Maternal Age of Menarche and Blood Pressure in Adolescence: Evidence from Hong Kong’s “Children of 1997” Birth Cohort

Tsz Chun Lai¹, Gabriel Matthew Leung¹, C. Mary Schooling¹,²*

¹ School of Public Health, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR, People’s Republic of China, ² City University of New York, School of Public Health and Hunter College, New York, New York, United States of America

* cms1@hku.hk

Abstract

Background

Age of puberty has declined substantially in developed settings and is now declining in the rest of the world with economic development. Early age of puberty is associated with non-communicable diseases in adulthood, and may be a long-term driver of population health with effects over generations. In a non-Western setting, we examined the association of maternal age of menarche with blood pressure in late childhood/adolescence.

Methods

We used generalised estimating equations to estimate the adjusted association of maternal age of menarche with age-, sex- and height-adjusted blood pressure z-score from 10 to 16 years in Hong Kong’s population-representative birth cohort, “Children of 1997” (n = 8327). We also assessed whether associations were mediated by body mass index (BMI) or pubertal stage.

Results

Earlier maternal age of menarche was associated with higher systolic blood pressure in adolescence [-0.02 z-score per year older maternal age of menarche, 95% confidence interval (CI) -0.04 to -0.003]. The association of maternal age of menarche with systolic blood pressure was mediated by adiposity and/or pubertal stage at 11 years. Maternal age of menarche was not associated with diastolic blood pressure.

Conclusion

Earlier maternal age of puberty was associated with higher systolic blood pressure, largely mediated by adiposity, highlighting the importance of tackling childhood obesity as a public health priority in view of the secular trend of declining age of puberty.
Introduction

There is a secular trend of decreasing age of onset of puberty globally, which may be stabilising in long-term developed settings but is more marked in rapidly developing settings [1]. Earlier age of puberty, within one generation, is consistently associated with chronic diseases in later life, including the metabolic syndrome [2], atherosclerosis [3], breast cancer [4] and testicular cancer [5], as well as cardiovascular disease risk factors, such as high blood pressure, in childhood and adolescence [3, 6, 7]. Hypertension is a major contributor to the global burden of disease [8], because of its role in cardiovascular disease. Blood pressure tracks from early life [9]. Drivers of blood pressure in children and adolescents may be intervention targets as well as providing etiologic insight concerning targets for cardiovascular disease prevention. Obesity, which may also have an early-life origin [10] and be partially driven by the secular trend of declining age of puberty [5], is a key driver of blood pressure [11, 12].

Whether associations of earlier puberty with non-communicable diseases are limited to one generation, or extend across generations has seldom been examined. All previous studies have found earlier maternal age of menarche associated with higher body mass index (BMI) in childhood [13–16]. A small study found a positive association of maternal age of menarche with systolic blood pressure in girls after 12 years of age [17]. To address this question more fully, we took advantage of a population-representative birth cohort, “Children of 1997”, from the developed non-Western setting of Hong Kong to assess the association of maternal age of menarche, i.e., age of first menstruation, with blood pressure. Given, earlier maternal age of menarche, was associated with higher BMI, in our cohort [16] as well as in other studies [13–15], we also assessed mediation by BMI, and in a complementary analysis mediation by pubertal stage.

Materials and Methods

Source of data

“Children of 1997” is a population-representative Chinese birth cohort (n = 8327) in Hong Kong, which has been described in detail elsewhere [18]. The study was initially established to investigate the impact of second-hand smoke exposure on infant health [19]. It covered 88% of all births from 1 April to 31 May 1997. Participants were recruited during their first post-natal visit to one of the 49 Maternal and Child Health Centres (MCHCs) in Hong Kong, where parents of all new-borns are encouraged to bring their infants for free post-natal check-ups and vaccinations until they are 5 years of age. Baseline information, including parental education, some information about parental migration status and birth characteristics (birth-weight, sex, gestational age), was collected using a self-administered questionnaire. Passive follow-up via record linkage was instituted in 2005 [18] to obtain (1) weight and height from birth to 5 years from the MCHCs (96% success); (2) annual measurements of weight and height (grade 1 onwards) and blood pressure (grade 5 onwards) from the Student Health Service, Department of Health, which provides free annual check-ups for all school students; and (3) death records from the Death Registry. In July 2008, Survey I, which focused on family history, including maternal age of menarche, was sent to the families. Additional postal surveys were conducted in 2010–2. Any missing data and discrepancies were reconciled between each wave of data collection.

Maternal age of menarche

Maternal age of menarche, which was ascertained at mothers’ age ranging from 26 to 59 years, was collected in Survey I. It was originally recorded in 10 categories in complete years: ≤9, 10,
11, 12, 13, 14, 15, 16, 17 and ≥18. To be consistent with previous similar studies [13, 14] and our previous study [16], it was re-categorised into 5 categories: ≤11, 12, 13, 14 and ≥15 years.

