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SUPPLEMENTARY MATERIAL

Preeclampsia and premature cardiovascular disease in a large UK pregnancy cohort of linked electronic health records: a CALIBER study

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SUPPLEMENTARY METHODS

CPRD and HES

The CPRD is taken from a representative sample of 701 UK National Health Service (NHS) primary care practices. Data are available on British National Formulary (BNF) prescription codes, and records of laboratory tests, diagnoses, anthropometric measurements, demographic characteristics, and medical procedures using the Read coding system.¹ Diagnoses relating to episodes of admitted patient care are recorded in HES using the ninth and tenth iterations of the International Classification of Diseases and Health-Related Problems (ICD9 and ICD10).² Elective and emergency procedures are recorded in HES using the Office of Population Censuses and Surveys Classification of Interventions and Procedures (OPCS) Version 4.³

The CPRD pregnancy register and HES maternity file

The CPRD pregnancy register was developed from the larger CPRD dataset to capture pregnancy episodes recorded within primary care and relevant data on the timing, duration, and outcome (livebirth, stillbirth, pregnancy loss) of each. The compilation of the register is based on an algorithm that uses a list of more than 4000 pregnancy-related Read codes and entity types, extracted from Clinical, Referral and Test files of all female patients between the ages of 11 and 49 years within CPRD. For cases in which pregnancies ended in a live birth, additional data from the linked baby record are available, such as gestational age at birth.

Using the Pregnancy Register, a complete pregnancy was flagged if the estimated duration of a pregnancy episode in the CPRD pregnancy register was at least 140 days (20 weeks), and the outcome category code was one of: 1=Livebirth; 2=Stillbirth; 3=1&2; 11=Delivery based on a third trimester pregnancy record; or 12=Delivery based on a late pregnancy (e.g. “Baby overdue”) record. Details on the compilation of the Pregnancy Register, including code lists, and algorithms for timing estimations are available from CPRD on request.

Inferred gestational ages were only calculated for a subset of HES records in which the maternity file did not contain delivery information for the pregnancy. In these participants gestational age data were derived from gestation at first antenatal appointment, date at first antenatal appointment, and end of pregnancy estimates, where available. If no gestational age was available or derivable, records were excluded.

Duplicated pregnancy records

There were 30 instances in which two separate CPRD entries matched the same HES pregnancy window. For these records, the combination of time windows across the overlapping records was calculated and the two with the longest overlap were counted as one pregnancy and those with the shortest overlap as separate pregnancies. See figure S1 for clarification of additional handling of manually identified duplicate records.

Baseline variables

Maternal age at delivery was the estimated age at end of pregnancy or delivery for each pregnancy record. Firstly, maternal age was extracted from both HES and CPRD variables. Where maternal age data were available in both datasets for the same pregnancy, the mean of the two records were retained. Maternal age was complete in the CPRD Pregnancy Register. By contrast, HES maternity files only record maternal age when a related delivery record exists, resulting in substantial missingness. Therefore, for missing records, maternal age was calculated using the estimated date at pregnancy end and date of birth from CPRD.

Maternal ethnicity was taken from the HES patient file. Missing records were recoded as a separate 'unknown' category. The original 12 categories recorded in HES were merged into four larger groups of: Asian (Bangladeshi, Indian, Pakistani, Other Asian), Black (Black Caribbean, Black African, Black Other), Other (Chinese, Mixed, Other), Unknown, and White.

2015 practice level Index of Multiple Deprivation (IMD) scores refer to measures of relative social deprivation mapped to postcodes within England, with a participant's General

Practitioner surgery as the reference address⁴. The score is recorded in deciles and combines a number of domains of deprivation such as employment, income, health, and crime. Higher scores indicate a higher level of deprivation.

Pre-pregnancy diabetes was defined by the presence of any diagnostic record of type one or two Diabetes Mellitus within CPRD or HES data (Table S1). Pre-pregnancy hypertension was either an inferred or diagnosed record of hypertension taken from the composite validated CALIBER phenotype⁵, that uses a combination of diagnostic codes, continuous blood pressure readings, and prescriptions for blood pressure lowering medications. Systemic lupus erythematosus (SLE) was defined by the presence of an ICD10 diagnosis code below the M32 branch prior to first pregnancy. Chronic kidney disease (CKD) was defined according to the presence of a relevant diagnostic code recorded in primary care, prior to the first index pregnancy (Table S1).

Estimates of parity were only available for women who had a pregnancy record in the HES maternity file, where the number of previous live births is recorded. A dichotomous variable for parity (nulliparity/multiparity) was constructed where data were available. BMI data were available from CPRD in continuous form and from HES in categorical groupings. The two were combined into a single categorical variable (Underweight (<18.5); Healthy (18.5-24.9); Overweight (25-29.9); Obese (30-39); Severely obese (>40)). These data were only available for 378,002 (29%) women. 725,959 (55.70%) women had available data on their parity status. Due to these significant proportions of missingness in these two variables, imputation of the remaining variables was deemed unsuitable and it was decided to leave them out of the final models and conduct sensitivity analyses to examine their effects instead in the sub-set with available data. For replication of Bartsch et al. summary data, available continuous BMI data in our study were re-categorised into BMI>25 and BMI>30 groupings.

Maternal smoking status was combined from the CALIBER variables for primary and secondary care smoking status. The smoking record closest to the start of the first pregnancy was used to identify either 'ever-smoker' or 'never smoker' categories.

Data on multi-fetal pregnancies were taken from HES delivery records with anything over 2 infants coded as 'multi-fetal'. Gestational diabetes (GDM) was defined according to the presence of one of a number of code-lists in either HES or CPRD (Table S1) within 20 weeks either side of the end of a pregnancy, no record was assumed to indicate no GDM.

Infant birthweight information was only available for HES recorded pregnancies. Any recorded birthweights under 100 grams (g) and over 6500 g were considered to be administrative errors and were recoded as NA. Preterm birth was defined as any end of pregnancy record prior to 37 weeks gestation.

SUPPLEMENTARY TABLES

Table S1 Overview of codes used to define exposure, covariate, and outcome variables and data sources for phenotypes that are not listed as starred phenotypes on the CALIBER data portal. *Details of the codes and algorithms used to create the CALIBER ‘starred’ phenotypes used in the study (hypertension, ischaemic stroke, intracerebral haemorrhage, subarachnoid haemorrhage, stroke not otherwise specified (NOS), myocardial infarction, atrial fibrillation, heart failure, stable angina, coronary heart disease NOS, peripheral arterial disease) are available in the CALIBER data portal (<https://www.caliberresearch.org/portal>)*

Variable	CPRD – Read code diagnoses	HES – ICD10 Hospital diagnoses
Preeclampsia	L124.00: Mild or unspecified pre-eclampsia L124.11; Mild pre-eclampsia L124.12: Toxaemia NOS L124000: Mild or unspecified pre-eclampsia unspecified L124100: Mild or unspecified pre-eclampsia - delivered L124200: Mild or unspecified pre-eclampsia - delivered with p/n comp L124300: Mild or unspecified pre-eclampsia - not delivered L124400: Mild or unspecified pre-eclampsia with p/n complication L124500: Mild pre-eclampsia	O14: Pre-eclampsia O14.0: Mild to moderate pre-eclampsia O14.1: Severe pre-eclampsia O14.2: HELLP syndrome O14.9: Pre-eclampsia, unspecified O15: Eclampsia O15.0: Eclampsia in pregnancy O15.1: Eclampsia in labour O15.2: Eclampsia in the puerperium O15.9: Eclampsia, unspecified as to time period

<p>L124600: Pre-eclampsia, unspecified</p> <p>L124z00: Mild or unspecified pre-eclampsia NOS</p> <p>L125.00: Severe pre-eclampsia</p> <p>L125000: Severe pre-eclampsia unspecified</p> <p>L125100: Severe pre-eclampsia - delivered</p> <p>L125200: Severe pre-eclampsia - delivered with postnatal complication</p> <p>L125300: Severe pre-eclampsia - not delivered</p> <p>L125400: Severe pre-eclampsia with postnatal complication</p> <p>L125z00: Severe pre-eclampsia NOS</p> <p>L126.00: Eclampsia</p> <p>L126000: Eclampsia unspecified</p> <p>L126100: Eclampsia - delivered</p> <p>L126200: Eclampsia - delivered with postnatal complication</p> <p>L126300: Eclampsia - not delivered</p> <p>L126400: Eclampsia with postnatal complication</p> <p>L126500: Eclampsia in pregnancy</p> <p>L126600: Eclampsia in labour</p> <p>L126z00: Eclampsia NOS</p>	
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L127.00: Pre-eclampsia or eclampsia with pre-existing hypertension

