Household income, fetal size and birth weight: an analysis of eight populations

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ABSTRACT

Background The age at onset of the association between poverty and poor health is not understood. Our hypothesis was that individuals from highest household income (HI), compared to those with lowest HI, will have increased fetal size in the second and third trimester and birth.

Methods. Second and third trimester fetal ultrasound measurements and birth measurements were obtained from eight cohorts. Results were analysed in cross-sectional two-stage individual patient data (IPD) analyses and also a longitudinal one-stage IPD analysis.

Results The eight cohorts included 21 714 individuals. In the two-stage (cross-sectional) IPD analysis, individuals from the highest HI category compared with those from the lowest HI category had larger head size at birth (mean difference 0.22 z score (0.07, 0.36)), in the third trimester (0.25 (0.16, 0.33)) and second trimester (0.11 (0.02, 0.19)). Weight was higher at birth in the highest HI category. In the one-stage (longitudinal) IPD analysis which included data from six cohorts (n=11 062), head size was larger (mean difference 0.13 (0.03, 0.23)) for individuals in the highest HI compared with lowest category, and this difference became greater between the second trimester and birth. Similarly, in the one-stage IPD, weight was heavier in second highest HI category compared with the lowest (mean difference 0.10 (0 .00, 0.20)) and the difference widened as pregnancy progressed. Length was not linked to HI category in the longitudinal model.

Conclusions The association between HI, an index of poverty, and fetal size is already present in the second trimester.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Poverty is associated with poor health outcomes throughout the life course.

⇒ Indices of poverty are associated with reduced birth weight.

WHAT THIS STUDY ADDS

⇒ Across eight different populations, we report an association between lower household income (HI) and reduced anthropometric measurements from the second trimester onwards.

⇒ The association was seen most clearly for fetal and neonatal head size, and was also present for weight but not length.

⇒ The magnitude of the association became greater as pregnancy progresses.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE AND/OR POLICY

⇒ Interventions which soften the impact of reduced household income on maternal and fetal well-being during all stages of pregnancy are needed, including those which encourage engagement with maternity services.

INTRODUCTION

Poverty is associated with reduced birth weight,[1 2] suggesting that exposure to poverty adversely impacts on health and well-being in antenatal life and extending throughout the life course.[3] Evidence that reduced birth weight is the first sign of health inequalities on the life course can be seen in studies linking small for gestational age (SGA) and increased risk for all cause adult mortality,[4] and in particular cardiovascular mortality.[4] There is a complex relationship between poverty, social determinants of health[5] and birth weight (online supplemental figure 1). Collectively these observations suggest that SGA is a consequence of poverty and is on a causal pathway between poverty and non-communicable diseases. SGA is also associated with lower childhood cognitive outcomes[6] and thus may be both a consequence and cause of reduced income.

Indices of poverty have been associated with reduced fetal measurements at birth [1 7] and a small number of randomised controlled trials have evaluated interventions aimed at reducing poverty in pregnant mothers, and one found that cash transfer programmes may lead to increased birth weight.[8]

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Further understanding is required to determine how close poverty and size at birth are on any causal pathway.

Our group has collected data from eight existing birth cohorts to study the relationship between household income (HI) and birth size. We reasoned that if a clear relationship was seen between household income ('the exposure') and size at birth ('the outcome') across several heterogeneous populations (differing by environment, lifestyle, ethnicity and healthcare setting), with adjustment for strong predictors of fetal size, this would argue for a relationship where HI was closely related to birth size. Our cohorts were selected because they also had fetal size in the second and third trimesters; this allowed us to determine the gestation at which any association between HI and birth size was first apparent.

Our hypothesis was that poverty (as evidenced by HI) will be associated with reduced fetal size in the second and third trimester and birth across populations from different countries. Our outcomes were fetal and birth measurements, SGA at birth and deceleration of fetal growth (DFG).

