SUPPLEMENTAL MATERIAL

Data S1.

Search terms

Synonyms of preterm birth (‘preterm delivery’ or ‘preterm birth’ or ‘premature delivery’ or ‘premature birth’) AND ‘ischaemic heart disease’ or ‘ischemic heart disease’ or ‘coronary artery disease’ or ‘coronary heart disease’ or ‘myocardial infarction’ or ‘acute coronary syndrome’ or ‘heart failure’ or ‘cardiac failure’ or ‘left ventricular systolic dysfunction’ or ‘stroke’ or ‘cerebrovascular disease’ or ‘cerebrovascular accident’ or ‘cardiomyopathy’ or ‘peripheral vascular disease’ or ‘cardiovascular disease’ or ‘cardiovascular morbidity’ or ‘cardiovascular mortality’.

Table S1. Study quality assessment overview.

Study ID	Representative of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of preterm birth	Demonstration that outcome of interest was not present at start of study	Comparability of cohort	Assessment of outcome	Follow-up duration to capture outcomes	Adequacy of follow-up	Total score
Bonamy 2011[1]	*	*	*	*	**	*	*	*	9
Catov 2007[2]	*	*			**		*	*	6
Catov 2010[3]	*	*	*	*	**	*	*	*	9
Cirillo 2015[4]	*	*	*	*	*	*	*	*	8
Davey Smith 2000[5]	*	*	*	*	*	*			6
Davey Smith 2005[6]	*	*	*	*	*	*	*		7
Freibert 2011[7]	*	*						*	3
Hastie 2011[8]	*	*	*		*	*	*	*	7
Hovi 2014[9]	*	*	*			*	*	*	6
Irgens 2001[10]	*	*	*	*	*	*	*	*	8
Kessous 2013[11]	*	*	*	*	**	*	*	*	9
Lykke 2010a[12] & Lykke 2010b[13]	*	*	*	*	**	*	*	*	9
Nardi 2006[14]		*		*	*	*	*		5
Ngo 2015[15]	*	*	*	*	*	*	*	*	8
Pell 2004[16] & Smith 2001[17]	*	*	*		*	*	*		6

Rich-Edwards 2015[18]	*	*	*	*	*	*	*	*	8
Tanz 2017[19]		*		*	*		*		4
Wang 2011[20]	*	*	*	*	*	*	*	*	8
Wikstrom 2005[21]	*	*	*		*	*	*	*	7

Table S2. Study quality assessment in detail.

Study ID	Representative of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of preterm birth	Demonstration that outcome of interest was not present at start of study	Comparability of cohort	Reliable ascertainment of outcomes	Follow-up duration to capture outcomes	Adequacy of follow-up
Bonamy 2011[1]	General cohort of women.	Controls from the same cohort.	From the Swedish Medical Birth Register.	Excluded women with a CVD event before their first delivery.	Adjusted for maternal age, birth year, highest income and highest education level before first delivery, country of birth, pregestational hypertension, pregestational diabetes mellitus, gestational diabetes mellitus, gestational hypertension, pre-eclampsia/eclampsia and maternal smoking at beginning of pregnancy.	ICD-8 to 10 codes from the hospital discharge register or the cause of death register. ICD-8: 411, 427.00, 427.10. ICD-9: 411B, 428. ICD-8/9: 410, 430-436. ICD-10: G45, I20.0, I21-22, I50, I60-64.	Median 11.8 years.	Database study.
Catov 2007[2]	General cohort of women.	Controls from the same cohort.	Self-reported.	Excluded women who reported pre-eclampsia or hypertension during pregnancy.	Adjusted for race, age at study baseline, systolic BP, log pulse wave velocity (from simultaneous carotid and femoral artery Doppler flow signals), insulin resistance, log	Self-reported and validated using an algorithm that assesses medication, physical examination, blood tests and ECG.	Mean 57 years.	All women followed up.

