

Maternal hypertensive disorder of pregnancy and offspring mortality in childhood, adolescence, and young adulthood: A national population-based cohort study

Supplementary Material

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Appendix S1. Detailed descriptions of registers used in this study^a

Register	Description	Reference
The Danish Civil Registration System (CRS)	The Danish Civil Registration System (CRS) has been established since 1968, and collects information on date of birth, emigration, and immigration, sex, and other vital status in a daily basis.	1
The Danish Medical Birth Register (DMBR)	The Danish Medical Birth Register (DMBR) includes Central Personal Register number (CPR) of new births, mothers, and fathers, as well as information on date of birth, birth characteristics such as sex, birth weight, gestational age, maternal characteristics such as maternal pre-pregnancy body mass index, maternal smoking during pregnancy. DMBR was established in 1968 and has been computerized since 1973.	2
The Danish National Patient Register (DNPR)	The Danish National Patient Register (DNPR) was established in 1977 and collects data from inpatient, outpatient and emergency hospital record (each visit for one record in register). Information includes dates of contact, primary and secondary discharge diagnoses, dates and procedures of surgery, certain treatment in hospitals, and other hospital related information. Diagnoses are classified according to the ICD-8 codes (<i>International Classification of Disease</i> codes, 8th revision) and ICD-10 codes thereafter.	3
The Danish Register of Causes of Death	The Danish Register of Causes of Death has been computerized since 1970 and the non-electronic data on deaths has been collected since 1924. This system has been collecting date of death, and underlying cause and	4

	contributory causes of death by law in Denmark. The ICD-8 was used to classify the causes of death during 1970-1993 and ICD-10 from 1994.	
The Danish Integrated Database for Longitudinal Labour Market Research	The Danish Integrated Database for Longitudinal Labour Market Research was established in 1981 and contains labour market and socioeconomic data.	5

^aDenmark has been providing public welfare, including universal health care, education, student assistance, disability pensions, and unemployment insurance through tax-funded services. There are population-based health databases in Denmark that regularly collect high-quality data, including individual medical data. All live births and new residents in Denmark have been assigned a unique 10-digit individual personal identification number (Central Personal Register number, CPR) since the 1960s. The CPR number links information across different national registers.

Appendix S2. Detailed descriptions of covariates and multiple imputation methods

Information on maternal and birth characteristics was retrieved from the Danish Medical Birth Register,² and socioeconomic factors were retrieved from the Danish Integrated Database for Longitudinal Labour Market Research,⁵ and the Danish Civil Registration System.¹ These included sex (male, female), singleton (yes, no), parity (1, 2, ≥ 3 children), birth year of the child (1977-1980, 5-year intervals during 1981-2015, and 2016-2018), maternal age (<20, 20-24, 25-29, 30-34, ≥ 35 years), maternal smoking during pregnancy (yes, no), maternal cohabitation (single, cohabitating), maternal residence (Copenhagen, big cities $\geq 100\ 000$ inhabitants, other places), maternal country of origin (Denmark, non-Denmark), maternal education before pregnancy (low: 0-9 years, medium: 10-14 years, high: ≥ 15 years), maternal income at birth (no income, 3 tertiles), maternal pre-pregnancy BMI (underweight: $<18.5\ \text{kg/m}^2$, normal: $18.5\text{-}24.9\ \text{kg/m}^2$, overweight: $25.0\text{-}29.9\ \text{kg/m}^2$, obese: $\geq 30.0\ \text{kg/m}^2$). Information on maternal history of diabetes and parental CVD history was obtained from the Danish National Patient Register.³

The frequency of missing data in this study was relatively low: 0.05% for sex, 1.64% for maternal education, 0.04% for maternal cohabitation, 0.02% for maternal income, and 0.97% for paternal history of CVD. The frequency of missing data for maternal smoking (available since 1991) was 3.44% and maternal BMI (available since 2004) was 3.65%.

Multiple imputation methods imputed with 10 replications was used to deal with missing values in this study.⁶ We imputed missing variables using the fully conditional specification (FCS) method in which logistic regression was used for categorical variables and predictive

mean matching for continuous variables. The imputation model included the following variables: maternal HDP (yes, no), offspring mortality (yes, no), sex of offspring (male, female), singleton births (yes, no), parity (1, 2, ≥ 3 children), birth year of the child (1977-1980, 5-year intervals during 1981-2015, and 2016-2018), maternal age (<20, 20-24, 25-29, 30-34, ≥ 35 years), maternal smoking during pregnancy (yes, no), maternal cohabitation (single, cohabitating), maternal residence (Copenhagen, big cities $\geq 100\ 000$ inhabitants, other places), maternal country of origin (Denmark, non-Denmark), maternal education before pregnancy (low 0-9 years, medium 10-14 years, high ≥ 15 years), maternal income at birth (no income, 3 tertiles), maternal pre-pregnancy BMI (underweight: < 18.5 kg/m², normal: 18.5-24.9 kg/m², overweight: 25.0-29.9 kg/m², obese: ≥ 30.0 kg/m²), maternal history of diabetes (yes, no), maternal and paternal history of CVD before childbirth (yes, no). As the data on maternal smoking was available since 1991 and data on maternal pre-pregnancy BMI was available since 2004, the imputation model for maternal smoking and maternal pre-pregnancy BMI was only restricted to offspring born since 1991 and 2004, respectively.

References

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2. Knudsen LB, Olsen J. The Danish Medical Birth Registry. *Danish medical bulletin*. Jun 1998;45(3):320-323.
3. Lynge E, Sandegaard JL, Rebolj M. The Danish National Patient Register. *Scandinavian journal of public health*. Jul 2011;39(7 Suppl):30-33.
4. Helweg-Larsen K. The Danish Register of Causes of Death. *Scandinavian journal of public health*. Jul 2011;39(7 Suppl):26-29.
5. Petersson F, Baadsgaard M, Thygesen LC. Danish registers on personal labour market affiliation. *Scandinavian journal of public health*. Jul 2011;39(7 Suppl):95-

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6. Sterne J A C, White I R, Carlin J B, Spratt M, Royston P, Kenward M G et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls BMJ 2009; 338 :b2393 doi:10.1136/bmj.b2393.

