Longitudinal and Life Course Studies • vol XX • no XX • 1–18 • © Authors 2025
Online ISSN 1757-9597 • https://doi.org/10.1332/17579597Y2025D000000038
Accepted for publication 14 January 2025 • First published online 10 February 2025

RESEARCH ARTICLE

Association between timing of motherhood and prospective cardiovascular biomarker risk factors: a twin study

Verena Schneider, verena.schneider.19@ucl.ac.uk
University College London, UK

Rebecca Lacey, rlacey@sgul.ac.uk
St George's University of London, UK

Giorgio Di Gessa, g.di-gessa@ucl.ac.uk
University College London, UK

Ruth Bowyer, ruth.c.bowyer@kcl.ac.uk
Claire Steves, claire.j.steves@kcl.ac.uk
King's College London, UK

Anne McMunn, a.mcmunn@ucl.ac.uk
University College London, UK

Background: Evidence suggests that transitioning to motherhood at a younger age is associated with higher levels of cardiovascular biomarker risk factors later in life. While early-life confounding factors alongside social and behavioural pathways contribute to this association, residual confounding may remain.
Objective: To investigate the relationship between age at first childbirth and later life cardiovascular biomarker risk factors (BMI, android/gynoid fat ratio, blood pressure, lipid profile), and environmental and genetic confounding in female twins.
Participants and setting: Participants were 2,204 mothers from the TwinsUK cohort (549 di-, 553 monozygotic twin pairs) who were 50 years or older and had data on age at first birth, at least one outcome, and selected covariates.
Methods: Generalised estimation equations were used to analyse (1) individual-level crude associations of age at first birth with the outcomes, (2) di- and monozygotic between and within-family estimates, and (3) covariate-adjusted associations.
Results: Individual-level analyses suggest that women with age at first birth <20 years (compared to 25–29 years) had higher mean BMI, android/gynoid fat ratio, and triglyceride levels after age 50. However, confidence intervals were wide. Considering within-family estimates, effect size reductions suggest partial confounding by early environmental factors, with associations for android/gynoid fat ratio persisting.

Conclusion: Family-level confounding plays a role in the link between age at first birth and cardiovascular biomarker risk factors. Age at first birth <20 may be associated with increased cardiovascular biomarker risk. Larger representative and/or twin studies are needed to assess these findings' significance, robustness to confounding, and specific pathways.

Keywords maternal age • cardiovascular biomarker risk factors • twin design • longitudinal studies • age at first birth

Key messages

- Young age at first birth is associated with adverse cardiovascular biomarker risk in later life.
- Uncertainties remain about residual confounding in this relationship.
- Co-twin control design findings highlight the role of early life family-level confounding.
- Young age at first birth remains a risk factor, particularly for android/gynoid fat ratio.

To cite this article: Schneider, V., Lacey, R., Di Gessa, G., Bowyer, R., Steves, C. and McMunn, A. (2025) Association between timing of motherhood and prospective cardiovascular biomarker risk factors: a twin study, *Longitudinal and Life Course Studies*, Early View, DOI: 10.1332/17579597Y2025D000000038

Several studies have reported negative associations between the age at which a woman has their first child and later life morbidity. For example, teenage mothers had higher odds of reporting fair/bad health (Grundy and Foverskov, 2016; Tomassini et al, 2018) or chronic conditions (Sironi, 2019) later in life compared to women with older ages at first birth across Western and Eastern European countries. Age at first birth seems to be particularly relevant to cardiovascular (CV) biomarkers and disease risk (Hardy et al, 2009; Lacey et al, 2017; Rosendaal and Pirkle, 2017; Sironi et al, 2020). Research conducted using British cohort studies (that is, 1958 National Child Development Study, 1946 National Survey of Health & Development) has consistently found that age at first birth before the age of 20 years was associated with later life higher CV biomarker risk factors (including BMI/obesity, blood pressure, lipid profiles and inflammation) compared to mothers with older ages at first birth (Hardy et al, 2009; Lacey et al, 2017; Sironi et al, 2020). However, unpacking the causal mechanisms in this association is complex, with evidence on selection effects and confounding due to childhood factors (Hardy et al, 2009; Lacey et al, 2017; Sironi et al, 2020).

Early life factors on the family and individual level complicate the relationship between age at first birth and later CV health. For example, household social disadvantages (for example, economic disadvantage or family disruption) are both associated with earlier parenthood (Kearney and Levine, 2012; Aluga and Okolie, 2021) and are themselves independent risk factors of worse CV health biomarker risk factors later in life (Stannard et al, 2022; Natale et al, 2023). On the individual level, those with worse early-life health may select into earlier parenthood due to fertility concerns and are more likely to have worse CV health later in life (Pool et al, 2021). Early pubertal development is related to earlier sexual activity and CV disease/biomarker risk factors later in life (Hardy et al, 2006; O'Kelly et al, 2022).

Considering the mechanisms of the association of age at first birth and later life CV biomarker risk factors, a number of pathways have been proposed. Physiological explanations for the association between mothers' age at first birth and later CV health include risks introduced through pregnancy-related changes, such as hypertension disorders and gestational diabetes, and their impact on later life outcomes (Parikh et al, 2016; Okoth et al, 2020; Sironi et al, 2020; O'Kelly et al, 2022). Women entering parenthood at an earlier age may be at greater long-term risk of these (Gunderson et al, 2012). However, studies including mothers and fathers and assessing social and behavioural pathways have suggested that the latter play a bigger role (Hardy et al, 2009; Grundy and Read, 2015; Lacey et al, 2017). Proposed social pathways suggest that early parenthood is more disruptive to education, careers and partnerships, thereby causing economic and social support disadvantages compared to older parents (Hardy et al, 2009; Lacey et al, 2017; Sironi et al, 2020). Furthermore, although parenting may motivate to exercise good health and fewer risky behaviours (Görlitz and Tamm, 2020), the association may also be explained by having less time to engage in health-promoting behaviours (Grundy and Read, 2015). Education may indeed both act as an early-life confounder or, considering continued education in adulthood, a mediator of the relationship between age at first birth and health. Finally, younger women at first birth are also more likely to have a higher number of total children, which may be an independent predictor of later CV health (Lawlor et al, 2003; Hardy et al, 2007).

Consistent with this, previous studies have found evidence for early-life confounding and mediating pathways in the association between age at first birth and CV biomarker risk factors. Hardy et al (2009) found the association of age at first birth with most CV biomarker risk factors in mothers was explained by confounding due to lower childhood and adult socioeconomic status, lower educational attainment, as well as lower physical activity levels and higher levels of smoking. However, associations with blood pressure remained. Lacey et al (2017) also found partial mediation via socioeconomic disadvantages, educational attainment, health behaviours, working status, marital status and number of children while controlling for early life confounding. Associations of age at first birth with BMI, blood pressure, HDL cholesterol and fibrinogen were only partially explained by these factors.

Hence, there remain uncertainties in explaining the relationship between age at first birth and later CV risk. One explanation could be unmeasured/residual confounding and measurement error. Available data may not fully capture confounding due to relevant early life factors. This is both because relevant confounders are not measured and included confounders are measured with error. It is also not clear whether genetic confounding could play a role in the association between age at first birth and CV biomarker risk factors.

