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ORIGINAL ARTICLE

Body mass index z-scores in the first 2 years of life were associated with adverse metabolic and anthropometric outcomes at 3 years of age

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Abstract

Aim: We investigated associations between body mass index (BMI) z-scores for children aged 0–2 years and the BMI z-scores, body fat percentage and metabolic risk factors at 3 years of age.

Methods: This was a secondary analysis of the Lifestyle in Pregnancy and Offspring randomised controlled trial, carried out at two university hospitals in Denmark. It comprised 149 mothers with BMI ≥30 kg/m^2 who did or did not receive a lifestyle intervention during pregnancy and a reference group of 97 mothers with normal-weight, with follow-up of their 3-year-old offspring. The children in these three groups were pooled for the data analyses, due to similar characteristics between groups. The BMI z-scores were calculated at 5 weeks, 5 months and 1, 2 and 3 years, using Danish reference groups. Their anthropometrics and metabolic outcomes were examined at 3 years of age.

Results: BMI z-scores at 5 months to 2 years were associated with BMI z-scores and body fat percentage at 3 years of age and BMI z-scores were not associated with metabolic risk factors at 3 years.

Conclusion: BMI z-scores from 5 weeks of age were associated with adverse anthropometric outcomes but not with metabolic risk factors at 3 years of age.

KEYWORDS
anthropometrics, body mass index, childhood obesity, early prevention, metabolic risk factors

Abbreviations: BMI, body mass index; HDL, high-density lipoprotein; IDF, International Diabetes Federation; LiP Offspring, lifestyle in pregnancy and offspring; LiP, lifestyle in pregnancy.

1 | INTRODUCTION

The prevalence of childhood obesity is continually increasing and poses a burden to public health worldwide.[1] Importantly, it has been shown that excessive growth in infancy has been associated with increased risk of cardiovascular disease, adverse metabolism and type 2 diabetes in later childhood and adult life.[2–8]

Metabolic syndrome is a widely established condition in adults, but has not been suitably defined in children under 10 years of age. A review suggested that the prevalence of adverse metabolic effects in children was increasing and that individuals with obesity carried the highest risk.[9]

Several studies have identified both slow and rapid growth trajectories in children as risk factors for adverse metabolic outcomes. However, studies that have investigated both metabolic and anthropometric outcomes are scarce. Few studies have explored growth in infancy and early childhood and their associations with adverse metabolism, overweight and body composition in adolescence.[10] Identifying crucial growth patterns at different ages during infancy may, therefore, provide an opportunity to develop early and targeted interventions for young children.[11]

The primary aim of this study was to investigate the associations between body mass index (BMI) z-scores for children aged 0–2 years and the BMI z-scores, body fat percentage and metabolic risk factors at age 3 years. We also aimed to investigate the association between BMI z-scores in early infancy and anthropometric measures and metabolic outcomes at 3 years of age. The data we used came from the Danish Lifestyle in Pregnancy and Offspring (LiP Offspring) cohort.[12] The measures included hip circumference, abdominal circumference, and skinfolds and the outcomes included fat mass, blood pressure, insulin resistance, fasting plasma glucose, plasma triglycerides and plasma total cholesterol.

Key Notes

- We investigated 246 mother–child dyads for associations between body mass index (BMI) z-scores in early infancy and weight and metabolic risk factors at 3 years of age.
- BMI z-scores at 5 months to 2 years were significantly associated with BMI z-scores and body fat percentage at 3 years of age.
- BMI z-scores from 5 weeks to 2 years were not associated with metabolic risk factors at 3 years of age.