Blood pressure

The outcomes were all measurements of systolic and diastolic blood pressure (SBP and DBP), usually measured every two years from ages 10 to 16 years. Blood pressure was measured on the right arm in a seated position after at least 10 minutes of rest with an age and size appropriate cuff size using a DINAMAP [20]. For systolic and/or diastolic blood pressure higher than 90th percentile for age, blood pressure was measured for a second time after at least 15 minutes of resting using a sphygmomanometer manually; the second reading was recorded. All measurements of SBP and DBP were considered as sex- age- and height-specific z-scores relative to the United States National High Blood Pressure Education Group reference in 2004 [21, 22], to ensure that any associations were not due to differences in these factors between participants.

Statistical analysis

We compared baseline characteristics by maternal age of menarche using $\chi^2$ tests. Adjusted associations of maternal age of menarche with blood pressure z-score in adolescence were estimated from generalised estimating equations (GEE) to account for correlation between blood pressure measurements of the same participant [23, 24]. We assessed whether the associations varied by maternal birthplace or sex from the heterogeneity across strata and the significance of the interaction terms (on an additive scale). Maternal age of menarche was also considered as continuous in years to assess the linear trend in order to avoid any bias from misclassification in groups [25].

Models were built sequentially to assess the role of confounding. Confounders were selected as likely common causes of maternal age of menarche and blood pressure [26]. Model 1 assessed the unadjusted association of maternal age of menarche with blood pressure z-score. Model 2 was adjusted for maternal education, household income, highest parental occupation, maternal age, maternal birthplace, sex and age at measurement. BMI and pubertal stage were considered as mediators rather than confounders because they are more likely factors on the pathway from maternal age of menarche to blood pressure at age 10 to 16 years than causes of maternal age of menarche. We assessed mediation by BMI z-score and Tanner stage at 11 years, which was clinically measured by doctors at the Student Health Service clinics, using Pearl’s mediation formula [27] from which we reported direct and indirect effects and the proportion mediated. We used the mediation package (version 4.4.5) in R for this analysis with 5000 bootstrap resamples to obtain 95% CIs. We assessed whether the association of maternal age of menarche and blood pressure at 11 years was mediated by BMI z-score or Tanner stage at 11 years using multivariable linear regression. The association of maternal age of menarche with blood pressure did not vary by BMI z-score at 11 years (p value for SBP = 0.66; p for DBP = 0.98) or Tanner stage at 11 years (p for SBP = 0.15; p for DBP = 0.33).

Given that our birth cohort is population-representative and has comprehensive baseline data concerning the participants’ and families’ characteristics, we used a combination of inverse probability weighting and multiple imputation to handle missing data [28]. Different missingness models were built, based on SEP, maternal age, parity, breastfeeding, sex and MCHC clinic, and the one with lowest Akaike information criterion was chosen. Inverse probability weights were then estimated from this model using logistic regression, to account for potential differences between those who provided maternal age of menarche in Survey I and those who did not. Missing values of factors in the missingness models were multiply imputed 10 times to ensure the sample size was not reduced. We used inverse probability weights in the
analyses. We also performed an available case analysis as a sensitivity analysis, i.e. deleting cases with missing data on variables on an analysis-by-analysis basis, for comparison. We also performed the analysis with blood pressure in mmHg and internally generated blood pressure z-scores to ensure that the choice of reference population was not biasing our results. Data were analysed using Stata version 13 (Stata Corp., College station, TX USA) and R version 3.3.0 (R Development Core Team, Vienna, Austria).

Ethics statement
Since our participants are children, informed consent was obtained from the parents, next of kin, caretakers or guardians (informants) on behalf of the participants by completing the questionnaire at enrolment as approved by The University of Hong Kong Medical Faculty Ethics Committee. Informed written consent for Survey I was obtained from a parent or guardian. Ethical approval for further studies was obtained from the University of Hong Kong-Hospital Authority Hong Kong West Cluster, Joint Institutional Review Board and/or the Ethics Committee of the Department of Health, Government of the Hong Kong SAR as appropriate.

Results
Of the original 8327 participants, as of 7th January 2016, 29 had permanently withdrawn. At the time of survey I (2008–09), 26 participants had permanently withdrawn, and 365 were not contactable, giving 7936 potential respondents to Survey I. Among them, 3679 responded and 3180 provided maternal age of menarche, of whom 7 were excluded for giving an invalid response. Among these 3172, after excluding another permanent withdrawal, 515 (16.2%) had maternal age of menarche of ≤11 years, 848 (26.7%) 12 years, 788 (24.8%) 13 years, 495 (15.6%) 14 years, and 526 (16.6%) ≥15 years. Most of the participants (85.7%) had at least one blood pressure measurement from 10 to 16 years. On average there were 1.97 measurements from ages 10 to 16 years for each participant.