The present study aimed to build on previous work investigating the association between age at first birth and subsequent CV risk factors and address confounding due to the childhood family environment and genetics using data from the TwinsUK registry (Verdi et al, 2019). Twin designs have the advantage that the design controls for (unmeasured) confounding due to shared early-life environmental factors and genetic predispositions. By using di- and monozygotic twin data, the present study aimed to decompose confounding due to early-life shared environmental and genetic factors, while also controlling for individual-level differences. Specifically, the research questions we aimed to address were:

1. What are the within-family associations between age at first birth and CV biomarker risk factors in mothers, that is, when accounting for confounding in the shared family environment (DZ twins) and/or shared genetics (MZ twins)?
2. What are the adjusted within-family associations between age at first birth and CV biomarker risk factors in mothers, when accounting for confounding in the shared family environment (DZ twins) and/or shared genetics (MZ twins) and confounding due to individual-level early life and adult factors?

Methods

Sample

This study analysed longitudinal data from mono- (MZ) and dizygotic (DZ) female twins in the TwinsUK dataset (Verdi et al, 2019). TwinsUK is the largest registry of adult volunteer twins in the UK and was set up in 1992 with data from over 15,000 twins between 18 and 100 years of age (TwinsUK, nd). The initial cohort of 7,000 volunteer female twins was found to be comparable to women in a British population cohort study (Verdi et al, 2019) for most age-matched characteristics except for weight (MZ twins had a lower weight). Multiple repeated biomarker measures and a range of data are collected from participants during clinical visits and via questionnaires (Verdi et al, 2019; Bowyer et al, 2022).

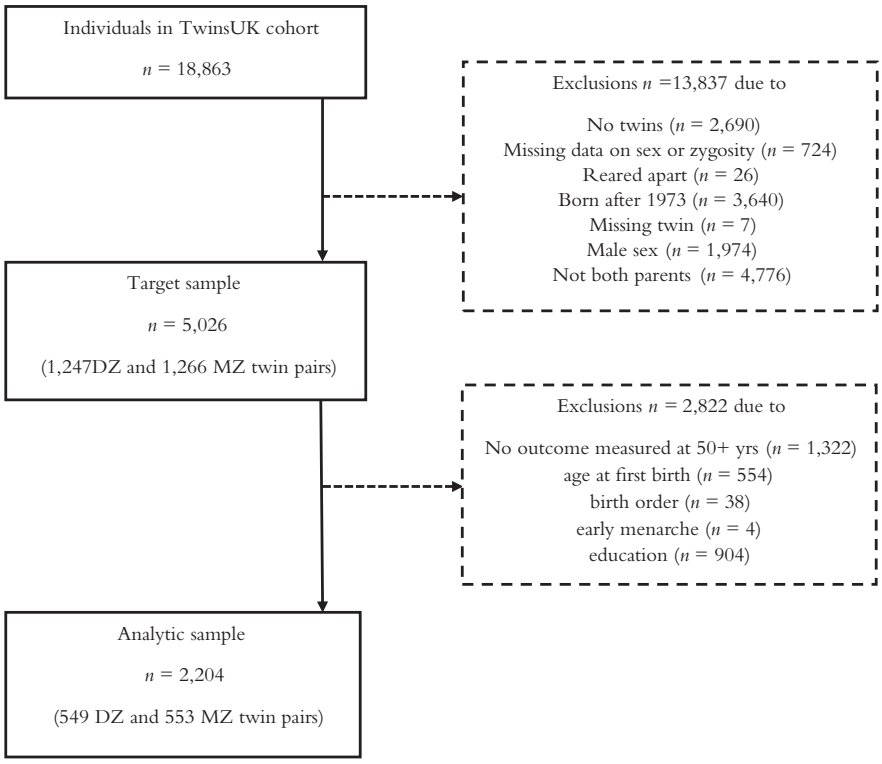
To be included in this particular study, twins needed to be born before 1974 (that is, be at least 50 years old), be biological mothers of at least one child each, and be reared in the same household (target sample; *N*=5,026; Figure 1). Furthermore, twins needed to have one available biomarker outcome measure (see next section) after reaching 50 years of age. The age at which the outcomes were measured needed to be identical within each twin pair. Furthermore, twins needed to have complete data on the exposure (age at first birth) and included covariates (see Figure 1 and measurement section). The final analytic sample (*N*=2,204) included 549 DZ and 553 MZ twin pairs. The analytic and target samples were similar in most characteristics (Table 1), however, the analytic sample consisted of a higher proportion of twins born between 1945 and 1954 and a slightly higher proportion of women with first childbirth at the ages 25–29 years versus 20–24 years. To account for any non-response bias in the analytic sample, non-response weights were created (Supplementary Text S1, Supplementary Figure S1).

Measures

Outcome measures

The study assessed BMI, android/gynoid fat ratio, systolic and diastolic blood pressure, fasting triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) cholesterol. The android/gynoid fat ratio compares fat distribution in the abdominal region (android) to that in the hips, buttocks and thighs (gynoid). This measure has been shown to be a stronger predictor of cardiovascular risk than general obesity measures (Okosun et al, 2015). As android fat is considered more harmful than gynoid fat, a higher ratio means elevated risk.

Figure 1: Flowchart of analytic sample



Notes: Abbreviations: DZ = dizygotic; MZ = monozygotic; yrs = years.

For blood pressure, repeat readings within the same visit were averaged. Due to a large number of individuals without repeat readings, the first measure was included in the main analysis. The impact of excluding the first blood pressure reading was explored in sensitivity analyses. LDL was either directly measured or derived from other lipid measures. Sensitivity analyses were conducted excluding derived LDL measures.

For each twin pair, biomarker outcome measures were from the clinical visit identified as the closest to and after the 50th birthday which were attended by both twins within 365 days of each other.

Exposure

The exposure variable was age at first birth. This was derived from repeated questionnaire data on family histories and ranged from 16 to 42 years of age. For the analysis, this was categorised into ages <20, 20–24, 25–29 (ref), 30–34 and ≥35.

Covariates

All models accounted for age at outcome measurement (continuous) and cohort (categorised into five levels by year of birth: <1935, 1935–1944, 1945–1954, 1955–1964, 1965–1974). Twin birth order was used to account for birth order differences. Age at first menstrual period was categorised into early menarche before 12 years of

Table 1: Characteristics of target population and participants included in the analytic sample

