some estimated mean differences but no changes in significance.

Systolic BP was significantly higher in VLBW young adults compared with controls (mean ± SD, 113.8 ± 12.6 mmHg vs 109.2 ± 10.5 mmHg; mean difference, 4.6 mmHg; 95% CI, 1.8-7.5 mmHg; $P = .002$), whereas diastolic BP was similar in the 2 groups (mean, 73.9 ± 9.4 mmHg vs 72.4 ± 8.7 mmHg; mean difference, 1.5 mmHg; 95% CI, -0.6 to 3.7 mmHg; $P = .17$). As shown in **Table V** (available at www.jpeds.com), a significant difference in systolic BP was seen only in males. These conclusions were unaltered when the data were adjusted for ethnicity. Five VLBW subjects, but no controls, were receiving antihypertension medication. More VLBW adults than controls had a systolic BP ≥130 mmHg or diastolic BP ≥85 mmHg or were taking medication (18.2% vs 8.0%; $P = .02$).

Tables VI and **VII** (available at www.jpeds.com) compare lipid, glucose, and insulin levels between the VLBW cohort and controls. Four subjects (3 VLBW, 1 control) either did not consent to blood testing or did not undergo a blood draw, and another 4 subjects (2 VLBW, 2 controls) were not fasting at

Table III. Growth and body composition (Mean, SD) by group status and gender

Measure	Females				Males			
	VLBW (N = 127)	Control (N = 64)	Mean difference (95% CI)	*P*	VLBW (N = 102)	Control (N = 36)	Mean difference (95% CI)	*P*
Height (cm)	161.3 (6.1)	166.6 (6.6)	−5.3 (−7.2 to −3.3)	<0.001	174.5 (5.8)	179.4 (6.9)	−4.9 (−7.3 to −2.6)	<0.001
Weight (kg)	70.8 (19.3)	81.0 (19.6)	−10.2 (−16.1 to −4.3)	<0.001	81.1 (17.9)	85.1 (15.9)	−4.0 (−10.7 to 2.7)	0.24
BMI (kg/m^2)	27.0 (6.8)	29.2 (7.0)	−2.1 (−4.2 to −0.1)	0.044	26.5 (5.5)	26.4 (4.9)	0.1 (−1.9 to 2.2)	0.90
Waist circumference (cm)	81.7 (14.8)	85.0 (15.1)	−3.3 (−7.9 to 1.2)	0.14	87.8 (14.3)	88.0 (10.7)	−0.2 (−5.3 to 5.0)	0.96
Hip circumference (cm)	101.0 (13.7)	106.3 (13.6)	−5.3 (−9.4 to −1.2)	0.012	99.7 (10.2)	102.2 (8.5)	−2.5 (−6.2 to 1.2)	0.19
Waist : Hip	0.81 (0.08)	0.80 (0.06)	0.01 (−0.01 to 0.03)	0.40	0.88 (0.08)	0.86 (0.06)	0.02 (−0.01 to 0.05)	0.20
Body fat percentage (%)	32.8 (9.8)	37.1 (7.5)	−4.3 (−7.1 to −1.5)	0.003	22.0 (8.5)	20.4 (7.2)	1.6 (−1.6 to 4.7)	0.33
Fat mass (kg)	24.9 (14.3)	31.5 (14.1)	−6.6 (−11.1 to −2.2)	0.004	19.3 (12.6)	18.3 (9.4)	1.0 (−3.6 to 5.5)	0.68
FFM (kg)	45.6 (5.5)	50.1 (7.3)	−4.5 (−6.4 to −2.6)	<0.001	62.0 (7.3)	66.8 (8.4)	−4.7 (−7.7 to −1.8)	0.002
TBW (kg)	33.4 (4.1)	36.7 (5.3)	−3.3 (−4.7 to −1.9)	<0.001	45.4 (5.4)	48.9 (6.1)	−3.5 (−5.6 to −1.3)	0.002

FFM: Fat Free Mass; TBW: Total Body Water.
Mean weight does not equal sum of mean fat mass + mean FFM due to small number of missing observations on body composition measures (9 VLBW, 4 controls).

