

## The Association Between Hypertensive Disorders in Pregnancy and the Risk of Developing Chronic Hypertension

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Xu J, Li T, Wang Y, Xue L, Miao Z, Long W, Xie K, Hu C and Ding H (2022) The Association Between Hypertensive Disorders in Pregnancy and the Risk of Developing Chronic Hypertension. Front. Cardiovasc. Med. 9:897771. doi: 10.3389/fcvm.2022.897771 **Objective:** This meta-analysis comprehensively evaluated the association between hypertensive disorders in pregnancy (HDP) and the risk of developing chronic hypertension and the associations between specific types of HDP, including preeclampsia (PE) and gestational hypertension (GH), and the risk of developing chronic hypertension.

Design: Systematic review and meta-analysis.

**Data Sources:** The PubMed, Embase and Cochrane Library databases were searched from inception to August 20, 2021.

**Methods:** Depending on heterogeneity, the combined odds ratio (OR) of the 95% confidence interval (CI) was obtained with a random-effects or fixed-effects model. We used meta-regression analysis to explore the sources of heterogeneity. We analyzed the OR value after adjusting for age and BMI at recruitment, prepregnancy BMI, age at first delivery, and other factors. Additionally, we evaluated the results of the subgroup analysis by the year of publication (< 2016,  $\geq$  2016), study design, sample size (< 500,  $\geq$  500), region (North and South America, Europe, and other regions) and NOS score (< 7,  $\geq$  7).

**Results:** Our systematic review and meta-analysis comprehensively explored the relationships between HDP, GH, and PE and chronic hypertension. Twenty-one articles that included 634,293 patients were included. The results of this systematic review and meta-analysis suggested that women with a history of HDP are almost 3.6 times more likely to develop chronic hypertension than those without a history of HDP, women with a history of GH are almost 6.2 times more likely to develop chronic hypertension than those without a history of PE are almost 3.2 times more likely to develop chronic hypertension than those without a history of PE. In addition, we further calculated the probability of developing chronic hypertension among patients with HDP or PE after adjusting for age and BMI at recruitment, prepregnancy BMI, age at first delivery, and other factors. The results suggested that women with a history of HDP are almost 2.47 times more likely to develop chronic hypertension than those

without a history of HDP and that women with a history of PE are almost 3.78 times more likely to develop chronic hypertension than those without a history of PE. People in Asian countries are more likely to develop chronic hypertension after HDP or PE, while American people are not at high relative risk.

**Conclusion:** These findings suggest that HDP, GH, and PE increase the likelihood of developing chronic hypertension. After adjustment for age and BMI at recruitment, prepregnancy BMI, age at first delivery, and other factors, patients with HDP or PE were still more likely to develop chronic hypertension. HDP may be a risk factor for chronic hypertension, independent of other risk factors. GH and PE, as types of HDP, may also be risk factors for chronic hypertension.

**Systematic Review Registration:** [www.ClinicalTrials.gov], identifier [CRD42021238599].

Keywords: hypertensive disorders in pregnancy (HDP), preeclampsia (PE), gestational hypertension (GH), hypertension, pooled odds ratios (ORs), confidence intervals (CIs), systematic review, meta-analysis

#### INTRODUCTION

Hypertension is one of the most common conditions that occur during pregnancy and the main cause of maternal death (1). Ten percent of pregnancies are affected by hypertension, especially those of primiparas. Hypertensive disorders in pregnancy (HDP) include a series of diseases classified as preeclampsia, eclampsia, gestational hypertension, pregnancy complicated with chronic hypertension and preeclampsia superimposed on chronic hypertension (2). Their definitions are shown in Table 1. HDP remains one of the leading causes of maternal and fetal disease incidence and mortality worldwide. Moreover, HDP is closely related to the patient's future health. A study found that women with prepregnancy hypertension and those with both HDP and prepregnancy hypertension had an increased risk of kidney disease 5 years after delivery (3). HDP increases the risk of future cardiovascular events and has been included in the guidelines for the risk assessment and prevention of stroke and cardiovascular disease (CVD) in women (4, 5). Recent evidence indicates that the incidence rate of HDP has increased over the past 30 years, suggesting that HDP, a sex-specific CVD risk factor, may become more important in the coming years (6, 7). A history of gestational hypertension/preeclampsia is related to subclinical atherosclerosis (increased carotid intimamedia thickness (IMT) and plaque) (8). Pregnancy-induced hypertension is even hereditary, affecting the cardiovascular health of offspring (9).

Studies have shown that women with preeclampsia have a higher risk of developing chronic hypertension. Indeed, comprehensive data show that 20% of women with eclampsia develop hypertension within 15 years (10). However, the risk varies depending on the population studied and the criteria used for diagnosis. According to a study, the risk of hypertension in Sweden 5–12 years after pregnancy is approximately 40% (11, 12). Three other studies reached similar conclusions (13–15). The correlation between HDP and chronic hypertension fluctuates greatly. The results were different depending on the region and follow-up years. There are many other confounding factors, such as race or country; studies have shown that African women with a history of pregnancy-induced hypertension, followed by Hispanic and Asian women, have the highest risk of future high blood pressure. Moreover, individuals with normal blood pressure showed better health-related quality of life than patients with hypertension. Although systemic hypertension has almost always been considered a clinically asymptomatic disease, it can impair the quality of life of patients (16, 17). Therefore, the early prevention of hypertension is necessary. If the association between gestational hypertension and chronic hypertension can be identified, the early prevention and treatment of HDP will greatly benefit the long-term health of patients.

