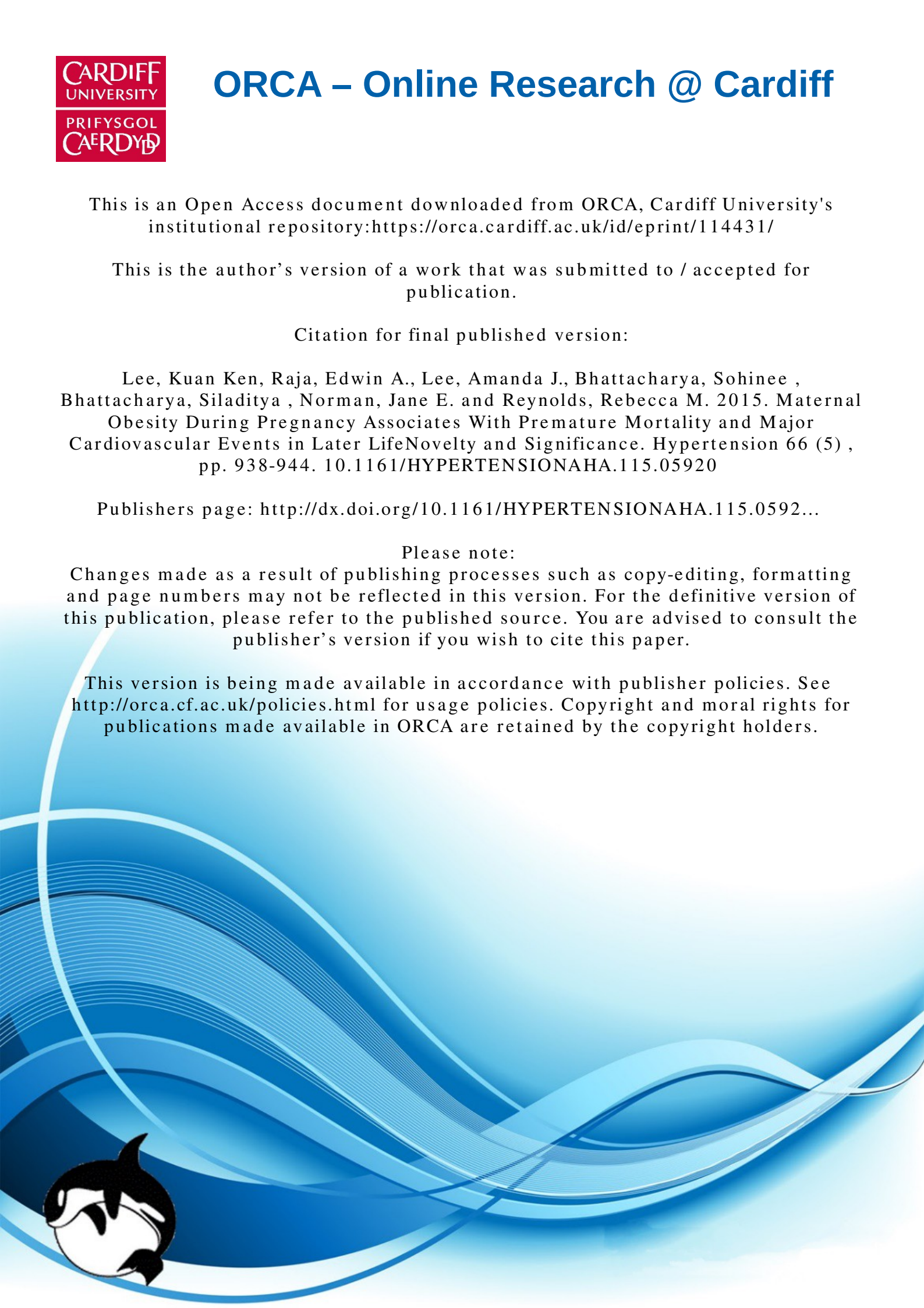

ONLINE SUPPLEMENTARY DATA

MATERNAL OBESITY DURING PREGNANCY ASSOCIATES WITH PREMATURE MORTALITY AND MAJOR CARDIOVASCULAR EVENTS IN LATER LIFE

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SHORT TITLE: OBESITY IN PREGNANCY AND PREMATURE MORTALITY

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METHODS

Ethics statement

Ethical approval was obtained from the North of Scotland Research Ethics Service (REC reference: 10/S11034/15). Approvals were also obtained from the steering committee of the AMND and the Privacy Advisory Committee of ISD, Scotland.

Subjects and methods

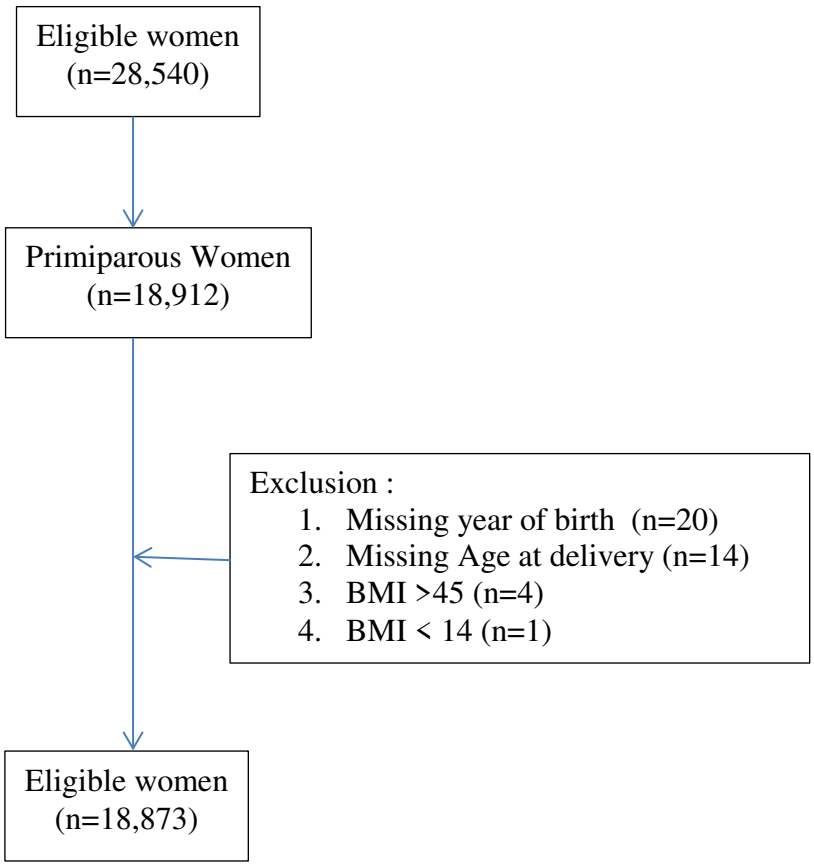
The Aberdeen Maternity and Neonatal Databank (AMND) has recorded information on all obstetric related events in women living in Aberdeen, Scotland since 1950 (detailed at www.abdn.ac.uk/amnd). In this cohort analysis, the exposure was maternal obesity during pregnancy and the outcomes were all cause mortality and hospital admission with a cardiovascular event (defined below) in later life. We identified all women from the AMND who delivered their first live singleton baby at term (≥37 weeks' gestation) between 1950 and 1976 and who had their weight recorded at their first antenatal visit. The women were grouped according to their BMI, calculated from height and weight measured at their first antenatal visit, using World Health Organisation criteria: underweight (BMI<18.5 kg/m^2), normal weight (BMI 18.5-24.9 kg/m^2), overweight (BMI 25-29.9 kg/m^2), and obese (BMI≥30 kg/m^2). Women's records were linked to the General Register of Deaths, Scotland, and the Scottish Morbidity Record systems (SMR01) of the Information and Services Division, NHS Scotland, by probability matching on name, date of birth, and postcode (zip code) to identify specific death and all hospital admissions for cardiovascular events. Where the community health index (CHI) number was available in the registers, this unique identifier was used for deterministic matching.