	Target population (*n* = 5,026)		Analytic sample (*n* = 2,204)		DZ (*n* = 1,098)		MZ (*n* = 1,272)	
	N	M(SD)/ N(valid %)	N	Weighted M(SD)/ N(valid %)	N	Weighted M(SD)/ N(valid %)	N	Weighted M(SD)/ N(valid %)
BMI (kg/m^2)	3,690	26.36 (4.74)	2,200	26.30 (4.63)	1,096	26.42 (4.72)	1,104	26.18 (4.53)
Android-gynoid fat ratio	2,806	0.95 (0.16)	2,006	0.95 (0.16)	986	0.95 (0.15)	1,020	0.96 (0.16)
Blood pressure								
Systolic (mmHg)	3,666	126.75 (17.35)	2,190	126.22 (17.25)	1,092	126.30 (17.10)	1,098	126.14 (17.42)
Diastolic (mmHg)	3,668	78.62 (10.58)	2,192	78.58 (10.67)	1,094	79.34 (10.72)	1,098	77.82 (10.58)
Lipids								
Triglycerides[a] (mmol/L)	2,594	0.96 (0.58)	1,944	0.96 (0.57)	964	0.99 (0.60)	980	0.93 (0.55)
HDL (mmol/L)	2,928	1.69 (0.47)	2,058	1.69 (0.46)	1,020	1.68 (0.44)	1,038	1.70 (0.48)
LDL (mmol/L)	2,922	3.48 (1.03)	2,058	3.50 (1.03)	1,020	3.48 (1.03)	1,038	3.51 (1.03)
Year of birth	5,026		2,204		1,098		1,106	
<1935		482 (9.59)		126 (5.72)		50 (4.55)		76 (6.87)
1935–1944		1,254 (24.95)		606 (27.50)		296 (26.96)		310 (28.03)
1945–1954		1,734 (34.50)		948 (43.01)		512 (46.63)		436 (39.42)
1955–1964		1,034 (20.57)		440 (19.96)		210 (19.13)		230 (20.80)
1965–1973		522 (10.39)		84 (3.81)		30 (2.73)		54 (4.88)
Age at first birth (years)	5,026		2,204		1,098		1,106	
N(%) missing		752 (14.96)						
< 20		341 (7.98)		161 (7.30)		80 (7.29)		81 (7.32)
20–24		1,516 (35.47)		717 (32.53)		385 (35.06)		332 (30.02)
25–29		1,581 (36.99)		877 (39.79)		407 (37.07)		470 (42.50)
30–34		657 (15.37)		345 (15.65)		172 (15.66)		173 (15.64)
≥ 35		179 (4.19)		104 (4.72)		54 (4.92)		50 (4.52)
N children	5,026		2,204		1,098		1,106	

(*Continued*)

Table 1: Continued

	Target population (*n* = 5,026)		Analytic sample (*n* = 2,204)		DZ (*n* = 1,098)		MZ (*n* = 1,272)	
	N	M(SD)/ N(valid %)	N	Weighted M(SD)/ N(valid %)	N	Weighted M(SD)/ N(valid %)	N	Weighted M(SD)/ N(valid %)
N(%) missing		2,159 (42.96)		765 (34.71)		335 (30.51)		430 (38.88)
1		354 (12.35)		166 (11.54)		98 (12.84)		68 (10.06)
2		1,496 (52.18)		793 (55.11)		401 (52.56)		392 (57.99)
≥ 3		1,017 (35.47)		480 (33.36)		264 (34.60)		216 (31.95)
Birth order	5,026		2,204		1,098		1,106	
N(%) missing		1,368 (27.22)						
1st		1,829 (50)		1,102 (50)		549 (50)		553 (50)
2nd		1,829 (50)		1,102 (50)		549 (50)		553 (50)
Early menarche	5,026		2,204		1,098		1,106	
N(%) missing		1,328 (26.42)						
<12 yrs		559 (15.12)		356 (16.15)		210 (19.13)		146 (13.20)
12+ yrs		3,139 (84.88)		1,848 (83.85)		888 (80.87)		960 (86.80)
Education	5,026		2,204		1,098		1,106	
N(%) missing		2,419 (48.13)						
No qualification		452 (17.34)		395 (17.92)		217 (19.76)		178 (16.09)
< A-levels		927 (35.56)		794 (36.03)		388 (35.34)		406 (36.71)
A-levels		119 (4.56)		107 (4.85)		53 (4.83)		54 (4.88)
Degree		1,109 (42.54)		908 (41.20)		440 (40.07)		468 (42.31)

Notes: [a] Distribution skewed; median and IQR are presented. Biomarker distributions have been winsorised at 0.5% and 99.5%. Abbreviations: BMI = body mass index; DZ = dizygotic; HDL = high-density lipoprotein; LDL = low-density lipoprotein; M = mean; MZ = monozygotic; SD = standard deviation.

age versus 12 years or older (O'Kelly et al, 2022). Highest educational attainment was categorised into a four-level variable (no qualification, <A-levels/ISCED Level 3, A-levels/ISCED Level 3, Degree/Tertiary education).

Data analysis

Analyses were conducted in R using the *geepack* package (Højsgaard et al, 2005) and weighted using non-response weights.

For each outcome, separate models were run to compare the standardised regression coefficients (Carlin et al, 2005; Baldwin et al, 2021): first, individual-level generalised estimating equation (GEE) models (with exchangeable correlation structure) were used to obtain standardised regression coefficients for the association between age at first birth and respective CV risk factors (Model 1). Second, co-twin control design GEE models were run for DZ and MZ twins separately to obtain between- and within-family standardised regression coefficients (Models 2 and 3). All models were run adjusted for age at outcome measurement and cohort and DZ and MZ models were further adjusted for birth order, early menarche (Models 4 and 6), and education (Models 5 and 7). Wald tests were conducted to assess differences between coefficients at the between- and the within-family level.

Sensitivity analyses

To assess the robustness of the results, several sensitivity analyses were conducted: first, models were rerun for blood pressure, excluding first readings (that is, those with only one reading were excluded), and for LDL. In the main analysis, LDL included directly measured LDL and derived measures (from other lipid measures where direct measures were not available). In sensitivity analyses, only directly measured LDL measures were included. Second, models decomposing between- and within-family variance were also run in the combined sample, that is, not stratified for DZ and MZ twins. While this does not permit the identification of environmental versus genetic factors in the interpretation, the combined sample provides an opportunity to assess the associations of age at first birth with outcomes in a larger sample. Third, to increase statistical power, (1) models were run with a binary exposure assessing associations for the group of women who had their first child before the age of 20, and (2) only minimally adjusted (crude) models were run for a larger sample.

Results

Characteristics of the sample

Table 1 describes the characteristics of the analytic sample (*N*=2,204). Most women in the sample were born between 1935 and 1954 (70.5%). The largest group had their first child between the ages 25 and 29 years old (39.8%; reference group). The majority of women had two (55.1%) or more children (33.4%) and two in five women had a degree (41.2%), while about 36.0% had no A-levels and 17.9% no qualification. About 16.2% of women had their menarche before the age of 12 years old.

Women had a mean BMI of 26.30 kg/m^2 (SD = 4.63), android/gynoid fat ratio of 0.95 (0.16), systolic blood pressure of 126 mmHg (17) and diastolic blood pressure of 79 mmHg (11). The triglycerides distribution was skewed and the median (interquartile range) is presented instead of means. Median triglycerides were 0.96 mmol/L (0.57), mean HDL 1.69 mmol/L (0.46) and mean LDL 3.50 mmol/L (1.03). The mean ages at biomarker measurement ranged from 55.5 (BMI, blood pressure) to 61.1 years of age (triglycerides) and age ranges were wide (up to 92 years).