METHODS

Study design

Data custodians of populations holding fetal ultrasound scan measurements identified from review articles[9–11] were contacted and asked to contribute individual patient data (IPD). Where it was not possible to share IPD, custodians were asked to provide aggregated descriptive data and analyse data locally for inclusion in a two-stage IPD analysis (according to a prespecified statistical analysis plan set out in our protocol, see online supplemental file 1). The outcomes were standardised anthropometric measurements made in the second and third trimesters (estimated fetal weight (EFW), biparietal diameter (BPD) and femur length (FL)) and at birth (weight, occipitofrontal circumference (OFC) and crown heel length (CHL)). Additional outcomes were SGA defined as <5th centile[12] and DFG, defined as a fall of ≥40 centiles between second trimester EFW and birth weight or, where EFW was <40th centile, we defined DFG as birth weight <1st centile.[12] EFW was calculated using the Hadlock formula with parameters abdominal circumference, BPD and FL.[13] The predictor of interest was HI (five categories defined by household income or parental occupation, online supplemental table 1). The analysis included one-stage and two-stage IPD (online supplemental figure 2). Cross-sectional two-stage IPD were undertaken (eg, how was HI associated with second trimester EFW adjusting for covariates?) as the principal analysis since this included the largest number of participants. Where IPD were available, one-stage IPD analysis was used for cross-sectional analysis to compare with the results from the two-stage IPD, and also for longitudinal analysis (eg, how was HI associated with second and third trimester EFW and birth weight? and how did this relationship change over time?).

Population details

The populations included were EDEN,[14] Generation R,[15] INMA,[16] London,[17] Project Viva,[18] Saudi,[19] SEATON[20] and Scandinavian SGA.[21] Details of each population are presented in online supplemental file 1. For INMA, London and SEATON, the index of HI was derived from the UK classification by paternal job and for SGA-Scand by maternal job, that is, classes I, II, IIIa, IIIb, IV and V (with IIIa and IIIb combined). For the remaining populations the annual household income was used (see online supplemental table 1). IPD were not provided from the Project Viva and Generation R populations. Maternal height was not available for the Saudi population, and the 50% centile height for girls aged 16 years (155 cm) was imputed for all individuals.[22] Generation R and SEATON included multiple pregnancies but did not include anthropometric measurements for these pregnancies.

Analysis

Standardisation of measurements

Fetal ultrasound measurements were standardised for gestational age using within-population values according to a standard method which derives z scores from mean and SD stratified by gestational weeks.[23] For between-population comparison, where IPD were available, the datasets were merged and standardised for gestation[23] as if they were from a single population. Birth measurements were standardised according to the WHO child growth standards[24] (which adjusts for gender) for all populations except Project Viva where an internal reference standard was used.

Two stage IPD analysis

Review Manager (V. 5.3) software was used to combine the mean differences in anthropometric measurements between highest HI category and the lowest HI category (reference) for each population (adjusted for fetal sex, population, maternal height, maternal smoking (categorised as yes or no), parity (categorised as 0, 1, 2 and >2) and maternal age). Analyses were also stratified for fetal sex and maternal smoking status. Random-effects models were applied where the I^2 value was >30%, otherwise fixed-effects models were used.

One-stage IPD analysis

For cross-sectional analyses, general linear regression models were created to compare differences in anthropometric measurements between the highest and lowest HI category and also the trends across all five HI categories, adjusting for the following variables: fetal sex, birth cohort population, maternal height, maternal smoking, parity and maternal age. For the longitudinal analysis, multilevel models (with AR1 covariance structure) were created to relate HI category to fetal measurements in the second and third trimester and at birth (ie, three levels). These analyses were adjusted for the variables included in the cross-sectional analysis. For weight, EFW in the second and third trimesters and birth weight were included. For head size, BPD in the second and third trimesters and OFC at birth were included. Finally, for length FL in the second and third trimester and CHL at birth were used. The following interaction terms were included: HI category*gestation (ie, second or third trimester or birth); HI category*population; and HI category*gestation*population. Logistic regression models were created to relate SGA (yes/no) and DFG (yes/no) to HI category adjusting for sex, population, maternal height, maternal smoking, parity and maternal age. IBM SSPS V.25.0 and STATA V.15 were used.

RESULTS

Population details

The eight populations included 21 714 individuals. IPD was provided for 11 062 individuals from six populations. Maternal and fetal characteristics differed between populations, for example the proportion in the highest HI category ranged from 1% to 61% and smoking prevalence from <1% to 57%, table 1. Not all anthropometric measurements were available from each population.