					IL-6, HDL cholesterol and statin use.			
Catov 2010[3]	General cohort of women.	Controls from the same cohort.	From the Danish Medical Birth Registry.	Excluded women with hospitalization for CVD or diabetes before the first birth during study period and those dying during delivery.	Adjusted for maternal age at first birth, parity, education, birth year. Excluded pre-eclampsia, SGA offspring and diabetes.	ICD-8 and 10 codes from the National Hospital Discharge Register. ICD-8: 410-414, 430-438, 440, 444, 452, 453. ICD-10: I20-25.5, I60-69.8, I70-70.9, I74, I81, I82.	Mean 28 years.	Database study.
Cirillo 2015[4]	General cohort of women.	Controls from the same cohort.	From medical records.	Not applicable as death outcome.	Adjusted for age, race, parity, BMI and smoking. Excluded pre-existing heart disease, multiple births, gestations <20 weeks and missing parity data.	ICD-7 to 10 codes in data linkage to California Vital Statistics and National Death Index. ICD-7: 420.1. ICD-8: 410, 412. ICD-9: 410, 411, 414, 429. ICD-10: I21, I24, I25.	Median 40 years.	<10% loss to follow-up.

Davey Smith 2000[5]	General cohort of women.	Controls from the same cohort.	From previous study records.	Not applicable as death outcome.	Adjusted for age, height, marital status, visits to private doctor, BP and hormone use during pregnancy,	From Finnish Central Population and Cause of Death registers.	Unclear.	Unclear.
Davey Smith 2005[6]	General cohort of parents.	Controls from the same cohort.	From the Swedish Medical Birth Register.	Not applicable as death outcome.	Adjusted for birth weight.	ICD-9 codes in the Swedish Cause of Death register. ICD-9: 390-459.	Mean 20.4 years.	Unclear.
Freibert 2011[7]	General cohort of women.	Controls from the same cohort.	Self-reported.	No.	Unadjusted.	Self-reported.	Unclear.	92.3% of all eligible women had complete data.
Hastie 2011[8]	General cohort of women.	Controls from the same cohort.	From routine national electronic records.	No.	Adjusted for age at delivery, height, deprivation category, birthweight decile, essential hypertension and pre-eclampsia.	ICD-8 to10 codes from electronic records. ICD-8/9: 410-414. ICD-10: I20-25.	Mean 22 years.	Database study.
Hovi 2014[9]	General cohort of women.	Controls from the same cohort.	From the Finnish Medical Birth Register.	No.	Unadjusted.	ICD-9 and 10 codes from the Hospital Discharge Register data and non-primary	Up to 22 years.	<1% loss to follow-up.

						care outpatient visit data. No details on exact ICD codes used.		
Irgens 2001[10]	General cohort of women.	Controls from the same cohort.	From the Medical Birth Registry of Norway.	Not applicable as death outcome.	Adjusted for age at delivery and year of birth of baby. Excluded pre-eclampsia.	ICD-8 and 9 codes from the Registry of Causes of Death. ICD-8/9: 410-429.	Median 13 years.	<10% loss to follow-up.
Kessous 2013[11]	General cohort of women.	Controls from the same cohort.	From the hospital perinatal database.	Excluded women with known CVD before or during the index pregnancy.	Adjusted for diabetes, gestational diabetes, obesity, age, pre-eclampsia, ethnicity, anaemia and induction of labour.	ICD-9 codes from the hospitalization database. ICD-9: 272.2, 272.4, 401.9, 402, 404, 404.9, 410, 411, 411.8, 411.81, 413, 413.9, 414, 414.8, 414.9, 415, 415.0, 427.5, 428.0, 428.1, 428.9, 429.9, 429.2, 436, 437, 437.1, 440, 440.2, 443.8, 443.89, 443.9, V810, V812, Z0045-Z0047, Z005,	Mean 10 years.	Database study.

						Z0065, Z3721-Z3723, Z37211, Z3610, Z3619, Z8852-Z8857, Z8877, Z8941, Z8943, Z8944, Z895.		
Lykke 2010a[12] & Lykke 2010b[13]	General cohort of women.	Controls from the same cohort.	From the National Patient Registry in Denmark.	Excluded pre-existing diabetes, cardiovascular diagnosis and women who died or emigrated 3 months after delivery.	Adjusted for maternal age at delivery, year of delivery, hypertensive pregnancy disorders, SGA or large-for-gestational-age offspring, placental abruption and stillbirth (Lykke 2010a). Adjusted for maternal age at delivery and year of delivery (Lykke 2010b).	ICD codes from the National Patient Registry (Lykke 2010a) or from cause of death registry or first cardiovascular diagnosis within 1 week prior to death (Lykke 2010b). ICD-8: 39-44, 45.145.8, 41.0-41.4, 427.09-427.11, 427.19, 427.99, 428.99, 429.00, 429.08, 429.09, 430-438.	Median 14.6 years (Lykke 2010a) or 14.8 years (Lykke 2010b).	<10% loss to follow-up.

