

SUPPLEMENTAL MATERIAL

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Supplemental Results.

Secondary Analyses.

In secondary analyses that examined associations between adverse pregnancy outcomes and ischemic heart disease subtypes, all HRs were higher for acute myocardial infarction but were also significantly elevated for angina. For example, associations between specific adverse pregnancy outcomes and risk of acute myocardial infarction or angina, respectively, at 0-46 years after delivery were: preterm delivery, 1.48 (95% CI, 1.43 to 1.54) vs. 1.32 (1.29 to 1.36); small for gestational age delivery, 1.38; (1.34 to 1.42) vs. 1.15 (1.13 to 1.18); preeclampsia, 1.49 (1.44 to 1.55) vs. 1.41 (1.37 to 1.45); other hypertensive disorders, 1.76 (1.59 to 1.94) vs. 1.56 (1.45 to 1.68); gestational diabetes, 1.73 (1.60 to 1.86) vs. 1.48 (1.39 to 1.57).

When restricting to women with a first delivery in 1990 or later (N=1,226,286), most HRs for ischemic heart disease were similar to those from the main analyses, except that the association between small for gestational age delivery and ischemic heart disease was no longer significant. For example, the adjusted HRs for ischemic heart disease at 0-46 years after delivery associated with specific adverse pregnancy outcomes among women with a first delivery in 1990 or later vs. the main model, respectively, were: preterm delivery, 1.40 (95% CI, 1.31 to 1.48) vs. 1.33 (1.30 to 1.37); small for gestational age delivery, 1.01 (0.95 to 1.07) vs. 1.18; (1.16 to 1.20); preeclampsia, 1.45 (1.35 to 1.56) vs. 1.39 (1.37 to 1.42); other hypertensive disorders, 1.69 (1.53 to 1.87) vs. 1.56 (1.47 to 1.65); gestational diabetes, 1.17 (1.04 to 1.31) vs. 1.45 (1.38 to 1.52).

Sensitivity Analyses.

In sensitivity analyses, all results were similar to the main results and the conclusions were unchanged. For example, when restricting to women with complete data as an alternative to multiple imputation, the adjusted HRs for ischemic heart disease at 0-46 years after delivery associated with specific adverse pregnancy outcomes were: 1.37 (95% CI, 1.32 to 1.42) for preterm delivery, 1.11 (1.08 to 1.15) for small for gestational age delivery, 1.40 (1.34 to 1.46) for preeclampsia, 1.61 (1.50 to 1.74) for other hypertensive disorders, and 1.20 (1.10 to 1.31) for gestational diabetes ($P<0.001$ for each). When coding missing data as a separate category, the corresponding HRs were 1.32 (95% CI, 1.29 to 1.35), 1.17 (1.15 to 1.19), 1.41 (1.38 to 1.44), 1.59 (1.50 to 1.69), and 1.45 (1.38 to 1.52) ($P<0.001$ for each). In addition, the corresponding HRs when repeating the main analyses while restricting to each woman's first delivery were 1.27 (95% CI, 1.22 to 1.32), 1.22 (1.19 to 1.25), 1.41 (1.36 to 1.45), 1.70 (1.50 to 1.92), and 1.80 (1.67 to 1.94) ($P<0.001$ for each).

As an alternative to censoring at death, competing risks models that accounted for death as a competing event yielded nearly identical results, due in part to the small number of deaths (3.0% of participants) in this relatively young cohort of women. For example, the adjusted HRs for ischemic heart disease at 0-46 years after delivery associated with specific adverse pregnancy outcomes in the competing risks model vs. main model, respectively, were: preterm delivery, 1.32 (95% CI, 1.29 to 1.36) vs. 1.33 (1.30 to 1.37); small for gestational age delivery, 1.18 (1.16 to 1.21) vs. 1.18; (1.16 to 1.20); preeclampsia, 1.38 (1.35 to 1.41) vs. 1.39 (1.37 to 1.42); other hypertensive disorders, 1.54 (1.45 to 1.63) vs. 1.56 (1.47 to 1.65); gestational diabetes, 1.44 (1.37 to 1.51) vs. 1.45 (1.38 to 1.52).

