

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email editorial.bmjopen@bmj.com

BMJ Open

Characterization of Infant BMI peak in urban China

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2016-015122
Article Type:	Research
Date Submitted by the Author:	28-Dec-2016
Complete List of Authors:	Sun, Jie; School of Public Health, Fudan, Department of Social Medicine; Jing'an Maternal and Child Health Care Center, Shanghai, Department of Child Health Care Nwaru, Bright; The University Of Edinburgh, Allergy & Respiratory Research Group, Centre for Population Health Sciences; University of Tampere, School of Health Sciences Hua, Jing; Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine, Department of Maternal and Child Health Care Li, Xiaohong; School of Public Health, Fudan University, Department of Health Policy and Management ; Innovation Center for Social Risk Governance in Health Wu, Zhuochun; School of Public Health, Fudan University, Department of Social Medicine; Innovation Center for Social Risk Governance in Health
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Paediatrics
Keywords:	Overweight, Obesity, Body mass index, Longitudinal Study, Infant

SCHOLARONE™
Manuscripts

only

Characterization of Infant BMI peak in urban China

Jie Sun^{1,2}, Bright I Nwaru^{3,4}, Jing Hua⁵, Xiaohong Li^{6,7}, Zhuochun Wu^{1,7}

Abstract

Objectives: Infant body mass index (BMI) peak, which has been studied in American and European, proves to be a useful indicator for predicting risk of childhood obesity. We aimed to first characterize infant BMI trajectories in a Chinese longitudinal cohort.

Methods: We used serial measurements (n=6-12) of weight and height from healthy term infants (n=2073) in a birth cohort established in urban Shanghai to estimate BMI growth curves from birth to 13.5 months by a polynomial regression model. The relationship between infant BMI peak and childhood BMI was examined using binary logistic analysis.

Results: Mean BMI peak was 18.33 kg/m² and occurred at 7.61 months. Boys (n=1022) had a higher average BMI peak (18.60 vs 18.07 kg/m², P<0.001) and earlier average timing (7.54 vs 7.67 months, P<0.05) than girls (n=1051). Higher (OR 3.11; 95% CI 2.64-3.66) and later timing (OR 1.35; 95% CI 1.22-1.50) of infant BMI peak were associated with increased risk of early childhood overweight. Similarly, higher magnitude (OR 2.76; 95% CI 2.05-3.73) and later timing (OR 1.34; 95% CI 1.08-1.67) of infant BMI peak were associated with increased risk of childhood obesity.

Conclusions: Infant BMI peak is valuable for predicting early childhood overweight and obesity in urban China. As this is first Chinese-based study on the topic, further studies are required to evaluate the utilization in other urban settings of China.

Key words: Body mass Index, Obesity, Overweight, Longitudinal Study, Infants

Word Count: 2739 words

¹Department of Social Medicine, School of Public Health, Fudan University, Shanghai, China.

²Department of Child Health Care, Jing'an Maternal and Child Health Care Center, Shanghai, China.

³School of Health Sciences, University of Tampere, Tampere, Finland.

⁴Asthma UK Centre for Applied Research, Usher Institute of Population Health Sciences and Informatics, University of Edinburgh, Edinburgh, UK.

⁵Department of Maternal and Child Health Care, Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine, Shanghai, China.

⁶Department of Health Policy and Management, School of Public Health, Fudan University, Shanghai, China.

⁷Innovation Center for Social Risk Governance in Health, Fudan University, Shanghai, China

Corresponding author: Zhuochun Wu, Department of Social Medicine, School of Public Health, Fudan University, Fax: 086-021-62309139, P.O. Box 250, 138 Yi Xue Yuan Road, Shanghai 200032, China. zcwu@shmu.edu.cn.

Strengths and limitations of this study

This is the first community-based cohort study in China to characterize infant BMI peak.

Association of BMI peak with risk of early childhood overweight and obesity will be evaluated.

It's a longitudinal cohort with careful repeated measurements of child growth parameters.

Only about 69.9% of all children in this age range had health records.

The data of parent's BMI and pregnancy weight gain were not available.

Introduction

The increasing prevalence of childhood overweight and obesity has become a serious public health crisis worldwide.¹⁻⁴ The worldwide prevalence of childhood overweight and obesity increased from 4.2% in 1990 to 6.7% in 2010.⁵ In urban areas of China, the prevalence of overweight and obesity among children aged 0-5 years increased from 5.3% in 2005 to 8.5% in 2010.⁶ Rapid weight gain in early infancy is related to later obesity and cardiovascular risk factors such as hypertension and impaired glucose tolerance in adulthood.⁷⁻¹¹ Although obesity results from the combined effects of genes, environment and lifestyle, rapid genetic changes could not have occurred to result in the rapid increase in prevalence being observed; consequently, environmental and behavioral factors are believed to be key drivers of the burden of obesity.¹² Therapeutic interventions have low cost-effectiveness and poor long-term effects, so infancy may be the most important period to initiate primary preventive strategies for overweight and obesity.¹³⁻¹⁵

Body mass index (BMI), a useful estimate of adiposity for children aged more than two years, correlates with future health outcomes.^{2,7} Based on international literature, few studies have evaluated the associations between infant BMI trajectories and childhood overweight and obesity.^{12,16-18} Weight-for-length percentile curves are often used but not with age-based changes that reflect different stages of infancy.¹⁶ BMI increases from birth and reaches a maximum called the 'BMI peak' around age 7-9 months, then, it decreases and reaches a nadir around age 4-6 years before increasing once more.¹⁶⁻¹⁸ From Silverwood et al onwards,

1
2
3 both age and BMI at BMI peak were positively associated with later BMI z-scores.¹⁷ So far,
4
5 several studies have used statistical models of growth trajectories to estimate the magnitude
6
7 and timing of infant BMI peak.¹⁶⁻²⁴
8
9

10 Ancestry-specific differences of Infant BMI peak have been demonstrated between
11
12 African-American and European populations.¹⁶ However, until date there has been no
13
14 previous study performed in China to demonstrate the utility of infant BMI peak for predicting
15
16 the risk of childhood overweight and obesity. Taking advantage of a population-based
17
18 longitudinal data set that has serial measurements for height and weight from birth into
19
20 childhood in Shanghai, we aimed to estimate the magnitude, timing of infant BMI peak, and to
21
22 study the association between infant BMI peak and overweight and obesity by age 2 years.
23
24
25
26

27 **Methods**

28 **Study Participants**

29
30
31
32
33 We obtained data from the Shanghai Jing'an District birth and health records, which is a
34
35 population-based longitudinal cohort. There are seventeen urban districts and one suburban
36
37 district in Shanghai, with a population of 19 million in 2009. Jing'an District is located at the
38
39 city center with a population of 248 thousand in 2009. "Providing free of charge health
40
41 examination to children aged 0-3 years" was a project funded by Shanghai government for
42
43 Jing'an children born from September 2009. The community health centers in the Jing'an
44
45 District provide routine basic medical services to the local community, including well-child
46
47 routine checks for infants and young children. A District Childcare Database for all local
48
49 health centers in this project was established and managed by the Jing'an maternal and child
50
51 health care center. With the information network, data on children's gender, gestational age,
52
53 birth weight, feeding and sleeping behaviors, amongst others were recorded by the nurses in
54
55 the health centers when they did the child health examination. All children were followed from
56
57 one month to two or three years old until they went to kindergarten.
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For this study, we used data from the Childcare Database for all children who were born from September 1st 2009 through September 1st 2013 and received care at the health centers of Jing'an district. The children were followed up from birth, with data collected at 1, 2, 4, 6, 9, 12, 18 and 24 months of age from all five communities in Jing'an District, representing 69.9% (7456/10674) of all children in this age range in Jing'an District. There were roughly 30% of children moving from Jing'an district to other districts of Shanghai during the study period, which resulted in the missing of the subjects. We gained approval (IRB#2015-TYSQ-03-11) for the current study from the Medical Research Ethics Committee, School of Public Health, Fudan University.

Inclusion and exclusion criteria

Inclusion criteria for infants included in the study were healthy singleton infants, born between 37 and 42 weeks gestational age without physical problems. Participants were also eligible if they had at least six measurements of height and weight in the first 13.5 months of life. This number and range of measurements were referred to BMI modeling set by the CHOP study in Philadelphia, USA.^{16,20} As BMI peak is around age 7-9 months, we included children who had at least one visit in the following age ranged 213-274 days. To test the relationship between infant BMI peak and childhood overweight and obesity, measurements for children at age two years were included when such data were available. There were 21.2% (2268/7456) infants eligible for analysis. Of these, we observed 85.9% (1949/2268) children from birth to age two years till September 1st 2015 (Table 1). Preterm infants (n =195), term infants with congenital defect (n=30) were excluded.

Anthropometric measures

Weight and length of children were measured using standardized procedures at the community health centers. Weight was measured by an electronic pediatric scale to the nearest 0.005 kg, and length to the nearest 0.1 cm. BMI z-score (BAZ) of children at age two years were calculated according to the 2006 World Health Organization (WHO) Child Growth

Standards using the WHO Anthro 2009 software.²⁵ The WHO Child Growth Standards was based on a multi-country study involving breastfed children from six geographically distinct sites.⁵ Overweight was defined as BAZ > +1 (BMI >85th percentile) while obesity was defined as BAZ>+2 (BMI >95th percentile). Normal weight was defined as $-1 \leq \text{BAZ} \leq +1$.^{1,13} Based on reports from previous studies,^{11,12,16,18} we extracted factors associated with childhood overweight from the electronic medical records. These factors were birth weight, sex, delivery mode mother's ages, duration of breastfeeding and sleeping data.(Table 2) Because this cohort was set up after birth, some information about pregnancy and parents information was not complete. We classified birth weight as the following categories: 1.5 to less than 2.5 kg, 2.5 to less than 4 kg, and greater than 4 kg.

BMI trajectory modeling

BMI peak was identified from subject-specific BMI growth curves established by serial BMI measurements. A polynomial regression model with quadratic terms was fit to the BMI measurements over time. Regression modeling was used for each child to fit the following equation:¹⁶

$$\text{BMI} = \beta_0 + [\beta_1 * (\text{age in days})] + [\beta_2 * (\text{age in days})^2]$$

The first inflection point occurred at less than 408 days and identified as BMI peak was derived from the equation. The magnitude and timing of BMI peak and velocity to peak were calculated for each subject from the model. The velocity to the peak was calculated using the following equation, with BMI at 14 days of age as the baseline measurement:¹⁸

$$(\text{BMI}_{\text{Peak}} - \text{BMI}_{14\text{days}}) / (\text{age}_{\text{BMI Peak}} - 14 \text{ days}).$$

The subjects who had a BMI peak within 14–408 days of life were defined as estimable (“fit”) BMI trajectories, while those who were not identifiable by the model were called inestimable (“not fit”) BMI trajectories.¹⁶

Statistical analysis

1
2
3 SPSS 20.0 statistical software was used for all analyses and metalab2014b for the BMI
4 trajectory modeling. Data were presented as mean with 95% confidence interval. Categorical
5 data were summarized by calculating percentages. The chi-square test and two-sampled t
6 tests were used to examine the differences between participants whose BMI trajectories were
7 estimable or not inestimable for the quadratic regression model and those who did or did not
8 have measurements at age two years. To evaluate the associations between covariates and
9 infant BMI peak characteristics and childhood BMI Z-scores, bivariate analyses were used by
10 one-way ANOVA with post hoc Bonferroni adjustments. Logistic regression was used to
11 assess the associations between infant BMI peak trajectories and childhood BMI Z-scores,
12 adjusting for other background characteristics. Statistical analyses were performed using
13 only the subjects with estimable BMI peak.¹⁶⁻¹⁹ All statistical tests were two-tailed and P
14 values <0.05 were considered statistically significant.
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Results

Description of the study population

The demographic and independent variables of the study population are presented in Table 3. There were 2268 infants eligible for analysis, 49.6% male and 50.4% female. Most had a normal birth weight of 2.5 to less than 4 kg (n=2073, 91.4%). Eighty-five percent (n =1949) of infants had follow-up data at least through the age of 2 years (Table 3). Evaluated by the WHO Child Growth Standards, 17.0% (n =332) infants were overweight (BAZ > +1) and 2.3% (n =44) obese (BAZ > +2) at age 2 years.

Results of infant BMI trajectory modeling

Individual BMI trajectories were estimable using the polynomial regression model for 91.4% of the sample, with reasonable fit (mean $R^2 = 0.70 \pm 0.23$). Mean BMI peak was 18.33 (95% CI 18.26-18.39) kg/m² and occurred at 7.61 (95% CI 7.55-7.67) months. Those subjects with inestimable BMI peak mostly showed either a BMI peak after 408 days of life or a decrease in BMI after birth. The prevalence of macrosomia (birth weight > 4kg) infants with inestimable infancy BMI peak were slightly higher than that with estimable ones (6.7% vs 11.3%, $P = 0.024$). Macrosomia born heavier reached their BMI peak much earlier, since some of them attained BMI peak measurements just after birth. There was no significant difference in other factors between subjects with estimable and inestimable peak BMI trajectories ($P > 0.05$). (Table 3)

Participants' characteristics in relation to infant BMI trajectories

Infant BMI trajectories were related to both sex and birth weight (Table 4). BMI peak was greater, and timing of peak BMI was earlier, in boys than in girls and in children of higher birth weight than those of lower birth weight. There was no statistical significant difference in velocity to BMI peak with regards to infant characteristics.

General characteristics of children at age two years

We tested for differences between infants who had BMI data with estimable BMI peak at age two years (n=1790) vs those who did not (n=159). There was no difference between the two groups in sex, birth weight, mother's age, duration of breastfeeding, duration of sleep ($P > 0.05$).

Association between infant BMI peak and childhood overweight and obesity

Table 5 shows the results of the association between BMI peak and risk of overweight and obesity at two years of age. When only the infant BMI peak was included in the model, higher magnitude and later timing of infant BMI peak increased the risk of overweight at two years. Furthermore, after adjustment for other infant background factors, higher magnitude (OR 3.11; 95% CI 2.64–3.66) and later timing (OR 1.35; 95% CI 1.22-1.50) of infant BMI peak each increased the risk of overweight at two years. The results were also similar with regards to childhood obesity (Table 5).

Discussion

Using a longitudinal data from a population-based cohort, we have demonstrated in the current analysis that infant BMI peak is useful for predicting childhood overweight and obesity in urban China. Boys had a higher average BMI peak and earlier average timing than girls. Principally, our results show that higher magnitude and later timing of infant BMI peak were each associated with increased risk of early childhood overweight and obesity.

This is the first community-based cohort study in China to characterize infant BMI peak and evaluate its association with risk of early childhood overweight and obesity. Our findings are therefore generalizable to children of similar age in Shanghai city, and to some degree by extension to other urban areas in China. The used data were routinely collected by the health centers where children are offered routine healthcare, such as immunization and physical examination; thus constitute a valid and reliable data set for addressing the study questions. The longitudinal nature of the cohort and the repeated measurements of height and weight parameters provided us with the opportunity to carefully model the BMI trajectories of infants. One limitation of our investigation was that only about 69.9% (7456/10674) of all children in this age range had health records and 85.9% of eligible children had complete follow-up data up to the age of two years, meaning that those with incomplete data were excluded from analysis and risk of selection bias may not be totally ruled out. Another weakness of the study is that the data of parent's BMI, pregnancy weight gain, gestational diabetes mellitus and income were not available, the reason being that the cohort was set up after birth and not prenatally.

So far, few studies have been conducted on the utility of infant BMI peak for predicting childhood overweight and obesity.¹⁶⁻¹⁸ The principal finding of our study that higher magnitude and later timing of infant BMI peak were each associated with increased risk of early childhood overweight and obesity is similar to previous research from the CHOP study

1
2
3 conducted in USA¹⁶ and the Uppsala Family Study in Europe.¹⁷ However, some findings of
4 the current study are not consistent with previous research. A 2010 prospective cohort show
5 that more rapid increases in weight for length in the first six months of life were associated
6 with sharply increased risk of childhood obesity.²⁶ Most previous studies used weight or BMI
7 at study-dependent fixed ages^{26,27} while ours was based on longitudinal and repeated
8 measures of height and weight. Our results also demonstrate that sex and birth weight
9 differences were shown in magnitude and timing of the peak but not in pre-peak velocity.^{16,18}
10 In some recent studies, later BMI peak was found for both girls and boys (8-9 months of age).
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

17,18,20 Furthermore, an earlier and higher BMI peak was found to be positively associated with birth weight.^{16,17} In our study, higher birth weight was not associated with a lower velocity, which was found by the CHOP study.¹⁶

There is no widely accepted method to model infant BMI peak, appropriate peak age range and the number and timing of serial measurements.²⁰ China is undergoing rapid social and economic developments with consequent improvement in nutritional status. Current estimates indicate that overweight and obesity are rising in China, including among children.⁴ However, given the lack of studies evaluating the utility of BMI peak for predicting later childhood overweight and obesity in China, as has been demonstrated in other contexts and shown to be ancestry-specific,¹⁶ it is therefore necessary to undertake such assessment, which will be useful in predicting early onset of obesity and serve as a springboard for planning appropriate interventions targeted at reducing the increasing trend of childhood overweight and obesity in urban China. It is unclear why infants in our study had earlier BMI peaks as (7-8 months) compared to infants from America and Europe (8-9 months),^{17,18,20} but as been demonstrated, such differences may reflect possible ancestry-specific BMI peaks across populations; therefore cross-cultural evaluations are required to ascertain the validity of this assertion. Understanding these differences may help design the protocol of public health interventions to control childhood obesity.^{28,29,30}

1
2
3
4
5
6 The principal finding of the current study suggests that infant BMI peak is useful in predicting
7 future risk of overweight and obesity in children in urban China; therefore infancy represents
8 a critical window of opportunity for the prevention of the emerging overweight and obesity
9 epidemic in children.
10
11
12
13

21 **Conclusion**

22
23
24 Using a community-based longitudinal cohort study with repeated measurements of infant
25 growth parameters, we have for the first time determined that infant BMI peak is valuable for
26 predicting early childhood overweight and obesity in urban China. Further studies are
27 required to evaluate the utilization in other urban settings of China.
28
29
30
31

32 **Acknowledgements**

33
34
35 We are grateful to the staff in Jing'an maternal and child health care center for data extraction.
36 We also acknowledge all children and their parent's for participating this project.
37
38
39

40 **Authors' contributions**

41
42
43 Jie Sun, Bright I Nwaru, and Zhuochun Wu were responsible for the study design, analysis of
44 the study and approval of the submitted and final version. Jing Hua and Xiaohong Li analyzed
45 the data, interpreted the results and commented on the manuscript.
46
47
48
49
50
51

52 **Funding**

53
54
55 This study was funded by National Natural Science Foundation of China [71573049]..
56
57
58
59
60

Ethics Approval

All procedures performed in this study were in accordance with the ethical standard. We gained approval (IRB#2015–TYSQ–03-11) for the current study from the Medical Research Ethics Committee, School of Public Health, Fudan University. Informed consent was obtained from all individual participants included in the study.

Competing interests

The authors declare that they have no conflict of interest.

References:

1. Neelon SEB, Andersen CS, Morgen CS, Kamper-Jørgensen M, Oken E, Gillman MW, et al. Early child care and obesity at 12 months of age in the Danish National Birth Cohort. *Int J Obes (Lond)* 2015;39:33-38.
2. Freedman DS, Mei Z, Srinivasan SR, Berenson GS, Dietz WH. Cardiovascular risk factors and excess adiposity among overweight children and adolescents: the Bogalusa Heart Study. *J Pediatr* 2007;150:12–17.
3. Skinner AC, Perrin EM, Skelton JA. Prevalence of obesity and severe obesity in US children, 1994-2014. *Obesity (Silver Spring)* 2016;24:1116-1123.
4. Ji C. Report on Childhood Obesity in China (4) Prevalence and Trends of Overweight and Obesity in Chinese Urban School-age Children and Adolescents, 1985-2000. *Biomed Environ Sci* 2007;20:100-106.
5. de Onis M, Blössner M, Borghi E. Global prevalence and trends of overweight and obesity among preschool children. *Am J Clin Nutr* 2010;92:1257–1264.
6. National Report on Nutritional status of children aged 0-6 year. *China: National health and Family Planning Commission*. China; 2012.
7. Andersen LG, Holst C, Michaelsen KF, Baker JL, Sørensen TI. Weight and weight gain during early infancy predict childhood obesity: a case- cohort study. *Int J Obes (Lond)* 2012;36:1306–1311.
8. Baird J, Fisher D, Lucas P, Kleijnen J, Roberts H, Law C. Being big or growing fast: systematic review of size and growth in infancy and later obesity. *BMJ* 2005;331:929.
9. Leunissen RW, Kerkhof GF, Stijnen T, Hokken-Koelega A. Timing and tempo of first-year rapid growth in relation to cardiovascular and metabolic risk profile in early adulthood. *JAMA* 2009;301:2234-2242.
10. Monteiro PO, Victora CG. Rapid growth in infancy and childhood and obesity in later life—a systematic review. *Obes Rev* 2005;6:143–154.
11. Weng SF, Redsell SA, Swift JA, Yang M, Glazebrook CP. Systematic review and meta-analyses of risk factors for childhood overweight identifiable during infancy. *Arch Dis Child* 2012;97:1019–1026.
12. Guo Y. Growth level of urban Chinese infants from birth to 2 years, body mass index Z scores' predicting model and its age trajectory in relation to maternal pre-pregnancy body weight status. *Huangzhong Technology University China*; 2013.
13. Ma JQ, Zhou LL, Hu YQ, Liu SS, Sheng XY . Association between feeding practices and weight status in young children. *BMC Pediatrics* 2015;15:97.
14. Gortmaker SL, Swinburn B, Levy D, Carter R, Mabry PL, Diane Finegood et al. Changing the Future of Obesity: Science, Policy and Action. *Lancet* 2011;378:838–847.
15. Robinson SM, Crozier SR, Harvey NC, Barton BD, Law CM, Godfrey KM, et al. Modifiable early-life risk factors for childhood adiposity and overweight: an analysis of their combined impact and potential for prevention. *Am J Clin Nutr* 2015;101:368-375.
16. Roy SM, Chesni A, Mentch F, Xiao R, Chiavacci R, Mitchell JA, et al. Body Mass Index (BMI) Trajectories in Infancy differ by population ancestry and may presage disparities in early childhood obesity. *J Clin Endocrinol Metab* 2015;100:1551-1560.

