Papers

Fetal growth and subsequent risk of breast cancer: results from long term follow up of Swedish cohort

V A McCormack, I dos Santos Silva, B L De Stavola, R Mohsen, D A Leon, H O Lithell

Abstract

Objective To investigate whether size at birth and rate of fetal growth influence the risk of breast cancer in adulthood.

Design Cohort identified from detailed birth records, with 97% follow up.

Setting Uppsala Academic Hospital, Sweden.

Participants 5358 singleton females born during 1915-29, alive and traced to the 1960 census.

Main outcome measures Incidence of breast cancer before (at age < 50 years) and after (≥ 50 years) the menopause.

Results Size at birth was positively associated with rates of breast cancer in premenopausal women. In women who weighed ≥ 4000 g at birth rates of breast cancer were 3.5 times (95% confidence interval 1.3 to 9.3) those in women of similar gestational age who weighed < 3000 g at birth. Rates in women in the top fifths of the distributions of birth length and head circumference were 3.4 (1.5 to 7.9) and 4.0 (1.6 to 10.0) times those in the lowest fifths (adjusted for gestational age). The effect of birth weight disappeared after adjustment for birth length or head circumference, whereas the effects of birth length and head circumference remained significant after adjustment for birth weight. For a given size at birth, gestational age was inversely associated with risk (P=0.03 for linear trend). Adjustment for markers of adult risk factors did not affect these findings. Birth size was not associated with rates of breast cancer in postmenopausal women.

Conclusions Size at birth, particularly length and head circumference, is associated with risk of breast cancer in women aged < 50 years. Fetal growth rate, as measured by birth size adjusted for gestational age, rather than size at birth may be the aetiologically relevant factor in premenopausal breast cancer.

Introduction

In 1990, Trichopoulos proposed the hypothesis that breast cancer may originate in utero.[1] Eight case-control studies,[2–9] one nested case-control study,[10] and one cohort study[11] have used birth weight as a marker of the in utero environment to investigate this hypothesis. Three studies found positive linear associations with birth weight,[9–11] while J shaped associations were found in four others.[3 4 6 7] The effect of other measures of birth size[3 5 9] and gestational age[5 10 17] have been examined more rarely.

We investigated possible associations between fetal growth and risk of breast cancer using data from a large Swedish cohort with long and virtually complete follow up. The cohort benefits from data on several birth characteristics and on markers of adult risk factors based on census data. These data allowed us to examine the independent effect of each measure of birth size on risk of breast cancer before and after the menopause, while controlling for some established risk factors for breast cancer. In addition, the availability of data on gestational age provide a unique opportunity to assess the effect of fetal growth rate, measured by birth size adjusted for gestational age, distinct from size at birth on risk of breast cancer.

Methods

Data sources

The Uppsala birth cohort comprises all people delivered at the Uppsala Academic Hospital during 1915-29.[12 13] The cohort was followed up initially through parish archives, which record all births, deaths, and changes of residence. Since the introduction of personal identity numbers in the 1950s records could be linked to the registers of deaths and migration and the Swedish Cancer Registry to provide the relevant data for computing incidence rates for breast cancer and to the 1960 and 1970 censuses for data on adult characteristics.

We analysed incidence of breast cancer in 5358 singleton females in this cohort for whom linkage to the 1960 census records was successful and for whom subsequent breast cancer registration (ICD-7 (international classification of diseases, seventh revision) code 170) could be ascertained through the Swedish Cancer Registry (established in 1958).

Birth characteristics recorded at the time of birth included birth weight (measured to the nearest 10 g), birth length (recorded to the nearest 0.5 cm), head circumference, gestational age (calculated as the time between the mother's last day of menses and delivery date), birth order (calculated as the mother's total previous live and stillbirths), and multiple births.

The 1960 and 1970 censuses provided information on proxy variables for some established risk factors for breast cancer. Age at first marriage and single marital status (recorded at 1960 census) were taken as correlates

Department of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London WC1E 7HT
V A McCormack
research fellow
I dos Santos Silva
clinical senior lecturer
B L De Stavola
senior lecturer
D A Leon
professor

Department of Geriatrics, Uppsala University, PO Box 609, S751-25 Uppsala, Sweden
R Mohsen
programmer
H O Lithell
professor

Correspondence to:
V A McCormack
valerie.mccormack@lshtm.ac.uk

Table 1 Baseline characteristics of eligible study participants by breast cancer status during follow up from 1960-98 and age at diagnosis, Uppsala birth cohort study. Figures are means (SD)