Appendix S3. Analysis codes for the study

```
/*Project          |maternal HDP and offspring mortality
/*Date            |2021-04-30
/*platform        |Windown 64 bit
/*SAS Version     |9.4
/*Dataset used    |Analysis.final

-----
*****Main Code*****
-----*/

/*Codes for association between maternal HDP and offspring
all-cause mortality*/

*create dataset for analysis;
*cox_time_fup: follow-up time;
data sla_data;
set analysis.final;
exp_cat=exp_cat_2;* define exposure as HDP 1 or 0;
run;

ods output Estimates=rrisk0;
ods select Estimates;
proc phreg data=sla_data fast nosummary;*crude HR for main
association;
class exp_cat(ref="0") /param=ref;
model cox_time_fup*outcome(0)=exp_cat/ties=efron rl;
estimate "exp_cat cHR1" exp_cat 1/exp cl;
run;

*adjusted model;
ods output Estimates=rrisk1;
ods select Estimates;
proc phreg data=sla_data fast nosummary;*adjusted HR for main
association;
class exp_cat(ref="0") singleton sex parity mageg msmoke
edu_cat mcohab mresid
cvd_total_m cvd_total_f dm_total_m morigin income_cat mbmi_cat
birth_yr_cat/param=ref;
model cox_time_fup*outcome(0)=exp_cat singleton sex parity
mageg msmoke edu_cat mcohab mresid
cvd_total_m cvd_total_f dm_total_m morigin income_cat mbmi_cat
```



```

birth_yr_cat/ties=efron rl;
estimate "exp_cat CHR1" exp_cat 1/exp cl;
run;

*specific types of exposure;
data sla_data;
set analysis.final;
exp_cat=exp_cat_8;* define exposure for subtypes;
run;

ods output Estimates=rrisk0;
ods select Estimates;
proc phreg data=sla_data fast nosummary;*crude HR for main
association;
class exp_cat(ref="0") /param=ref;
model cox_time_fup*outcome(0)=exp_cat/ties=efron rl;
estimate "exp_cat CHR1" exp_cat 1/exp cl;
estimate "exp_cat CHR2" exp_cat 0 1/exp cl;
estimate "exp_cat CHR3" exp_cat 0 0 1/exp cl;
estimate "exp_cat CHR4" exp_cat 0 0 0 1/exp cl;
estimate "exp_cat CHR5" exp_cat 0 0 0 0 1/exp cl;
estimate "exp_cat CHR6" exp_cat 0 0 0 0 0 1/exp cl;
estimate "exp_cat CHR7" exp_cat 0 0 0 0 0 0 1/exp cl;
run;

*adjusted model;
ods output Estimates=rrisk1;
ods select Estimates;
proc phreg data=sla_data fast nosummary;*adjusted HR for main
association;
class exp_cat(ref="0") singleton sex parity mageg msmove
edu_cat mcohab mresid
cvd_total_m cvd_total_f dm_total_m morigin income_cat mbmi_cat
birth_yr_cat/param=ref;
model cox_time_fup*outcome(0)=exp_cat singleton sex parity
mageg msmove edu_cat mcohab mresid
cvd_total_m cvd_total_f dm_total_m morigin income_cat mbmi_cat
birth_yr_cat/ties=efron rl;
estimate "exp_cat CHR1" exp_cat 1/exp cl;
estimate "exp_cat CHR2" exp_cat 0 1/exp cl;
estimate "exp_cat CHR3" exp_cat 0 0 1/exp cl;
estimate "exp_cat CHR4" exp_cat 0 0 0 1/exp cl;
estimate "exp_cat CHR5" exp_cat 0 0 0 0 1/exp cl;
estimate "exp_cat CHR6" exp_cat 0 0 0 0 0 1/exp cl;

```

```

estimate "exp_cat cHR7" exp_cat 0 0 0 0 0 0 1/exp cl;
run;

/*Codes for cause-specific mortality*/

%macro specific (outcome_num,name);
data sla_data;
set analysis.final;
exp_cat=exp_cat_2;
outcome=outcome&outcome_num;
run;

ods output Estimates=rrisk0;
ods select Estimates;
proc phreg data=sla_data fast nosummary;*crude HR for main
association;
class exp_cat(ref="0") /param=ref;
model cox_time_fup*outcome(0)=exp_cat/ties=efron rl;
estimate "exp_cat cHR1" exp_cat 1/exp cl;
run;

*adjusted model;
ods output Estimates=rrisk1;
ods select Estimates;
proc phreg data=sla_data fast nosummary;*adjusted HR for main
association;
class exp_cat(ref="0") singleton sex parity mageg msmoke
edu_cat mcohab mresid
cvd_total_m cvd_total_f dm_total_m morigin income_cat mbmi_cat
birth_yr_cat/param=ref;
model cox_time_fup*outcome(0)=exp_cat singleton sex parity
mageg msmoke edu_cat mcohab mresid
cvd_total_m cvd_total_f dm_total_m morigin income_cat mbmi_cat
birth_yr_cat/ties=efron rl;
estimate "exp_cat cHR1" exp_cat 1/exp cl;
run;

%mend;

%specific(1,cvd);
%specific(2,cancer);
%specific(3,infectious);
%specific(4,metabolic);

```

```
%specific(5,mental);  
%specific(6,nervous);  
%specific(7,respiratory);  
%specific(8,digestive);  
%specific(9,musculoskeletal);  
%specific(10,genitourinary);  
%specific(11,perinatal);  
%specific(12,malformation);  
%specific(13,external);  
%specific(14,other);
```

Table S1. Exposure classification of hypertensive disorder of pregnancy from the International Classification of Diseases, the 8th and 10th versions (ICD-8 and ICD-10) ^a

	ICD-8	ICD-10
Pre-eclampsia and eclampsia		
Moderate pre-eclampsia	63703	O14.0
Severe pre-eclampsia	63704	O14.1
HELLP syndrome		O14.2
Unspecified pre-eclampsia	63709	O14.9
Eclampsia	63719	O15
Gestational hypertension		
Gestational (pregnancy-induced) hypertension	63700	O13
Unspecified maternal hypertension	76029	O16
Pre-gestational hypertension		
Essential hypertension	40009	I10
Hypertensive heart disease	40019 40029	I11
Hypertensive renal disease	40039	I12
Hypertensive heart and renal disease	40099	I13
Secondary hypertension	40199	I15
Pre-existing hypertension complicating pregnancy		O10
Pre-eclampsia superimposed on chronic hypertension		O11

^a Information on maternal hypertensive disorder of pregnancy came from the Danish National Patient Register.

Table S2. Outcome classification of cause of death from the International Classification of Diseases, the 8th and 10th versions (ICD-8 and ICD-10)^a

Cause of Deaths	ICD-8	ICD-10
All cause of death	000-E999	A00-Y89
Specific causes of death		
Infectious and parasitic diseases	000-136	A00-B99
Malignant neoplasms	140-209	C00-C97
Endocrine, nutritional and metabolic diseases	240-279	E00-E89
Mental and behavioural disorders	290-315	F01-F99
Diseases of the nervous system and the sense organs	320-389	G00-H95
Diseases of the circulatory system	390-444.1, 444.3-458,	I00-I99
Diseases of the respiratory system	460-519	J00-J99
Diseases of the digestive system	520-577, 444.2	K00-K92
Diseases of the musculoskeletal system or connective tissue	710-738	M00-M99
Diseases of the genitourinary system	580-629, 792	N00-N99
Certain conditions originating in the perinatal period	760-779	P00-P96
Congenital malformations and chromosomal abnormalities	740-759	Q00-Q99
External causes of morbidity and mortality	E800-E999	V01-Y89

^a Information on deaths came from the Danish Cause of Death Register.

Table S3. Associations between maternal HDP and all-cause mortality in offspring of sibling pairs

	Exposure	No. of deaths	Follow-up time (person years)	Rate (1/10⁵ person years)	cHR (95%CI)	aHR^b (95%CI)
Half-sibling^a	No maternal HDP	16174	37453153.37	43.18	1.0 (reference)	1.0 (reference)
	Maternal HDP	842	1446608.97	58.21	1.27 (1.13 to 1.43)	1.15 (1.01 to 1.30)
Full-sibling^a	No maternal HDP	13606	33472377.85	40.65	1.0 (reference)	1.0 (reference)
	Maternal HDP	699	1290702.57	54.16	1.30 (1.14 to 1.48)	1.19 (1.04 to 1.36)

Abbreviations: HDP, hypertensive disorder of pregnancy; cHR, crude hazard ratio; aHR, adjusted hazard ratio.

^a Half-sibling: sibling pairs of offspring born to the same mother; full-sibling: sibling pairs of offspring born to the same father and mother.

^b Offspring's age as time scale, adjusted for calendar year, sex, singleton, parity, birth year of the child, maternal age, maternal smoking, maternal cohabitation, maternal country of origin, maternal residence, maternal education, maternal income at birth, maternal pre-pregnancy BMI, maternal history of diabetes and parental CVD before childbirth.

Table S4. Association between paternal hypertension before pregnancy and all-cause mortality in offspring

Exposure	No. of deaths	Follow-up time (person years)	Rate (1/10⁵ person years)	cHR (95%CI)	aHR^a (95%CI)
No paternal hypertension	20070	47221473.65	42.50	1.0 (reference)	1.0 (reference)
Paternal hypertension	70	153041.87	45.74	0.97 (0.77 to 1.23)	1.20 (0.94 to 1.54)

Abbreviations: cHR, crude hazard ratio; aHR, adjusted hazard ratio.

^a Offspring's age as time scale, adjusted for calendar year, sex, singleton, parity, birth year of the child, maternal age, maternal smoking, maternal cohabitation, maternal country of origin, maternal residence, maternal education, maternal income at birth, maternal pre-pregnancy BMI, maternal history of diabetes and parental CVD before childbirth.