Table 1 shows that earlier maternal age of menarche was associated with higher education, higher household income and higher parental occupation. Mothers who were born in the rest of China or elsewhere had later age of menarche. Maternal age of menarche was not associated with maternal age.

The association of maternal age of menarche with blood pressure did not vary by sex (p for SBP = 0.48; p for DBP = 0.43) or maternal birthplace (p for SBP = 0.89, p for DBP = 0.92). Table 2 shows that younger maternal age of menarche was not associated with SBP in Model 1. However, after adjustment for maternal education, household income, highest parental occupation, maternal age, maternal birthplace, sex and age at measurement (Model 2) younger maternal age of menarche was associated with higher SBP. Maternal age of menarche was not associated with DBP at puberty in any model. The association of maternal age of menarche with SBP was partially mediated by BMI z-score at 11 years (63.3%) or by Tanner stage at 11 years (41.8%) (Table 3).

Sensitivity analyses using blood pressure in mmHg gave similar results (S1 Table), with younger maternal age of menarche associated with higher SBP (Model 2) but not with DBP. Results were also similar using internally generated blood pressure z-score (S2 Table) and in available case analysis (S3 Table). An available case analysis using blood pressure in mmHg also showed that older maternal age of menarche was associated with lower SBP, but was not associated with DBP (S4 Table).

Discussion
In this large, prospective, population-representative birth cohort from an under-studied non-Western setting, we found a graded association of maternal age of menarche with SBP in late adolescence.
childhood/adolescence, which was largely explained by adiposity and/or earlier pubertal timing. Maternal age of menarche was not associated with DBP. Our study adds by demonstrating an inter-generational association of earlier puberty with blood pressure, possibly partially driven by the association of earlier maternal age of menarche with greater adiposity and/or with earlier pubertal timing.

In this population-representative study, blood pressure and anthropometric measurements were taken regularly by trained nurses. Nonetheless our study has several limitations. First, maternal age of menarche was self-reported. Age of menarche is a watershed event with good recall years later [29]. Non-differential recall error usually biases towards the null. Second, we have missing data on exposures and some confounders. We used a combination of inverse probability weighting and multiple imputation to handle the missing data, because it is more difficult to fulfil the assumptions required for available case analysis than analysis of imputed data. The combination of inverse probability weighting and multiple imputation allowed us to capitalise on the data we have and increased efficiency [28]. Third, children with lower SEP were less likely to be followed up. However, we included parental education in the inverse

| Characteristics                  | n   | ≤11 (n = 515) | 12 (n = 848) | 13 (n = 788) | 14 (n = 495) | ≥15 (n = 526) | p-value |
|----------------------------------|-----|--------------|--------------|--------------|--------------|--------------|---------|
| Child’s sex                      |     |              |              |              |              |              | 0.19    |
| Girl                             | 1711| 54.8         | 53.1         | 54.2         | 50.1         | 57.6         |         |
| Boy                              | 1462| 45.2         | 46.9         | 45.8         | 49.9         | 42.4         |         |
| Maternal education               |     |              |              |              |              |              | <0.001  |
| Grade 9 or below                 | 1195| 28.0         | 28.4         | 32.9         | 43.4         | 64.1         |         |
| Grade 10–11                      | 1443| 54.4         | 51.4         | 49.0         | 40.0         | 27.1         |         |
| Grade 12 or above                | 533 | 17.7         | 20.2         | 18.2         | 16.6         | 8.8          |         |
| Household income per head at birth in quintiles (mean ± SD) |     |              |              |              |              |              | <0.001  |
| 1st quintile (HK$ 1751 ± 413)    | 505 | 11.3         | 12.9         | 14.9         | 20.7         | 34.8         |         |
| 2nd quintile (HK$ 2856 ± 325)    | 538 | 15.6         | 14.6         | 17.3         | 22.1         | 29.8         |         |
| 3rd quintile (HK$ 4362 ± 556)    | 555 | 21.5         | 19.0         | 21.5         | 18.9         | 17.3         |         |
| 4th quintile (HK$ 6822 ± 886)    | 610 | 26.5         | 25.9         | 23.2         | 19.6         | 9.3          |         |
| 5th quintile (HK$ 14850 ± 16050) | 610 | 25.2         | 27.6         | 23.1         | 18.9         | 8.9          |         |
| Highest parental occupation at birth |     |              |              |              |              |              | <0.001  |
| I (professional)                 | 752 | 30.8         | 33.2         | 28.4         | 22.4         | 15.2         |         |
| II (managerial)                  | 413 | 16.8         | 15.4         | 15.2         | 14.2         | 12.2         |         |
| III (nonmanual skilled)          | 812 | 29.9         | 29.6         | 29.4         | 32.6         | 24.7         |         |
| IIIM (manual skilled)            | 444 | 10.9         | 12.1         | 15.2         | 17.5         | 27.9         |         |
| IV (semi-skilled)                | 275 | 9.2          | 8.4          | 9.6          | 9.9          | 13.8         |         |
| V (unskilled)                    | 78  | 2.4          | 1.2          | 2.3          | 3.5          | 6.1          |         |
| Maternal birthplace              |     |              |              |              |              |              | <0.001  |
| Rest of China or elsewhere       | 1205| 21.6         | 24.2         | 35.3         | 45.2         | 74.3         |         |
| Hong Kong                        | 1958| 78.4         | 75.8         | 64.7         | 54.8         | 25.7         |         |
| Maternal age at birth            |     |              |              |              |              |              | 0.06    |
| ≤24 years                        | 294 | 12.2         | 9.2          | 7.9          | 7.5          | 10.3         |         |
| 25–29 years                      | 980 | 30.3         | 28.5         | 29.7         | 33.9         | 34.4         |         |
| 30–34 years                      | 1269| 36.9         | 42.0         | 42.0         | 40.6         | 36.5         |         |
| ≥35 years                        | 627 | 20.6         | 20.3         | 20.4         | 18.0         | 18.7         |         |