Study Outcomes and follow-up

We defined cardiovascular events in women according to hospital discharge data codes (ICD, international classification of diseases versions 9 and 10) consistent with angina (I20), myocardial infarction (I21-I23, I25), stroke

(I61, I63, I64), other cerebrovascular disease (I60, I62, I65-69), transient ischaemic attack (G45), peripheral artery disease (I70-I79), and other cardiovascular disease (I00, I01, I02, I05-I13, I15, I26-I28, I30-I52, I80-I89, I95, I97, I98, I99, Z95, R074, M31). Major Adverse Cardiovascular Event (MACE) was defined as a composite of death, myocardial infarction, stroke or peripheral arterial disease, whichever occurred first. All women included in this study were followed up from their first antenatal visit between 1950 and 1976 up to the 1st January 2012 (see Flow chart).

Flow Chart of Population Selection



Statistical analysis

Data were analysed with SPSS version 21.0 (SPSS Inc., Chicago, IL, USA) and Stata version 13 (Stata Corp, Texas). Chi-square, ANOVA and Kruskal-wallis tests were used to compare baseline characteristics of women across the different BMI categories. Two Cox proportional hazards models were used to examine the relationship between BMI and time to mortality/cardiovascular event/MACE or censoring. The first model was the standard approach in which the primary time scale was time on study (defined as time between age at delivery and 'event') with age at delivery included as a confounder. The second model used age as the primary time scale, and age at delivery as the year at entry in order to control for the stronger effects of age in later life. The results of this second model are reported in the paper, whilst the results of the first model were considered as a sensitivity analysis and are reported in the supplement.

For analyses of BMI as a categorical variable, Kaplan-Meier survival curves were constructed to illustrate mortality and MACE at different ages of women. Cox survival analysis was used to examine the relationship between maternal BMI (underweight, overweight or obese in pregnancy compared to women with normal BMI) and cardiovascular events\death\MACE. Multivariate survival analysis was conducted to adjust for potential confounding factors extracted from the AMND including husband/partner's social class, smoking status, gestation at BMI measurement, age at delivery, clinically diagnosed pre-eclampsia and low birth weight (<2500g). The proportionality of hazards was examined by comparing observed and predicted survival curves, plotting smoothed scaled schoenfeld residuals against time and examination of the schoenfeld residual for global test (no violations were detected).

In the second set of analyses, to model the non-linear relationship between maternal BMI at pregnancy and mortality/MACE, a restricted cubic spline (RCS) procedure was adopted. This uses multiple polynomial line segments within the range of BMI, the boundaries of these line segments being called knots. Two internal knots were

considered for the model at maternal BMI values of 21.3 and 23.6 with two boundary knots at 14.6 and 44.5. The mean maternal BMI in the data was 22.8 kg/m^2so BMI 23 kg/m^2 was taken as the reference value in the calculation of the hazards of mortality/ MACE. A spline function was assumed to be significant if the p-value for the model chi-square was < 0.05 and the association was assumed to be non-linear if the spline coefficients differ significantly from each other based on the Wald test for linearity.

All analyses were done (i) for all women with the first maternal weight measured at any time during pregnancy and (ii) for the subset of women with first weight recorded before 20 weeks' gestation to avoid the additional influences of weight gain during pregnancy, which might be an independent risk factor for the outcomes of interest.

To examine the influence of parity on outcomes we first included adjustment for parity in all models described above. A group-based trajectory modelling, also referred to as a semi-parametric mixture model was applied using traj plugin in Stata to identify maternal BMI trajectories across pregnancies. We then examined all outcomes according to change in maternal BMI between first and last pregnancy among women with more than one pregnancy, using women who had gained or lost less than 1 BMI unit (weight stable) as the reference category. A p-value < 0.05 was considered to be statistically significant throughout all analyses.

Table S1. Baseline characteristics of mothers by maternal body mass index (BMI)

(n=18873)	**Maternal BMI (WHO) category**				
	Underweight n= 701	Normal n= 14459	Overweight n= 3260	Obese n= 452	P value
Age at delivery (years)	23.4 (3.80)	23.2 (4.2)	23.7 (4.8)	24.6 (5.1)	<0.001
Gestation when BMI was measured (weeks):					
In all women	13 (11, 15)	15 (12, 19)	17 (13, 24)	17 (13, 25)	<0.001
In subgroup measured before 20 weeks	13 (11, 15)	14 (11, 16)	14 (11, 16)	14 (11, 16)	<0.001
No (%) of mothers by social class:					
I-IIIa non-manual	205 (29.3)	3693 (25.5)	672 (20.6)	82 (18.1)	<0.001
IIIb manual-V	429 (61.1)	8764 (60.6)	1932 (59.3)	247 (54.7)	
Missing	67 (9.5)	2003 (13.9)	656 (20.1)	123 (27.2)	
Gestation at delivery (weeks)	40.4 (1.4)	40.5 (1.4)	40.4 (1.4)	40.2 (±.6)	<0.001
No (%) of Smokers	82 (11.7)	2279 (15.7)	626 (19.2)	129 (28.5)	<0.001
No (%) of Pre-eclampsia	26 (3.7)	683 (4.7)	230 (7.1)	39 (8.6)	<0.001
No (%) of Low Birth Weight (<2500g)	56 (8.0)	602 (4.2)	109 (3.3)	9 (2.0)	<0.001

Figures are mean (SD), median (IQR) or n (%) as appropriate

Table S2. Hazard ratios and 95% confidence intervals (CI) for cardiovascular events according to maternal BMI category among women with BMI measurement before 20 weeks gestation. Data analysed using age as the primary time scale, and age at delivery as the year of entry.