Table S5. Associations between maternal HDP and all-cause mortality in offspring according to SGA^a

SGA	Exposure	No. of deaths	Follow-up time (person years)	Rate (1/10⁵ person years)	cHR (95%CI)	aHR^b (95%CI)
Yes	No maternal HDP	2972	4095316.55	72.57	1.0 (reference)	1.0 (reference)
	Maternal HDP	294	272846.85	107.75	1.42 (1.26 to 1.60)	1.53 (1.36 to 1.73)
No	No maternal HDP	16147	41439062.17	38.97	1.0 (reference)	1.0 (reference)
	Maternal HDP	727	1567289.95	46.39	1.16 (1.08 to 1.25)	1.12 (1.04 to 1.21)

Abbreviations: HDP, hypertensive disorder of pregnancy; SGA, small for gestational age; cHR, crude hazard ratio; aHR, adjusted hazard ratio.

^a SGA defined as infants whose birthweight below the 10th percentile for infants of the same gestational age, sex, and birth year

^b Offspring's age as time scale, adjusted for calendar year, sex, singleton, parity, birth year of the child, maternal age, maternal smoking, maternal cohabitation, maternal country of origin, maternal residence, maternal education, maternal income at birth, maternal pre-pregnancy BMI, maternal history of diabetes and parental CVD before childbirth.

Table S6. Subanalyses of the association between maternal HDP and all-cause mortality in offspring

	Exposure	No. of deaths	Follow-up time (person years)	Rate (1/10⁵ person years)	cHR (95%CI)	aHR^a (95%CI)
Additional adjustment for paternal hypertension	No maternal HDP	19119	45534378.72	41.99	1.0 (Reference)	1.0 (Reference)
	Maternal HDP	1021	1840136.80	55.49	1.28 (1.21 to 1.37)	1.26 (1.18 to 1.34)
	Pre-eclampsia or Eclampsia	798	1337690.23	59.66	1.42 (1.32 to 1.52)	1.30 (1.21 to 1.40)
	Pre-eclampsia	781	1324978.47	58.94	1.40 (1.30 to 1.50)	1.29 (1.20 to 1.38)
	Moderate	423	1013731.05	41.73	1.00 (0.91 to 1.10)	0.90 (0.82 to 0.99)
	Severe	279	208803.94	133.62	3.10 (2.75 to 3.49)	3.00 (2.66 to 3.37)
	HELLP syndrome	30	18671.24	160.67	3.11 (2.18 to 4.45)	4.78 (3.34 to 6.84)
	Unspecified	49	83772.24	58.49	1.44 (1.09 to 1.91)	1.31 (0.99 to 1.73)
	Eclampsia	17	12711.76	133.73	3.17 (1.97 to 5.10)	2.89 (1.80 to 4.65)
	Hypertension	223	502446.57	44.38	0.96 (0.84 to 1.10)	1.12 (0.98 to 1.27)
	Pregestational hypertension	81	181836.48	44.55	0.90 (0.72 to 1.12)	1.26 (1.01 to 1.57)
	Gestational hypertension	142	320610.09	44.29	1.00 (0.85 to 1.18)	1.05 (0.89 to 1.24)
Offspring born after 1991	No maternal HDP	6897	22161734.73	31.12	1.0 (Reference)	1.0 (Reference)
	Maternal HDP	440	918811.23	47.89	1.46 (1.33 to 1.61)	1.40 (1.27 to 1.55)
	Pre-eclampsia or Eclampsia	337	619593.37	54.39	1.72 (1.54 to 1.92)	1.54 (1.38 to 1.72)
	Pre-eclampsia	329	612917.05	53.68	1.70 (1.52 to 1.90)	1.52 (1.36 to 1.70)
	Moderate	137	440245.69	31.12	0.99 (0.84 to 1.17)	0.90 (0.76 to 1.06)
	Severe	138	117289.26	117.66	3.65 (3.09 to 4.32)	3.18 (2.68 to 3.77)
	HELLP syndrome	30	18671.24	160.67	4.49 (3.13 to 6.42)	4.61 (3.22 to 6.61)
	Unspecified	24	36710.85	65.38	2.21 (1.48 to 3.30)	1.86 (1.25 to 2.78)
	Eclampsia	8	6676.32	119.83	3.85 (1.92 to 7.70)	3.45 (1.72 to 6.89)

	Hypertension	103	299217.86	34.42	0.97 (0.80 to 1.18)	1.08 (0.89 to 1.32)
	Pregestational hypertension	58	145461.64	39.87	1.10 (0.85 to 1.42)	1.28 (0.98 to 1.65)
	Gestational hypertension	45	153756.22	29.27	0.85 (0.63 to 1.14)	0.91 (0.68 to 1.22)
Offspring born after 1994	No maternal HDP	5218	17255033.13	30.24	1.0 (Reference)	1.0 (Reference)
	Maternal HDP	345	736186.88	46.86	1.46 (1.31 to 1.63)	1.39 (1.24 to 1.55)
	Pre-eclampsia or Eclampsia	262	476813.12	54.95	1.78 (1.57 to 2.02)	1.56 (1.38 to 1.77)
	Pre-eclampsia	257	471680.12	54.49	1.76 (1.56 to 2.00)	1.55 (1.36 to 1.76)
	Moderate	99	336148.10	29.45	0.96 (0.79 to 1.17)	0.86 (0.70 to 1.05)
	Severe	116	92899.28	124.87	3.98 (3.31 to 4.78)	3.28 (2.72 to 3.95)
	HELLP syndrome	27	18352.42	147.12	4.42 (3.03 to 6.45)	4.14 (2.84 to 6.06)
	Unspecified	15	24280.32	61.78	2.11 (1.27 to 3.51)	1.91 (1.15 to 3.17)
	Eclampsia ^b	-	5133.00	97.41	3.21 (1.34 to 7.72)	2.74 (1.14 to 6.58)
	Hypertension	83	259373.76	32.00	0.94 (0.76 to 1.17)	1.02 (0.82 to 1.27)
	Pregestational hypertension	48	134081.02	35.80	1.04 (0.78 to 1.38)	1.15 (0.86 to 1.53)
	Gestational hypertension	35	125292.74	27.93	0.83 (0.59 to 1.15)	0.89 (0.64 to 1.24)
Offspring born after 2004	No maternal HDP	1904	5628441.07	33.83	1.0 (Reference)	1.0 (Reference)
	Maternal HDP	120	287392.56	41.75	1.20 (1.00 to 1.44)	1.05 (0.87 to 1.27)
	Pre-eclampsia or Eclampsia	95	163632.13	58.06	1.68 (1.37 to 2.06)	1.36 (1.10 to 1.67)
	Pre-eclampsia	94	161962.64	58.04	1.68 (1.36 to 2.06)	1.36 (1.10 to 1.67)
	Moderate	31	112054.80	27.67	0.80 (0.56 to 1.14)	0.66 (0.46 to 0.95)
	Severe	42	33829.56	124.15	3.58 (2.64 to 4.86)	2.67 (1.96 to 3.64)
	HELLP syndrome	16	8897.57	179.82	5.34 (3.26 to 8.73)	4.28 (2.61 to 7.02)
	Unspecified ^b	-	7180.70	69.63	2.12 (0.88 to 5.11)	1.73 (0.72 to 4.16)
	Eclampsia ^b	-	1669.49	59.90	1.75 (0.25 to 12.44)	1.50 (0.21 to 10.68)
	Hypertension	25	123760.44	20.20	0.57 (0.39 to 0.85)	0.57 (0.38 to 0.84)
	Pregestational hypertension	17	68548.02	24.80	0.72 (0.45 to 1.16)	0.70 (0.44 to 1.14)