2 | METHODS

2.1 | Study design and participants

This was a secondary analysis of data from the LiP Offspring study by Tanvig et al.,[12] which was a follow-up study of the Lifestyle in Pregnancy (LiP) randomised controlled trial.[13] The original LiP study was conducted between October 2007 and October 2010 at Odense University Hospital and Aarhus University Hospital, Denmark. The inclusion criteria were: pre-pregnancy BMI of 30–45 kg/m^2 and maternal age of 18–40 years. We excluded prior serious obstetric complications, chronic diseases, gestational diabetes diagnosed in early pregnancy, alcohol or drug abuse, not speaking Danish and multiple pregnancies.[14] Pregnant women aged 18–40 years who met the inclusion criteria were recruited at 10–14 weeks of gestation, as determined by ultrasound.

Participants were randomised to either a lifestyle intervention group that comprised dietary counselling and physical activity or to a control group.[14]

In the subsequent LiP Offspring study, women with a normal weight pre-pregnancy BMI of 18.5–24.9 kg/m^2 and their offspring were identified from electronic patient records after pregnancy by Tanvig et al.[12] This external reference group comprised the 97/325 (30%) mother–child dyads who were eligible and agreed to participate.

We found that 304 of the 360 women randomised to the LiP study were still in the study at the time of delivery. However, three delivered stillborn infants, leaving 301 mother–child dyads eligible for the LiP Offspring follow-up study and 149 dyads (50%) took part (Figure 1).

Non-Danish speakers were excluded from the original LiP study and it was coincidental that only Caucasian mothers were recruited. Caucasian ethnicity was chosen as an eligibility criterion when the external reference group was recruited. The other inclusion criteria were singleton infants born between 39 ± 0 and 40 ± 6 weeks/days from 2008 to 2009 to healthy mothers of with a normal pre-pregnancy BMI of 18.5–24.9 kg/m^2. Women in the external reference group had comparable maternal age and parity as the LiP mothers and gave birth to similar proportions of male and female babies with similar gestational ages at delivery.[12]

Thus, the LiP Offspring study included three types of mother–child dyads: the offspring of the intervention and control groups of mothers with obesity and an external reference group of normal-weight mothers. In this secondary analysis the three groups were pooled.

The women in the original LiP groups completed a baseline questionnaire in early pregnancy that provided information about maternal characteristics, including employment and education. These questionnaires were repeated at 35 weeks of gestation and 6 months postpartum. At the postpartum visit, women in the original LiP groups completed questionnaires about breastfeeding and their child's growth during the first 6 months of life during postpartum visits. The maternal characteristics for the external reference group were obtained from questionnaires when the children were examined at 3 years of age.[15]

2.2 | Anthropometrics and metabolic outcomes

The 3-year-old children were examined by a physician and a research laboratory technician.[15] These examinations included blood

