**Associations of young and old maternal age at childbirth with childhood and adult outcomes in the offspring; prospective study in five low and middle-income countries (COHORTS collaboration)**

Brief title: Maternal age and offspring health and human capital

**Caroline HD Fall DM**, chdf@mrc.soton.ac.uk MRC Lifecourse Epidemiology Unit, University of Southampton, UK; **Harshpal Singh Sachdev MD**, hpssachdev@gmail.com Sitaram Bhartia Institute of Science and Research, New Delhi, India; **Clive Osmond PhD**, co@mrc.soton.ac.uk MRC Lifecourse Epidemiology Unit, University of Southampton, UK; **Maria Clara Restrepo-Mendez PhD**, mcrestrepo@equidade.org Universidade Federal de Pelotas, Brazil; **Cesar Victora MD**, cvictora@gmail.com Universidade Federal de Pelotas, Brazil; **Reynaldo Martorell PhD**, rmart77@emory.edu Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, USA; **Aryeh D Stein PhD**, aryeh.stein@emory.edu Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, USA; **Shikha Sinha BSc**, shikhakk2002@yahoo.co.in Sitaram Bhartia Institute of Science and Research, New Delhi, India; **Nikhil Tandon MD**, nikhil\_tandon@hotmail.com All India Institute of Medical Sciences, New Delhi, India; **Linda Adair PhD**, linda\_adair@unc.edu Department of Nutrition, University of North Carolina at Chapel Hill, USA; **Isabelita Bas MHSS**, abetbas@yahoo.com Office of Population Studies Foundation, University of San Carlos, Cebu, Philippines; **Shane Norris PhD**, san@global.co.za Medical Research Council Developmental Pathways for Health Research Unit, Witwatersrand University, Johannesburg, South Africa; **Linda M Richter PhD**, lrichter@hsrc.ac.za Human Sciences Research Council, Durban, South Africa, **and the COHORTS investigators**

Author for correspondence: Professor Caroline HD Fall, MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton General Hospital, Tremona Road, Southampton, UK SO16 6YD; Tel: +44 (0)2380 777624; Fax: +44 (0)2380 704021; E-mail: chdf@mrc.soton.ac.uk

**Word count (main text): 2999**

**ABSTRACT**

**Background:** Both young and advanced maternal age is associated with adverse birth and child outcomes. Few studies have examined these associations in low- and middle-income countries (LMICs) and none have studied adult outcomes in the offspring.

**Methods:** Pooled data from five birth cohorts (total N=19,403) in Brazil, Guatemala, India, the Philippines and South Africa were used to examine associations of maternal age with offspring birth weight, gestational age, height-for-age and weight-for-height Z-scores in childhood, attained schooling, and adult height, body composition (BMI, waist circumference, fat and lean mass) and cardiometabolic risk factors (blood pressure and fasting plasma glucose concentration), along with binary variables derived from these. Analyses were unadjusted and adjusted for maternal socio-economic status, height and parity, and breastfeeding duration.

**Findings:** In unadjusted analyses, younger (<19 years) and older (>35 years) maternal age was associated with lower birth weight, gestational age, child nutritional status and schooling. Associations with younger maternal age remained after adjustment; odds ratios (OR) for low birth weight, pre-term birth, 2-year stunting and failure to complete secondary schooling were 1·18 (95% CI: 1·02,1·36), 1·26 (1·03,1·53), 1·46 (1·25,1·70) and 1·38 (1·18,1·62) respectively compared with mothers aged 20-24 years. After adjustment, older maternal age remained associated with increased risk of pre-term birth (OR=1·33 (1·05,1·67)) but children of older mothers had less 2-year stunting (OR=0·64 (0·54,0·77)) and failure to complete secondary schooling (OR=0·59 (0·48,0·71)). Offspring of both younger and older mothers had higher adult fasting glucose concentrations (~0·05 mmol/l).

**Interpretation:** Children of young mothers in LMICs are disadvantaged at birth and in childhood nutrition and schooling. Efforts to prevent early childbearing should be strengthened. After adjusting for confounders, children of older mothers have advantages in nutritional status and schooling. Extremes of maternal age may be associated with disturbed offspring glucose metabolism.

**Funding:** Wellcome Trust, Bill and Melinda Gates Foundation

**Key words:** Maternal age, Adolescent pregnancy, Low birth weight, Pre-term birth, Stunting, Schooling, Adult height, Adult body composition, Adult glucose metabolism, Adult blood pressure

**INTRODUCTION**

Young maternal age at childbearing (< 19 years) is associated with an increased risk of pre-term birth and intra-uterine growth restriction, infant mortality and child undernutrition.1-12 These associations result from behavioural, social and biological factors. Younger mothers may breastfeed for a shorter duration3,13 and be behaviourally immature and therefore less able to attend to their infant’s needs. They tend to have lower socio-economic status, less schooling and less stable partnerships. If still growing, their nutritional needs compete with those of the fetus.14

Advanced maternal age (> 35 years) is associated with increased stillbirths, pre-term births, intra-uterine growth restriction and chromosomal abnormalities.15-18 Again, these result from multiple factors. In some settings, older mothers have lower socio-economic status, less schooling and higher parity, while in others they are educated women who have delayed pregnancy for career reasons. Older mothers are at higher risk of obesity, diabetes and hypertension, and associated pregnancy complications.

There has been recent interest in the developmental origins of human capital and adult disease, especially cardiovascular disease and its risk factors hypertension and diabetes.19 Studies from high-income countries report more educational under-achievement in children of younger mothers.20 Some studies have shown higher childhood blood pressure in the offspring of older mothers.21-24 No published studies have examined associations between maternal age and adult cardiovascular disease risk factors.

Most studies linking maternal age to child outcomes are from high-income countries (HICs). However, young maternal age is more common in LMICs (fertility rate among women aged <19 years approximately 103 per 1000 women/year) than in HICs (21/1000).25 More young mothers in LMICs may be physically immature because of delayed completion of growth among undernourished girls. Confounding effects of socio-economic status may differ in LMICS; for example, in some settings, young age at marriage is a norm and not necessarily associated with deprivation.3,10

COHORTS (Consortium for Health Orientated Research in Transitioning Societies) is a collaboration of five birth cohorts from LMICs, in which mothers were recruited before or during pregnancy, and the children followed up to adulthood.26 This paper explores associations of maternal age with birth outcomes, child nutritional status and schooling, and adult size, body composition and cardiometabolic risk factors. We adjusted for socio-economic confounding factors, and explored maternal height, breastfeeding duration and parity as potential mediators of associations.

**METHODS**

The cohorts include the 1982 Pelotas Cohort (Brazil); the Institute of Nutrition of Central America and Panama Nutrition Trial Cohort (Guatemala); the New Delhi Cohort (India); the Cebu Longitudinal Health and Nutrition Survey (Philippines) and the Birth to Twenty Cohort (South Africa) (**eTable 1**).26 All studies were approved by appropriate institutional ethics committees.

*Exposure*

The mother’s age at the birth of the index child was calculated from data obtained at interview before or during pregnancy, or (South Africa) from birth notification forms.

*Outcomes*

*Birth:* Birth weight was measured by researchers (Brazil, India, Guatemala) or obtained from hospital records (Philippines, South Africa). Gestational age was calculated from the last menstrual period date obtained by prospective surveillance (Guatemala, India), from the mother at recruitment (Philippines) or from medical records (Brazil, South Africa). In the Philippines, gestational age was obtained for low birth weight babies by newborn clinical assessment.27 Low birth weight (LBW) was defined as <2500g, pre-term birth as gestational age <37 weeks, and smallness-for-gestational-age (SGA) as BW below the age- and sex-specific 10th percentile of a US reference population.28

*Childhood:* In all sites, post-natal weight and height were measured longitudinally using standardized methods. Measurements at two years were available in all sites, and 4-year measurements in all except the Philippines, where the next available age (8·5 years) was used to define ‘mid-childhood’ size. Height and weight-for-height were converted into Z-scores (HAZ and WHZ) using the WHO reference ([www.who.int/growthref/en](http://www.who.int/growthref/en)). Stunting and wasting were defined as HAZ and WHZ below -2 SDs respectively. Breastfeeding data were recorded prospectively using different methods in each cohort; for this analysis we used duration in months of any breastfeeding (as opposed to exclusive breastfeeding), which was available for all cohorts except India.