Supplemental Table 1. ICD codes for and frequency of adverse pregnancy outcomes, other ischemic heart disease risk factors, and ischemic heart disease.

	<i>ICD-8</i>	<i>ICD-9</i>	<i>ICD-10</i>	n (%)
APOs				
Preterm delivery ^a	--	--	--	194,751 (8.8)
Small for gestational age ^a	--	--	--	314,605 (14.3)
Preeclampsia	637	624.4-624.7	O14-O15	132,543 (6.0)
Other hypertensive disorders	400-404	401-405, 642.0-642.3, 642.9	I10-I15, O10-O11, O13, O16	34,186 (1.6)
Gestational diabetes	--	648.0, 648.8	O24	36,269 (1.7)
Risk factors at baseline				
Hypertension	400-404	401-405	I10-I15	2,966 (0.1)
Diabetes	250	250	E10-E14	10,045 (0.5)
Hyperlipidemia ^b	272	272	E78	1,826 (0.1)
IHD (any)				
Acute myocardial infarction	410-414	410-414	I20-I25	83,881 (3.8)
Acute myocardial infarction	410	410	I21-I23	46,386 (2.1)
Angina pectoris	413	413	I-20	32,462 (1.5)
Other acute IHD	411	411	I-24	671 (<0.1)
Other chronic IHD	412, 414	412, 414	I-25	4,362 (0.2)

^aPreterm delivery (<37 completed weeks) and small for gestational age (infant birth weight <10th percentile for gestational age) were identified based on reported gestational age at birth and birth weight in the Swedish Medical Birth Register.

^bHyperlipidemia was identified based on the diagnoses specified and/or prescription of lipid-modifying medications (Anatomical Therapeutic Chemical Classification System code C10) in the Swedish Pharmacy Register, which includes all prescriptions dispensed nationwide since July 1, 2005.

APO = adverse pregnancy outcome, *ICD* = *International Classification of Diseases*, IHD = ischemic heart disease

Supplemental Table 2. Prevalence of combinations of adverse pregnancy outcomes.

		SGA	PEC	OHD	GD
		n (%)	n (%)	n (%)	n (%)
PTD	Ever	31,822 (1.4)	25,451 (1.2)	5,269 (0.2)	10,368 (0.5)
	Same pregnancy	10,329 (0.5)	13,151 (0.6)	2,064 (0.1)	5,999 (0.3)
SGA	Ever	--	28,602 (1.3)	7,037 (0.3)	5,138 (0.2)
	Same pregnancy	--	12,009 (0.5)	3,150 (0.1)	2,465 (0.1)
PEC	Ever		--	4,651 (0.2)	4,033 (0.2)
	Same pregnancy		--	0 (0.0)	2,291 (0.1)
OHD	Ever			--	1,373 (0.1)
	Same pregnancy			--	912 (<0.1)

GD = gestational diabetes, OHD = other hypertensive disorders of pregnancy, PEC = preeclampsia, PTD = preterm delivery, SGA = small for gestational age delivery

Supplemental Table 3. Associations between number of adverse pregnancy outcomes and subsequent risk of ischemic heart disease.