*Numbers may not add up to 100% due to rounding*
probability weights. Fourth, blood pressure was measured with oscillometric devices, or rechecked by sphygmomanometer if the reading exceeded the 90th percentile. Oscillometric devices have slight differences from the gold standard mercury sphygmomanometer [30, 31]. However our analysis is unlikely to be biased differentially by these differences. Fifth, a reference population from the US was chosen for converting blood pressure into z-scores, since there is no published reference for Hong Kong adolescents. The choice of reference population is unlikely to affect the internal comparisons made here, results using internally generated z-scores were similar (S2 Table).

Despite the associations of earlier puberty with many chronic diseases, associations with blood pressure have been inconsistent across settings [32]. For instance, two previous studies, one from the US [33] and the other from China [34], found age of menarche was not associated with blood pressure in later life. In a British cohort, the association was only evident in men [35]. Where an association of earlier puberty with blood pressure was observed, adiposity did not fully explain the association in adolescence [3, 36] or mid-life [2, 37]. However, in the present study, the intergenerational association of earlier puberty with higher blood pressure in

### Table 2. Adjusted association of maternal age of menarche with blood pressure z-score (with reference to CDC Growth Chart) in adolescence (from 10 to 16 years) in the “Children of 1997” Birth Cohort from Hong Kong.

| Maternal age of menarche (years) | ≤11  | 12  | 13  | 14  | >15 | Model n | β    | 95%CI   | β    | 95%CI   | β    | 95%CI   | β    | 95%CI   | β for trend | 95%CI |
|---------------------------------|------|-----|-----|-----|-----|---------|------|---------|------|---------|------|---------|------|---------|-------------|------|
| Systolic blood pressure        |      |     |     |     |     | 1 2977  | -0.05| -0.14 to 0.04 | -0.05| -0.14 to 0.05 | -0.04| -0.14 to 0.07 | -0.11| -0.22 to -0.01 | -0.01| -0.03 to 0.01 |
|                                | 2 2977 | Ref. | -0.05| -0.14 to 0.04 | -0.05| -0.15 to 0.04 | -0.07| -0.18 to 0.03 | -0.16| -0.27 to -0.05 | -0.02| -0.04 to -0.00 |
| Diastolic blood pressure       | 1 2977 | Ref. | 0.00 | -0.04 to 0.05 | 0.00 | -0.05 to 0.05 | 0.00 | -0.05 to 0.06 | 0.03 | -0.02 to 0.08 | 0.01 | -0.00 to 0.02 |
|                                | 2 2977 | Ref. | 0.00 | -0.05 to 0.05 | -0.01| -0.06 to 0.04 | -0.02| -0.07 to 0.03 | -0.01| -0.07 to 0.05 | -0.00| -0.01 to 0.01 |

Model 1 is the crude model. Model 2 adjusted for maternal age, maternal education, maternal birthplace, highest parental occupation, household income, sex and age at measurement. β-coefficients represent the change in blood pressure z-score (1-unit change in SBP z-score is approximately 10.6 mm Hg and 1-unit change in DBP z-score is approximately 11.3 mm Hg).

doi:10.1371/journal.pone.0159855.t002

### Table 3. Total, direct, and indirect effects of maternal age of menarche and 95% CI on systolic and diastolic blood pressure z-score at 11 years with the proportion mediated by BMI z-score and Tanner stage at 11 years.