*Adult:* Height, weight and waist circumference were measured using standardized techniques. Fat and fat-free mass were measured using site-specific methods, as previously described.29 In Brazil, bioelectrical impedance was measured and results corrected based on a validation study that used isotopic methods; data are only available for men. In Guatemala, weight, height, and abdominal circumference were measured and entered into a hydrostatic-weighing validated equation. The India and Philippine cohorts used published equations that have been validated for use in Asian populations for estimating body fat from skinfold measures. South Africa used dual x-ray absorptiometry (Hologic Delphi). Fat mass was calculated as % body fat x body weight, and fat free mass as weight - fat mass. Overweight was defined as a body mass index (BMI) ≥25 kg/m2 and obesity as BMI >30 kg/m2. Blood pressure (BP) was measured seated, after a 5-10 minute rest, using appropriate cuff-sizes and a variety of devices, as previously described.30 ‘Elevated BP’ was defined as systolic BP≥130 or diastolic BP≥85.31 Fasting glucose was measured in all sites except Brazil, where a random sample was collected and glucose values adjusted for time since the last meal.32 Impaired fasting glucose (IFG) was defined as a fasting glucose ≥6·1 and <7·0 mmol/l and diabetes as a value ≥7·0 mmol/l.33 Pregnant women were excluded from all these analyses.

*Confounding and mediating variables*

Socio-economic status was considered a potential confounding factor and was assessed using five variables: maternal schooling, marital status, wealth index, urban/rural residence and race. Wealth index was a score derived in each cohort based on type of housing and ownership of household assets (**eTable 2**). The Brazil, India and South Africa cohorts are urban, and the Guatemala cohort is rural; in the mixed Philippine cohort, an ‘urbanicity index’ was used.34 Brazil and South Africa had white, black, Asian and ‘other’ racial sub-groups. Maternal height was potentially both a confounder of maternal age effects (due to secular trends in height) and a mediator (due to younger mothers not having attained final height). Maternal parity and breastfeeding duration were potential mediators (older mothers tend to have higher parity and younger mothers may breastfeed for a shorter time). Parity was coded as 1, 2, 3 or >4.

*Statistical Methods*

Maternal age and at least one outcome were available for 19,403 of 22,188 mothers (87%). The number for whom outcomes were available diminished with age at follow-up; for example N=17,903 (81%) for birth weight and N=10,376 (47%) for adult BP. The maternal age distribution was similar in successive waves of follow-up (**eTable 3**). For each outcome we used the maximum sample with available data (**Table 1**). To test the representativeness of our analysis sample, we compared maternal age in those included in the analysis (with data for any childhood or adult outcome of interest) and those not included, using t tests (**eTable 4**). We used maternal age as a continuous variable where possible, but used categories (<19, >35, and 5-year intervening bands) to check for linearity and for tables, figures and odds ratio calculations. Percentage body fat and wealth index were non-normally distributed and were Fisher-Yates transformed.35 We first analysed associations between maternal age and outcomes in each cohort using multiple linear regression for continuous outcomes and multiple logistic regression for dichotomous outcomes. We assessed non-linear associations using quadratic terms. We then produced pooled analyses, including main effects for each cohort and interaction terms for cohort and control variables. We tested for heterogeneity among cohorts using F tests, comparing sums of squares explained when effects were or were not allowed to vary across sites.35 We used a sequence of regression models: (1) adjusted for sex, and adult age (adult outcomes only); (2) further adjusted for socio-economic variables; (3) further adjusted for maternal height; (4) further adjusted for breastfeeding duration; (5) further adjusted for parity. Missing maternal wealth and schooling values were imputed using regression analysis of known values on other socio-economic variables. Missing maternal height values were not imputed, and a dummy variable (0,1) to represent missingness was included in regression models. The Guatemala cohort is based on a randomised controlled trial of a protein and energy supplement for pregnant women and children26; it comprises children living in the trial villages who were born or were <7 years of age at any time from 1969-1977. We tested for interactions between maternal age and intervention group in this cohort, but found no consistent evidence of interactions. In Guatemala the 2344 participants came from 768 families; in India the 5395 came from 5313 families; there were no siblings in the other cohorts. We used linear mixed modelling to assess whether siblings affected the associations of outcomes with maternal age, and found they made little difference (**eFigure 1**). We therefore present our findings without adjustment for sibships. All analyses were performed using IBM SPSS version 21 and STATA version 12.

**RESULTS**

Table 1 shows the characteristics of the participants. Mean (range) maternal age was 26 (12-49) years, similar in all cohorts; 20-24 years was the most numerous category (eTable 2).

*Confounding and mediating variables*

The percentage of mothers who were married was 44% in South Africa and >90% in the other cohorts (Table 1). Mean maternal schooling ranged from 1·3 years (Guatemala) to 9·5 years (South Africa). Most mothers in Guatemala were of parity four or higher, compared with ~35% (India, Philippines) and 16% (Brazil, South Africa). Associations of the confounding/mediating variables with maternal age and study outcomes varied among the cohorts (**Table 2**). Older maternal age was associated with being married, having less schooling but greater wealth, longer breastfeeding duration and higher parity. Maternal height was positively related to maternal age in the Philippines, and there were inverted U-shaped relationships in the other cohorts, with shorter height in mothers <19 years and >35 years (non-linear data not shown). Maternal married status, higher schooling and wealth, white race (Brazil, South Africa), urbanicity (Philippines) and taller height were associated with higher birth weight, and child size and schooling. Blood pressure was highest in black participants and lowest in Asians (Brazil, South Africa).

*Maternal age and birth outcomes*

Birth weight rose with increasing maternal age, with a downturn among the oldest mothers (**Figure 1**). Adjusting for socio-economic factors, maternal height and breastfeeding made little difference to this pattern. Adjusting for maternal parity attenuated the association, though maternal age <19 years remained associated with lower birth weight. There were similar findings for LBW (OR 1.18, **Table 3**) and SGA (OR 1·10 [95%CI 0.94, 1.24] in the fully adjusted model). Maternal age showed an inverted U-shaped association with gestational age which changed very little with adjustment (Figure 1). Gestational age was shorter by 0·1 (95%CI 0·0,0·3) and 0·4 weeks (95%CI 0·3,0·6) in mothers aged <19 and >35 respectively in the fully adjusted model, and odds ratios for pre-term birth were 1·26 and 1·33 respectively (Table 3). These associations showed no site-sex heterogeneity (Figure 1**, eTables 5&6, eFigures 2&3**).

*Maternal age and child nutrition, schooling and adult height*

Maternal age also showed inverted U-shaped associations with 2-year HAZ and WHZ, mid-childhood HAZ, attained schooling and adult height (Figure 1, eTable 5). Adjusting for socio-economic factors attenuated these associations, though maternal age <19 years remained associated with lower values. Adjustment for maternal height and breastfeeding made little difference. Adjustment for parity changed the shape of the associations (Figure 1); while young maternal age remained associated with poorer outcomes, maternal age >25 years was associated with better outcomes. In the fully adjusted model, 2-year HAZ was lower by 0·23 (95%CI 0·16,0·29) for maternal age <19 years, and higher by 0·24 (95%CI 0·17,0·32) for maternal age >35 years. Corresponding data for schooling were -0·38 years (95%CI -0·54,-0·21) and +0·72 years (95%CI 0·53,0·92) and for adult height -0·63 cm (-1·00, -0·26) and +0·77 cm (0·34, 1·20). The associations was little changed after further adjustment for birth weight. There were similar findings for 2-year stunting and wasting, and failure to complete secondary schooling (Table 3). There was significant site-sex heterogeneity for these outcomes, mainly due to more linear associations in some cohorts, less marked in fully adjusted models (eTables 5&6, **eFigures 4-7**).

*Maternal age and adult body composition and cardiometabolic risk factors*

Systolic blood pressure was positively and linearly related to maternal age (Figure 1, eTable 5, **eFigure 8**) but this was non-significant after adjustment for socio-economic factors. Fasting glucose showed a U-shaped association with maternal age (Figure 1, eTable 5) which remained after full adjustment. Mean fasting glucose was higher by 0·05 (95%CI -0·01,0·10) and 0·06 (95%CI -0·01, 0·12) mmol/l in offspring of mothers aged <19 years and >35 years respectively. This association was little changed after further adjustment for birth weight. There was significant site-sex heterogeneity, due to more linear associations in some cohorts (**eFigure 9**). None of the body composition or other cardiometabolic outcomes was related to maternal age (Table 3, eTables 5&6).

*Parity*

The change in associations between maternal age and outcomes after adjusting for parity indicated strong effects of parity itself. **Figure 2** shows these effects on birth weight, 2-year HAZ and schooling. At any parity, birth weight increased with maternal age up to a threshold around 25-30 years and then decreased, while 2-year HAZ and schooling increased up to around 30-35 year, and remained high. At any maternal age, higher parity was associated with higher birth weight (especially marked for the difference between parity 1 and 2), but lower 2-year HAZ and years of schooling. Higher parity was not associated with lower gestational age or higher risk of pre-term birth in young or older mothers.