	IHD cases	Rate ^a	HR (95% CI) ^b	P
0-46 years after first delivery				
0 APOs	50,574	136.0	Reference	
1 APO	22,959	186.6	1.24 (1.22, 1.26)	<0.001
2 APOs	7,001	229.0	1.46 (1.43, 1.50)	<0.001
≥3 APOs	3,347	308.2	1.75 (1.69, 1.82)	<0.001
Per each additional APO			1.21 (1.20, 1.22)	<0.001
<10 years after first delivery				
0 APOs	2,183	14.8	Reference	
1 APO	876	19.9	1.29 (1.19, 1.39)	<0.001
2 APOs	309	34.1	1.80 (1.59, 2.03)	<0.001
≥3 APOs	151	58.4	2.26 (1.89, 2.70)	<0.001
Per each additional APO			1.32 (1.26, 1.38)	<0.001
10-19 years after first delivery				
0 APOs	6,067	58.2	Reference	
1 APO	2,784	79.7	1.33 (1.27, 1.39)	<0.001
2 APOs	975	102.6	1.73 (1.61, 1.85)	<0.001
≥3 APOs	531	145.0	2.07 (1.88, 2.28)	<0.001
Per each additional APO			1.30 (1.27, 1.33)	<0.001
20-29 years after first delivery				
0 APOs	15,719	217.8	Reference	
1 APO	7,345	284.1	1.29 (1.25, 1.32)	<0.001
2 APOs	2,292	321.9	1.53 (1.47, 1.60)	<0.001
≥3 APOs	1,181	420.1	1.95 (1.84, 2.08)	<0.001
Per each additional APO			1.25 (1.23, 1.27)	<0.001
30-46 years after first delivery				
0 APOs	26,605	558.1	Reference	
1 APO	11,954	655.1	1.20 (1.18, 1.23)	<0.001
2 APOs	3,425	701.9	1.37 (1.32, 1.42)	<0.001
≥3 APOs	1,484	823.5	1.62 (1.53, 1.71)	<0.001
Per each additional APO			1.18 (1.16, 1.19)	<0.001

^aIHD incidence rate per 100,000 person-years.

^bAdjusted for maternal age, year of delivery, parity, education, employment, income, country of origin, BMI, smoking, prior history of hypertension, diabetes, or hyperlipidemia, and all other APOs.

APO = adverse pregnancy outcome, CI = confidence interval, HR = hazard ratio, IHD = ischemic heart disease

Supplemental Table 4. Summary of interaction results.

Interaction	Additive	Multiplicative
PTD * SGA	None ($P=0.86$)	None ($P=0.09$)
PTD * PEC	Positive ($P<0.001$)	None ($P=0.18$)
PTD * OHD	Positive ($P=0.003$)	None ($P=0.11$)
PTD * GD	Positive ($P<0.001$)	Positive ($P=0.04$)
SGA * PEC	None ($P=0.99$)	None ($P=0.06$)
SGA * OHD	None ($P=0.25$)	None ($P=0.79$)
SGA * GD	Negative ($P=0.02$)	Negative ($P<0.001$)
PEC * OHD	None ($P=0.24$)	Negative ($P=0.002$)
PEC * GD	Positive ($P=0.003$)	None ($P=0.15$)
OHD * GD	None ($P=0.19$)	Negative ($P=0.009$)

GD = gestational diabetes, OHD = other hypertensive disorders of pregnancy, PEC = preeclampsia, PTD = preterm delivery, SGA = small for gestational age infant

Supplemental Table 5. Interactions between preterm delivery and preeclampsia (1973-2015) in relation to risk of ischemic heart disease through 2018, Sweden.

	Pregnancy duration				HRs (95% CI) for preterm vs. full-term within preeclampsia strata
	Full-term (39-41 wks)		Preterm (<37 wks)		
	No. (rate) ^a	HR (95% CI) ^b	No. (rate) ^a	HR (95% CI) ^b	
Preeclampsia					
No	43,518 (137.0)	Reference	7,734 (197.3)	1.33 (1.30, 1.36);	1.33 (1.30, 1.36);
Yes	5,076 (252.1)	1.37 (1.33, 1.41);	1,690 (297.4)	1.90 (1.81, 1.99);	1.38 (1.31, 1.46);
HRs (95% CI) associated with preeclampsia (yes vs. no) within pregnancy duration strata		1.37 (1.33, 1.41);		1.43 (1.35, 1.51);	
Interaction on additive scale: RERI (95% CI)			0.20 (0.10, 0.30); <i>P</i> <0.001		
Interaction on multiplicative scale: HR ratio (95% CI)			1.04 (0.98, 1.11); <i>P</i> =0.18		

^aNumber of IHD cases (incidence rate per 100,000 person-years).

^bAdjusted for maternal age, year of delivery, parity, education, employment, income, country of origin, BMI, smoking, prior history of hypertension, diabetes, or hyperlipidemia, and other adverse pregnancy outcomes (small for gestational age, other hypertensive disorders, gestational diabetes).