L127000: Pre-eclampsia or eclampsia with hypertension unspecified

L127100: Pre-eclampsia or eclampsia with hypertension - delivered

L127200: Pre-eclampsia or eclampsia with hypertension - del+p/n comp

L127300: Pre-eclampsia or eclampsia with hypertension - not delivered

L127400: Pre-eclampsia or eclampsia with hypertension + p/n comp

L127z00: Pre-eclampsia or eclampsia + pre-existing hypertension NOS

L129.00: Moderate pre-eclampsia

L12A.00: HELLP - Syndrome haemolysis, elev liver enzyme low platelets

L12B.00: Proteinuric hypertension of pregnancy

Lyu1.00: [X]Oedema,proteinuria+hypertens in pregnancy,childbrth,puerp

Q000.11 Fetus affected by maternal toxemia

<p>HDP</p>	<p><i>All codes listed above AND:</i></p> <p>L123.00: Transient hypertension of pregnancy</p> <p>L123000: Transient hypertension of pregnancy unspecified</p> <p>L123100: Transient hypertension of pregnancy - delivered</p> <p>L123200: Transient hypertension of pregnancy - deliv with p/n comp</p> <p>L123300: Transient hypertension of pregnancy - not delivered</p> <p>L123400: Transient hypertension of pregnancy + postnatal complication</p> <p>L123500: Gestational hypertension</p> <p>L123600: Transient hypertension of pregnancy</p> <p>L123z00: Transient hypertension of pregnancy NOS</p> <p>L120.00: Benign essential hypertension in pregnancy/childbirth/puerp</p> <p>L120000: Benign essential hypertension in preg/childb/puerp unspec</p> <p>L120100: Benign essential hypertension in preg/childb/puerp - deliv</p>	<p><i>All codes listed above AND:</i></p> <p>O13; Gestational (pregnancy induced) hypertension</p> <p>O10: Pre-existing hypertension complicating pregnancy, childbirth and the puerperium</p> <p>O10.0: Pre-existing essential hypertension complicating pregnancy, childbirth and the puerperium</p> <p>O10.9: Unspecified pre-existing hypertension complicating pregnancy, childbirth and the puerperium</p> <p>O11: Pre-eclampsia superimposed on chronic hypertension</p> <p>O16: Unspecified maternal hypertension</p> <p>O10.1: Pre-existing hypertensive heart disease complicating pregnancy, childbirth and the puerperium</p> <p>O10.2: Pre-existing hypertensive renal disease complicating pregnancy, childbirth and the puerperium</p> <p>O10.3: Pre-existing hypertensive heart and renal disease complicating pregnancy, childbirth and the puerperium</p> <p>O10.4: Pre-existing secondary hypertension complicating pregnancy, childbirth and the puerperium</p>
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L120200: Benign ess hypert in preg/childb/puerp - deliv with p/n
comp

L120300: Benign essential hypertension in preg/childb/puerp-not
deliv

L120400: Benign essential hypertension in preg/childb/puerp +p/n
comp

L120z00: Benign essential hypertension in preg/childb/puerp NOS

L122.00: Other pre-existing hypertension in preg/childbirth/puerp

L122000: Other pre-existing hypertension in preg/childb/puerp
unspec

L122100: Other pre-existing hypertension in preg/childb/puerp -
deliv

L122300: Other pre-exist hypertension in preg/childb/puerp-not
deliv

L122z00: Other pre-existing hypertension in preg/childb/puerp
NOS

L128.00: Pre-exist hypertension compl preg childbirth and
puerperium

L128000 Pre-exist hyperten heart dis compl preg
childbth+puerperium

L128200	Pre-exist 2ndry hypertens comp preg childbth and puerperium
L121.00	Renal hypertension in pregnancy/childbirth/puerperium
L121000	Renal hypertension in pregnancy/childbirth/puerp unspecified
L121100	Renal hypertension in pregnancy/childbirth/puerp - delivered
L121200	Renal hypertension in preg/childb/puerp -deliv with p/n comp
L121300	Renal hypertension in preg/childbirth/puerp - not delivered
L121z00	Renal hypertension in pregnancy/childbirth/puerperium NOS
L12..00	Hypertension complicating pregnancy/childbirth/puerperium
L12z.00	Unspecified hypertension in pregnancy/childbirth/puerperium
L12z000	Unspecified hypertension in preg/childb/puerp unspecified

	<p>L12z100 Unspecified hypertension in preg/childb/puerp - delivered</p> <p>L12z200 Unspecified hypertension in preg/childb/puerp -del +p/n comp</p> <p>L12z300 Unspecified hypertension in preg/childb/puerp - not deliv</p> <p>L12z400 Unspecified hypertension in preg/childb/puerp with p/n comp</p> <p>L12zz00 Unspecified hypertension in preg/childb/puerp NOS</p> <p>Q000.00 Fetus or neonate affected by maternal hypertensive disease</p>	
Diabetes	<p>6761: Diabetic pre-pregnancy counselling</p> <p>7276: Pan retinal photocoagulation for diabetes</p> <p>9360: Patient held diabetic record issued</p> <p>13AB.00: Diabetic lipid lowering diet</p> <p>13AC.00: Diabetic weight reducing diet</p> <p>13B1.00: Diabetic diet</p> <p>2BBF.00: Retinal abnormality - diabetes related</p> <p>2BBk.00: O/E - right eye stable treated prolif diabetic retinopathy</p>	<p>E10 Insulin-dependent diabetes mellitus</p> <p>E11 Non-insulin-dependent diabetes mellitus</p> <p>E13 Other specified diabetes mellitus</p> <p>E14 Unspecified diabetes mellitus</p> <p>G590 Diabetic mononeuropathy</p> <p>G632 Diabetic polyneuropathy</p> <p>H280 Diabetic cataract</p> <p>H360 Diabetic retinopathy</p>

2BBL.00: O/E - diabetic maculopathy present both eyes
2BBL.00: O/E - left eye stable treated prolif diabetic retinopathy
2BBM.00: O/E - diabetic maculopathy absent both eyes
2BBo.00: O/E - sight threatening diabetic retinopathy
2BBP.00: O/E - right eye background diabetic retinopathy
2BBQ.00: O/E - left eye background diabetic retinopathy
2BBR.00: O/E - right eye preproliferative diabetic retinopathy
2BBS.00: O/E - left eye preproliferative diabetic retinopathy
2BBT.00: O/E - right eye proliferative diabetic retinopathy
2BBV.00: O/E - left eye proliferative diabetic retinopathy
2BBW.00: O/E - right eye diabetic maculopathy
2BBX.00: O/E - left eye diabetic maculopathy
2G51000: Foot abnormality - diabetes related
2G5A.00: O/E - Right diabetic foot at risk
2G5B.00: O/E - Left diabetic foot at risk
2G5C.00: Foot abnormality - diabetes related
2G5E.00: O/E - Right diabetic foot at low risk
2G5F.00: O/E - Right diabetic foot at moderate risk
2G5G.00: O/E - Right diabetic foot at high risk
2G5H.00: O/E - Right diabetic foot - ulcerated

M142 Diabetic arthropathy
N083 Glomerular disorders in diabetes mellitus
O240 Diabetes mellitus in pregnancy: Pre-existing diabetes mellitus, insulin-dependent
O241 Diabetes mellitus in pregnancy: Pre-existing diabetes mellitus, non-insulin-dependent
O243 Diabetes mellitus in pregnancy: Pre-existing diabetes mellitus, unspecified