**DISCUSSION**

*Summary*

This study, using data from five population-based cohorts in LMICs, is one of the largest relating maternal age to birth and childhood outcomes with adjustment for multiple confounders, and the first to relate maternal age to adult outcomes. Children of young mothers and mothers of advanced age had an increased risk of low birth weight and pre-term birth, stunting in infancy, short adult height, poor schooling and higher adult fasting glucose concentrations. The disadvantages of young maternal age were independent of socio-economic status, height, breastfeeding duration and parity. With the exception of pre-term birth and adult plasma glucose concentration, the disadvantages associated with older maternal age were greatly reduced after adjustment for co-variables, especially parity, and older maternal age was associated with distinct advantages for children’s height and schooling. Apart from glucose, maternal age was unrelated to offspring cardiometabolic risk factors or body composition.

*Young mothers*

Children of mothers aged <19 years had a 20-30% increased risk of low birth weight and pre-term birth. This is consistent with a large body of evidence that teenage motherhood is detrimental to the newborn.1-12,36 Studies that sub-categorised teenage births showed the most adverse effects at the youngest ages.2-4,6,9,11 The mechanisms for these effects are important for policy8; for example, if they are explained by socio-economic factors, interventions that simply delay age at marriage may have little impact. In our study, adjusting for socio-economic factors attenuated the associations, but they remained significant. This suggests that there are biological and/or behavioural factors not captured by maternal height, breastfeeding duration or parity. This is supported by the similarity of findings in different settings.1-12 Several recent studies in the UK and USA have reported that the risk of pre-term birth among teenage mothers is increased more for second time than for first time mothers.37,38 The reasons for this are unknown, but in a high income setting, having more than one birth as a teenager may identify a group with high-risk behaviours. We found no evidence of a similar association in our data from LMICs.

Children of mothers aged <19 years had a 30-40% increased risk of 2-year stunting and of failure to complete secondary schooling. These associations remained after full adjustment, although residual confounding cannot be ruled out. The associations with poorer child nutritional status, especially stunting, are consistent with other studies.39 The effects could be mediated by maternal inexperience and/or lack of autonomy leading to sub-optimal feeding, hygiene and healthcare-seeking behaviours3, which we did not measure. Children of young mothers in LMICs have higher mortality, sometimes increasing with the age of the child, suggesting effects of the post-natal environment.3,9 Studies from high-income countries have also shown poorer school attainment and/or cognitive function in children of teenage mothers, independent of socio-economic factors20,40-42, possibly because of poorer care and stimulation. There are no previous publications on schooling in relation to maternal age from LMICs.

In recognition of the disadvantages of young motherhood, most countries have a minimum legal marriage age, but it is often ignored. In many LMICs, 20-30% of girls aged 15-19 years are married, and in some 40-50%.36,40 Early marriage has implications for women themselves, truncating their education and violating their human rights.36,43 The situation is improving in many places, but worsening in others, and the disparity in teenage fertility rates between HICs and LMICs is widening.25 Our findings highlight the importance of continued and strengthened measures to discourage early marriage and childbirth.

*Older mothers*

Independent of confounders, and consistent with other data from both HICs and LMICs,16-18 mothers >35 years of age had a 30% increased risk of pre-term birth. However, in our fully adjusted data, older maternal age was an advantage for the child’s nutritional status, schooling and adult height. These associations were strong (the fully-adjusted OR for non-completion of secondary education was 0·59) and have not been reported before from LMICs. They may be related to better child-rearing practices by more experienced and/or empowered women.40-42

*Cardiometabolic risk factors*

We found a U-shaped association between maternal age and fasting glucose concentration in the adult offspring. Offspring of younger and older mothers had concentrations approximately 0·05 mmol/l higher than the reference group, an association that was not evident for IGT/diabetes. This previously unreported association requires replication. The effect in older mothers could be due to obesity and/or diabetes in pregnancy, but we have no data to examine this. Offspring body composition and other cardiometabolic risk markers were unrelated to maternal age.

*Strengths and limitations*

Strengths of the study are a large sample size, information on confounding factors recorded prospectively, and comparable outcomes in all sites. We did not know maternal age at menarche and so could not examine effects of ‘gynaecological age’. We lacked data on maternal smoking, diet and supplement use, other aspects of infant/childhood diet (apart from breastfeeding), and paternal factors, and so residual confounding cannot be ruled out. We cannot exclude confounding by unmeasured genetic and/or familial factors, recently shown in a large Swedish cohort using sibling- and cousin-comparisons to account for an association between young maternal age and attention-deficit hyperactivity disorder in the children.44 Adult outcomes were measured using different techniques in the different cohorts, although all were accepted methods; these differences may contribute additional ‘noise’ in the data, which would tend to reduce associations. Other limitations were losses to follow-up and missing data. Two-year outcomes were available for ~80% of the cohort in Brazil and the Philippines but only 45-50% in Guatemala (where many children were enrolled after age 2 years), India and South Africa. Percentages for adult blood pressure were >70% (Brazil), >50% (Guatemala, Philippines and South Africa) and 14% in India. Comparisons between participants and non-participants showed differences among cohorts in maternal, child and adult measurements that varied in strength and direction; we adjusted for each maternal factor independently within each cohort to allow for the varied ways in which they were related to outcomes.

*Conclusions*

Children of teenage mothers in LMICs are disadvantaged at birth and during childhood and have reduced human capital. Measures to prevent young motherhood should be strengthened and young mothers should be helped to improve their children’s nutrition and education. Our data show that children of older mothers are at increased risk of pre-term birth, and may have higher plasma glucose concentrations in adult life. However, at a given socio-economic level and parity, children of older mothers have advantages in terms of childhood nutrition and educational attainment.

**Research in context**

**Systematic review**

We searched PubMed for studies describing the relationship of maternal age to birth outcomes, child nutritional status, attained schooling, and adult body composition and cardiometabolic risk factors in the offspring. There is a large literature documenting an increased risk of adverse birth outcomes when the mother is very young (<19 years) or of advanced age (>35 years). Young motherhood is also associated with increased undernutrition and poor educational attainment in the children. This literature, especially that relating to advanced maternal age, is overwhelmingly dominated by studies from high income countries. Few studies in any setting have examined advanced maternal age as a predictor of childhood outcomes, and none have examined young or advanced maternal age as predictors of adult body composition and cardiometabolic risk factors.

**Interpretation**

Our study pooled data from five birth cohorts in low- and middle-income countries (LMICs) creating a large samples size (N=~17,000 for birth outcomes, ~13,000 for child outcomes and ~10,000 for adult outcomes). All studies collected maternal age at childbirth (exposure), and (outcomes) longitudinal measurements of the children’s weight and height, attained schooling, and adult body composition and cardiometabolic risk factors. They also collected data on maternal socio-economic status, parity and height, and duration of breastfeeding, which may confound the relationship of maternal age with these outcomes. We confirmed that young maternal age was associated with an increased risk of low birth weight, pre-term and small-for-gestational-age births, stunting and wasting in infancy and childhood and failure to complete secondary education. The associations were attenuated by adjustment for confounding factors, but remained significant. This suggests that they result from biological and/or behavioural immaturity of the mother. The results reinforce the arguments for low- and middle-income countries to strengthen measures to prevent early marriage and childbearing. We confirmed that advanced maternal age was associated with an increased risk of pre-term birth, independent of confounders. After adjusting for confounders, higher maternal age was associated with better child nutritional status and more schooling, suggesting that, other factors being equal, children of more mature mothers are advantaged nutritionally and educationally. Adult body composition and blood pressure were unrelated to maternal age, but fasting plasma glucose concentrations were higher in offspring of young and old mothers. This has not been reported before and should be replicated in other studies, but suggests that there may be effects of maternal age on fetal/child development which programme adult glucose metabolism.

**Competing interests**

All authors declare that we have no conflicts of interest.

**Acknowledgements**

**Author contributions:** The authors have no relevant conflict of interest to disclose. The COHORTS group designed the research. CHDF, HSS, CO, MCR-M, CV, RM, ADS, SS, NT, LA, IB, SN, LMR conducted the research. CO and CHDF analyzed the data and drafted the manuscript, and all authors contributed to critical revision of the manuscript. CO and CHDF had primary responsibility for final content. All authors read and approved the final manuscript. CO and CHDF had full access to all the data and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Funding support:** COHORTS is supported by the Wellcome Trust (UK), the Bill and Melinda Gates Foundation and the US National Institutes of Health. Funding for the individual cohorts was as follows: Guatemala (US National Institutes of Health; US National Science Foundation); Pelotas (Wellcome Trust); New Delhi (Indian Council of Medical Research, US National Center for Health Statistics; Medical Research Council (UK); British Heart Foundation), Birth-to-twenty (Wellcome Trust, Human Sciences Research Council, South African Medical Research Council, Mellon Foundation, South-African Netherlands Programme on Alternative Development, Anglo American Chairman’s Fund, University of the Witwatersrand), Cebu (US National Institutes of Health). The funding sources played no role in the design and conduct of the study, management, analysis and interpretation of the data, preparation, review or approval of the manuscript, and decision to submit the manuscript for publication.