#### Mediation by BMI z-score

| Total effect | Direct effect | Indirect effect | Proportion mediated |
|--------------|---------------|----------------|-------------------|
| Systolic blood pressure | -0.012 | -0.005 | -0.008 | 0.633 |
| Diastolic blood pressure | 0.000 | -0.001 | 0.000 | N/A |

#### Mediation by Tanner stage

| Total effect | Direct effect | Indirect effect | Proportion mediated |
|--------------|---------------|----------------|-------------------|
| Systolic blood pressure | -0.012 | -0.007 | -0.005 | 0.418 |
| Diastolic blood pressure | -0.001 | -0.001 | 0.000 | N/A |

Models adjusted for maternal age, maternal education, maternal birthplace, highest parental occupation, household income, sex and age at measurement.

doi:10.1371/journal.pone.0159855.t003
adolescence was partially mediated by adiposity and/or pubertal stage. Differences in intergenerational associations for blood pressure and adiposity suggest that blood pressure and adiposity have to some extent different drivers. As such, declining age of puberty over generations [38] might drive obesity more than blood pressure. However, an association could emerge in adulthood. A previous small study found maternal age of menarche associated with higher SBP only in a subset of girls, which might be a chance finding on stratification [17], however, the study is too small to be definitive. To our knowledge, this is the first study investigating intergenerational associations of timing of puberty with blood pressure outside a Western setting, as well as assessing the mediating role of adiposity. At a general level our findings are consistent with the disassociation of secular trends in obesity and blood pressure [39, 40], because maternal pubertal timing might be more relevant to childhood obesity than blood pressure. A secular trend of increasing obesity without a parallel trend in blood pressure has occurred in Western settings for adults [41] and children [40, 42], and also in Asia [43] and other rapidly developing settings [44].

Our finding that an association of earlier maternal age of menarche with higher systolic blood pressure was partially mediated by BMI could indicate that maternal age of menarche operates largely by a mechanism that affects obesity but does not extend to blood pressure. This pattern of associations could have arisen for a number of reasons. First, as well as the association of earlier menarche with cardiovascular risk, obesity also appears to promote earlier puberty [45], whilst blood pressure does not, making a relation of maternal age of menarche with blood pressure less likely. Shared genetic architecture could drive both age of menarche and obesity, but not blood pressure. Genome-wide association studies (GWAS) show common genetic variants, including ADCY3-PDMC and PXMP3, [46] drive both age of menarche and adiposity. In contrast, a shared genetic basis for timing of puberty and blood pressure has not yet been found, although GWAS has to date has only explained a small percentage of the variance in blood pressure (<1%), for reasons that are unclear [47]. Finally, we assessed blood pressure in late childhood and early adolescence. The factors underlying the relation of maternal age of menarche with offspring characteristics may have greater impact at a stage when the drivers of growth affect adiposity more than blood pressure. Alternatively, earlier maternal age of menarche may be associated with a lifestyle that protects more against high blood pressure than obesity, for example a plentiful but low salt diet.

**Conclusions**

In a recently developed, non-Western setting, earlier maternal age of menarche was associated with higher systolic blood pressure in late childhood/adolescence, but the association was partially explained by adiposity and/or earlier pubertal timing, suggesting that the association of falling age of menarche with blood pressure, or possibly other non-communicable diseases in adulthood, might be partially driven by adiposity. Our study highlights the importance of tackling childhood obesity as a public health strategy to reduce population cardiovascular risk.

**Supporting Information**

S1 Table. Adjusted association of maternal age of menarche with blood pressure in adolescence (from 10 to 16 years) in the “Children of 1997” Birth Cohort from Hong Kong.

S2 Table. Adjusted association of maternal age of menarche with internal blood pressure z-score in adolescence (from 10 to 16 years) in the “Children of 1997” Birth Cohort from Hong Kong.
S3 Table. Adjusted association of maternal age of menarche with blood pressure z-score (with reference to CDC Growth Chart) in adolescence (from 10 to 16 years) in the “Children of 1997” Birth Cohort from Hong Kong (complete case analysis).

(DoCX)

S4 Table. Adjusted association of maternal age of menarche with blood pressure in adolescence (from 10 to 16 years) in the “Children of 1997” Birth Cohort from Hong Kong (complete case analysis).

(AcCX)

Acknowledgments
The authors thank colleagues at the Student Health Service and Family Health Service of the Department of Health for their assistance and collaboration.

Author Contributions
Conceived and designed the experiments: TCL GML CMS. Analyzed the data: TCL. Wrote the paper: TCL CMS. Critically appraise and revised the contents of the manuscript: TCL GML CMS.