	Gestational hypertension	8	55212.42	14.49	0.40 (0.20 to 0.80)	0.40 (0.20 to 0.80)
Complete case analysis	No maternal HDP	1741	5945848.11	29.28	1.0 (Reference)	1.0 (Reference)
	Maternal HDP	105	297367.76	35.31	1.16 (0.95 to 1.41)	1.01 (0.83 to 1.23)
	Pre-eclampsia or Eclampsia	80	170220.86	47.00	1.56 (1.25 to 1.95)	1.26 (1.00 to 1.58)
	Pre-eclampsia	77	168625.80	45.66	1.52 (1.21 to 1.91)	1.22 (0.97 to 1.54)
	Moderate	29	117535.33	24.67	0.82 (0.57 to 1.18)	0.67 (0.46 to 0.97)
	Severe	33	33978.11	97.12	3.21 (2.27 to 4.52)	2.44 (1.72 to 3.46)
	HELLP syndrome	12	9098.51	131.89	4.45 (2.52 to 7.86)	3.69 (2.09 to 6.52)
	Unspecified ^b	-	8013.84	37.44	1.33 (0.43 to 4.12)	1.06 (0.34 to 3.29)
	Eclampsia ^b	-	1595.06	188.08	6.21 (2.00 to 19.27)	5.44 (1.75 to 16.88)
	Hypertension	25	127146.90	19.66	0.64 (0.43 to 0.95)	0.62 (0.42 to 0.92)
	Pre-gestational hypertension	17	69808.37	24.35	0.80 (0.50 to 1.29)	0.79 (0.49 to 1.27)
	Gestational hypertension	8	57338.52	13.95	0.45 (0.22 to 0.89)	0.43 (0.21 to 0.86)
	Singleton births	No maternal HDP	17946	44270955.38	40.54	1.0 (Reference)
Maternal HDP		927	1719042.47	53.93	1.30 (1.21 to 1.38)	1.32 (1.23 to 1.41)
Pre-eclampsia or Eclampsia		714	1236530.82	57.74	1.43 (1.32 to 1.54)	1.37 (1.27 to 1.48)
Pre-eclampsia		699	1224683.31	57.08	1.41 (1.30 to 1.52)	1.35 (1.25 to 1.46)
Moderate		377	942828.29	39.99	0.99 (0.89 to 1.10)	0.93 (0.84 to 1.03)
Severe		246	186405.07	131.97	3.20 (2.82 to 3.63)	3.35 (2.96 to 3.81)
HELLP syndrome		28	16092.63	173.99	3.59 (2.48 to 5.20)	6.36 (4.39 to 9.23)
Unspecified ^d		48	79357.33	60.49	1.55 (1.16 to 2.05)	1.44 (1.09 to 1.91)
Eclampsia		15	11847.51	126.61	3.10 (1.87 to 5.15)	2.94 (1.77 to 4.87)
Hypertension		213	482511.65	44.14	1.00 (0.87 to 1.14)	1.17 (1.02 to 1.34)
Pre-gestational hypertension		77	174686.64	44.08	0.94 (0.75 to 1.17)	1.33 (1.06 to 1.67)
Gestational hypertension		136	307825.01	44.18	1.03 (0.87 to 1.22)	1.10 (0.93 to 1.31)
Excluding individuals exposed to		No maternal HDP	19119	45534378.72	41.99	1.0 (Reference)

pregestational hypertension						
	Maternal HDP	940	1658300.32	56.68	1.33 (1.25 to 1.42)	1.26 (1.18 to 1.34)
	Pre-eclampsia or Eclampsia	798	1337690.23	59.66	1.42 (1.32 to 1.52)	1.30 (1.21 to 1.40)
	Pre-eclampsia	781	1324978.47	58.94	1.40 (1.30 to 1.50)	1.29 (1.20 to 1.38)
	Moderate	423	1013731.05	41.73	1.00 (0.91 to 1.10)	0.90 (0.82 to 0.99)
	Severe	279	208803.94	133.62	3.10 (2.75 to 3.49)	2.99 (2.66 to 3.37)
	HELLP syndrome	30	18671.24	160.67	3.11 (2.18 to 4.45)	4.79 (3.34 to 6.86)
	Unspecified	49	83772.24	58.49	1.44 (1.09 to 1.91)	1.30 (0.98 to 1.72)
	Eclampsia	17	12711.76	133.73	3.17 (1.97 to 5.10)	2.88 (1.79 to 4.63)
	Gestational hypertension	142	320610.09	44.29	1.00 (0.85 to 1.18)	1.06 (0.90 to 1.25)
Additional adjustment for Charlson Comorbidity Index scores	No maternal HDP	19119	45534378.72	41.99	1.0 (Reference)	1.0 (Reference)
	Maternal HDP	1021	1840136.80	55.49	1.28 (1.21 to 1.37)	1.25 (1.18 to 1.34)
	Pre-eclampsia or Eclampsia	798	1337690.23	59.66	1.42 (1.32 to 1.52)	1.30 (1.21 to 1.39)
	Pre-eclampsia	781	1324978.47	58.94	1.40 (1.30 to 1.50)	1.28 (1.19 to 1.38)
	Moderate	423	1013731.05	41.73	1.00 (0.91 to 1.10)	0.90 (0.82 to 0.99)
	Severe	279	208803.94	133.62	3.10 (2.75 to 3.49)	2.98 (2.64 to 3.36)
	HELLP syndrome	30	18671.24	160.67	3.11 (2.18 to 4.45)	4.78 (3.34 to 6.85)
	Unspecified	49	83772.24	58.49	1.44 (1.09 to 1.91)	1.30 (0.98 to 1.72)
	Eclampsia	17	12711.76	133.73	3.17 (1.97 to 5.10)	2.87 (1.79 to 4.63)
	Hypertension	223	502446.57	44.38	0.96 (0.84 to 1.10)	1.11 (0.98 to 1.27)
	Pregestational hypertension	81	181836.48	44.55	0.90 (0.72 to 1.12)	1.25 (1.00 to 1.56)
	Gestational hypertension	142	320610.09	44.29	1.00 (0.85 to 1.18)	1.05 (0.89 to 1.24)
All livebirths in 1977-2018	No maternal HDP	21943	50108433.17	43.79	1.0 (Reference)	1.0 (Reference)

	Maternal HDP	1117	1996266.80	55.95	1.24 (1.17 to 1.32)	1.22 (1.14 to 1.29)
	Pre-eclampsia or Eclampsia	877	1461390.61	60.01	1.37 (1.28 to 1.46)	1.26 (1.18 to 1.35)
	Pre-eclampsia	857	1446772.00	59.24	1.35 (1.26 to 1.44)	1.25 (1.16 to 1.33)
	Moderate	479	1119415.24	42.79	0.98 (0.89 to 1.07)	0.89 (0.81 to 0.98)
	Severe	290	217826.07	133.13	2.97 (2.64 to 3.33)	2.91 (2.59 to 3.27)
	HELLP syndrome	30	18730.61	160.17	2.99 (2.09 to 4.27)	4.73 (3.30 to 6.77)
	Unspecified	58	90800.08	63.88	1.51 (1.17 to 1.95)	1.35 (1.04 to 1.74)
	Eclampsia	20	14618.60	136.81	3.11 (2.00 to 4.82)	2.69 (1.74 to 4.18)
	Hypertension	240	534876.19	44.87	0.94 (0.82 to 1.06)	1.07 (0.94 to 1.22)
	Pregestational hypertension	83	185439.29	44.76	0.87 (0.70 to 1.08)	1.20 (0.96 to 1.49)
	Gestational hypertension	157	349436.90	44.93	0.98 (0.83 to 1.14)	1.03 (0.88 to 1.20)

Abbreviations: HDP, hypertensive disorder of pregnancy; cHR, crude hazard ratio; aHR, adjusted hazard ratio.

^a Offspring's age as time scale, adjusted for calendar year, sex, singleton, parity, birth year of the child, maternal age, maternal smoking, maternal cohabitation, maternal country of origin, maternal residence, maternal education, maternal income at birth, maternal pre-pregnancy BMI, maternal history of diabetes and parental CVD before childbirth.