Table 1 Descriptive summary of characteristics of participants in the included populations

		Population							
		EDEN (France)	Generation R (Netherlands)	INMA (Spain)	London	Project Viva (USA)	Saudi	SEATON (UK)	Scandinavia SGA (Sweden, Norway)
Mean maternal age at delivery, year (SD)		25.5 (4.9)	29.9 (5.4)	32.0 (4.2)	30.8 (5.6)	32.6 (5.2)	28.3 (5.3)	29.4 (5.6)	28.5 (4.3)
% Maternal smoking during pregnancy (n/n)		18% (331/1891)	27% (2188/8242)	32% (765/2410)	28% (462/1650)	13% (266/2107)	0.5% (4/501)	30% (593/1999)	57% (997/1855)
Parity	0	45% (847/1902)	55% (5178/9400)	56% (1391/2475)	53% (870/1650)	48% (1017/2128	28% (243/878)	49% (986/1999)	
	1	37% (698/1902)	30% (2835/9400)	37% (916/2475)	30% (490/1650)	36% (761/2128)	24% (209/878)	35% (693/1999)	69% (1342/1943)
	2	14% (258/1902)	11% (984/9400)	6% (143/2475)	10% (164/1650)	12% (253/2128)	19% (170/878)	12% (231/1999)	31% (601/1943)
	≥3	5% (89/1902)	4% (403/9400)	1% (25/2475)	8% (126/1650)	5% (97/2128)	29% (256/878)	5% (89/1999)	
Mean maternal height (SD), cm		164 (6) n=1881	168 (7) n=6628	163 (6) n=2476	165 (7) n=1644	165 (7) n=2118	NA	163 (6) n=1999	166 (6) n=1931
Mean maternal weight (SD), kg		62.1 (13.3) n=1867	69.5 (13.3) n=8838	NA	64.0 (11.4) n=1548	67.7 (15.9) n=2116	NA	66.9 (13.3) n=1999	59.2 (10.2) n=1928
Household income	1 (most poor)	17% (317/1895)	12% (835/6712)	13% (315/2476)	11% (117/1650)	NA	10% (103/1076)	3% (45/1818)	9% (133/1520)
	2	30% (564/1895)	14% (912/6712)	40% (993/2476)	13% (206/1650)	5% (85/1874)	20% (214/1076)	9% (162/1818)	26% (398/1520)
	3	26% (499/1895)	8% (564/6712)	26% (639/2476)	22% (355/1650)	11% (208/1874)	32% (345/1076)	37% (671/1818)	58% (877/1520)
	4	16% (294/1895)	12% (753/6712)	12% (289/2476)	42% (688/1650)	23% (435/1874)	20% (213/1076)	29% (522/1818)	6% (98/1520)
	5 (least poor)	12% (221/1895)	54% (3648/6712)	10% (240/2476)	14% (224/1650)	61% (1146/1874)	18% (201/1076)	23% (418/1818)	1% (14/1520)
% Male offspring (n/n)		53% (1000/1903)	51% (4812/9503)	48% (1197/2473)	52% (767/1484)	51% (1096/2128)	52% (547/1063)	51% (963/1906)	51% (988/1944)
Mean second trimester BPD z score†		0.0904 (n=1873)	NA	0.1027 (n=2312)	0.2727 (n=1574)	NA	−0.3536 (n=525)	−0.6140 (n=1482)	0.1408 (n=1844)
Mean second trimester AC z score†		0.0923 (n=1820)		−0.0124 (n=2307)	−0.1825 (n=1560)		−0.1680 (n=562)	0.4222 (n=568)	NA
Mean second trimester FL z score†		0.1106 (n=1865)		0.1498 (n=2306)	−0.1059 (n=1549)		0.0130 (n=585)	−0.3263 (n=1476)	0.0476 (n=1816)
Mean second trimester EFW z score†		0.1201 (n=1797)		0.0470 (n=22 920	−0.1799 (n=1530)		−0.0776 (n=480)	−0.0195 (n=562)	NA
Mean third trimester BDP z score†		−0.1157 (n=1816)		−0.1013 (n=2238)	0.3706 (n=1216)		−0.4207 (n=442)	−0.3132 (n=279)	0.1900 (n=1366)
Mean third trimester AC z score†		−0.1786 (n=1792)		0.1146 (n=2233)	0.0430 (n=1378		−0.0835 (n=631)	0.2198 (n=262)	NA
Mean third trimester FL z score†		−0.1157 (n=1814)		0.0624 (n=2227)	−0.0699 (n=1378)		−0.0013 (n=635)	−0.1489 (n=279)	0.1548 (n=1354)
Mean third trimester EFW z score†		−0.1812 n=1771		0.0772 (n=2213)	0.0977 (n=1213)		−0.0773 (n=434)	0.2645 n=246)	NA
Mean birth weight (SD), g		3211 (428) n=1741	3409 (564) n=6591‡	3277 (442) n=2426	3433 (497) n=1443	3500 (525) (n=2082)	3117 (446) n=938	3411 (625) n=1508	35 156 (514) n=1667
Mean birth length (SD), cm		50 (2) n=1789	NA	50 (2) n=2377	50 (2) n=1409	50 (2) (n=1055)	51 (3) n=911	50 (2) n=1421	50 (2) n=16 559
Mean occipitofrontal circumference (SD), cm		34.2 (1.6) n=1790	NA	34.3 (1.4) n=2379	34.6 (1.5) n=1416	34.1 (1.3) (n=1161)	34.1 (1.4) n=896	35.0 (1.3) n=1424	35.09 (1.4) n=1650