Characteristic	No cancer (n=4999)	Age <50 years at diagnosis (n=63)	Age ≥50 years at diagnosis (n=296)
Birth weight (g)	3396 (497)	3491 (528)	3406 (500)
Birth length (cm)	50.4 (2.2)	50.7 (2.4)	50.6 (2.3)
Ponderal index (kg/m³)	26.4 (2.7)	26.6 (3.0)	26.2 (2.4)
Head circumference (cm)	34.4 (1.4)	34.7 (1.3)	34.5 (1.5)
Gestational age (weeks)	40.0 (2.0)	39.7 (2.4)	39.9 (1.9)
Maternal age (years)	28.3 (6.5)	28.4 (6.6)	28.3 (6.1)
Age in 1960* (years)	37.6 (4.2)	35.7 (4.5)	37.4 (4.4)

*Start of follow up.

for age at first birth and a crude indicator of nulliparity, respectively; the largest number of children aged less than 15 years living in the household in 1960 or, if available, 1970 as a proxy for parity; and educational level, personal car possession, and occupation in 1960 as markers of adult socioeconomic circumstances.

Statistical methods

We categorised birth weight into four groups (<3000 g, 3000-3499 g, 3500-3999 g, ≥4000 g) for ease of comparison with other studies.[10][11] Ponderal index, a measure of weight relative to length, was calculated as weight/height[3]. Gestational age was categorised into four groups (30-38, 39, 40, and ≥41 completed weeks of gestation). Birth length, head circumference, and ponderal index were divided into approximate fifths (exact fifths could not be defined due to the discrete nature of the data).

Follow up was calculated from 1 November 1960, the census date, to the date of first diagnosis of breast cancer, emigration, death, or end of follow up (31 December 1998), whichever occurred first. We estimated the effect of each birth characteristic on risk of breast cancer as rate ratios using a Cox proportional hazards regression model, where age defined the time scale. To adjust for cohort effects we stratified the models[14] by five year birth cohorts (1915-9, 1920-4, and 1925-9). As breast cancer may have a different aetiology before and after the menopause we examined associations separately at ages <50 years and at older ages, hereafter referred to as premenopausal and postmenopausal ages, respectively. Confidence intervals were computed with robust standard errors to account for correlations among siblings[15] and Wald tests were used to assess linearity of effects among consecutive exposure categories.

We adjusted for gestational age by including this covariate in Cox models. When we used z scores of birth characteristics for each gestational age (standardised birth characteristics within each gestational week) our results were similar and thus are not reported here.

Results

During 1915-29, 6977 girls were born at the Uppsala Academic Hospital, of whom 6552 singletons survived. By 1960, 710 had died and 65 had emigrated. We found personal identity numbers (introduced in the early 1950s) for 5586 (97%) women. Of these, 5538 were successfully linked to the 1960 census. We

Table 2 Rate ratios* (95% confidence intervals) and P value for linear test for trend for incidence of breast cancer at premenopausal ages (<50 years) by selected birth characteristics