- 1
2
3 17. Silverwood RJ, De Stavola BL, Cole TJ, Leo DA. BMI peak in infancy as a predictor for later BMI in the
4 Uppsala Family Study. *In J Obes (Lond)* 2009;33:929-937.
5
6 18. Jensen SM, Ritz C, Ejlerskov KT, Mølgaard C, Michaelsen KF. Infant BMI peak, breastfeeding, and body
7 composition at age 3y. *Am J Clin Nutr* 2015;101:319-325.
8
9 19. WHO Multicentre Growth Reference Study Group. WHO Child Growth Standards: Length/height-for-age,
10 Weight-for-age, Weight-for-length, Weight-for-height, and Body Mass Index-for-age: Methods and
11 Development. Geneva: World Health Organization, 2006. Available from:
12 <http://www.who.int/childgrowth/standards/en/>
13
14 20. Wen X, Kleinman K, Gillman MW, Rifas-Shiman SL, Taveras EM. Childhood body mass index
15 trajectories: modeling, characterizing, pairwise correlations and socio-demographic predictors of trajectory
16 characteristics. *BMC Med Res Methodol* 2012;12:38.
17
18 21. Chivers P, Hands B, Parker H, Bulsara M, Beilin LJ, Kendall GE et al. Body mass index, adiposity
19 rebound and early feeding in a longitudinal cohort (Raine Study). *In J Obes (Lond)* 2010;34:1169-1176.
20
21 22. Johnson W, Choh AC, Lee M, Towne B, Czerwinski SA, Demerath EW. Characterization of the Infant BMI
22 Peak: Sex Differences, Birth Year Cohort Effects, Association with Concurrent Adiposity, and Heritability. *Am*
23 *J Hum Biol* 2013;25:378-388.
24
25 23. Giles LC, Whitrow MJ, Davies MJ, Davies CE, Rumbold AR, Moore VM. Growth trajectories in early
26 childhood, their relationship with antenatal and postnatal factors, and development of obesity by age 9 years:
27 results from an Australian birth cohort study. *Int J Obes (Lond)* 2015;39:1049-1056.
28
29 24. Sovio U, Kaakinen M, Tzoulaki I, Das S, Ruokonen A, Pouta A, et al. How do changes in body mass index
30 in infancy and childhood associate with cardiometabolic profile in adulthood? Findings from the Northern
31 Finland Birth Cohort 1966 Study. *Int J Obes (Lond)* 2014;38:53-59.
32
33 25. WHO. Anthro for personal computers, version 3. Software for assessing growth and development of the
34 world's children. Geneva: WHO, 2009. Available from: <http://www.who.int/childgrowth/software/en/>
35
36 26. Taveras EM, Rifas-Shiman S, Belfort MB, Kleinman KP, Oken E, Gillman MW. Weight status in the first 6
37 months of life and obesity at 3 years of age. *Pediatrics* 2009;123:1177-1183.
38
39 27. Guo B, Mei H, Yang S, Zhang J. Prenatal factors associated with high BMI status of infants and
40 toddlers. *Chin J Pediatr* 2014;52:464-467.
41
42 28. Taveras EM, Gillman MW, Kleinman KP, Rich-Edwards JW, Rifas-Shiman SL. Racial/Ethnic Differences
43 in Early Life Risk Factors for Childhood obesity. *Pediatrics* 2010;125:686-695.
44
45 29. Taveras EM, Gillman MW, Kleinman KP, Rich-Edwards JW, Rifas-Shiman SL. Reducing racial/ethnic
46 disparities in childhood obesity: the role of early life risk factors. *Jama Pediatrics* 2013;167:1-7.
47
48 30. Zilanawala A, Davis-Kean P, Nazroo J, Sacker A, Simonton S, Kelly Y.
49 Race/ethnic disparities in early childhood BMI, obesity and overweight in the
50 United Kingdom and United States. *Int J Obes (Lond)* 2015;39:520-529.
51
52
53
54
55
56
57
58
59
60

Table 1 Description of children eligible in the study

Year	Eligible children n	Children with data at age 2y n (%)
2009	190	169 (88.9)
2010	413	369 (89.3)
2011	606	545 (89.9)
2012	660	571 (86.5)
2013	399	295 (73.9)
Total number	2268	1949 (85.9)

For peer review only

Table 2 Description of dependent and independent variables

Variable	Description
Dependent Variables	
Overweight	1-if yes at age 2y 0-otherwise
Obesity	1-if yes at age 2y 0-otherwise
Independent variables	
Sex	1-male 0-female
Delivery Mode	1-Cesarean Section 0-Vaginal Birth
Mother Age	1-above 35y 0-otherwise
Duration of Breastfeeding	Continuous variable
Duration of Sleep	Continuous variable
Birth Weight	Continuous variable
Magnitude of BMI Peak	Continuous variable
Timing of BMI Peak	Continuous variable
Velocity to BMI Peak	Continuous variable

Table 3 Participants' characteristics by subjects with "estimable"* and "inestimable"# BMI peak

Characteristics	n	Estimable *, n (%)	Inestimable #, n (%)
Total number	2268	2073	195
Sex			
Male	1126	1022 (49.3)	104 (53.3)
Female	1142	1051 (50.7)	91 (46.7)
Birth weight			
1.5 to <2.5kg	35	30 (1.4)	5 (2.6)
2.5 to <4.0kg	2073	1905 (91.9)	168 (86.2)
≥4kg	160	138 (6.7)^a	22 (11.3)
Delivery mode			
Vaginal birth	1086	989 (47.7)	97 (49.7)
Cesarean section	1182	1084 (52.3)	98 (50.3)
Mother Age			
>35y	176	159 (7.7)	17 (8.7)
≤35y	2092	1914 (92.3)	178 (91.3)
Total number with data at age 2y	1949	1790 (86.3)	159 (81.5)
Total number overweight and obese at age 2y	332	313 (17.5)	19 (11.9)
Total number and obese at age	44	43 (2.4)	1 (0.6)

a.P<0.05

* Estimable: fit and identifiable BMI peak within 14–408 days of life.

Inestimable: Not fit and identifiable.

Chi-square tests were used to examine the differences between Estimable or Inestimable group.

Table 4 Infant characteristics in relation to infant BMI peak trajectories

		infant BMI peak, kg/m ² , Mean (95% CI)	Age at Infant BMI peak, mo, Mean (95% CI)	Velocity to Peak, kg/m ² , mo. Mean (95% CI)
Total	n=2073	18.33(18.26-18.39)	7.61(7.55-7.67)	0.43(0.42-0.44)
Sex				
	male (n=1022)	18.60(18.21-18.69)^a	7.54(7.46-7.63)^b	0.42(0.41-0.43)
	female (n=1051)	18.07(17.98-18.16)	7.67(7.59-7.76)	0.43(0.42-0.44)
Birth Weight				
	1.5 to <2.5kg(n=30)	17.63(17.13-18.13)	8.13(7.56-8.70)	0.44(0.35-0.53)
	2.5 to <4.0kg(n=1905)	18.27(18.21-18.34)	7.63(7.57-7.70)	0.43(0.42-0.44)
	>=4kg(n=138)	19.25(18.97-19.52)^b	7.11(6.88-7.34)^a	0.39(0.35-0.42)
Delivery Mode				
	Vaginal birth (n=989)	18.24(18.14-18.34)	7.64(7.56-7.73)	0.43(0.42-0.44)
	Cesarean section (n=1084)	18.41(18.32-18.50)^a	7.58(7.49-7.66)	0.43(0.42-0.44)
Mother Age				
	>35y(n=159)	18.42(18.18-18.66)	7.61(7.49-7.82)	0.44(0.41-0.48)
	<=35y(n=1914)	18.32(18.25-18.39)	7.61(7.55-7.67)	0.42(0.41-0.43)

a.P<0.001 b.P<0.05

The analysis includes only infants who had BMI peak within 0-408 days and whose BMI trajectories were estimable by the quadratic model.

Bivariate comparison was performed using one-way ANOVA with post hoc Bonferroni multiple comparison test.

Table 5 Association between infant BMI peak and overweight and obesity at age 2 years

	Overweight at 2y (n=1790)		Obesity at 2y (n=1790)	
	Model containing infant BMI trajectory characteristics alone	Initial model plus all independent variables	Model containing infant BMI trajectory characteristics alone	Initial model plus all independent variables
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Magnitude of BMI peak, kg/m ²)	2.94(2.54-3.40)^a	3.11(2.64-3.66)^a	2.76(2.11-3.60)^a	2.76(2.05-3.73)^a
Timing of BMI peak, mo	1.36(1.23-1.51)^b	1.35(1.22-1.50)^a	1.33(1.08-1.65)^b	1.34(1.08-1.67)^b
Velocity to BMI peak, kg/m ² mo	0.17(0.07-0.40)^c	0.14(0.06-0.35)^a	0.10(0.02-0.56)^b	0.11(0.02-0.68)^c
male(vs female) birth weight,g(continuous)		0.66(0.49-0.89)^b		0.94(0.48-1.85)
Duration of breastfeeding(continuous)		1.00(1.00-1.00)		1.00(0.99-1.00)
Duration of Sleep(continuous)		0.97(0.94-1.01)		0.92(0.84-1.01)
Cesarean section(vs Vaginal Birth)		0.89(0.77-1.02)		0.88(0.63-1.23)
Mother Age(>35y vs <=35y)		1.09(0.82-1.45)		0.87(0.45-1.65)
		0.69(0.39-1.22)		0.75(0.21-2.62)

a.P<0.001 b.P<0.01 c.P<0.05

The analysis includes only infants who had BMI peak within 0-408 days and whose BMI trajectories were estimable by the quadratic model.

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any pre-specified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-4, Table-1
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	4
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5, Table-2
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4,5
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5,6
		(b) Describe any methods used to examine subgroups and interactions	6
		(c) Explain how missing data were addressed	4
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	4

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 3
		(b) Indicate number of participants with missing data for each variable of interest	Table 3
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	4
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	7
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8, Table 5
		(b) Report category boundaries when continuous variables were categorized	Table 3, 4
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	10
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Infant BMI Peak as a predictor of overweight and obesity at age 2 years in a Chinese community-based cohort

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2016-015122.R1
Article Type:	Research
Date Submitted by the Author:	13-Jun-2017
Complete List of Authors:	Sun, Jie; School of Public Health, Fudan, Department of Social Medicine; Jing'an Maternal and Child Health Care Center, Shanghai, Department of Child Health Care Nwaru, Bright; The University Of Edinburgh, Allergy & Respiratory Research Group, Centre for Population Health Sciences; University of Tampere, School of Health Sciences Hua, Jing; Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine, Department of Maternal and Child Health Care Li, Xiaohong; School of Public Health, Fudan University, Department of Health Policy and Management ; Innovation Center for Social Risk Governance in Health Wu, Zhuochun; School of Public Health, Fudan University, Department of Social Medicine; Innovation Center for Social Risk Governance in Health
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Paediatrics
Keywords:	Overweight, Obesity, Body mass index, Longitudinal Study, Infant

SCHOLARONE™
Manuscripts

Infant BMI peak as a predictor of overweight and obesity at age 2 years in a Chinese community-based cohort

Jie Sun^{1,2}, Bright I Nwaru^{3,4}, Jing Hua⁵, Xiaohong Li^{6,7}, Zhuochun Wu^{1,7}

Abstract

Objectives: Infant body mass index (BMI) peak, which has been studied in American and European populations and proved to be a useful indicator for predicting risk of childhood obesity, has not been assessed in China. We aimed to characterize infant BMI trajectories in a Chinese longitudinal cohort and to evaluate whether BMI peak can predict overweight and obesity at age 2 years.

Methods: Serial measurements (n=6-12) of weight and length from healthy term infants (n=2073) in a birth cohort established in urban Shanghai were conducted to estimate BMI growth curves from birth to 13.5 months using a polynomial regression model. BMI peak characteristics [age (in months) and magnitude (BMI; in kg/m²) at peak and pre-peak velocities (in kg/m²/month)] were estimated. The relationship between infant BMI peak and childhood BMI at age 2 years was examined using binary logistic analysis.

Results: Mean age at peak BMI was 7.61 months, with a magnitude of 18.33 kg/m². Boys (n=1022) had a higher average peak BMI (18.60 vs. 18.07 kg/m², P<0.001) and earlier average timing of achieving peak value (7.54 vs. 7.67 months, P<0.05) than girls (n=1051). With the peak BMI value increasing by 1 kg/m² or the peak time by 1 month every time, the risk of overweight at age 2 years increased by 2.11 times (OR 3.11; 95% CI 2.64-3.66) and 35% (OR 1.35; 95% CI 1.21-1.50) respectively. Similarly, higher magnitude (OR 2.69; 95% CI 2.00-3.61) and later timing (OR 1.35; 95% CI 1.08-1.68) of infant BMI peak were associated with increased risk of childhood obesity at age 2 years.

Conclusions: Infant BMI peak is proved to be valuable for predicting early childhood overweight and obesity in urban Shanghai. Since this is the first Chinese community-based cohort study on the topic, further studies are required for other infant populations in different areas of China.

Key words: Body mass Index, Obesity, Overweight, Longitudinal Study, Infants

Word Count: 3694 words

¹Department of Social Medicine, School of Public Health, Fudan University, Shanghai, China.

²Department of Child Health Care, Jing'an Maternal and Child Health Care Center, Shanghai, China.

³School of Health Sciences, University of Tampere, Tampere, Finland.

⁴Asthma UK Centre for Applied Research, Usher Institute of Population Health Sciences and Informatics, University of Edinburgh, Edinburgh, UK.

⁵Department of Maternal and Child Health Care, Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine,

1
2
3 Shanghai, China.

4
5 ⁶Department of Health Policy and Management, School of Public Health, Fudan University, Shanghai,China.

6
7 ⁷Innovation Center for Social Risk Governance in Health, Fudan University, Shanghai, China

8 Corresponding author:Zhuochun Wu , Department of Social Medicine , School of Public Health, Fudan University, Fax:
9 086-021-62309139, P.O. Box 250,138 Yi Xue Yuan Road, Shanghai 200032, China . zcwu@shmu.edu.cn.

10 11 **Strengths and limitations of this study**

12 This is the first community-based cohort study in China to characterize infant BMI peak.

13 Association of BMI peak with risk of early childhood overweight and obesity will be evaluated.

14 It's a longitudinal cohort with careful repeated measurements of child growth parameters.

15 Only about 69.9% of all children in this age range had health records.

16 The data of parent's BMI and pregnancy weight gain were not available.

17 18 19 20 21 22 23 24 25 26 **Introduction**

27
28 The worldwide overweight prevalence among children aged under 5 years has risen from 4.8%
29 in 1990 to 6.1% in 2014. The current worldwide obesity epidemic is a serious public health
30 crisis. ⁽¹⁻⁵⁾ In 2014, almost half (48%) of them lived in Asia. ⁽⁵⁾ In urban areas of China, the
31 prevalence increased from 5.3% in 2005 to 8.5% in 2010. ⁽⁶⁾ Rapid weight gain in early infancy
32 is related to later obesity and cardiovascular risk factors such as hypertension and impaired
33 glucose tolerance in adulthood. ⁽⁷⁻¹¹⁾ Although obesity results from the combined effects of
34 genes, environment and lifestyle, rapid genetic changes could not have occurred to result in
35 the rapid increase in prevalence being observed; consequently, environmental and
36 behavioral factors are believed to be key drivers of the burden of obesity. ⁽¹²⁾ Therapeutic
37 interventions have low cost-effectiveness and poor long-term effects, so infancy may be the
38 most important period to initiate primary preventive strategies for overweight and
39 obesity. ⁽¹³⁻¹⁵⁾

40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
Body mass index (BMI), a useful estimate of adiposity for children aged more than two years,
correlates with future health outcomes. ^(2, 7) It's reported that even a modest reduction in BMI
z-score after one year of obesity intervention was associated with improvement in several

1
2
3 cardiovascular risk factors.⁽¹⁶⁾ In young children, waist-to-height-ratio (WHtR) is not superior
4 to BMI in estimating body fat percentage, nor is WHtR better correlated with cardiometabolic
5 risk factors than BMI in overweight/obese children.⁽¹⁷⁾ One study in Singapore suggests an
6 important impact of early BMI development on later metabolic outcomes in Asian
7 populations.⁽¹⁸⁾
8
9

10
11
12 Based on international literature, few studies have evaluated the associations between infant
13 BMI trajectories and childhood overweight and obesity.^(12, 19-21) Weight-for-length percentile
14 curves are often used but not with age-based changes that reflect different stages of
15 infancy.⁽¹⁹⁾ BMI increases from birth and reaches a maximum called the 'BMI peak' around
16 age 7-9 months, then, it decreases and reaches a nadir around age 4-6 years before
17 increasing once more.⁽¹⁹⁻²¹⁾ From Silverwood et al onwards, both age and magnitude at peak
18 were positively associated with later BMI z-scores.⁽²⁰⁾ So far, several studies have used
19 statistical models of growth trajectories to estimate the magnitude and timing of infant BMI
20 peak.⁽¹⁸⁻²⁷⁾
21
22

23
24 Ancestry-specific differences of Infant BMI peak have been demonstrated between
25 African-American and European populations.⁽¹⁹⁾ However, until date there has been no
26 previous study performed in China to demonstrate the utility of infant BMI peak for predicting
27 the risk of childhood overweight and obesity. It is possible that different modeling methods
28 (such as natural cubic splines, fractional polynomials) used to derive BMI peak
29 characteristics could account for the observed differences across populations.⁽¹⁸⁾ To make
30 comparison with other populations, we referred to BMI modeling set by the CHOP study in
31 Philadelphia, USA.^(19, 23) Taking advantage of a community-based longitudinal data set that
32 has serial measurements for length and weight from birth into childhood in Shanghai, we
33 aimed to estimate the BMI peak characteristics to study the association between infant BMI
34 peak and overweight and obesity at age 2 years.
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Methods

Study Participants

We obtained data from the Shanghai Jing'an District birth and health records, which is a community-based longitudinal cohort. There are seventeen urban districts and one suburban district in Shanghai, with a population of 19 million in 2009. Jing'an District is located at the city center with a population of 248 thousand in 2009. "Providing free of charge health examination to children aged 0-3 years" was a project funded by Shanghai government for Jing'an children born from September 2009. The community health centers in the Jing'an District provide well-child routine checks for infants and young children. A District Childcare Database for all health centers in this project was established and managed by the Jing'an maternal and child health care center. With the information network, data on children's gender, gestational age, birthweight, feeding and sleeping behaviors, amongst others were recorded by the nurses in the health centers when they did the child health examination. All children were followed from one month to two or three years old until they went to kindergarten.

For this study, we used data from the Childcare Database for all children who were born from September 1st 2009 through September 1st 2013 and received care at the health centers of Jing'an district. The children were followed up from birth, with data collected at 1, 2, 4, 6, 9, 12, 18 and 24 months of age from all five communities in Jing'an District, representing 69.9% (7456/10674) of all children in this age range in Jing'an District. There were roughly 30% of children moving from Jing'an district to other districts of Shanghai during the study period, which resulted in the loss to follow-up. We gained approval (IRB#2015-TYSQ-03-11) for the current study from the Medical Research Ethics Committee, School of Public Health, Fudan University.

Inclusion and exclusion criteria

Inclusion criteria for infants included in the study were healthy singleton infants, born between 37 and 42 weeks gestational age without physical problems. Participants were eligible if they had at least six measurements of length and weight in the first 13.5 months of life. This number and range of measurements were referred to BMI modeling set by the CHOP study in Philadelphia, USA.^(19, 23) As age of BMI peak is around 7-9 months, we included children who had at least one visit in the following age ranged 213-274 days. To test the relationship between infant BMI peak and childhood overweight and obesity, measurements for children at age 2 years were included when such data were available. Preterm infants (n =289), term twins(n =52), post-term infants(n =11) and term infants with congenital defect (n=30) were excluded. There were 21.2% (2268/7456) infants eligible for analysis. Of these, we observed 85.9% (1949/2268) children from birth to age two years till September 1st 2015 (Figure 1). To assess potential selection bias, we compared demographics and birth characteristics of the analytic sample (n=2268) to the excluded healthy singleton infants (n=4806). There were no substantial differences in sex, birthweight, maternal age or overweight and obese rates at age 2 years of the two samples. (Supplemental Table 1)

Anthropometric measures

Weight and length of children were measured by the same type of instruments at the community health centers. Weight for infants (0-18months) was measured by an electronic pediatric scale (SECA 376 Weighing Scale) to the nearest 0.005 kg. Weight for toddlers (19-24months) was measured by another type of scale (SECA 704c Weighing Scale) to the nearest 0.05kg. Recumbent length was measured from the top of the head to soles of feet using an infant mat (SECA416 Mobile Measuring Mat) to the nearest 0.1 cm. BMI z-score (BAZ) of children at age two years were calculated according to the 2006 World Health Organization (WHO) Child Growth Standards using the WHO Anthro 2009 software.⁽²⁸⁾The

1
2
3 WHO Child Growth Standards was based on a multi-country study involving breastfed
4 children from six geographically distinct sites.⁽⁵⁾ Overweight was defined as BAZ > +1
5 (BMI >85th percentile) while obesity was defined as BAZ>+2 (BMI >97th percentile). Normal
6 weight was defined as $-1 \leq BAZ \leq +1$.^(1, 13) Based on reports from previous studies,^(11, 12, 19, 21)
7 we extracted factors associated with childhood overweight from the electronic medical
8 records. These factors were birthweight, sex, delivery mode, maternal ages, duration of
9 breastfeeding and sleeping data. Parents recalled to feeding and sleeping questions in
10 follow-ups. They reported the age in months at which breastfeeding was stopped. Sleep
11 duration in hours was recorded at age 2 years. Because this cohort was set up after birth,
12 some information about pregnancy and parents information was not available.
13
14
15
16
17
18
19
20
21
22
23

24 **BMI trajectory modeling**

25
26 BMI peak was identified from subject-specific BMI growth curves established by serial BMI
27 measurements. (Figure 2) A polynomial regression model with quadratic terms was fit to the
28 BMI measurements over time. Regression modeling was used for each child to fit the
29 following equation:⁽¹⁹⁾
30
31
32
33

$$34 \text{ BMI} = \beta_0 + \beta_1(\text{age in days}) + \beta_2(\text{age in days})^2$$

35
36
37
38
39
40
41 The first inflection point occurred at less than 408 days and identified as BMI peak was
42 derived from the equation. The magnitude and timing of BMI peak could be found by taking
43 derivatives as follows:
44
45
46
47

$$48 \text{ BMI}' = 2\beta_2(\text{age in days}) + \beta_1 = 0$$

49
50
51 Thus,

$$52 \text{ } T_{peak} = -\frac{\beta_1}{2\beta_2}$$

$$BMI_{peak} = \frac{4\beta_0 \beta_2 - \beta_1^2}{4\beta_2}$$

T_{peak} is the timing of BMI peak and BMI_{peak} is the magnitude of BMI peak.