For the six populations where individual patient data were available (ie, excluding Generation R and Project Viva), all variables except offspring sex differed between populations (p<0.001).
Fetal size ultrasound Z scores were standardised across six populations to allow direct comparison using the methodology of Cantonwine *et al*.[23]
*Maternal age at recruitment.
†These z scores were derived using data from the six populations where individual data were available and therefore allow direct comparison between populations.
‡Numbers for infants whose maternal deprivation status was determined.
BPD, biparietal diameter; FEW, estimated fetal weight; FL, femur length; NA, not available.

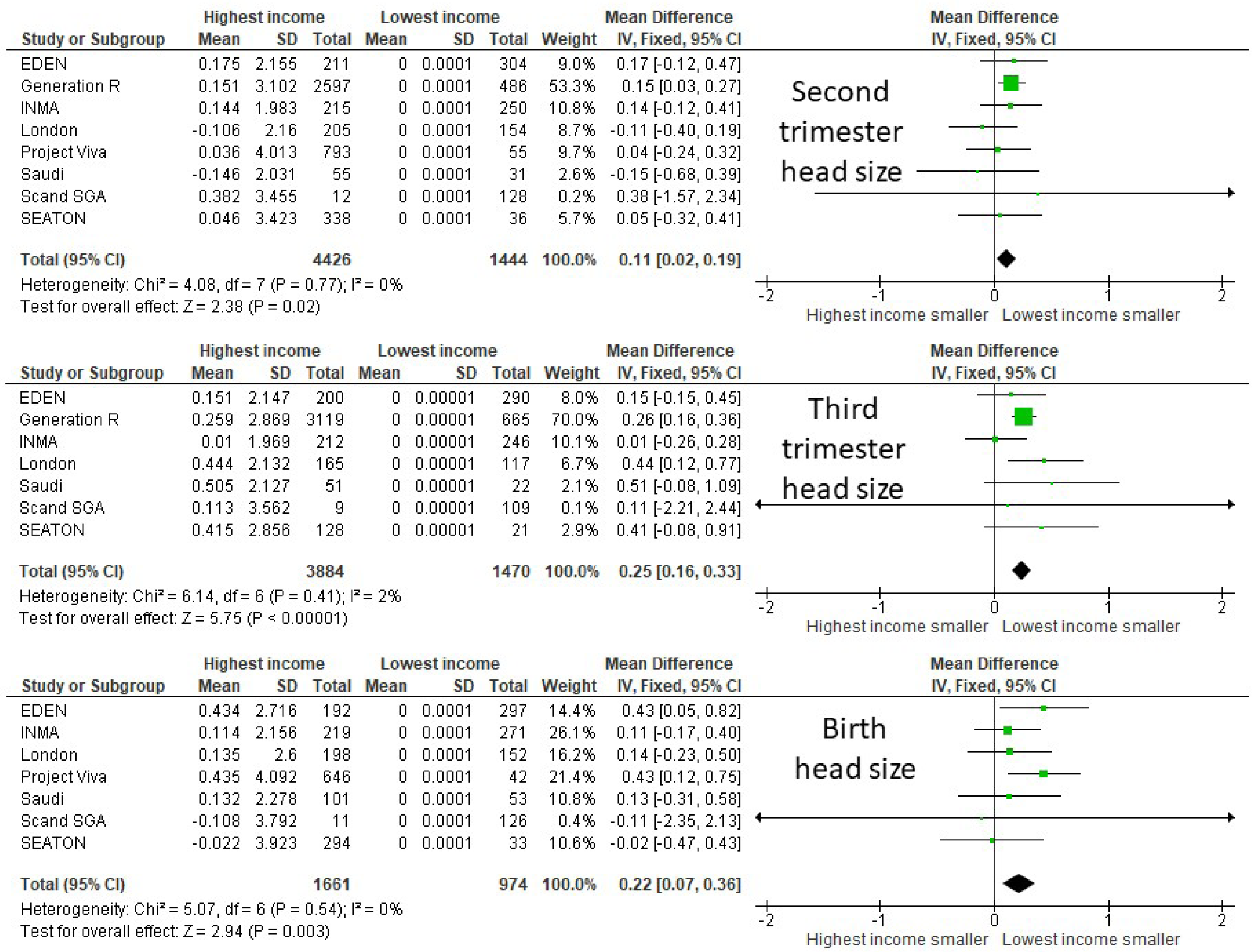

Figure 1 Forest plots from the two-stage individual patient data analysis demonstrating the difference in head size between individual in the highest and lowest household income categories across the populations where data were available. Second and third trimester head size was biparietal diameter. Birth head size was occipitofrontal circumference. The results from each population were adjusted for sex, maternal height, maternal smoking, parity and maternal age.

Two stage IPD analysis: cross-sectional analysis

Mean birth weight (online supplemental figure 3) and OFC (figure 1) were higher in those in the highest compared with the lowest HI category by 0.24 z scores (95% CI 0.12 to 0.35) and 0.22 z scores (95% CI 0.07 to 0.36), respectively (table 2). Third and second trimester BPD were also higher in the highest HI category by a mean of 0.25 z scores (95% CI 0.16 to 0.33) and 0.11 z scores (95% CI 0.02 to 0.19), respectively (figure 1, table 2). Second trimester FL was shorter (mean difference 0.09 z scores (0.01, 0.17)) for the highest compared with the lowest HI category, (online supplemental figure 4). When data from the Generation R cohort (the largest contributor of data) was excluded from the analysis, results were mostly unchanged although the difference in second trimester BPD was no longer significant (online supplemental table 2). The results for all individuals were similar to when males and females were considered separately (online supplemental tables 3 and 4). When offspring of mothers who smoked were considered separately (online supplemental table 5), the magnitude of differences between highest and lowest HI categories for birth weight, birth length and third trimester EFW and FL was greater compared with the results in table 2. Online supplement table 6 presents measurements of individuals whose mothers did not smoke. Within individual populations, measurements were larger for those in the highest compared with the lowest HI category as follows: Second trimester BPD for participants in Generation R; third trimester BPD for Generation R and London; OFC for Eden and Project Viva; birth weight for Generation R and Project Viva, (online supplemental figure 3); in Generation R second and third trimester FL was shorter and for Project Viva CHL was longer in the highest HI group compared with the lowest HI group (online supplemental figure 4).

One-stage IPD: cross-sectional analysis

OFC was higher for the highest HI relative to lowest category (mean difference 0.18 z scores (95% CI 0.07 to 0.28), and OFC differed across the five HI categories (table 3). Third trimester BPD was larger in the higher relative to lowest HI category (0.14 (95% CI 0.03 to 0.24), and the comparison for second trimester BPD approached significance in the one-stage IPD (p=0.070). These results were not substantially altered by excluding data from the Saudi population (where maternal height was imputed) (online supplemental table 7). The difference in birth weight between highest and lowest HI categories seen in the two stage IPD was not present in the one-stage analysis but there was a

Table 2 Results from two-stage individual patient data analysis showing cross-sectional differences in Z scores of anthropometric measurements in second and third trimester and at birth between individuals in the highest and lowest household income (HI) categories

