Supplementary Online Content

Crump C, Sundquist J, Sundquist K. Preterm delivery and long-term risk of hypertension in women. *JAMA Cardiol.* Published online October 13, 2021. doi:10.1001/jamacardio.2021.4127

eMethods. Supplemental Methods

eResults. Supplemental Results

eReferences

eTable 1. International Classification of Diseases (ICD) Codes Used in the Analyses.

eTable 2. Associations Between Number of Preterm Deliveries and Subsequent Risk of Chronic

Hypertension Among Women With at Least Two Singleton Deliveries

eTable 3. Spontaneous or Medically Indicated Delivery and Subsequent Risk of Chronic

Hypertension, Sweden, 1990-2015

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Supplemental Methods

Spline curves were used to present adjusted hazard ratios (HRs) and unadjusted risk differences for hypertension by time since delivery for different pregnancy durations (Figure 1). Secondary analyses were performed to examine: (1) hypertension risks associated with recurrent preterm delivery; (2) hypertension risks associated with spontaneous vs. medically indicated preterm delivery, which was systematically recorded starting in 1990 (N=2,645,898 deliveries among 1,447,549 women; maximum 26 years of follow-up); (3) among women with 2 deliveries, potential variation in hypertension risks by whether the 1st delivery was preterm but not the 2nd vs. the 2nd delivery was preterm but not the 1st; and (4) hypertension risks after further adjusting for oral contraceptive use, which was available from nationwide pharmacy records starting July 1, 2005 (N=1,116,307 deliveries among 723,655 women; maximum 10.5 years of follow-up). This last analysis explored oral contraceptive use as a potential confounder because it has been associated with hypertension¹ and may potentially (but not always^{2,3}) be more common after preterm delivery.

Sensitivity analyses were performed that (1) excluded women with preeclampsia or other hypertensive disorders of pregnancy (n=182,879; 8.3%) as an alternative to adjusting for these conditions; (2) ascertained hypertension based on \geq 2 (rather than \geq 1) diagnoses from any outpatient and/or inpatient settings; (3) ascertained hypertension based on \geq 2 outpatient diagnoses within any 2-year period or \geq 1 inpatient diagnosis; and (4) restricted to each woman's first delivery instead of time-dependent modeling of her shortest pregnancy.

eResults. Supplemental Results

Among women with 2 deliveries, there was no significant difference in risk of hypertension among those whose 1st delivery was preterm but not the 2nd (e.g., 0-43 years of follow-up: adjusted HR, 1.19; 95% CI, 1.15-1.22) vs. those whose 2nd delivery was preterm but not the 1st (1.23; 1.19-1.26) (*P* for difference in HRs = 0.07).

Additional adjustment for oral contraceptive use in the main analyses made no difference in risk estimates. In the full model, the hazard ratio (HR) for hypertension comparing preterm with full-term delivery was 1.47 (95% CI, 1.41-1.54; P<0.001) either with or without further adjusting for oral contraceptive use (maximum follow-up, 10.5 years).

In sensitivity analyses that examined alternatives to multiple imputation for missing data, all results were similar to the main findings and the conclusions were unchanged. For example, comparing preterm with full-term delivery, the adjusted HR for hypertension at 0-43 years of follow-up was 1.29 (95% CI, 1.27-1.31; P<0.001) when restricting to women with complete data, and 1.24 (1.23-1.26; P<0.001) when coding missing data as a separate category.

When hypertension was ascertained based on ≥ 2 (rather than ≥ 1) diagnoses, or based on ≥ 2 outpatient diagnoses within any 2-year period or ≥ 1 inpatient diagnosis, the risk estimates also were negligibly changed. For example, comparing preterm with full-term delivery, the adjusted HRs for hypertension at 0-43 years of follow-up using these two different ascertainment approaches were 1.24 (95% CI, 1.23-1.26; *P*<0.001) and 1.26 (1.25-1.28; *P*<0.001), respectively. In addition, the corresponding HR when focusing on each woman's first delivery, instead of her shortest pregnancy adjusted for parity, was 1.29 (95% CI, 1.26-1.32; *P*<0.001).