^b Less than 6 cases are not allowed to report.

Table S7. Association between maternal HDP and all-cause mortality in offspring using restricted cubic splines for continuous covariates

Exposure	No. of deaths	Follow-up time (person years)	Rate (1/10⁵ person years)	cHR (95%CI)	aHR^a (95%CI)
No maternal HDP	19119	45534378.72	41.99	1.0 (Reference)	1.0 (reference)
Maternal HDP	1021	1840136.80	55.49	1.28 (1.21 to 1.37)	1.29 (1.20 to 1.37)

Abbreviations: HDP, hypertensive disorder of pregnancy; cHR, crude hazard ratio; aHR, adjusted hazard ratio.

^a Offspring's age as time scale, adjusted for calendar year, country, sex, singleton, parity, birth year of the child, maternal age, maternal smoking, maternal cohabitation, maternal country of origin, maternal residence, maternal education, maternal income at birth, maternal pre-pregnancy BMI, maternal history of diabetes and CVD before childbirth, parental history of CVD before childbirth.

Table S8. The risk of all-cause mortality in offspring according to the timing and severity of maternal pre-eclampsia based on different cutoff points of 35 or 36 weeks for timing of pre-eclampsia^a

	No. of deaths	Follow-up time (person years)	Rate (1/10 ⁵ person years)	cHR(95%CI)	aHR ^b (95%CI)
Timing of pre-eclampsia defined by 35 weeks of gestation					
No maternal HDP	19119	45534378.72	41.99	1.0 (Reference)	1.0 (Reference)
By timing of pre-eclampsia					
Late-onset	300	848998.87	35.34	0.86 (0.77 to 0.97)	0.77 (0.68 to 0.86)
Early-onset	432	392207.36	110.15	2.45 (2.23 to 2.69)	2.45 (2.23 to 2.70)
By severity of pre-eclampsia					
Moderate	423	1013731.05	41.73	1.00 (0.91 to 1.10)	0.90 (0.82 to 0.99)
Severe and HELLP	309	227475.18	135.84	3.10 (2.77 to 3.47)	3.10 (2.77 to 3.47)
Interaction for timing and severity of pre-eclampsia					
Late-onset * Moderate	253	739662.19	34.20	0.84 (0.74 to 0.95)	0.74 (0.65 to 0.84)
Late-onset * Severe/HELLP	47	109336.68	42.99	0.99 (0.74 to 1.32)	0.96 (0.72 to 1.27)
Early-onset * Moderate	170	274068.86	62.03	1.37 (1.18 to 1.59)	1.35 (1.16 to 1.57)
Early-onset * Severe/HELLP	262	118138.50	221.77	5.02 (4.45 to 5.67)	5.22 (4.62 to 5.91)
Timing of pre-eclampsia defined by 36 weeks of gestation					
No maternal HDP	19119	45534378.72	41.99	1.0 (Reference)	1.0 (Reference)
By timing of pre-eclampsia					
Late-onset	254	751540.72	33.80	0.83 (0.73 to 0.93)	0.74 (0.65 to 0.84)
Early-onset	478	489665.51	97.62	2.21 (2.02 to 2.42)	2.13 (1.94 to 2.34)
By severity of pre-eclampsia					
Moderate	423	1013731.05	41.73	1.00 (0.91 to 1.10)	0.90 (0.82 to 0.99)
Severe and HELLP	309	227475.18	135.84	3.10 (2.77 to 3.47)	3.10 (2.77 to 3.47)
Interaction for timing and severity of pre-eclampsia					
Late-onset * Moderate	224	663368.13	33.77	0.83 (0.73 to 0.95)	0.73 (0.64 to 0.84)
Late-onset * Severe/HELLP	30	88172.59	34.02	0.78 (0.55 to 1.12)	0.77 (0.54 to 1.10)
Early-onset * Moderate	199	350362.92	56.80	1.28 (1.12 to 1.48)	1.22 (1.06 to 1.40)

Early-onset * Severe/HELLP	279	139302.59	200.28	4.55 (4.05 to 5.13)	4.61 (4.09 to 5.20)
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Abbreviations: HDP, hypertensive disorder of pregnancy; cHR, crude hazard ratio; aHR, adjusted hazard ratio.

^a Includes moderate pre-eclampsia, severe pre-eclampsia, and HELLP syndrome.

^b Offspring's age as time scale, adjusted for calendar year, country, sex, singleton, parity, birth year of the child, maternal age, maternal smoking, maternal cohabitation, maternal country of origin, maternal residence, maternal education, maternal income at birth, maternal pre-pregnancy BMI, maternal history of diabetes and CVD before childbirth, parental history of CVD before childbirth.

Table S9. Associations between maternal HDP and all-cause mortality in offspring according to different follow up years

Follow up years	Exposure	No. of Deaths	Follow-up time (person years)	Rate (1/10⁵ person years)	cHR (95%CI)	aHR^a (95%CI)
0~5	No maternal HDP	10650	10853890.38	98.12	1.0 (reference)	1.0 (reference)
	Maternal HDP	656	466792.64	140.53	1.42 (1.31 to 1.54)	1.39 (1.29 to 1.51)
0~10	No maternal HDP	11721	20286705.48	57.78	1.0 (reference)	1.0 (reference)
	Maternal HDP	687	854286.15	80.42	1.36 (1.26 to 1.46)	1.34 (1.24 to 1.45)
0~15	No maternal HDP	12627	28244542.46	44.71	1.0 (reference)	1.0 (reference)
	Maternal HDP	723	1166762.02	61.97	1.33 (1.24 to 1.44)	1.32 (1.22 to 1.42)
0~20	No maternal HDP	14504	34694942.03	41.80	1.0 (reference)	1.0 (reference)
	Maternal HDP	809	1415746.72	57.14	1.32 (1.23 to 1.41)	1.30 (1.21 to 1.39)
0~25	No maternal HDP	16409	39599421.39	41.44	1.0 (reference)	1.0 (reference)
	Maternal HDP	907	1605513.46	56.49	1.32 (1.23 to 1.41)	1.30 (1.21 to 1.39)
0~30	No maternal HDP	17708	42904382.08	41.27	1.0 (reference)	1.0 (reference)
	Maternal HDP	962	1735817.59	55.42	1.30 (1.22 to 1.39)	1.28 (1.20 to 1.37)
0~35	No maternal HDP	18622	44799855.16	41.57	1.0 (reference)	1.0 (reference)
	Maternal HDP	997	1812016.11	55.02	1.28 (1.20 to 1.37)	1.26 (1.18 to 1.34)
0~41	No maternal HDP	19119	45534378.72	41.99	1.0 (reference)	1.0 (reference)
	Maternal HDP	1021	1840136.80	55.49	1.28 (1.21 to 1.37)	1.26 (1.18 to 1.34)

Abbreviations: HDP, hypertensive disorder of pregnancy; cHR, crude hazard ratio; aHR, adjusted hazard ratio.

^a Offspring's age as time scale, adjusted for calendar year, country, sex, singleton, parity, birth year of the child, maternal age, maternal smoking, maternal cohabitation, maternal country of origin, maternal residence, maternal education, maternal income at birth, maternal pre-pregnancy BMI, maternal history of diabetes and CVD before childbirth, parental history of CVD before childbirth.

Table S10. Associations between maternal HDP and all-cause mortality in offspring in different age groups

Age of offspring	Exposure	No. of Deaths	Follow-up time (person years)	Rate (1/10 ⁵ person years)	cHR (95%CI)	aHR ^a (95%CI)
0~18	No maternal HDP	13561	32298425.78	41.99	1.0 (reference)	1.0 (reference)
	Maternal HDP	762	1323402.82	57.58	1.32 (1.22 to 1.42)	1.30 (1.21 to 1.40)
≥19	No maternal HDP	5558	13235952.95	41.99	1.0 (reference)	1.0 (reference)
	Maternal HDP	259	516733.98	50.12	1.19 (1.05 to 1.35)	1.14 (1.01 to 1.29)

Abbreviations: HDP, hypertensive disorder of pregnancy; cHR, crude hazard ratio; aHR, adjusted hazard ratio.