<p>2G5I.00: O/E - Left diabetic foot at low risk</p> <p>2G5J.00: O/E - Left diabetic foot at moderate risk</p> <p>2G5K.00: O/E - Left diabetic foot at high risk</p> <p>2G5L.00: O/E - Left diabetic foot - ulcerated</p> <p>2G5V.00: O/E - right chronic diabetic foot ulcer</p> <p>2G5W.00: O/E - left chronic diabetic foot ulcer</p> <p>66A3.00: Diabetic on diet only</p> <p>66A4.00: Diabetic on oral treatment</p> <p>66A5.00: Diabetic on insulin</p> <p>66A8.00: Has seen dietician - diabetes</p> <p>66A9.00: Understands diet - diabetes</p> <p>66Aa.00: Diabetic diet - poor compliance</p> <p>66AA.11: Injection sites - diabetic</p> <p>66Ab.00: Diabetic foot examination</p> <p>66Ac.00: Diabetic peripheral neuropathy screening</p> <p>66AD.00: Fundoscopy - diabetic check</p> <p>66AG.00: Diabetic drug side effects</p> <p>66Ag.00: Insulin needles changed daily</p> <p>66AH.00: Diabetic treatment changed</p> <p>66Ah.00: Insulin needles changed for each injection</p>	
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<p>66Al.00: Diabetic - good control</p> <p>66Ai.00: Diabetic 6 month review</p> <p>66AJ.00: Diabetic - poor control</p> <p>66Aj.00: Insulin needles changed less than once a day</p> <p>66AJ.11: Unstable diabetes</p> <p>66AJ100: Brittle diabetes</p> <p>66AJz00: Diabetic - poor control NOS</p> <p>66AK.00: Diabetic - cooperative patient</p> <p>66AL.00: Diabetic-uncooperative patient</p> <p>66Am.00: Insulin dose changed</p> <p>66An.00: Diabetes type 1 review</p> <p>66AN.00: Date diabetic treatment start</p> <p>66Ao.00: Diabetes type 2 review</p> <p>66AO.00: Date diabetic treatment stopp.</p> <p>66AP.00: Diabetes: practice programme</p> <p>66Ap.00: Insulin treatment initiated</p> <p>66AQ.00: Diabetes: shared care programme</p> <p>66Aq.00: Diabetic foot screen</p> <p>66AR.00: Diabetes management plan given</p> <p>66AS.00: Diabetic annual review</p>	
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<p>66AT.00: Annual diabetic blood test</p> <p>66AU.00: Diabetes care by hospital only</p> <p>66AV.00: Diabetic on insulin and oral treatment</p> <p>66AW.00: Diabetic foot risk assessment</p> <p>66AX.00: Diabetes: shared care in pregnancy - diabetol and obstet</p> <p>66AY.00: Diabetic diet - good compliance</p> <p>68A7.00: Diabetic retinopathy screening</p> <p>68A9.00: Diabetic retinopathy screening offered</p> <p>68AB.00: Diabetic digital retinopathy screening offered</p> <p>7L10000: Continuous subcutaneous infusion of insulin</p> <p>7L19800: Subcutaneous injection of insulin</p> <p>889A.00: Diab mellit insulin-glucose infus acute myocardial infarct</p> <p>8A13.00: Diabetic stabilisation</p> <p>8B3I.00: Diabetes medication review</p> <p>8BL2.00: Patient on maximal tolerated therapy for diabetes</p> <p>8CA4100: Pt advised re diabetic diet</p> <p>8CAQ.00: Advice about blood glucose control</p> <p>8CP2.00: Transition of diabetes care options discussed</p> <p>8H2J.00: Admit diabetic emergency</p> <p>8H3O.00: Non-urgent diabetic admission</p>	
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<p>8H7r.00: Refer to diabetic foot screener</p> <p>8HBG.00: Diabetic retinopathy 12 month review</p> <p>8HBH.00: Diabetic retinopathy 6 month review</p> <p>8HI1.00: Referral for diabetic retinopathy screening</p> <p>8HLE.00: Diabetology D.V. done</p> <p>8I3k.00: Insulin therapy declined</p> <p>8I3W.00: Diabetic foot examination declined</p> <p>8I3X.00: Diabetic retinopathy screening refused</p> <p>8I57.00: Patient held diabetic record declined</p> <p>9OLD.00: Diabetic patient unsuitable for digital retinal photography</p> <p>C10..00: Diabetes mellitus</p> <p>C100.00: Diabetes mellitus with no mention of complication</p> <p>C100000: Diabetes mellitus, juvenile type, no mention of complication</p> <p>C100011: Insulin dependent diabetes mellitus</p> <p>C100100: Diabetes mellitus, adult onset, no mention of complication</p> <p>C100111: Maturity onset diabetes</p> <p>C100112: Non-insulin dependent diabetes mellitus</p>	
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<p>C100z00: Diabetes mellitus NOS with no mention of complication</p> <p>C101.00: Diabetes mellitus with ketoacidosis</p> <p>C101000: Diabetes mellitus, juvenile type, with ketoacidosis</p> <p>C101100: Diabetes mellitus, adult onset, with ketoacidosis</p> <p>C101y00: Other specified diabetes mellitus with ketoacidosis</p> <p>C101z00: Diabetes mellitus NOS with ketoacidosis</p> <p>C102.00: Diabetes mellitus with hyperosmolar coma</p> <p>C102000: Diabetes mellitus, juvenile type, with hyperosmolar coma</p> <p>C102100: Diabetes mellitus, adult onset, with hyperosmolar coma</p> <p>C102z00: Diabetes mellitus NOS with hyperosmolar coma</p> <p>C103.00: Diabetes mellitus with ketoacidotic coma</p> <p>C103000: Diabetes mellitus, juvenile type, with ketoacidotic coma</p> <p>C103100: Diabetes mellitus, adult onset, with ketoacidotic coma</p> <p>C103y00: Other specified diabetes mellitus with coma</p> <p>C103z00: Diabetes mellitus NOS with ketoacidotic coma</p> <p>C104.00: Diabetes mellitus with renal manifestation</p> <p>C104.11: Diabetic nephropathy</p> <p>C104000: Diabetes mellitus, juvenile type, with renal manifestation</p> <p>C104100: Diabetes mellitus, adult onset, with renal manifestation</p>	
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<p>C104y00: Other specified diabetes mellitus with renal complications</p> <p>C104z00: Diabetes mellitus with nephropathy NOS</p> <p>C105.00: Diabetes mellitus with ophthalmic manifestation</p> <p>C105000: Diabetes mellitus, juvenile type, + ophthalmic manifestation</p> <p>C105100: Diabetes mellitus, adult onset, + ophthalmic manifestation</p> <p>C105y00: Other specified diabetes mellitus with ophthalmic complicatn</p> <p>C105z00: Diabetes mellitus NOS with ophthalmic manifestation</p> <p>C106.00: Diabetes mellitus with neurological manifestation</p> <p>C106.11: Diabetic amyotrophy</p> <p>C106.12: Diabetes mellitus with neuropathy</p> <p>C106.13: Diabetes mellitus with polyneuropathy</p> <p>C106000: Diabetes mellitus, juvenile, + neurological manifestation</p> <p>C106100: Diabetes mellitus, adult onset, + neurological manifestation</p> <p>C106y00: Other specified diabetes mellitus with neurological comps</p>	
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<p>C106z00: Diabetes mellitus NOS with neurological manifestation</p> <p>C107.00: Diabetes mellitus with peripheral circulatory disorder</p> <p>C107.11: Diabetes mellitus with gangrene</p> <p>C107.12: Diabetes with gangrene</p> <p>C107000: Diabetes mellitus, juvenile +peripheral circulatory disorder</p> <p>C107100: Diabetes mellitus, adult, + peripheral circulatory disorder</p> <p>C107200: Diabetes mellitus, adult with gangrene</p> <p>C107300: IDDM with peripheral circulatory disorder</p> <p>C107400: NIDDM with peripheral circulatory disorder</p> <p>C107z00: Diabetes mellitus NOS with peripheral circulatory disorder</p> <p>C108.00: Insulin dependent diabetes mellitus</p> <p>C108.11: IDDM-Insulin dependent diabetes mellitus</p> <p>C108.12: Type 1 diabetes mellitus</p> <p>C108.13: Type I diabetes mellitus</p> <p>C108000: Insulin-dependent diabetes mellitus with renal complications</p> <p>C108011: Type I diabetes mellitus with renal complications</p> <p>C108012: Type 1 diabetes mellitus with renal complications</p>	
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<p>C108100: Insulin-dependent diabetes mellitus with ophthalmic comps</p> <p>C108200: Insulin-dependent diabetes mellitus with neurological comps</p> <p>C108211: Type I diabetes mellitus with neurological complications</p> <p>C108212: Type 1 diabetes mellitus with neurological complications</p> <p>C108300: Insulin dependent diabetes mellitus with multiple complicatn</p> <p>C108400: Unstable insulin dependant diabetes mellitus</p> <p>C108411: Unstable type I diabetes mellitus</p> <p>C108412: Unstable type 1 diabetes mellitus</p> <p>C108500: Insulin dependent diabetes mellitus with ulcer</p> <p>C108511: Type I diabetes mellitus with ulcer</p> <p>C108512: Type 1 diabetes mellitus with ulcer</p> <p>C108600: Insulin dependent diabetes mellitus with gangrene</p> <p>C108700: Insulin dependent diabetes mellitus with retinopathy</p> <p>C108711: Type I diabetes mellitus with retinopathy</p> <p>C108712: Type 1 diabetes mellitus with retinopathy</p> <p>C108800: Insulin dependant diabetes mellitus - poor control</p> <p>C108811: Type I diabetes mellitus - poor control</p>	
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<p>C108812: Type 1 diabetes mellitus - poor control</p> <p>C108900: Insulin dependant diabetes maturity onset</p> <p>C108911: Type I diabetes mellitus maturity onset</p> <p>C108912: Type 1 diabetes mellitus maturity onset</p> <p>C108A00: Insulin-dependent diabetes without complication</p> <p>C108A11: Type I diabetes mellitus without complication</p> <p>C108B00: Insulin dependent diabetes mellitus with mononeuropathy</p> <p>C108C00: Insulin dependent diabetes mellitus with polyneuropathy</p> <p>C108D00: Insulin dependent diabetes mellitus with nephropathy</p> <p>C108D11: Type I diabetes mellitus with nephropathy</p> <p>C108E00: Insulin dependent diabetes mellitus with hypoglycaemic coma</p> <p>C108E11: Type I diabetes mellitus with hypoglycaemic coma</p> <p>C108E12: Type 1 diabetes mellitus with hypoglycaemic coma</p> <p>C108F00: Insulin dependent diabetes mellitus with diabetic cataract</p> <p>C108F11: Type I diabetes mellitus with diabetic cataract</p> <p>C108G00: Insulin dependent diab mell with peripheral angiopathy</p> <p>C108H00: Insulin dependent diabetes mellitus with arthropathy</p>	
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<p>C108H11: Type I diabetes mellitus with arthropathy</p> <p>C108J00: Insulin dependent diab mell with neuropathic arthropathy</p> <p>C108J11: Type I diabetes mellitus with neuropathic arthropathy</p> <p>C108J12: Type 1 diabetes mellitus with neuropathic arthropathy</p> <p>C108y00: Other specified diabetes mellitus with multiple comps</p> <p>C108z00: Unspecified diabetes mellitus with multiple complications</p> <p>C109.00: Non-insulin dependent diabetes mellitus</p> <p>C109.11: NIDDM - Non-insulin dependent diabetes mellitus</p> <p>C109.12: Type 2 diabetes mellitus</p> <p>C109.13: Type II diabetes mellitus</p> <p>C109000: Non-insulin-dependent diabetes mellitus with renal comps</p> <p>C109011: Type II diabetes mellitus with renal complications</p> <p>C109012: Type 2 diabetes mellitus with renal complications</p> <p>C109100: Non-insulin-dependent diabetes mellitus with ophthalm comps</p> <p>C109111: Type II diabetes mellitus with ophthalmic complications</p> <p>C109112: Type 2 diabetes mellitus with ophthalmic complications</p>	
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C109200: Non-insulin-dependent diabetes mellitus with neuro
comps