Table VIII. Prevalence of the metabolic syndrome in the VLBW cohort and controls

Sex	VLBW		Controls		*P* value
	n	%	n	%	
Female	125	12.8	61	13.1	.95
Male	99	22.2	36	11.1	.15
Total*	224	17.0	97	12.4	.30

*Total excludes 5 VLBW and 3 controls who had no blood tests or were not fasting when blood was obtained.

the time of testing, so their results from tests involving fasting were excluded. There were no significant differences in any of these comparisons, although the proportion of subjects with lipid measurements in the optimal range was consistently slightly lower in the VLBW cohort compared with controls. One VLBW adult and 3 control adults had been previously diagnosed with diabetes. A higher proportion of VLBW subjects than controls (30.5% vs 26.0%) had a fasting insulin value >11.5 μU/mL (80 pmol/L), the upper limit of our laboratory's reference range. A measure which combines both glucose and insulin measurements to provide data on insulin resistance (HOMA-IR) also showed no differences, but a slightly greater proportion of VLBW participants had values outside the recommended range. Adjusting data for sex and ethnicity did not affect these results (**Tables VI** and **VII**).

We found no differences between the VLBW cohort and controls in serum creatinine level, estimated glomerular filtration rate, or urine albumin creatinine clearance (data not shown). There also were no significant differences in the prevalence of the metabolic syndrome between the VLBW cohort and controls, both within the total population and when stratified by sex (**Table VIII**).

Table IX presents factors associated with the metabolic syndrome in the VLBW cohort. On univariate analysis, the only factors significantly associated with the metabolic syndrome were Māori/Pacific Island ethnicity, birth at <28 weeks of gestation, and BMI >90th percentile at age 7-8 years. Similar results were obtained for weight >90th percentile at 7-8 years, or when BMI or weight was considered as a continuous variable (data not shown).

On logistic regression, male sex, gestational age <28 weeks, Māori/Pacific Island ethnicity, and BMI >90th percentile at age 7-8 years were all significant predictors for having the metabolic syndrome at age 27-29 years all with an OR close to 3 (**Table X**). Extension of the model to test for sex by risk factor interactions, and likewise for ethnicity, showed no evidence of significant interactions.

Table XI (available at www.jpeds.com) shows the associations (OR; 95% CI) between risk factors and individual components of the metabolic syndrome.

Discussion

In this prospectively enrolled national cohort of VLBW young adults born in New Zealand in 1986, we did not find a significant difference in the prevalence of the metabolic

Table IX. Factors associated with the metabolic syndrome in the VLBW cohort (N = 224)

	Metabolic syndrome			
Factors	No (n = 186), %	Yes (n = 38), %	OR (95% CI)	*P* value
Male sex	41.4	57.9	1.9 (0.9-3.9)	.06
Māori/Pacific Island ethnicity	25.8	55.3	3.6 (1.7-7.3)	.001
ELBW (<1000 g)	25.8	36.8	1.7 (0.8-3.5)	.17
Extremely preterm (<28 wk)	21.5	42.1	2.6 (1.3-5.5)	.01
SGA	32.3	29.0	0.9 (0.4-1.8)	.69
ANS	57.5	47.4	0.7 (0.3-1.3)	.25
Maternal smoking during pregnancy	19.6	31.6	1.9 (0.9-4.0)	.11
PET	23.7	26.3	1.2 (0.5-2.6)	.73
Cesarean delivery birth	60.2	55.3	0.8 (0.4-1.6)	.57
Multiple birth	25.8	18.4	0.6 (0.3-1.6)	.34
Breastfed*	76.0	69.4	0.7 (0.3-1.6)	.40
Current smoker	29.6	34.2	1.2 (0.6-2.6)	.57
BMI >90th percentile (age 7-8 y)	6.6	23.7	4.4 (1.7-11.4)	.001
Weight >90th percentile (age 7-8 y)	6.6	23.7	4.4 (1.7-11.4)	.001

PET, preeclamptic toxemia.
Five VLBW adults were excluded either because they declined blood testing or blood was not drawn.
*Breastfed after birth, including with expressed breast milk.