CI = confidence interval, HR = hazard ratio, IHD = ischemic heart disease, RERI = relative excess risk due to interaction

Supplemental Table 6. Interactions between preterm delivery and other hypertensive disorders of pregnancy (1973-2015) in relation to risk of ischemic heart disease through 2018, Sweden.

	Pregnancy duration				HRs (95% CI) for preterm vs. full-term within OHD strata
	Full-term (39-41 wks)		Preterm (<37 wks)		
	No. (rate) ^a	HR (95% CI) ^b	No. (rate) ^a	HR (95% CI) ^b	
Other hypertensive disorders					
No	48,101 (143.7)	Reference	9,100 (206.9)	1.33 (1.30, 1.36);	1.33 (1.30, 1.36);
Yes	493 (161.3)	1.52 (1.39, 1.66);	324 (358.8)	2.29 (2.05, 2.57);	1.51 (1.30, 1.72);
HRs (95% CI) associated with OHD (yes vs. no) within pregnancy duration strata		1.52 (1.39, 1.66);		1.72 (1.62, 1.92);	
Interaction on additive scale: RERI (95% CI)			0.44 (0.15, 0.73);	<i>P</i> =0.003	
Interaction on multiplicative scale: HR ratio (95% CI)			1.13 (0.97, 1.30);	<i>P</i> =0.11	

^aNumber of IHD cases (incidence rate per 100,000 person-years).

^bAdjusted for maternal age, year of delivery, parity, education, employment, income, country of origin, BMI, smoking, prior history of hypertension, diabetes, or hyperlipidemia, and other adverse pregnancy outcomes (small for gestational age, preeclampsia, gestational diabetes).

CI = confidence interval, HR = hazard ratio, IHD = ischemic heart disease, OHD = other hypertensive disorders of pregnancy, RERI = relative excess risk due to interaction

Supplemental Table 7. Interactions between preterm delivery and gestational diabetes (1973-2015) in relation to risk of ischemic heart disease through 2018, Sweden.

	Pregnancy duration				HRs (95% CI) for preterm vs. full-term within GD strata
	Full-term (39-41 wks)		Preterm (<37 wks)		
	No. (rate) ^a	HR (95% CI) ^b	No. (rate) ^a	HR (95% CI) ^b	
Gestational diabetes					
No	48,047 (143.3)	Reference	8,540 (199.3)	1.33 (1.30, 1.36);	1.33 (1.30, 1.36);
Yes	547 (210.4)	1.26 (1.15, 1.37);	884 (434.5)	1.89 (1.75, 2.03);	1.50 (1.34, 1.66);
HRs (95% CI) associated with GD (yes vs. no) within pregnancy duration strata		1.26 (1.15, 1.37);		1.42 (1.31, 1.53);	
Interaction on additive scale: RERI (95% CI)			0.30 (0.13, 0.47);	<i>P</i> <0.001	
Interaction on multiplicative scale: HR ratio (95% CI)			1.13 (1.01, 1.25);	<i>P</i> =0.04	

^aNumber of IHD cases (incidence rate per 100,000 person-years).

^bAdjusted for maternal age, year of delivery, parity, education, employment, income, country of origin, BMI, smoking, prior history of hypertension, diabetes, or hyperlipidemia, and other adverse pregnancy outcomes (small for gestational age, preeclampsia, other hypertensive disorders).

CI = confidence interval, GD = gestational diabetes, HR = hazard ratio, IHD = ischemic heart disease, RERI = relative excess risk due to interaction

Supplemental Table 8. Interactions between preeclampsia and gestational diabetes (1973-2015) in relation to risk of ischemic heart disease through 2018, Sweden.