eReferences

- 1. Liu H, Yao J, Wang W, Zhang D. Association between duration of oral contraceptive use and risk of hypertension: A meta-analysis. *J Clin Hypertens (Greenwich)*. 2017;19(10):1032-1041.
- 2. Toscano M, Li D, Dye T, Olson-Chen C. Antepartum Contraceptive Counseling in Women with Preterm Birth. *Am J Perinatol.* 2019;36(12):1310-1316.
- 3. Robbins CL, Farr SL, Zapata LB, D'Angelo DV, Callaghan WM. Postpartum contraceptive use among women with a recent preterm birth. *Am J Obstet Gynecol*. 2015;213(4):508 e501-509.

eTable 1. International Classification of Diseases (ICD) codes used in the analyses.

Diagnosis	ICD-8	ICD-9	<i>ICD</i> -10
Hypertension	400-404	401-405	110-115
Preeclampsia	637	624.4-624.7	014-015
Other hypertensive disorders	400-404	401-405, 642.0-	I10-I15, O10-O11,
of pregnancy		642.3, 642.9	O13, O15-O16
Diabetes mellitus	250	250, 648.0, 648.8	E10-E14, O24

	Cases	Rate ^a	HR (95% CI) ^ь	Р
0-43 years after first delivery				
0 preterm	183,711	637.9	Reference	
1 preterm	22,229	790.7	1.22 (1.20, 1.24)	<0.001
≥2 preterm	5,406	866.3	1.37 (1.34, 1.41)	<0.001
Per additional preterm delivery			1.18 (1.17, 1.19)	<0.001
<10 years after first delivery				
0 preterm	10,245	84.9	Reference	
1 preterm	1,976	169.8	1.70 (1.62, 1.78)	<0.001
≥2 preterm	630	243.5	2.31 (2.13, 2.50)	<0.001
Per additional preterm delivery			1.51 (1.47, 1.56)	<0.001
10-19 years after first delivery				
0 preterm	27,795	315.1	Reference	
1 preterm	4,044	463.6	1.37 (1.32, 1.42)	<0.001
≥2 preterm	1,055	540.2	1.62 (1.52, 1.72)	<0.001
Per additional preterm delivery			1.28 (1.26, 1.31)	<0.001
20-29 years after first delivery				
0 preterm	67,294	1215.0	Reference	
1 preterm	7,882	1435.8	1.15 (1.12, 1.18)	<0.001
≥2 preterm	1,909	1550.4	1.24 (1.19, 1.30)	<0.001
Per additional preterm delivery			1.12 (1.10, 1.14)	<0.001
30-43 years after first delivery				
0 preterm	78,377	3298.4	Reference	
1 preterm	8,327	3687.8	1.11 (1.09, 1.14)	<0.001
≥2 preterm	1,812	3865.3	1.19 (1.13, 1.24)	<0.001
Per additional preterm delivery			1.10 (1.08, 1.11)	<0.001

eTable 2. Associations between number of preterm deliveries and subsequent risk of chronic hypertension among women with at least two singleton deliveries.

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

^bAdjusted for maternal age, year of delivery, parity, education, employment, income, region of origin, BMI, smoking, preeclampsia, other hypertensive disorders of pregnancy, and diabetes.

	Cases	Rate ^a	HR (95% CI) ^b	Р
Preterm				
Spontaneous	2,734	613.2	1.25 (1.21, 1.30)	<0.001
Medically indicated	5,097	1247.2	1.46 (1.42, 1.50)	<0.001
Early term				
Spontaneous	10,559	511.5	1.08 (1.06, 1.10)	<0.001
Medically indicated	11,668	875.8	1.30 (1.27, 1.33)	<0.001
Full-term	67,982	494.6	Reference	

eTable 3. Spontaneous or medically indicated delivery and subsequent risk of chronic hypertension, Sweden, 1990-2015.

^aHypertension incidence rate per 100,000 person-years. ^bAdjusted for maternal age, year of delivery, parity, education, employment, income, region of origin, BMI, smoking, preeclampsia, other hypertensive disorders of pregnancy, and diabetes.