**Additional COHORTS investigators: Pelotas Birth Cohort** (Brazil): Fernando C Barros fcbarros.epi@gmail.com, Denise Gigante denise.epi@gmail.com, Pedro C Hallal prchallal@terra.com.br, Bernardo L Horta blhorta@gmail.com (Universidade Federal de Pelotas, Pelotas); **INCAP Nutrition Trial Cohort Study** (Guatemala): Manual Ramirez-Zea mramirez@incap.int (Instituto de Nutrición de Centra América y Panamá (INCAP), Guatemala); **New Delhi Birth Cohort Study** (India): Santosh K Bhargava drskbhargava@yahoo.com (Sunderlal Jain Hospital, New Delhi), Lakshmi Ramakrishnan lakshmy\_ram@yahoo.com, Dorairaj Prabhakaran dprabhakaran@ccdcindia.org (Centre for the Control of Chronic Diseases, New Delhi), K Srinath Reddy ksrinath.reddy@phfi.org (Public Health Foundation of India, New Delhi); Anita Khalil anitakhalil@yahoo.com (The Heart Centre, New Delhi), Poornima Prabhakaran poornimaap@yahoo.co.uk (Public Health Foundation of India, Delhi), SK Dey Biswas biswasskd@icmr.org.in (Indian Council of Medical Research, New Delhi), Siddarth Ramji sumisid@vsnl.com (Maulana Azad Medical College, New Delhi); **Cebu Longitudinal Health and Nutrition Study** (Philippines): Judith Borja judithborja@gmail.com, Nanette Lee nanette\_rlee@yahoo.com (Office of Population Studies, University of San Carlos, Cebu City); Darren L Dahly ddahly@ucc.ie (University of Cork, Eire); Christopher W Kuzawa kuzawa@northwestern.edu (Northwestern University, Evanston IL); **Birth to Twenty Cohort** (South Africa): Alan Stein alan.stein@psych.ox.ac.uk (University of Oxford, Oxford).

**REFERENCES**

1. Paranjothy S, Broughton H, Adappa R, Fone D. Teenage pregnancy: who suffers? *Arch Dis Child* 2009; **94**: 239-45.
2. DuPlessis HM, Bell R, Richards T. Adolescent pregnancy; understanding the impact of age and race on outcomes*. J Adolescent Health* 1997; **20**: 187-97.
3. LeGrand TK, Mbacke CS. Teenage pregnancy and child health in the urban Sahel. *Stud Fam Planning* 1993; **24**: 137-49.
4. Conde-Agudelo A, Belizan JM, Lammers C. Maternal-perinatal morbidity and mortality associated with adolescent pregnancy in Latin America: cross-sectional survey. *Am J Obs Gyn* 2005; **192**: 342-9.
5. Markovitz BP, Cook R, Flick LH, Leet TL. Socioeconomic factors and adolescent pregnancy outcomes; distinctions between neonatal and postneonatal deaths? *BMC Public Health* 2005; **5**: 79.
6. Sharma V, Katz J, Mullany LC et al. Young maternal age and the risk of neonatal mortality in rural Nepal. *Arch Paediatr Adolesc Med* 2008; **162**: 828-35.
7. DeVienne CM, Creveuil C, Dreyfus M. Does young maternal age increase the risk of adverse obstetric, fetal and neonatal outcomes: a cohort study. *Eur J Obstet Gynecol Reprod Biol* 2009; **147**: 151-156.
8. Lawlor DA, Mortensen L, Andersen AM. Mechanisms underlying the associations of maternal age with adverse perinatal outcomes: a sibling study of 264 695 Danish women and their firstborn offspring. *Int J Epidemiol* 2011; **40**: 1205-14.
9. Restrepo-Mendez MC, Barros AJD, Santos IS et al. Childbearing during adolescence and offspring mortality: findings from three population-based cohorts in southern Brazil. *BMC Public Health* 2011; **11**: 781.
10. Alam N. Teenage motherhood and infant mortality in Bangladesh: maternal age-dependent effect of parity one. *J Biosocial Sci* 2000; **32**: 229-36.
11. Gibbs C, Wendt A, Peters S, Hogue CJ. The impact of early age at first childbirth on maternal and infant health. *Paed Perinat Epidemiol* 2012; **26 (suppl 1)**; 259-84.
12. Borja J, Adair LS. Assessing the net effect of young maternal age on birth weight. *Am J Hum Biol* 2003; **15**: 733-740.
13. Wambach KA, Cole C. Breastfeeding and adolescents. *J Obs Gynecol Neonatal Nurs* 2000; **29**: 282-94.
14. Scholl TO, Hediger ML. A review of the epidemiology of nutrition and adolescent pregnancy: maternal growth during pregnancy and its effects on the fetus. *J Am Coll Nutr* 1993; **12**: 101-7.
15. Carolan M, Frankowska D. Advanced maternal age and adverse perinatal outcome; a review of the evidence. *Midwifery* 2011; **27**: 793-801.
16. Ngowa JDK, Ngassam A, Dohbit JS, Nzedjom C, Kasia JM. Pregnancy outcome at advanced maternal age in a group of African women in two teaching hospitals in Yaounde, Cameroon. *Pan African Med J* 2013; **14**: 134.
17. Kenny LC, Lavender T, McNamee R, O’Neill SM, Mills T, Khashan AS. Advanced maternal age and adverse pregnancy outcome: evidence from a large contemporary cohort. PLoS One 2013; 8: e56583. doi: 10·1371/journal.pone·0056583.
18. Newburn-Cook CV, Onyskiw JE. Is older maternal age a risk factor for pre-term birth and fetal growth restriction; a systematic review. *Health Care Women Int* 2005; **26**: 852-75.
19. Victora CG, Adair L, Fall C et al and the Maternal and Child Undernutrition Study Group. Maternal and child undernutrition: consequences for adult health and human capital. *Lancet* 2008; **371**: 340-357.
20. Shaw M, Lawlor D, Najman JM. Teenage children of teenage mothers: psychological, behavioural and health outcomes from an Australian prospective longitudinal study. *Soc Sci Med* 2006; **62**: 2526-2539.
21. Whincup PH, Cook DG, Shaper AG. Early influences on blood pressure: a study of children aged 5-7 years. *BMJ* 1989; **299**: 587-91.
22. Lawlor DA, Naiman JM, Sterne J, Williamns GM, Ebrahim S, Davey Smith G. Associations of parental, birth and early life characteristics with systolic blood pressure at 5 years of age: findings from the Mater-University study of pregnancy and its outcomes. *Circulation* 2004; **110**: 2417-23.
23. Gillman MW, Rich-Edwards JW, Rifas-Shiman SL et al. Maternal age and other predictors of newborn blood pressure. *J Pediatr* 2004; **144**: 240-5.
24. Roberts RJ, Leary SD, Smith GD, Ness AR and ALSPAC study team. Maternal age in pregnancy and offspring blood pressure in childhood in the Avon Longitudinal Study of Parents and Children (ALSPAC). *J Hum Hyperten* 2005; **19**: 893-900.
25. United Nations; Dept of Economic and Social Affairs, Population Division. World Fertility Patterns 2009. [http://www.un.org/esa/population/publications/worldfertility2009/worldfertility2009.htm Accessed January 2014](http://www.un.org/esa/population/publications/worldfertility2009/worldfertility2009.htm%20%20Accessed%20January%202014).
26. Richter LM, Victora CG, Hallal PC, Adair LS, Bhargava SK, Fall CH, et al. Cohort Profile: The Consortium of Health-Orientated Research in Transitioning Societies. *Int J Epidemiol* 2012; **41**: 621-6.
27. Ballard JL, Novak KK, Driver M. A simplified score for assessment of fetal maturation of newly born infants. *J Pediatrics* 1979; **95**: 769-74.
28. Williams RL, Creasy RK, Cunningham GC, Hawes WE, Norris FD, Tashiro M. Fetal growth and perinatal viability in California. *Obstet Gynecol* 1982; **59**: 624-32.
29. Kuzawa C, Hallal P, Adair L et al. Birth weight, postnatal weight gain and adult body composition in five low and middle income countries. *Am J Hum Biol* 2012; **24**: 5-13.
30. Adair LS, Martorell R, Stein AD et al. Size at birth, weight gain in infancy and childhood, and adult blood pressure in five low and middle income country cohorts: When does weight gain matter? *Am J Clin Nutr* 2009; **89**: 1383-92.
31. International Diabetes Federation. The IDF consensus worldwide definition of the metabolic syndrome. Brussels, 2006, International Diabetes Federation.
32. Norris SA, Osmond C, Gigante D et al. Size at birth, weight gain in infancy and childhood, and adult diabetes risk in five low- or middle-income country birth cohorts. *Diabetes Care* 2012; 35: 72-79.
33. World Health Organization. Definition, diagnosis and classification of diabetes mellitus and its complications. Report of a WHO consultation. Part 1: Diagnosis and Classification of Diabetes Mellitus. WHO, Geneva, 1999.
34. Adair L, Dahly D. Quantifying the urban environment; a scale measure of urbanicity outperforms the rural-urban dichotomy. *Soc Sci Med* 2007; **64**: 1407-19.
35. Armitage P, Berry G, Matthews JNS. Statistical methods in medical research. 4th Edition. Oxford, Blackwell Science Ltd, 2002.
36. United Nations Population Fund (UNFPA). Marrying too young; end child marriage. UNFPA, New York, 2012.
37. Smith GCS, Pell JP. Teenage pregnancy and risk of adverse perinatal outcomes associated with first and second births: population based retrospective cohort study. *BMJ* 2001; **323**: 476-9.
38. Khashan AS, Baker PN, Kenny LC. Preterm birth and reduced birthweight in first and second teenage pregnancies; a register-based cohort study. *BMC Pregnancy Childbirth* 2010; **10**: 36.
39. Raj A, Saggurti N, Winter M et al. The effect of maternal child marriage on morbidity and mortality of children under 5 in India: cross-sectional study of a nationally representative sample. *BMJ* 2010; **340**: b4258.
40. Boden JM, Fergusson DM, John Horwood L. Early motherhood and subsequent life outcomes. *J Child Psychol Psychiatry* 2008; **49**: 151-60.
41. Fergusson DM, Woodward LJ. Maternal age and educational and psychological outcomes in early adulthood. *J Child Psychol Psychiatry* 1999; **40**: 479-89.
42. Morinis J, Carson C, Quigley MA. Effect of teenage motherhood on cognitive outcomes in children: a population-based cohort study. *Arch Dis Child* 2013; **98**: 959-64.
43. United Nations. World Marriage Patterns 2000. <http://www.un.org/esa/population/publications/worldmarriage/worldmarriagepatterns2000.pdf> Accessed January 2014.
44. Chang Z, Lichtenstein P, D’Onofrio BM, Almquist C, Kuja-Halkola R, Sjolander A, Larsson H. Maternal age at childbirth and risk for ADHD in offspring: a population-based cohort study. *Int J Epidemiol* 2014; **43**: 1815-24.