The pre-peak velocity was calculated using the following equation, with BMI at 14 days of age as the baseline measurement to avoid the period of neonatal weight loss seen in the first two weeks of life.⁽²¹⁾

$$(BMI_{Peak} - BMI_{14days}) / (T_{peak} - 14 \text{ days}).$$

The subjects who had a BMI peak within 14–408 days of life were defined as estimable (“fit”) BMI trajectories, while those who were not identifiable by the model were called inestimable (“not fit”) BMI trajectories.⁽¹⁹⁾

Statistical analysis

SPSS 20.0 statistical software was used for all analyses and metalab2014b for the BMI trajectory modeling. Data were presented as mean with 95% confidence interval. Categorical data were summarized by calculating percentages. The chi-square test and two-sampled t tests were used to examine the differences between participants whose BMI trajectories were estimable or inestimable for the quadratic regression model and those who did or did not have measurements at age two years. We classified birthweight as the following categories: 1.5 to less than 2.5 kg, 2.5 to less than 4 kg, and greater than 4 kg in the chi-square test. (Table 1)

To evaluate the associations between covariates and infant BMI peak characteristics and childhood BMI Z-scores, bivariate analyses were used by one-way ANOVA with post hoc Bonferroni adjustments. (Table 2) BMI peak characteristics [age (in months) and magnitude (BMI; in kg/m²) at peak and pre-peak velocities (kg/m²/month)] were estimated. The correlations between the estimated BMI peak characteristics were assessed by Pearson correlation analysis. (Supplemental Table 2) Logistic regression was used to assess the

1
2
3 associations between BMI peak characteristics and childhood overweight (BAZ > +1) or
4 obesity (BAZ > +2), adjusting for other background characteristics. Gender, delivery mode
5 and maternal ages were defined as categorical variables. Birthweight, duration of
6 breastfeeding and sleeping were defined as continuous variable. We derived
7 birthweight-for-gestational-age z-scores using references from International standards for
8 newborn.⁽²⁹⁾ (Table 3) Statistical analyses were performed using only the subjects with
9 estimable BMI peak.⁽¹⁹⁻²²⁾ All statistical tests were two-tailed and P values <0.05 were
10 considered statistically significant.
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Results

Description of the study population

The demographic and independent variables of the study population are presented in Table 1. There were 2268 infants eligible for analysis, 49.6% male and 50.4% female. Most had a normal birthweight of 2.5 to less than 4 kg (n=2073, 91.4%). Eighty-five percent (n =1949) of infants had follow-up data at least through the age of 2 years (Table 1). Evaluated by the WHO Child Growth Standards, 17.0% (n =332) infants were overweight (BAZ > +1) and 2.3% (n =44) obese (BAZ > +2) at age 2 years.

Results of infant BMI trajectory modeling

Individual BMI trajectories were estimable using the polynomial regression model for 91.4% of the sample, with reasonable fit (mean $R^2=0.70\pm 0.23$). Mean magnitude of BMI peak was 18.33 (95% CI 18.26-18.39) kg/m^2 and occurred at 7.61 (95% CI 7.55-7.67) months. (Supplemental Figure1) Those subjects with inestimable BMI peak mostly showed either a BMI peak after 408 days of life or a decrease in BMI after birth. The prevalence of macrosomia (birthweight>4kg) infants with inestimable infancy BMI peak were slightly higher than that with estimable ones (6.7% vs 11.3%, $P=0.024$). Macrosomia born heavier reached their BMI peak much earlier, since some of them attained BMI peak measurements just after birth. There was no significant difference in other factors between subjects with estimable and inestimable peak BMI ($P>0.05$). (Table 1)

Participants' characteristics in relation to infant BMI trajectories

Infant BMI trajectories were related to both sex and birthweight (Table 2). The magnitude of BMI peak was greater, and timing of peak BMI was earlier, in boys than in girls and in children of higher birthweight than those of lower birthweight. There was no statistical significant difference in pre-peak velocities with regards to infant characteristics.

General characteristics of children at age two years

We tested for differences between infants who had BMI data with estimable BMI peak at age two years (n=1790) vs. those who did not (n=159). There was no difference between the two groups in sex, birthweight, maternal age, duration of breastfeeding, duration of sleep and overweight rates at age 2 years. ($P > 0.05$).

Association between infant BMI peak and childhood overweight and obesity

Table 3 shows the results of the association between BMI peak and risk of overweight and obesity at two years of age. When only the infant BMI peak was included in the model, higher magnitude and later timing of infant BMI peak increased the risk of overweight at two years. Furthermore, after adjustment for other infant background factors, higher magnitude (OR 3.11; 95% CI 2.64–3.66) and later timing (OR 1.35; 95% CI 1.21-1.50) of infant BMI peak each increased the risk of overweight at two years. The results were also similar with regards to childhood obesity (Table 3).

Discussion

Using a longitudinal data from a community-based cohort, we have demonstrated in the current analysis that infant BMI peak is useful for predicting childhood overweight and obesity in urban China. Boys had a higher average BMI peak and earlier average timing than girls. Principally, our results show that higher magnitude and later timing of infant BMI peak were each associated with increased risk of early childhood overweight and obesity.

This is the first community-based cohort study in China to characterize infant BMI peak and evaluate its association with risk of early childhood overweight and obesity. Overweight and obesity increased remarkably both in rural and urban areas of China.⁽³⁰⁾ Our findings are therefore generalizable to children of similar age in Shanghai city, and to some degree by extension to other areas in China. The used data were routinely collected by the health centers where children are offered routine healthcare, such as immunization and physical examination; thus constitute a valid and reliable data set for addressing the study questions. The longitudinal nature of the cohort and the repeated measurements of length and weight parameters provided us with the opportunity to carefully model the BMI trajectories of infants. One limitation of our investigation was that only about 69.9% (7456/10674) of all children in this age range had health records and 85.9% of eligible children had complete follow-up data up to the age 2 years, meaning that those with incomplete data were excluded from analysis and risk of selection bias may not be totally ruled out. Another weakness of the study is that the data of parent's BMI, pregnancy weight gain, gestational diabetes mellitus and income were not available, the reason being that the cohort was set up after birth and not prenatally. Thirdly, the BMI peak is estimation and not the true peak. A potential problem of using estimated BMI peak relates to the uncertainty in subsequent regression models.⁽¹⁸⁾

So far, few studies have been conducted on the utility of infant BMI peak for predicting childhood overweight and obesity.⁽¹⁹⁻²¹⁾ The principal finding of our study that higher

1
2
3 magnitude and later timing of infant BMI peak were each associated with increased risk of
4 early childhood overweight and obesity is similar to previous research from the CHOP study
5 conducted in USA⁽¹⁹⁾ and the Uppsala Family Study in Europe.⁽²⁰⁾ However, some findings of
6 the current study are not consistent with previous research. A 2010 prospective cohort show
7 that more rapid increases in weight for length in the first six months of life were associated
8 with sharply increased risk of childhood obesity.⁽³¹⁾ Most previous studies used weight or BMI
9 at study-dependent fixed ages^(31, 32) while ours was based on longitudinal and repeated
10 measures of length and weight. Our results also demonstrate that sex and birthweight
11 differences were shown in magnitude and timing of the peak but not in pre-peak velocity.^(19, 21)
12 In some recent studies, later BMI peak was found for both girls and boys (8-9 months of age)
13 in European or American populations.^(20, 21, 23) Girls peaked slightly later than boys in both
14 populations. However, one recent study conducted in Singapore suggests that Asian children
15 peak earlier (6 months) and that sex does not significantly influence age at peak in Asian
16 infants. Different modeling methods could account for the observed differences in BMI peak
17 characteristics across populations.⁽¹⁸⁾ The effect of breastfeeding might also explain the
18 different age of BMI peak across genders and populations. Further research is needed to
19 demonstrate the clinical relevance of the small differences. Furthermore, an earlier and
20 higher BMI peak was found to be positively associated with birthweight.^(19, 20) In our study,
21 higher birthweight was not associated with a lower velocity, which was found by the CHOP
22 study.⁽¹⁹⁾

23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47 There is no widely accepted method to model infant BMI peak, appropriate peak age range
48 and the number and timing of serial measurements.⁽²³⁾ China is undergoing rapid social and
49 economic developments with consequent improvement in nutritional status. Current
50 estimates indicate that overweight and obesity are rising in China, including among children.⁽⁴⁾
51
52
53
54 However, given the lack of studies evaluating the utility of BMI peak for predicting later
55 childhood overweight and obesity in China, as has been demonstrated in other contexts and
56
57
58
59
60

1
2
3 shown to be ancestry-specific,⁽¹⁹⁾ it is therefore necessary to undertake such assessment,
4 which will be useful in predicting early onset of obesity and serve as a springboard for
5 planning appropriate interventions targeted at reducing the increasing trend of childhood
6 overweight and obesity in urban China. It is unclear why infants in our study had earlier BMI
7 peaks as (7-8 months) compared to infants from America and Europe (8-9 months),^(20, 21, 23)
8 but as been demonstrated, such differences may reflect possible ancestry-specific BMI peaks
9 across populations; therefore cross-cultural evaluations are required to ascertain the validity
10 of this assertion. Understanding these differences may help design the protocol of public
11 health interventions to control childhood obesity.⁽³³⁻³⁵⁾
12
13
14
15
16
17
18
19
20
21
22
23
24

25 The principal finding of the current study suggests that infant BMI peak is useful in predicting
26 future risk of overweight and obesity in children in urban China; therefore infancy represents
27 a critical window of opportunity for the prevention of the emerging overweight and obesity
28 epidemic in children.
29
30
31
32
33
34
35
36
37
38

39 **Conclusion**

40
41
42 Using a community-based longitudinal cohort study with repeated measurements of infant
43 growth parameters, we have for the first time determined that infant BMI peak is valuable for
44 predicting early childhood overweight and obesity in urban China. Further studies are
45 required for other infant populations in different areas of China.
46
47
48
49

50 **Acknowledgements**

51
52
53
54 We are grateful to the staff in Jing'an maternal and child health care center for data extraction.
55
56 We also acknowledge all children and their parent's for participation.
57
58
59
60

Authors' contributions

JieSun, Bright I Nwaru, and ZhuochunWu were responsible for the study design, analysis of the study and approval of the submitted and final version. Jing Hua and Xiaohong Li analyzed the data, interpreted the results and commented on the manuscript.

Funding

This study was funded by National Natural Science Foundation of China [71573049].

Ethics Approval

All procedures performed in this study were in accordance with the ethical standard. We gained approval (IRB#2015-TYSQ-03-11) for the current study from the Medical Research Ethics Committee, School of Public Health, Fudan University. Informed consent was obtained from all individual participants included in the study.

Competing interests

The authors declare that they have no conflict of interest.

Data Sharing Statement

No additional data are available.

References:

1. Benjamin Neelon SE, Schou Andersen C, Schmidt Morgen C, Kamper-Jorgensen M, Oken E, Gillman MW, et al. Early child care and obesity at 12 months of age in the Danish National Birth Cohort. *International journal of obesity* (2005). 2015;39(1):33-8.
2. Freedman DS, Mei Z, Srinivasan SR, Berenson GS, Dietz WH. Cardiovascular risk factors and excess adiposity among overweight children and adolescents: the Bogalusa Heart Study. *The Journal of pediatrics*. 2007;150(1):12-7.e2.
3. Skinner AC, Perrin EM, Skelton JA. Prevalence of obesity and severe obesity in US children, 1999-2014. *Obesity (Silver Spring, Md)*. 2016;24(5):1116-23.
4. Ji CY. Report on childhood obesity in China (4) prevalence and trends of overweight and obesity in Chinese urban school-age children and adolescents, 1985-2000. *Biomedical and environmental sciences : BES*. 2007;20(1):1-10.
5. Commission presents its final report, calling for high-level action to address major health challenge. Available from <http://www.who.int/end-childhood-obesity/news/launch-final-report/en/>. 2016.
6. Commission. CNhaFP. National Report on Nutritional status of children aged 0-6 year. China:National health and Family Planning Commission. China;. 2012.
7. Andersen LG, Holst C, Michaelsen KF, Baker JL, Sorensen TI. Weight and weight gain during early infancy predict childhood obesity: a case-cohort study. *International journal of obesity* (2005). 2012;36(10):1306-11.
8. Baird J, Fisher D, Lucas P, Kleijnen J, Roberts H, Law C. Being big or growing fast: systematic review of size and growth in infancy and later obesity. *BMJ (Clinical research ed)*. 2005;331(7522):929.
9. Leunissen RW, Kerkhof GF, Stijnen T, Hokken-Koelega A. Timing and tempo of first-year rapid growth in relation to cardiovascular and metabolic risk profile in early adulthood. *Jama*. 2009;301(21):2234-42.
10. Monteiro PO, Victora CG. Rapid growth in infancy and childhood and obesity in later life--a systematic review. *Obesity reviews : an official journal of the International Association for the Study of Obesity*. 2005;6(2):143-54.
11. Weng SF, Redsell SA, Swift JA, Yang M, Glazebrook CP. Systematic review and meta-analyses of risk factors for childhood overweight identifiable during infancy. *Archives of disease in childhood*. 2012;97(12):1019-26.
12. Guo Y. Growth level of urban Chinese infants from birth to 2 years, body mass index Z scores' predicting model and its age trajectory in relation to maternal pre-pregnancy body weight status. 2013.
13. Ma JQ, Zhou LL, Hu YQ, Liu SS, Sheng XY. Association between feeding practices and weight status in young children. *BMC pediatrics*. 2015;15:97.
14. Gortmaker SL, Swinburn BA, Levy D, Carter R, Mabry PL, Finegood DT, et al. Changing the future of obesity: science, policy, and action. *Lancet (London, England)*. 2011;378(9793):838-47.

- 1
2
3 15. Robinson SM, Crozier SR, Harvey NC, Barton BD, Law CM, Godfrey KM, et al.
4 Modifiable early-life risk factors for childhood adiposity and overweight: an analysis of
5 their combined impact and potential for prevention. *The American journal of clinical*
6 *nutrition*. 2015;101(2):368-75.
7
8 16. Kolsgaard ML, Joner G, Brunborg C, Anderssen SA, Tonstad S, Andersen LF.
9 Reduction in BMI z-score and improvement in cardiometabolic risk factors in obese
10 children and adolescents. *The Oslo Adiposity Intervention Study - a hospital/public*
11 *health nurse combined treatment*. *BMC pediatrics*. 2011;11:47.
12
13 17. Sijtsma A, Bocca G, L'Abée C, Liem ET, Sauer PJ, Corpeleijn E. Waist-to-height ratio,
14 waist circumference and BMI as indicators of percentage fat mass and cardiometabolic
15 risk factors in children aged 3-7 years. *Clinical nutrition (Edinburgh, Scotland)*.
16 2014;33(2):311-5.
17
18 18. Aris IM, Bernard JY, Chen LW, Tint MT, Pang WW, Lim WY, et al. Infant body mass
19 index peak and early childhood cardio-metabolic risk markers in a multi-ethnic Asian
20 birth cohort. *International journal of epidemiology*. 2016.
21
22 19. Roy SM, Chesi A, Mentch F, Xiao R, Chiavacci R, Mitchell JA, et al. Body mass index
23 (BMI) trajectories in infancy differ by population ancestry and may presage disparities
24 in early childhood obesity. *The Journal of clinical endocrinology and metabolism*.
25 2015;100(4):1551-60.
26
27 20. Silverwood RJ, De Stavola BL, Cole TJ, Leon DA. BMI peak in infancy as a predictor
28 for later BMI in the Uppsala Family Study. *International journal of obesity (2005)*.
29 2009;33(8):929-37.
30
31 21. Jensen SM, Ritz C, Ejlerskov KT, Molgaard C, Michaelsen KF. Infant BMI peak,
32 breastfeeding, and body composition at age 3 y. *The American journal of clinical*
33 *nutrition*. 2015;101(2):319-25.
34
35 22. WHO Multicentre Growth Reference Study Group. WHO Child Growth Standards:
36 Length/height-for-age, Weight-for-age, Weight-for-length, Weight-for-height, and Body
37 Mass Index-for-age: Methods and Development. Geneva:World Health
38 Organization,2006. Available from: <http://www.who.int/childgrowth/standards/en/>.
39 2006.
40
41 23. Wen X, Kleinman K, Gillman MW, Rifas-Shiman SL, Taveras EM. Childhood body
42 mass index trajectories: modeling, characterizing, pairwise correlations and
43 socio-demographic predictors of trajectory characteristics. *BMC medical research*
44 *methodology*. 2012;12:38.
45
46 24. Chivers P, Hands B, Parker H, Bulsara M, Beilin LJ, Kendall GE, et al. Body mass index,
47 adiposity rebound and early feeding in a longitudinal cohort (Raine Study).
48 *International journal of obesity (2005)*. 2010;34(7):1169-76.
49
50 25. Johnson W, Choh AC, Lee M, Towne B, Czerwinski SA, Demerath EW.
51 Characterization of the infant BMI peak: sex differences, birth year cohort effects,
52 association with concurrent adiposity, and heritability. *American journal of human*
53 *biology : the official journal of the Human Biology Council*. 2013;25(3):378-88.
54
55 26. Giles LC, Whitrow MJ, Davies MJ, Davies CE, Rumbold AR, Moore VM. Growth
56
57
58
59
60

- trajectories in early childhood, their relationship with antenatal and postnatal factors, and development of obesity by age 9 years: results from an Australian birth cohort study. *International journal of obesity* (2005). 2015;39(7):1049-56.
27. Sovio U, Kaakinen M, Tzoulaki I, Das S, Ruokonen A, Pouta A, et al. How do changes in body mass index in infancy and childhood associate with cardiometabolic profile in adulthood? Findings from the Northern Finland Birth Cohort 1966 Study. *International journal of obesity* (2005). 2014;38(1):53-9.
28. WHO. Anthro for personal computers, version 3. Software for assessing growth and development of the world's children. Geneva: WHO,2009. Available from: <http://www.who.int/childgrowth/software/en/>. 2009.
29. Villar J, Cheikh Ismail L, Victora CG, Ohuma EO, Bertino E, Altman DG, et al. International standards for newborn weight, length, and head circumference by gestational age and sex: the Newborn Cross-Sectional Study of the INTERGROWTH-21st Project. *Lancet* (London, England). 2014;384(9946):857-68.
30. Zhang YX, Wang SR. Rural-urban comparison in prevalence of overweight and obesity among adolescents in Shandong, China. *Annals of human biology*. 2013;40(3):294-7.
31. Taveras EM, Rifas-Shiman SL, Belfort MB, Kleinman KP, Oken E, Gillman MW. Weight status in the first 6 months of life and obesity at 3 years of age. *Pediatrics*. 2009;123(4):1177-83.
32. Guo B, Mei H, Yang S, Zhang J. [Prenatal factors associated with high BMI status of infants and toddlers]. *Zhonghua er ke za zhi = Chinese journal of pediatrics*. 2014;52(6):464-7.
33. Taveras EM, Gillman MW, Kleinman K, Rich-Edwards JW, Rifas-Shiman SL. Racial/ethnic differences in early-life risk factors for childhood obesity. *Pediatrics*. 2010;125(4):686-95.
34. Taveras EM, Gillman MW, Kleinman KP, Rich-Edwards JW, Rifas-Shiman SL. Reducing racial/ethnic disparities in childhood obesity: the role of early life risk factors. *JAMA pediatrics*. 2013;167(8):731-8.
35. Zilanawala A, Davis-Kean P, Nazroo J, Sacker A, Simonton S, Kelly Y. Race/ethnic disparities in early childhood BMI, obesity and overweight in the United Kingdom and United States. *International journal of obesity* (2005). 2015;39(3):520-9.

Table 1 Participants' characteristics by subjects with "estimable"* and "inestimable"# BMI peak

Characteristics	n	Estimable*, n (%)	Inestimable#, n (%)
Total number	2268	2073	195
Gender			
Male	1126	1022 (49.3)	104 (53.3)
Female	1142	1051 (50.7)	91 (46.7)
Birth weight			
1.5 to <2.5kg	35	30 (1.4)	5 (2.6)
2.5 to <4.0kg	2073	1905 (91.9)	168 (86.2)
≥4kg	160	138 (6.7)^a	22 (11.3)
Delivery mode			
Vaginal birth	1086	989 (47.7)	97 (49.7)
Cesarean section	1182	1084 (52.3)	98 (50.3)
Maternal Age			
>35y	176	159 (7.7)	17 (8.7)
≤35y	2092	1914 (92.3)	178 (91.3)
Total number with data at age 2y	1949	1790 (86.3)	159 (81.5)
Total number of overweight and obese at age 2y	332	313 (17.5)	19 (11.9)
Total number of obese at age 2y	44	43 (2.4)	1 (0.6)

a.P<0.05

*Estimable: fit and identifiable BMI peak within 14–408 days of life.

Inestimable: Not fit and identifiable.

Chi-square tests were used to examine the differences between Estimable or Inestimable group.

Table 2 Infant characteristics in relation to infant BMI peak trajectories

		Magnitude(kg/m ²), Mean (95% CI)	Age(months), Mean (95% CI)	Pre-peak velocities(kg/m ² /month) Mean (95% CI)
Total	n=2073	18.33(18.26-18.39)	7.61(7.55-7.67)	0.43(0.42-0.44)
Gender				
	male (n=1022)	18.60(18.21-18.69)^a	7.54(7.46-7.63)^b	0.42(0.41-0.43)
	female (n=1051)	18.07(17.98-18.16)	7.67(7.59-7.76)	0.43(0.42-0.44)
Birth Weight				
	1.5 to <2.5kg(n=30)	17.63(17.13-18.13)	8.13(7.56-8.70)	0.44(0.35-0.53)
	2.5 to <4.0kg(n=1905)	18.27(18.21-18.34)	7.63(7.57-7.70)	0.43(0.42-0.44)
	>=4kg(n=138)	19.25(18.97-19.52)^b	7.11(6.88-7.34)^a	0.39(0.35-0.42)
Delivery Mode				
	Vaginal birth (n=989)	18.24(18.14-18.34)	7.64(7.56-7.73)	0.43(0.42-0.44)
	Cesarean section (n=1084)	18.41(18.32-18.50)^a	7.58(7.49-7.66)	0.43(0.42-0.44)
Maternal Age				
	>35y(n=159)	18.42(18.18-18.66)	7.61(7.49-7.82)	0.44(0.41-0.48)
	<=35y(n=1914)	18.32(18.25-18.39)	7.61(7.55-7.67)	0.42(0.41-0.43)

a.P<0.001 b.P<0.05

The analysis includes only infants who had BMI peak within 0-408 days and whose BMI trajectories were estimable by the quadratic model.