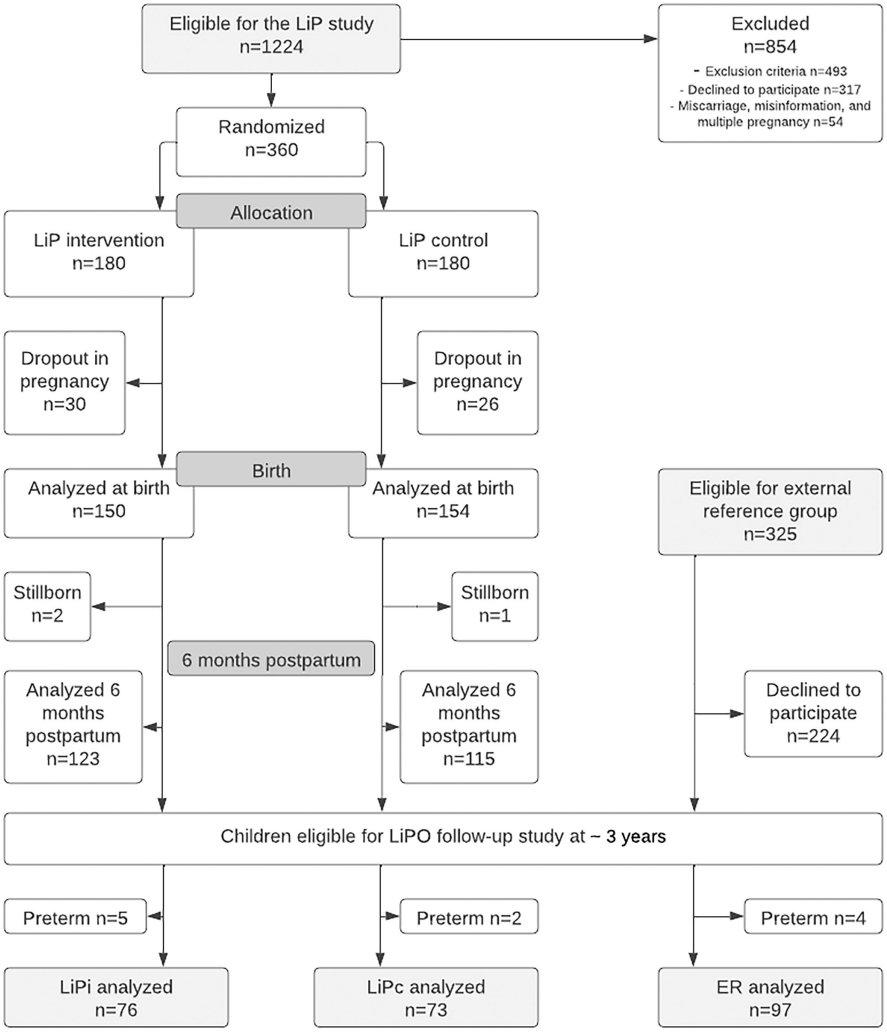

FIGURE 1 Participation rates during the LiP and LiP Offspring studies. ER, external reference; LiP Offspring, Lifestyle in Pregnancy and Offspring; LiP, Lifestyle in Pregnancy; LiPc, LiP control group, LiPi, LiP intervention group.

samples, blood pressure measurements, skinfolds, height, weight, hip circumference and abdominal circumference. The collection of the anthropometrics and metabolic outcomes has previously been described in detail.[12,13] Paediatric medical records were reviewed, and data on the weight and length/height of the children at up to 2 years of age were collected from routine visits to general practitioners, as part of the routine Danish programme.[13]

The children's BMI at 5 weeks, 5 months, 1, 2 and 3 years were calculated as weight divided by the square of height. The BMIs were expressed as z-scores, based on age and sex specific reference groups for Danish infants. The reference groups were based on a national sample used to generate the current Danish height and weight reference, by using 29 106 measurements carried out in 1965–1977.[16]

Lean body mass, body fat mass and body fat percentage were determined using dual energy X-ray scans, as described in the LiP Offspring paper.[13]

2.3 | Metabolic risk factors

A range of metabolic risk factors were used, including abdominal circumference, blood pressure and fasting levels of plasma glucose, insulin, triglycerides and high-density lipoprotein (HDL). We defined two different clusters of metabolic risk factors. The first, the LiP Offspring metabolic group, used the sample population's 90th percentiles. These comprised abdominal circumference ≥ 51 cm, HDL < 0.9 mmol/L, triglycerides ≥ 1.2 mmol/L, fasting glucose ≥ 5.8 mmol/L and systolic blood pressure ≥ 107 mmHg. The second used the International Diabetes Federation's (IDF) definition of high-risk metabolism in adolescents and these are referred to as the IDF metabolic group. These comprised an abdominal circumference ≥ 90th percentile, HDL < 1.03 mmol/L, Triglycerides ≥ 1.7 mmol/L, fasting glucose ≥ 5.6 mmol/L and systolic blood pressure ≥ 130 mmHg. We categorised the children as high risk if they had a high abdominal circumference and two or more of the following: low HDL, high triglycerides, high fasting glucose, and high systolic or diastolic blood pressure, according to the above groups.[17]

2.4 | Statistical analysis

We pooled children from the three LiP Offspring groups for all the analyses. Descriptive analyses used one-way ANOVA and the

Chi-squared test. Associations between BMI z-scores and the two groups of metabolic risk factors at 3 years of age were identified using univariate and multivariate logistic regression. BMI z-scores, body fat percentage and secondary outcomes at 3 years of age were included as continuous outcomes and analysed using simple and multiple linear regression. All models were adjusted for potential confounders: maternal BMI in early pregnancy, maternal age, smoking during pregnancy, educational level, gestational weight gain, offspring gender and breastfeeding. Estimates are presented as odds ratio (OR) and 95% confidence intervals (95% CI).