		Mean difference between highest and lowest HI category	No of populations	No in highest HI category	No in lowest HI category	I^2
Birth measurements	Birth weight	0.24 (0.12, 0.35) p<0.0001	8	5300	1739	25%
	Crown heel length	−0.01 (−0.21, 0.20) p=0.95	7*	1597	933	38%
	Occipito frontal circumference	0.22 (0.07, 0.36) p=0.003	7*	1661	974	0%
Third trimester measurements	Estimated fetal weight	0.08 (−0.01, 0.18) p=0.08	6†	3923	1384	0%
	Femur length	−0.07 (−0.16, 0.01) p=0.080	7‡	4008	1536	28%
	Biparietal diameter	0.25 (0.16, 0.33) p<0.001	7‡	3884	1470	2%
Second trimester measurements	Estimated fetal weight	0.05 (−0.05, 0.14) p=0.32	7§	4275	1436	0%
	Femur length	−0.09 (−0.17, −0.01) p=0.003	8	4958	1757	6%
	Biparietal diameter	0.11 (0.02, 0.19) p=0.02	8	4426	1444	0%

Data were not available from all populations for the following analyses.
The analyses from each cohort adjusted for fetal sex, maternal age, parity, height and smoking.
*Generation R.
†Project Viva and Scandinavian SGA.
‡Project Viva.
§Scandinavian SGA.
SGA, small for gestational age.

significant change in birth weight across all five HI categories. In the one-stage analyses, the difference in second trimester FL between highest and lowest HI categories in the two stage IPD (table 2) was not apparent in the one-stage model, althoughthe mean difference in second trimester FL approached significance (p=0.068) with the longer measurement being associated with higher HI (table 3). There were 498 (4.8%) individuals with low birth weight (LBW, ie, <2.5 kg), and the OR for LBW were 1.6 (95% CI 1.0 to 2.6) p=0.046 for the lowest vs highest HI category.

One-stage IPD: longitudinal analysis

Weight in the middle and second highest HI categories was higher than the lowest HI category, and the interaction term between HI category and gestation (ie, second trimester, third trimester and birth) was significant (p=0.017) (table 4 and online supplemental figure 5). Head size was greater for individuals in the second highest and highest HI category relative to lowest HI category and interaction terms were significant for both HI category and trimester (p=0.027) and HI category, trimester and population (p=0.005) (table 4). Length did not differ between HI categories (table 4).

SGA AND DFG RATE

The proportions with SGA in highest HI to lowest HI categories were as follows: 6.2% (75/1210), 4.9% (97/1977), 5.5% (164/2962), 7.3% (164/2232) and 6.9% (79/11530. With adjustment, the p value for trend across HI categories was 0.033. The proportions with DFG in highest HI to lowest HI categories were as follows: 14.4% (117/810), 11.0% (146/1326), 14.1% (239/1699), 15.0% (257/1709) and 14.6% (110/752), p=0.085.

DISCUSSION

This study related household income (HI) to fetal size and growth between the second trimester and birth using data collected from eight different countries. We found that higher HI was associated with larger fetal head size and weight but not

Table 3 Results from one-stage individual patient data analysis showing cross-sectional differences in Z scores for anthropometric measurements in second and third trimester and at birth measurements between individuals in the highest and lowest household income (HI) categories also the trend across HI categories

		One-stage individual patient data analysis			
		P value for trend across HI categories	Mean difference between highest and lowest HI category	No in highest HI category	No in lowest HI category
Birth measurements	Birth weight	0.023	0.05 (−0.05, 0.15) p=0.31	1065	901
	Crown heel length	0.070	−0.07 (−0.18, 0.04) p=0.22	1034	903
	Occipito frontal circumference	0.001	0.18 (0.07, 0.28) p=0.001	1033	903
Third trimester measurements	Estimated fetal weight	0.285	0.08 (−0.03, 0.19) p=0.14	736	682
	Femur length	0.623	0.03 (−0.07, 0.13) p=0.54	807	833
	Biparietal diameter or head circumference	0.018	0.14 (0.03, 0.24) p=0.009	765	805
Second trimester measurements	Estimated fetal weight	0.117	0.07 (−0.04, 0.17) p=0.22	803	729
	Femur length	0.161	0.09 (−0.01, 0.18) p=0.068	1040	898
	Biparietal diameter or head circumference	0.231	0.09 (−0.01, 0.18) p=0.070	1036	903

Data from the following populations were included: EDEN, INMA, London, Saudi, SEATON and Scandinavian SGA. The analysis adjusted for sex, maternal age, parity, height, smoking and the population. Maternal height in the Saudi population was missing and a value of 155 cm was imputed.[22] Online supplemental table 2 presents results excluding the Saudi population.
SGA, small for gestational age.