Bivariate comparison was performed using one-way ANOVA with post hoc Bonferroni multiple comparison test.

Table 3 Association between BMI peak characteristics and overweight and obesity at age 2 years

Model	Overweight at 2y (n=1790)		Obesity at 2y (n=1790)	
	containing infant BMI trajectory characteristics alone	Initial model plus all independent variables	Model containing infant BMI trajectory characteristics alone	Initial model plus all independent variables
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Magnitude(kg/m ²)	2.94(2.54-3.40)^a	3.11(2.64-3.66)^a	2.76(2.11-3.60)^a	2.69(2.00-3.61)^a
Age (months)	1.36(1.23-1.51)^a	1.35(1.21-1.50)^a	1.33(1.08-1.65)^b	1.35(1.08-1.68)^b
Pre-peak velocities(kg/m ² /month)	0.17(0.07-0.40)^a	0.14(0.06-0.34)^a	0.10(0.02-0.56)^b	0.12(0.02-0.74)^c
male(vs female)		0.67(0.49-0.90)^b		0.99(0.51-1.96)
birth weight z score,(continuous)		1.06(0.89-1.26)		1.24(0.84-1.82)
Duration of breastfeeding(continuous)		0.97(0.93-1.01)		0.92(0.84-1.01)
Duration of Sleep(continuous)		0.89(0.77-1.02)		0.89(0.63-1.24)
Cesarean section(vs Vaginal Birth)		1.08(0.81-1.44)		0.80(0.42-1.54)
Mother Age(>35y vs<=35y)		0.68(0.38-1.21)		0.74(0.21-2.59)

a.P<0.001 b.P<0.01 c.P<0.05

The analysis includes only infants who had BMI peak within 0-408 days and whose BMI trajectories were estimable by the quadratic model.

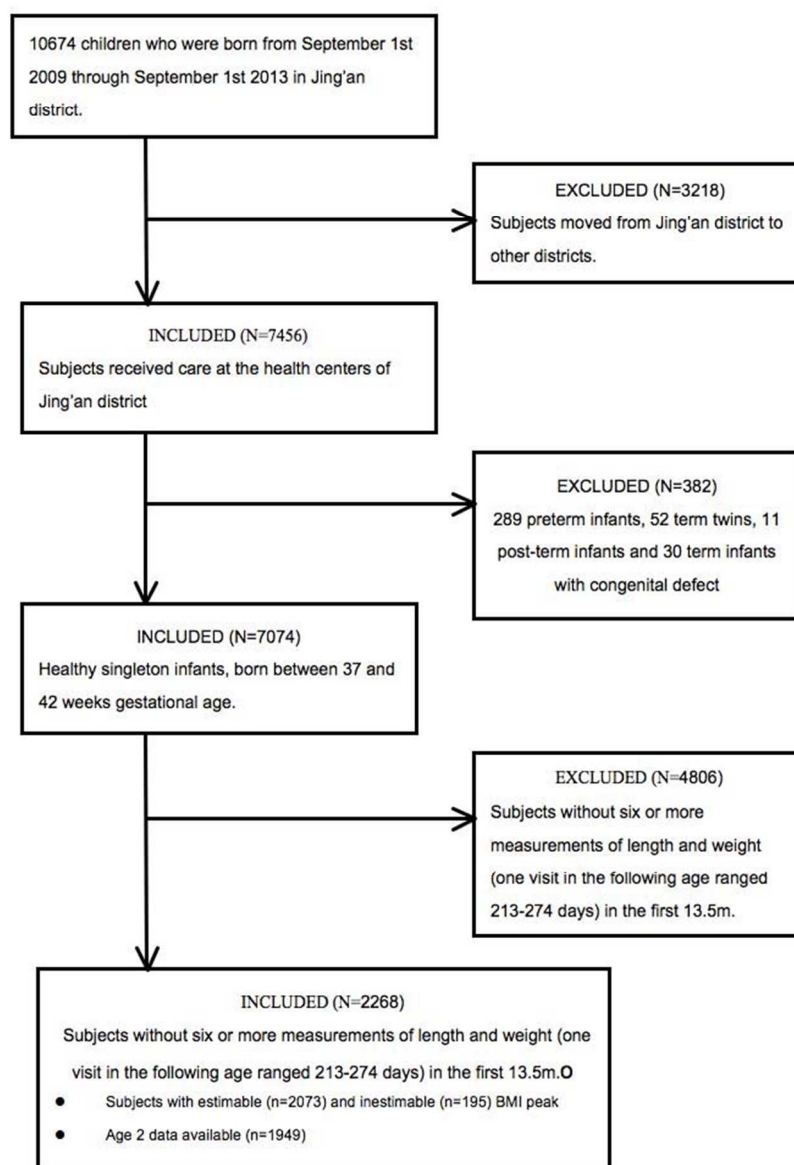


Figure1 Recruitment flow chart and study sample

64x83mm (300 x 300 DPI)

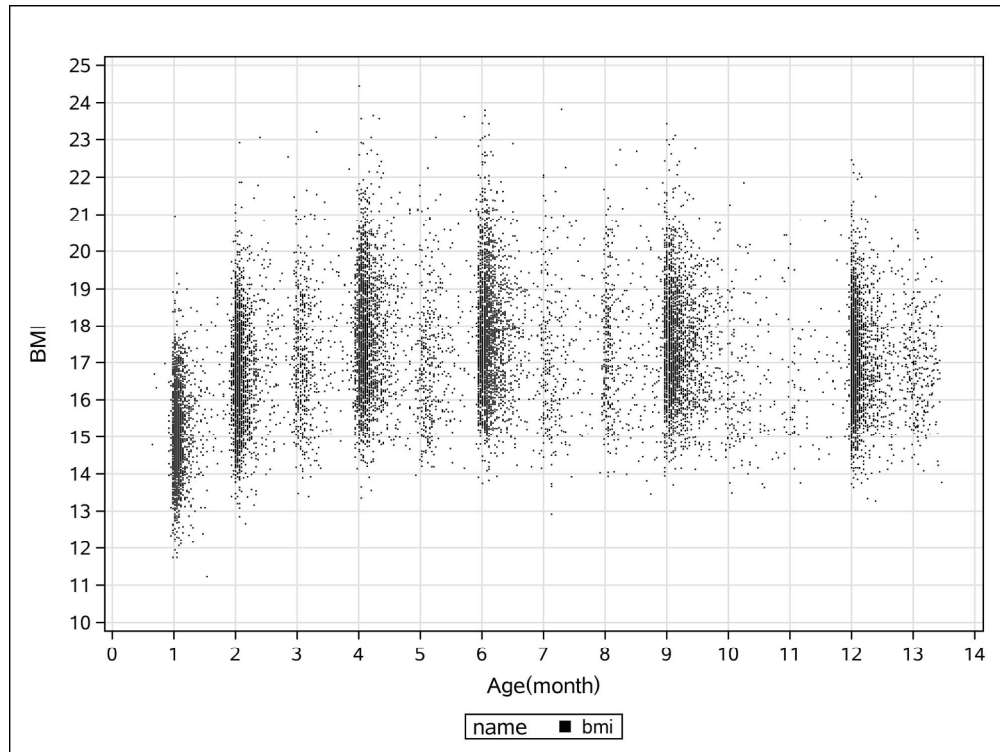


Figure 2 Plot of BMI data by age from birth to 13.5 months

169x127mm (300 x 300 DPI)

Supplemental Table 1 Characteristics of the analytic and excluded healthy singleton infants

Characteristics	n	Included, n (%)	Excluded, n (%)
Total number	7074	2268(32.1)	4806(67.9)
Gender			
Male	3468	1126 (49.6)	2342 (48.7)
Female	3606	1142(50.4)	2464 (51.3)
Birth weight			
<4.0kg	6609	2108(92.9)	4501 (93.7)
≥4kg	465	160 (7.1)	305(6.3)
Maternal Age			
>35y	570	176 (7.8)	394 (8.2)
≤35y	6504	2092(92.2)	4412(91.8)
Total number with data at age 2y	1949	1949 (85.9)^a	2282 (47.4)
Total number of overweight and obese at age 2y	751	330 (16.9)	421 (18.4)
Total number of obese at age 2y	99	44 (2.3)	55(2.4)

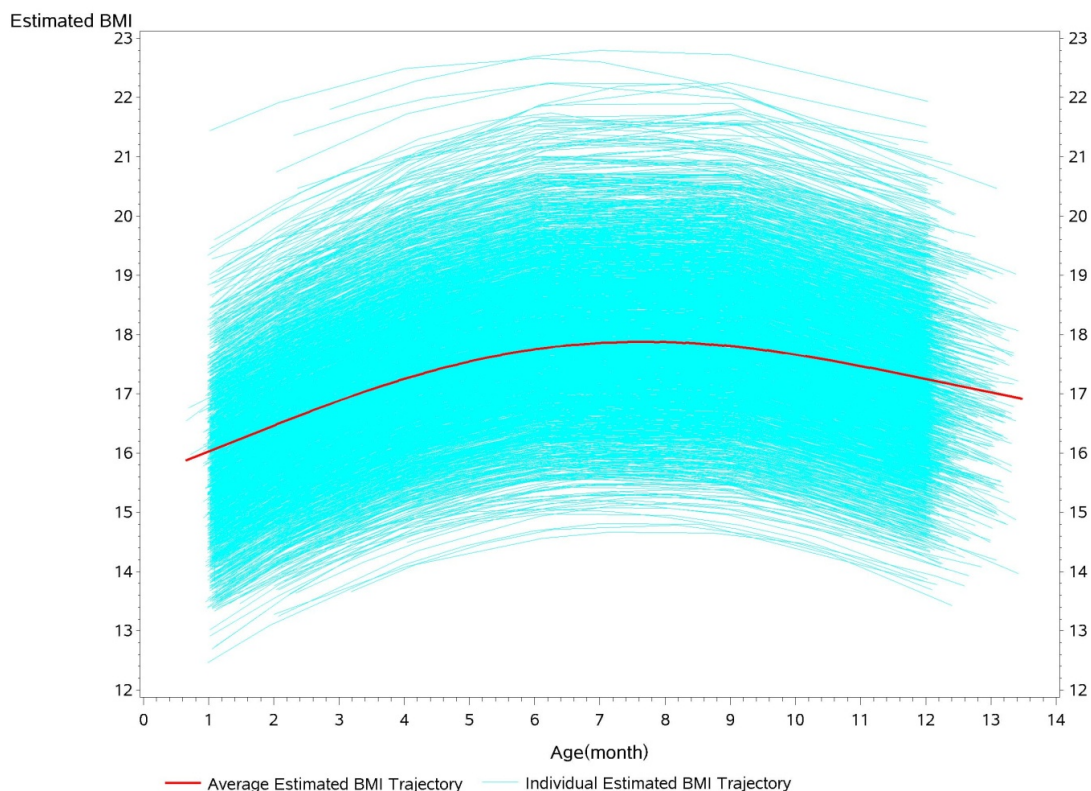
a.P<0.05

Chi-square tests were used to examine the differences between included or excluded group.

Supplemental Table 2: Correlation matrix of infancy BMI characteristics

	Age of BMI Peak, mo	Pre-peak velocities, kg/m2/mo
Magnitude of BMI peak, kg/m2	0.03	0.654**
Age of BMI Peak, mo		0.09**

Significance is noted as: ** $p \leq 0.01$.



Supplemental Figure1 Infant Estimated BMI trajectory by polynomial regression model

Only

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any pre-specified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-4, Figure 1
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6, Figure 1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8-9
		(b) Describe any methods used to examine subgroups and interactions	8
		(c) Explain how missing data were addressed	6
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	6

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Figure 1
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1, Supplemental Table 1
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	5
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	8
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 3
		(b) Report category boundaries when continuous variables were categorized	8
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

For peer review only

BMJ Open

Infant BMI Peak as a predictor of overweight and obesity at age 2 years in a Chinese community-based cohort

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2016-015122.R2
Article Type:	Research
Date Submitted by the Author:	16-Jul-2017
Complete List of Authors:	Sun, Jie; School of Public Health, Fudan, Department of Social Medicine; Jing'an Maternal and Child Health Care Center, Shanghai, Department of Child Health Care Nwaru, Bright; The University Of Edinburgh, Allergy & Respiratory Research Group, Centre for Population Health Sciences; University of Tampere, School of Health Sciences Hua, Jing; Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine, Department of Maternal and Child Health Care Li, Xiaohong; School of Public Health, Fudan University, Department of Health Policy and Management ; Innovation Center for Social Risk Governance in Health Wu, Zhuochun; School of Public Health, Fudan University, Department of Social Medicine; Innovation Center for Social Risk Governance in Health
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Paediatrics
Keywords:	Overweight, Obesity, Body mass index, Longitudinal Study, Infant

SCHOLARONE™
Manuscripts

Infant BMI peak as a predictor of overweight and obesity at age 2 years in a Chinese community-based cohort

Jie Sun^{1,2}, Bright I Nwaru^{3,4,5}, Jing Hua⁶, Xiaohong Li^{7,8}, Zhuochun Wu^{1,8}

Abstract

Objectives: Infant body mass index (BMI) peak has proven to be a useful indicator for predicting childhood obesity risk in American and European populations. However, it has not been assessed in China. We characterized infant BMI trajectories in a Chinese longitudinal cohort and evaluated whether BMI peak can predict overweight and obesity at age 2 years.

Methods: Serial measurements (n=6-12) of weight and length were taken from healthy term infants (n=2073) in a birth cohort established in urban Shanghai. Measurements were used to estimate BMI growth curves from birth to 13.5 months using a polynomial regression model. BMI peak characteristics, including age (in months) and magnitude (BMI, in kg/m²) at peak and pre-peak velocities (in kg/m²/month), were estimated. The relationship between infant BMI peak and childhood BMI at age 2 years was examined using binary logistic analysis.

Results: Mean age at peak BMI was 7.61 months, with a magnitude of 18.33 kg/m². Boys (n=1022) had a higher average peak BMI (18.60 vs. 18.07 kg/m², P<0.001) and earlier average achievement of peak value (7.54 vs. 7.67 months, P<0.05) than girls (n=1051). With 1 kg/m² increase in peak BMI and one month increase in peak time, the risk of overweight at age 2 years increased by 2.11 times (OR 3.11; 95% CI 2.64-3.66) and 35% (OR 1.35; 95% CI 1.21-1.50), respectively. Similarly, higher BMI magnitude (OR 2.69; 95% CI 2.00-3.61) and later timing of infant BMI peak (OR 1.35; 95% CI 1.08-1.68) were associated with an increased risk of childhood obesity at age 2 years.

Conclusions: We have shown that infant BMI peak is valuable for predicting early childhood overweight and obesity in urban Shanghai. Because this is the first Chinese community-based cohort study of this nature, future research is required to examine infant populations in other areas of China.

Key words: Body mass Index, Obesity, Overweight, Longitudinal Study, Infants

Word Count: 3883 words

¹Department of Social Medicine, School of Public Health, Fudan University, Shanghai, China.

²Department of Child Health Care, Jing'an Maternal and Child Health Care Center, Shanghai, China.

³School of Health Sciences, University of Tampere, Tampere, Finland.

⁴Asthma UK Centre for Applied Research, Usher Institute of Population Health Sciences and Informatics, University of Edinburgh, Edinburgh, UK.

⁵Krefting Research Centre, Institute of Medicine, University of Gothenburg, Gothenburg, Sweden

⁶Department of Maternal and Child Health Care, Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine,

1
2
3 Shanghai, China.

4
5 ⁷Department of Health Policy and Management, School of Public Health, Fudan University, Shanghai,China.

6
7 ⁸Innovation Center for Social Risk Governance in Health, Fudan University, Shanghai, China

8
9 Corresponding author: Zhuochun Wu, Department of Social Medicine, School of Public Health, Fudan University, Fax:
10 086-021-62309139, P.O. Box 250,138 Yi Xue Yuan Road, Shanghai 200032, China . zcwu@shmu.edu.cn.

11 **Strengths and limitations of this study**

12
13 We have demonstrated here for the first time that infant BMI peak is an effective predictor for childhood obesity
14 in Shanghai, an urban city in China.

15
16 The longitudinal cohort with careful repeated measurements of child growth parameters provided the
17 opportunity to characterize infant BMI peak over the first year of life.

18
19 As we lacked data on parent's BMI and pregnancy weight gain, we could ascertain the influence of these on
20 infant BMI peak and contribution to childhood overweight and obesity.

21
22 Selection bias may exist in our study because 14.1% of the infants that were measured did not complete the
23 follow-up at 2 years old.

24 **Introduction**

25
26
27
28
29 The worldwide overweight prevalence among children aged under 5 years has risen from 4.8%
30 in 1990 to 6.1% in 2014.⁽¹⁾ The current worldwide obesity epidemic is a serious public health
31 crisis.⁽¹⁻⁵⁾ In 2014, almost half (48%) of obese individuals lived in Asia.⁽¹⁾ In urban areas of
32 China, the prevalence of overweight increased from 5.3% in 2005 to 8.5% in 2010.⁽⁶⁾ Rapid
33 weight gain in early infancy is related to the adult development of obesity and cardiovascular
34 risk factors, including hypertension and impaired glucose tolerance.⁽⁷⁻¹¹⁾ Environmental and
35 behavioral factors are believed to be key drivers of obesity because although obesity is
36 genetically influenced, genetic changes cannot explain the rapid increase in the prevalence
37 of obesity.⁽¹²⁾ Therapeutic interventions in adulthood have poor long-term effects and are not
38 cost effective, therefore the introduction of primary preventive strategies during infancy may
39 be more important to reduce the risk of being overweight and obese.⁽¹³⁻¹⁵⁾

40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
90
91
92
93
94
95
96
97
98
99
100
101
102
103
104
105
106
107
108
109
110
111
112
113
114
115
116
117
118
119
120
121
122
123
124
125
126
127
128
129
130
131
132
133
134
135
136
137
138
139
140
141
142
143
144
145
146
147
148
149
150
151
152
153
154
155
156
157
158
159
160
161
162
163
164
165
166
167
168
169
170
171
172
173
174
175
176
177
178
179
180
181
182
183
184
185
186
187
188
189
190
191
192
193
194
195
196
197
198
199
200
201
202
203
204
205
206
207
208
209
210
211
212
213
214
215
216
217
218
219
220
221
222
223
224
225
226
227
228
229
230
231
232
233
234
235
236
237
238
239
240
241
242
243
244
245
246
247
248
249
250
251
252
253
254
255
256
257
258
259
260
261
262
263
264
265
266
267
268
269
270
271
272
273
274
275
276
277
278
279
280
281
282
283
284
285
286
287
288
289
290
291
292
293
294
295
296
297
298
299
300
301
302
303
304
305
306
307
308
309
310
311
312
313
314
315
316
317
318
319
320
321
322
323
324
325
326
327
328
329
330
331
332
333
334
335
336
337
338
339
340
341
342
343
344
345
346
347
348
349
350
351
352
353
354
355
356
357
358
359
360
361
362
363
364
365
366
367
368
369
370
371
372
373
374
375
376
377
378
379
380
381
382
383
384
385
386
387
388
389
390
391
392
393
394
395
396
397
398
399
400
401
402
403
404
405
406
407
408
409
410
411
412
413
414
415
416
417
418
419
420
421
422
423
424
425
426
427
428
429
430
431
432
433
434
435
436
437
438
439
440
441
442
443
444
445
446
447
448
449
450
451
452
453
454
455
456
457
458
459
460
461
462
463
464
465
466
467
468
469
470
471
472
473
474
475
476
477
478
479
480
481
482
483
484
485
486
487
488
489
490
491
492
493
494
495
496
497
498
499
500
501
502
503
504
505
506
507
508
509
510
511
512
513
514
515
516
517
518
519
520
521
522
523
524
525
526
527
528
529
530
531
532
533
534
535
536
537
538
539
540
541
542
543
544
545
546
547
548
549
550
551
552
553
554
555
556
557
558
559
560
561
562
563
564
565
566
567
568
569
570
571
572
573
574
575
576
577
578
579
580
581
582
583
584
585
586
587
588
589
590
591
592
593
594
595
596
597
598
599
600
601
602
603
604
605
606
607
608
609
610
611
612
613
614
615
616
617
618
619
620
621
622
623
624
625
626
627
628
629
630
631
632
633
634
635
636
637
638
639
640
641
642
643
644
645
646
647
648
649
650
651
652
653
654
655
656
657
658
659
660
661
662
663
664
665
666
667
668
669
670
671
672
673
674
675
676
677
678
679
680
681
682
683
684
685
686
687
688
689
690
691
692
693
694
695
696
697
698
699
700
701
702
703
704
705
706
707
708
709
710
711
712
713
714
715
716
717
718
719
720
721
722
723
724
725
726
727
728
729
730
731
732
733
734
735
736
737
738
739
740
741
742
743
744
745
746
747
748
749
750
751
752
753
754
755
756
757
758
759
760
761
762
763
764
765
766
767
768
769
770
771
772
773
774
775
776
777
778
779
780
781
782
783
784
785
786
787
788
789
790
791
792
793
794
795
796
797
798
799
800
801
802
803
804
805
806
807
808
809
810
811
812
813
814
815
816
817
818
819
820
821
822
823
824
825
826
827
828
829
830
831
832
833
834
835
836
837
838
839
840
841
842
843
844
845
846
847
848
849
850
851
852
853
854
855
856
857
858
859
860
861
862
863
864
865
866
867
868
869
870
871
872
873
874
875
876
877
878
879
880
881
882
883
884
885
886
887
888
889
890
891
892
893
894
895
896
897
898
899
900
901
902
903
904
905
906
907
908
909
910
911
912
913
914
915
916
917
918
919
920
921
922
923
924
925
926
927
928
929
930
931
932
933
934
935
936
937
938
939
940
941
942
943
944
945
946
947
948
949
950
951
952
953
954
955
956
957
958
959
960
961
962
963
964
965
966
967
968
969
970
971
972
973
974
975
976
977
978
979
980
981
982
983
984
985
986
987
988
989
990
991
992
993
994
995
996
997
998
999
1000

1
2
3 WHtR better correlated with cardiometabolic risk factors than BMI in overweight/obese
4 children.⁽¹⁷⁾ One study in Singapore suggested that early BMI may have an important impact
5 on later metabolic outcomes in Asian populations.⁽¹⁸⁾
6
7