Endpoint		Hazard ratio (95% CI)		
	No (%) of events	Unadjusted	Adjusted*	Adjusted†
All cardiovascular events combined				
Mother underweight	115 (17.2)	0.94 (0.78, 1.14)	0.97 (0.80, 1.17)	0.97 (0.80, 1.17)
Mother normal weight	1928 (17.5)	1.00	1.00	1.00
Mother overweight	393 (19.8)	**1.25** (1.12, 1.39)	**1.19** (1.07, 1.33)	**1.21** (1.08, 1.35)
Mother obese	55 (20.7)	**1.47** (1.13, 1.93)	**1.30** (1.00, 1.71)	**1.35** (1.03, 1.77)
MACE (Death, MI, Stroke, PAD)				
Mother underweight	117 (17.5)	**1.26** (1.05, 1.52)	**1.28** (1.06, 1.54)	**1.24** (1.03, 1.50)
Mother normal weight	1483 (13.4)	1.00	1.00	1.00
Mother overweight	294 (14.8)	1.19 (1.05, 1.35)	**1.17** (1.03, 1.32)	**1.19** (1.05, 1.35)
Mother obese	42 (15.8)	**1.43** (1.05, 1.94)	1.34 (0.99, 1.83)	**1.43** (1.05, 1.94)
Angina				
Mother underweight	12 (1.8)	0.65 (0.37, 1.16)	0.67 (0.37, 1.19)	0.66 (0.37, 1.19)
Mother normal weight	288 (2.6)	1.00	1.00	1.00
Mother overweight	48 (2.4)	1.01 (0.75, 1.38)	0.97 (0.72, 1.32)	0.99 (0.73, 1.34)
Mother obese	12 (4.5)	**2.17** (1.22, 3.86)	**2.00** (1.12, 3.57)	**2.11** (1.18, 3.77)
Myocardial Infarction				
Mother underweight	20 (3.0)	1.18 (0.75, 1.86)	1.23 (0.78, 1.93)	1.22 (0.77, 1.92)
Mother normal weight	267 (2.4)	1.00	1.00	1.00
Mother overweight	57 (2.9)	1.30 (0.98, 1.73)	1.25 (0.94, 1.66)	1.28 (0.96, 1.70)
Mother obese	6 (2.3)	1.18 (0.52, 2.64)	1.06 (0.47, 2.39)	1.12 (0.50, 2.52)
Stroke				
Mother underweight	10 (1.5)	0.89 (0.47, 1.68)	0.91 (0.48, 1.72)	0.90 (0.47, 1.70)
Mother normal weight	176 (1.6)	1.00	1.00	1.00
Mother overweight	33 (1.7)	1.14 (0.79 1.66)	1.11 (0.77, 1.62)	1.15 (0.79, 1.66)
Mother obese	4 (1.5)	1.20 (0.44, 3.23)	1.09 (0.41, 2.95)	1.18 (0.44, 3.19)
Other cerebrovascular disease				
Mother underweight	14 (2.1)	1.18 (0.69, 2.04)	1.22 (0.71, 2.10)	1.20 (0.70, 2.07)
Mother normal weight	186 (1.7)	1.00	1.00	1.00
Mother overweight	33 (1.7)	1.08 (0.74, 1.56)	1.03 (0.71, 1.49)	1.06 (0.73, 1.53)
Mother obese	5 (1.9)	1.38 (0.57, 3.36)	1.23 (0.50, 2.99)	1.30 (0.53, 3.18)
Peripheral arterial disease				
Mother underweight	16 (2.4)	1.34 (0.81, 2.24)	1.37 (0.82, 2.28)	1.34 (0.80, 2.24)
Mother normal weight	187 (1.7)	1.00	1.00	1.00
Mother overweight	49 (2.5)	**1.60** (1.17, 2.19)	**1.53** (1.12, 2.10)	**1.59** (1.15, 2.17)
Mother obese	11 (4.2)	**3.08** (1.68, 5.66)	**2.74** (1.49, 5.04)	**2.97** (1.61, 5.48)
Other cardiovascular disease				
Mother underweight	97 (14.5)	0.89 (0.73, 1.09)	0.91 (0.74, 1.12)	0.91 (0.74, 1.12)
Mother normal weight	1707 (15.5)	1.00	1.00	1.00
Mother overweight	360 (18.2)	**1.29** (1.15, 1.45)	**1.24** (1.11, 1.39)	**1.25** (1.12, 1.40)
Mother obese	50 (18.8)	**1.52** (1.15, 2.01)	**1.35** (1.02, 1.79)	**1.39** (1.05, 1.84)

*Adjusted for husband/partner's social class, smoking status, gestational age, pre-eclampsia and low birth weight.
†Adjusted for husband/partner's social class, smoking status, gestational age, pre-eclampsia, low birth weight and parity
MACE= Major adverse cardiac event defined by Death, Myocardial Infarction, Stroke or Peripheral arterial disease

Table S3. Hazard ratios and 95% confidence intervals (CI) for all deaths by maternal BMI category. Analysis conducted as sensitivity analysis using the time scale as time-on-study.

Sample	No (%) of deaths	Hazard ratio (95% CI) Unadjusted	Adjusted†
Complete sample (n=18 912)			
Mother underweight	90 (12.8)	1.16 (0.94, 1.44)	1.16 (0.93, 1.43)
Mother normal weight	1514 (10.5)	1.00	1.00
Mother overweight	348 (10.7)	**1.13** (1.01, 1.27)	1.09 (0.97, 1.23)
Mother obese	53 (11.7)	**1.49** (1.13, 1.96)	**1.37** (1.04, 1.80)
Subgroup with BMI measured <20 weeks (n=13 690)			
Mother underweight	87 (13.0)	1.19 (0.95, 1.48)	1.19 (0.96, 1.49)
Mother normal weight	1152 (10.4)	1.00	1.00
Mother overweight	235 (11.9)	**1.27** (1.10, 1.46)	**1.21** (1.05, 1.40)
Mother obese	33 (12.4)	**1.52** (1.08, 2.15)	1.40 (0.99, 1.98)

†Adjusted for husband/partner's social class, smoking status, gestational age, mother's age at delivery, pre-eclampsia and low birth weight.

Table S4a. Hazard ratios and 95% confidence intervals (CI) for cardiovascular events according to maternal BMI category among all women

Endpoint	No (%) of events	Hazard ratio (95% CI) Unadjusted	Adjusted†
All cardiovascular events combined			
Mother underweight	120 (17.0)	0.97 (0.80, 1.16)	0.95 (0.79, 1.15)
Mother normal weight	2430 (16.8)	1.00	1.00
Mother overweight	588 (18.0)	**1.22** (1.12, 1.34)	**1.26** (1.15, 1.38)
Mother obese	82 (18.1)	**1.52** (1.22, 1.89)	**1.52** (1.22, 1.90)
MACE (Death, MI, Stroke, PAD)			
Mother underweight	121 (17.3)	**1.24** (1.03, 1.49)	**1.24** (1.03, 1.49)
Mother normal weight	1929 (13.3)	1.00	1.00
Mother overweight	443 (13.6)	1.14 (1.02, 1.26)	1.11 (1.00, 1.23)
Mother obese	67 (14.8)	**1.50** (1.18, 1.92)	**1.39** (1.09, 1.78)
Angina			
Mother underweight	14 (2.0)	0.75 (0.44, 1.28)	0.74 (0.43, 1.26)
Mother normal weight	358 (2.5)	1.00	1.00
Mother overweight	69 (2.1)	0.98 (0.75, 1.26)	1.04 (0.80, 1.35)
Mother obese	16 (3.5)	**2.08** (1.26, 3.44)	**2.27** (1.37, 3.76)
Myocardial Infarction			
Mother underweight	21 (3.0)	1.24 (0.80, 1.92)	1.24 (0.80, 1.94)
Mother normal weight	329 (2.3)	1.00	1.00
Mother overweight	83 (2.6)	**1.28** (1.01, 1.63)	**1.29** (1.01, 1.65)
Mother obese	12 (2.7)	1.70 (0.96, 3.03)	1.66 (0.93, 2.97)
Stroke			
Mother underweight	10 (1.4)	0.89 (0.47, 1.67)	0.87 (0.46, 1.64)
Mother normal weight	217 (1.5)	1.00	1.00
Mother overweight	47 (1.4)	1.10 (0.80, 1.51)	1.11 (0.80, 1.53)
Mother obese	6 (1.3)	1.30 (0.58, 2.93)	1.27 (0.56, 2.87)
Other cerebrovascular disease			
Mother underweight	14 (2.0)	1.16 (0.68, 1.99)	1.17 (0.68, 2.00)
Mother normal weight	233 (1.6)	1.00	1.00
Mother overweight	59 (1.8)	1.28 (0.96, 1.71)	1.25 (0.94, 1.68)
Mother obese	6 (1.3)	1.19 (0.53, 2.67)	1.08 (0.48, 2.43)
Peripheral arterial disease			
Mother underweight	16 (2.3)	1.32 (0.80, 2.19)	1.28 (0.77, 2.13)
Mother normal weight	234 (1.6)	1.00	1.00
Mother overweight	70 (2.2)	**1.52** (1.16, 1.98)	**1.53** (1.17, 2.01)
Mother obese	14 (3.1)	**2.80** (1.63, 4.80)	**2.67** (1.55, 4.61)
Other cardiovascular disease			
Mother underweight	101 (14.4)	0.92 (0.75, 1.12)	0.90 (0.73, 1.10)
Mother normal weight	2135 (14.8)	1.00	1.00
Mother overweight	533 (16.4)	**1.26** (1.15, 1.39)	**1.31** (1.19, 1.44)
Mother obese	77 (16.8)	**1.64** (1.30, 2.05)	**1.65** (1.31, 2.08)