syndrome at age 27-29 years compared with term-born controls. There also were no significant differences between the VLBW cohort and controls in the prevalence of components of the metabolic syndrome except for systolic BP. There was heterogeneity in these findings between males and females. Female VLBW participants had significantly lower BMI, fat mass, and body fat percentage than controls, whereas males did not. However, both male and female VLBW subjects had significantly lower fat-free mass compared with controls. A systematic review by Parkinson et al similarly found no differences for most features of the metabolic syndrome in preterm-born late adolescents and adults compared with term-born late adolescents and adults other than higher BP and higher low-density lipoprotein levels in the former group.[3]

In our VLBW cohort, male sex, gestational age <28 weeks, Māori/Pacific Island ethnicity, and a BMI >90th percentile at age 7-8 years were all significant predictors of the metabolic syndrome in young adulthood. Unlike several other studies of preterm and general population cohorts,[20,21] we did not have any data on growth measures between hospital discharge and age 7-8 years, but in agreement with these and other reports, our data suggest that the scene is already set by age 8 years as far as an obesogenic phenotype is concerned. In a study from northern Finland of preterm infants and controls assessed at a mean age of 23 years, the mean BMI was 23.0 in control males and 22.0 in control females,[22] considerably lower than the 26.4 and 29.2 in our controls, suggesting that to some extent, individuals tend to follow growth patterns that are the norm for a particular society. Taken together, these data suggest that excessive growth trajectories should, at least in theory, be amenable to societal interventions aimed specifically at the early childhood years. The Finnish study did find that early preterm (<34 weeks) and late preterm (34-36 weeks) young adults had ORs of 3.7 and 2.5, respectively, for meeting the metabolic syndrome criteria compared with controls after adjustment for sex, age, and cohort status.[22] Our finding that gestational age <28 weeks had an OR of 2.8 for meeting the metabolic syndrome criteria as a young adult is noteworthy in that many more such infants are now surviving compared with the 1980s, but requires confirmation from other studies.

Table X. Logistic regression model predicting the metabolic syndrome in the VLBW cohort (N = 224)

Variable	B (SE)	OR (95% CI)	*P* value
Male sex	1.05 (0.41)	2.9 (1.3-6.3)	.01
Extremely preterm (<28 wk)	1.03 (0.41)	2.8 (1.2-6.3)	.01
Māori/Pacific Island ethnicity	1.24 (0.39)	3.4 (1.6-7.5)	.002
BMI >90th percentile (age 7-8 y)	1.31 (0.53)	3.7 (1.3-10.5)	.01

Five VLBW adults were excluded either because they declined blood testing or blood was not drawn.

The heterogeneity in body composition outcomes and the metabolic syndrome incidence between males and females raises several questions. Sex differences in the long-term effects of various feeding regimens have been reported in both animal models and preterm infants.[23] We found no differences in breast feeding rates between males (74.3%) and females (75.4%) in our VLBW cohort, and being breastfed was not associated with the metabolic syndrome or most of its components. We do not have sufficient data to explore this issue further, but agree with Harding et al that further study is needed to assess the long-term effects of early nutrition and growth and how they might differ by sex.[23]

Higher systolic BP in former very-preterm-born infants has been consistently reported.[24] In their meta-analysis of 16 published studies, Parkinson et al reported that mean systolic BP was 4.2 mmHg higher in former preterm infants compared with controls,[3] similar to our findings. Data for diastolic BP are less clear, however; Parkinson et al found a significantly higher diastolic BP (mean, 2.6 mmHg higher) in preterm-born adults,[3] but several other studies have reported no difference.[6] A report from the Helsinki VLBW study found significantly higher seated diastolic BP, but not ambulatory diastolic BP, in preterm-born adults.[10] In a meta-regression, the preterm-term difference was greater in women than in men, in contrast to our findings, in which a significant difference in systolic BP was seen only in men.[3]

The mechanisms leading to higher BP in VLBW adults remain unclear,[25,26] as does whether prematurity independently increases the risk of higher BP or whether this is related mainly to small size as a consequence of intrauterine growth retardation, as suggested by Cheung et al.[27] We did not identify small for gestational age status to be predictive of elevated blood pressure. Reports from the Dutch Project on Preterm and Small for Gestational Age study of infants born very preterm or VLBW in 1983 have documented reduced renal growth in very-preterm-born adults[28] and have shown that despite normal renal function, lower birth weight was associated with higher serum creatinine concentration and higher microalbumin excretion at age 19 years.[29] A further report from the POPS study noted a significantly lower glomerular filtration rate associated with antenatal corticosteroid exposure (20.5% of the cohort), although this was in the normal range.[11] We found no differences in serum creatinine, estimated glomerular filtration rate, or urine albumin creatinine clearance between our VLBW cohort and controls. In addition, there was no effect of antenatal corticosteroid exposure on BP in our cohort, in agreement with data at age 30 years reported by the Auckland Steroid Trial.[30]