Table 4 Results from the longitudinal one-stage IPD analysis where mixed level models were used to determine whether the relationship between household income (HI) and fetal anthropometric measurements changed over the period between the second trimester and birth

Anthropometric measurement	Household income category					Interaction term between HI category and trimester	Interaction term between income category, trimester and population
	Lowest HI category	Second lowest HI category	Middle HI category	Second highest HI category	Highest HI category		
Mean z score weight relative to lowest income category (95% CI)	Reference	0.03 (−0.06 to 0.12)	0.09 (0.00 to 0.18) p=0.044	0.10 (−0.00 to 0.20) p=0.036	0.08 (−0.03 to 0.19)	P=0.017	NS
Mean z score head size relative to lowest income category (95% CI)	Reference	0.03 (−0.06 to 0.12)	0.06 (−0.03 to 0.14)	0.12 (0.03 to 0.23) p=0.002	0.13 (0.03 to 0.23) p=0.004	P=0.027	P=0.005
Mean z score length relative to lowest income category (95% CI)	Reference	0.03 (−0.06 to 0.11)	0.07 (−0.02 to 0.15)	0.06 (−0.03 to 0.15)	0.03 (−0.07 to 0.13)	NS	NS

In these analyses data from Project Viva and Generation R were not included. Weight was defined as estimated fetal weight in the second and third trimesters and actual weight at birth. Head size was defined as biparietal diameter or head circumference in the second and third trimesters and occipitofrontal circumference at birth. Length was defined as femur length in the second and third trimesters and crown heel length at birth. All measurements were z scores using the method of Cantonwine *et al*[23] using each individual population as its own reference and WHO standard for birth measurements.[24] The covariates also included in the analysis were sex, parity, maternal smoking, maternal age and maternal height. The regression coefficients for anthropometric measurements are from main effects models. The p values are from models which included interaction terms between trimester * income category and between trimester * income category * population.
IPD, individual patient data; NS, not significant.

length from the second half of pregnancy compared with lowest HI. These results argue for a relationship where HI is closely related to birth size. Interventions aimed at softening the impact of poverty on pregnant mothers could reduce incidence of SGA and the associated burden of excessive morbidity and mortality throughout the life course. Systematic reviews have found that nutritional[25] and smoking cessation[26] interventions may reduce SGA incidence, but more large high-quality randomised controlled trials are needed.

There is no ideal index of socioeconomic status or poverty and we acknowledge that HI as defined in our study is best considered a partial measure of 'socioeconomic disadvantage'. Socioeconomic disadvantage is a multidimensional characteristic. Alternative indices of socioeconomic status or poverty include duration of parental full-time education and deprivation, and poverty itself can be defined in many ways including absolute or relative poverty.[27] The lack of a gold-standard definition of socioeconomic status or poverty means that, for example, in Norway a truck driver would be categorised as having lower social class than a physician but nonetheless the former might have a higher HI. Household income is the most widely used measure of (relative) poverty in the European Union[27] where the majority of our cohorts were recruited. Despite the limitation of using HI (as defined in our study) across eight different populations we were able to find a consistent relationship with fetal size and growth and this suggests that there is a close and potentially causal relationship between socioeconomic disadvantage and fetal well-being.