						ICD-10: G45, I0-9, I20-25, I50, I51.3, I51.9, I60-67.		
Nardi 2006[14]	Teachers covered by a health insurance scheme.	Controls from the same cohort.	Self-reported.	Not applicable as death outcome.	Unadjusted. Excluded pre-existing MI, angina, psychiatric disorders and unspecified other cardiac and non-cardiac diseases.	Death from CHD using ICD-9 codes from insurance and national databases. ICD-9: 410-414.	Mean 5.2 years from study enrolment.	19% loss to follow-up.
Ngo 2015[15]	General cohort of women.	Controls from the same cohort.	From the perinatal data collection.	Excluded chronic hypertension or hypertensive disorders of pregnancy, CVD event prior to last birth, CVD event within 42 days of last birth and death	Adjusted for age, country of birth, socioeconomic status, parity, SGA offspring, diabetes, gestational diabetes and smoking.	ICD-10 codes from national datasets. ICD-10: G45.0-45.2, G45.4, G45.8, G45.9, G46, I20-25, I25.2, I50, I60-66, I67.0-67.2, I67.4-67.9, I68.1, I68.2, I68.8, I69.	Median 7.5 years.	Linkage proportion for records >98%.

				before follow-up period.				
Pell 2004[16] & Smith 2001[17]	General cohort of women.	Controls from the same cohort.	From routine maternity hospital records.	No.	Excluded stillbirths. Adjusted for age, height, deprivation category, pre-eclampsia, lowest birth weight quintiles and previous spontaneous miscarriage (Pell 2004). Additional adjustment for essential hypertension, but not previous miscarriage (Smith 2001).	ICD-9 and 10 codes from the Scottish Morbidity Record system and General Registrar's Office. ICD-9: 410-414, 430-438. ICD-10: G44, I-20-25, I60-69,	14-19 years.	11.9% (Pell 2004) or 4.4% (Smith 2001) loss to follow-up.
Rich-Edwards 2015[18]	General cohort of women.	Controls from the same cohort.	From the Medical Birth Registry of Norway.	Not applicable as death outcome.	Adjusted for year of delivery, age and education at first birth.	ICD-8 to 10 codes in the National Cause of Death Registry. ICD-8/9: 410-414, 430-438. ICD-10: I20-25, I60-69.	Median 24.8 years.	8.3% loss to follow-up.
Tanz 2017[19]	Registered nurses.	Controls from the same cohort.	Self-reported.	Excluded pre-existing MI or stroke.	Excluded hypertensive disorders of pregnancy. Adjusted for age at first birth, age in 1989, ethnicity, parental education, pre-pregnancy BMI, smoking, Alternative	Self-reported then verified with medical records.	Median 32 years.	32% of eligible women had missing data.

					Healthy Eating Index score, alcohol intake, physical activity at 18 years of age, oral contraceptive use, chronic hypertension, hypercholesterolaemia, type 2 diabetes and family history of MI or stroke before 60 years of age.			
Wang 2011[20]	General cohort of women.	Controls from the same cohort.	From National Health Insurance program database.	Excluded pre-existing stroke or hypertension.	Adjusted for age, urbanization level, diabetes, hyperlipidaemia, CHD, abruption, lupus and thrombophilia.	ICD-9 codes from the national database. ICD-9: 430-437, 674.0, A290-294, A299.	Mean 6.4 years.	Database study.
Wikstrom 2005[21]	General cohort of women.	Controls from same cohort.	ICD codes from Swedish Medical Register.	Excluded hypertension and diabetes.	Adjusted for age, socio-economic level, category of hospital in which the first child was born.	ICD-9 and ICD-10 codes from hospital discharge register and cause of death register. ICD-9: 410-414. ICD=10: I20-25.	15 years.	3.15% died or emigrated.

BMI=body mass index, BP=blood pressure, CHD=coronary heart disease, CVD=cardiovascular diseases, ECG=electrocardiogram, HDL=high-density lipoprotein, IL=interleukin, MI=myocardial infarction, SGA=small-for-gestational age.

Table S3. Cardiovascular risk factor profile of preterm birth and term birth groups in the included studies. GDM=gestational diabetes, HBW=high birth weight >2500g, LBW=low birth weight <2500g, BMI=body mass index, N.S.=non-significant, SE=socio-economic, SEIFA=socio-economic indexes for areas, SGA=small-for-gestational age, wk=weeks gestation.