Former preterm infants have been reported to have impairments in glucose homeostasis in early childhood, adolescence, and beyond.[4,12,26,31-34] Hovi et al assessed 166 VLBW young adults (age 18-27 years; 50% of 329 survivors of the Helsinki cohort born in 1985-1987) compared with 86 controls born at term using a 75-g oral glucose tolerance test.[9] Notably, the mean BMI was 21.9 for the VLBW group and 22.4 for the control group. The VLBW young adults had significantly higher fasting insulin values and increased calculated insulin resistance (by the HOMA-IR) compared with controls.[9] In a follow-up of a regional cohort of extremely low birth weight (ELBW; <1000 g) infants at a mean age of 32 years, Morrison reported significantly higher fasting glucose, insulin and HOMA-IR in ELBW adults compared with controls.[13] On a 75-g oral glucose tolerance test, the ELBW adults were found to have a 3- to 4-fold increased risk of dysglycemia, as defined by the Canadian Diabetes Association. In common with our New Zealand cohort, a high proportion (48%) of the ELBW adults had been exposed to antenatal steroids, but there was no relationship between antenatal corticosteroid exposure and dysglycemia.[13]

In contrast to these reports, here we found no difference between VLBW adults and controls in mean fasting insulin concentrations or HOMA-IR, although a greater proportion of the VLBW cohort exceeded the upper limit of our laboratory norm for insulin. Increasing BMI is correlated with an increased fasting insulin and is directly related to insulin resistance and is a risk factor for type 2 diabetes mellitus and cardiovascular disease.[35] In a high proportion of both the VLBW cohort and controls (21% and 17%, respectively), a combination of BMI>30 and elevated fasting insulin level triggered a feedback letter to the participant and his or her general practitioner noting the increased risk of developing type 2 diabetes in the future.

Strengths of the present study include the prospectively enrolled national population-based cohort born in a single year, 50% of which were exposed to antenatal corticosteroids, and the high cohort retention during longitudinal follow-up. Weaknesses include recruitment of the cohort by birth weight, although this was typical for the 1980s, and birth weight is a more precise measurement than gestational age, the unavailability of longitudinal data for the controls, and the relatively small number of participants. In particular, the sample size precluded an in-depth assessment of between sex differences in metabolic risk. In addition, we did not collect growth or other data for the period between initial hospital discharge and age 7-8 years in the VLBW cohort. At age 27-29 years, our examination schedule was limited by time and funding.

In conclusion, in this follow-up of a national cohort of VLBW young adults compared with term-born controls, we found associations between VLBW and shorter stature and higher systolic BP. Overall, however, there was little evidence of any metabolic consequences of being born VLBW, at least by the late 20s. It is possible that our sample is too small to show significant differences, and whether differences will emerge later in life remain to be seen. ■