	Preeclampsia				HRs (95% CI) for preeclampsia (yes vs. no) within GD strata
	No. (rate) ^a	No HR (95% CI) ^b	No. (rate) ^a	Yes HR (95% CI) ^b	
Gestational diabetes					
No	71,908 (145.9)	Reference	9,633 (264.1)	1.39 (1.36, 1.42);	1.39 (1.36, 1.42);
Yes	1,930 (306.0)	1.43 (1.36, 1.50);	410 (553.5)	2.16 (1.95, 2.39);	1.51 (1.35, 1.67);
HRs (95% CI) associated with GD (yes vs. no) within preeclampsia strata		1.43 (1.36, 1.50);		1.55 (1.39, 1.71);	
Interaction on additive scale: RERI (95% CI)			0.34 (0.12, 0.56);	<i>P</i> =0.003	
Interaction on multiplicative scale: HR ratio (95% CI)			1.09 (0.97, 1.21);	<i>P</i> =0.15	

^aNumber of IHD cases (incidence rate per 100,000 person-years).

^bAdjusted for maternal age, year of delivery, parity, education, employment, income, country of origin, BMI, smoking, prior history of hypertension, diabetes, or hyperlipidemia, and other adverse pregnancy outcomes (preterm delivery, small for gestational age, other hypertensive disorders).

CI = confidence interval, GD = gestational diabetes, HR = hazard ratio, IHD = ischemic heart disease, RERI = relative excess risk due to interaction

Supplemental Table 9. Associations between adverse pregnancy outcomes and subsequent risk of ischemic heart disease within 10 years following delivery, stratified on calendar year of delivery.