8
9
10 Few studies have evaluated the associations between infant BMI trajectory and childhood
11 overweight and obesity.^(12, 19-21) Weight-for-length percentile curves are often used but do not
12 account for the age-based changes that reflect different stages of infancy.⁽¹⁹⁾ BMI increases
13 from birth and reaches a maximum called the 'BMI peak' around age 7-9 months old, and
14 then decreases and reaches a nadir around age 4-6 years old before increasing once
15 again.⁽¹⁹⁻²¹⁾ According to Silverwood et al, both age and magnitude of BMI peak were
16 positively associated with later BMI z-scores.⁽²⁰⁾ Additionally, several studies have used
17 statistical models of growth trajectories to estimate the magnitude and timing of infant BMI
18 peak.⁽¹⁸⁻²⁷⁾
19
20
21
22
23
24
25
26
27

28 Ancestry-specific differences in Infant BMI peak are found between African-American and
29 European populations.⁽¹⁹⁾ However, to date there have been no studies performed in China to
30 demonstrate the utility of infant BMI peak for predicting the risk of childhood overweight and
31 obesity. In order to form comparisons with other populations, we referred to a BMI modeling
32 set by a cohort study in Philadelphia, USA^(19, 23) Using a community-based longitudinal data
33 set of serial measurements of length and weight from birth to childhood in Shanghai, we
34 aimed to estimate the BMI peak characteristics in order to study the association between the
35 infant BMI peak and overweight and obesity at age 2 years.
36
37
38
39
40
41
42
43
44
45
46
47

48 **Methods**

49 **Study Participants**

50
51
52 We obtained our community-based longitudinal cohort data from the Shanghai Jing'an
53 District birth and health records. Shanghai has a population of 19 million, as of 2009, and is
54 divided into seventeen urban districts and one suburban district. Jing'an District is located at
55
56
57
58
59
60

1
2
3 the city center and has a population of 248,000, as of 2009. "Providing free of charge health
4 examination to children aged 0-3 years" was a project funded by the Shanghai government
5 for Jing'an children born from September 2009 onwards. Community health centers in the
6
7 Jing'an District provide routine well-child checks for infants and young children. A District
8
9 Childcare Database for all health centers in this project was established and managed by the
10
11 Jing'an maternal and child health care center. For the Childcare Database, health center
12
13 nurses record children's gender, gestational age, birthweight, feeding and sleeping behaviors,
14
15 and other information during the child health examination. All children were followed from
16
17 the age of one month to two or three years old until they went to kindergarten.
18
19
20

21
22 For this study, we used data from the Childcare Database for all children who were born from
23
24 September 1st 2009 to September 1st 2013 and received care at the Jing'an District health
25
26 centers. Children were followed from birth, with data collected at 1, 2, 4, 6, 9, 12, 18 and 24
27
28 months of age from all five communities in Jing'an District, representing 69.9% (7456/10674)
29
30 of all children in this age range in Jing'an District. Roughly 30% of children moved from
31
32 Jing'an district to other districts of Shanghai during the study period, which resulted in a loss
33
34 of follow-up in these cases. We gained approval (IRB#2015-TYSQ-03-11) for the current
35
36 study from the Medical Research Ethics Committee, School of Public Health, Fudan
37
38 University.
39
40
41
42
43

44 **Inclusion and exclusion criteria**

45
46 Inclusion criteria for the infants in this study specified healthy single births, a gestational age
47
48 between 37 and 42 weeks, and no physical problems. Participants were included if they had
49
50 at least six measurements of length and weight in the first 13.5 months of life. The number
51
52 and range of measurements were determined by the BMI modeling set by a cohort study in
53
54 Philadelphia, USA.^(19, 23) Because the BMI peak occurs around 7-9 months old, we included
55
56 children who had at least one health examination visit between 213-274 days old. To test the
57
58
59
60

1
2
3 relationship between infant BMI peak and childhood overweight and obesity, we included
4 measurements for children at 2 years old when the data was available. Preterm infants (n =
5 289), term twins (n = 52), post-term infants (n = 11), and term infants with congenital defects
6 (n = 30) were excluded. These children have different curve characteristics than normal term
7 children.⁽²⁸⁾ We used exclusion criteria similar to the Philadelphia cohort study to compare
8 peak BMI with other populations.⁽¹⁹⁾ There were 21.2% (2268/7456) infants eligible for
9 analysis. Of these, we observed 85.9% (1949/2268) children from birth to age two years, i.e.
10 until September 1st 2015 (Figure 1). To assess potential selection bias, we compared
11 demographics and birth characteristics of the analytic sample (n=2268) to the excluded
12 healthy singleton infants (n=4806). There were no substantial differences in sex, birthweight,
13 maternal age or overweight and obese rates at age 2 years of the two samples.
14 (Supplemental Table 1)
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30

31 **Anthropometric measures**

32
33 Weight and length of children were measured by the same type of instruments at the
34 community health centers. Weight for infants (0-18 months) was measured by an electronic
35 pediatric scale (SECA 376 Weighing Scale) to the nearest 0.005 kg. Weight for toddlers
36 (19-24 months) was measured by another type of scale (SECA 704c Weighing Scale) to the
37 nearest 0.05 kg. Recumbent length was measured from the top of the head to soles of feet
38 using an infant mat (SECA416 Mobile Measuring Mat) to the nearest 0.1 cm. BMI z-score
39 (BAZ) of children at age two years were calculated according to the 2006 World Health
40 Organization (WHO) Child Growth Standards using the WHO Anthro 2009 software.⁽²⁹⁾The
41 WHO Child Growth Standards was based on a multi-country study involving breastfed
42 children from six geographically distinct sites.⁽¹⁾ Overweight was defined as BAZ > +1
43 (BMI >85th percentile) while obesity was defined as BAZ > + 2 (BMI >97th percentile). Normal
44 weight was defined as $-1 \leq \text{BAZ} \leq +1$.^(2, 13) Based on reports from previous studies,^(11, 12, 19, 21)
45 we extracted factors associated with childhood overweight from the electronic medical
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

records. These factors were birthweight, sex, delivery mode, maternal age, duration of breastfeeding and sleeping data. Parents answered to feeding and sleeping questions in follow-ups. They reported the age in months at which breastfeeding was stopped. Sleep duration in hours was recorded at age 2 years. Because this cohort was set up after birth, some information about pregnancy and parents information was not available.

BMI trajectory modeling

BMI peak was identified from subject-specific BMI growth curves established by serial BMI measurements. (Figure 2) A polynomial regression model with quadratic terms was fit to the BMI measurements over time. Regression modeling was used for each child to fit the following equation: ⁽¹⁹⁾

$$BMI = \beta_0 + \beta_1(\text{age in days}) + \beta_2(\text{age in days})^2$$

The first inflection point occurred at less than 408 days as derived from the equation and this was identified as BMI peak. The magnitude and timing of BMI peak were found by taking derivatives as follows:

$$BMI' = 2\beta_2(\text{age in days}) + \beta_1 = 0$$

Thus,

$$T_{peak} = -\frac{\beta_1}{2\beta_2}$$

$$BMI_{peak} = \frac{4\beta_0\beta_2 - \beta_1^2}{4\beta_2}$$

T_{peak} is the timing of BMI peak and BMI_{peak} is the magnitude of BMI peak.

1
2
3 The pre-peak velocity was calculated using the following equation, with BMI at 14 days of age
4 as the baseline measurement to avoid the period of neonatal weight loss seen in the first two
5 weeks of life.⁽²¹⁾
6
7

$$(BMI_{Peak} - BMI_{14days}) / (T_{peak} - 14 \text{ days}).$$

8
9
10
11
12
13 The subjects who had a BMI peak within 14 – 408 days of life were defined as estimable (“fit”)
14 BMI trajectories, while those who were not identifiable by the model were called inestimable
15 (“not fit”) BMI trajectories.⁽¹⁹⁾
16
17

18 19 20 **Statistical analysis**

21
22
23 SPSS 20.0 statistical software was used for all analyses and metalab2014b for the BMI
24 trajectory modeling. Data were presented as mean with 95% confidence interval. Categorical
25 data were summarized by calculating percentages. The chi-square test and two-sampled t
26 tests were used to examine the differences between participants whose BMI trajectories were
27 estimable or inestimable for the quadratic regression model and those who did or did not
28 have measurements at age two years. We classified birthweight as the following categories:
29 1.5 to less than 2.5 kg, 2.5 to less than 4 kg, and equal to or greater than 4 kg in the
30 chi-square test. (Table 1)
31
32

33
34
35 To evaluate the associations between covariates and infant BMI peak characteristics and
36 childhood BMI Z-scores, bivariate analyses were used by one-way ANOVA with post hoc
37 Bonferroni adjustments. (Table 2) BMI peak characteristics [age (in months) and magnitude
38 (BMI; in kg/m²) at peak and pre-peak velocities (kg/m²/month)] were estimated. The
39 correlations between the estimated BMI peak characteristics were assessed by pearson
40 correlation analysis. (Supplemental Table 2) Logistic regression was used to assess the
41 associations between BMI peak characteristics and childhood overweight (BAZ > +1) or
42 obesity (BAZ > +2), adjusting for other background characteristics. Gender, delivery mode
43 and maternal ages were defined as categorical variables. Birthweight, duration of
44 breastfeeding and sleeping were defined as continuous variable. We derived
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 birthweight-for-gestational-age z-scores using references from International standards for
4 newborn.⁽³⁰⁾ (Table 3) The coefficient of determination denoted R^2 was used to describe the
5 fit of every subject-specific curve. Statistical analyses were performed using only the subjects
6 with estimable BMI peak.⁽¹⁹⁻²²⁾ All statistical tests were two-tailed and P values <0.05 were
7 considered statistically significant.
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

Results

Description of the study population

The demographic characteristics of the study population are presented in Table 1. There were 2268 infants eligible for analysis, 49.6% male and 50.4% female. Most had a normal birthweight of 2.5 to less than 4 kg (n=2073, 91.4%). Eighty-five percent (n =1949) of infants had follow-up data at least through the age of 2 years (Table 1). Evaluated by the WHO Child Growth Standards, 17.0% (n =332) infants were overweight (BAZ > +1) and 2.3% (n =44) obese (BAZ > +2) at age 2 years.

Results of infant BMI trajectory modeling

Individual BMI trajectories were estimable using the polynomial regression model for 91.4% of the sample, with reasonable fit (mean $R^2=0.70\pm0.23$). Mean magnitude of BMI peak was 18.33 (95% CI 18.26-18.39) kg/m^2 and occurred at 7.61 (95% CI 7.55-7.67) months. (Supplemental Figure1) Those subjects with inestimable BMI peak mostly showed either a BMI peak after 408 days of life or a decrease in BMI after birth. The prevalence of macrosomia (birthweight>4kg) infants with inestimable infancy BMI peak were higher than that with estimable ones (6.7% vs 11.3%, $P =0.024$). Heavier macrosomia infants reached their BMI peak much earlier than other infants, since some of them attained BMI peak measurements just after birth. There was no significant difference in other factors between subjects with estimable and inestimable peak BMI ($P>0.05$). (Table 1)

Participants' characteristics in relation to infant BMI trajectories

Infant BMI trajectories were related to both sex and birthweight (Table 2). The magnitude of BMI peak was greater, and timing of peak BMI was earlier, in boys than in girls and in children of higher birthweight than those of lower birthweight. There was no statistical significant difference in pre-peak velocities with regards to infant characteristics.

General characteristics of children at age two years

We tested for differences between infants who had BMI data with estimable BMI peak at age two years (n=1790) vs. those who did not (n=159). There was no statistical difference between the two groups in sex, birthweight, maternal age, duration of breastfeeding, duration of sleep and overweight rates at age 2 years. ($P > 0.05$).

Association between infant BMI peak and childhood overweight and obesity

Table 3 shows the results of the association between BMI peak and risk of overweight and obesity at two years of age. When only the infant BMI peak was included in the model, higher magnitude and later timing of infant BMI peak increased the risk of overweight at two years. Furthermore, after adjustment for other infant background factors, higher magnitude (OR 3.11; 95% CI 2.64–3.66) and later timing (OR 1.35; 95% CI 1.21-1.50) of infant BMI peak each increased the risk of overweight at two years. The results were also similar with regards to childhood obesity (Table 3).

Discussion

Using a longitudinal set from a community-based cohort, we have demonstrated in the current analysis that infant BMI peak is useful for predicting childhood overweight and obesity in urban China. Boys had a higher average BMI peak and earlier average timing to achieve peak BMI than girls. Principally, our results show that higher BMI magnitude and later timing of infant BMI peak were each associated with increased risk of early childhood overweight and obesity.

This is the first community-based cohort study in China to characterize infant BMI peak and evaluate its association with risk of being overweight and obesity in early childhood. There have been remarkable increases in overweight and obesity in both rural and urban areas of China.⁽³¹⁾ Our findings can therefore be generalized to similarly aged children in Shanghai city and, to some degree, be extended to other areas in China. The data used in our analysis were routinely collected by the health centers where children are offered routine healthcare, such as immunizations and physical examination; thus, the collected measurements are a valid and reliable data set for addressing the study questions. The longitudinal nature of the cohort data and the repeated measurements of length and weight parameters provided us with the opportunity to carefully model infant BMI trajectories of infants over the course of the first year of life. A limitation of our investigation was that only about 69.9% (7456/10674) of all children in this age range had health records that only 85.9% of eligible children had complete follow-up data up to 2 years of age. Because children with incomplete data were excluded from the analysis, the risk of selection bias cannot be totally ruled out. Another weakness of the study is that the data concerning parent's BMI, pregnancy weight gain, gestational diabetes mellitus and income were not available, because the cohort was defined after birth and not prenatally. Additionally, the reliability of the anthropometric measurements could not be ascertained due to the retrospective nature of the cohort. Finally, the recorded BMI peak is estimation and not the true peak. Use of estimated BMI peak is potentially related to uncertainty in subsequent regression models.⁽¹⁸⁾

1
2
3 Few studies have investigated the utility of infant BMI peak in predicting childhood overweight
4 and obesity.⁽¹⁹⁻²¹⁾ Principally, we found that higher BMI magnitude and later timing of infant
5 BMI peak were each associated with increased risk of early childhood overweight and obesity.
6
7 This result is similar to previous research from the cohort study conducted in USA⁽¹⁹⁾ and the
8 Uppsala Family Study in Europe.⁽²⁰⁾ However, some of our findings are not consistent with
9 previous research. A 2010 prospective cohort study showed that more rapid increases in
10 weight for length in the first six months of life were associated with a sharp increase in
11 childhood obesity risk.⁽³²⁾ Although most previous studies used weight or BMI at
12 study-dependent fixed ages,^(32, 33) our work was based on longitudinal and repeated
13 measures of length and weight. Our results also demonstrate the differences in sex and
14 birthweight were associated with BMI magnitude and timing of the BMI peak, but not with
15 pre-peak velocity.^(19, 21) In recent studies, later timing of the BMI peak was observed in both
16 girls and boys (8-9 months of age) from European or American populations.^(20, 21, 23) Girls
17 peaked slightly later than boys in both populations. However, one recent study conducted in
18 Singapore suggested that Asian children peak earlier (6 months) than European or American
19 children and that sex does not significantly influence age at BMI peak in Asian infants.
20 Notably, that study used natural cubic splines, compared to our analysis that used a
21 polynomial regression model. It is possible that the use of different modeling methods to
22 derive BMI peak characteristics could account for the observed differences across
23 populations.⁽¹⁸⁾ Also, the effect of breastfeeding may also explain the different ages of BMI
24 peak observed across genders and populations. Further research is needed to demonstrate
25 the clinical relevance of these small differences in BMI peak across populations. Furthermore,
26 a previous study found a positive association between an earlier and higher BMI peak and
27 birthweight.^(19, 20) In our study, higher birthweight was not associated with a lower velocity,
28 which was found by the Philadelphia cohort study.⁽¹⁹⁾

29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
There is no widely accepted method to model infant BMI peak, appropriate peak age range
and the number and timing of serial measurements.⁽²³⁾ China is undergoing rapid social and
economic developments, which is accompanied by an improvement in nutritional status.

1
2
3 Current estimates indicate that overweight and obesity are rising in China, including in
4 children.⁽⁵⁾ However, there has been a lack of studies evaluating the utility of BMI peak for
5 predicting risk for being overweight or obese in later childhood in China, although BMI peak
6 has been demonstrated to be ancestry-specific.⁽¹⁹⁾ Therefore, these findings can be used to
7 help predict the early onset of obesity and to serve as a springboard for planning appropriate
8 interventions to reduce the increasing trend of childhood overweightness and obesity in
9 urban China. It is unclear why infants in our study had earlier BMI peaks (7-8 months) than
10 infants from America and Europe (8-9 months),^(20, 21, 23) but it has been demonstrated that
11 such differences may reflect ancestry-specific BMI peaks across populations.⁽¹⁹⁾ For this
12 reason, cross-cultural investigations are required to determine the validity of this assertion.
13 Understanding these differences may influence the design of public health intervention
14 protocols to address childhood obesity.⁽³⁴⁻³⁶⁾

27 Conclusion

28
29
30 Using a community-based longitudinal cohort study with repeated measurements of infant
31 growth parameters, we have for the first time determined that infant BMI peak is a useful
32 metric to predict early childhood overweight and obesity in urban China. Our findings suggest
33 that higher magnitude and later timing of infant BMI peak increased the risk of early childhood
34 overweight and obesity. Infancy therefore represents a critical window of opportunity to
35 prevent the emerging epidemic of overweight and obesity in children. Further studies from
36 other urban populations in China are required in order to confirm or question our
37 observations.
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Acknowledgements

We are grateful to the staff in Jing'an maternal and child health care center for data extraction.

We also acknowledge all children and their parent's for participation.

Authors' contributions

JieSun, Bright I Nwaru, and ZhuochunWu were responsible for the study design, analysis of the study and approval of the submitted and final version. Jing Hua and Xiaohong Li analyzed the data, interpreted the results and commented on the manuscript.

Funding

This study was funded by National Natural Science Foundation of China [71573049].

Ethics Approval

All procedures performed in this study were in accordance with the ethical standard. We gained approval (IRB#2015-TYSQ-03-11) for the current study from the Medical Research Ethics Committee, School of Public Health, Fudan University. Informed consent was obtained from all individual participants included in the study.

Competing interests

The authors declare that they have no conflict of interest.

Data Sharing Statement

No additional data are available.

References:

1. Commission presents its final report, calling for high-level action to address major health challenge. Available from <http://www.who.int/end-childhood-obesity/news/launch-final-report/en/>. 2016.
2. Benjamin Neelon SE, Schou Andersen C, Schmidt Morgen C, Kamper-Jorgensen M, Oken E, Gillman MW, et al. Early child care and obesity at 12 months of age in the Danish National Birth Cohort. *International journal of obesity* (2005). 2015;39(1):33-8.
3. Freedman DS, Mei Z, Srinivasan SR, Berenson GS, Dietz WH. Cardiovascular risk factors and excess adiposity among overweight children and adolescents: the Bogalusa Heart Study. *The Journal of pediatrics*. 2007;150(1):12-7.e2.
4. Skinner AC, Perrin EM, Skelton JA. Prevalence of obesity and severe obesity in US children, 1999-2014. *Obesity* (Silver Spring, Md). 2016;24(5):1116-23.
5. Ji CY. Report on childhood obesity in China (4) prevalence and trends of overweight and obesity in Chinese urban school-age children and adolescents, 1985-2000. *Biomedical and environmental sciences : BES*. 2007;20(1):1-10.
6. Commission. CNhaFP. National Report on Nutritional status of children aged 0-6 year. China:National health and Family Planning Commission. China;. 2012.
7. Andersen LG, Holst C, Michaelsen KF, Baker JL, Sorensen TI. Weight and weight gain during early infancy predict childhood obesity: a case-cohort study. *International journal of obesity* (2005). 2012;36(10):1306-11.
8. Baird J, Fisher D, Lucas P, Kleijnen J, Roberts H, Law C. Being big or growing fast: systematic review of size and growth in infancy and later obesity. *BMJ (Clinical research ed)*. 2005;331(7522):929.
9. Leunissen RW, Kerkhof GF, Stijnen T, Hokken-Koelega A. Timing and tempo of first-year rapid growth in relation to cardiovascular and metabolic risk profile in early adulthood. *Jama*. 2009;301(21):2234-42.
10. Monteiro PO, Victora CG. Rapid growth in infancy and childhood and obesity in later life--a systematic review. *Obesity reviews : an official journal of the International Association for the Study of Obesity*. 2005;6(2):143-54.
11. Weng SF, Redsell SA, Swift JA, Yang M, Glazebrook CP. Systematic review and meta-analyses of risk factors for childhood overweight identifiable during infancy. *Archives of disease in childhood*. 2012;97(12):1019-26.
12. Guo Y. Growth level of urban Chinese infants from birth to 2 years, body mass index Z scores' predicting model and its age trajectory in relation to maternal pre-pregnancy body weight status. 2013.
13. Ma JQ, Zhou LL, Hu YQ, Liu SS, Sheng XY. Association between feeding practices and weight status in young children. *BMC pediatrics*. 2015;15:97.
14. Gortmaker SL, Swinburn BA, Levy D, Carter R, Mabry PL, Finegood DT, et al. Changing the future of obesity: science, policy, and action. *Lancet (London, England)*. 2011;378(9793):838-47.
15. Robinson SM, Crozier SR, Harvey NC, Barton BD, Law CM, Godfrey KM, et al. Modifiable early-life risk factors for childhood adiposity and overweight: an analysis of their combined impact and potential for prevention. *The American journal of clinical nutrition*. 2015;101(2):368-75.
16. Kolsgaard ML, Joner G, Brunborg C, Anderssen SA, Tonstad S, Andersen LF. Reduction in BMI z-score and improvement in cardiometabolic risk factors in obese children and adolescents. *The Oslo Adiposity*

- 1
2
3 Intervention Study - a hospital/public health nurse combined treatment. BMC pediatrics. 2011;11:47.
4
5 17. Sijtsma A, Bocca G, L'Abée C, Liem ET, Sauer PJ, Corpeleijn E. Waist-to-height ratio, waist
6 circumference and BMI as indicators of percentage fat mass and cardiometabolic risk factors in children
7 aged 3-7 years. Clinical nutrition (Edinburgh, Scotland). 2014;33(2):311-5.
8
9 18. Aris IM, Bernard JY, Chen LW, Tint MT, Pang WW, Lim WY, et al. Infant body mass index peak and early
10 childhood cardio-metabolic risk markers in a multi-ethnic Asian birth cohort. International journal of
11 epidemiology. 2016.
12
13 19. Roy SM, Chesi A, Mentch F, Xiao R, Chiavacci R, Mitchell JA, et al. Body mass index (BMI) trajectories
14 in infancy differ by population ancestry and may presage disparities in early childhood obesity. The
15 Journal of clinical endocrinology and metabolism. 2015;100(4):1551-60.
16
17 20. Silverwood RJ, De Stavola BL, Cole TJ, Leon DA. BMI peak in infancy as a predictor for later BMI in the
18 Uppsala Family Study. International journal of obesity (2005). 2009;33(8):929-37.
19
20 21. Jensen SM, Ritz C, Ejlerskov KT, Molgaard C, Michaelsen KF. Infant BMI peak, breastfeeding, and body
21 composition at age 3 y. The American journal of clinical nutrition. 2015;101(2):319-25.
22
23 22. WHO Multicentre Growth Reference Study Group. WHO Child Growth Standards:
24 Length/height-for-age, Weight-for-age, Weight-for-length, Weight-for-height, and Body Mass
25 Index-for-age: Methods and Development. Geneva:World Health Organization,2006. Available from:
26 <http://www.who.int/childgrowth/standards/en/>. 2006.
27
28 23. Wen X, Kleinman K, Gillman MW, Rifas-Shiman SL, Taveras EM. Childhood body mass index
29 trajectories: modeling, characterizing, pairwise correlations and socio-demographic predictors of
30 trajectory characteristics. BMC medical research methodology. 2012;12:38.
31
32 24. Chivers P, Hands B, Parker H, Bulsara M, Beilin LJ, Kendall GE, et al. Body mass index, adiposity
33 rebound and early feeding in a longitudinal cohort (Raine Study). International journal of obesity (2005).
34 2010;34(7):1169-76.
35
36 25. Johnson W, Choh AC, Lee M, Towne B, Czerwinski SA, Demerath EW. Characterization of the infant
37 BMI peak: sex differences, birth year cohort effects, association with concurrent adiposity, and heritability.
38 American journal of human biology : the official journal of the Human Biology Council.
39 2013;25(3):378-88.
40
41 26. Giles LC, Whitrow MJ, Davies MJ, Davies CE, Rumbold AR, Moore VM. Growth trajectories in early
42 childhood, their relationship with antenatal and postnatal factors, and development of obesity by age 9
43 years: results from an Australian birth cohort study. International journal of obesity (2005).
44 2015;39(7):1049-56.
45
46 27. Sovio U, Kaakinen M, Tzoulaki I, Das S, Ruokonen A, Pouta A, et al. How do changes in body mass
47 index in infancy and childhood associate with cardiometabolic profile in adulthood? Findings from the
48 Northern Finland Birth Cohort 1966 Study. International journal of obesity (2005). 2014;38(1):53-9.
49
50 28. Fenton TR, Nasser R, Eliasziw M, Kim JH, Bilan D, Sauve R. Validating the weight gain of preterm
51 infants between the reference growth curve of the fetus and the term infant. BMC pediatrics. 2013;13:92.
52
53 29. WHO. Anthro for personal computers, version 3. Software for assessing growth and development of
54 the world's children. Geneva: WHO,2009. Available from: <http://www.who.int/childgrowth/software/en/>.
55 2009.
56
57 30. Villar J, Cheikh Ismail L, Victora CG, Ohuma EO, Bertino E, Altman DG, et al. International standards
58 for newborn weight, length, and head circumference by gestational age and sex: the Newborn
59
60

1
2
3 Cross-Sectional Study of the INTERGROWTH-21st Project. *Lancet* (London, England).