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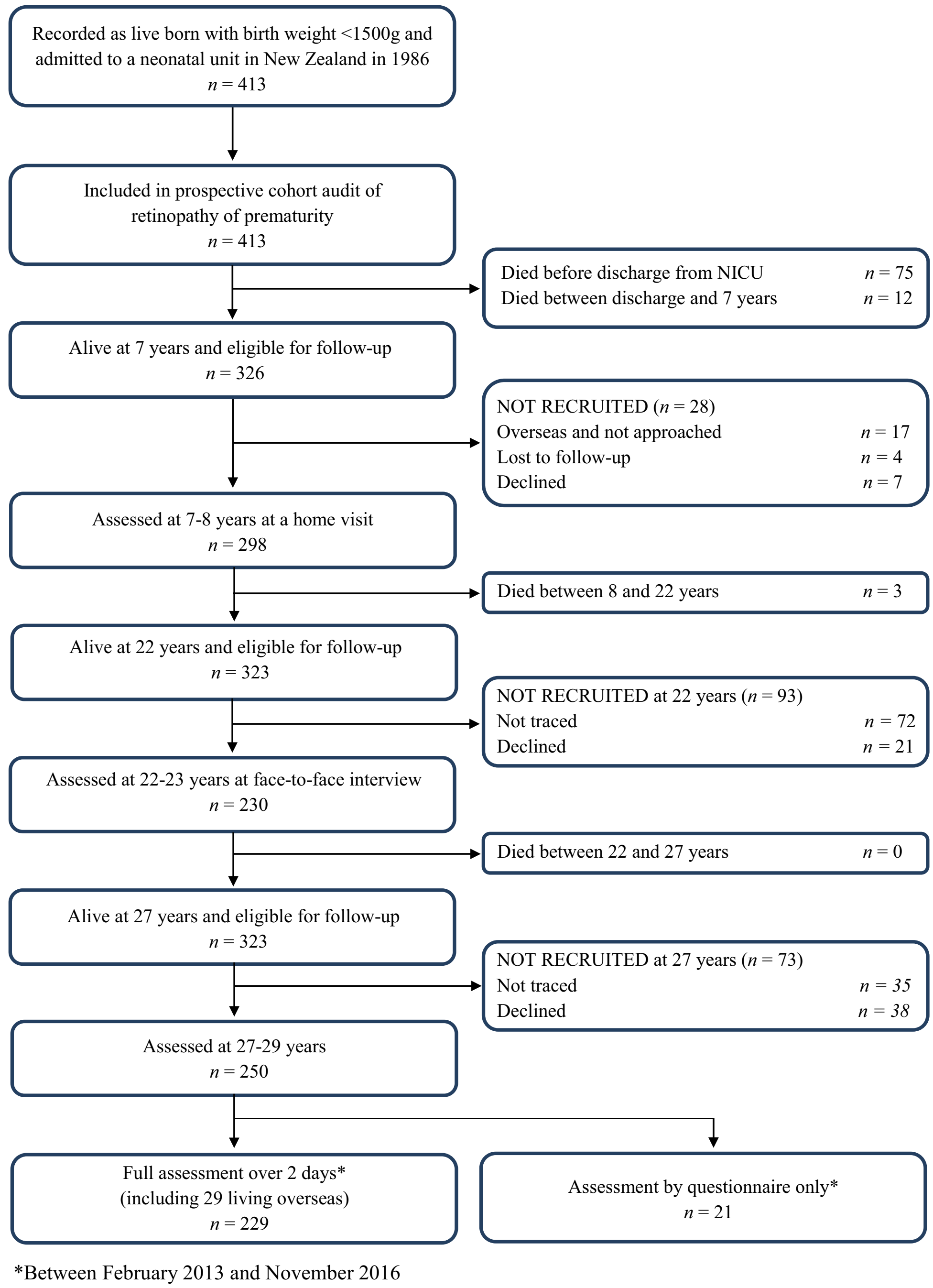

Figure. Cohort flow chart. *NICU*, neonatal intensive care unit.

Table I. International Diabetes Federation definition of the metabolic syndrome[17]

Measure	Categorical cut points
Central obesity	Elevated waist circumference (ethnicity-specific)
	Plus any 2 of the following:
Elevated triglycerides	≥150 mg/dL (1.7 mmol/L)*
Reduced HDL-C	≤ 40 mg/dL (1.0 mmol/L) in males*
	≤ 50 mg/dL (1.3 mmol/L) in females*
Elevated BP	Systolic ≥130 mmHg or diastolic ≥85 mmHg†
Elevated fasting glucose	Fasting plasma glucose >100 mg/dL (5.6 mmol/L)‡

HDL-C, high-density lipoprotein cholesterol.
*Or specific treatment for this lipid abnormality.
†Or treatment of previously diagnosed hypertension.
‡Or previously diagnosed type 2 diabetes.