†Adjusted for husband/partner's social class, smoking status, gestational age, mother's age at delivery, pre-eclampsia and birth weight.
MACE= Major adverse cardiac event defined by Death, Myocardial Infarction, Stroke or Peripheral arterial disease

Table S4b. Hazard ratios and 95% confidence intervals (CI) for cardiovascular events according to maternal BMI category among women with BMI measurement <20 weeks gestation

Endpoint	No (%) of events	Hazard ratio (95% CI) Unadjusted	Adjusted†
All cardiovascular events combined			
Mother underweight	115 (17.2)	0.94 (0.78, 1.13)	0.96 (0.79, 1.15)
Mother normal weight	1928 (17.5)	1.00	1.00
Mother overweight	393 (19.8)	**1.30** (1.17, 1.45)	**1.29** (1.16, 1.44)
Mother obese	55 (20.7)	**1.60** (1.22, 2.09)	**1.51** (1.16, 1.98)
MACE (Death, MI, Stroke, PAD)			
Mother underweight	117 (17.5)	**1.25** (1.04, 1.51)	**1.27** (1.05 , 1.53)
Mother normal weight	1483 (13.4)	1.00	1.00
Mother overweight	294 (14.8)	1.24 (1.09, 1.40)	**1.19** (1.05, 1.35)
Mother obese	42 (15.8)	**1.53** (1.12, 2.07)	**1.40** (1.03, 1.91)
Angina			
Mother underweight	12 (1.8)	0.65 (0.36, 1.15)	0.65 (0.36, 1.15)
Mother normal weight	288 (2.6)	1.00	1.00
Mother overweight	48 (2.4)	1.07 (0.79, 1.45)	1.11 (0.81, 1.51)
Mother obese	12 (4.5)	**2.40** (1.34, 4.27)	**2.47** (1.38, 4.41)
Myocardial Infarction			
Mother underweight	20 (3.0)	1.17 (0.74, 1.84)	1.21 (0.76, 1.90)
Mother normal weight	267 (2.4)	1.00	1.00
Mother overweight	57 (2.9)	1.37 (1.03, 1.83)	**1.36** (1.02, 1.81)
Mother obese	6 (2.3)	1.29 (0.58, 2.90)	1.22 (0.54, 2.74)
Stroke			
Mother underweight	10 (1.5)	0.88 (0.47, 1.66)	0.90 (0.47, 1.70)
Mother normal weight	176 (1.6)	1.00	1.00
Mother overweight	33 (1.7)	1.21 (0.83, 1.75)	1.18 (0.81, 1.72)
Mother obese	4 (1.5)	1.32 (0.49, 3.55)	1.21 (0.45, 3.28)
Other cerebrovascular disease			
Mother underweight	14 (2.1)	1.17 (0.68, 2.02)	1.20 (0.70, 2.08)
Mother normal weight	186 (1.7)	1.00	1.00
Mother overweight	33 (1.7)	1.14 (0.78, 1.65)	1.10 (0.76, 1.59)
Mother obese	5 (1.9)	1.53 (0.63, 3.72)	1.39 (0.57, 3.39)
Peripheral arterial disease			
Mother underweight	16 (2.4)	1.33 (0.80, 2.22)	1.36 (0.82, 2.27)
Mother normal weight	187 (1.7)	1.00	1.00
Mother overweight	49 (2.5)	**1.69** (1.23, 2.32)	**1.64** (1.19, 2.25)
Mother obese	11 (4.2)	**3.40** (1.85, 6.24)	**3.08** (1.67, 5.67)
Other cardiovascular disease			
Mother underweight	97 (14.5)	0.89 (0.72, 1.09)	0.90 (0.73, 1.10)
Mother normal weight	1707 (15.5)	1.00	1.00
Mother overweight	360 (18.2)	**1.35** (1.21, 1.52)	**1.34** (1.20, 1.51)
Mother obese	50 (18.8)	**1.65** (1.24, 2.19)	**1.56** (1.18, 2.07)

†Adjusted for husband/partner's soc class, smoking status, gestational age, mothe age at delivery, pre-eclampsia and low bir weight.
MACE= Major adverse cardiac event defined by Death, Myocardial Infarction, Stroke or Peripheral arterial disease

Table S5. Hazard ratios and 95% confidence intervals for cardiovascular events according to first pregnancy maternal BMI category and change in BMI between first and last pregnancy among women with more than one pregnancy (n=5,552)