The number of observations varied with each model, because of some missing data for both independent and dependent variables.

All analyses were performed using Stata Statistical Software, Release 17 (StataCorp Texas, USA), with a two-sided significance level of 0.05.

2.5 | Ethics

The local ethics committee of the Region of Southern Denmark and the Danish Data Protection Agency approved the LiP and LiP Offspring studies, which complied with the Declaration of Helsinki. They were registered at clinicaltrials.gov as: NCT00530439, NCT01918319 and NCT01918423. The mothers provided written, informed consent.

3 | RESULTS

We examined 246 mother–child dyads: 76 from the LiP Offspring intervention group, 73 from the LiP Offspring control group and 97 from the external reference group. They were examined at follow up at a mean of 2.8 (range 2.5–3.2 years) years of age. The three groups were pooled for data analysis, because there were no differences in offspring characteristics between the groups.

Maternal and childhood characteristics are presented in Table 1. There were no differences in maternal characteristics between the LiP Offspring intervention and control groups. The mothers of the external reference group had significantly lower pre-gestational BMI, higher gestational weight gain and longer duration of breastfeeding than the LiP Offspring intervention and LiP Offspring control groups respectively.

At 3 years of age, there were no differences in the children in the LiP Offspring intervention and control group and external reference group with regard to fat and lean body mass, insulin resistance, body fat percentage and fasting plasma glucose. In total, 2.1% of the external reference group, 5.3% of the LiP Offspring intervention group and 4.1% of the LiP Offspring control group met the LiP Offspring group definition of metabolic risk factors.

In the external reference group, 3.1% met the IDF metabolic group definition, compared to 5.3% and 5.5% in the LiP Offspring intervention and LiP Offspring control children, respectively. There were no significant differences in the measurements used to define the LiP Offspring and IDF metabolic group between the two LiP Offspring groups and the external reference group.

The highest BMI z-scores at 3 years of age we found in the LiP Offspring intervention group (0.13). They were lower in the LiP Offspring control group (−0.18) and lowest in the external reference group (−0.21).

3.1 | Primary outcomes

After adjustment for potential confounders, BMI z-scores at 5 weeks to 2 years were significantly associated with BMI z-scores at 3 years. The coefficient ranges for these two ages were 0.3–0.6, and 0.03–0.04, respectively (Table 2).

BMI z-scores at 5 months, 1 and 2 years were associated with body fat percentage at 3 years (coefficient range: 0.03–0.04, *p*-value: <0.001) (Table 2).

BMI z-scores from 5 weeks to 2 years of age were not associated with the LiP Offspring metabolic nor the IDF metabolic group (Table 2).

3.2 | Secondary outcomes

The associations between BMI z-scores at the different ages of the children and secondary outcomes at 3 years of age are also presented in Table 2. At 5 weeks, BMI z-score was positively associated with BMI z-score, abdominal circumference, hip circumference, subscapular skinfold and fat body mass. Infant BMI z-scores from 5 months to 2 years were positively associated with abdominal circumference, hip circumference, triceps skinfold, subscapular skinfold, lean body mass, fat body mass, diastolic and systolic blood pressure at the 3-year examinations.

3.3 | Sensitivity and supplementary analyses

Table 2 excludes secondary outcomes without significant associations. Log transformation did not change the results. Sub-group analyses of the primary outcomes, stratified by sex, did not differ from the main analyses and showed no differences between sexes.