4 2014;384(9946):857-68.

5
6 31. Zhang YX, Wang SR. Rural-urban comparison in prevalence of overweight and obesity among
7 adolescents in Shandong, China. *Annals of human biology*. 2013;40(3):294-7.

8
9 32. Taveras EM, Rifas-Shiman SL, Belfort MB, Kleinman KP, Oken E, Gillman MW. Weight status in the first
10 6 months of life and obesity at 3 years of age. *Pediatrics*. 2009;123(4):1177-83.

11
12 33. Guo B, Mei H, Yang S, Zhang J. [Prenatal factors associated with high BMI status of infants and
13 toddlers]. *Zhonghua er ke za zhi = Chinese journal of pediatrics*. 2014;52(6):464-7.

14
15 34. Taveras EM, Gillman MW, Kleinman K, Rich-Edwards JW, Rifas-Shiman SL. Racial/ethnic differences
16 in early-life risk factors for childhood obesity. *Pediatrics*. 2010;125(4):686-95.

17
18 35. Taveras EM, Gillman MW, Kleinman KP, Rich-Edwards JW, Rifas-Shiman SL. Reducing racial/ethnic
19 disparities in childhood obesity: the role of early life risk factors. *JAMA pediatrics*. 2013;167(8):731-8.

20
21 36. Zilanawala A, Davis-Kean P, Nazroo J, Sacker A, Simonton S, Kelly Y. Race/ethnic disparities in early
22 childhood BMI, obesity and overweight in the United Kingdom and United States. *International journal of
23 obesity (2005)*. 2015;39(3):520-9.

Table 1 Participants' characteristics by subjects with "estimable"* and "inestimable"# BMI peak

Characteristics	n	Estimable*, n (%)	Inestimable#, n (%)
Total number	2268	2073	195
Gender			
Male	1126	1022 (49.3)	104 (53.3)
Female	1142	1051 (50.7)	91 (46.7)
Birth weight			
1.5 to <2.5kg	35	30 (1.4)	5 (2.6)
2.5 to <4.0kg	2073	1905 (91.9)	168 (86.2)
≥4kg	160	138 (6.7)^a	22 (11.3)
Delivery mode			
Vaginal birth	1086	989 (47.7)	97 (49.7)
Cesarean section	1182	1084 (52.3)	98 (50.3)
Maternal Age			
>35y	176	159 (7.7)	17 (8.7)
≤35y	2092	1914 (92.3)	178 (91.3)
Total number with data at age 2y	1949	1790 (86.3)	159 (81.5)
Total number of overweight and obese at age 2y	332	313 (17.5)	19 (11.9)
Total number of obese at age 2y	44	43 (2.4)	1 (0.6)

a.P<0.05

*Estimable: fit and identifiable BMI peak within 14–408 days of life.

Inestimable: Not fit and identifiable.

Chi-square tests were used to examine the differences between Estimable or Inestimable group.

Table 2 Infant characteristics in relation to infant BMI peak trajectories

		Magnitude(kg/m ²), Mean (95% CI)	Age(months), Mean (95% CI)	Pre-peak velocities(kg/m ² /month) Mean (95% CI)
Total	n=2073	18.33(18.26-18.39)	7.61(7.55-7.67)	0.43(0.42-0.44)
Gender				
	male (n=1022)	18.60(18.21-18.69)^a	7.54(7.46-7.63)^b	0.42(0.41-0.43)
	female (n=1051)	18.07(17.98-18.16)	7.67(7.59-7.76)	0.43(0.42-0.44)
Birth Weight				
	1.5 to <2.5kg(n=30)	17.63(17.13-18.13)	8.13(7.56-8.70)	0.44(0.35-0.53)
	2.5 to <4.0kg(n=1905)	18.27(18.21-18.34)	7.63(7.57-7.70)	0.43(0.42-0.44)
	>=4kg(n=138)	19.25(18.97-19.52)^b	7.11(6.88-7.34)^a	0.39(0.35-0.42)
Delivery Mode				
	Vaginal birth (n=989)	18.24(18.14-18.34)	7.64(7.56-7.73)	0.43(0.42-0.44)
	Cesarean section (n=1084)	18.41(18.32-18.50)^a	7.58(7.49-7.66)	0.43(0.42-0.44)
Maternal Age				
	>35y(n=159)	18.42(18.18-18.66)	7.61(7.49-7.82)	0.44(0.41-0.48)
	<=35y(n=1914)	18.32(18.25-18.39)	7.61(7.55-7.67)	0.42(0.41-0.43)

a.P<0.001 b.P<0.05

The analysis includes only infants who had BMI peak within 0-408 days and whose BMI trajectories were estimable by the quadratic model.

Bivariate comparison was performed using one-way ANOVA with post hoc Bonferroni multiple comparison test.

Table 3 Association between BMI peak characteristics and overweight and obesity at age 2 years

	Overweight at 2y (n=1790)		Obesity at 2y (n=1790)	
	Model containing infant BMI trajectory characteristics alone	Initial model plus all independent variables	Model containing infant BMI trajectory characteristics alone	Initial model plus all independent variables
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Magnitude(kg/m ²)	2.94(2.54-3.40)^a	3.11(2.64-3.66)^a	2.76(2.11-3.60)^a	2.69(2.00-3.61)^a
Age (months)	1.36(1.23-1.51)^a	1.35(1.21-1.50)^a	1.33(1.08-1.65)^b	1.35(1.08-1.68)^b
Pre-peak velocities(kg/m ² /month)	0.17(0.07-0.40)^a	0.14(0.06-0.34)^a	0.10(0.02-0.56)^b	0.12(0.02-0.74)^c
male(vs female)		0.67(0.49-0.90)^b		0.99(0.51-1.96)
birth weight z score.(continuous)		1.06(0.89-1.26)		1.24(0.84-1.82)
Duration of breastfeeding(continuous)		0.97(0.93-1.01)		0.92(0.84-1.01)
Duration of Sleep(continuous)		0.89(0.77-1.02)		0.89(0.63-1.24)
Cesarean section(vs Vaginal Birth)		1.08(0.81-1.44)		0.80(0.42-1.54)
Mother Age(>35y vs<=35y)		0.68(0.38-1.21)		0.74(0.21-2.59)

a.P<0.001 b.P<0.01 c.P<0.05

The analysis includes only infants who had BMI peak within 0-408 days and whose BMI trajectories were estimable by the quadratic model.

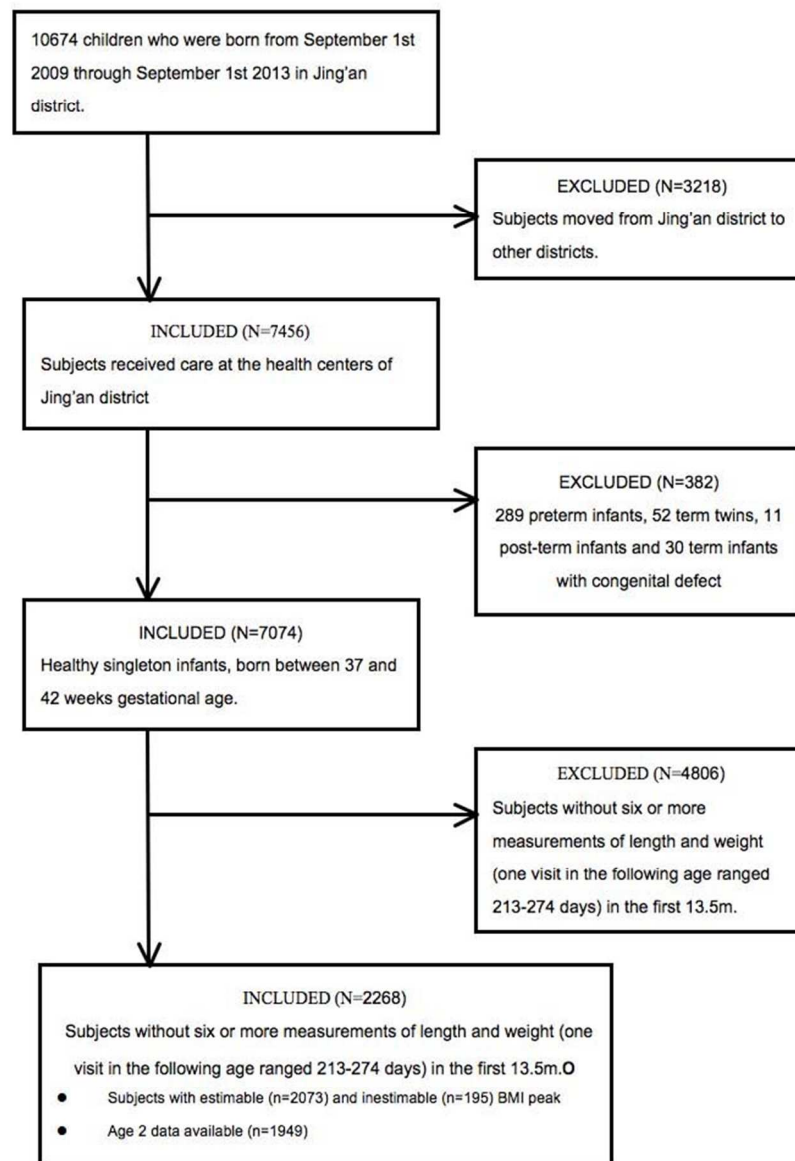


Figure1 Recruitment flow chart and study sample

64x83mm (300 x 300 DPI)

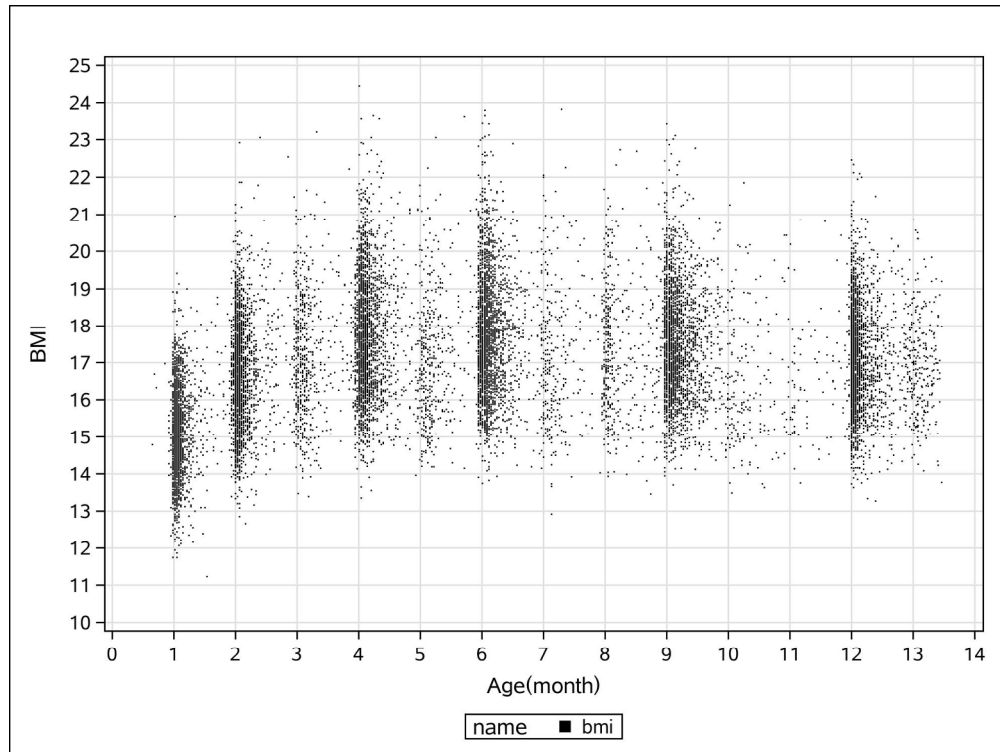


Figure 2 Plot of BMI data by age from birth to 13.5 months

169x127mm (300 x 300 DPI)

Supplemental Table 1 Characteristics of the analytic and excluded healthy singleton infants

Characteristics	n	Included, n (%)	Excluded, n (%)
Total number	7074	2268(32.1)	4806(67.9)
Gender			
Male	3468	1126 (49.6)	2342 (48.7)
Female	3606	1142(50.4)	2464 (51.3)
Birth weight			
<4.0kg	6609	2108(92.9)	4501 (93.7)
≥4kg	465	160 (7.1)	305(6.3)
Maternal Age			
>35y	570	176 (7.8)	394 (8.2)
≤35y	6504	2092(92.2)	4412(91.8)
Total number with data at age 2y	1949	1949 (85.9)^a	2282 (47.4)
Total number of overweight and obese at age 2y	751	330 (16.9)	421 (18.4)
Total number of obese at age 2y	99	44 (2.3)	55(2.4)

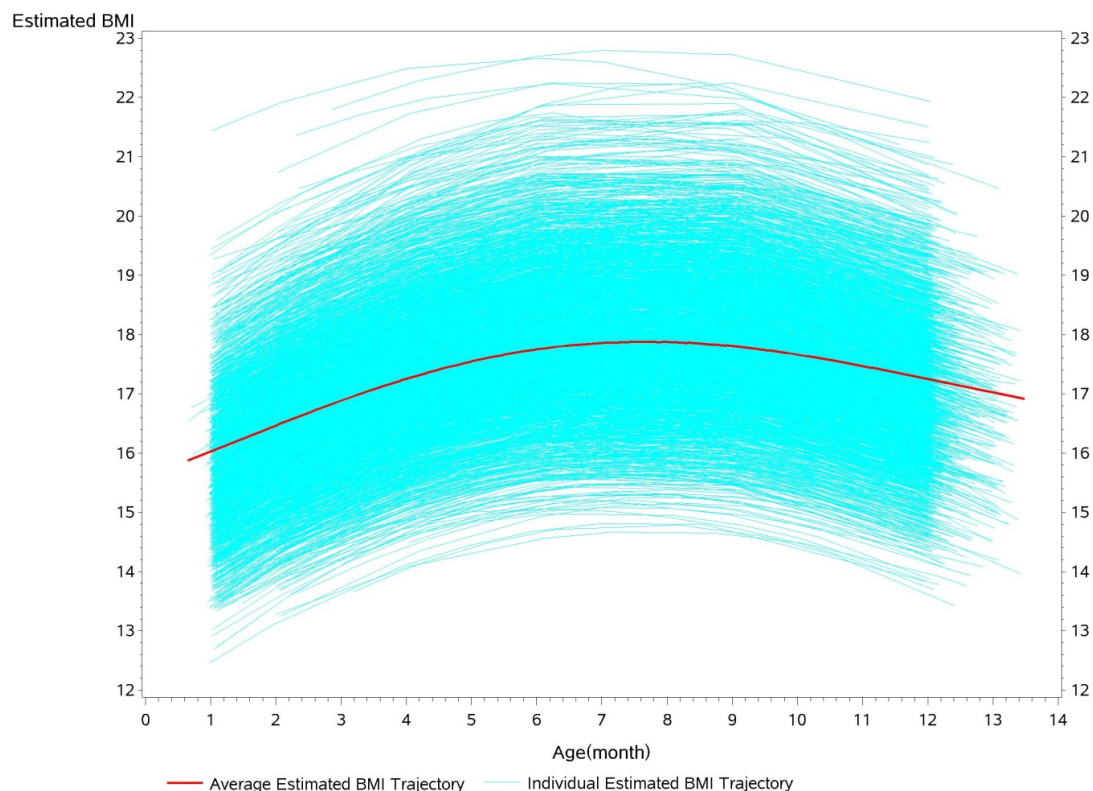
a.P<0.05

Chi-square tests were used to examine the differences between included or excluded group.

Supplemental Table 2: Correlation matrix of infancy BMI characteristics

	Age of BMI Peak, mo	Pre-peak velocities, kg/m2/mo
Magnitude of BMI peak, kg/m2	0.03	0.654**
Age of BMI Peak, mo		0.09**

Significance is noted as: ** $p \leq 0.01$.



Supplemental Figure1 Infant Estimated BMI trajectory by polynomial regression model

Only

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any pre-specified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-4,Figure1
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6,Figure 1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8-9
		(b) Describe any methods used to examine subgroups and interactions	8
		(c) Explain how missing data were addressed	6
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	6

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Figure 1
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1, Supplemental Table 1
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	5
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	8
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 3
		(b) Report category boundaries when continuous variables were categorized	8
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

For peer review only

BMJ Open

Infant BMI Peak as a predictor of overweight and obesity at age 2 years in a Chinese community-based cohort

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2016-015122.R3
Article Type:	Research
Date Submitted by the Author:	06-Aug-2017
Complete List of Authors:	Sun, Jie; School of Public Health, Fudan, Department of Social Medicine; Jing'an Maternal and Child Health Care Center, Shanghai, Department of Child Health Care Nwaru, Bright; The University Of Edinburgh, Allergy & Respiratory Research Group, Centre for Population Health Sciences; University of Tampere, School of Health Sciences Hua, Jing; Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine, Department of Maternal and Child Health Care Li, Xiaohong; School of Public Health, Fudan University, Department of Health Policy and Management ; Innovation Center for Social Risk Governance in Health Wu, Zhuochun; School of Public Health, Fudan University, Department of Social Medicine; Innovation Center for Social Risk Governance in Health
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Paediatrics
Keywords:	Overweight, Obesity, Body mass index, Longitudinal Study, Infant

SCHOLARONE™
Manuscripts

Infant BMI peak as a predictor of overweight and obesity at age 2 years in a Chinese community-based cohort

Jie Sun^{1,2}, Bright I Nwaru^{3,4,5}, Jing Hua⁶, Xiaohong Li^{7,8}, Zhuochun Wu^{1,8}

Abstract

Objectives: Infant body mass index (BMI) peak has proven to be a useful indicator for predicting childhood obesity risk in American and European populations. However, it has not been assessed in China. We characterized infant BMI trajectories in a Chinese longitudinal cohort and evaluated whether BMI peak can predict overweight and obesity at age 2 years.

Methods: Serial measurements (n=6-12) of weight and length were taken from healthy term infants (n=2073) in a birth cohort established in urban Shanghai. Measurements were used to estimate BMI growth curves from birth to 13.5 months using a polynomial regression model. BMI peak characteristics, including age (in months) and magnitude (BMI, in kg/m²) at peak and pre-peak velocities (in kg/m²/month), were estimated. The relationship between infant BMI peak and childhood BMI at age 2 years was examined using binary logistic analysis.

Results: Mean age at peak BMI was 7.61 months, with a magnitude of 18.33 kg/m². Boys (n=1022) had a higher average peak BMI (18.60 vs. 18.07 kg/m², P<0.001) and earlier average achievement of peak value (7.54 vs. 7.67 months, P<0.05) than girls (n=1051). With 1 kg/m² increase in peak BMI and one month increase in peak time, the risk of overweight at age 2 years increased by 2.11 times (OR 3.11; 95% CI 2.64-3.66) and 35% (OR 1.35; 95% CI 1.21-1.50), respectively. Similarly, higher BMI magnitude (OR 2.69; 95% CI 2.00-3.61) and later timing of infant BMI peak (OR 1.35; 95% CI 1.08-1.68) were associated with an increased risk of childhood obesity at age 2 years.

Conclusions: We have shown that infant BMI peak is valuable for predicting early childhood overweight and obesity in urban Shanghai. Because this is the first Chinese community-based cohort study of this nature, future research is required to examine infant populations in other areas of China.

Key words: Body mass Index, Obesity, Overweight, Longitudinal Study, Infants

Word Count: 3883 words

¹Department of Social Medicine, School of Public Health, Fudan University, Shanghai, China.