C109211: Type II diabetes mellitus with neurological complications

C109212: Type 2 diabetes mellitus with neurological complications

C109300: Non-insulin-dependent diabetes mellitus with multiple
comps

C109400: Non-insulin dependent diabetes mellitus with ulcer

C109411: Type II diabetes mellitus with ulcer

C109412: Type 2 diabetes mellitus with ulcer

C109500: Non-insulin dependent diabetes mellitus with gangrene

C109511: Type II diabetes mellitus with gangrene

C109512: Type 2 diabetes mellitus with gangrene

C109600: Non-insulin-dependent diabetes mellitus with
retinopathy

C109611: Type II diabetes mellitus with retinopathy

C109612: Type 2 diabetes mellitus with retinopathy

C109700: Non-insulin dependant diabetes mellitus - poor control

C109711: Type II diabetes mellitus - poor control

C109712: Type 2 diabetes mellitus - poor control

C109900: Non-insulin-dependent diabetes mellitus without complication

C109A00: Non-insulin dependent diabetes mellitus with mononeuropathy

C109A11: Type II diabetes mellitus with mononeuropathy

C109B00: Non-insulin dependent diabetes mellitus with polyneuropathy

C109B11: Type II diabetes mellitus with polyneuropathy

C109C00: Non-insulin dependent diabetes mellitus with nephropathy

C109C11: Type II diabetes mellitus with nephropathy

C109C12: Type 2 diabetes mellitus with nephropathy

C109D00: Non-insulin dependent diabetes mellitus with hypoglycaemia

C109D11: Type II diabetes mellitus with hypoglycaemic coma

C109D12: Type 2 diabetes mellitus with hypoglycaemic coma

C109E00: Non-insulin dependent diabetes mellitus with diabetic cataract

C109E11: Type II diabetes mellitus with diabetic cataract

C109E12: Type 2 diabetes mellitus with diabetic cataract

<p>C109F00: Non-insulin-dependent d m with peripheral angiopath</p> <p>C109F11: Type II diabetes mellitus with peripheral angiopathy</p> <p>C109F12: Type 2 diabetes mellitus with peripheral angiopathy</p> <p>C109G00: Non-insulin dependent diabetes mellitus with arthropathy</p> <p>C109G11: Type II diabetes mellitus with arthropathy</p> <p>C109G12: Type 2 diabetes mellitus with arthropathy</p> <p>C109H00: Non-insulin dependent d m with neuropathic arthropathy</p> <p>C109H11: Type II diabetes mellitus with neuropathic arthropathy</p> <p>C109H12: Type 2 diabetes mellitus with neuropathic arthropathy</p> <p>C109J00: Insulin treated Type 2 diabetes mellitus</p> <p>C109J11: Insulin treated non-insulin dependent diabetes mellitus</p> <p>C109J12: Insulin treated Type II diabetes mellitus</p> <p>C109K00: Hyperosmolar non-ketotic state in type 2 diabetes mellitus</p> <p>C10A.00: Malnutrition-related diabetes mellitus</p> <p>C10A000: Malnutrition-related diabetes mellitus with coma</p> <p>C10A100: Malnutrition-related diabetes mellitus with ketoacidosis</p> <p>C10B.00: Diabetes mellitus induced by steroids</p>	
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C10B000: Steroid induced diabetes mellitus without complication