Endpoint	No (%) of events	Hazard ratio (95% CI) Unadjusted	Adjusted†
Death			
First Pre-pregnancy BMI			
Mother underweight	41 (17.3)	1.02 (0.74, 1.40)	1.02 (0.74, 1.40)
Mother normal weight	721 (16.3)	1.00	1.00
Mother overweight	144 (17.5)	1.13 (0.94, 1.35)	1.11 (0.92, 1.33)
Mother obese	14 (19.4)	1.37 (0.81, 2.32)	1.38 (0.81, 2.36)
Change in BMI			
No Change	364 (16.3)	1.00	1.00
Negative Change	100 (16.4)	1.07 (0.86, 1.34)	1.03 (0.81, 1.30)
Positive change	456 (16.8)	1.04 (0.91, 1.20)	0.97 (0.85, 1.12)
All cardiovascular events combined			
First Pre-pregnancy BMI			
Mother underweight	47 (19.8)	0.82 (0.62, 1.11)	0.82 (0.61, 1.10)
Mother normal weight	1013 (22.9)	1.00	1.00
Mother overweight	202 (24.5)	1.16 (0.99, 1.35)	1.11 (0.95, 1.30)
Mother obese	19 (26.4)	1.45 (0.92, 2.28)	1.34 (0.85, 2.12)
Change in BMI			
No Change	466 (20.9)	1.00	1.00
Negative Change	121 (19.9)	1.03 (0.84, 1.25)	0.97 (0.95, 1.30)
Positive change	694 (25.6)	**1.26** (1.12, 1.41)	1.34 (0.85, 1.12)
MACE (Death, MI, Stroke, PAD)			
First Pre-pregnancy BMI			
Mother underweight	52 (21.9)	1.04 (0.79, 1.38)	1.05 (0.80, 1.40)
Mother normal weight	899 (20.4)	1.00	1.00
Mother overweight	182 (22.1)	1.16 (0.99, 1.36)	1.11 (0.94, 1.31)
Mother obese	19 (26.4)	1.52 (0.96, 2.39)	1.48 (0.93, 2.34)
Change in BMI			
No Change	443 (19.9)	1.00	1.00
Negative Change	128 (21.0)	1.13 (0.93, 1.38)	1.08 (0.88, 1.33)
Positive change	581 (21.4)	1.09 (0.97, 1.24)	1.02 (0.90, 1.16)
Angina			
First Pre-pregnancy BMI			
Mother underweight	7 (3.0)	0.75 (0.35, 1.60)	0.78 (0.37, 1.67)
Mother normal weight	167 (3.8)	1.00	1.00
Mother overweight	29 (3.5)	0.99 (0.67, 1.48)	0.95 (0.65, 1.42)
Mother obese	6 (8.3)	**2.65** (1.17, 5.99)	**2.80** (1.22, 6.40)
Change in BMI			
No Change	76 (3.4)	1.00	1.00
Negative Change	15 (2.5)	0.77 (0.44, 1.34)	0.65 (0.37, 1.15)
Positive change	118 (4.4)	1.30 (0.97, 1.73)	1.20 (0.89, 1.61)

Myocardial Infarction			
First Pre-pregnancy BMI			
Mother underweight	9 (3.8)	1.07 (0.55, 2.11)	1.08 (0.55, 2.13)
Mother normal weight	150 (3.4)	1.00	1.00
Mother overweight	40 (4.9)	**1.53** (1.08, 2.16)	**1.47** (1.03, 2.10)
Mother obese	2 (2.8)	0.97 (0.24, 3.93)	0.89 (0.22, 3.63)
Change in BMI			
No Change	75 (3.4)	1.00	1.00
Negative Change	19 (3.1)	1.00 (0.60, 1.66)	0.93 (0.55, 1.58)
Positive change	107 (3.9)	1.19 (0.89, 1.60)	1.08 (0.80, 1.47)
Stroke			
First Pre-pregnancy BMI			
Mother underweight	4 (1.7)	0.67 (0.25, 1.81)	0.62 (0.23, 1.69)
Mother normal weight	106 (2.4)	1.00	1.00
Mother overweight	24 (2.9)	1.30 (0.84, 2.03)	1.32 (0.84, 2.08)
Mother obese	3 (4.2)	2.08 (0.66, 6.55)	1.83 (0.56, 5.99)
Change in BMI			
No Change	56 (2.5)	1.00	1.00
Negative Change	12 (2.0)	0.85 (0.45, 1.58)	0.80 (0.42, 1.52)
Positive change	69 (2.5)	1.02 (0.72, 1.46)	0.94 (0.65, 1.35)
Other cerebrovascular disease			
First Pre-pregnancy BMI			
Mother underweight	4 (1.7)	0.62 (0.23, 1.69)	0.60 (0.22, 1.60)
Mother normal weight	114 (2.6)	1.00	1.00
Mother overweight	21 (2.6)	1.06 (0.67, 1.69)	1.09 (0.68, 1.75)
Mother obese	2 (2.8)	1.29 (0.32, 5.22)	1.42 (0.35, 5.84)
Change in BMI			
No Change	61 (2.7)	1.00	1.00
Negative Change	14 (2.3)	0.91 (0.51, 1.62)	0.91 (0.50, 1.66)
Positive change	66 (2.4)	0.90 (0.64, 1.28)	0.84 (0.59, 1.20)
Peripheral arterial disease			
First Pre-pregnancy BMI			
Mother underweight	5 (2.1)	0.76 (0.31, 1.87)	0.76 (0.31, 1.87)
Mother normal weight	116 (2.6)	1.00	1.00
Mother overweight	28 (3.4)	1.39 (0.92, 2.10)	1.31 (0.86, 2.00)
Mother obese	4 (5.6)	2.57 (0.95, 6.97)	2.25 (0.81, 6.32)
Change in BMI			
No Change	51 (2.3)	1.00	1.00
Negative Change	17 (2.8)	1.32 (0.76, 2.29)	1.23 (0.69, 2.18)
Positive change	85 (3.1)	1.39 (0.98, 1.97)	1.25 (0.88, 1.78)
Other cardiovascular disease			
First Pre-pregnancy BMI			
Mother underweight	40 (16.9)	0.81 (0.59, 1.11)	0.80 (0.58, 1.09)
Mother normal weight	875 (19.8)	1.00	1.00
Mother overweight	185 (22.4)	**1.23** (1.05, 1.44)	**1.18** (1.01, 1.39)
Mother obese	17 (23.6)	1.51 (0.93, 2.44)	1.39 (0.85, 2.25)
Change in BMI			
No Change	398 (17.9)	1.00	1.00
Negative Change	103 (16.9)	1.02 (0.82, 1.27)	0.96 (0.77, 1.20)
Positive change	616 (22.7)	**1.30** (1.15, 1.48)	**1.24** (1.09, 1.41)

†Adjusted for husband/partner's soc class, smoking status, gestational age, pre-eclampsia , low birth weight and parity. MACE= Major adverse cardiac event defined by Death, Myocardial Infarction, Stroke or Peripheral arterial disease