Birth size measure	No of women† (n=5358)	No of cases (n=63)	Crude analysis	Adjusted for gestational age	Adjusted for gestational age and adult risk factors‡
Birth weight (g):					
<3000	991	7	1	1	1
3000-3499	2111	21	1.46 (0.62 to 3.43)	1.63 (0.70 to 3.79)	1.61 (0.69 to 3.77)
3500-3999	1674	24	2.09 (0.90 to 4.85)	2.48 (1.02 to 6.01)	2.43 (1.00 to 5.94)
≥4000	576	11	2.78 (1.08 to 7.15)	3.47 (1.30 to 9.27)	3.48 (1.29 to 9.38)
Linear trend			P=0.01	P=0.006	P=0.006
Birth length§ (cm):					
≤49.0	1493	9	1	1	1
49.5, 50.0	1136	13	1.93 (0.83 to 4.50)	2.13 (0.91 to 4.98)	2.10 (0.89 to 4.94)
50.5, 51.0	1074	16	2.60 (1.15 to 5.86)	2.99 (1.32 to 6.75)	2.94 (1.30 to 6.67)
51.5, 52.0	774	13	3.10 (1.32 to 7.24)	3.60 (1.54 to 8.40)	3.53 (1.50 to 8.31)
≥52.5	861	12	2.72 (1.16 to 6.41)	3.37 (1.45 to 7.85)	3.40 (1.45 to 8.01)
Linear trend			P=0.003	P<0.001	P<0.001
Ponderal index (kg/m³):					
<24.4	1107	10	1	1	1
24.4-25.7	1049	11	1.06 (0.44 to 2.56)	1.07 (0.45 to 2.58)	1.06 (0.44 to 2.53)
25.8-27.0	1121	14	1.20 (0.52 to 2.78)	1.25 (0.54 to 2.89)	1.25 (0.54 to 2.88)
27.1-28.4	1014	13	1.21 (0.51 to 2.84)	1.25 (0.53 to 2.94)	1.24 (0.52 to 2.93)
≥28.5	1046	15	1.34 (0.58 to 3.09)	1.38 (0.59 to 3.22)	1.42 (0.61 to 3.32)
Linear trend			P=0.44	P=0.41	P=0.37
Head circumference (cm):					
<33.8	1384	7	1	1	1
33.8-34.0	997	10	2.03 (0.77 to 5.32)	2.17 (0.82 to 5.71)	2.12 (0.81 to 5.58)
34.1-35.0	1559	24	3.14 (1.36 to 7.24)	3.50 (1.52 to 8.04)	3.36 (1.46 to 7.73)
35.1-35.9	344	7	4.35 (1.54 to 12.29)	5.05 (1.71 to 14.83)	5.05 (1.72 to 14.83)
≥36.0	917	14	3.39 (1.35 to 8.52)	3.98 (1.58 to 10.00)	3.91 (1.54 to 9.93)
Linear trend			P=0.001	P<0.001	P<0.001

*Estimated from Cox survival model, stratified on period of birth (1915-9, 1920-4, 1925-9) and with robust standard errors to account for correlations among siblings.
†Total numbers do not always add up to 5358 because of missing data on specific birth characteristic.
‡Other factors as measured in 1960: marital status, children in the home (0, 1-2, 3-4, ≥5), age at first marriage (<25, 25-29, 30-34, ≥35 years, unmarried), level of education attained (non-academic, A levels, academic), personal car possession (yes/no), occupation (supervisor/non-manual, manual, self employed, unemployed).
§Recorded to the nearest 0.5 cm.

Table 3 Rate ratios* (95% confidence intervals) and P value for linear test for trend for breast cancer incidence at postmenopausal ages (≥50 years) by selected birth characteristics

Birth size measure	No of women† (n=5173)	No of cases (n=296)	Crude analysis	Adjusted for gestational age	Adjusted for gestational age and adult risk factors‡
Birth weight (g):					
<3000	954	60	1	1	1
3000-3499	2044	102	0.75 (0.55 to 1.03)	0.75 (0.54 to 1.03)	0.75 (0.54 to 1.03)
3500-3999	1617	101	0.98 (0.71 to 1.35)	0.98 (0.70 to 1.36)	0.97 (0.69 to 1.35)
≥4000	552	32	0.89 (0.58 to 1.37)	0.88 (0.56 to 1.37)	0.87 (0.56 to 1.36)
Linear trend			P=0.83	P=0.83	P=0.87
Birth length§ (cm):					
≤49.0	1442	77	1	1	1
49.5, 50.0	1096	58	0.97 (0.69 to 1.36)	0.97 (0.69 to 1.37)	0.97 (0.69 to 1.36)
50.5, 51.0	1040	66	1.15 (0.83 to 1.60)	1.16 (0.84 to 1.62)	1.13 (0.81 to 1.58)
51.5, 52.0	742	34	0.81 (0.54 to 1.21)	0.82 (0.54 to 1.23)	0.80 (0.53 to 1.21)
≥52.5	833	59	1.29 (0.92 to 1.82)	1.30 (0.92 to 1.85)	1.29 (0.91 to 1.84)
Linear trend			P=0.34	P=0.34	P=0.38
Ponderal index (kg/m^3):					
<24.4	1076	66	1	1	1
24.4-25.7	1010	55	0.89 (0.63 to 1.28)	0.90 (0.63 to 1.28)	0.88 (0.62 to 1.26)
25.8-27.0	1089	65	1.01 (0.72 to 1.42)	1.01 (0.72 to 1.43)	0.99 (0.71 to 1.40)
27.1-28.4	976	58	1.02 (0.72 to 1.46)	1.02 (0.72 to 1.46)	1.02 (0.71 to 1.45)
≥28.5	1001	50	0.85 (0.59 to 1.23)	0.85 (0.59 to 1.23)	0.85 (0.59 to 1.23)
Linear trend			P=0.68	P=0.67	P=0.67
Head circumference (cm):					
<33.8	1335	80	1	1	1
33.8-34.0	967	42	0.70 (0.48 to 1.02)	0.70 (0.49 to 1.02)	0.69 (0.48 to 1.01)
34.1-35.0	1501	77	0.83 (0.61 to 1.13)	0.83 (0.60 to 1.14)	0.82 (0.60 to 1.13)
35.1-35.9	331	20	0.99 (0.60 to 1.62)	0.99 (0.60 to 1.62)	0.97 (0.59 to 1.61)
≥36.0	883	65	1.16 (0.84 to 1.61)	1.16 (0.83 to 1.62)	1.14 (0.81 to 1.60)
Linear trend			P=0.26	P=0.26	P=0.29