Table II. Demographic and perinatal data for the VLBW cohort and controls

Measure	VLBW, assessed (N = 229)	VLBW, not assessed* (N = 94)	*P* value†	Controls (N = 100)	*P* value‡
Age at assessment, y, mean ± SD	28.5 ± 1.1			28.3 ± 0.9	.13
Male sex, % (n)	44.5 (102)	53.2 (50)	.16	36.0 (36)	.15
Māori/Pacific Islander, % (n)	31.0 (71)	34.0 (32)	.59	21.0 (21)	.06
Birth weight, g, mean ± SD	1133 ± 237	1192 ± 230	.04	3372 ± 565	<.001
Birth weight <1000 g, % (n)	28.0 (64)	21.3 (20)	.21		
Gestation, wk, mean ± SD	29.2 ± 2.5	29.3 ± 2.4	.82		
<28 wk gestation, % (n)	24.9 (57)	24.5 (23)	.94		
SGA, % (n)	31.4 (72)	22.3 (21)	.10		
RDS, % (n)	54.6 (125)	60.6 (57)	.32		
BPD, % (n)	20.1 (46)	23.4 (22)	.51		
ANS, % (n)	56.3 (129)	59.6 (56)	.59		
ROP, % (n)	19.7 (45)	20.7 (18)	.92		
Any neurosensory disability at age 7-8 y, % (n)	23.0 (51)	31.1 (23)	.16		
Moderate/severe disability at age 7-8 y, % (n)	5.9 (13)	18.9 (14)	.001		

ANS, antenatal steroids (any); *BPD*, bronchopulmonary dysplasia (oxygen requirement at 36 weeks postmenstrual age); *RDS*, respiratory distress syndrome; *ROP*, retinopathy of prematurity; *SGA*, small for gestational age (birth weight <10th percentile).
Moderate or severe disability at age 7-8 years was defined as cerebral palsy in nonambulant children or in ambulant children causing considerable limitation of movement, bilateral sensorineural deafness requiring hearing aids, bilateral blindness, or an IQ score of >2 SD below the test mean (<70) on the Revised Wechsler Intelligence Scale for Children (WISC-R).[15]
*Includes 73 with no follow-up (35 not able to be contacted [13 known to be overseas], 38 contacted but declined) and 21 not assessed in Christchurch but who consented to an interview.
†Comparisons of VLBW assessed and not assessed by the *t* test or χ^2 test.
‡Comparisons of VLBW assessed and controls by the *t* test or χ^2 test.

Table IV. Mean differences between the VLBW cohort and controls in growth and body composition, adjusted for ethnicity

	Females		Males	
Measures	Mean difference (95% CI)	*P* value	Mean difference (95% CI)	*P* value
Height, cm	-5.4 (-7.3 to -3.5)	<.001	-5.1 (-7.5 to -2.7)	<.001
Weight, kg	-10.9 (-16.6 to -5.2)	<.001	-6.2 (-12.6 to 0.3)	.062
BMI, kg/m^2	-2.3 (-4.4 to -0.3)	.025	-0.5 (-2.5 to 1.5)	.60
Waist circumference, cm	-4.0 (-8.3 to 0.4)	.076	-1.1 (-6.3 to 4.0)	.66
Hip circumference, cm	-5.7 (-9.8 to -1.6)	.006	-3.5 (-7.2 to 0.2)	.062
Waist/hip ratio	0.01 (-0.01 to 0.03)	.53	0.01 (-0.01 to 0.05)	.23
Body fat percentage, %	-4.4 (-7.2 to -1.6)	.002	0.6 (-2.5 to 3.7)	.69
Fat mass, kg	-6.9 (-11.2 to -2.5)	.002	-0.5 (-4.9 to 3.9)	.82
FFM, kg	-4.6 (-6.5 to -2.8)	<.001	-5.4 (-8.3 to -2.5)	<.001
TBW, kg	-3.4 (-4.8 to -2.0)	<.001	-4.0 (-6.1 to -1.8)	<.001

FFM, fat-free mass; *TBW*, total body water.

Table V. BP by group status and sex

	Females						Males					
Measures	VLBW (n = 127), mean ± SD	Control (n = 64), mean ± SD	Mean difference (95% CI)	*P* value	Mean difference* (95% CI)	*P* value	VLBW (n = 102), mean ± SD	Control (n = 36), mean ± SD	Mean difference (95% CI)	*P* value	Mean difference* (95% CI)	*P* value
SBP, mmHg	108.8 ± 11.2	106.3 ± 9.1	2.5 (-0.7 to 5.7)	.12	2.5 (-0.8 to 5.7)	.13	120.0 ± 11.6	114.3 ± 10.9	5.7 (1.3-10.1)	.01	5.0 (0.5-9.4)	.028
DBP, mmHg	71.0 ± 8.2	70.9 ± 8.4	0.1 (-2.4 to 2.6)	.94	0.0 (-2.5 to 2.5)	.94	77.6 ± 9.5	75.1 ± 8.6	2.5 (-1.1 to 6.0)	.17	1.4 (-2.1 to 4.8)	.17

DBP, diastolic BP; *SBP*, systolic BP.
*Adjusted for ethnicity.