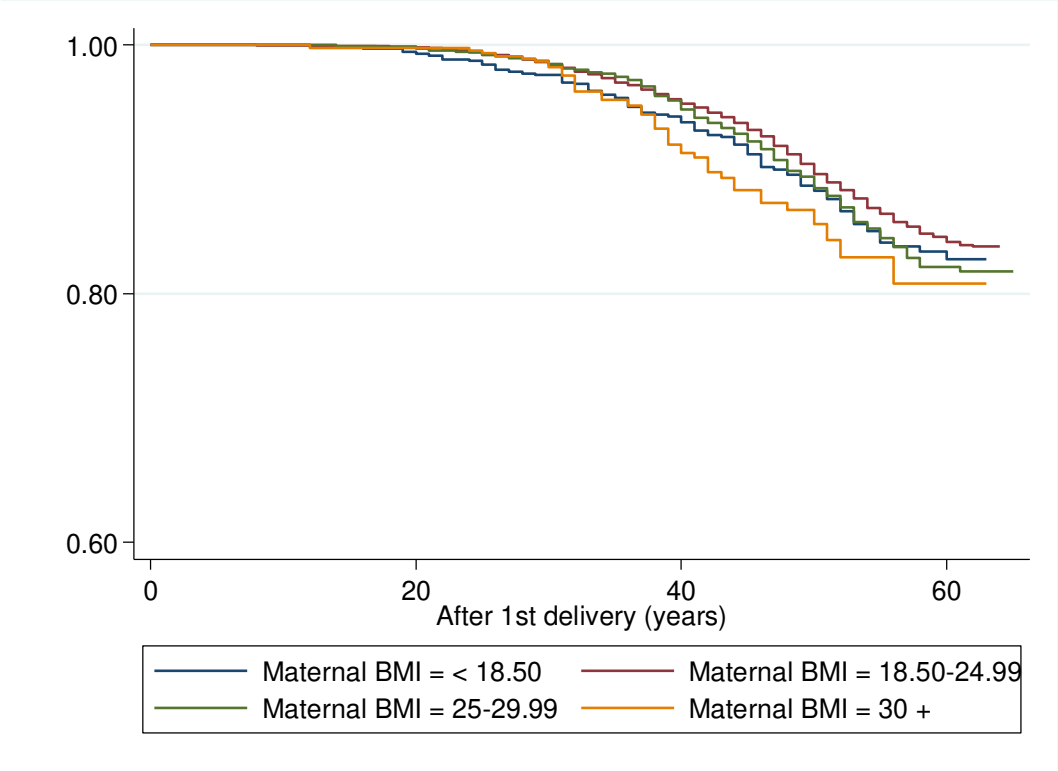


Figure S1a: Kaplan-Meier curves for death rates according to maternal BMI

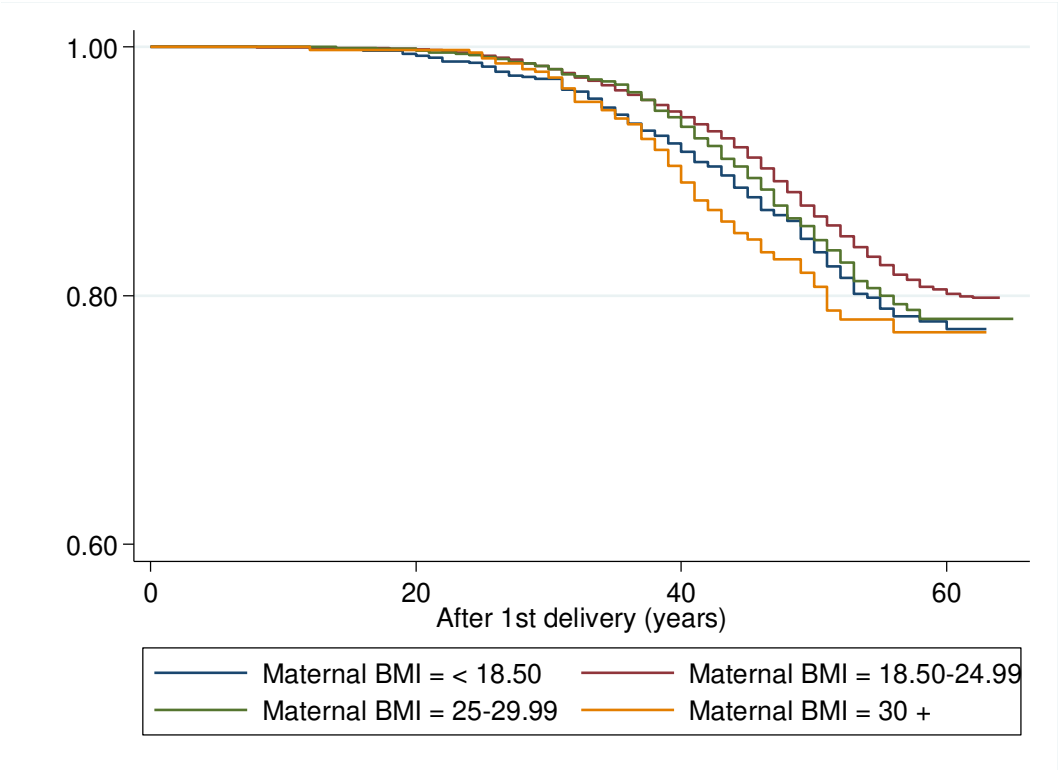


Figure S1 b: Kaplan-Meier curves for MACE according to maternal BMI

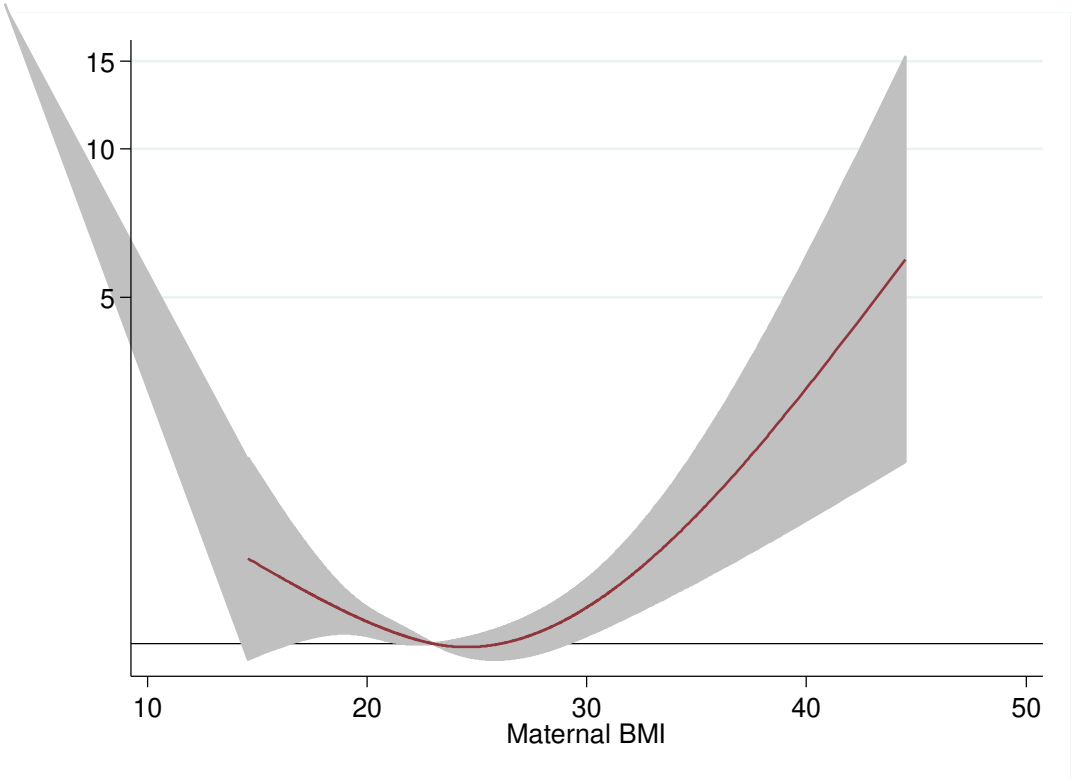


Figure S2a. Spline graph of all cause mortality Hazard ratio (95% CI) for Maternal BMI (* after adjusting for age at delivery, social class, smoking, gestation of measurement of BMI, preeclampsia and low birthweight (<2500g)).