4 | DISCUSSION

This was a secondary analysis of the 246 mother–child dyads from the LiP Offspring study. It showed that BMI z-scores from 5 weeks to 2 years of age were all significantly and positively associated with BMI z-scores at 3 years of age. BMI z-scores from 5 months to 2 years of age were also significantly and positively associated with body fat percentage at 3 years of age. BMI z-scores from 5 weeks were not associated with the metabolic risk factor groups. This could be due to few children meeting the definitions.

TABLE 1 Maternal and childhood characteristics at baseline and follow-up for the LiP Offspring groups.

	Summary statistics			Number above the 90th percentile			
	LiP Offspring intervention	LiP Offspring control	External reference	LiP Offspring intervention	LiP Offspring control	External reference	
	n = 76	*n* = 73	*n* = 97	*n* = 76	*n* = 73	*n* = 97	Total, *n*
Maternal characteristics							
Pre-gestational BMI, kg/m^2[a]	34.1 ± 3.3	34.4 ± 3.1	22 ± 1.7				246
Maternal age	29.4 ± 4.0	29.1 ± 4.3	30.2 ± 4.1				246
Gestational Weight Gain, kg[a]	7.9 ± 4.6	8.5 ± 4.1	15.9 ± 5.2				243
School >12 years	58 (76.3)	48 (65.8)	97 (100)				246
Smoking in pregnancy	6 (9.2)	6 (9)	10 (10.5)				246
Breastfeeding >4 months[a]	41 (63.1)	38 (56.7)	73 (76.8)				246
Childhood characteristics 0–2 years							
Gender, males	37 (48.7)	41 (56.2)	50 (51.5)				246
Birthweight, g	3767.7 ± 482	3647.7 ± 435	3554.6 ± 433				246
BMI z-score							
5 weeks	0.5 ± 0.9	0.5 ± 1.0	0.3 ± 1.0				193
5 months	0.01 ± 1.5	0.02 ± 1.1	−0.1 ± 1.0				209
1 year	−0.3 ± 1.0	−0.4 ± 1.4	−0.6 ± 1.1				207
2 years	−0.2 ± 1.1	−0.4 ± 1.1	−0.5 ± 1.1				168
Outcomes at 3 years							
BMI z-score	0.1 ± 1.1	−0.2 ± 1.1	−0.2 ± 0.9	16 (21.1)	5 (6.9)	4 (4.1)	246
Abdominal circumference, cm	48.7 ± 3.0	47.9 ± 3.3	48.2 ± 2.8	10 (14.1)	3 (13)	10 (10.3)	237
Hip circumference, cm	51.1 ± 2.9	50.1 ± 3.2	50.4 ± 3.0	9 (13.4)	4 (6.3)	12 (12.4)	228
Triceps skinfold, mm	8.5 ± 1.7	8.3 ± 2.0	8.2 ± 1.6	6 (8.8)	10 (15.9)	7 (7.9)	220
Subscapular skinfold, mm	6.3 ± 1.6	6 ± 1.1	5.8 ± 1.2	7 (10.5)	5 (8.2)	9 (10.5)	214
Lean body mass, g	9180 ± 981	8996 ± 966	8611 ± 995	6 (18.8)	3 (10.3)	4 (7.0)	118
Fat body mass, g	2201 ± 899	2095 ± 633	1953 ± 720	6 (18.8)	3 (10.3)	3 (5.3)	118
Body fat percentage, %	0.2 ± 0.1	0.2 ± 0.1	0.2 ± 0.1	4 (12.5)	3 (10.3)	6 (10.5)	118
Diastolic blood pressure, mmHg	64.4 ± 5.1	62.9 ± 5.4	64.5 ± 5.8	4 (6.5)	5 (9.3)	13 (15.7)	199
Systolic blood pressure, mmHg	98.7 ± 7.2	98.3 ± 6.4	97.5 ± 7.3	6 (9.7)	7 (13)	8 (9.6)	199
Fasting plasma glucose, mmol/L	5.1 ± 0.6	5.1 ± 0.6	5 ± 0.5	9 (15.5)	8 (13.6)	7 (8.0)	205
HOMA-IR	5.1 ± 4.3	3.6 ± 3.5	3.2 ± 3.2	8 (21.1)	4 (7.8)	3 (4.9)	150
Total cholesterol, mmol/L	3.9 ± 0.7	4.0 ± 0.7	4 ± 0.7	4 (11.8)	5 (10.2)	6 (10.0)	143
HDL cholesterol, mmol/L	1.2 ± 0.2	1.3 ± 0.3	1.2 ± 0.3	2 (5.9)[b]	1 (2.0)[b]	5 (8.3)[b]	143
LDL cholesterol, mmol/L	2.4 ± 0.5	2.3 ± 0.5	2.4 ± 0.6	6 (17.7)	4 (8.2)	12 (20.0)	143
Triglycerides, mmol/L	0.8 ± 0.2	0.9 ± 0.5	0.8 ± 0.8	4 (11.8)	10 (20.4)	6 (10.2)	142
Metabolic risk factors LiP Offspring group[c]	4 (5.3)	3 (4.1)	2 (2.1)				
Metabolic risk factors IDF group[d]	4 (5.3)	4 (5.5)	3 (3.1)				