Table VI. Lipid levels

Measures	VLBW (n = 226)	Controls (n = 99)	Unadjusted: Mean difference (95% CI)	Unadjusted: *P* value	Adjusted*: Mean difference (95% CI)	Adjusted*: *P* value
Total cholesterol, mg/dL						
Mean ± SD	178 ± 32	177 ± 41	0.7 (-7.7 to 9.0)	.88	0.9 (-7.7 to 9.4)	.84
% optimal (<155; <4 mmol/L)	20.8	24.2		.49		
Triglycerides, mg/dL†						
Mean ± SD	111 ± 60	99 ± 64	12.1 (-2.5 to 26.6)	.10	12.0 (-2.8 to 26.7)	.11
% optimal (<151; <1.7 mmol/L)	79.7	87.9		.07		
HDL-C, mg/dL						
Mean ± SD	51 ± 38	48 ± 12	2.8 (-4.9 to 10.5)	.47	2.4 (-5.4 to 10.3)	.54
% optimal (>39; >1 mmol/L)	78.8	79.8		.83		
Total cholesterol:HDL-C ratio						
Mean ± SD	3.8 ± 1.1	3.8 ± 1.1	0.04 (-0.23 to 0.30)	.79	0.09 (-0.17 to 0.35)	.50
% optimal (<4.5)	73.3	77.6		.42		
LDL-C, mg/dL						
Mean ± SD	107 ± 29	108 ± 29	-0.4 (-7.2 to 6.4)	.92	0.7 (-6.3 to 7.6)	.85
% optimal (<97; <2.5 mmol/L)	35.1	36.7		.78		

LDL-C, low-density lipoprotein cholesterol.
*Adjusted for sex and ethnicity.
†Reanalysis of triglycerides data using a log10 transformation to account to non-normality yielded the following estimates of the geometric mean (95% CI) difference between VLBW and controls: unadjusted, 9.8 (0.2-18.3), *P* = .044; adjusted, 9.9 (2.0-18.5), *P* = .046.

Table VII. Glucose/insulin levels*

Measures	VLBW (n = 224)	Controls (n = 97)	Unadjusted: Mean difference (95% CI)	Unadjusted: *P* value	Adjusted‡: Mean difference (95% CI)	Adjusted‡: *P* value
Fasting blood insulin, μU/mL						
Mean ± SD	10.5 ± 8.1	9.7 ± 4.7	0.8 (-1.0 to 2.5)	.38	0.5 (-1.3 to 2.2)	.61
% in recommended range (1.4-11.4; 10-80 pmol/L)	69.5	74.0		.42		
Fasting blood glucose, mg/dL						
Mean ± SD	91 ± 9	91 ± 16	-0.2 (-3.0 to 2.7)	.91	-0.2 (-3.0 to 2.7)	.91
% in recommended range (63-108; 3.5-6.0 mmol/L)	98.2	94.9		.09		
Hemoglobin A1c						
Mean ± SD	31.9 ± 4.4	31.1 ± 6.2	0.79 (-0.41 to 2.00)	.19	0.53 (-0.65 to 1.71)	.38
% in recommended range (20-40)	96.9	95.9		.66		
HOMA-IR§						
Mean ± SD	2.3 ± 1.9	2.1 ± 1.2	0.19 (-0.22 to 0.60)	.37	0.12 (-0.29 to 0.53)	.57
% in recommended range (males, <2.25; females, <2.1)†	62.2	64.6		.68		

SI units were converted to metric mass units as follows: glucose, mmol/L x 18 = mg/dL; insulin, pmol/L ÷ 7 = μU/mL
*Excludes 5 participants with nonfasting blood tests (3 VLBW, 2 controls).
†Based on cutpoints for 30-year-old nondiabetics used by Gayoso-Diz et al.[19]
‡Adjusted for sex and ethnicity.
§Reanalysis of HOMA-IR data using a log10 transformation to account for non-normality yielded the following estimates of the geometric mean (95% CI) difference between VLBW and controls: unadjusted, .01 (-0.24 to 0.30), *P* = .92; adjusted, 0.094 (-0.17 to 0.39), *P* = .50.