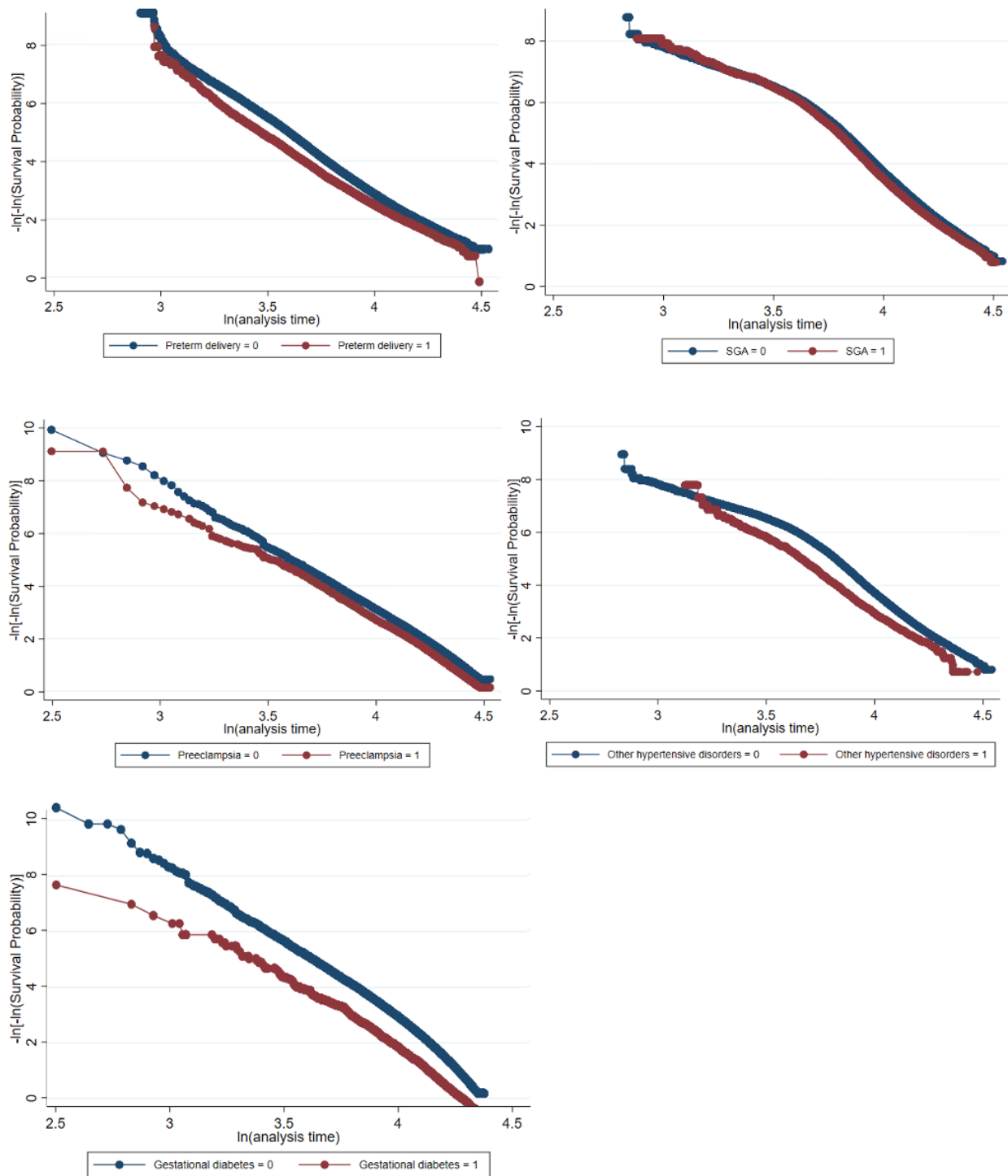
	IHD cases	Rate ^a	Reduced model ^b HR (95% CI)	Full model ^c HR (95% CI)
1973-1979				
Preterm delivery	57	22.7	1.73 (1.28, 2.34)	1.50 (1.10, 2.05)
Small for gestational age	98	13.0	1.67 (1.32, 2.10)	1.64 (1.30, 2.07)
Preeclampsia	68	16.4	1.47 (1.12, 1.92)	1.47 (1.12, 1.93)
Other hypertensive disorders	20	58.6	2.94 (1.94, 4.44)	2.67 (1.79, 4.01)
Gestational diabetes	22	54.4	3.37 (2.20, 5.16)	2.83 (1.82, 4.41)
1980-1989				
Preterm delivery	129	27.1	2.31 (1.87, 2.87)	2.06 (1.66, 2.56)
Small for gestational age	166	18.6	1.78 (1.48, 2.13)	1.66 (1.39, 2.00)
Preeclampsia	118	26.4	2.09 (1.69, 2.57)	1.85 (1.50, 2.28)
Other hypertensive disorders	28	82.0	4.12 (2.72, 6.22)	3.74 (2.50, 5.61)
Gestational diabetes	22	38.6	2.48 (1.68, 3.65)	2.04 (1.39, 2.99)
1990-1999				
Preterm delivery	242	44.5	2.28 (1.94, 2.67)	2.10 (1.78, 2.46)
Small for gestational age	194	24.1	1.14 (0.97, 1.33)	1.06 (0.91, 1.24)
Preeclampsia	117	45.1	2.03 (1.66, 2.47)	1.68 (1.37, 2.05)
Other hypertensive disorders	65	62.0	2.73 (2.14, 3.48)	2.46 (1.93, 3.13)
Gestational diabetes	22	40.3	1.34 (0.95, 1.90)	1.20 (0.85, 1.70)
2000-2009				
Preterm delivery	356	75.2	1.75 (1.55, 1.98)	1.62 (1.43, 1.84)
Small for gestational age	316	47.3	1.13 (1.00, 1.28)	1.09 (0.96, 1.23)
Preeclampsia	187	77.7	1.65 (1.41, 1.92)	1.42 (1.22, 1.67)
Other hypertensive disorders	101	110.0	2.13 (1.76, 2.58)	2.00 (1.65, 2.42)
Gestational diabetes	87	90.2	1.49 (1.22, 1.83)	1.34 (1.09, 1.65)

^aIschemic heart disease incidence rate per 100,000 person-years.