Note: Data are given as mean ± SD, or as number (*N*) and percentage (%).

Abbreviation: HOMA-IR, homeostasis model assessment of insulin resistance.

[a] $p < 0.05$ (External reference vs. LiP Offspring control).

[b] Numbers below the 10th percentile.

[c] Number of children in the LiP Offspring metabolic group.

[d] Number of children in the IDF metabolic group.

TABLE 2 Adjusted analyses of BMI z-scores from 5 weeks to 2 years of age and anthropometric and metabolic outcomes at 3 years of age.

	5 weeks, BMI z-score ($n = 193$)		5 months, BMI z-score ($n = 209$)		1 year, BMI z-score ($n = 207$)		2 years, BMI z-score ($n = 168$)	
Outcomes at 3 years	**Adjusted[a] OR**	***N***	**Adjusted[a] OR**	***N***	**Adjusted[a] OR**	***N***	**Adjusted[a] OR**	***N***
Metabolic risk factors								
LiP Offspring metabolic group[c]	3.16 (0.90 to 11.14)	84	1.60 (0.81 to 3.16)	90	1.23 (0.78 to 3.42)	90	3.34 (0.96 to 11.67)	75
IDF metabolic group[17]	2.71 (0.83 to 8.84)	88	1.27 (0.74 to 2.19)	94	1.77 (0.94 to 3.33)	96	2.64 (0.77 to 9.04)	99
	Adjusted[b] coefficient	***N***	**Adjusted[b] coefficient**	***N***	**Adjusted[b] coefficient**	***N***	**Adjusted[b] coefficient**	***N***
Anthropometrics								
BMI z-score	**0.30 (0.16 to 0.45)***	94	**0.47 (0.36 to 0.58)***	101	**0.6 (0.46 to 0.66)***	102	**0.6 (0.51 to 0.73)***	84
Abdominal circumference, cm	**0.50 (0.003 to 0.9)*****	91	**0.6 (0.27 to 1.0)***	98	**1.2 (0.87 to 0.1.57)***	99	**1.1 (0.76 to 1.53)***	82
Hip circumference, cm	**0.50 (0.004 to 0.9)*****	85	**1 (0.63 to 1.38)***	92	**1.4 (1.1 to 1.79)***	92	**1.5 (1.14 to 1.91)***	77
Triceps skinfold, mm	0.27 (−0.02 to 0.73)	85	**0.4 (0.15 to 0.61)***	93	**0.5 (0.28 to 0.74)***	93	**0.5 (0.24 to 0.72)***	79
Subscapular skinfold, mm	0.25 (−0.15 to 0.66)	83	**0.3 (0.14 to 0.50)***	90	**0.5 (0.29 to 0.65)***	90	**0.4 (0.17 to 0.59)***	76
Metabolic outcomes								
Lean body mass, g	249 (−78 to 577)	50	**344 (158-529)***	52	**427 (255-600)***	54	**359 (145-574)***	43
Fat body mass, g	**184 (11-357)*****	50	**368 (234-502)***	52	**400 (277-523)***	54	**428 (296-560)***	43
Body fat percentage	0.01 (−0.02 to 0.04)	50	**0.03 (0.02 to 0.05)***	52	**0.03 (0.02 to 0.05)***	54	**0.04 (0.03 to 0.05)***	43
Diastolic blood pressure, mmHg	0.88 (−49 to 2.26)	77	**1 (0.26 to 1.82)****	82	**1.3 (0.49 to 2.18)****	82	**1.1 (0.21 to 1.99)*****	71
Systolic blood pressure, mmHg	0.47 (−1.32 to 2.25)	77	**1 (0.01 to 1.9)*****	82	**2.2 (1.19 to 3.24)***	82	**1.4 (0.34 to 2.54)*****	71
Fasting blood glucose, mmol/L	0.08 (−0.09 to 0.24)	79	0.003 (−0.11 to 0.11)	85	**0.1 (0.002 to 0.2)*****	86	0.05 (−0.08 to 0.17)	71