*Estimated from Cox survival model, stratified on period of birth (1915-9, 1920-4, 1925-9) and with robust standard errors to account for correlations among siblings.

†Total numbers do not always add up to 5173 because of missing data on specific birth characteristic.

‡Other factors as measured in 1960: marital status, children in the home (0, 1-2, 3-4, ≥5), age at first marriage (<25, 25-29, 30-34, ≥35 years, unmarried), level of education attained (non-academic, A levels, academic), personal car possession (yes/no), occupation (supervisor/non-manual, manual, self employed, unemployed).

§Recorded to the nearest 0.5 cm.

excluded four women with a diagnosis of breast cancer before the 1960 census. As most of the analyses required gestational age we also excluded 159 women with unknown gestational age and 17 with an unlikely value of less than 30 weeks. Thus we included 5358 women in the reported analyses.

There were 359 cases of breast cancer during the 38 year follow up. Cases were identified through cancer registration, with the exception of three whom we identified through death certificates only. The median age at diagnosis was 62 years (range 36-82), with 63 cases occurring in women aged under 50 years. In addition, 1197 (22%) women, who had never been diagnosed with breast cancer, died from other causes (median age 68 years, range 31-83) and 37 (0.7%) emigrated during follow up (median age 49, range 31-74).

Table 1 describes the baseline characteristics by breast cancer status and, for cases, by age at diagnosis. Women who developed breast cancer at premenopausal ages had, on average, a larger birth size but a shorter gestational age than those who did not.

There were positive and significant linear trends in rates of breast cancer at premenopausal ages among categories of birth weight, length, and head circumference (table 2). Each of these associations strengthened considerably after we adjusted for gestational age. Rates of breast cancer were 3-4 times higher in women who were in the highest category of any of these measures of birth size compared with those of similar gestational age in the lowest category. Ponderal index showed a positive but non-significant association with risk of premenopausal breast cancer, which did not

alter after we adjusted for gestational age. Women of a higher birth order were at a slightly increased but non-significant risk (results not shown), but this effect disappeared after we adjusted for birth weight (P=0.98 for linear trend). Maternal age showed no clear pattern with rates of premenopausal breast cancer (results not shown). There was no evidence of associations between any of the birth size measures available in this study and rates of postmenopausal breast cancer (table 3).

In contrast with the positive associations between measures of birth size and premenopausal risk, for a given birth size a shorter gestation was associated with a significant increase in risk (table 4). No such association was seen for postmenopausal ages.

Simultaneous modelling of the birth size variables and gestational age showed that head circumference was the measure with the strongest independent association with risk of premenopausal breast cancer (table 5). The association with birth weight was greatly reduced and no longer significant after we adjusted for either birth length or head circumference, whereas that for birth length remained of borderline significance after we adjusted for birth weight.

The proxy markers for risk factors for breast cancer had effects in the expected direction. Rates of breast cancer at all ages were higher in women who were single (rate ratio 1.11, 95% confidence interval 0.76 to 1.63, for single v married women), married later (1.46, 1.06 to 2.01, for women who married at ages 30-34 v women who married before age 25), or lived in households with fewer children (1.29, 0.93 to 1.80, for women with no children at home v those with 3 or 4). Rates were also

Table 4 Rate ratios* (95% confidence interval) and P values for linear trend for incidence of breast cancer at premenopausal and postmenopausal ages by gestational age