Table XI. Associations between risk factors and components of the metabolic syndrome in the VLBW cohort (N = 224)

Risk factors	OR (95% CI)				
	Elevated waist circumference*	Elevated triglycerides†	Reduced HDL-C†	Elevated BP§	Elevated fasting glucose¶
Male sex	0.5 (0.3-0.8)	2.3 (1.2-4.6)**	0.5 (0.3-0.9)**	5.0 (2.3-10.9)††	2.0 (0.9-4.2)
Māori/Pacific Island ethnicity	2.9 (1.6-5.3)‡‡	2.0 (1.0-4.0)**	2.7 (1.5-4.7)**	1.1 (0.5-2.3)	1.1 (0.5-2.4)
ELBW (<1000 g)	1.3 (0.7-2.3)	1.2 (0.6-2.4)	1.9 (1.1-3.5)**	1.0 (0.5-2.1)	1.5 (0.7-3.3)
Extremely preterm (<28 wk)	2.1 (1.1-3.8)**	1.6 (0.8-3.2)	1.9 (1.0-3.5)**	1.2 (0.5-2.6)	1.3 (0.6-2.9)
SGA status	1.0 (0.6-1.8)	1.2 (0.6-2.4)	1.7 (0.98-3.1)	1.2 (0.6-2.4)	0.6 (0.3-1.4)
ANS	1.1 (0.6-1.9)	0.7 (0.3-1.3)	1.2 (0.7-2.1)	0.8 (0.4-1.7)	1.8 (0.8-3.9)
Maternal smoking during pregnancy	1.9 (1.0-3.6)**	1.6 (0.7-3.3)	1.8 (0.9-3.3)	0.9 (0.4-2.1)	1.1 (0.5-2.7)
PET	0.7 (0.4-1.4)	1.0 (0.5-2.1)	1.9 (1.0-3.5)**	1.9 (0.9-4.0)	1.9 (0.9-4.2)
Cesarean delivery birth	1.0 (0.6-1.8)	1.1 (0.6-2.1)	0.9 (0.5-1.5)	2.0 (0.9-4.3)	1.3 (0.6-2.8)
Multiple birth	1.1 (0.6-2.0)	0.8 (0.4-1.8)	0.7 (0.4-1.4)	0.7 (0.3-1.7)	1.6 (0.7-3.5)
Breastfed	0.8 (0.4-1.5)	1.0 (0.5-2.1)	0.5 (0.3-0.9)**	1.3 (0.6-3.1)	0.8 (0.4-1.9)
Current smoker	0.8 (0.5-1.5)	1.1 (0.6-2.3)	2.5 (1.4-4.5)**	0.9 (0.4-1.8)	1.1 (0.5-2.4)
BMI >90th percentile (age 7-8 y)	18.9 (4.3-83.4)††	2.6 (1.0-6.7)**	3.4 (1.3-8.8)‡‡	1.5 (0.5-4.4)	1.3 (0.4-4.2)
Weight >90th percentile (age 7-8 y)	8.1 (2.6-24.9)††	1.6 (0.6-4.4)	2.2 (0.9-5.4)	2.0 (0.7-5.6)	0.9 (0.3-3.3)
Height >90th percentile (age 7-8 y)	1.9 (0.6-5.9)**	1.1 (0.3-4.3)	0.7 (0.2-2.2)	—§§	1.0 (0.2-4.7)

PET, preeclamptic toxemia.
Breastfed includes any breastfeeding following birth.
*>80 cm in females, >94 cm in males.
†>150 mg/dL (1.7 mmol/L).
‡<50 mg/dL (1.3 mmol/L) in females, <40 mg/dL (1.0 mmol/L) in males.
§Systolic BP >130 mmHg and/or diastolic BP >85 mmHg.
¶>100 mg/L (5.6 mmol/L).
***P* < .05.
††*P* < .001.
‡‡*P* < .01.
§§Unable to estimate (zero cell).