^a Offspring's age as time scale, adjusted for calendar year, sex, singleton, parity, birth year of the child, maternal age, maternal smoking, maternal cohabitation, maternal country of origin, maternal residence, maternal education, maternal income at birth, maternal pre-pregnancy BMI, maternal history of diabetes and parental CVD before childbirth.

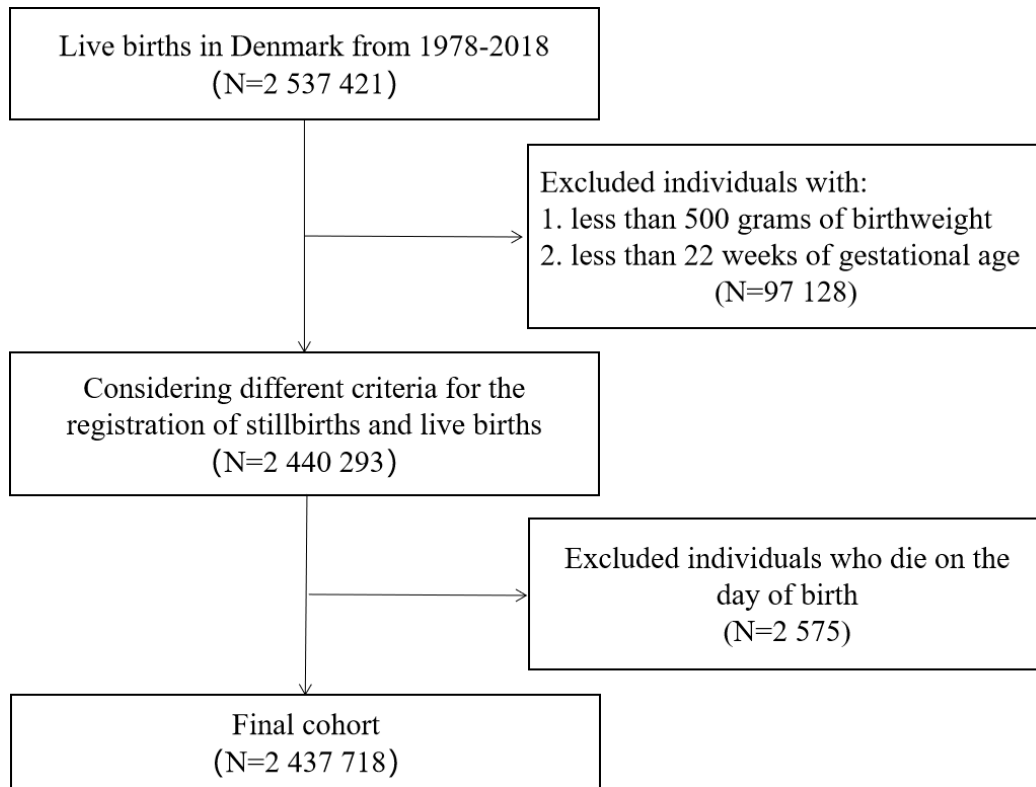


Figure S1. Flow chart of the study population

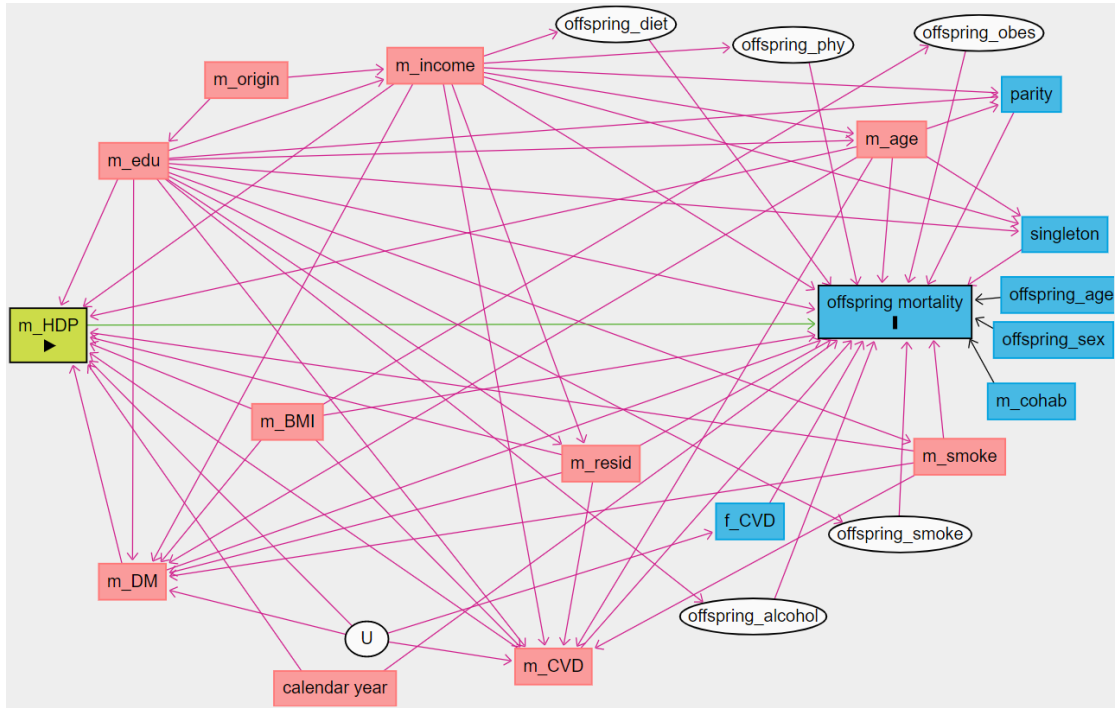


Figure S2. Causal diagram showing selection of covariates for confounding control

^am_HPD: maternal hypertensive disorder of pregnancy, m_age: maternal age, m_smoke: maternal smoking, m_edu: maternal education, m_income: maternal income, m_cohab: maternal cohabitation, m_origin: maternal country of origin, m_resid: maternal residence at birth, m_BMI: maternal BMI, m_CVD: maternal history of CVD before childbirth, m_DM: maternal history of diabetes before childbirth, f_CVD: paternal history of CVD before childbirth, offspring_diet: offspring diet, offspring_phy: offspring physical activity, offspring_obes: offspring obesity, offspring_smoke: offspring smoking status, offspring_alcohol: offspring alcohol use; U: unmeasured variables