Gestational age (weeks)	No of women†	No of cases	Crude analysis	Adjusted for birth size measures‡	Adjusted for birth size measures‡ and adult life risk factors§
Premenopausal (<50 years):					
30-38	1252	17	1.35 (0.68 to 2.69)	2.10 (1.05 to 4.21)	2.06 (1.02 to 4.16)
39	1118	12	1.10 (0.51 to 2.33)	1.35 (0.65 to 2.80)	1.30 (0.61 to 2.77)
40	1321	18	1.38 (0.71 to 2.68)	1.51 (0.78 to 2.92)	1.45 (0.74 to 2.85)
≥41	1494	15	1	1	1
Linear trend			P=0.34	P=0.03	P=0.03
Postmenopausal (≥50 years):					
30-38	1205	68	0.93 (0.67 to 1.28)	0.96 (0.69 to 1.35)	0.95 (0.68 to 1.34)
39	1077	62	0.93 (0.67 to 1.29)	0.97 (0.70 to 1.35)	0.96 (0.69 to 1.34)
40	1271	67	0.87 (0.63 to 1.20)	0.90 (0.65 to 1.23)	0.88 (0.64 to 1.22)
≥41	1448	86	1	1	1
Linear trend			P=0.72	P=0.64	P=0.66

*Estimated from Cox survival model, stratified on period of birth (1915-9, 1920-4, 1925-9) and with robust standard errors to account for correlations among siblings.
†Analyses restricted to women with complete data for gestational age, birth weight, birth length, and head circumference.
‡Length, weight, and head circumference.
§Other factors as measured in 1960: marital status, children in the home (0, 1-2, 3-4, ≥5), age at first marriage (<25, 25-29, 30-34, ≥35 years, unmarried), level of education attained (non-academic, A levels, academic), personal car possession (yes/no), occupation (supervisor/non-manual, manual, self employed, unemployed).

higher in women who were supervisors or non-manual workers, had their own car, and had had an academic education. There was, however, no evidence that the associations between the birth characteristics and risk of breast cancer were confounded by these adult characteristics (see tables 2 and 4) nor by maternal socioeconomic status at birth (results not shown).

Discussion

Main findings

We have found strong evidence of positive associations between measures of birth size and risk of premenopausal breast cancer, which persisted after we adjusted for markers of adult risk factors and were strengthened after we adjusted for gestational age. In addition, for a given birth size a shorter gestation was associated with

a significantly increased risk of premenopausal breast cancer. The positive association with birth size and independent inverse association with gestational age indicate that the rate of fetal growth may underlie the association between birth size and risk of early breast cancer. There was no evidence of an association with postmenopausal risk.

The Uppsala birth cohort study comprises a large population based cohort with long and almost complete follow up and enough events to enable separate analysis at premenopausal and postmenopausal ages. Data on a large number of birth measurements allowed us to examine their independent effects and their effects adjusted for gestational age so we could obtain a measure of the fetal growth rate. As birth characteristics were measured and recorded at the

Table 5 Mutually adjusted rate ratios* (95% confidence interval) and P value for linear test for trend for incidence of breast cancer at premenopausal ages (<50 years) by selected measures of birth size

Birth size measure	Adjusted for gestational age† only	Adjusted for gestational age† and			
		Birth weight	Birth length	Head circumference	Other two measures
Birth weight (g):					
<3000	1	—	1	1	1
3000-3499	1.63 (0.70 to 3.79)	—	1.00 (0.41 to 2.44)	0.99 (0.44 to 2.24)	0.70 (0.30 to 1.63)
3500-3999	2.48 (1.02 to 6.01)	—	1.20 (0.44 to 3.30)	1.18 (0.51 to 2.72)	0.70 (0.27 to 1.78)
≥4000	3.47 (1.30 to 9.27)	—	1.58 (0.45 to 5.52)	1.32 (0.48 to 3.60)	0.73 (0.22 to 2.44)
Linear trend	P=0.006	—	P=0.37	P=0.47	P=0.79
Birth length‡ (cm):					
≤49.0	1	1	—	1	1
49.5 to 50.0	2.13 (0.91 to 4.98)	2.03 (0.88 to 4.69)	—	1.61 (0.71 to 3.64)	1.80 (0.80 to 4.07)
50.5 to 51.0	2.99 (1.32 to 6.75)	2.69 (1.16 to 6.22)	—	1.90 (0.89 to 4.06)	2.18 (0.96 to 4.94)
51.5 to 52.0	3.60 (1.54 to 8.40)	3.00 (1.15 to 7.86)	—	2.31 (0.99 to 5.42)	2.64 (1.02 to 6.81)
≥52.5	3.37 (1.45 to 7.85)	2.59 (0.90 to 7.47)	—	2.03 (0.88 to 4.68)	2.30 (0.83 to 6.39)
Linear trend	P<0.001	P=0.09	—	P=0.06	P=0.12
Head circumference (cm):					
<33.8	1	1	1	—	1
33.8-34.0	2.17 (0.82 to 5.71)	2.11 (0.80 to 5.52)	1.87 (0.72 to 4.87)	—	2.03 (0.78 to 5.27)
34.1-35.0	3.50 (1.52 to 8.04)	3.27 (1.48 to 7.20)	2.68 (1.19 to 6.04)	—	2.95 (1.35 to 6.46)
35.1-35.9	5.05 (1.71 to 14.83)	4.49 (1.63 to 12.37)	3.67 (1.29 to 10.44)	—	3.99 (1.46 to 10.87)
≥36.0	3.98 (1.58 to 10.00)	3.40 (1.31 to 8.83)	2.73 (1.07 to 7.00)	—	2.97 (1.15 to 7.66)
Linear trend	P<0.001	P=0.006	P=0.02	—	P=0.02