Table 2 describes unadjusted weighted means for each outcome by age at first birth for a sample of a randomly selected twin from each family (*N*=1,102). The means suggest that there were higher BMI, android/gynoid fat ratio, and

Table 2: Unadjusted weighted means (95% CI) of CV risk factor by age at first birth in a random single twin sample (*N*=1,102)

	< 20 yrs	20-24 yrs	25-29 yrs	30-34 yrs	≥ 35 yrs
BMI (kg/m^2)	27.19 (26.19; 28.19)	26.67 (26.18; 27.16)	26.08 (25.65; 26.51)	26.08 (25.39; 26.77)	26.76 (25.25; 28.27)
Android-gynoid fat ratio	1.00 (0.96; 1.04)	0.97 (0.95; 0.99)	0.93 (0.91; 0.95)	0.95 (0.93; 0.97)	0.92 (0.86; 0.98)
Blood pressure					
Systolic (mmHg)	125.37 (121.82; 128.92)	127.02 (125.37; 128.67)	125.51 (123.82; 127.20)	126.87 (123.91; 129.83)	125.09 (120.19; 129.99)
Diastolic (mmHg)	77.44 (75.13; 79.75)	79.12 (78.06; 80.18)	78.2 (77.12; 79.28)	78.11 (76.23; 79.99)	78.09 (74.70; 81.48)
Lipids					
Triglycerides[a] (mmol/L)	1.01 (0.79; 1.44)	0.98 (0.76; 1.38)	0.94 (0.73; 1.23)	0.93 (0.76; 1.31)	0.86 (0.69; 1.31)
HDL (mmol/L)	1.61 (1.49; 1.73)	1.66 (1.62; 1.70)	1.69 (1.65; 1.73)	1.73 (1.65; 1.81)	1.91 (1.77; 2.05)
LDL (mmol/L)	3.50 (3.26; 3.74)	3.57 (3.45; 3.69)	3.42 (3.32; 3.52)	3.48 (3.32; 3.64)	3.26 (3.01; 3.51)

Notes: [a]Distribution skewed; median and IQR are presented. Distributions have been winsorised at 0.5% and 99.5%. Abbreviations: BMI = body mass index; CI = confidence interval; CV = cardiovascular; HDL = high-density lipoprotein; LDL = low-density lipoprotein; yrs = years.

triglycerides and lower mean HDL in women who had their first child before their 20th birthday compared to older ages at first birth. However, confidence intervals are overlapping.

Association between age at first birth and CV biomarker risk factors

Results from age and cohort-adjusted models suggest that compared to women having their first child between the ages of 25 and 29, women with age at first birth <20 had higher mean BMI (standardised β = 0.21; 95% CI = -0.01, 0.43), android/gynoid fat ratio (standardised β = 0.38; 95% CI = 0.15, 0.61), and triglyceride levels (standardised β = 0.22; 95% CI = -0.02, 0.45; Table 3; Supplementary figures S2–S8). Age at first birth between the ages of 20 and 24 was also associated with higher BMI (standardised β = 0.14; 95% CI = 0.00, 0.27), android/gynoid fat ratio (standardised β = 0.20; 95% CI = 0.05, 0.34), triglycerides (standardised β = 0.14; 95% CI = -0.01, 0.30) and LDL (standardised β = 0.13; 95% CI = -0.02, 0.28), while women who had a first child after their 35th birthday had higher HDL (standardised β = 0.43; 95% CI = 0.12, 0.74), compared to age at first birth between 25 and 29 years.

What are the DZ within-family associations between age at first birth and CV biomarker risk factors in mothers, that is, when accounting for confounding in the shared family environment?

Differences in the between- and within-family standardised estimates from the DZ co-twin control design were assessed to understand the impact of the shared environment, that is, the effect of differences between individuals in the same twin-dyad who shared their childhood household versus differences between families. Between-family coefficients were similar to or larger than the individual-level coefficients

Table 3: Minimally adjusted standardised regression coefficients (95% CI) for individual-level, DZ and MZ weighted co-twin design models (Models 1–3)

	Model 1 (individual-level)	Model 2 (DZ)		Model 3 (MZ)	
		Between-family	Within-family	Between-family	Within-family
BMI (N=1,100; N_{DZ}=548; N_{MZ}=552)					
<20	0.21 (–0.01; 0.43)	0.48 (0.00; 0.96)*	–0.30 (–0.85; 0.26)*	0.41 (0.00; 0.82)	0.02 (–0.48; 0.52)
20–24	0.14 (0.00; 0.27)	0.15 (–0.11; 0.41)	0.09 (–0.21; 0.38)	0.23 (–0.02; 0.49)	–0.14 (–0.42; 0.14)
25–29	ref	ref	ref	ref	ref
30–34	0.00 (–0.18; 0.18)	–0.11 (–0.46; 0.23)	0.09 (–0.26; 0.43)	0.04 (–0.29; 0.37)	0.07 (–0.28; 0.41)
>=35	0.12 (–0.21; 0.44)	–0.29 (–0.90; 0.31)	0.13 (–0.51; 0.78)	0.19 (–0.40; 0.77)	0.57 (0.11; 1.04)
Android/gynoid fat ratio (N=1,003; N_{DZ}=493; N_{MZ}=510)					
<20	0.38 (0.15; 0.61)	0.43 (–0.01; 0.87)	–0.14 (–0.68; 0.41)	0.42 (–0.02; 0.87)	0.65 (0.08; 1.22)
20–24	0.20 (0.05; 0.34)	0.03 (–0.25; 0.30)	0.15 (–0.16; 0.46)	0.27 (0.00; 0.54)	0.30 (–0.01; 0.61)
25–29	ref	ref	ref	ref	ref
30–34	0.11 (–0.09; 0.30)	–0.33 (–0.67; 0.00)*	0.27 (–0.13; 0.67)*	0.27 (–0.08; 0.63)	0.18 (–0.20; 0.56)
>=35	–0.09 (–0.42; 0.24)	–0.43 (–0.94; 0.09)	–0.06 (–0.64; 0.51)	–0.19 (–0.87; 0.50)	0.44 (–0.35; 1.22)
Systolic blood pressure (N=1,095; N_{DZ}=546; N_{MZ}=549)					
<20	0.08 (–0.15; 0.31)	0.14 (–0.33; 0.60)	–0.12 (–0.51; 0.28)	0.13 (–0.32; 0.58)	0.10 (–0.45; 0.64)
20–24	0.09 (–0.05; 0.23)	0.06 (–0.21; 0.32)	–0.28 (–0.61; 0.05)	0.31 (0.03; 0.59)	0.20 (–0.09; 0.48)
25–29	ref	ref	ref	ref	ref
30–34	0.13 (–0.07; 0.32)	0.13 (–0.27; 0.54)	–0.02 (–0.37; 0.34)	0.24 (–0.14; 0.62)	0.14 (–0.23; 0.51)
>=35	–0.02 (–0.33; 0.29)	–0.06 (–0.64; 0.52)	–0.14 (–0.76; 0.47)	–0.10 (–0.60; 0.40)	0.28 (–0.27; 0.83)
Diastolic blood pressure (N=1,096; N_{DZ}=547; N_{MZ}=549)					
<20	0.00 (–0.23; 0.24)	0.13 (–0.37; 0.64)	–0.40 (–0.92; 0.12)	0.12 (–0.36; 0.60)	0.06 (–0.48; 0.61)
20–24	0.08 (–0.06; 0.22)	–0.04 (–0.30; 0.22)	–0.23 (–0.54; 0.08)	0.30 (0.04; 0.57)	0.17 (–0.12; 0.46)
25–29	ref	ref	ref	ref	ref
30–34	0.02 (–0.18; 0.21)	–0.14 (–0.52; 0.23)	–0.21 (–0.58; 0.16)	0.20 (–0.17; 0.57)	0.17 (–0.25; 0.59)
>=35	0.00 (–0.33; 0.33)	0.23 (–0.39; 0.84)	–0.29 (–0.97; 0.38)	–0.02 (–0.58; 0.53)	0.03 (–0.57; 0.63)
Triglycerides[a] (N=972; N_{DZ}=482; N_{MZ}=490)					
<20	0.22 (–0.02; 0.45)	0.33 (–0.13; 0.78)	0.06 (–0.50; 0.61)	0.30 (–0.13; 0.72)	0.09 (–0.43; 0.62)
20–24	0.14 (–0.01; 0.30)	0.13 (–0.18; 0.43)	0.03 (–0.31; 0.38)	0.24 (–0.04; 0.52)	0.06 (–0.27; 0.38)