C10C.00: Diabetes mellitus autosomal dominant

C10C.11: Maturity onset diabetes in youth

C10C.12: Maturity onset diabetes in youth type 1

C10D.00: Diabetes mellitus autosomal dominant type 2

C10D.11: Maturity onset diabetes in youth type 2

C10E.00: Type 1 diabetes mellitus

C10E.11: Type I diabetes mellitus

C10E.12: Insulin dependent diabetes mellitus

C10E000: Type 1 diabetes mellitus with renal complications

C10E100: Type 1 diabetes mellitus with ophthalmic complications

C10E112: Insulin-dependent diabetes mellitus with ophthalmic
comps

C10E200: Type 1 diabetes mellitus with neurological complications

C10E300: Type 1 diabetes mellitus with multiple complications

C10E311: Type I diabetes mellitus with multiple complications

C10E312: Insulin dependent diabetes mellitus with multiple
complicat

C10E400: Unstable type 1 diabetes mellitus

C10E411: Unstable type I diabetes mellitus

<p>C10E412: Unstable insulin dependent diabetes mellitus</p> <p>C10E500: Type 1 diabetes mellitus with ulcer</p> <p>C10E511: Type I diabetes mellitus with ulcer</p> <p>C10E512: Insulin dependent diabetes mellitus with ulcer</p> <p>C10E600: Type 1 diabetes mellitus with gangrene</p> <p>C10E700: Type 1 diabetes mellitus with retinopathy</p> <p>C10E711: Type I diabetes mellitus with retinopathy</p> <p>C10E712: Insulin dependent diabetes mellitus with retinopathy</p> <p>C10E800: Type 1 diabetes mellitus - poor control</p> <p>C10E812: Insulin dependent diabetes mellitus - poor control</p> <p>C10E900: Type 1 diabetes mellitus maturity onset</p> <p>C10E911: Type I diabetes mellitus maturity onset</p> <p>C10E912: Insulin dependent diabetes maturity onset</p> <p>C10EA00: Type 1 diabetes mellitus without complication</p> <p>C10EA11: Type I diabetes mellitus without complication</p> <p>C10EB00: Type 1 diabetes mellitus with mononeuropathy</p> <p>C10EC00: Type 1 diabetes mellitus with polyneuropathy</p> <p>C10EC11: Type I diabetes mellitus with polyneuropathy</p> <p>C10ED00: Type 1 diabetes mellitus with nephropathy</p> <p>C10EE00: Type 1 diabetes mellitus with hypoglycaemic coma</p>	
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<p>C10EF00: Type 1 diabetes mellitus with diabetic cataract</p> <p>C10EG00: Type 1 diabetes mellitus with peripheral angiopathy</p> <p>C10EH00: Type 1 diabetes mellitus with arthropathy</p> <p>C10EJ00: Type 1 diabetes mellitus with neuropathic arthropathy</p> <p>C10EK00: Type 1 diabetes mellitus with persistent proteinuria</p> <p>C10EL00: Type 1 diabetes mellitus with persistent microalbuminuria</p> <p>C10EM00: Type 1 diabetes mellitus with ketoacidosis</p> <p>C10EM11: Type I diabetes mellitus with ketoacidosis</p> <p>C10EN00: Type 1 diabetes mellitus with ketoacidotic coma</p> <p>C10EN11: Type I diabetes mellitus with ketoacidotic coma</p> <p>C10EP00: Type 1 diabetes mellitus with exudative maculopathy</p> <p>C10EP11: Type I diabetes mellitus with exudative maculopathy</p> <p>C10EQ00: Type 1 diabetes mellitus with gastroparesis</p> <p>C10ER00: Latent autoimmune diabetes mellitus in adult</p> <p>C10F.00: Type 2 diabetes mellitus</p> <p>C10F.11: Type II diabetes mellitus</p> <p>C10F000: Type 2 diabetes mellitus with renal complications</p> <p>C10F011: Type II diabetes mellitus with renal complications</p> <p>C10F100: Type 2 diabetes mellitus with ophthalmic complications</p>	
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<p>C10F200: Type 2 diabetes mellitus with neurological complications</p> <p>C10F211: Type II diabetes mellitus with neurological complications</p> <p>C10F300: Type 2 diabetes mellitus with multiple complications</p> <p>C10F311: Type II diabetes mellitus with multiple complications</p> <p>C10F400: Type 2 diabetes mellitus with ulcer</p> <p>C10F411: Type II diabetes mellitus with ulcer</p> <p>C10F500: Type 2 diabetes mellitus with gangrene</p> <p>C10F600: Type 2 diabetes mellitus with retinopathy</p> <p>C10F611: Type II diabetes mellitus with retinopathy</p> <p>C10F700: Type 2 diabetes mellitus - poor control</p> <p>C10F711: Type II diabetes mellitus - poor control</p> <p>C10F900: Type 2 diabetes mellitus without complication</p> <p>C10F911: Type II diabetes mellitus without complication</p> <p>C10FA00: Type 2 diabetes mellitus with mononeuropathy</p> <p>C10FA11: Type II diabetes mellitus with mononeuropathy</p> <p>C10FB00: Type 2 diabetes mellitus with polyneuropathy</p> <p>C10FB11: Type II diabetes mellitus with polyneuropathy</p> <p>C10FC00: Type 2 diabetes mellitus with nephropathy</p> <p>C10FD00: Type 2 diabetes mellitus with hypoglycaemic coma</p> <p>C10FD11: Type II diabetes mellitus with hypoglycaemic coma</p>	
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<p>C10FE00: Type 2 diabetes mellitus with diabetic cataract</p> <p>C10FE11: Type II diabetes mellitus with diabetic cataract</p> <p>C10FF00: Type 2 diabetes mellitus with peripheral angiopathy</p> <p>C10FG00: Type 2 diabetes mellitus with arthropathy</p> <p>C10FH00: Type 2 diabetes mellitus with neuropathic arthropathy</p> <p>C10FJ00: Insulin treated Type 2 diabetes mellitus</p> <p>C10FJ11: Insulin treated Type II diabetes mellitus</p> <p>C10FK00: Hyperosmolar non-ketotic state in type 2 diabetes mellitus</p> <p>C10FL00: Type 2 diabetes mellitus with persistent proteinuria</p> <p>C10FL11: Type II diabetes mellitus with persistent proteinuria</p> <p>C10FM00: Type 2 diabetes mellitus with persistent microalbuminuria</p> <p>C10FM11: Type II diabetes mellitus with persistent microalbuminuria</p> <p>C10FN00: Type 2 diabetes mellitus with ketoacidosis</p> <p>C10FP00: Type 2 diabetes mellitus with ketoacidotic coma</p> <p>C10FQ00: Type 2 diabetes mellitus with exudative maculopathy</p> <p>C10FR00: Type 2 diabetes mellitus with gastroparesis</p> <p>C10M.00: Lipoatrophic diabetes mellitus</p>	
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<p>C10y.00: Diabetes mellitus with other specified manifestation</p> <p>C10y100: Diabetes mellitus, adult, + other specified manifestation</p> <p>C10yy00: Other specified diabetes mellitus with other spec comps</p> <p>C10yz00: Diabetes mellitus NOS with other specified manifestation</p> <p>C10z.00: Diabetes mellitus with unspecified complication</p> <p>C10z000: Diabetes mellitus, juvenile type, + unspecified complication</p> <p>C10z100: Diabetes mellitus, adult onset, + unspecified complication</p> <p>C10zy00: Other specified diabetes mellitus with unspecified comps</p> <p>C10zz00: Diabetes mellitus NOS with unspecified complication</p> <p>C314.11: Renal diabetes</p> <p>C350011: Bronzed diabetes</p> <p>Cyu2.00: [X]Diabetes mellitus</p> <p>Cyu2000: [X]Other specified diabetes mellitus</p> <p>F171100: Autonomic neuropathy due to diabetes</p> <p>F345000: Diabetic mononeuritis multiplex</p> <p>F35z000: Diabetic mononeuritis NOS</p> <p>F372.00: Polyneuropathy in diabetes</p> <p>F372.11: Diabetic polyneuropathy</p>	
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<p>F372.12: Diabetic neuropathy</p> <p>F372000: Acute painful diabetic neuropathy</p> <p>F372100: Chronic painful diabetic neuropathy</p> <p>F372200: Asymptomatic diabetic neuropathy</p> <p>F381300: Myasthenic syndrome due to diabetic amyotrophy</p> <p>F381311: Diabetic amyotrophy</p> <p>F3y0.00: Diabetic mononeuropathy</p> <p>F420.00: Diabetic retinopathy</p> <p>F420000: Background diabetic retinopathy</p> <p>F420100: Proliferative diabetic retinopathy</p> <p>F420200: Preproliferative diabetic retinopathy</p> <p>F420300: Advanced diabetic maculopathy</p> <p>F420400: Diabetic maculopathy</p> <p>F420500: Advanced diabetic retinal disease</p> <p>F420600: Non proliferative diabetic retinopathy</p> <p>F420700: High risk proliferative diabetic retinopathy</p> <p>F420800: High risk non proliferative diabetic retinopathy</p> <p>F420z00: Diabetic retinopathy NOS</p> <p>F440700: Diabetic iritis</p> <p>F464000: Diabetic cataract</p>	
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<p>G73y000: Diabetic peripheral angiopathy</p> <p>K01x100: Nephrotic syndrome in diabetes mellitus</p> <p>K01x111: Kimmelstiel - Wilson disease</p> <p>L180500: Pre-existing diabetes mellitus, insulin-dependent</p> <p>L180600: Pre-existing diabetes mellitus, non-insulin-dependent</p> <p>L180X00: Pre-existing diabetes mellitus, unspecified</p> <p>M037200: Cellulitis in diabetic foot</p> <p>M21yC00: Insulin lipohypertrophy</p> <p>M21yC11: Insulin site lipohypertrophy</p> <p>M271000: Ischaemic ulcer diabetic foot</p> <p>M271100: Neuropathic diabetic ulcer - foot</p> <p>M271200: Mixed diabetic ulcer - foot</p> <p>N030000: Diabetic cheiroarthropathy</p> <p>N030011: Diabetic cheiropathy</p> <p>N030100: Diabetic Charcot arthropathy</p> <p>Q441.00: Neonatal diabetes mellitus</p> <p>R054200: [D]Gangrene of toe in diabetic</p> <p>R054300: [D]Widespread diabetic foot gangrene</p> <p>TJ23.00: Adverse reaction to insulins and antidiabetic agents</p> <p>TJ23z00: Adverse reaction to insulins and antidiabetic agents NOS</p>	
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	<p>U602311: [X] Adverse reaction to insulins and antidiabetic agents</p> <p>ZC2C800: Dietary advice for diabetes mellitus</p> <p>ZC2C900: Dietary advice for type I diabetes</p> <p>ZC2CA00: Dietary advice for type II diabetes</p> <p>ZRbH.00: Perceived control of insulin-dependent diabetes</p> <p>ZV65312: [V]Dietary counselling in diabetes mellitus</p>	
Gestational diabetes	<p>O244 Diabetes mellitus arising in pregnancy</p> <p>O249 Diabetes mellitus in pregnancy, unspecified</p>	<p>Pre-existing type 1 diabetes mellitus O24.0</p> <p>Pre-existing type 2 diabetes mellitus O24.1</p> <p>Pre-existing diabetes mellitus, unspecified O24.3</p> <p>Pre-existing malnutrition-related diabetes mellitus O24.2</p> <p>Diabetes mellitus in pregnancy O24</p> <p>Diabetes mellitus arising in pregnancy O24.4</p> <p>Diabetes mellitus in pregnancy, unspecified O24.9</p>
Chronic kidney disease	<p>1Z10.00: Chronic kidney disease stage 1</p> <p>1Z17.00: Chronic kidney disease stage 1 with proteinuria</p> <p>1Z17.11: CKD stage 1 with proteinuria</p> <p>1Z18.00: Chronic kidney disease stage 1 without proteinuria</p> <p>1Z11.00: Chronic kidney disease stage 2</p> <p>1Z19.00: Chronic kidney disease stage 2 with proteinuria</p>	