*Estimated from Cox survival model to stratified on period of birth (1915-9 to 1920-4 to 1925-9) and with robust standard errors to account for correlations among siblings.
†Gestational age: 30-38, 39, 40, ≥41 completed weeks of gestation.
‡Recorded to nearest 0.5 cm.

timeof birth they were not affected by recall bias. Other than measures of birth size, however, we did not have any other information about intrauterine factors. We adjusted for risk factors in adult life using proxy markers obtained from census data, although there is still potential for residual confounding. Ascertainment of cases of breast cancer during follow up was virtually complete,[16] but a few cases in young women might have been missed if they were diagnosed before the start of follow up in 1960.

Comparison with other studies

Our findings are consistent with those from a British cohort[11] and a case-control study nested within the nurses' health study,[10] in which positive associations were found with birth weight, particularly at young ages. We did not find evidence for a J shaped association as has been reported elsewhere.[3 4 6 7] Our observed positive association with birth length agrees with findings from two other studies.[3 9] Also Ekbom et al found a significantly increased risk in women who had been born very prematurely,[5 17] though no such association was found in the nurses' health study.[10] However, in the nurses' health study maturity at birth was recalled by the participants' mothers and was thus prone to greater error than in our study. Lastly, our adjustment for gestational age or stratification by menopausal status, or both, may have led to differences in magnitude of effects with respect to other studies.[9–11]

We found that the associations of birth length and head circumference with premenopausal risk were stronger than those for birth weight and that there was no association with ponderal index, suggesting that linear (bone) growth may be a more sensitive indicator of the relevant biological processes. Length at birth is a stronger predictor of adult height than birth weight.[18 19] Thus, the association of adult height with risk of breast cancer[20] may in part reflect prenatal as well as postnatal influences.

Biological plausibility and implications

Trichopoulos hypothesised that prenatal exposure to high concentrations of pregnancy oestrogens influences risk of breast cancer.[1] The mammary gland starts to develop in utero, when it is in a partially undifferentiated state, and high concentrations of growth factors may result in an increased number of stem cells or increased mitosis, or both. But although there is strong evidence that a woman's endogenous oestrogen concentrations are important in the aetiology of postmenopausal breast cancer,[21] their role at premenopausal ages is less clear.[22] Our findings are consistent with those from recent prospective studies that have shown a strong association between high circulating concentrations of insulin-like growth factor I in adulthood and subsequent risk of premenopausal, but not postmenopausal, breast cancer.[23 24]

In public health terms, if the findings were real, large birth size would be responsible for only a small proportion of the total number of cases of breast cancer in any population as the incidence at premenopausal ages is low. The association of larger size at birth with an increased risk of premenopausal breast cancer should be considered in light of its opposite association with ischaemic heart disease,[13] a much more common condition.

What is already known on this topic

There is some evidence that birth weight is related to risk of breast cancer

The exact nature of any association and whether it differs at premenopausal and postmenopausal ages is unclear

Few studies have examined the effect of other measures of birth size and of gestational age

What this study adds

There are strong positive associations between measures of birth size and rates of breast cancer at premenopausal ages that persisted after adjustment for adult risk factors

For a given birth size, gestational age was inversely associated with risk, suggesting that the rate of fetal growth may be aetiologically relevant to premenopausal breast cancer

There was no association between birth characteristics and rates of breast cancer at postmenopausal ages

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In summary, our results provide strong evidence that there is real association between birth size and risk of breast cancer at premenopausal ages and that fetal growth rate, rather than size at birth alone, may be the aetiological relevant factor.

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