(*Continued*)

Table 3: Continued

	Model 1 (individual-level)	Model 2 (DZ)		Model 3 (MZ)	
		Between-family	Within-family	Between-family	Within-family
25–29	ref	ref	ref	ref	ref
30–34	0.05 (–0.14; 0.24)	0.03 (–0.39; 0.45)	0.00 (–0.40; 0.39)	0.07 (–0.26; 0.41)	0.16 (–0.19; 0.51)
>=35	–0.02 (–0.37; 0.34)	0.14 (–0.62; 0.89)	0.23 (–0.51; 0.97)	–0.27 (–0.80; 0.26)	–0.20 (–0.71; 0.32)
HDL (N=1,029; N_{DZ}=510; N_{MZ}=519)					
<20	–0.13 (–0.39; 0.14)	–0.15 (–0.60; 0.30)	0.11 (–0.49; 0.70)	–0.33 (–0.81; 0.16)	0.10 (–0.45; 0.66)
20–24	–0.04 (–0.19; 0.11)	0.07 (–0.17; 0.30)	0.02 (–0.34; 0.37)	–0.16 (–0.46; 0.14)	0.06 (–0.26; 0.37)
25–29	ref	ref	ref	ref	ref
30–34	0.10 (–0.09; 0.29)	0.26 (–0.17; 0.70)	0.32 (–0.04; 0.67)	–0.04 (–0.41; 0.34)	–0.18 (–0.56; 0.20)
>=35	0.43 (0.12; 0.74)	0.63 (0.10; 1.17)	0.28 (–0.23; 0.79)	0.77 (0.15; 1.39)	0.00 (–0.67; 0.68)
LDL (N=1,029; N_{DZ}=510; N_{MZ}=519)					
<20	0.05 (–0.21; 0.31)	–0.45 (–0.89; 0.00)	0.22 (–0.35; 0.78)	0.15 (–0.40; 0.70)	0.30 (–0.30; 0.91)
20–24	0.13 (–0.02; 0.28)	0.02 (–0.24; 0.28)	0.16 (–0.19; 0.51)	0.17 (–0.12; 0.46)	0.21 (–0.13; 0.54)
25–29	ref	ref	ref	ref	ref
30–34	0.08 (–0.10; 0.27)	–0.28 (–0.65; 0.08)	0.21 (–0.15; 0.57)	0.27 (–0.09; 0.63)	0.07 (–0.29; 0.43)
>=35	–0.12 (–0.38; 0.15)	–0.11 (–0.68; 0.46)	–0.12 (–0.69; 0.45)	–0.18 (–0.72; 0.35)	–0.05 (–0.60; 0.51)

Notes: [a] Distribution skewed; log transformed. Distributions have been winsorised at 0.5% and 99.5%. Models are adjusted for age at measurement and cohort. * = significant different within- and between-level effects. Abbreviations: BMI = body mass index; CI = confidence interval; DZ = dizygotic; HDL = high-density lipoprotein; LDL = low-density lipoprotein; MZ = monozygotic.

(Table 3; Supplementary figures S2–S8). For example, compared to age at first birth between 25 and 29 years, between-family coefficients suggested that women who had their first child before their 20th birthday had a standardised $\beta = 0.48$ SDs (95% CI = 0.00; 0.96) higher BMI after the age of 50. In within-family estimates, these effects were not sustained and the point estimate had an opposite effect direction (standardised $\beta = -0.30$; 95% CI = -0.85, 0.26). Larger differences in between- and within-family standardised coefficients were seen in the youngest and oldest age at first birth categories, but confidence intervals were wide and the Wald tests for difference were mostly not significant.

What are the MZ within-family associations between age at first birth and CV biomarker risk factors in mothers, that is, when accounting for confounding in the shared family environment and shared genetics?

Differences in the standardised between- and within-family estimates from the MZ co-twin control design were assessed to understand the impact of the shared environment and genetics, that is, the effect of differences between individuals in the same twin-dyad who shared their childhood household and

genetics versus differences between families. As with the DZ results, standardised between-family coefficients were mostly similar or larger than the individual-level coefficients, while on the within-family level, these were not sustained (Table 3; Supplementary figures S2–S8). However, exceptions were seen for android/gynoid fat ratio (standardised β = 0.65; 95% CI = 0.08, 1.22), suggesting higher means for age at first birth <20 compared to 25 to 29 years. Women who have their first child after their 35th birthday had higher BMIs later in life (standardised β = 0.57; 95% CI = 0.11, 1.04), independent of early-life environmental and genetic factors.

Table 4: Adjusted standardised within-family regression coefficients (95% CI) from weighted DZ and MZ co-twin design models adjusted for age at measurement, cohort, age at menarche, and birth order (Models 4 and 6) and additionally for education (Models 5 and 7)