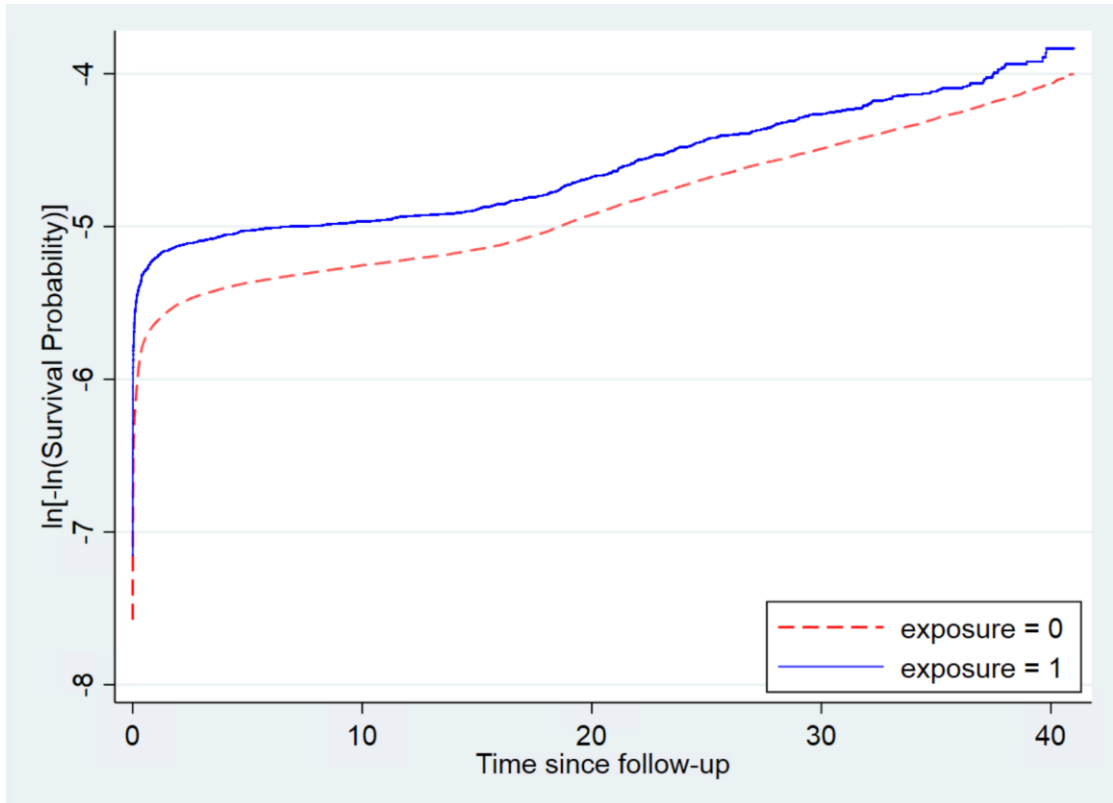
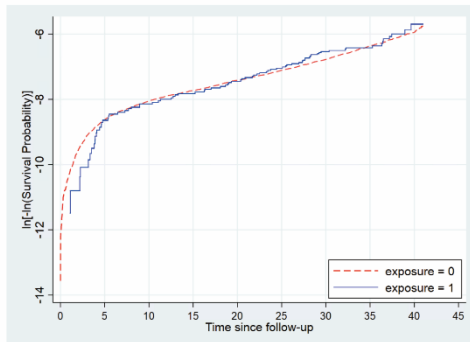
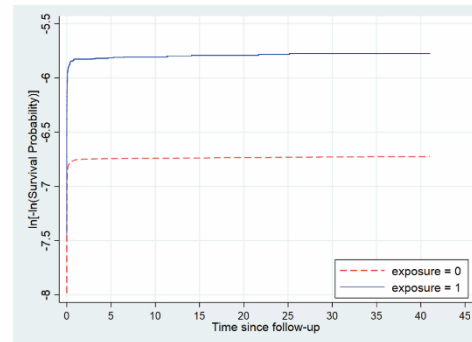


Figure S3. The log-minus-log survival curve for maternal HDP and all-cause mortality in offspring

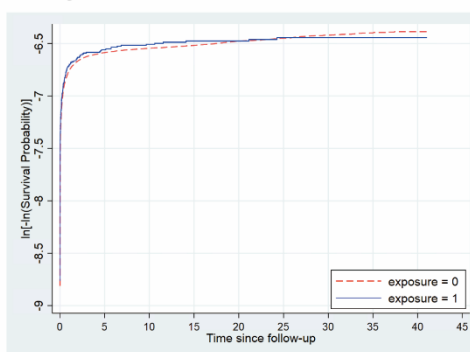
A. Malignant neoplasms



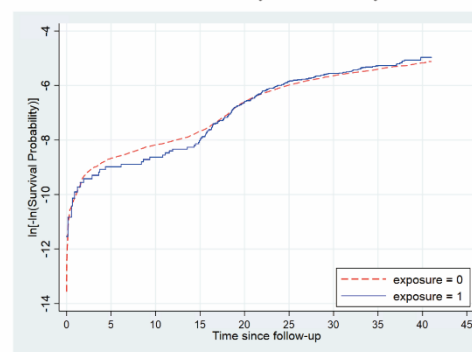
B. Certain conditions originating in the perinatal period



C. Congenital malformations and chromosomal abnormalities



D. External causes of morbidity and mortality



E. Other causes

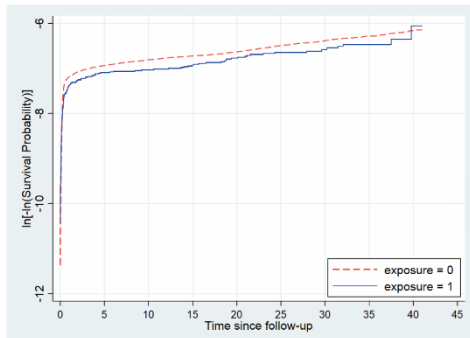


Figure S4. The log-minus-log survival curves for maternal HDP and cause-specific mortality in offspring

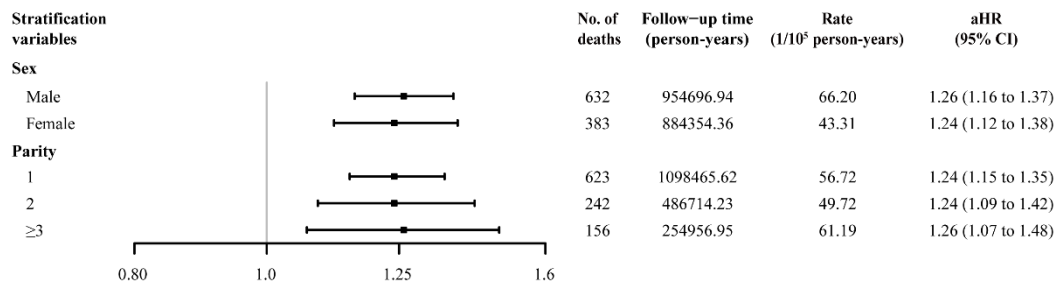


Figure S5. Associations between maternal HDP and all-cause mortality in offspring by sex and parity

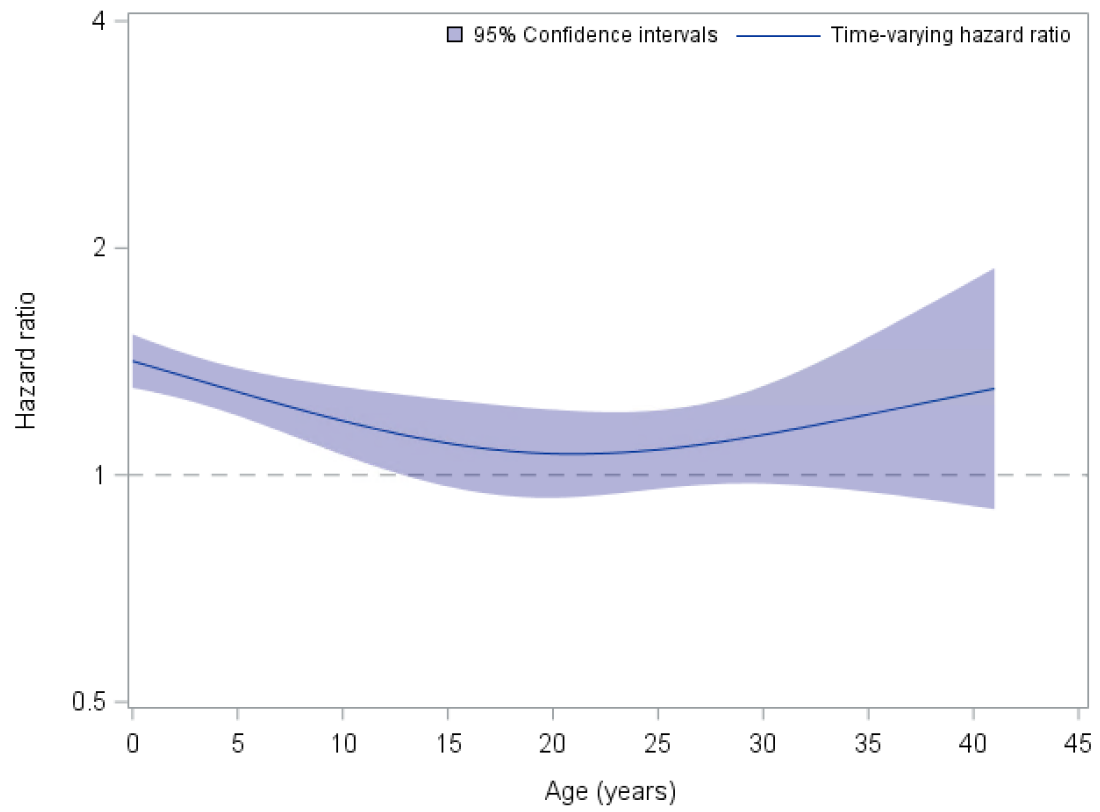


Figure S6. Change of all-cause mortality risk over offspring age among offspring exposed to maternal HDP compared to unexposed offspring