Study ID	**Risk factor profile**	**During pregnancy / study enrolment**			**At follow-up**		
		Preterm	**Term**	***p* value**	**Preterm**	**Term**	***p* value**
Bonamy 2011[1]	Not available	-	-	-	-	-	-
Catov 2007[2]	Age (year)	23.1	HBW 23.7 LBW 22.0	-	72.9	HBW 73.0 LBW 73.4	-
	Black race (%)	-	-	-	51.9	HBW 41.5 LBW 63.2	-
	Low SE status (%)	-	-	-	22.2	HBW 14.2 LBW 18.4	-
	Ever smoker (%)	-	-	-	66.7	HBW 41.7 LBW 47.4	-
	BMI (kg/m^2)	-	-	-	27.8	HBW 28.3 LBW 26.7	-
	Triacylglycerol (mg/dL)	-	-	-	139.5	HBW 141.3 LBW	-

						163.7	
	Fasting glucose (mg/dL)	-	-	-	104.0	HBW 101.4	-
						LBW 98.0	
	Fasting insulin (IU/mL)	-	-	-	9.8	HBW 8.2	-
						LBW 10.7	
	Hypertension (%)	-	-	-	70.4	HBW 59.8	-
						LBW 71.1	
	Diabetes (%)	-	-	-	7.7	HBW 9.5	-
						LBW 7.9	
Catov 2010[3]	Age (year)	25.2	25.7	-	-	-	-
	Basic education (%)	51.1	44.1	<0.001	-	-	-
	Pre-eclampsia (%)	5.0	3.2	<0.001	-	-	-
	SGA (%)	13.1	9.2	<0.001	-	-	-
Cirillo 2015[4]	Not available	-	-	-	-	-	-
Davey Smith 2000[5]	Not available	-	-	-	-	-	-
Davey Smith 2005[6]	Not available	-	-	-	-	-	-
Freibert 2010[7]	Age (year)	-	-	-	59.6	60.3	-
	Education ≤12 years (%)	-	-	-	38	36.4	-
	Ever smoker (%)	-	-	-	44	40	-

Hastie 2011[8]	Age (year)	24	25	<0.001	-	-	-
	High deprivation quintile using Carstairs index (%)	7.9	6.7	<0.001	-	-	-
	Hypertension (%)	0.4	0.1	<0.001	-	-	-
	Pre-eclampsia (%)	8.8	8.1	<0.001	-	-	-
Hovi 2014[9]	Not available	-	-	-	-	-	-
Irgens 2001[10]	Not available	-	-	-	-	-	-
Kessous 2013[11]	Age (years)	28.1	29.9	0.001	-	-	-
	Jewish (%)	52.6	70.4	0.001	-	-	-
	GDM and Diabetes (%)	8.3	8.2	N.S.	-	-	-
	Obesity (%)	1.1	2.0	0.001	-	-	-
Lykke 2010a[12] & Lykke 2010b[13]	Not available	-	-	-	-	-	-
Nardi 2006[14]	Not available	-	-	-	-	-	-
Ngo 2015[15]	High deprivation using SEIFA index (%)	24.0	20.9	-	-	-	-
	Ever smoker (%)	30.0	28.3	-	-	-	-
	Diabetes (%)	1.3	0.4	-	-	-	-
Pell 2004[16] & Smith 2001[17]	Not available	-	-	-	-	-	-
	Age (year)	23.7	23.9	-	-	-	-

Rich-Edwards 2015[18]	Education <high school (%)	53.6	46.4	-	-	-	-
Tanz 2017[19]	Age (year)	<32 wk 27.5	27	-	-	-	-
		≥32 to <37 wk 27.8					
	BMI≥30 (%)	<32 wk 4.0	3.1	-	-	-	-
		≥32 to <37 wk 3.4					
	Caucasian (%)	<32 wk 91.0	92.9	-	-	-	-
		≥32 to <37 wk 90.9					
	Ever smoker (%)	<32 wk 33.0	31.8	-	-	-	-
		≥32 to <37 wk 30.9					
Wang 2011[20]	Not available	-	-	-	-	-	-
Wikstrom 2005[21]	Not available	-	-	-	-	-	-

Table S4. Sensitivity analysis with regards to singleton and multiple pregnancies.