References
1. Karlberg J. Secular trends in pubertal development. Hormone research. 2002; 57 Suppl 2:19–30. Epub 2002/06/18. doi: 10.1097/0b013e3181567a2d. PMID:12065922.
2. Heys M, Schooling CM, Jiang C, Cowling B, Lao X, Zhang W, et al. Age of menarche and the metabolic syndrome in China. Epidemiology. 2007; 18(6):746–9. Epub 2007/10/06. doi: 10.1097/EDE.0b013e3181567a1f. PMID: 17917601.
3. Remsberg KE, Demerath EW, Schubert CM, Chumlea WC, Sun SS, Siervogel RM. Early Menarche and the Development of Cardiovascular Disease Risk Factors in Adolescent Girls: The Fels Longitudinal Study. Journal of Clinical Endocrinology & Metabolism. 2005; 90(5):2718–24. doi: 10.1210/jc.2004-1991.
4. Ritte R, Lukanova A, Tjonneland A, Olsen A, Overvad K, Mersiie S, et al. Height, age at menarche and risk of hormone receptor-positive and -negative breast cancer: a cohort study. International journal of cancer. 2013; 132(11):2619–29. Epub 2012/10/24. doi: 10.1002/int.27913. PMID: 23090881.
5. Golub MS, Collman GW, Foster PM, Kimmel WC, Reiter EO, et al. Public health implications of altered puberty timing. Pediatrics. 2008; 121 Suppl 3:S218–30. Epub 2008/02/15. doi: 10.1542/peds.2007-1813G. PMID: 18245514.
6. Boyne MS, Thame M, Osmond C, Fraser RA, Gabay L, Taylor-Bryan C, et al. The effect of earlier puberty on cardiometabolic risk factors in Afro-Caribbean children. Journal of pediatric endocrinology & metabolism: JPEM. 2014; 27(5–6):453–60. Epub 2014/01/29. doi: 10.1515/jpem-2013-0324. PMID: 24468602.
7. Koziel S, Kolodziej H, Ulijaszek S. Body size, fat distribution, menarcheal age and blood pressure in 14-year-old girls. European journal of epidemiology. 2001; 17(12):1111–5. Epub 2003/01/18. PMID: 12530770.
8. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012; 380(9869):2224–33. Epub 2012/12/19. doi: 10.1016/s0140-6736(12)61766-8. PMID: 23245609; PubMed Central PMCID: PMC3415651.
9. Raitakari OT, Juonala M, Kahonen M, Taittonen L, Maki-Torkko N, et al. Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study. Jama. 2003; 290(17):2277–83. Epub 2003/11/06. doi: 10.1001/jama.290.17.2277. PMID: 14601886.
10. Godfrey KM, Gluckman PD, Hanson MA. Developmental origins of metabolic disease: life course and intergenerational perspectives. Trends in endocrinology and metabolism: TEM. 2010; 21(4):199–205. Epub 2010/01/19. doi: 10.1016/j.tem.2009.12.008. PMID: 20080045.
11. Bot M, Spijkerman AM, Twisk JW, Verschuren WM. Weight change over five-year periods and number of components of the metabolic syndrome in a Dutch cohort. European journal of epidemiology. 2010; 25(2):125–33. Epub 2010/01/22. doi:10.1007/s10654-009-9419-7 PMID: 20091093; PubMed Central PMCID: PMCPMC2821620.

12. Nguyen NT, Magno CP, Lane KT, Hinojosa MW, Lane JS. Association of hypertension, diabetes, dyslipidemia, and metabolic syndrome with obesity: findings from the National Health and Nutrition Examination Survey, 1999 to 2004. Journal of the American College of Surgeons. 2008; 207(6):928–34. Epub 2009/02/03. doi:10.1016/j.jamcollsurg.2008.08.022 PMID: 19183541.

13. Basso O, Pennell ML, Chen A, Longnecker MP. Mother’s age at menarche and offspring size. International journal of obesity (2005). 2010; 34(12):1766–71. Epub 2010/06/16. doi:10.1038/ijo.2010.104 PMID: 20548308; PubMed Central PMCID: PMCPMC3005766.

14. Ong KK, Northstone K, Wells JCK, Rubin C, Ness AR, Golding J, et al. Earlier Mother’s Age at Menarche Predicts Rapid Infancy Growth and Childhood Obesity. PLoS Med. 2007; 4(4):e132. doi:10.1371/journal.pmed.0040132 PMID: 17455989

15. Min J, Li Z, Liu X, Wang Y. The association between early menarche and offspring’s obesity risk in early childhood was modified by gestational weight gain. Obesity (Silver Spring, Md). 2014; 22(1):19–23. Epub 2013/07/10. doi:10.1002/oby.20567. PMID: 23836480; PubMed Central PMCID: PMCPMC4036118.