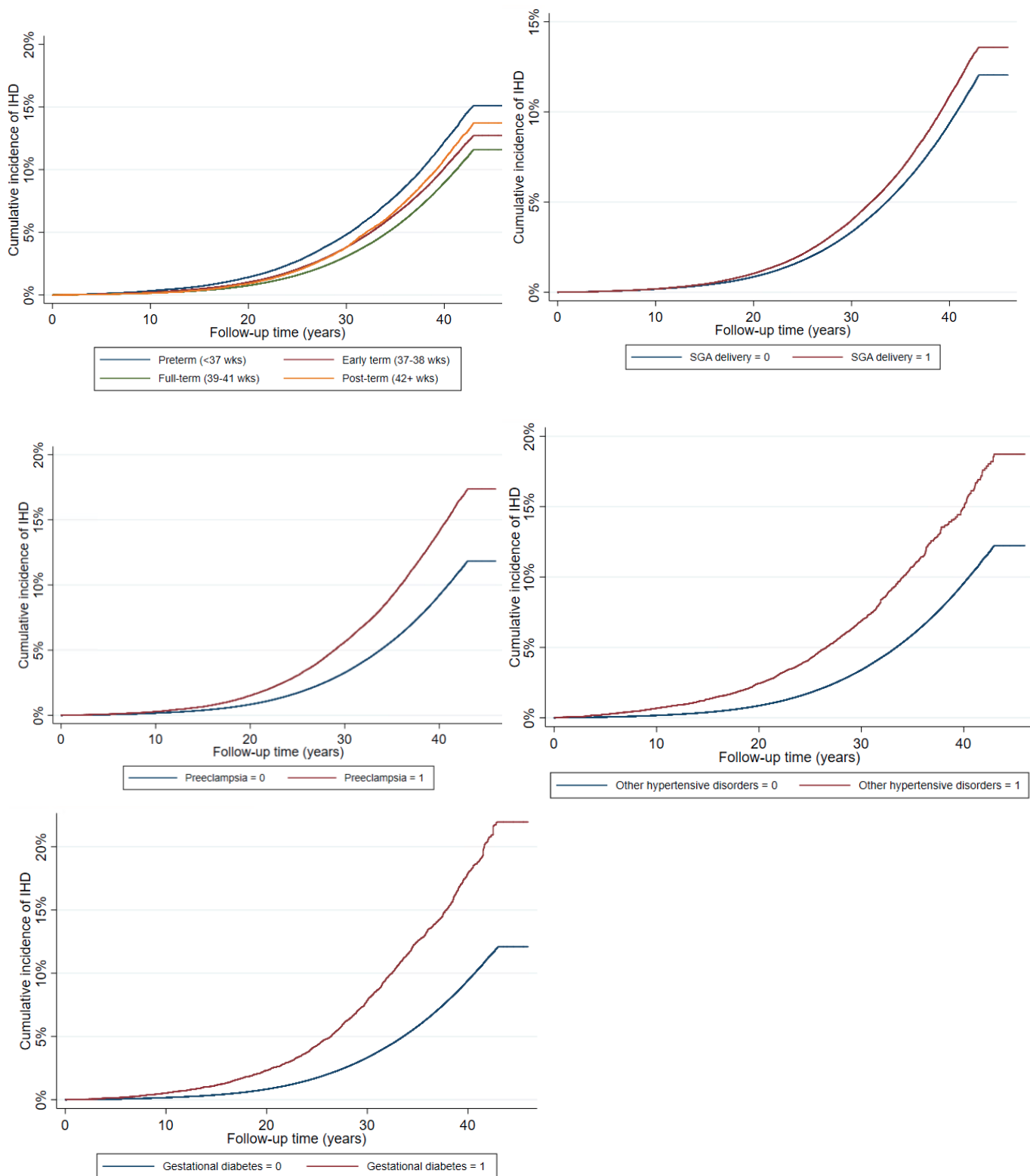
^bAdjusted for maternal age, year of delivery, parity, education, employment, income, country of origin, BMI, smoking, and prior history of hypertension, diabetes, or hyperlipidemia.

^cAdjusted for the same covariates as above and all other adverse pregnancy outcomes.

CI = confidence interval, HR = hazard ratio, IHD = ischemic heart disease



Supplemental Figure 1. Log-log plots for associations between adverse pregnancy outcomes and subsequent risk of ischemic heart disease at 0-46 years of follow-up.



Supplemental Figure 2. Cumulative incidence of ischemic heart disease at 0-46 years of follow-up associated with specific adverse pregnancy outcomes.