Outcomes	**Singleton pregnancies only**	**Singleton and multiple pregnancies**
CVD	1.56 [1.27, 1.93], n=5	1.56 [1.32, 1.84], n=8
CVD death	1.95 [1.79, 2.12], n=4	1.81 [1.55, 2.10], n=5
CHD	1.48 [1.36, 1.61], n=4	1.50 [1.39, 1.62], n=6
CHD death	2.07 [1.76, 2.44], n=3	2.02 [1.78, 2.30], n=5
Stroke	1.69 [1.54, 1.85], n=3	1.65 [1.51, 1.79], n=5

Table S5. Sensitivity analysis with regards to the year each study was commenced.

Outcomes	**Study year before 1990**	**Study year after 1990**	**Study year before 1970**	**Study year after 1970**
CVD	1.51 [1.20, 1.90], n=5	1.62 [1.46, 1.80], n=3	-	-
CVD death	-	-	1.91 [1.68, 2.16], n=2	1.74 [1.36, 2.23], n=3
CHD	1.46 [1.34, 1.59], n=4	1.64 [1.44, 1.87], n=2	-	-
CHD death	-	-	2.17 [1.92, 2.46], n=3	1.61 [1.26, 2.07], n=2
Stroke	1.60 [1.33, 1.93], n=3	1.67 [1.45, 1.93], n=2	-	-

Table S6. Sensitivity analysis with regards to study quality score.

Outcomes	**Study quality score ≤6**	**Study quality score ≥7**
CVD	1.59 [1.38, 1.83], n=4	1.53 [1.18, 1.97], n=4
CVD death	2.06 [1.22, 3.47], n=1	1.79 [1.51, 2.11], n=4
CHD	1.65 [1.34, 2.03], n=2	1.48 [1.36, 1.61], n=4
CHD death	1.54 [1.04, 2.28], n=1	2.10 [1.87, 2.36], n=4
Stroke	1.55 [1.05, 2.29], n=2	1.67 [1.52, 1.83], n=3

Table S7. Sensitivity analysis with regards to study location.

Outcomes	**Study location: Europe**	**Study location: U.S.**	**Study location: other**
CVD	1.54 [1.23, 1.92], n=5	1.73 [0.87, 3.46], n=2	1.65 [1.49, 1.82], n=1
CVD death	1.81 [1.55, 2.10], n=5	-	-
CHD	1.45 [1.32, 1.60], n=3	1.65 [1.34, 2.03], n=2	1.61 [1.40, 1.86], n=1
CHD death	1.98 [1.69, 2.33], n=4	2.10 [1.43, 3.08], n=1	-
Stroke	1.70 [1.51, 1.90], n=2	1.28 [0.95, 1.72], n=1	1.67 [1.45, 1.93], n=2

Table S8. Sensitivity analysis with regards to whether the study excluded women with pre-existing cardiovascular disease.

Outcomes	**Pre-existing CVD excluded**	**Pre-existing CVD not excluded**
CVD	1.54 [1.24, 1.92], n=6	1.65 [1.46, 1.85], n=2
CVD death	1.98 [1.77, 2.21], n=2	1.54 [1.02, 2.33], n=3
CHD	1.45 [1.33, 1.57], n=4	1.59 [1.48, 1.71], n=2
CHD death	-	2.02 [1.78, 2.30], n=5
Stroke	1.63 [1.49, 1.78], n=4	1.91 [1.35, 2.70], n=1