	Model 4 (DZ)	Model 5 (DZ)	Model 6 (MZ)	Model 7 (MZ)
BMI (N_{DZ}=548; N_{MZ}=552)				
<20	–0.31 (–0.87; 0.24)	–0.29 (–0.84; 0.27)	–0.03 (–0.53; 0.47)	–0.05 (–0.55; 0.44)
20–24	0.10 (–0.19; 0.39)	0.10 (–0.19; 0.39)	–0.15 (–0.43; 0.13)	–0.15 (–0.43; 0.14)
25–29	ref	ref	ref	ref
30–34	0.09 (–0.26; 0.43)	0.11 (–0.24; 0.47)	0.06 (–0.28; 0.41)	0.06 (–0.28; 0.40)
>=35	0.18 (–0.45; 0.81)	0.19 (–0.43; 0.80)	0.57 (0.11; 1.02)	0.57 (0.12; 1.01)
Android/gynoid fat ratio (N_{DZ}=493; N_{MZ}=510)				
<20	–0.14 (–0.69; 0.41)	–0.13 (–0.67; 0.41)	0.59 (0.03; 1.15)	0.56 (0.00; 1.13)
20–24	0.15 (–0.16; 0.46)	0.15 (–0.16; 0.46)	0.28 (–0.03; 0.59)	0.28 (–0.03; 0.59)
25–29	ref	ref	ref	ref
30–34	0.27 (–0.14; 0.67)*	0.28 (–0.13; 0.68)	0.18 (–0.20; 0.56)	0.18 (–0.21; 0.56)
>=35	–0.05 (–0.62; 0.53)	–0.04 (–0.62; 0.53)	0.42 (–0.36; 1.20)	0.43 (–0.35; 1.21)
Systolic blood pressure (N_{DZ}=546; N_{MZ}=549)				
<20	–0.07 (–0.47; 0.33)	–0.04 (–0.42; 0.36)	0.11 (–0.43; 0.64)	0.10 (–0.43; 0.64)
20–24	–0.28 (–0.61; 0.04)	–0.28 (–0.60; 0.04)	0.20 (–0.09; 0.49)	0.20 (–0.09; 0.49)
25–29	ref	ref	ref	ref
30–34	–0.05 (–0.41; 0.31)	–0.01 (–0.36; 0.35)	0.13 (–0.24; 0.50)	0.13 (–0.24; 0.50)
>=35	–0.11 (–0.7; 0.49)	–0.10 (–0.71; 0.52)	0.26 (–0.30; 0.81)	0.26 (–0.30; 0.81)
Diastolic blood pressure (N_{DZ}=547; N_{MZ}=549)				
<20	–0.37 (–0.89; 0.16)	–0.35 (–0.88; 0.18)	0.05 (–0.49; 0.59)	0.05 (–0.49; 0.59)
20–24	–0.23 (–0.53; 0.08)	–0.23 (–0.53; 0.08)	0.17 (–0.13; 0.46)	0.17 (–0.13; 0.47)
25–29	ref	ref	ref	ref
30–34	–0.24 (–0.62; 0.14)	–0.22 (–0.60; 0.15)	0.16 (–0.27; 0.58)	0.16 (–0.27; 0.58)
>=35	–0.25 (–0.90; 0.40)	–0.24 (–0.90; 0.41)	0.00 (–0.60; 0.60)	0.00 (–0.60; 0.60)
Triglycerides[a] (N_{DZ}=482; N_{MZ}=490)				
<20	0.00 (–0.56; 0.55)	–0.01 (–0.56; 0.54)	0.05 (–0.46; 0.57)	0.04 (–0.48; 0.56)
20–24	0.07 (–0.27; 0.41)	0.07 (–0.27; 0.42)	0.04 (–0.29; 0.36)	0.04 (–0.29; 0.36)
25–29	ref	ref	ref	ref
30–34	0.02 (–0.36; 0.41)	0.01 (–0.37; 0.40)	0.15 (–0.20; 0.50)	0.15 (–0.21; 0.50)
>=35	0.27 (–0.46; 1.01)	0.27 (–0.46; 1.01)	–0.22 (–0.72; 0.28)	–0.22 (–0.72; 0.28)

(*Continued*)

Table 4: Continued

	Model 4 (DZ)	Model 5 (DZ)	Model 6 (MZ)	Model 7 (MZ)
HDL (N_{DZ}=510; N_{MZ}=519)				
<20	0.11 (–0.48; 0.70)	0.07 (–0.51; 0.66)	0.12 (–0.44; 0.68)	0.15 (–0.41; 0.70)
20–24	0.01 (–0.35; 0.37)	0.01 (–0.34; 0.36)	0.06 (–0.25; 0.38)	0.06 (–0.25; 0.38)
25–29	ref	ref	ref	ref
30–34	0.31 (–0.04; 0.67)	0.28 (–0.08; 0.64)	–0.18 (–0.56; 0.20)	–0.18 (–0.57; 0.21)
>=35	0.26 (–0.25; 0.76)	0.25 (–0.24; 0.73)	–0.01 (–0.68; 0.67)	–0.01 (–0.67; 0.66)
LDL (N_{DZ}=510; N_{MZ}=519)				
<20	0.20 (–0.36; 0.77)	0.18 (–0.39; 0.74)	0.28 (–0.32; 0.88)	0.29 (–0.32; 0.89)
20–24	0.17 (–0.18; 0.52)	0.17 (–0.18; 0.52)	0.20 (–0.13; 0.54)	0.20 (–0.13; 0.54)
25–29	ref	ref	ref	ref
30–34	0.21 (–0.15; 0.57)	0.19 (–0.18; 0.55)	0.08 (–0.28; 0.44)	0.08 (–0.28; 0.44)
>=35	–0.08 (–0.65; 0.49)	–0.09 (–0.66; 0.48)	–0.03 (–0.59; 0.52)	–0.03 (–0.59; 0.52)

Notes: [a] Distribution skewed; log transformed. Distributions have been winsorised at 0.5% and 99.5%. * = significant different within- and between-level effects. Abbreviations: BMI = body mass index; CI = confidence interval; DZ = dizygotic; HDL = high-density lipoprotein; LDL = low-density lipoprotein; MZ = monozygotic.

What are the adjusted within-family associations between age at first birth and CV biomarker risk factors in mothers, that is, when accounting for confounding in the shared family environment (DZ twins) and/or shared genetics (MZ twins) and confounding due to individual-level early life and adult factors?

Further adjustment for individual-level covariates birth order, age at menarche, and educational attainment did not substantially alter the standardised within-family effect sizes and interpretation in most instances (Table 4; Supplementary figures S2–S8).

Sensitivity analyses

Trends in standardised effect sizes from models unstratified by zygosity, from unweighted models and sensitivity analyses excluding first blood pressure, excluding calculated LDL measurements, using a binary exposure or a larger sample for crude analyses did not substantially alter the main interpretation of the findings (Supplementary tables S1–S8). Specifically, the finding from MZ within-family effects that age at first birth <20 years was associated with a higher android/gynoid fat ratio later in life was replicated across models (point estimate range: standardised β = 0.35–0.68), however, with varying confidence intervals.

Discussion

Individual level analyses suggest that women with age at first birth <20 years had higher mean BMI, android/gynoid fat ratio, and triglyceride levels later in life compared to women who had their first child between 25 and 29 years of age. Age at first birth between the ages of 20 and 24 was also associated with higher mean BMI, android/gynoid fat ratio, LDL and triglyceride levels after the age of 50. However, confidence intervals were wide and differences between standardised between and within-family coefficients indicate that confounding due to the shared family environment and, potentially, genetic factors play a role in this association. Considering fully adjusted MZ within-family coefficients, results suggest that age at first birth <20 years may

be associated with increased android/gynoid fat ratio, independent of shared early-life environmental factors, genetic factors and confounding via birth order, early menarche and education. While confidence intervals were wide, this was a robust finding in sensitivity analyses.

These findings add to and extend previous literature. This study's individual-level results for women with younger age (that is, <20 years) at first birth replicate previous findings of increased CV risk for younger age at first birth (Hardy et al, 2009; Lacey et al, 2017; Sironi et al, 2020). Considering the MZ within-family coefficients, associations between age at first birth before the age of 20 with increased android/gynoid fat ratio were maintained, although with wide confidence intervals. Previous studies have shown that associations can partially be explained by confounding in early life, as well as social and behavioural pathways (Hardy et al, 2009; Lacey et al, 2017). This study adds to the previous findings by allowing for more stringent control of confounding due to the early-life family environment and genetics. In most instances, further control for individual-level confounders including education did little to change the size of the effect.