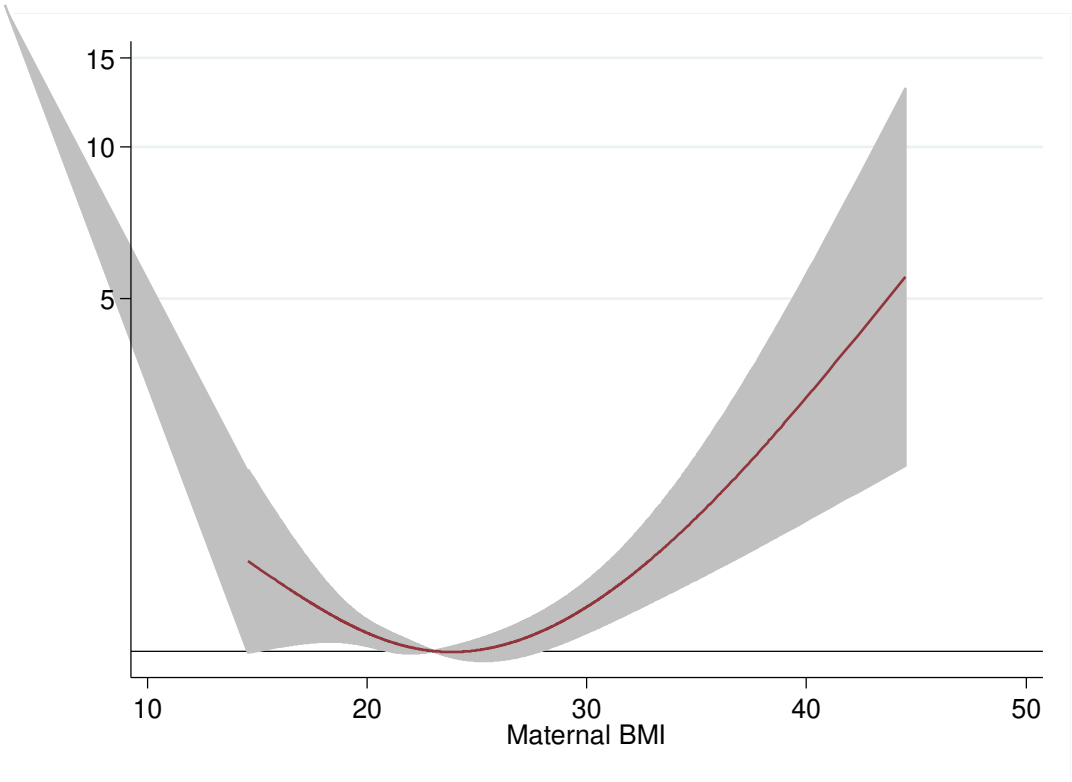


Figure S2b Spline graph of MACE Hazard ratio (95% CI) for Maternal BMI (*after adjusting for age at delivery, social class, smoking, gestation of measurement of BMI, preeclampsia and low birthweight (<2500g)).

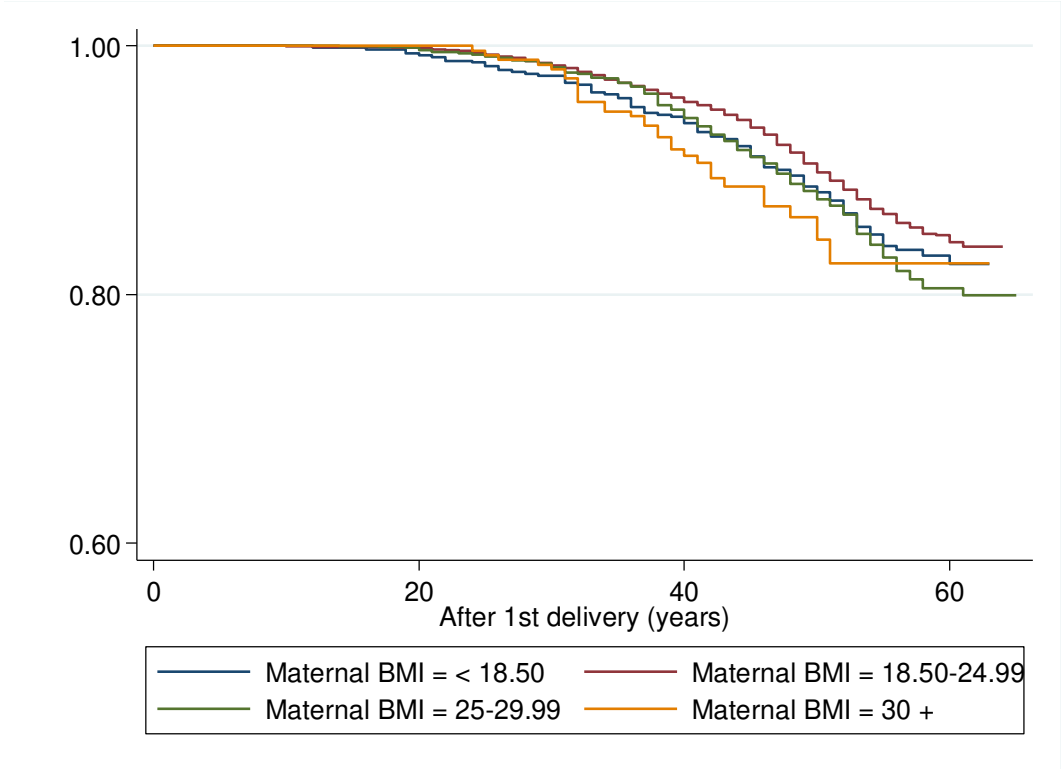


Figure S3a: Kaplan-Meier curves for all cause death rates according to maternal BMI among women with BMI measurement <20 weeks gestation

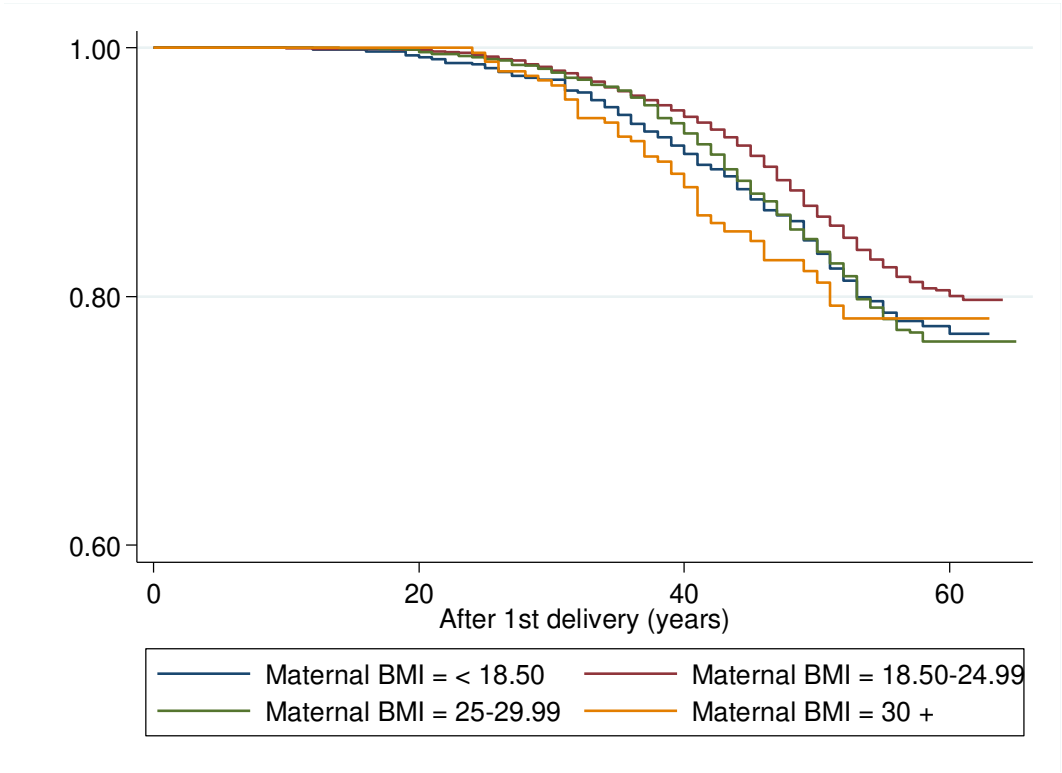


Figure S3 b: Kaplan-Meier curves for MACE according to maternal BMI among women with BMI measurement <20 weeks gestation