1Z19.11: CKD stage 2 with proteinuria	
1Z1A.00: Chronic kidney disease stage 2 without proteinuria	
1Z1A.11: CKD stage 2 without proteinuria	
1Z12.00: Chronic kidney disease stage 3	
1Z15.00: Chronic kidney disease stage 3A	
1Z16.00: Chronic kidney disease stage 3B	
1Z1B.00: Chronic kidney disease stage 3 with proteinuria	
1Z1B.11: CKD stage 3 with proteinuria	
1Z1C.00: Chronic kidney disease stage 3 without proteinuria	
1Z1C.11: CKD stage 3 without proteinuria	
1Z1D.00: Chronic kidney disease stage 3A with proteinuria	
1Z1D.11: CKD stage 3A with proteinuria	
1Z1E.00: Chronic kidney disease stage 3A without proteinuria	
1Z1E.11: CKD stage 3A without proteinuria	
1Z1F.00: Chronic kidney disease stage 3B with proteinuria	
1Z1F.11: CKD stage 3B with proteinuria	
1Z1G.00: Chronic kidney disease stage 3B without proteinuria	
1Z13.00: Chronic kidney disease stage 4	
1Z1H.00: Chronic kidney disease stage 4 with proteinuria	
1Z1J.00: Chronic kidney disease stage 4 without proteinuria	

	1Z1J.11: CKD stage 4 without proteinuria	
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	1Z14.00: Chronic kidney disease stage 5	
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	1Z1K.00: Chronic kidney disease stage 5 with proteinuria	
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	1Z1L.00: Chronic kidney disease stage 5 without proteinuria	
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	1Z1L.11: CKD stage 5 without proteinuria	
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Table S2: Comparison between study attributes of Bartsch et al⁶ and current study

	Bartsch et al	Current study
Study inclusion	<ul style="list-style-type: none"> -Study period: 2000 to 2015 -Cohort study design with minimum samples size of 1000 pregnancies -Numbers of patients with/without the risk factor and with /without preeclampsia were provided to enable pooled effect size calculation -Evaluated each risk factor up to 16 weeks gestation or earlier -Studies investigating association between preeclampsia and at least one risk factor in a previous pregnancy (history of preeclampsia, placental abruption, intrauterine growth restriction, stillbirth) or in the current pregnancy (nulliparity, advanced maternal age, high body mass index, chronic 	<ul style="list-style-type: none"> -Study period: 1996-2016 -Electronic health records study with all women in CPRD eligible for linkage with HES and with record of 'completed' pregnancy either in primary or secondary care within cohort inclusion dates and between ages of 11-49 at pregnancy. -Evaluated each risk factor from five years prior to pregnancy and up to 16 weeks gestation

	<p>hypertension, prepregnancy diabetes, CKD, SLE, ALS, ART, multi-fetal pregnancy)</p> <p>-92 studies included in the meta-analysis</p>	
Exposure (definition, comparison)	<p>[(MeSH terms “pre-eclampsia, eclampsia, HELLP syndrome, toxemia”) OR (keywords “preeclampsia, pre-eclampsia, eclampsia, HELLP syndrome, toxemia”)]</p>	<p>PE as defined by code list (see methods) and presence of a record within 20 weeks either side of estimate of pregnancy end.</p>
Confounding	<p>No adjustment</p>	<p>No adjustment</p>
Model	<p>Unadjusted relative risk for each risk factor from the raw numbers and then a pooled relative risk and 95% CI for each risk factor and I² heterogeneity calculated</p>	<p>Unadjusted relative risk for each risk factor from the raw numbers with 95% CI</p>

Table S3 – with adjustment for potential mediating effects of post-pregnancy hypertension with robust standard errors

Composite outcome	Preeclampsia HR (95% CI)	P	% difference with model 1	HDP HR (95% CI)	P	% difference with model 1	Preterm preeclampsia HR (95% CI)	P	% difference with model 1
All stroke	1.68 (1.30-2.18)	9.55e-5	24.44	1.65 (1.40-1.94)	1.26e-9	21.69	2.79 (1.48-5.25)	0.0015	15.96
Cardiac atherosclerotic	1.45 (1.32-1.59)	1.17e-14	32.84	1.53 (1.45-1.62)	<2e-16	25.35	1.78 (1.34-2.36)	6.24e-05	17.89
All peripheral disease	1.60 (1.12-2.29)	0.0097	26.83	1.35 (1.07-1.72)	0.012	36.36	1.44 (0.46-4.48)	0.53	64.8
Other cardiovascular	1.43 (1.15-1.76)	0.00098	48.81	1.22 (1.06-1.40)	0.0047	58.49	1.60 (0.88-2.92)	0.12	52.38
All CVD	1.45 (1.34-1.57)	<2e-16	34.78	1.49 (1.41-1.56)	<2e-16	27.94	1.87 (1.47-2.37)	2.51e-07	22.32

Table S4 – Sensitivity analysis of BMI 5 years with preeclampsia exposure with robust standard errors

Composite outcome	HR (95% CI)	P	% difference with model 1	N events	N events full cohort
All stroke	1.58 (1.11-2.25)	0.01	15.94	553	1698
Cardiac atherosclerotic	1.23 (1.10-1.39)	0.00056	66.67	5832	14309
All peripheral disease	1.66 (1.04-2.63)	0.033	20.73	288	852
Other cardiovascular	1.41 (1.06-1.87)	0.018	51.19	877	2620
All CVD	1.24 (1.11-1.38)	9.67e-05	66.67	7217	18624

Table S5: Forest plot of adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) for 12 cardiovascular outcomes and relevant composites, given exposure to Preeclampsia with preterm birth. All HRs were computed using a cox proportional hazards model with time-dependent exposure and adjusted for effects of maternal ethnicity, maternal age, pre-pregnancy diabetes, pre-pregnancy hypertension and index of multiple deprivation with robust SE using clustering for patient ID.

Outcome	Unadjusted		Adjusted	
	Preeclampsia HR (95% CI)	P	Preeclampsia HR (95% CI)	P
Ischaemic stroke	2.71 (2.03-3.62)	1.38E-11	2 (1.48-2.7)	6.13E-06
Intracerebral haemorrhage	1.7 (0.975-2.96)	0.0615	1.52 (0.861-2.68)	0.148
Subarachnoid haemorrhage	2.21 (1.52-3.21)	3.22E-05	1.85 (1.26-2.72)	0.00175
Stroke NOS	3.83 (2.58-5.68)	2.42E-11	2.89 (1.92-4.34)	3.24E-07
All stroke	2.4 (1.94-2.95)	2.22E-16	1.9 (1.53-2.35)	5.32E-09
Myocardial infarction	3.71 (2.85-4.82)	<2.2E-16	2.53 (1.91-3.36)	9.35E-11
Stable angina	2.04 (1.88-2.22)	<2.2E-16	1.64 (1.51-1.78)	<2.2E-16
Unstable angina	2.99 (2.13-4.2)	2.18E-10	2.14 (1.49-3.08)	3.49E-05
Coronary heart disease NOS	3.04 (2.52-3.66)	<2.2E-16	2.29 (1.89-2.79)	1.11E-16

Cardiac atherosclerotic	2.08 (1.92-2.25)	<2.2E-16	1.67 (1.54-1.81)	<2.2E-16
Peripheral arterial disease	2.44 (1.8-3.31)	8.79E-09	1.88 (1.37-2.56)	7.63E-05
Abdominal aortic aneurysm	1.7 (0.537-5.41)	0.365	0.628 (0.179-2.21)	0.468
All peripheral disease	2.37 (1.76-3.18)	1.36E-08	1.82 (1.34-2.46)	0.000119
Heart failure	2.87 (2.24-3.67)	1.11E-16	2.13 (1.64-2.76)	1.35E-08
Atrial fibrillation	2.19 (1.76-2.72)	1.36E-12	1.73 (1.38-2.16)	1.81E-06
Other cardiovascular	2.31 (1.95-2.75)	<2.2E-16	1.84 (1.54-2.19)	2.11E-11
CVD death	2.7 (1.93-3.76)	5.14E-09	2.12 (1.49-2.99)	2.36E-05
All CVD	2.07 (1.94-2.22)	<2.2E-16	1.69 (1.57-1.81)	<2.2E-16
Hypertension	4.87 (4.72-5.03)	<2.2E-16	4.47 (4.32-4.62)	<2.2E-16

Bold = P<0.05

Table S6: Forest plot of adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) for 12 cardiovascular outcomes and relevant composites, given exposure to Hypertensive disorders of pregnancy. All HRs were computed using a cox proportional hazards model with time-dependent exposure and adjusted for effects of maternal ethnicity, maternal age, pre-pregnancy diabetes, pre-pregnancy hypertension and index of multiple deprivation with robust SE using clustering for patient ID.