To our knowledge, this is the first study to assess the association between age at first birth and later life CV biomarker risk factors using a co-twin design. While the co-twin design's strengths are the ability to account for confounding of family-level and genetic factors, this study also had several limitations: First, the sample size was small, resulting in wide confidence intervals. This limited the interpretation of findings for other age-at-first-birth groups in the present study. The interpretations presented here focus mainly on the <20 age at first birth group where results showed stronger and more consistent associations, and sensitivity analyses are presented to assess the robustness of the results.

Second, the statistical power for within-family effects was low (only 61.1% of DZ and 57.9% of MZ twins were in different categories from their twin). Within-family effects are also more vulnerable to bias arising from measurement error or unmeasured confounding (Frisell et al, 2012). Therefore, we were cautious with genetic interpretations of the within-family effect differences in DZ and MZ twins. It might be tempting to attribute such differences to the increased shared genetics in MZ pairs and therefore infer genetic confounding is driving an association. However, this interpretation hinges on the assumption that MZ twins share the environment to the same extent as DZ twins (equal environment assumption); an assumption which has been challenged (Felson, 2014). We recommend further research into possible genetic confounding of age at first birth and CV risk before drawing conclusions.

Third, the volunteer sample and survival bias mean that the study sample is unlikely to be representative of the general population and further exclusions in the definition of a complete case sample could have increased bias. Although the latter was accounted for by creating non-response sample weights, we were only able to compute these weights based on a limited set of variables and we cannot account fully for sample representativeness.

Fourth, due to data availability and impacts on sample size, the present study was not able to assess social, economic and behavioural pathways to explain the remaining association between age at first birth and CV risk or adjust more comprehensively for individual-level confounding (for example, baseline health). Although relevant social, economic and behavioural measures were available in the TwinsUK dataset,

these were measured at different ages and most unsuitable for consideration as a mediator/ mechanism between the age at first birth and the outcome (measured at 50+ years). This reduces the comparability to other studies (Hardy et al, 2009; Lacey et al, 2017). For example, it is possible that adult social, economic and behavioural factors would explain the MZ within-family associations for android/gynoid fat ratio, but this could not be determined in the present study. Other individual-level unmeasured confounders may also play a role, such as baseline health. For example, poor health or high BMI in early life may lead to both earlier menarche and be associated with later life health. A related limitation is that women's highest education was collected when they were 50 years and above as educational data pre-dating the birth of their first child was not available. Educational attainment can therefore both be a confounder (that is, educational attainment up to age at first birth) and mediator (that is, continued education after the birth of the first child), and it is possible that effect sizes were over-adjusted. However, findings suggest that educational attainment added little more to what was already accounted for by included confounders and the (shared) early-life environment with the latter being a well-known predictor of later educational attainment (Fergusson et al, 2008).

Fifth, large missingness of data on use of antihypertensives and statins meant that we could not account for these in the blood pressure and cholesterol outcomes. Both would have introduced bias in the outcomes and decreased precision.

Finally, measures for exposure and covariates were derived from questions from different waves of data collection which had slightly different wording. Where possible, multiple responses over time were used for quality control; however, it is possible that the different measures may have introduced measurement error. Similarly, there was a wide age range at which questionnaire data and clinical measures were collected.

These findings have implications for research with future studies benefitting from larger and more representative (twin) samples. There are also practical implications to identify parents most at risk of adverse CV health later in life, early on. This study suggests that both early life and (young) parenthood are key life periods/events for parents' prospective health outcomes. Studying the most influential pathways in this association (Hardy et al, 2009; Lacey et al, 2017) can help to identify the type of support young parents need. While physiological pathways have also been proposed including risks introduced through pregnancy-related changes (Gunderson et al, 2012), evidence of non-gender specific associations and behavioural and social pathways in mothers and fathers lend more support to bio-social explanations (Hardy et al, 2009; Lacey et al, 2017). Evidence from cross-country comparisons suggests that social and economic country-level differences may modify the risk associated with early parenthood (Grundy and Foverskov, 2016), for example via social norms and family-supportive policies.

In conclusion, this co-twin design study suggests that the early-life family environment and, potentially, genetics play a role in the association between young age at first birth and later life adverse CV risk. Young age at first birth may be associated with CV risks, particularly due to a higher android/gynoid fat ratio later in life, independent of vulnerabilities in the family environment and genetic factors. Larger representative and/or twin studies are needed to provide further support to these findings, and to understand the nature of confounding, the specific pathways and points for intervention.

Funding

VS is funded by the ESRC-BBSRC Soc-B Centre for Doctoral Training (Grant ref: ES/T00200X/1). TwinsUK is funded by the Wellcome Trust (Grant ref: 212904/Z/18/Z), Medical Research Council, Versus Arthritis, European Union Horizon 2020, Chronic Disease Research Foundation (CDRF), Zoe Ltd, the National Institute for Health and Care Research (NIHR) Clinical Research Network (CRN) and Biomedical Research Centre based at Guy's and St Thomas' NHS Foundation Trust in partnership with King's College London. We also acknowledge support from the King's Together Seed Fund which initiated the collaboration leading to this work.

Acknowledgements

We would like to thank the participants in the TwinsUK for their participation and ongoing support. We would also like to thank the Department of Twin Research for managing the TwinsUK database.

Data availability statement

The TwinsUK data are available on request via the TwinsUK website: https://twinsuk.ac.uk/resources-for-researchers/our-data/.

Ethics statement

This study is a secondary analysis of TwinsUK data. TwinsUK is an ongoing longitudinal survey which has received ethical approval for its data collection from NHS Research Ethics Committees at the Department of Twin Research and Genetic Epidemiology, King's College London. Participants provide informed consent upon joining TwinsUK and have the right to withdraw consent and data at any point.

Conflict of interest

The authors declare that there is no conflict of interest.

References

Aluga, D. and Okolie, E.A. (2021) Socioeconomic determinants of teenage pregnancy and early motherhood in the United Kingdom: a perspective, *Health Promotion Perspectives*, 11(4): 426–29. doi: 10.34172/hpp.2021.52

Baldwin, J.R., Ayorech, Z., Rijsdijk, F.V., Schoeler, T. and Pingault, J.B. (2021) Cyber-victimisation and mental health in young people: a co-twin control study, *Psychological Medicine*, 51(15): 2620–30. doi: 10.1017/S0033291720001178

Bowyer, R.C.E., Abbasian, G., García, M.P., Anastasiou, A., Lachance, G., Thompson, E.J., et al (2022) Diverging destinies: 'social' data within the TwinsUK cohort, *Wellcome Open Research*, 7. doi: 10.12688/wellcomeopenres.17139.1

Carlin, J.B., Gurrin, L.C., Sterne, J.A., Morley, R. and Dwyer, T. (2005) Regression models for twin studies: a critical review, *International Journal of Epidemiology*, 34(5): 1089–99. doi: 10.1093/ije/dyi153