**Table 1: Maternal age, birth, child and adult outcomes, socio-economic variables and maternal height, breast feeding and parity in the five cohorts**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **BRAZIL** | **GUATEMALA** | **INDIA** | **PHILIPPINES** | **SOUTH AFRICA** |
|  | **Mean (SD) or N (%)\*** | **N** | **Mean (SD) or N (%)\*** | **N** | **Mean (SD) or N (%)\*** | **N** | **Mean (SD) or N (%)\*** | **N** | **Mean (SD) or N (%)\*** | **N** |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **N Original cohort** |  |  | 5913 |  |  | 2392 |  |  | 7530 |  |  | 3080 |  |  | 3273 |
| **N with maternal age** |  |  | 5912 |  |  | 2344 |  |  | 5395 |  |  | 3080 |  |  | 3271 |
| **N with maternal age and any outcome of interest** |  |  | 5910 |  |  | 1942 |  |  | 5203 |  |  | 3078 |  |  | 3270 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Maternal age (yr)** | **25·8** | (6·1) | 5910 | **27·2** | (7·2) | 1942 | **26·0** | (5·2) | 5203 | **26·3** | (6·0) | 3078 | **26·0** | (6·1) | 3270 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Child outcomes:** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Birth weight (g)** | **3190** | (568) | 5804 | **3048** | (492) | 973 | **2792** | (440) | 4832 | **2988** | (438) | 3029 | **3070** | (513) | 3265 |
| **Low birth weight\*** | **640** | (11·0) | 5804 | **136** | (14·0) | 973 | **1393** | (28·8) | 4832 | **448** | (14·8) | 3029 | **420** | (12·9) | 3265 |
| **Small for gestational age\*** | **683** | (14.9) | 4596 | **233** | (31.1) | 748 | **361** | (40.9) | 883 | **735** | (24.5) | 2999 | **453** | (14.3) | 3166 |
| **Gestation (weeks)** | **39·3** | (1·9) | 4600 | **39·3** | (3·0) | 851 | **38·9** | (2·6) | 937 | **38·7** | (2·2) | 3048 | **38·1** | (1·9) | 3169 |
| **Pre-term birth\*** | **289** | (6·3) | 4600 | **109** | (12·8) | 851 | **141** | (15·0) | 937 | **466** | (15·3) | 3048 | **388** | (12·2) | 3169 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Height (Z) at 2y** | **-0·67** | (1·25) | 4835 | **-2·91** | (1·15) | 1079 | **-2·01** | (1·23) | 3697 | **-2·41** | (1·15) | 2504 | **-1·16** | (1·12) | 1804 |
| **Weight for height (Z) at 2y** | **0·56** | (0·99) | 4832 | **-0·28** | (0·90) | 1076 | **-0·66** | (1·03) | 3666 | **-0·62** | (0·96) | 2502 | **0·19** | (1·35) | 1803 |
| **Stunted at 2y\*** | **667** | (13·8) | 4835 | **858** | (79·5) | 1079 | **1841** | (49·8) | 3697 | **1558** | (62·2) | 2504 | **372** | (20·6) | 1804 |
| **Wasted at 2y\*** | **40** | (0·8) | 4832 | **52** | (4·8) | 1076 | **362** | (9·9) | 3666 | **182** | (7·3) | 2502 | **86** | (4·8) | 1803 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Height (Z) mc** | **-0·66** | (1·11) | 4651 | **-2·42** | (0·97) | 998 | **-1·98** | (1·06) | 3197 | **-2·05** | (0·94) | 2261 | **-0·91** | (0·93) | 1804 |
| **Weight for height (Z) mc** | **0·63** | (1·01) | 4648 | **0·32** | (0·83) | 998 | **-0·17** | (0·88) | 3173 | **-0·81** | (0·89) | 2261 | **0·18** | (1·03) | 1804 |
| **Stunted mc\*** | **505** | (10·9) | 4651 | **672** | (67·3) | 998 | **1547** | (48·4) | 3197 | **1215** | (53·7) | 2261 | **212** | (11·8) | 1804 |
| **Wasted mc\*** | **15** | (0·3) | 4648 | **2** | (0·2) | 998 | **72** | (2·3) | 3173 | **195** | (8·6) | 2261 | **29** | (1·6) | 1804 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Adult outcomes:** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Age (years)** | **22·7** | (0·4) | 4193 | **32·4** | (4·1) | 1297 | **29·1** | (1·3) | 1038 | **21·2** | (0·9) | 2040 | **18·1** | (0·5) | 1989 |
| **Attained schooling (yrs)** | **9·3** | (3·2) | 4076 | **4·7** | (3·4) | 1458 | **13·2** | (3·4) | 1038 | **10·0** | (3·0) | 2069 | **11·1** | (1·5) | 2036 |
| **Failed to finish 20 school\*** | **1974** | (48·4) | 4076 | **1369** | (93·9) | 1458 | **145** | (14·0) | 1038 | **613** | (29·6) | 2069 | **781** | (38·4) | 2036 |
| **Height (cm) Men** | **173·7** | (6·9) | 2207 | **162·8** | (6·0) | 552 | **169·3** | (6·4) | 590 | **163·0** | (5·9) | 1079 | **171·0** | (7·5) | 933 |
|  **Women** | **160·8** | (6·2) | 1979 | **150·6** | (5·6) | 608 | **154·3** | (5·1) | 446 | **151·2** | (5·5) | 958 | **159·7** | (6·3) | 1000 |
| **Short stature\*** | **167** | (4·0) | 4186 | **535** | (46·1) | 1160 | **161** | (15·5) | 1036 | **864** | (42·4) | 2037 | **151** | (7·8) | 1933 |
| **Body mass index (kg/m2)** | **23·6** | (4·4) | 4185 | **25·9** | (4·4) | 1160 | **24·4** | (4·6) | 1036 | **20·6** | (3·1) | 2032 | **21·7** | (4·2) | 1932 |
| **Waist circ (cm) Men** | **80·9** | (10·1) | 2205 | **86·7** | (9·1) | 540 | **88·9** | (11·7) | 590 | **72·0** | (7·5) | 1077 | **-** | - | - |
|  **Women** | **74·9** | (10·6) | 1978 | **92·4** | (12·1) | 604 | **78·6** | (12·4) | 448 | **67·6** | (7·2) | 951 | **-** | - | - |
| **Overweight\*** | **1190** | (28·4) | 4185 | **603** | (52·0) | 1160 | **465** | (44·9) | 1036 | **176** | (8·7) | 2032 | **330** | (17·1) | 1932 |
| **Obesity\*** | **341** | (8.1) | 4185 | **202** | (17.4) | 1160 | **94** | (9.1) | 1036 | **32** | (1.6) | 2032 | **104** | (5.4) | 1932 |
| **Fat mass (kg) Men** | **12·2** | (5·1) | 1952 | **14·0** | (6·6) | 540 | **17·2** | (6·9) | 588 | **9·7** | (4·5) | 988 | **8·7** | (5·0) | 879 |
|  **Women** | **-** | - | - | **22·3** | (9·1) | 602 | **20·3** | (8·1) | 446 | **15·4** | (4·6) | 822 | **19·4** | (7·7) | 936 |
| **Lean mass (kg) Men** | **60·3** | (9·7) | 1952 | **51·4** | (5·4) | 540 | **53·4** | (7·8) | 588 | **46·4** | (5·8) | 988 | **51·0** | (6·7) | 879 |
|  **Women** | **-** | - | - | **38·9** | (3·6) | 602 | **37·6** | (5·6) | 446 | **31·0** | (4·2) | 822 | **39·0** | (5·4) | 936 |
| **Body fat (%) Men** | **16·3** | (3·8) | 2196 | **20·5** | (6·6) | 540 | **23·5** | (6·0) | 588 | **16·7** | (5·1) | 988 | **14·1** | (5·3) | 883 |
|  **Women** | **-** | - | - | **35·1** | (7·3) | 602 | **33·7** | (7·5) | 446 | **32·7** | (4·8) | 822 | **32·3** | (6·6) | 939 |
| **Systolic BP (mmHg)** | **117·7** | (15·0) | 4188 | **112·1** | (12·9) | 1248 | **113·0** | (12·2) | 1033 | **105·9** | (12·2) | 2036 | **117·6** | (10·7) | 1871 |
| **Diastolic BP (mmHg)** | **73·8** | (11·4) | 4188 | **70·8** | (9·5) | 1248 | **75·3** | (10·0) | 1033 | **72·1** | (10·0) | 2042 | **71·4** | (8·5) | 1871 |
| **Elevated BP\*** | **1384** | (33·0) | 4188 | **224** | (17·9) | 1248 | **342** | (33·1) | 1033 | **589** | (28·8) | 2044 | **400** | (21·4) | 1871 |
| **Fasting glucose (mmol/l)** | **5·02** | (0·73) | 3612 | **5·20** | (1·11) | 985 | **5·43** | (1·01) | 1013 | **4·63** | (0·55) | 1703 | **4·62** | (0·45) | 1189 |
| **IFG/DM\*** | **281** | (7·8) | 3618 | **60** | (6·1) | 991 | **184** | (18·1) | 1014 | **16** | (0·9) | 1703 | **10** | (0·8) | 1194 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Covariates** |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| **Mother married\*** | **5422** | (91·8) | 5905 | **1557** | (91·5) | 1701 | **5200** | (100·0) | 5201 | **2963** | (97·5) | 3038 | **1414** | (43·5) | 3248 |
| **Maternal education (y)** | **6·5** | (4·2) | 5910 | **1·3** | (1·6) | 1913 | **5·1** | (4·6) | 5203 | **7·1** | (3·3) | 3078 | **9·5** | (3·0) | 3048 |
| **Maternal wealth** | **3·3** | (1·2) | 4988 | **-0·12** | (0·93) | 1784 | **4·1** | (1·2) | 5190 | **3·5** | (2·6) | 3077 | **3·9** | (1·6) | 2857 |
| **Race White\*** | **3457** | (75·5) | 4580 | **0** | - | 1942 | **0** | - | 5203 | **0** | - | 3078 | **207** | (6·3) | 3270 |
|  **Black\*** | **711** | (15·5) | 4580 | **0** | - | 1942 | **0** | - | 5203 | **0** | - | 3078 | **2567** | (78·5) | 3270 |
|  **Asian\*** | **76** | (1·7) | 4580 | **0** | - | 1942 | **5203** | (100) | 5203 | **3078** | (100) | 3078 | **115** | (3·5) | 3270 |
|  **Other\*** | **336** | (7·3) | 4580 | **1942** | (100) | 1942 | **0** | - | 5203 | **0** | - | 3078 | **381** | (11·7) | 3270 |
| **Urban score** |  | **Urban** |  |  | **Rural** |  |  | **Urban** |  | **30·6** | (12·6) | 3078 |  | **Urban** |  |
| **Maternal height (cm)** | **156·4** | (6·0) | 5804 | **148·5** | (5·2) | 1604 | **151·8** | (5·5) | 1296 | **150·6** | (5·0) | 3078 | **158·8** | (6·1) | 1757 |
| **Breastfeeding None\*** | **420** | (9·4) | 4489 | **7** | (0·7) | 988 | **-** | - | - | **204** | (7·6) | 2668 | **203** | (8·5) | 2390 |
|  **<6 m\*** | **2562** | (57·1) | 4489 | **40** | (4·0) | 988 | **-** | - | - | **397** | (14·9) | 2668 | **745** | (31·2) | 2390 |
|  **<1 y\*** | **690** | (15·4) | 4489 | **149** | (15·1) | 988 | **-** | - | - | **353** | (13·2) | 2668 | **368** | (15·4) | 2390 |
|  **≥1 y\*** | **817** | (18·2) | 4489 | **792** | (80·2) | 988 | **-** | - | - | **1714** | (64·2) | 2668 | **1074** | (44·9) | 2390 |
| **Maternal parity 1\*** | **2321** | (39·3) | 5908 | **310** | (16·0) | 1938 | **77·2** | (17·2) | 4492 | **686** | (22·3) | 3078 | **1197** | (36·6) | 3270 |
|  **2\*** | **1659** | (28·1) | 5908 | **295** | (15·2) | 1938 | **1140** | (25·4) | 4492 | **693** | (22·5) | 3078 | **988** | (30·2) | 3270 |
|  **3\*** | **965** | (16·3) | 5908 | **272** | (14·0) | 1938 | **1000** | (22·3) | 4492 | **598** | (19·4) | 3078 | **578** | (17·7) | 3270 |
|  **4+\*** | **963** | (16·3) | 5908 | **1061** | (54·7) | 1938 | **1580** | (35·2) | 4492 | **1101** | (35·8) | 3078 | **507** | (15·5) | 3270 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