²Department of Child Health Care, Jing'an Maternal and Child Health Care Center, Shanghai, China.

³School of Health Sciences, University of Tampere, Tampere, Finland.

⁴Asthma UK Centre for Applied Research, Usher Institute of Population Health Sciences and Informatics, University of Edinburgh, Edinburgh, UK.

⁵Krefting Research Centre, Institute of Medicine, University of Gothenburg, Gothenburg, Sweden

⁶Department of Maternal and Child Health Care, Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine,

1
2
3 Shanghai, China.

4
5 ⁷Department of Health Policy and Management, School of Public Health, Fudan University, Shanghai,China.

6
7 ⁸Innovation Center for Social Risk Governance in Health, Fudan University, Shanghai, China

8
9 Corresponding author: Zhuochun Wu, Department of Social Medicine, School of Public Health, Fudan University, Fax:
10 086-021-62309139, P.O. Box 250,138 Yi Xue Yuan Road, Shanghai 200032, China . zcwu@shmu.edu.cn.

11 **Strengths and limitations of this study**

12
13 The longitudinal cohort with careful repeated measurements of child growth parameters provided the
14 opportunity to characterize infant BMI peak over the first year of life.

15
16 As we lacked data on parent's BMI and pregnancy weight gain, we could not ascertain the influence of these on
17 infant BMI peak and contribution to childhood overweight and obesity.

18
19 Selection bias may exist in our study because 14.1% of the infants that were measured did not complete the
20 follow-up at 2 years old.

21 **Introduction**

22
23 The worldwide overweight prevalence among children aged under 5 years has risen from 4.8%
24 in 1990 to 6.1% in 2014.⁽¹⁾ The current worldwide obesity epidemic is a serious public health
25 crisis.⁽¹⁻⁵⁾ In 2014, almost half (48%) of obese individuals lived in Asia.⁽¹⁾ In urban areas of
26 China, the prevalence of overweight increased from 5.3% in 2005 to 8.5% in 2010.⁽⁶⁾ Rapid
27 weight gain in early infancy is related to the adult development of obesity and cardiovascular
28 risk factors, including hypertension and impaired glucose tolerance.⁽⁷⁻¹¹⁾ Environmental and
29 behavioral factors are believed to be key drivers of obesity because although obesity is
30 genetically influenced, genetic changes cannot explain the rapid increase in the prevalence
31 of obesity.⁽¹²⁾ Therapeutic interventions in adulthood have poor long-term effects and are not
32 cost effective, therefore the introduction of primary preventive strategies during infancy may
33 be more important to reduce the risk of being overweight and obese.⁽¹³⁻¹⁵⁾

34
35 Body mass index (BMI), a useful estimate of adiposity for children aged more than two years,
36 correlates with future health outcomes.^(3, 7) A modest reduction in BMI z-score after one year
37 of obesity intervention may improve several cardiovascular risk factors.⁽¹⁶⁾ In young children,
38 waist-to-height-ratio (WHtR) is not superior to BMI in estimating body fat percentage, nor is
39 WHtR better correlated with cardiometabolic risk factors than BMI in overweight/obese

1
2
3 children.⁽¹⁷⁾ One study in Singapore suggested that early BMI may have an important impact
4
5 on later metabolic outcomes in Asian populations.⁽¹⁸⁾
6
7

8
9 Few studies have evaluated the associations between infant BMI trajectory and childhood
10
11 overweight and obesity.^(12, 19-21) Weight-for-length percentile curves are often used but do not
12
13 account for the age-based changes that reflect different stages of infancy.⁽¹⁹⁾ BMI increases
14
15 from birth and reaches a maximum called the 'BMI peak' around age 7-9 months old, and
16
17 then decreases and reaches a nadir around age 4-6 years old before increasing once
18
19 again.⁽¹⁹⁻²¹⁾ According to Silverwood et al, both age and magnitude of BMI peak were
20
21 positively associated with later BMI z-scores.⁽²⁰⁾ Additionally, several studies have used
22
23 statistical models of growth trajectories to estimate the magnitude and timing of infant BMI
24
25 peak.⁽¹⁸⁻²⁷⁾

26
27 Ancestry-specific differences in Infant BMI peak are found between African-American and
28
29 European populations.⁽¹⁹⁾ However, to date there have been no studies performed in China to
30
31 demonstrate the utility of infant BMI peak for predicting the risk of childhood overweight and
32
33 obesity. In order to form comparisons with other populations, we referred to a BMI modeling
34
35 set by a cohort study in Philadelphia, USA ^(19, 23) Using a community-based longitudinal data
36
37 set of serial measurements of length and weight from birth to childhood in Shanghai, we
38
39 aimed to estimate the BMI peak characteristics in order to study the association between the
40
41 infant BMI peak and overweight and obesity at age 2 years.
42
43
44
45

46 **Methods**

47 **Study Participants**

48
49 We obtained our community-based longitudinal cohort data from the Shanghai Jing'an
50
51 District birth and health records. Shanghai has a population of 19 million, as of 2009, and is
52
53 divided into seventeen urban districts and one suburban district. Jing'an District is located at
54
55 the city center and has a population of 248,000, as of 2009. "Providing free of charge health
56
57
58
59
60

1
2
3 examination to children aged 0-3 years" was a project funded by the Shanghai government
4 for Jing'an children born from September 2009 onwards. Community health centers in the
5 Jing'an District provide routine well-child checks for infants and young children. A District
6 Childcare Database for all health centers in this project was established and managed by the
7 Jing'an maternal and child health care center. For the Childcare Database, health center
8 nurses record children's gender, gestational age, birthweight, feeding and sleeping behaviors,
9 and other information during the child health examination. All children were followed from
10 the age of one month to two or three years old until they went to kindergarten.
11
12

13
14
15 For this study, we used data from the Childcare Database for all children who were born from
16 September 1st 2009 to September 1st 2013 and received care at the Jing'an District health
17 centers. Children were followed from birth, with data collected at 1, 2, 4, 6, 9, 12, 18 and 24
18 months of age from all five communities in Jing'an District, representing 69.9% (7456/10674)
19 of all children in this age range in Jing'an District. Roughly 30% of children moved from
20 Jing'an district to other districts of Shanghai during the study period, which resulted in a loss
21 of follow-up in these cases. We gained approval (IRB#2015-TYSQ-03-11) for the current
22 study from the Medical Research Ethics Committee, School of Public Health, Fudan
23 University.
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41

42 **Inclusion and exclusion criteria**

43
44 Inclusion criteria for the infants in this study specified healthy single births, a gestational age
45 between 37 and 42 weeks, and no physical problems. Participants were included if they had
46 at least six measurements of length and weight in the first 13.5 months of life. The number
47 and range of measurements were determined by the BMI modeling set by a cohort study in
48 Philadelphia, USA.^(19, 23) Because the BMI peak occurs around 7-9 months old, we included
49 children who had at least one health examination visit between 213-274 days old. To test the
50 relationship between infant BMI peak and childhood overweight and obesity, we included
51
52
53
54
55
56
57
58
59
60

1
2
3 measurements for children at 2 years old when the data was available. Preterm infants (n =
4 289), term twins (n = 52), post-term infants (n = 11), and term infants with congenital defects
5 (n = 30) were excluded. These children have different curve characteristics than normal term
6 children.⁽²⁸⁾ We used exclusion criteria similar to the Philadelphia cohort study to compare
7 peak BMI with other populations.⁽¹⁹⁾ There were 21.2% (2268/7456) infants eligible for
8 analysis. Of these, we observed 85.9% (1949/2268) children from birth to age two years, i.e.
9 until September 1st 2015 (Figure 1). To assess potential selection bias, we compared
10 demographics and birth characteristics of the analytic sample (n=2268) to the excluded
11 healthy singleton infants (n=4806). There were no substantial differences in sex, birthweight,
12 maternal age or overweight and obese rates at age 2 years of the two samples.
13 (Supplemental Table 1)
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28

29 **Anthropometric measures**

30
31
32 Weight and length of children were measured by the same type of instruments at the
33 community health centers. Weight for infants (0-18 months) was measured by an electronic
34 pediatric scale (SECA 376 Weighing Scale) to the nearest 0.005 kg. Weight for toddlers
35 (19-24 months) was measured by another type of scale (SECA 704c Weighing Scale) to the
36 nearest 0.05 kg. Recumbent length was measured from the top of the head to soles of feet
37 using an infant mat (SECA416 Mobile Measuring Mat) to the nearest 0.1 cm. BMI z-score
38 (BAZ) of children at age two years were calculated according to the 2006 World Health
39 Organization (WHO) Child Growth Standards using the WHO Anthro 2009 software.⁽²⁹⁾ The
40 WHO Child Growth Standards was based on a multi-country study involving breastfed
41 children from six geographically distinct sites.⁽¹⁾ Overweight was defined as BAZ > +1
42 (BMI >85th percentile) while obesity was defined as BAZ > + 2 (BMI >97th percentile). Normal
43 weight was defined as $-1 \leq \text{BAZ} \leq +1$.^(2, 13) Based on reports from previous studies,^(11, 12, 19, 21)
44 we extracted factors associated with childhood overweight from the electronic medical
45 records. These factors were birthweight, sex, delivery mode, maternal age, duration of
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

breastfeeding and sleeping data. Parents answered to feeding and sleeping questions in follow-ups. They reported the age in months at which breastfeeding was stopped. Sleep duration in hours was recorded at age 2 years. Because this cohort was set up after birth, some information about pregnancy and parents information was not available.

BMI trajectory modeling

BMI peak was identified from subject-specific BMI growth curves established by serial BMI measurements. (Figure 2) A polynomial regression model with quadratic terms was fit to the BMI measurements over time. Regression modeling was used for each child to fit the following equation: ⁽¹⁹⁾

$$BMI = \beta_0 + \beta_1(\text{age in days}) + \beta_2(\text{age in days})^2$$

The first inflection point occurred at less than 408 days as derived from the equation and this was identified as BMI peak. The magnitude and timing of BMI peak were found by taking derivatives as follows:

$$BMI' = 2\beta_2(\text{age in days}) + \beta_1 = 0$$

Thus,

$$T_{peak} = -\frac{\beta_1}{2\beta_2}$$

$$BMI_{peak} = \frac{4\beta_0\beta_2 - \beta_1^2}{4\beta_2}$$

T_{peak} is the timing of BMI peak and BMI_{peak} is the magnitude of BMI peak.

The pre-peak velocity was calculated using the following equation, with BMI at 14 days of age as the baseline measurement to avoid the period of neonatal weight loss seen in the first two weeks of life.⁽²¹⁾

$$(BMI_{Peak} - BMI_{14days}) / (T_{peak} - 14 \text{ days}).$$

The subjects who had a BMI peak within 14 – 408 days of life were defined as estimable (“fit”) BMI trajectories, while those who were not identifiable by the model were called inestimable (“not fit”) BMI trajectories.⁽¹⁹⁾

Statistical analysis

SPSS 20.0 statistical software was used for all analyses and metalab2014b for the BMI trajectory modeling. Data were presented as mean with 95% confidence interval. Categorical data were summarized by calculating percentages. The chi-square test and two-sampled t tests were used to examine the differences between participants whose BMI trajectories were estimable or inestimable for the quadratic regression model and those who did or did not have measurements at age two years. We classified birthweight as the following categories: 1.5 to less than 2.5 kg, 2.5 to less than 4 kg, and equal to or greater than 4 kg in the chi-square test. (Table 1)

To evaluate the associations between covariates and infant BMI peak characteristics and childhood BMI Z-scores, bivariate analyses were used by one-way ANOVA with post hoc Bonferroni adjustments. (Table 2) BMI peak characteristics [age (in months) and magnitude (BMI; in kg/m²) at peak and pre-peak velocities (kg/m²/month)] were estimated. The correlations between the estimated BMI peak characteristics were assessed by Pearson correlation analysis. (Supplemental Table 2) Logistic regression was used to assess the associations between BMI peak characteristics and childhood overweight (BAZ > +1) or obesity (BAZ > +2), adjusting for other background characteristics. Gender, delivery mode and maternal ages were defined as categorical variables. Birthweight, duration of breastfeeding and sleeping were defined as continuous variable. We derived birthweight-for-gestational-age z-scores using references from International standards for newborn.⁽³⁰⁾ (Table 3) The coefficient of determination denoted R² was used to describe the fit of every subject-specific curve. Statistical analyses were performed using only the subjects

1
2
3 with estimable BMI peak.⁽¹⁹⁻²²⁾ All statistical tests were two-tailed and P values <0.05 were
4
5 considered statistically significant.
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

Results

Description of the study population

The demographic characteristics of the study population are presented in Table 1. There were 2268 infants eligible for analysis, 49.6% male and 50.4% female. Most had a normal birthweight of 2.5 to less than 4 kg (n=2073, 91.4%). Eighty-five percent (n =1949) of infants had follow-up data at least through the age of 2 years (Table 1). Evaluated by the WHO Child Growth Standards, 17.0% (n =332) infants were overweight (BAZ > +1) and 2.3% (n =44) obese (BAZ > +2) at age 2 years.

Results of infant BMI trajectory modeling

Individual BMI trajectories were estimable using the polynomial regression model for 91.4% of the sample, with reasonable fit (mean $R^2=0.70\pm 0.23$). Mean magnitude of BMI peak was 18.33 (95% CI 18.26-18.39) kg/m^2 and occurred at 7.61 (95% CI 7.55-7.67) months. (Supplemental Figure1) Those subjects with inestimable BMI peak mostly showed either a BMI peak after 408 days of life or a decrease in BMI after birth. The prevalence of macrosomia (birthweight>4kg) infants with inestimable infancy BMI peak were higher than that with estimable ones (6.7% vs 11.3%, $P =0.024$). Heavier macrosomia infants reached their BMI peak much earlier than other infants, since some of them attained BMI peak measurements just after birth. There was no significant difference in other factors between subjects with estimable and inestimable peak BMI ($P>0.05$). (Table 1)

Participants' characteristics in relation to infant BMI trajectories

Infant BMI trajectories were related to both sex and birthweight (Table 2). The magnitude of BMI peak was greater, and timing of peak BMI was earlier, in boys than in girls and in children of higher birthweight than those of lower birthweight. There was no statistical significant difference in pre-peak velocities with regards to infant characteristics.

General characteristics of children at age two years

We tested for differences between infants who had BMI data with estimable BMI peak at age two years (n=1790) vs. those who did not (n=159). There was no statistical difference between the two groups in sex, birthweight, maternal age, duration of breastfeeding, duration of sleep and overweight rates at age 2 years. ($P > 0.05$).

Association between infant BMI peak and childhood overweight and obesity

Table 3 shows the results of the association between BMI peak and risk of overweight and obesity at two years of age. When only the infant BMI peak was included in the model, higher magnitude and later timing of infant BMI peak increased the risk of overweight at two years. Furthermore, after adjustment for other infant background factors, higher magnitude (OR 3.11; 95% CI 2.64–3.66) and later timing (OR 1.35; 95% CI 1.21-1.50) of infant BMI peak each increased the risk of overweight at two years. The results were also similar with regards to childhood obesity (Table 3).

Discussion

Using a longitudinal set from a community-based cohort, we have demonstrated in the current analysis that infant BMI peak is useful for predicting childhood overweight and obesity in urban China. Boys had a higher average BMI peak and earlier average timing to achieve peak BMI than girls. Principally, our results show that higher BMI magnitude and later timing of infant BMI peak were each associated with increased risk of early childhood overweight and obesity.

This is the first community-based cohort study in China to characterize infant BMI peak and evaluate its association with risk of being overweight and obesity in early childhood. There have been remarkable increases in overweight and obesity in both rural and urban areas of China.⁽³¹⁾ Our findings can therefore be generalized to similarly aged children in Shanghai city and, to some degree, be extended to other areas in China. The longitudinal nature of the cohort data and the repeated measurements of length and weight parameters provided us with the opportunity to carefully model infant BMI trajectories of infants over the course of the first year of life. A limitation of our investigation was that only about 69.9% (7456/10674) of all children in this age range had health records that only 85.9% of eligible children had complete follow-up data up to 2 years of age. Because children with incomplete data were excluded from the analysis, the risk of selection bias cannot be totally ruled out. Another weakness of the study is that the data concerning parent's BMI, pregnancy weight gain, gestational diabetes mellitus and income were not available, because the cohort was defined after birth and not prenatally. Additionally, the reliability of the anthropometric measurements could not be ascertained due to the retrospective nature of the cohort. We acknowledge that the generated from routinely collected data may potentially influence the generalizability of the findings. Finally, the recorded BMI peak is estimation and not the true peak. Use of estimated BMI peak is potentially related to uncertainty in subsequent regression models.⁽¹⁸⁾

Few studies have investigated the utility of infant BMI peak in predicting childhood overweight and obesity.⁽¹⁹⁻²¹⁾ Principally, we found that higher BMI magnitude and later timing of infant

1
2
3 BMI peak were each associated with increased risk of early childhood overweight and obesity.
4
5 This result is similar to previous research from the cohort study conducted in USA⁽¹⁹⁾ and the
6
7 Uppsala Family Study in Europe.⁽²⁰⁾ However, some of our findings are not consistent with
8
9 previous research. A 2010 prospective cohort study showed that more rapid increases in
10
11 weight for length in the first six months of life were associated with a sharp increase in
12
13 childhood obesity risk.⁽³²⁾ Although most previous studies used weight or BMI at
14
15 study-dependent fixed ages,^(32, 33) our work was based on longitudinal and repeated
16
17 measures of length and weight. Our results also demonstrate the differences in sex and
18
19 birthweight were associated with BMI magnitude and timing of the BMI peak, but not with
20
21 pre-peak velocity.^(19, 21) In recent studies, later timing of the BMI peak was observed in both
22
23 girls and boys (8-9 months of age) from European or American populations.^(20, 21, 23) Girls
24
25 peaked slightly later than boys in both populations. However, one recent study conducted in
26
27 Singapore suggested that Asian children peak earlier (6 months) than European or American
28
29 children and that sex does not significantly influence age at BMI peak in Asian infants.
30
31 Notably, that study used natural cubic splines, compared to our analysis that used a
32
33 polynomial regression model. It is possible that the use of different modeling methods to
34
35 derive BMI peak characteristics could account for the observed differences across
36
37 populations.⁽¹⁸⁾ Also, the effect of breastfeeding may also explain the different ages of BMI
38
39 peak observed across genders and populations. Further research is needed to demonstrate
40
41 the clinical relevance of these small differences in BMI peak across populations. Furthermore,
42
43 a previous study found a positive association between an earlier and higher BMI peak and
44
45 birthweight.^(19, 20) In our study, higher birthweight was not associated with a lower velocity,
46
47 which was found by the Philadelphia cohort study.⁽¹⁹⁾

48
49 There is no widely accepted method to model infant BMI peak, appropriate peak age range
50
51 and the number and timing of serial measurements.⁽²³⁾ China is undergoing rapid social and
52
53 economic developments, which is accompanied by an improvement in nutritional status.
54
55 Current estimates indicate that overweight and obesity are rising in China, including in
56
57 children.⁽⁵⁾ However, there has been a lack of studies evaluating the utility of BMI peak for
58
59

1
2
3 predicting risk for being overweight or obese in later childhood in China, although BMI peak
4 has been demonstrated to be ancestry-specific.⁽¹⁹⁾ Therefore, these findings can be used to
5 help predict the early onset of obesity and to serve as a springboard for planning appropriate
6 interventions to reduce the increasing trend of childhood overweightness and obesity in
7 urban China. It is unclear why infants in our study had earlier BMI peaks (7-8 months) than
8 infants from America and Europe (8-9 months),^(20, 21, 23) but it has been demonstrated that
9 such differences may reflect ancestry-specific BMI peaks across populations.⁽¹⁹⁾ For this
10 reason, cross-cultural investigations are required to determine the validity of this assertion.
11 Understanding these differences may influence the design of public health intervention
12 protocols to address childhood obesity.⁽³⁴⁻³⁶⁾

23 **Conclusion**

24
25
26 Using a community-based longitudinal cohort study with repeated measurements of infant
27 growth parameters, we have for the first time determined that infant BMI peak is a useful
28 metric to predict early childhood overweight and obesity in urban China. Our findings suggest
29 that higher magnitude and later timing of infant BMI peak increased the risk of early childhood
30 overweight and obesity. Infancy therefore represents a critical window of opportunity to
31 prevent the emerging epidemic of overweight and obesity in children. Further studies from
32 other urban populations in China are required in order to confirm or question our
33 observations.
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Acknowledgements

We are grateful to the staff in Jing'an maternal and child health care center for data extraction.

We also acknowledge all children and their parent's for participation.

Authors' contributions

JieSun, Bright I Nwaru, and ZhuochunWu were responsible for the study design, analysis of the study and approval of the submitted and final version. Jing Hua and Xiaohong Li analyzed the data, interpreted the results and commented on the manuscript.

Funding

This study was funded by National Natural Science Foundation of China [71573049].

Ethics Approval

All procedures performed in this study were in accordance with the ethical standard. We gained approval (IRB#2015-TYSQ-03-11) for the current study from the Medical Research Ethics Committee, School of Public Health, Fudan University. Informed consent was obtained from all individual participants included in the study.

Competing interests

The authors declare that they have no conflict of interest.

Data Sharing Statement

No additional data are available.