Figure S1. PRISMA checklist

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Preterm Delivery and Future Risk of Maternal Cardiovascular Disease: A Systematic Review and Meta-Analysis.	1
ABSTRACT			
Structured summary	2	*Background*: Preterm delivery (<37 weeks gestational age) affects 11% of all pregnancies, but data are conflicting whether preterm birth is associated with long-term adverse maternal cardiovascular outcomes. *Objectives*: To systematically evaluate and summarize the evidence on the relationship between preterm birth and future maternal risk of cardiovascular diseases. *Data sources*: A systematic search was conducted using MEDLINE and EMBASE from inception to October 2017. Manual searching for additional articles was also conducted by reviewing the bibliography of relevant review articles and published systematic reviews. Search terms were: Synonyms of preterm birth ('preterm delivery' or 'preterm birth' or 'premature delivery' or 'premature birth') AND 'ischaemic heart disease' or 'ischemic heart disease' or 'coronary artery disease' or 'coronary heart disease' or 'myocardial infarction' or 'acute coronary syndrome' or 'heart failure' or 'cardiac failure' or 'left ventricular systolic dysfunction' or 'stroke' or 'cerebrovascular disease' or 'cerebrovascular accident' or 'cardiomyopathy' or 'peripheral vascular disease' or 'cardiovascular disease' or 'cardiovascular morbidity' or 'cardiovascular mortality'. *Study selection*: The included studies had at least two groups (one with preterm birth and one with term birth) and reported sufficient data to allow for accurate risk estimates to be calculated. There was no restriction based on language, cohort type, study design or duration of follow-up. *Data extraction*: Independent double data extraction was done by four reviewers using predefined data fields, including study quality indicators. *Study appraisal and synthesis methods*: Study quality was assessed based on the recommendations of the Newcastle-Ottawa Quality Assessment Scale for cohort studies. We used RevMan Version 5.3.5 (Nordic Cochrane Centre) to conduct random effects meta-analysis using the inverse variance method for pooling log risk ratios (RRs).	5 6 7 8

		Results: Twenty-one studies with over 5.8 million women, including over 338,000 women with previous preterm deliveries, were identified. Meta-analysis of studies that adjusted for potential confounders showed that preterm birth was associated with an increased risk of maternal future cardiovascular disease (risk ratio (RR) 1.43, 95% CI 1.18, 1.72), cardiovascular disease death (RR 1.78, 95% CI 1.42, 2.21), coronary heart disease (RR 1.49, 95% CI 1.38, 1.60), coronary heart disease death (RR 2.10, 95% CI 1.87, 2.36), and stroke (RR 1.65, 95% CI 1.51, 1.79). Sensitivity analysis showed that the highest risks occurred when the preterm deliveries occurred before 32 weeks gestation or were medically indicated. *Limitations*: The limitations of this study include the risk of confounding and being unable to attribute causality of future cardiovascular disease to preterm delivery. There may be inherent publication bias, recall bias or inaccuracies in historical data collection. Heterogeneity may have arisen due to differences in the study population, research methodology, period of conducting the study, and inherent differences between the studies. *Conclusions*: Preterm delivery is associated with an increase in future maternal adverse cardiovascular outcomes, including a two-fold increase in deaths due to coronary heart disease. These findings support the assessment of preterm delivery in cardiovascular risk assessment in women. *Systematic review registration number*: PROSPERO CRD42017068455	16 17
INTRODUCTION			
Rationale	3	Preterm birth (<37 weeks gestational age) affects 11% of all pregnancies. Pregnancy is characterized by a challenge to the cardiovascular system. This physiological stress for most women is uncomplicated but for women who experience preterm birth, this adverse pregnancy outcome may serve to identify women at risk for cardiovascular disease who would not have been detected using traditional risk assessment tools at a time when it may be possible to alter their risk trajectory. It remains unclear whether preterm delivery is an independent risk factor for future cardiovascular disease or an early marker of women with background high-risk profiles for future cardiovascular disease. The pathogenesis of preterm birth remains poorly understood.	5
Objectives	4	To systematically evaluate and summarize the evidence on the relationship between preterm birth and future maternal risk of cardiovascular diseases, we reviewed studies that compared long-term adverse cardiovascular outcomes between women with and without preterm birth in postnatal women.	6
METHODS			
Protocol and registration	5	Available from: http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017068455 Protocol registration number: PROSPERO CRD42017068455	6
Eligibility criteria	6	*Participants*: postnatal women. *Comparisons*: Preterm birth versus term birth. *Outcome measures*: ischaemic heart disease, coronary artery disease, coronary heart disease, myocardial infarction, acute coronary syndrome, heart failure, cardiac failure, left ventricular systolic dysfunction,	6