mc = mid-childhood. Low birth weight (LBW) was defined as <2500g, pre-term birth as gestational age <37 weeks, and smallness-for-gestational-age (SGA) as a BW below the age- and sex-specific 10th percentile of a US reference population.27 Stunting and wasting were defined as height-for-age and weigh-for-age Z-scores (WHO standard) below -2 SDs respectively. Short adult stature was defined as <-2 SDs for height according to 18-year values in the WHO standard. Adult overweight was defined as a body mass index (BMI) ≥25 kg/m2. Elevated BP was defined as systolic BP≥130 or diastolic BP≥85.30 Impaired fasting glucose (IFG) was defined as a fasting glucose ≥6•1 but <7•0 mmol/l and diabetes as a value ≥7•0 mmol/l.32 In the mixed urban and rural Philippine cohort an ‘urbanicity index’ was used.33 Maternal wealth was defined differently in each cohort, based on type of housing and/or household assets (see eTable 2). Breastfeeding duration was not available for India. Imputed values were used for maternal schooling (Brazil N=7 (0.1%), Guatemala N=64 (3.3%), India N=9 (0.17%), Philippines N=0, South Africa N=341 (10.4%)) and maternal wealth (Brazil N=922 (15.6%), Guatemala N=158 (8.1%), India N=13 (2.5%), Philippines N=1 (0.03%), South Africa N=413 (12.6%)). Maternal height was missing for 106 in Brazil (1.8%), 338 in Guatemala (17.4%), 3907 in India (75.1%), 0 in the Philippines and 1513 (46.3%) in South Africa.