References:

1. Commission presents its final report, calling for high-level action to address major health challenge. Available from <http://www.who.int/end-childhood-obesity/news/launch-final-report/en/>. 2016.
2. Benjamin Neelon SE, Schou Andersen C, Schmidt Morgen C, Kamper-Jorgensen M, Oken E, Gillman MW, et al. Early child care and obesity at 12 months of age in the Danish National Birth Cohort. *International journal of obesity* (2005). 2015;39(1):33-8.
3. Freedman DS, Mei Z, Srinivasan SR, Berenson GS, Dietz WH. Cardiovascular risk factors and excess adiposity among overweight children and adolescents: the Bogalusa Heart Study. *The Journal of pediatrics*. 2007;150(1):12-7.e2.
4. Skinner AC, Perrin EM, Skelton JA. Prevalence of obesity and severe obesity in US children, 1999-2014. *Obesity* (Silver Spring, Md). 2016;24(5):1116-23.
5. Ji CY. Report on childhood obesity in China (4) prevalence and trends of overweight and obesity in Chinese urban school-age children and adolescents, 1985-2000. *Biomedical and environmental sciences : BES*. 2007;20(1):1-10.
6. Commission. CNhaFP. National Report on Nutritional status of children aged 0-6 year. China:National health and Family Planning Commission. China;. 2012.
7. Andersen LG, Holst C, Michaelsen KF, Baker JL, Sorensen TI. Weight and weight gain during early infancy predict childhood obesity: a case-cohort study. *International journal of obesity* (2005). 2012;36(10):1306-11.
8. Baird J, Fisher D, Lucas P, Kleijnen J, Roberts H, Law C. Being big or growing fast: systematic review of size and growth in infancy and later obesity. *BMJ (Clinical research ed)*. 2005;331(7522):929.
9. Leunissen RW, Kerkhof GF, Stijnen T, Hokken-Koelega A. Timing and tempo of first-year rapid growth in relation to cardiovascular and metabolic risk profile in early adulthood. *Jama*. 2009;301(21):2234-42.
10. Monteiro PO, Victora CG. Rapid growth in infancy and childhood and obesity in later life--a systematic review. *Obesity reviews : an official journal of the International Association for the Study of Obesity*. 2005;6(2):143-54.
11. Weng SF, Redsell SA, Swift JA, Yang M, Glazebrook CP. Systematic review and meta-analyses of risk factors for childhood overweight identifiable during infancy. *Archives of disease in childhood*. 2012;97(12):1019-26.
12. Guo Y. Growth level of urban Chinese infants from birth to 2 years, body mass index Z scores' predicting model and its age trajectory in relation to maternal pre-pregnancy body weight status. 2013.
13. Ma JQ, Zhou LL, Hu YQ, Liu SS, Sheng XY. Association between feeding practices and weight status in young children. *BMC pediatrics*. 2015;15:97.
14. Gortmaker SL, Swinburn BA, Levy D, Carter R, Mabry PL, Finegood DT, et al. Changing the future of obesity: science, policy, and action. *Lancet (London, England)*. 2011;378(9793):838-47.
15. Robinson SM, Crozier SR, Harvey NC, Barton BD, Law CM, Godfrey KM, et al. Modifiable early-life risk factors for childhood adiposity and overweight: an analysis of their combined impact and potential for prevention. *The American journal of clinical nutrition*. 2015;101(2):368-75.
16. Kolsgaard ML, Joner G, Brunborg C, Anderssen SA, Tonstad S, Andersen LF. Reduction in BMI z-score and improvement in cardiometabolic risk factors in obese children and adolescents. *The Oslo Adiposity*

- 1
2
3 Intervention Study - a hospital/public health nurse combined treatment. BMC pediatrics. 2011;11:47.
- 4 17. Sijtsma A, Bocca G, L'Abée C, Liem ET, Sauer PJ, Corpeleijn E. Waist-to-height ratio, waist
5 circumference and BMI as indicators of percentage fat mass and cardiometabolic risk factors in children
6 aged 3-7 years. Clinical nutrition (Edinburgh, Scotland). 2014;33(2):311-5.
- 7 18. Aris IM, Bernard JY, Chen LW, Tint MT, Pang WW, Lim WY, et al. Infant body mass index peak and early
8 childhood cardio-metabolic risk markers in a multi-ethnic Asian birth cohort. International journal of
9 epidemiology. 2016.
- 10 19. Roy SM, Chesi A, Mentch F, Xiao R, Chiavacci R, Mitchell JA, et al. Body mass index (BMI) trajectories
11 in infancy differ by population ancestry and may presage disparities in early childhood obesity. The
12 Journal of clinical endocrinology and metabolism. 2015;100(4):1551-60.
- 13 20. Silverwood RJ, De Stavola BL, Cole TJ, Leon DA. BMI peak in infancy as a predictor for later BMI in the
14 Uppsala Family Study. International journal of obesity (2005). 2009;33(8):929-37.
- 15 21. Jensen SM, Ritz C, Ejlerskov KT, Molgaard C, Michaelsen KF. Infant BMI peak, breastfeeding, and body
16 composition at age 3 y. The American journal of clinical nutrition. 2015;101(2):319-25.
- 17 22. WHO Multicentre Growth Reference Study Group. WHO Child Growth Standards:
18 Length/height-for-age, Weight-for-age, Weight-for-length, Weight-for-height, and Body Mass
19 Index-for-age: Methods and Development. Geneva:World Health Organization,2006. Available from:
20 <http://www.who.int/childgrowth/standards/en/>. 2006.
- 21 23. Wen X, Kleinman K, Gillman MW, Rifas-Shiman SL, Taveras EM. Childhood body mass index
22 trajectories: modeling, characterizing, pairwise correlations and socio-demographic predictors of
23 trajectory characteristics. BMC medical research methodology. 2012;12:38.
- 24 24. Chivers P, Hands B, Parker H, Bulsara M, Beilin LJ, Kendall GE, et al. Body mass index, adiposity
25 rebound and early feeding in a longitudinal cohort (Raine Study). International journal of obesity (2005).
26 2010;34(7):1169-76.
- 27 25. Johnson W, Choh AC, Lee M, Towne B, Czerwinski SA, Demerath EW. Characterization of the infant
28 BMI peak: sex differences, birth year cohort effects, association with concurrent adiposity, and heritability.
29 American journal of human biology : the official journal of the Human Biology Council.
30 2013;25(3):378-88.
- 31 26. Giles LC, Whitrow MJ, Davies MJ, Davies CE, Rumbold AR, Moore VM. Growth trajectories in early
32 childhood, their relationship with antenatal and postnatal factors, and development of obesity by age 9
33 years: results from an Australian birth cohort study. International journal of obesity (2005).
34 2015;39(7):1049-56.
- 35 27. Sovio U, Kaakinen M, Tzoulaki I, Das S, Ruokonen A, Pouta A, et al. How do changes in body mass
36 index in infancy and childhood associate with cardiometabolic profile in adulthood? Findings from the
37 Northern Finland Birth Cohort 1966 Study. International journal of obesity (2005). 2014;38(1):53-9.
- 38 28. Fenton TR, Nasser R, Eliasziw M, Kim JH, Bilan D, Sauve R. Validating the weight gain of preterm
39 infants between the reference growth curve of the fetus and the term infant. BMC pediatrics. 2013;13:92.
- 40 29. WHO. Anthro for personal computers, version 3. Software for assessing growth and development of
41 the world's children. Geneva: WHO,2009. Available from: <http://www.who.int/childgrowth/software/en/>.
42 2009.
- 43 30. Villar J, Cheikh Ismail L, Victora CG, Ohuma EO, Bertino E, Altman DG, et al. International standards
44 for newborn weight, length, and head circumference by gestational age and sex: the Newborn
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 Cross-Sectional Study of the INTERGROWTH-21st Project. *Lancet* (London, England).
4 2014;384(9946):857-68.

5
6 31. Zhang YX, Wang SR. Rural-urban comparison in prevalence of overweight and obesity among
7 adolescents in Shandong, China. *Annals of human biology*. 2013;40(3):294-7.

8
9 32. Taveras EM, Rifas-Shiman SL, Belfort MB, Kleinman KP, Oken E, Gillman MW. Weight status in the first
10 6 months of life and obesity at 3 years of age. *Pediatrics*. 2009;123(4):1177-83.

11
12 33. Guo B, Mei H, Yang S, Zhang J. [Prenatal factors associated with high BMI status of infants and
13 toddlers]. *Zhonghua er ke za zhi = Chinese journal of pediatrics*. 2014;52(6):464-7.

14
15 34. Taveras EM, Gillman MW, Kleinman K, Rich-Edwards JW, Rifas-Shiman SL. Racial/ethnic differences
16 in early-life risk factors for childhood obesity. *Pediatrics*. 2010;125(4):686-95.

17
18 35. Taveras EM, Gillman MW, Kleinman KP, Rich-Edwards JW, Rifas-Shiman SL. Reducing racial/ethnic
19 disparities in childhood obesity: the role of early life risk factors. *JAMA pediatrics*. 2013;167(8):731-8.

20
21 36. Zilanawala A, Davis-Kean P, Nazroo J, Sacker A, Simonton S, Kelly Y. Race/ethnic disparities in early
22 childhood BMI, obesity and overweight in the United Kingdom and United States. *International journal of
23 obesity (2005)*. 2015;39(3):520-9.

Table 1 Participants' characteristics by subjects with "estimable"* and "inestimable"# BMI peak

Characteristics	n	Estimable*, n (%)	Inestimable#, n (%)
Total number	2268	2073	195
Gender			
Male	1126	1022 (49.3)	104 (53.3)
Female	1142	1051 (50.7)	91 (46.7)
Birth weight			
1.5 to <2.5kg	35	30 (1.4)	5 (2.6)
2.5 to <4.0kg	2073	1905 (91.9)	168 (86.2)
≥4kg	160	138 (6.7)^a	22 (11.3)
Delivery mode			
Vaginal birth	1086	989 (47.7)	97 (49.7)
Cesarean section	1182	1084 (52.3)	98 (50.3)
Maternal Age			
>35y	176	159 (7.7)	17 (8.7)
≤35y	2092	1914 (92.3)	178 (91.3)
Total number with data at age 2y	1949	1790 (86.3)	159 (81.5)
Total number of overweight and obese at age 2y	332	313 (17.5)	19 (11.9)
Total number of obese at age 2y	44	43 (2.4)	1 (0.6)

a.P<0.05

*Estimable: fit and identifiable BMI peak within 14–408 days of life.

Inestimable: Not fit and identifiable.

Chi-square tests were used to examine the differences between Estimable or Inestimable group.

Table 2 Infant characteristics in relation to infant BMI peak trajectories

		Magnitude(kg/m ²), Mean (95% CI)	Age(months), Mean (95% CI)	Pre-peak velocities(kg/m ² /month) Mean (95% CI)
Total	n=2073	18.33(18.26-18.39)	7.61(7.55-7.67)	0.43(0.42-0.44)
Gender				
	male (n=1022)	18.60(18.21-18.69)^a	7.54(7.46-7.63)^b	0.42(0.41-0.43)
	female (n=1051)	18.07(17.98-18.16)	7.67(7.59-7.76)	0.43(0.42-0.44)
Birth Weight				
	1.5 to <2.5kg(n=30)	17.63(17.13-18.13)	8.13(7.56-8.70)	0.44(0.35-0.53)
	2.5 to <4.0kg(n=1905)	18.27(18.21-18.34)	7.63(7.57-7.70)	0.43(0.42-0.44)
	>=4kg(n=138)	19.25(18.97-19.52)^b	7.11(6.88-7.34)^a	0.39(0.35-0.42)
Delivery Mode				
	Vaginal birth (n=989)	18.24(18.14-18.34)	7.64(7.56-7.73)	0.43(0.42-0.44)
	Cesarean section (n=1084)	18.41(18.32-18.50)^a	7.58(7.49-7.66)	0.43(0.42-0.44)
Maternal Age				
	>35y(n=159)	18.42(18.18-18.66)	7.61(7.49-7.82)	0.44(0.41-0.48)
	<=35y(n=1914)	18.32(18.25-18.39)	7.61(7.55-7.67)	0.42(0.41-0.43)

a.P<0.001 b.P<0.05

The analysis includes only infants who had BMI peak within 0-408 days and whose BMI trajectories were estimable by the quadratic model.

Bivariate comparison was performed using one-way ANOVA with post hoc Bonferroni multiple comparison test.

Table 3 Association between BMI peak characteristics and overweight and obesity at age 2 years

	Overweight at 2y (n=1790)		Obesity at 2y (n=1790)	
	Model containing infant BMI trajectory characteristics alone	Initial model plus all independent variables	Model containing infant BMI trajectory characteristics alone	Initial model plus all independent variables
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Magnitude(kg/m ²)	2.94(2.54-3.40)^a	3.11(2.64-3.66)^a	2.76(2.11-3.60)^a	2.69(2.00-3.61)^a
Age (months)	1.36(1.23-1.51)^a	1.35(1.21-1.50)^a	1.33(1.08-1.65)^b	1.35(1.08-1.68)^b
Pre-peak velocities(kg/m ² /month)	0.17(0.07-0.40)^a	0.14(0.06-0.34)^a	0.10(0.02-0.56)^b	0.12(0.02-0.74)^c
male(vs female)		0.67(0.49-0.90)^b		0.99(0.51-1.96)
birth weight z score.(continuous)		1.06(0.89-1.26)		1.24(0.84-1.82)
Duration of breastfeeding(continuous)		0.97(0.93-1.01)		0.92(0.84-1.01)
Duration of Sleep(continuous)		0.89(0.77-1.02)		0.89(0.63-1.24)
Cesarean section(vs Vaginal Birth)		1.08(0.81-1.44)		0.80(0.42-1.54)
Mother Age(>35y vs<=35y)		0.68(0.38-1.21)		0.74(0.21-2.59)

a.P<0.001 b.P<0.01 c.P<0.05

The analysis includes only infants who had BMI peak within 0-408 days and whose BMI trajectories were estimable by the quadratic model.

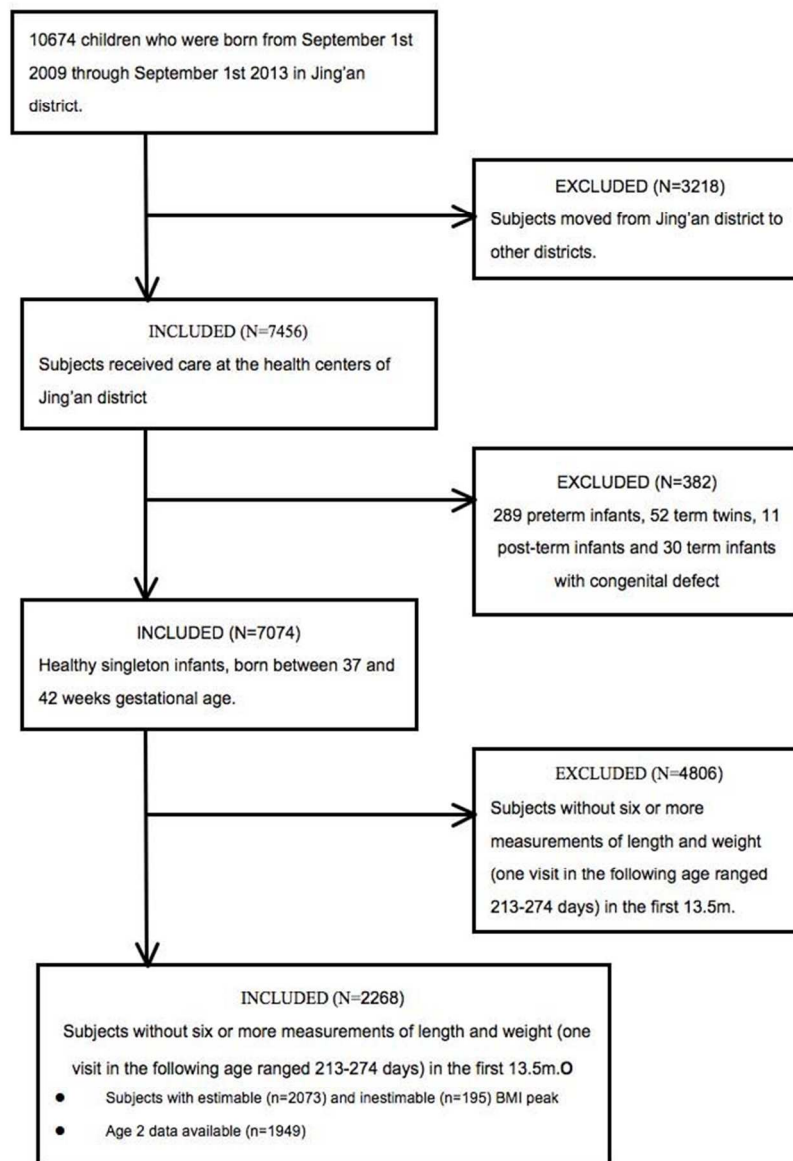


Figure1 Recruitment flow chart and study sample

64x83mm (300 x 300 DPI)

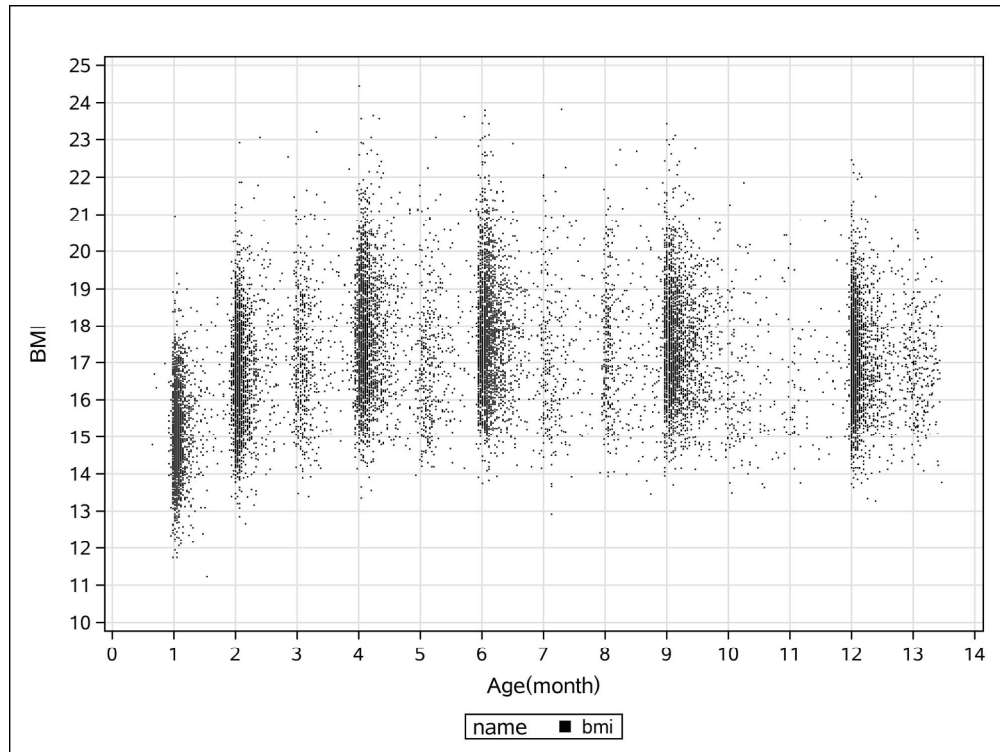


Figure 2 Plot of BMI data by age from birth to 13.5 months

169x127mm (300 x 300 DPI)

Supplemental Table 1 Characteristics of the analytic and excluded healthy singleton infants

Characteristics	n	Included, n (%)	Excluded, n (%)
Total number	7074	2268(32.1)	4806(67.9)
Gender			
Male	3468	1126 (49.6)	2342 (48.7)
Female	3606	1142(50.4)	2464 (51.3)
Birth weight			
<4.0kg	6609	2108(92.9)	4501 (93.7)
≥4kg	465	160 (7.1)	305(6.3)
Maternal Age			
>35y	570	176 (7.8)	394 (8.2)
≤35y	6504	2092(92.2)	4412(91.8)
Total number with data at age 2y	1949	1949 (85.9)^a	2282 (47.4)
Total number of overweight and obese at age 2y	751	330 (16.9)	421 (18.4)
Total number of obese at age 2y	99	44 (2.3)	55(2.4)

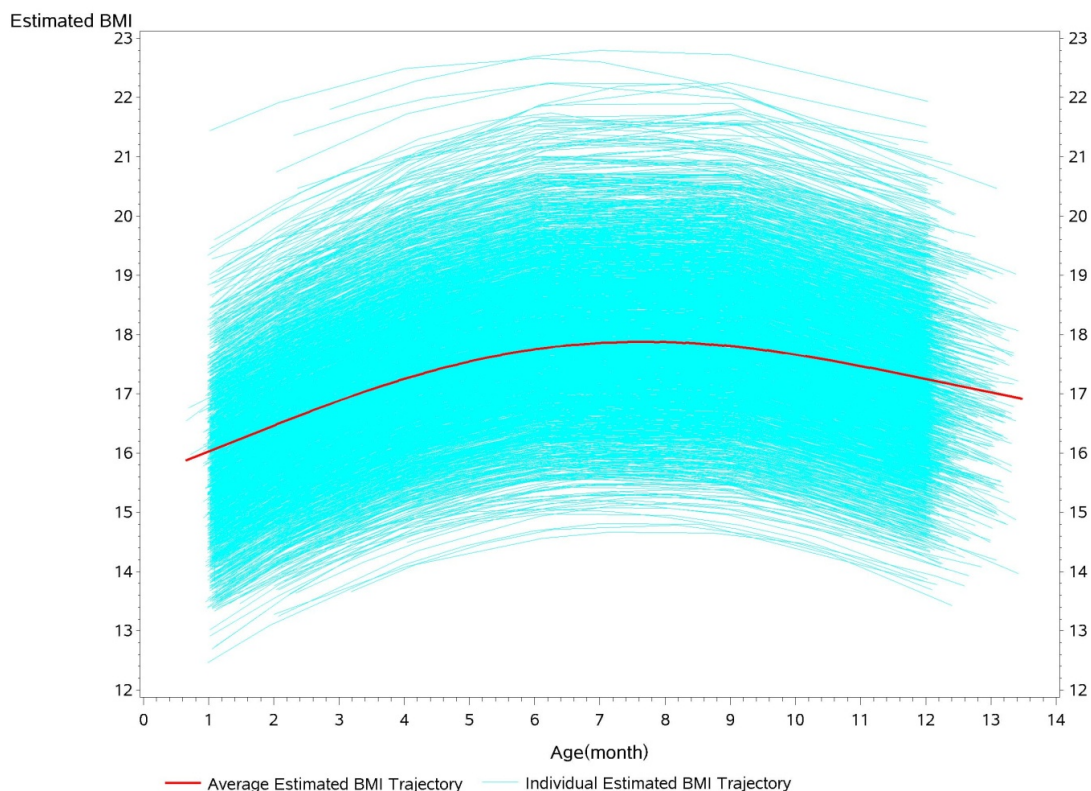
a.P<0.05

Chi-square tests were used to examine the differences between included or excluded group.

Supplemental Table 2: Correlation matrix of infancy BMI characteristics

	Age of BMI Peak, mo	Pre-peak velocities, kg/m ² /mo
Magnitude of BMI peak, kg/m ²	0.03	0.654**
Age of BMI Peak, mo		0.09**

Significance is noted as: ** p ≤ 0.01.



Supplemental Figure1 Infant Estimated BMI trajectory by polynomial regression model

Only

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any pre-specified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-4, Figure 1
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-8
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	6, Figure 1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	8-9
		(b) Describe any methods used to examine subgroups and interactions	8
		(c) Explain how missing data were addressed	6
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed	6

		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	
		(e) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Figure 1
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1, Supplemental Table 1
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	5
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	8
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 3
		(b) Report category boundaries when continuous variables were categorized	8
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.

For peer review only