Outcome	Unadjusted		Adjusted	
	HDP HR (95% CI)	HDP P	HDP HR (95% CI)	HDP P
Ischaemic stroke	2.25 (1.85-2.73)	1.11E-16	1.72 (1.39-2.12)	4.16E-07
Intracerebral haemorrhage	1.85 (1.34-2.55)	0.000162	1.71 (1.24-2.36)	0.00102
Subarachnoid haemorrhage	2.33 (1.86-2.92)	1.38E-13	1.99 (1.57-2.52)	1.39E-08
Stroke NOS	2.58 (1.93-3.45)	1.65E-10	1.99 (1.46-2.71)	1.36E-05
All stroke	2.25 (1.97-2.57)	<2.2E-16	1.83 (1.59-2.1)	<2.2E-16
Myocardial infarction	3.4 (2.85-4.06)	<2.2E-16	2.48 (2.04-3.01)	<2.2E-16
Stable angina	2.05 (1.95-2.16)	<2.2E-16	1.66 (1.58-1.75)	<2.2E-16
Unstable angina	2.85 (2.29-3.54)	<2.2E-16	2.14 (1.67-2.74)	1.47E-09
Coronary heart disease NOS	3 (2.66-3.38)	<2.2E-16	2.37 (2.08-2.69)	<2.2E-16
Cardiac atherosclerotic	2.1 (2-2.2)	<2.2E-16	1.71 (1.62-1.79)	<2.2E-16
Peripheral arterial disease	1.93 (1.58-2.37)	2.49E-10	1.56 (1.26-1.93)	4.12E-05

Abdominal aortic aneurysm	1.88 (0.968-3.66)	0.0621	0.721 (0.312-1.67)	0.444
All peripheral disease	1.93 (1.58-2.35)	6.19E-11	1.55 (1.26-1.9)	2.97E-05
Heart failure	2.01 (1.69-2.39)	6.88E-15	1.54 (1.28-1.86)	6.18E-06
Atrial fibrillation	1.9 (1.65-2.18)	<2.2E-16	1.5 (1.29-1.75)	1.37E-07
Other cardiovascular	1.9 (1.7-2.13)	<2.2E-16	1.53 (1.36-1.73)	5.40E-12
CVD death	2.58 (2.09-3.19)	<2.2E-16	2.15 (1.72-2.68)	2.11E-11
All CVD	2.04 (1.96-2.13)	<2.2E-16	1.68 (1.61-1.76)	<2.2E-16
Hypertension	4.42 (4.33-4.52)	<2.2E-16	4.15 (4.06-4.24)	<2.2E-16

Bold P<0.05

Table S7: Forest plot of adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) for 12 cardiovascular outcomes and relevant composites, given exposure to Preeclampsia with preterm birth. All HRs were computed using a cox proportional hazards model with time-dependent exposure and adjusted for effects of maternal ethnicity, maternal age, pre-pregnancy diabetes, pre-pregnancy hypertension and index of multiple deprivation with robust SE using clustering for patient ID.

Outcome	Unadjusted		Adjusted	
	Preterm preeclampsia	Preterm preeclampsia	Preterm preeclampsia	Preterm preeclampsia
	HR (95% CI)	P	HR (95% CI)	P
Ischaemic stroke	6.32 (3.28-12.2)	3.83E-08	3.42 (1.73-6.74)	0.000396
Intracerebral haemorrhage	4.69 (1.51-14.6)	0.0077	3.11 (0.948-10.2)	0.0612
Subarachnoid haemorrhage	3.89 (1.46-10.4)	0.00677	2.59 (0.947-7.1)	0.0639
Stroke NOS	8.58 (3.55-20.8)	1.88E-06	4.49 (1.84-11)	0.000983
All stroke	5.17 (3.16-8.46)	6.16E-11	3.13 (1.88-5.19)	1.07E-05

Myocardial infarction	5.93 (2.82-12.5)	2.80E-06	2.53 (1.15-5.57)	0.0206
Stable angina	2.28 (1.76-2.96)	4.85E-10	1.77 (1.36-2.31)	2.21E-05
Unstable angina	6.54 (2.92-14.6)	4.85E-06	2.69 (1.16-6.21)	0.0209
Coronary heart disease NOS	7.15 (4.6-11.1)	<2.2E-16	3.49 (2.2-5.54)	1.08E-07
Cardiac atherosclerotic	2.54 (2.01-3.23)	1.57E-14	1.95 (1.53-2.48)	6.41E-08
Peripheral arterial disease	3.45 (1.43-8.31)	0.00582	2 (0.823-4.85)	0.126
Abdominal aortic aneurysm	6.8 (0.946-49)	0.0569	1.32 (0.159-11)	0.796
All peripheral disease	3.83 (1.72-8.56)	0.00104	2.25 (1-5.08)	0.0496
Heart failure	4.11 (2.05-8.23)	6.96E-05	2 (0.97-4.12)	0.0603
Atrial fibrillation	3.14 (1.69-5.85)	0.00031	1.98 (1.06-3.72)	0.033

Other cardiovascular	3.7 (2.33-5.88)	3.25E-08	2.26 (1.41-3.63)	0.000719
CVD death	5.86 (2.62-13.1)	1.65E-05	3.19 (1.39-7.36)	0.00636
All CVD	2.79 (2.28-3.41)	<2.2E-16	2.12 (1.73-2.6)	3.31E-13
Hypertension	6.14 (5.59-6.75)	<2.2E-16	5.65 (5.1-6.26)	<2.2E-16

Bold P <0.05

Table S8; Comparison of HR with impact of non-CVD mortality as a competing risk on CVD events.

	Original HR (95% CI)	HR adjusted for competing risk of non-cvd mortality (95% CI)
Stroke all	1.9 (1.53-2.35)	1.89 (1.53-2.35)
Cardio atherosclerotic	1.67 (1.54-1.81)	1.67 (1.54-1.81)
Other cardio	1.84 (1.54-2.19)	1.83 (1.53-2.19)
Peripheral all	1.82 (1.34-2.46)	1.81 (1.34-2.45)
All CVD	1.69 (1.57-1.81)	1.89 (1.53-2.35)