16. Lai TC, Au Yeung SL, Lin SL, Leung GM, Schooling CM. Maternal age of menarche and adiposity: evidence from Hong Kong’s "Children of 1997" birth cohort. Epidemiology. 2016. Epub 2016/01/26. doi:10.1097/ede.0000000000000448 PMID: 26906956.

17. Jelenkovic A, Rebato E. Association of maternal menarcheal age with anthropometric dimensions and blood pressure in children from Greater Bilbao. Annals of human biology. 2015;1–8. Epub 2015/08/06. PMID: 26243478.

18. Schooling CM, Hui LL, Ho LM, Lam TH, Leung GM. Cohort profile: ‘children of 1997”: a Hong Kong Chinese birth cohort. International journal of epidemiology. 2012; 41(3):611–20. Epub 2011/01/13. doi:10.1093/ije/dys243 PMID: 21224275.

19. Lam TH, Leung GM, Ho LM. The effects of environmental tobacco smoke on health services utilization in the first eighteen months of life. Pediatrics. 2001; 107(5):E91. Epub 2001/06/05. PMID: 11389289.

20. Kwok MK, Freeman G, Lin SL, Lam TH, Schooling CM. Simulated growth trajectories and blood pressure in adolescence: Hong Kong's Chinese Birth Cohort. Journal of hypertension. 2013; 31(9):1785–97. Epub 2013/06/12. doi:10.1097/HJH.0b013e32832f62ea PMID: 23751966.

21. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics. 2004; 114(2 Suppl 4th Report):555–76. Epub 2004/08/03. PMID: 15286277.

22. Kwok MK, Au Yeung SL, Leung GM, Schooling CM. Birth weight, infant growth, and adolescent blood pressure using twin status as an instrumental variable in a Chinese birth cohort: "Children of 1997". Annals of epidemiology. 2014; 24(7):509–15. Epub 2014/05/24. doi:10.1016/j.annepidem.2014.04.005 PMID: 24854183.

23. Ballinger GA. Using Generalized Estimating Equations for Longitudinal Data Analysis. Organizational Research Methods. 2004; 7(2):127–50. doi:10.1177/1094428104263672

24. Twisk JWR. Applied longitudinal data analysis for epidemiology a practical guide. Cambridge, UK; New York: Cambridge University Press; 2003. xvi, 301 p. p.

25. Bennette C, Vickers A. Against quantiles: categorization of continuous variables in epidemiologic research, and its discontents. BMC Medical Research Methodology. 2012; 12(1):21. doi:10.1186/1471-2288-12-21

26. VanderWeele TJ, Shpitser I. A new criterion for confounder selection. Biometrics. 2011; 67(4):1406–13. Epub 2011/06/02. doi:10.1111/j.1541-0420.2011.01619.x PMID: 21627630; PubMed Central PMCID: PMCPMC3166439.

27. Pearl J. The causal mediation formula—a guide to the assessment of pathways and mechanisms. Prevention science: the official journal of the Society for Prevention Research. 2012; 13(4):426–36. Epub 2012/03/16. doi:10.1007/s11121-011-0270-y PMID: 22419385.

28. Seaman SR, White IR, Copas AJ, Li L. Combining multiple imputation and inverse-probability weighting. Biometrics. 2012; 68(1):129–37. Epub 2011/11/05. doi:10.1111/j.1541-0420.2011.01666.x PMID: 22050039; PubMed Central PMCID: PMCPMC3412287.

29. Must A, Phillips SM, Naumova EN, Blum M, Harris S, Dawson-Hughes B, et al. Recall of early menstrual history and menarcheal body size: after 30 years, how well do women remember? American journal of epidemiology. 2002; 155(7):872–9. Epub 2002/03/27. PMID: 11914195.
30. Urbina EM, Khoury PR, McCoy CE, Daniels SR, Dolan LM, Kimball TR. Comparison of mercury blood pressure readings with oscillometric and central blood pressure in predicting target organ damage in youth. Blood pressure monitoring. 2015. Epub 2015/02/04. doi: 10.1097/mbp.0000000000000110 PMID: 25647284.

31. Wong SN, Tz Sung RY, Leung LC. Validation of three oscillometric blood pressure devices against auscultatory mercury sphygmomanometer in children. Blood pressure monitoring. 2006; 11(5):81–91. Epub 2006/08/26. doi: 10.1097/01.mbp.0000209082.09623.b4 PMID: 16932037.

32. Prentice P, Viner RM. Pubertal timing and adult obesity and cardiometabolic risk in women and men: a systematic review and meta-analysis. Int J Obes. 2013; 37(8):1036–43. doi: 10.1038/ijo.2012.177

33. Frontini MG, Srinivasan SR, Berenson GS. Longitudinal changes in risk variables underlying metabolic Syndrome X from childhood to young adulthood in female subjects with a history of early menarche: the Bogalusa Heart Study. International journal of obesity and related metabolic disorders. 2003; 27(11):1398–404. Epub 2003/10/24. doi: 10.1038/sj.ijo.0802422 PMID: 14574352.