The association between increased HI and increased size was most clearly seen for head size, and was also present for weight but not for length. We cannot explain the lack of association between HI and length; increased variation in ultrasound measurement of length compared with head size[28] could explain a lack of association with antenatal length, but not with birth length since measurement error will be comparable between length and head size at birth. Our study design reduced confounding by including important covariates in the analysis and also by incorporating data from populations where lifestyle, environment and healthcare systems differed. Although we do not provide evidence of causation, our results fulfil these Bradford Hill criteria for causation[29]: plausibility, consistency, temporality and biological gradient. More effective interventions in the first half of pregnancy, or preferably preconceptionally, which lessen the impact of poverty on fetal growth need to be developed. Such interventions could be expected to lessen morbidity and mortality from the perinatal period and throughout the life course.[4]

The relationship between higher HI and fetal size differed for measurement of head size, weight and length. Growth in fetal head size, weight and length may genuinely be differentially affected by different exposures, for example the association between maternal smoking and small size is apparent for length in the second trimester before becoming evident for all measurements in the third trimester.[9] In contrast, increased air pollution is only consistently associated with reduced fetal head size in the third trimester but not weight and length.[11] Fetal weight but not length is reduced by factors present in the second half of pregnancy, for example, placental insufficiency, maternal malnutrition, and this might at least explain the relationship between lower HI and reduced fetal weight but not length. The inter observer variability for ultrasound measurements of head circumference is approximately 4% and twice this value for other measurements,[28] and this increased precision for measurements of head size may partly explain the clearer relationship between HI and head size relative to weight and length.

There are a number of limitations to our study. First, although the same definition of parental social class was used for four populations, different cut-offs of HI were used for the remaining four populations and this may have weakened any relation between HI and fetal and neonatal measurements. Second, in two cohorts (Generation R and Project Viva) the majority of participants were in the highest HI category and under-representation of individuals in the lowest HI category may have artificially reduced the magnitude of an association between higher HI and larger size. Differences in head and weight measurements were nonetheless present and these persisted in the one-stage analysis where data from the two populations were not included. Third, there were different findings for comparisons between highest and lowest HI groups for birth weight and second trimester FL between the cross-sectional two stage (table 2) and one-stage (table 3) IPD. The relationship between FL and HI is at least partly explained by inclusion of data from Generation R cohort in only the two-stage analysis where these data had a greater than 50% weight (or influence). A further limitation is that we did not consider how ethnicity may have influenced the results, but ethnic variation in at least four of the included cohorts (London, Saudi, SEATON and SGA-Scand) was very limited. Finally, our study included data collected over a 25-year period (from 1986 in Scandinavian SGA to 2011 in Saudi) and over this period environmental and social exposures may have changed weakening the associations described.

Our study was not designed to describe the mechanism where poverty leads to reduced fetal size, but we believe our findings give some useful insights. The associations described are likely to be independent of maternal smoking, an exposure known to be associated with reduced fetal size,[9] since some of the differences observed for the whole population were of greater magnitude when only offspring of mothers who smoked were considered. We cannot exclude the possibility of collider bias where smoking is part of any causal mechanism linking HI and reduced fetal size. There were two populations (Scandinavian SGA and SEATON) where there was no within-population difference for any measurement compared between highest and lowest HI categories and this might at least in part be explained by the advanced welfare state in Scandinavian countries and the UK which softened the impact of poverty on health, although in second UK population (London) third trimester head size was smaller in the lowest relative to highest HI category. An analysis which considered the potential relevance of wealth distribution within and between nations on associations between HI and fetal size was not possible due to the limited number of nations included but may be of considerable interest.

Assuming that our study design reduced the impact of lifestyle and environment on the relationship between HI and fetal size, we speculate that limited access to and engagement with healthcare services among the poorest may be relevant. Mothers in poor communities are known to engage with maternity services later into pregnancy (or not at all) compared with mothers in more affluent communities.[30] Ethnic categories who are not fluent with the language of a country are likely to live in the poorest communities and lack of understanding of local healthcare services may present a challenge to engagement with healthcare services. Poverty can make parents face difficult choices and travel to a maternity clinic may be seen as discretionary in the context of feeding and clothing a family. In addition to engagement with maternity services, pregnant mothers who have socioeconomic disadvantage also have sedentary behaviour and poor diet and these lifestyle factors may impact on fetal size and growth.[31]

In summary, our results suggest a meaningful relationship between lower HI and smaller fetal weight and head size and supports calls for antenatal interventions to prevent non communicable diseases in postnatal life.[32] Interventions could focus on the poorest communities and reasonably be expected to yield societal benefits over many decades.

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