**Table 2: Associations of potential confounding and mediating variables with maternal age and offspring birth weight, gestational age at delivery, size at age two years, education and adult height, systolic blood pressure and fasting glucose**

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Covariate** | **Site** | **Feature** | **Maternal****age****(years)** | **Birth****weight****(g)** | **Gestational****age****(weeks)** | **Height at****age 2y****(z)** | **Weight****for height****at age 2y****(z)** | **Schooling****(years)** | **Adult height****(cm)** | **Systolic****blood****pressure****(mm Hg)** | **Fasting glucose (mmol/l)** |
|  |  |  |  |  |  |  |  |  |  |  |  |
| **Maternal****schooling****(correlation)** | **Brazil** |  | 0·06\*\*\* | 0·09\*\*\* | -0·03 | 0·31\*\*\* | 0·14\*\*\* | 0·51\*\*\* | 0·12\*\*\* | -0·01 | -0·03 |
| **Guatemala** |  | -0·05\* | 0·08\* | -0·01 | 0·06 | 0·01 | 0·28\*\*\* | 0·12\*\*\* | -0·00 | -0·06\* |
| **India** |  | -0·12\*\*\* | 0·17\*\*\* | -0·02 | 0·45\*\*\* | 0·28\*\*\* | 0·38\*\*\* | 0·12\*\*\* | 0·00 | 0·02 |
| **Philippines** |  | -0·05\*\* | 0·05\* | 0·04 | 0·33\*\*\* | 0·13\*\*\* | 0·46\*\*\* | 0·14\*\*\* | 0·04 | -0·03 |
| **South Africa** |  | -0·15\*\*\* | 0·06\*\* | 0·06\*\* | 0·16\*\*\* | -0·01 | 0·21\*\*\* | 0·05\* | -0·09\*\*\* | -0·03 |
|  |  |  |  |  |  |  |  |  |  |  |  |
| **Marital****status****(mean)** | **Brazil** | **Married** | 26·1 | 3203 | 39·3 | -0·65 | 0·56 | 9·4 | 167·6 | 117·8 | 5·03 |
| **Single** | 22·5\*\*\* | 3046\*\*\* | 39·3 | -0·91\*\*\* | 0·53 | 8·4\*\*\* | 167·1 | 116·5 | 4·99 |
| **Guatemala** | **Married** | 27·9 | 3075 | 39·4 | -2·88 | -0·26 | 4·7 | 156·6 | 112·2 | 5·23 |
| **Single** | 26·1\*\* | 2896\*\* | 38·4\* | -3·20\* | -0·53\*\* | 4·0\* | 155·8 | 111·7 | 5·18 |
| **Philippines** | **Married** | 26·5 | 2993 | 38·7 | -2·41 | -0·62 | 10·0 | 157·5 | 105·8 | 4·63 |
| **Single** | 21·8\*\*\* | 2852\*\* | 38·5 | -2·34 | -0·58 | 9·9 | 157·6 | 105·3 | 4·45\* |
| **South Africa** | **Married** | 28·4 | 3098 | 38·4 | -1·02 | 0·02 | 11·1 | 166·1\*\*\* | 118·1 | 4·64 |
| **Single** | 24·1\*\*\* | 3051\*\* | 38·0\*\*\* | -1·25\*\*\* | 0·30\*\*\* | 11·0 | 164·6 | 117·3 | 4·61 |
|  |  |  |  |  |  |  |  |  |  |  |  |
| **Wealth****(correlation)** | **Brazil** |  | 0·22\*\*\* | 0·11\*\*\* | -0·04\* | 0·34\*\*\* | 0·17\*\*\* | 0·47\*\*\* | 0·10\*\*\* | -0·00 | -0·06\*\* |
| **Guatemala** |  | 0·02 | 0·11\*\* | -0·01 | 0·14\*\*\* | 0·09\*\* | 0·23\*\*\* | 0·10\*\* | 0·03 | -0·01 |
| **India** |  | 0·11\*\*\* | 0·13\*\*\* | -0·01 | 0·23\*\*\* | 0·17\*\*\* | 0·22\*\*\* | 0·05 | 0·03 | 0·02 |
| **Philippines** |  | 0·09\*\*\* | 0·08\*\*\* | 0·02 | 0·26\*\*\* | 0·15\*\*\* | 0·24\*\*\* | 0·12\*\*\* | 0·04 | -0·01 |
| **South Africa** |  | 0·02 | 0·02 | 0·06\*\* | 0·19\*\*\* | -0·05 | 0·16\*\*\* | 0·03 | -0·06\* | 0·03 |
|  |  |  |  |  |  |  |  |  |  |  |  |
| **Urban****(correlation)** | **Philippines** |  | -0·06\*\* | 0·04\* | -0·01 | 0·15\*\*\* | -0·04 | 0·20\*\*\* | 0·04 | 0·01 | -0·02 |
|  |  |  |  |  |  |  |  |  |  |  |  |
| **Race****(mean)** | **Brazil** | **White** | 26·0 | 3247\*\*\* | 39·4 | -0·55\*\*\* | 0·61\*\*\* | 9·8\*\*\* | 167·9\* | 117·3\*\* | 5·02 |
| **Black** | 25·8 | 3139\*\*\* | 39·2 | -1·10\*\*\* | 0·44\*\*\* | 8·2\*\*\* | 166·7\* | 119·4\*\* | 5·00 |
| **Asian** | 25·2 | 3225\*\*\* | 39·7 | -0·98\*\*\* | 0·38\*\*\* | 8·3\*\*\* | 166·1\* | 115·8\*\* | 5·04 |
| **Other** | 26·3 | 3207\*\*\* | 39·3 | -0·99\*\*\* | 0·47\*\*\* | 7·8\*\*\* | 167·1\* | 119·1\*\* | 5·13 |
| **South Africa** | **White** | 27·8\*\*\* | 3197\*\*\* | 39·0\*\*\* | -0·37\*\*\* | 0·36\*\*\* | 11·6\*\*\* | 169·8\*\* | 114·3\*\*\* | N/A |
| **Black** | 25·9\*\*\* | 3077\*\*\* | 37·9\*\*\* | -1·24\*\*\* | 0·35\*\*\* | 11·1\*\*\* | 165·0\*\* | 118·0\*\*\* | 4·62 |
| **Asian** | 26·3\*\*\* | 2911\*\*\* | 38·8\*\*\* | -0·77\*\*\* | -0·58\*\*\* | 11·6\*\*\* | 167·1\*\* | 111·0\*\*\* | 4·86 |
| **Other** | 25·6\*\*\* | 3007\*\*\* | 38·9\*\*\* | -1·13\*\*\* | -0·51\*\*\* | 10·7\*\*\* | 164·9\*\* | 116·1\*\*\* | 4·63 |
|  |  |  |  |  |  |  |  |  |  |  |  |
| **Maternal****height****(correlation)** | **Brazil** |  | -0·00 | 0·18\*\*\* | 0·04\*\* | 0·38\*\*\* | 0·13\*\*\* | 0·19\*\*\* | 0·38\*\*\* | 0·03 | -0·01 |
| **Guatemala** |  | -0·01 | 0·14\*\*\* | -0·02 | 0·30\*\*\* | 0·07\* | 0·10\*\*\* | 0·32\*\*\* | 0·03 | 0·01 |
| **India** |  | -0·02 | 0·09\*\*\* | -0·00 | 0·20\*\*\* | 0·08\*\*\* | 0·04 | 0·14\*\*\* | -0·03 | 0·07\* |
| **Philippines** |  | 0·06\*\* | 0·20\*\*\* | 0·01 | 0·32\*\*\* | 0·14\*\*\* | 0·13\*\*\* | 0·34\*\*\* | 0·04 | -0·00 |
| **South Africa** |  | 0·01 | 0·09\*\*\* | 0·02 | 0·16\*\*\* | 0·03 | 0·04 | 0·27\*\*\* | 0·09\*\*\* | 0·02\* |
| **Breastfeeding duration****(correlation)** | **Brazil** |  | 0·09\*\*\* | 0·09\*\*\* | 0·04\* | -0·01 | -0·05\*\*\* | 0·02 | 0·02 | 0·02 | 0·00 |
| **Guatemala** |  | 0·13\*\*\* | 0·06 | 0·03 | 0·13\*\*\* | -0·11\*\* | -0·02 | 0·05 | 0·07 | 0·06 |
| **Philippines** |  | 0·04\* | 0·05\*\* | 0·04\* | -0·09\*\*\* | -0·12\*\*\* | -0·20\*\*\* | -0·05\* | -0·01 | 0·03 |
| **South Africa** |  | -0·01 | 0·04 | 0·01 | -0·12\*\*\* | 0·04 | 0·00 | 0·00 | 0·04 | -0·04 |
| **Parity****(correlation)** | **Brazil** |  | 0·53\*\*\* | 0·07\*\*\* | -0·04\* | -0·16\*\*\* | -0·09\*\*\* | -0·22\*\*\* | -0·06\*\*\* | -0·01 | -0·00 |
| **Guatemala** |  | 0·67\*\*\* | 0·21\*\*\* | 0·01 | -0·04 | 0·03 | -0·10\*\*\* | -0·01 | -0·00 | 0·02 |
| **India** |  | 0·50\*\*\* | 0·08\*\*\* | 0·07\* | -0·21\*\*\* | -0·11\*\*\* | -0·19\*\*\* | -0·12\*\*\* | -0·03 | -0·05 |
| **Philippines** |  | 0·64\*\*\* | 0·17\*\*\* | 0·03 | -0·20\*\*\* | -0·06\*\* | -0·14\*\*\* | -0·03 | -0·01 | 0·04 |
| **South Africa** |  | 0·68\*\*\* | 0·08\*\*\* | 0·06\*\* | -0·06\* | -0·02 | -0·09\*\*\* | 0·04 | 0·10\*\*\* | 0·00 |
|  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |

All participants in India were married. N/A=no available data. The Brazil, India and South Africa studies were set in exclusively urban areas. The Guatemala study was set in an exclusively rural area. Participants in India and the Philippines were classified as “Asian” and in Guatemala as “Other”. Breastfeeding duration was not available for India. \* signifies p<0·05; \*\* p<0·01; \*\*\* p<0·001. P-values for marital status are from a 2-sample t-test; those for race are from a 3 degree of freedom F-test

**Table 3: Odds ratios for low birth weight, pre-term birth, 2-year stunting and wasting, non-completion of secondary education, and adult overweight/obesity, elevated blood pressure and abnormal glucose tolerance**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Maternal age (y)** | **Low Birth Weight** | **Pre-term****birth** | **2-year Stunting**  | **2-year Wasting**  | **Non-completion** **of 2O schooling** | **Adult over-weight/ obesity** | **Adult elevated blood pressure** | **Adult IFG/DM** |
| **Model 1** (adjusted for sex only) |
| **<19** | **1·43** | 1·26,1·62 | **1·44** | 1·21,1·72 | **1·37** | 1·20,1·56 | **1·12** | 0·86,1·46 | **1·32** | 1·15,1·51 | **1·07** | 0·92,1·25 | **1·00** | 0·87,1·16 | **0·87** | 0·64,1·18 |
| **20-24** | **1·00** | ref | **1·00** | ref | **1·00** | ref | **1·00** | ref | **1·00** | ref | **1·00** | ref | **1·00** | ref | **1·00** | ref |
| **25-29** | **0·83** | 0·75,0·92 | **0·91** | 0·78,1·06 | **0·84** | 0·76,0·93 | **0·91** | 0·75,1·11 | **0·80** | 0·72,0·90 | **0·96** | 0·84,1·08 | **1·05** | 0·94,1·19 | **0·98** | 0·78,1·23 |
| **30-34** | **0·82** | 0·72,0·93 | **0·91** | 0·77,1·08 | **0·93** | 0·83,1·04 | **1·05** | 0·84,1·31 | **0·86** | 0·76,0·98 | **1·06** | 0·92,1·21 | **1·11** | 0·97,1·27 | **0·69** | 0·52,0·91 |
| **≥35** | **0·94** | 0·81,1·08 | **1·30** | 1·08,1·57 | **1·18** | 1·03,1·35 | **0·97** | 0·74,1·28 | **0·99** | 0·85,1·16 | **1·01** | 0·86,1·19 | **1·08** | 0·92,1·26 | **1·06** | 0·79,1·41 |
| P1 | <0·001 | 0·29 | 0·02 | 0·64 | <0·001 | 0·76 | 0·17 | 0·86 |
| P2 | <0·001 | <0·001 | <0·001 | 0·16 | <0·001 | 0·74 | 0·35 | 0·29 |
| **Model 2** (adjusted for sex and socio-economic factors) |
| **<19** | **1·36** | 1·19,1·56 | **1·35** | 1·12,1·62 | **1·23** | 1·06,1·41 | **1·05** | 0·80,1·38 | **1·13** | 0·97,1·31 | **1·11** | 0·95,1·29 | **1·00** | 0·86,1·16 | **0·87** | 0·64,1·19 |
| **20-24** | **1·00** | ref | **1·00** | ref | **1·00** | ref | **1·00** | ref | **1·00** | ref | **1·00** | ref | **1·00** | ref | **1·00** | ref |
| **25-29** | **0·87** | 0·78,0·97 | **0·91** | 0·77,1·06 | **0·88** | 0·79,0·98 | **0·95** | 0·77,1·16 | **0·87** | 0·77,0·99 | **0·95** | 0·84,1·08 | **1·04** | 0·93,1·18 | **0·98** | 0·78,1·23 |
| **30-34** | **0·83** | 0·73,0·94 | **0·92** | 0·77,1·10 | **0·87** | 0·77,0·99 | **0·98** | 0·78,1·23 | **0·87** | 0·76,1·01 | **1·05** | 0·91,1·21 | **1·10** | 0·96,1·25 | **0·69** | 0·52,0·92 |
| **≥35** | **0·92** | 0·79,1·07 | **1·28** | 1·04,1·56 | **0·97** | 0·83,1·13 | **0·79** | 0·59,1·06 | **0·88** | 0·74,1·05 | **1·02** | 0·87,1·21 | **1·06** | 0·90,1·24 | **1·05** | 0·78,1·43 |
| P1 | <0·001 | 0·69 | 0·001 | 0·19 | 0·001 | 0·59 | 0·30 | 0·88 |
| P2 | <0·001 | <0·001 | 0·003 | 0·92 | 0·10 | 0·56 | 0·35 | 0·22 |
| **Model 5** (adjusted for sex, socio-economic factors, maternal height, breastfeeding duration and parity) |
| **<19** | **1·18** | 1·02,1·36 | **1·26** | 1·03,1·53 | **1·46** | 1·25,1·70 | **1·11** | 0·83,1·49 | **1·38** | 1·18,1·62 | **1·10** | 0·94,1·29 | **0·95** | 0·81,1·11 | **0·87** | 0·63,1·20 |
| **20-24** | **1·00** | ref | **1·00** | ref | **1·00** | Ref | **1·00** | Ref | **1·00** | Ref | **1·00** | Ref | **1·00** | Ref | **1·00** | Ref |
| **25-29** | **0·96** | 0·85,1·08 | **0·96** | 0·81,1·14 | **0·72** | 0·63,0·81 | **0·84** | 0·68,1·04 | **0·71** | 0·62,0·81 | **0·98** | 0·86,1·12 | **1·07** | 0·94,1·21 | **0·98** | 0·77,1·25 |
| **30-34** | **0·94** | 0·82,1·09 | **0·96** | 0·79,1·18 | **0·63** | 0·54,0·73 | **0·82** | 0·63,1·06 | **0·63** | 0·53,0·74 | **1·12** | 0·96,1·30 | **1·13** | 0·97,1·31 | **0·69** | 0·51,0·94 |
| **≥35** | **1·03** | 0·86,1·23 | **1·33** | 1·05,1·67 | **0·64** | 0·54,0·77 | **0·66** | 0·48,0·90 | **0·59** | 0·48,0·71 | **1·13** | 0·94,1·36 | **1·08** | 0·90,1·29 | **1·03** | 0·74,1·44 |
| P1 | 0·14 | 0·37 | <0·001 | 0·01 | <0·001 | 0·44 | 0·18 | 0·94 |
| P2 | 0·001 | <0·001 | <0·001 | 0·32 | 0·001 | 0·69 | 0·09 | 0·16 |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

P1: p value for linear association; P2: p value for quadratic association; p values derived using logistic regression, with maternal age and maternal age2 as continuous variables and outcomes as binary; IFG=Impaired fasting glucose, DM=diabetes, N/A=not applicable

**Figure legends**

**Figure 1: Associations of maternal age with birth weight, gestational age, 2-year height and weight-for-height Z scores, years of schooling, adult height, systolic blood pressure and fasting plasma glucose**

*Footnote:* Each point represents the amount by which the outcome differs from the value obtained for offspring of mothers aged 20-24 years. These estimates are shown with 95% confidence intervals, and they are obtained by pooling across all five studies. Three of the five models discussed in the text are included. Model 1 is adjusted for sex and age. Model 2 is further adjusted for maternal marital status, schooling, wealth, race and urbanicity. Models 3 and 4, in which further adjustment is made for maternal height and breastfeeding duration respectively, are not shown because the results were similar to Model 2. Model 5 is further adjusted for parity. Four p-values are shown: “*p lin*” is from a test for linear trend in the outcome with mother’s age; “*p quad*” is from a test for quadratic trend in the outcome with mother’s age; “*het lin*” is the F-test p-value for heterogeneity in the linear trends in the five studies; “*het quad*” is the F-test p-value for heterogeneity in the quadratic trends in the five studies. All four p values are derived using maternal age as a continuous variable.

**Figure 2: Relationship of maternal age and parity to birth weight, 2-year height Z-score and years of schooling (adjusted for maternal socio-economic status and height)**

*Footnote:*Outcomes (birth weight, height Z score at age two years, and schooling) were adjusted for study site and sex. Within each parity group (1, 2, 3, 4+) cubic regression was used to model how maternal age was associated with each outcome. The fitted regression lines were plotted for the central 95% of maternal ages for the parity group.