34. Qiu C, Chen H, Wen J, Zhu P, Lin F, Huang B, et al. Associations between age at menarche and menopause with cardiovascular disease, diabetes, and osteoporosis in Chinese women. The Journal of clinical endocrinology and metabolism. 2013; 98(4):1612–21. Epub 2013/03/09. doi: 10.1210/jc.2012-2919 PMID: 23471979.

35. Hardy R, Kuh D, Whincup PH, Wadsworth ME. Age at puberty and adult blood pressure and body size in a British birth cohort study. Journal of hypertension. 2006; 24(1):59–66. Epub 2005/12/07. PMID: 16331102.

36. Chen X, Wang Y. The influence of sexual maturation on blood pressure and body fatness in African-American adolescent girls and boys. American journal of human biology. 2009; 21(1):105–12. Epub 2008/10/24. doi: 10.1002/ajhb.20832 PMID: 18942713.

37. Hulanicka B, Lipowicz A, Kowalisko A. Relationship between early puberty and the risk of hypertension/overweight at age 50: evidence for a modified Barker hypothesis among Polish youth. Economics and human biology. 2007; 5(1):48–60. Epub 2007/02/13. doi: 10.1016/j.ehb.2006.12.001 PMID: 17291841.

38. Huen KF, Leung SS, Lau JT, Cheung AY, Leung NK, Chiu MC. Secular trend in the sexual maturation of southern Chinese girls. Acta paediatrica (Oslo, Norway: 1992). 1997; 86(10):1121–4. Epub 1997/11/14. PMID: 9350897.

39. Freedman DS, Goodman A, Contreras OA, DasMahapatra P, Srinivasan SR, Berenson GS. Secular trends in BMI and blood pressure among children and adolescents: the Bogalusa Heart Study. Pediatrics. 2012; 130(1):e159–66. Epub 2012/06/06. doi: 10.1542/peds.2011-3302 PMID: 22665416; PubMed Central PMCID: PMCPMC3382918.

40. Chiolero A, Bovet P, Paradis G, Paccaud F. Has blood pressure increased in children in response to the obesity epidemic? Pediatrics. 2007; 119(3):544–53. Epub 2007/03/03. doi: 10.1542/peds.2006-2136 PMID: 17332208.

41. Hulman A, Tabak AG, Nyari TA, Vistisen D, Kivimaki M, Brunner EJ, et al. Effect of secular trends on age-related trajectories of cardiovascular risk factors: the Whitehall II longitudinal study 1985–2009. International journal of epidemiology. 2014; 43(3):866–77. Epub 2014/01/28. doi: 10.1093/ije/dyt279 PMID: 24464190; PubMed Central PMCID: PMCPMC4052135.

42. Muntner P, He J, Cutler JA, Wildman RP, Whelton PK. Trends in blood pressure among children and adolescents: the Bogalusa Heart Study. Circulation. 2011; 124(4):397–404. Epub 2011/07/07. doi: 10.1161/circulationaha.110.15126439.

43. Khang YH, Lynch JW. Exploring determinants of secular decreases in childhood blood pressure and hypertension. Circulation. 2011; 124(4):397–405. Epub 2011/07/07. doi: 10.1161/circulationaha.110.014399 PMID: 21730305.

44. Chiolero A, Paradis G, Madeleine G, Hanley JA, Paccaud F, Bovet P. Discordant secular trends in elevated blood pressure and obesity in children and adolescents in a rapidly developing country. Circulation. 2009; 119(4):558–65. Epub 2009/01/21. doi: 10.1161/circulationaha.108.796276 PMID: 19153270.

45. Kaplowitz PB. Link between body fat and the timing of puberty. Pediatrics. 2008; 121 Suppl 3:S208–17. Epub 2008/02/15. doi: 10.1542/peds.2007-1813F PMID: 18245513.

46. Johnson W, Choh AC, Curran JE, Czerwinski SA, Bellis C, Dyer TD, et al. Genetic risk for earlier menarche also influences prepubertal body mass index. Am J Phys Anthropol. 2013; 150(1):10–20. Epub 2013/01/04. doi: 10.1002/ajpa.22121 PMID: 23283660; PubMed Central PMCID: PMCPMC3539227.

47. Ehret GB, Munroe PB, Rice KM, Bochud M, Johnson AD, Chasman DJ, et al. Genetic variants in novel pathways influence blood pressure and cardiovascular disease risk. Nature. 2011; 478(7367):103–9. Epub 2011/09/13. doi: 10.1038/nature10405 PMID: 21909115; PubMed Central PMCID: PMCPmc3340926.