SUPPLEMENTAL FIGURE LEGENDS

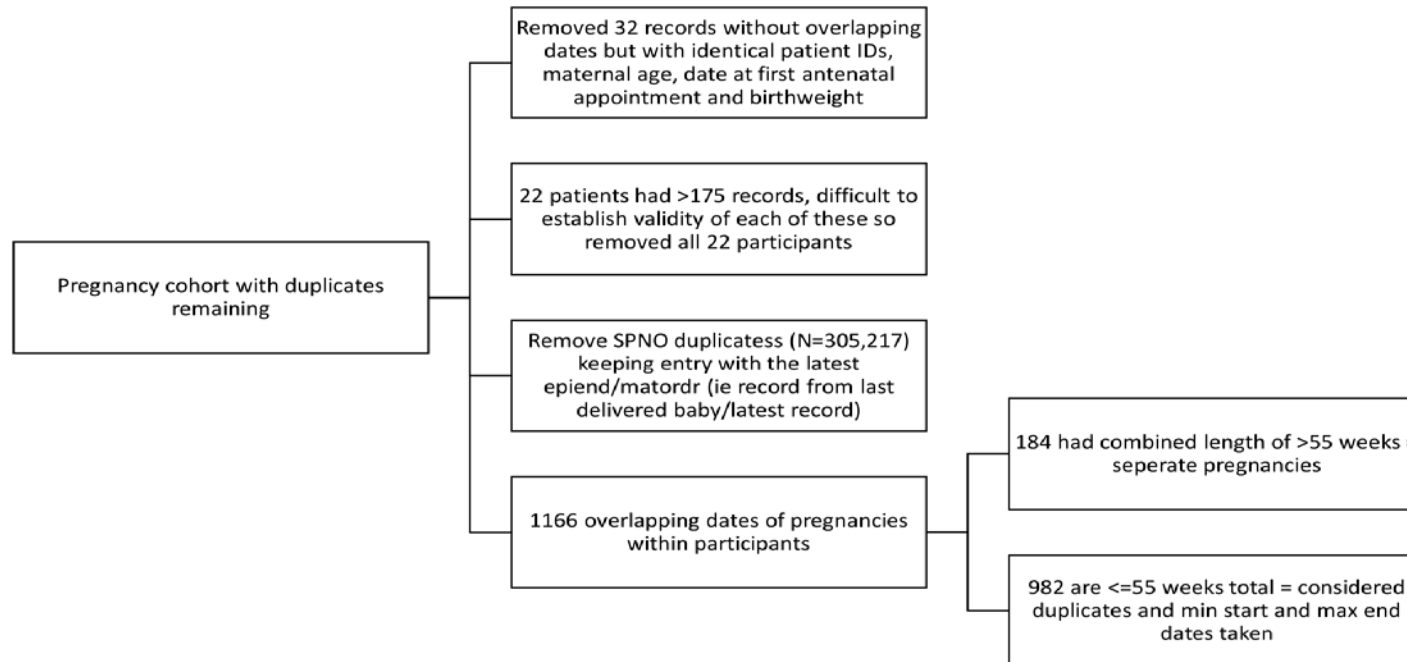


Figure S1: Dealing with duplicates and merging primary and secondary care pregnancy records

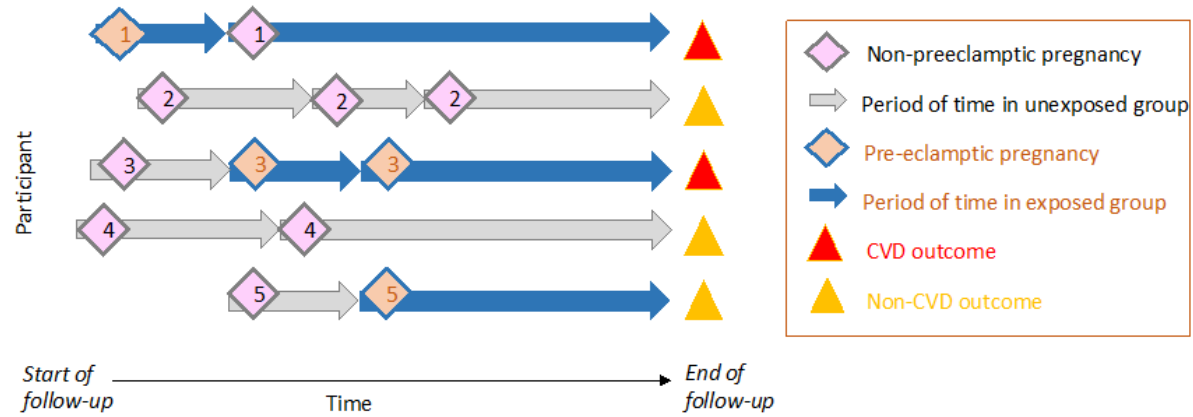


Figure S2: Schematic to explain time-varying exposure model used to investigate association between preeclampsia and cardiovascular outcomes, enabling inclusion of multiple pregnancies per woman in our cohort.

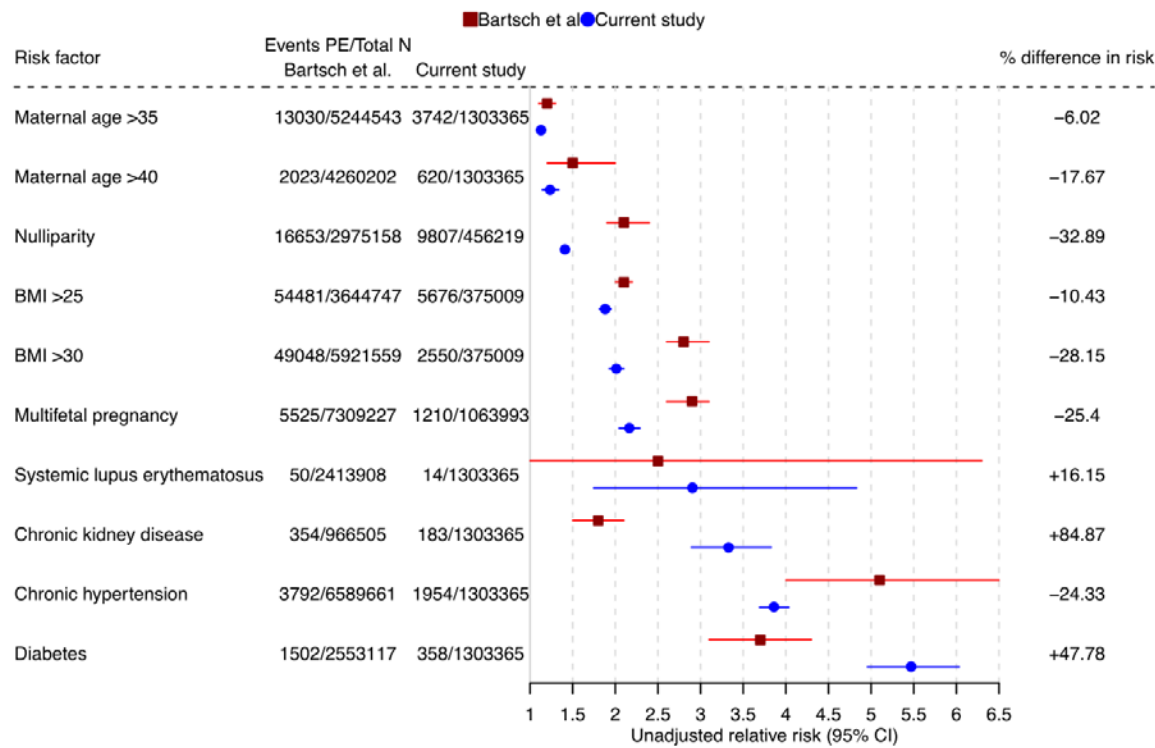


Figure S3: Comparison of relative risk of preeclampsia for a selection of pre-pregnancy risk factors, between Bartsch et al (2016) systematic review and current dataset. Risk factors and preeclampsia status relate to first recorded pregnancy in cohort. Percentage difference in risk was calculated as the point estimate for the relative risk for each risk factor in the current study minus the point estimate for the Bartsh et al study.

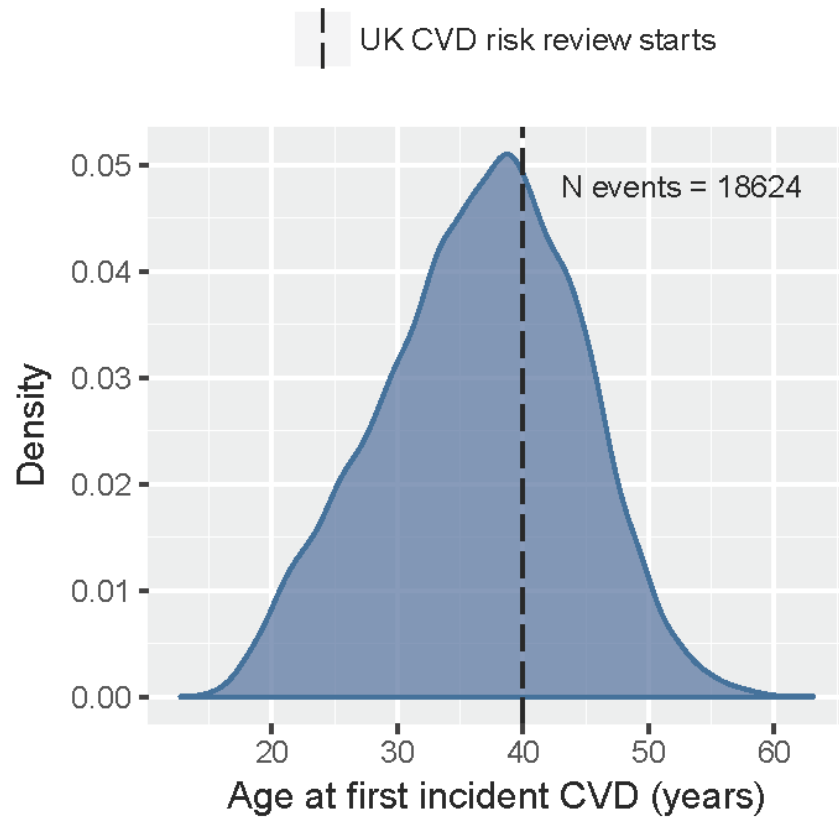


Figure S4: Age at event density distributions for first incident of any cardiovascular outcome for women in the present study. Dotted line is age at first cardiovascular risk screen in UK (40 years).

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