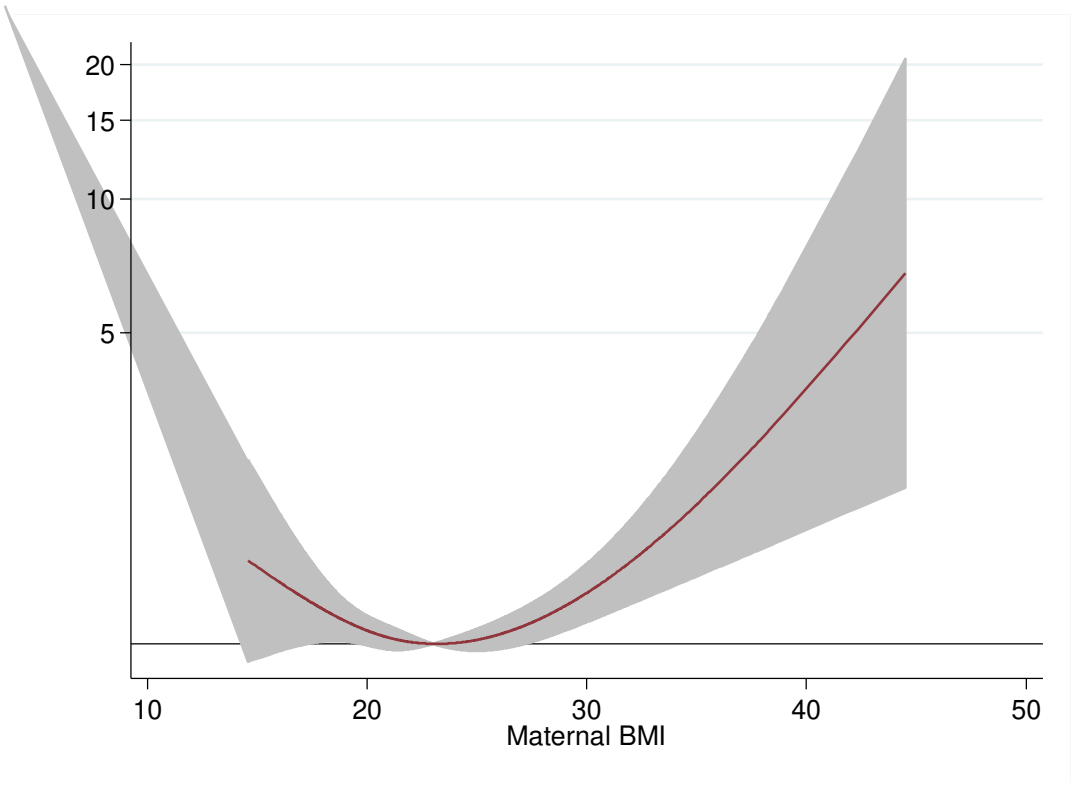


Figure S4a. Spline graph of mortality Hazard ratio (95% CI) for Maternal BMI (*after adjusting for age at delivery, social class, smoking, gestation of measurement of BMI, preeclampsia and low birthweight (<2500g) among women with BMI measurement <20 weeks gestation).

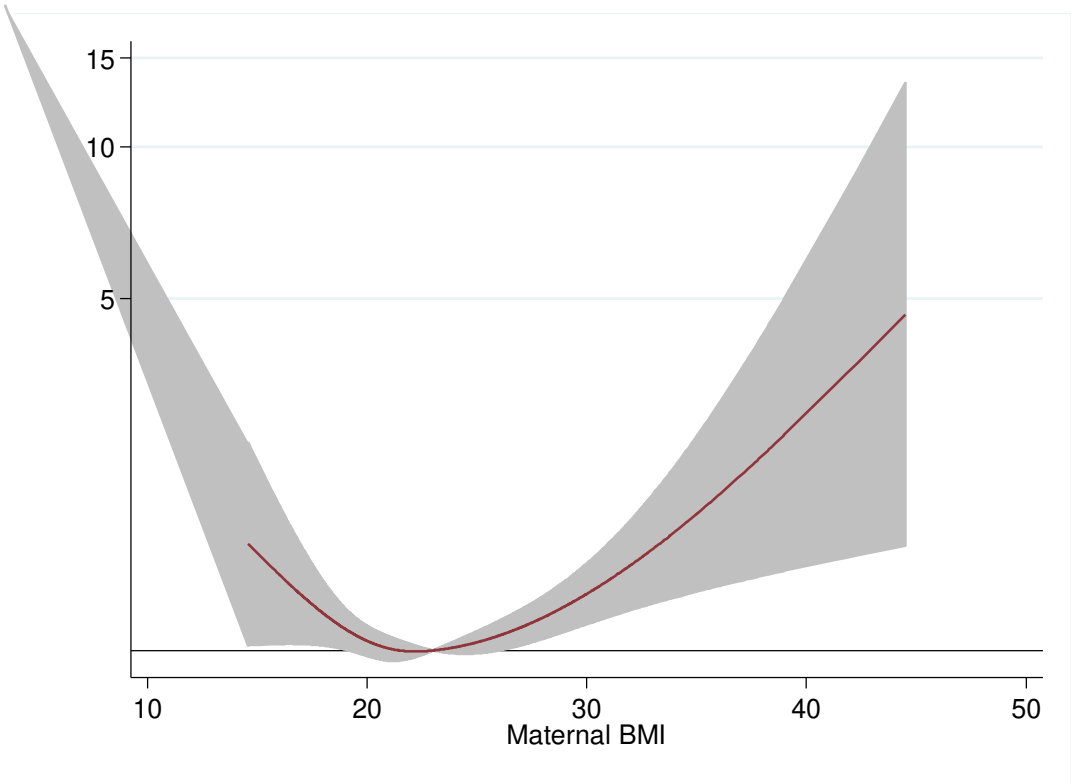


Figure S4b Spline graph of MACE Hazard ratio (95% CI) for Maternal BMI (*after adjusting for age at delivery, social class, smoking, gestation of measurement of BMI, preeclampsia and low birthweight (<2500g) among women with BMI measurement <20 weeks gestation).

Figure S5 BMI trajectories across pregnancies among 5552 women with more than one pregnancy

The semi-parametric mixture model utilises the first BMI at each pregnancy and considers each of the woman's trajectories and group similar trajectories together as clusters so that the women within the trajectory-cluster have similar trajectories and different between cluster trajectories. The model identified six different BMI trajectories (each trajectory indicated by different coloured line).