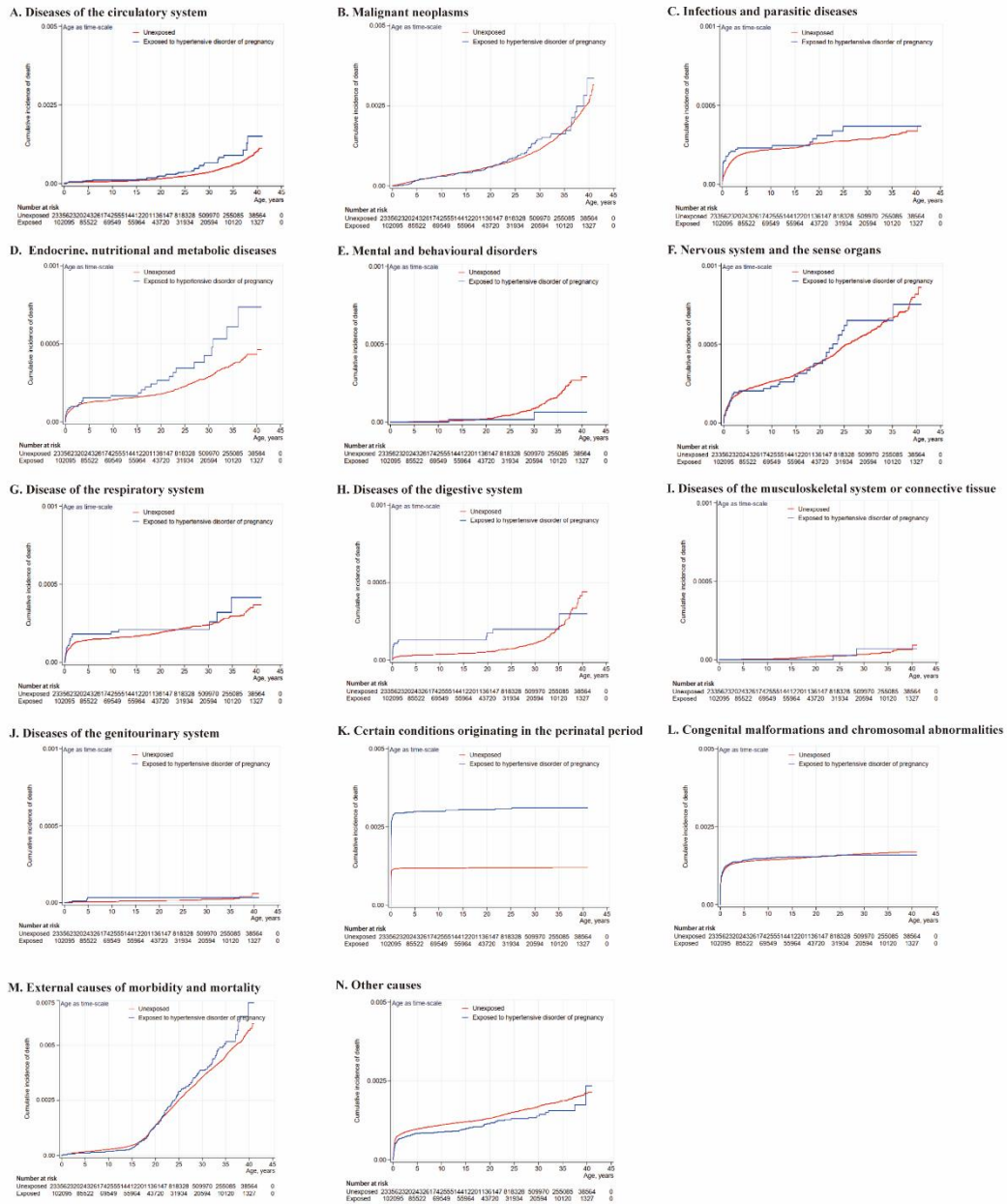
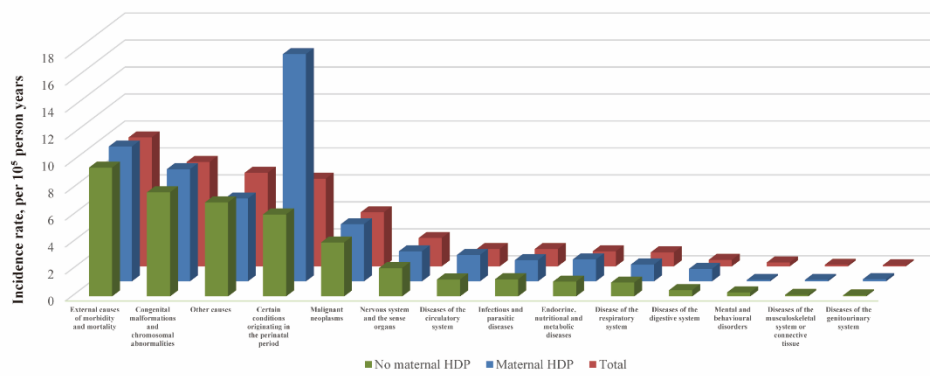


Figure S7. Cumulative incidence of cause-specific mortality among offspring exposed and unexposed to maternal HDP



Exposure	Cause-specific mortality													
	External causes of morbidity and mortality	Congenital malformations and chromosomal abnormalities	Other causes	Certain conditions originating in the perinatal period	Malignant neoplasms	Nervous system and the sense organs	Diseases of the circulatory system	Infectious and parasitic diseases	Endocrine, nutritional and metabolic diseases	Disease of the respiratory system	Diseases of the digestive system	Mental and behavioural disorders	Diseases of the musculoskeletal system or connective tissue	Diseases of the genitourinary system
No maternal HDP	9.54(9.26-9.83)	7.72(7.47-7.98)	6.97(6.73-7.22)	6.08(5.86-6.31)	3.99(3.82-4.18)	2.10(1.97-2.23)	1.26(1.16-1.36)	1.27(1.17-1.38)	1.09(1.00-1.19)	1.03(0.94-1.12)	0.46(0.40-0.53)	0.29(0.25-0.35)	0.11(0.09-0.15)	0.07(0.05-0.10)
Maternal HDP	10.00(8.65-11.55)	8.31(7.10-9.74)	6.14(5.11-7.38)	16.85(15.07-18.83)	4.24(3.40-5.29)	2.23(1.64-3.03)	1.96(1.41-2.71)	1.58(1.10-2.27)	1.63(1.14-2.33)	1.25(0.83-1.88)	0.92(0.57-1.49)	0.11(0.03-0.43)	0.11(0.03-0.43)	0.16(0.05-0.51)
Total	9.56(9.29-9.84)	7.74(7.49-8.00)	6.94(6.71-7.18)	6.50(6.27-6.73)	4.00(3.83-4.19)	2.10(1.98-2.24)	1.28(1.19-1.39)	1.28(1.18-1.39)	1.11(1.02-1.21)	1.03(0.95-1.13)	0.48(0.43-0.55)	0.29(0.24-0.34)	0.11(0.09-0.15)	0.08(0.06-0.11)

Figure S8. Incidence rates (95% CIs) of cause-specific mortality according to maternal HDP