		stroke, cerebrovascular disease, cerebrovascular accident, cardiomyopathy, peripheral vascular disease, cardiovascular disease, cardiovascular morbidity, cardiovascular mortality. *Study characteristics*: the included studies had at least two groups (one with preterm birth and one with term birth) and reported sufficient data to allow for accurate risk estimates to be calculated. There was no restriction based on language, cohort type, study design or duration of follow-up.	
Information sources	7	Searches were conducted using the databases MEDLINE and EMBASE from inception to present. Manual searching for additional articles was also conducted by reviewing the bibliography of relevant review articles and published systematic reviews. The last search was run on 7th October 2017.	7
Search	8	Synonyms of preterm birth ('preterm delivery' or 'preterm birth' or 'premature delivery' or 'premature birth') AND 'ischaemic heart disease' or 'ischemic heart disease' or 'coronary artery disease' or 'coronary heart disease' or 'myocardial infarction' or 'acute coronary syndrome' or 'heart failure' or 'cardiac failure' or 'left ventricular systolic dysfunction' or 'stroke' or 'cerebrovascular disease' or 'cerebrovascular accident' or 'cardiomyopathy' or 'peripheral vascular disease' or 'cardiovascular disease' or 'cardiovascular morbidity' or 'cardiovascular mortality'.	Supplemental methods 2.
Study selection	9	Eligibility assessment was performed independently by 2 reviewers. Disagreements between reviewers were resolved by using the eligibility assessment by PW, who is a more experienced researcher.	7
Data collection process	10	Independent double data extraction was done by 4 reviewers using predefined data fields, including study quality indicators. Disagreements between reviewers were resolved by consensus. If no agreement could be reached, the decision was made by PW. The information was obtained from published data.	7
Data items	11	Data were collected on study design, year, country, number of participants, mean age, parity, cohort characteristics, definition and ascertainment of preterm birth, ascertainment of outcomes, timing of assessment, adequacy of follow-up and results. Where possible, we chose to pool adjusted risk estimates from primary studies and when these data were not available, raw data were used to calculate unadjusted risk estimates.	7, 8
Risk of bias in individual studies	12	Each study was individually assessed for quality based on the recommendations of the Newcastle-Ottawa Quality Assessment Scale for cohort studies by independent reviewers. No studies were excluded following quality assessment.	7
Summary measures	13	We conducted random effects meta-analysis using the inverse variance method for pooling log risk ratios.	8
Synthesis of results	14	Studies were pooled in meta-analysis with subgroups based on whether or not the study used adjustments to account for confounders. Statistical heterogeneity was assessed using the I^2 statistic.	8
Risk of bias across studies	15	In the case for an analysis where there is more than 10 studies and little evidence of heterogeneity, we planned to perform funnel plots to assess for publication bias.	8
Additional analyses	16	Sensitivity analysis was performed to consider the follow-up duration of the studies (<10 years, 10-30 years, and >30 years), gestation (<32 weeks versus 32-37 weeks) and recurrence (1 recurrence versus ≥2	8

		recurrence) of preterm births, and whether the preterm births occurred spontaneously or were medically indicated.	
RESULTS			
Study selection	17	See flow diagram in figure 1.	Figure 1
Study characteristics	18	See table 1.	Table 1
Risk of bias within studies	19	See supplemental table 1 and 2.	Supplemental tables 1 and 2.
Results of individual studies	20	See table 2, figures 2-4.	Table 2, figures 2-4.
Synthesis of results	21	See figures 2-4.	Figures 2-4.
Risk of bias across studies	22	We did not perform funnel plots to assess for publication bias as less than 10 studies were included in each analysis.	11
Additional analysis	23	See table 3 and supplemental table 4.	Table 3 and supplemental table 4.
DISCUSSION			
Summary of evidence	24	We found that preterm delivery is associated with an increased maternal risk for future incident cardiovascular events, cardiovascular death, coronary heart disease events, coronary heart disease death and stroke. The adjusted risk ranged between 1.4 to 2–fold compared to those without a history of preterm birth. This increased risk is greatest in preterm births that occur before 32 weeks in gestation or in those that are delivered for medical indications such as fetal growth restriction or pre-eclampsia. For the composite cardiovascular disease and coronary heart disease outcomes, the risks are higher in women with a greater number of recurrent preterm births.	13
Limitations	25	*Outcome level*: The limitations of this study include the risk of confounding and being unable to attribute causality of future cardiovascular disease to preterm delivery. Heterogeneity may have arisen due to differences in the study population, research methodology, period of conducting the study, and inherent differences between the studies.	16

		Review level: There may be inherent publication bias, recall bias or inaccuracies in historical data collection.	
Conclusions	26	In keeping with current recommendations, our study highlights the importance of advising women with preterm births about their increased cardiovascular risk and advocating and supporting lifestyle and behavioural changes to control their modifiable risk factors. These findings support the assessment of preterm delivery in cardiovascular risk assessment in women, with the 6-week postpartum visit the ideal place for this to occur.	17
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