Note: Bold data refer to statistically significant results.

Abbreviation: *N*, Number of observations in each model.

[a]Adjusted for maternal BMI at inclusion, gestational weight gain, maternal education (>12 years of school), maternal age, and gender.

[b]Adjusted for maternal BMI, gestational weight gain, maternal education (>12 years of school), breastfeeding for at least 4 months, smoking during pregnancy, maternal age, and gender.

[c]High abdominal circumference and two or more: abdominal circumference ≥ 52 cm; HDL < 0.9 mmol/L; Triglycerides ≥ 1.2 mmol/L; fasting glucose ≥ 5.8 mmol/L; systolic blood pressure ≥ 107 mmHg.

*$p \leq 0.001$; **$p \leq 0.01$; ***$p \leq 0.05$.

Early onset obesity, as young as 5 years of age, has been related to a higher metabolic risk in adolescence.[18] A Dutch cohort study found an association between growth in infancy and later adverse cardiovascular outcomes,[19] which supported the association between early growth patterns and adverse outcomes later in life. The lack of significant associations between BMI z-scores and metabolic risk factors at 3 years of age in our study may suggest that infant BMI z-scores were not really able to predict the onset of metabolic risk factors. Having said that, BMI z-scores from 5 weeks of age were associated with other factors related to metabolic risk, such as BMI z-scores, fat mass and abdominal circumference.

Few studies have investigated infant BMIs, but Sun et al.[20] found that when BMI peaked between birth and 13.5 months, it predicted obesity at 2 years of age in a Chinese community-based cohort. The associations between infant BMI z-scores and adverse outcomes at 3 years of age that were identified in our study may be present before that age, but patterns of growth and development may vary across different populations. In our study, BMI z-scores at 5 weeks were only associated with a few outcomes after adjustment, so attention to the child's BMI z-score may be more effective after 5 months of age and not 5 weeks.

We adjusted for total gestational weight gain and maternal BMI in our analyses, since we in this study were interested in BMI z-score in early age as predictors for adverse outcomes at 3 years of age, independent of the maternal weight factors. In previous publications we have shown that offspring of normal-weight mothers were comparable to offspring from LiP Offspring groups at 3 years of age.[13,14] However, other previous studies have indicated that maternal obesity before pregnancy is the strongest independent risk factor for neonatal adiposity and children being large for gestational age.[21,22]

In a Finnish child cohort, Nedelec et al.[23] found that an early-increase in the BMI trajectory was the highest risk for obesity compared to the normal trajectory. A stable low BMI trajectory from birth to 3.5 years of age resulted in a reduced BMI z-score at 9 years of age.[23] In contrast, stable high and accelerating trajectories were related to increased body size at that age.[24] The overall findings suggested that the speed of growth or weight gain, and not just a high BMI, may be associated with later adverse outcomes. Our present study was not able to identify growth trajectories, due to the small number of time points. This means that they described associations for each time point and not the impact of when, how much or how fast a child's BMI changed.