Felson, J. (2014) What can we learn from twin studies? A comprehensive evaluation of the equal environments assumption, *Social Science Research*, 43: 184–99. doi: 10.1016/j.ssresearch.2013.10.004

Fergusson, D.M., Horwood, L.J. and Boden, J.M. (2008) The transmission of social inequality: examination of the linkages between family socioeconomic status in childhood and educational achievement in young adulthood, *Research in Social Stratification and Mobility*, 26(3): 277–95. doi: 10.1016/j.rssm.2008.05.001

Frisell, T., Öberg, S., Kuja-Halkola, R. and Sjölander, A. (2012) Sibling comparison designs: bias from non-shared confounders and measurement error, *Epidemiology*, 23(5): 713–20. doi: 10.1097/EDE.0b013e31825fa230

Görlitz, K. and Tamm, M. (2020) Parenthood, risk attitudes and risky behavior, *Journal of Economic Psychology*, 79: 102189. doi: 10.1016/j.joep.2019.102189

Grundy, E. and Read, S. (2015) Pathways from fertility history to later life health: results from analyses of the English longitudinal study of ageing, *Demographic Research*, S22(4): 107–46. doi: 10.4054/demres.2015.32.4

Grundy, E. and Foverskov, E. (2016) Age at first birth and later life health in Western and Eastern Europe, *Population and Development Review*, 42(2): 245–69. doi: 10.1111/j.1728-4457.2016.00128.x

Gunderson, E.P., Schreiber, G., Striegel-Moore, R., Hudes, M., Daniels, S., Biro, F.M., et al (2012) Pregnancy during adolescence has lasting adverse effects on blood lipids: a 10-year longitudinal study of black and white females, *Journal of Clinical Lipidology*, 6(2): 139–49. doi: 10.1016/j.jacl.2011.12.004

Hardy, R., Kuh, D., Whincup, P.H. and Wadsworth, M.E.J. (2006) Age at puberty and adult blood pressure and body size in a British birth cohort study, *Journal of Hypertension*, 24(1). doi: 10.1097/01.hjh.0000198033.14848.93

Hardy, R., Lawlor, D.A., Black, S., Wadsworth, M.E. and Kuh, D. (2007) Number of children and coronary heart disease risk factors in men and women from a British birth cohort, *BJOG*, 114(6): 721–30.

Hardy, R., Lawlor, D.A., Black, S., Mishra, G.D. and Kuh, D. (2009) Age at birth of first child and coronary heart disease risk factors at age 53 years in men and women: British birth cohort study, *Journal of Epidemiology and Community Health*, 63(2): 99–105. doi: 10.1136/jech.2008.076943

Højsgaard, S., Halekoh, U. and Yan, J. (2005) The R Package geepack for generalized estimating equations, *Journal of Statistical Software*, 15(2): 1–11.

Kearney, M.S. and Levine, P.B. (2012) Why is the teen birth rate in the United States so high and why does it matter?, *Journal of Economic Perspectives*, 26(2): 141–66. doi: 10.1257/jep.26.2.141

Lacey, R.E., Kumari, M., Sacker, A. and McMunn, A. (2017) Age at first birth and cardiovascular risk factors in the 1958 British birth cohort, *Journal of Epidemiology and Community Health*, 71(7): 691–8. doi: 10.1136/jech-2016-208196

Lawlor, D.A., Emberson, J.R., Ebrahim, S., Whincup, P.H., Wannamethee, S.G., Walker, M., et al (2003) Is the association between parity and coronary heart disease due to biological effects of pregnancy or adverse lifestyle risk factors associated with child-rearing?, *Circulation*, 107(9): 1260–64. doi: 10.1161/01.cir.0000053441.43495.1a

Natale, B.N., Manuck, S.B., Shaw, D.S., Matthews, K.A., Muldoon, M.F., Wright, A.G.C., et al (2023) Systemic inflammation contributes to the association between childhood socioeconomic disadvantage and midlife cardiometabolic risk, *Annals of Behavioral Medicine*, 57(1): 26–37. doi: 10.1093/abm/kaac004

O'Kelly, A.C., Michos, E.D., Shufelt, C.L., Vermunt, J.V., Minissian, M.B., Quesada, O., et al (2022) Pregnancy and reproductive risk factors for cardiovascular disease in women, *Circulation Research*, 130(4): 652–72. doi: 10.1161/CIRCRESAHA.121.319895

Okosun, I.S., Seale, J.P. and Lyn, R. (2015) Commingling effect of gynoid and android fat patterns on cardiometabolic dysregulation in normal weight American adults, *Nutrition & Diabetes*, 5(5): e155–e55. doi: 10.1038/nutd.2015.5

Okoth, K., Chandan, J.S., Marshall, T., Thangaratinam, S., Thomas, G.N., Nirantharakumar, K., et al (2020) Association between the reproductive health of young women and cardiovascular disease in later life: umbrella review, *BMJ*, 371: m3502. doi: 10.1136/bmj.m3502

Parikh, N.I., Jeppson, R.P., Berger, J.S., Eaton, C.B., Kroenke, C.H., LeBlanc, E.S., et al (2016) Reproductive risk factors and coronary heart disease in the women's health initiative observational study, *Circulation*, 133(22): 2149–58. doi: 10.1161/CIRCULATIONAHA.115.017854

Pool, L.R., Aguayo, L., Brzezinski, M., Perak, A.M., Davis, M.M., Greenland, P., et al (2021) Childhood risk factors and adulthood cardiovascular disease: a systematic review, *Journal of Pediatrics*, 232: 118–26. doi: 10.1016/j.jpeds.2021.01.053

Rosendaal, N.T.A. and Pirkle, C.M. (2017) Age at first birth and risk of later-life cardiovascular disease: a systematic review of the literature, its limitation, and recommendations for future research, *BMC Public Health*, 17(1): 627. doi: 10.1186/s12889-017-4519-x

Sironi, M. (2019) Fertility histories and chronic conditions later in life in Europe, *European Journal of Ageing*, 16(3): 259–72. doi: 10.1007/s10433-018-0494-z

Sironi, M., Ploubidis, G.B. and Grundy, E.M. (2020) Fertility history and biomarkers using prospective data: evidence from the 1958 national child development study, *Demography*, 57(2): 529–58. doi: 10.1007/s13524-020-00855-x

Stannard, S., Berrington, A. and Alwan, N.A. (2022) The mediating pathways between parental separation in childhood and offspring hypertension at midlife, *Scientific Reports*, 12(1): 7062. doi: 10.1038/s41598-022-11007-z

Tomassini, C., Di Gessa, G. and Egidi, V. (2018) Fertility histories and health in later life in Italy, in G. Doblhammer and J. Gumà (eds) *A Demographic Perspective on Gender, Family and Health in Europe*, Cham: Springer International Publishing, pp 263–81.

TwinsUK (nd) What is TwinsUK?, https://twinsuk.ac.uk/about-us/what-is-twinsuk/.

Verdi, S., Abbasian, G., Bowyer, R.C.E., Lachance, G., Yarand, D., Christofidou, P., et al (2019) TwinsUK: the UK adult twin registry update, *Twin Research and Human Genetics*, 22(6): 523–9. doi: 10.1017/thg.2019.65