It may be useful to establish a definition of high-risk metabolism in small children in order to compare results from different studies based on specific risk factors and cut-off points. The clinical implications of this study should be interpreted with caution, as other factors are important for children's development and future health. Being overly focused on weight and weight loss could potentially worry and stress parents and children.

4.1 | Strengths and limitations

The main strength of our study was the detailed examinations of mother–child dyads in both pregnancy and early childhood. It was possible to include a wide range of potential confounders, which increased the validity of the study.

The post hoc analyses performed by Tanvig et al.[13] on our data source found no differences in BMI z-score or maternal and infant characteristics between participants with information on all outcomes and those with missing values. This indicated that no systematic bias was present.

To our knowledge, this was the first study to include a wide range of metabolic and anthropometric factors, including dual energy X-ray scans, in children as young as 0–3 years.

Women were excluded if they could not speak enough Danish to understand the questionnaire. The fact that only Caucasian mothers, who were not representative of the general population of pregnant women in Denmark, took part was an ethnic profile limitation of our study.

The limitations also included the risk of attrition bias, due to the loss to follow-up from the LiP to LiP Offspring study. This resulted in a smaller sample size and increased the risk of misclassification bias. The limitations also included the risk of social desirability and recall bias, as some of the information was based on the questionnaires, such as the duration and intensity of breastfeeding and maternal height. Factors that were not adjusted for were dietary habits, which may have affected their growth and weight in early childhood. Another limitation was measuring the length and height of children under 2 years of age that can be challenging and imprecise.

The lack of a definition for metabolic syndrome in young children made comparing studies on risk factors difficult. The IDF has produced a consensus statement for adults and children aged 10–16 years, but it does not apply to younger children.[17] For example the blood pressure criterion of 130 mmHg or more would be very high in children under 10. However, no other definition exists for children, so we used the IDF definition to inform the IDF group of metabolic risk factors. Some of the criteria in the IDF definition were very unlikely to be met by 3-year-old children. This meant that the IDF group was smaller than it would have been if we had used other criteria values to define this group.

Body fat percentage is not used in daily clinical settings, because dual energy X-ray scans are not routinely performed, but this measure adds much information to BMI z-scores and was a better measure for our research questions.

Danish health professionals routinely monitor measurements such as BMI-for-age and weight-for-length curves in infants and young children and assess their general well-being based on multiple factors, such as observing the home environment and anthropometrics. These results may simplify the monitoring of children's growth and well-being or provide awareness of the possible applications of BMI z-scores.

5 | CONCLUSION

There are some indications that adverse anthropometric outcomes are apparent as early as 3 years of age. Further research on the clinical

implications could include cut-off points for BMI z-scores to identify children with the highest risks of future adverse outcomes. A long-term follow-up study of the LiP Offspring children at age 14 years is investigating how infant growth and metabolism may predict later onset obesity, body composition and metabolic dysfunction.

AUTHOR CONTRIBUTIONS

Mikala E. Jakobsen: Conceptualization; formal analysis; methodology; writing – original draft. **Louise L. Stentebjerg:** Writing – review and editing. **Mette H. Tanvig:** Data curation; writing – review and editing. **Jan S. Jørgensen:** Writing – review and editing. **Per G. Ovesen:** Writing – review and editing. **Henrik T. Christesen:** Writing – review and editing. **Dorte M. Jensen:** Conceptualization; project administration; supervision; writing – original draft. **Christina A. Vinter:** Data curation; supervision; writing – original draft.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

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