This systematic review and meta-analysis assessed recent reports to explore the association between HDP and chronic hypertension and evaluate the associations between specific types of HDP, including preeclampsia (PE), and gestational hypertension (GH), and the risk of developing chronic hypertension. We analyzed both crude and adjusted OR values to better determine the relationships between the variables and the stability of the results. We also conducted subgroup analysis by country and year to analyze the relationship between HDP and chronic hypertension.

#### METHODS

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (18).

## Protocol, Eligibility Criteria, Information Sources, and Search Strategy

This review was based on a prior design recommended by a systematic review and meta-analysis. The PubMed, EMBASE, and Cochrane Library databases were searched electronically in August 2021 using a combination of terms, keywords and

#### TABLE 1 | Definition of HDPs.

Type of HDPs	Definition
Gestational hypertension	Hypertension occurring after 20 weeks of pregnancy, systolic blood pressure $\geq$ 140 mmHg and (or) diastolic blood pressure $\geq$ 90 mmHg, and a return to normal blood pressure within 12 weeks after delivery; urinary protein (–); the diagnosis can be made after delivery.
Preeclampsia	<ul> <li>Systolic blood pressure ≥ 140 mmHg and (or) diastolic blood pressure ≥ 90 mmHg after 20 weeks of pregnancy, accompanied by urinary protein ≥ 0.3 g/24 h, or random urinary protein (+)</li> <li>Or without proteinuria, but combined with any of the following:</li> <li>Thrombocytopenia (platelets &lt; 100) × 10<sup>9</sup>/L)</li> <li>Liver function impairment (serum transaminase level is more than twice the normal value)</li> <li>Renal function impairment (serum creatinine level &gt; 1.1 mg/dl or more than twice the normal value)</li> <li>Pulmonary edema</li> <li>New central nervous system abnormalities or visual impairment</li> </ul>
Eclampsia	Convulsions that cannot be explained by other reasons occurring on the basis of preeclampsia.
Preeclampsia superimposed on chronic hypertension	There was no proteinuria before pregnancy, and proteinuria was present after 20 weeks of pregnancy in women with chronic hypertension; or proteinuria was present before pregnancy, and proteinuria increased significantly after pregnancy; or blood pressure rises further; or thrombocytopenia < 100 × 10 <sup>9/</sup> L; or other serious manifestations such as liver and kidney function damage, pulmonary edema, nervous system abnormalities, or visual impairment.
Pregnancy complicated with chronic hypertension	Systolic blood pressure $\geq$ 140 mmHg and (or) diastolic blood pressure $\geq$ 90 mmHg before 20 weeks of pregnancy (excluding trophoblastic diseases), and there was no significant aggravation during pregnancy; or hypertension was first diagnosed after 20 weeks of pregnancy and continued beyond 12 weeks postpartum.

word variants related to the medical subject headings (MeSH) "hypertension, pregnancy," "preeclampsia," "eclampsia" and "hypertension." We used Endnote x9 to remove duplicate articles and then browsed the titles and summaries to exclude unrelated articles. Reviews, meta-analyses, articles lacking relevant data, letters and abstracts were excluded. There were no time or language restrictions. The reference lists of relevant articles and comments were manually searched for additional reports. The study was registered in the Prospero database (Registration number: CRD42021238599).

# Study Selection, Data Collection, and Data Items

The main outcome was the incidence rate of chronic hypertension in patients with HDP or with the specific types PE and GH. We included case-control studies and cohort studies that provided data on how many patients developed hypertension several years after delivery. The research period of the different studies varied: the span was large, and the time period ranged from 1 to 30 years. Hypertension was defined as a systolic blood pressure (SBP) > 140 mmHg and/or a diastolic blood pressure (DBP)  $\geq$  90 mmHg occurring more than once in a clinical environment. The use of antihypertensive drugs and lower thresholds for defining hypertension were also included in the diagnostic criteria. When data were available, only patients affected by HDP, PE, and GH were considered in the analysis. We excluded studies in which chronic hypertension was present before pregnancy or before 20 weeks of gestation. If a study included patients with chronic hypertension, we considered only the articles that provided the number of patients with chronic hypertension. In addition, we did not include articles about the incidence rate of postpartum hypertension within 1 year of delivery.

Two researchers, Xu and Wang, independently performed all abstract screenings. The two researchers retrieved and

independently evaluated the full texts of potentially eligible studies. Any inconsistencies or differences were discussed with a third reviewer, and a consensus was reached. Several articles were translated into languages other than English to determine whether they were suitable for inclusion. The reviewers extracted data on the study characteristics and results, especially the author, year, location, study type, population size, and reported results. If multiple studies with the same endpoint were published for the same cohort, the report containing the most comprehensive population information was used to avoid population overlap.

### **Risk of Bias and Study Quality**

The quality of the included studies was assessed using the Newcastle-Ottawa Scale (NOS) for cohort and case-control studies, which was developed by Schokker et al. to assess the quality of non-randomized studies (19). With this protocol, the maximum score for each study was 9. Studies with a score  $\geq$  7 were considered high-quality articles. The two authors independently reviewed each study and determined whether it was eligible for inclusion in our meta-analysis. If there were any differences, the third author joined the discussion. Since the NOS could not be used to fully evaluate the potential confounding factors in the study analysis, information on which confounding factors were considered in each study was further extracted. Publication bias was assessed by a funnel plot using Begg's and Egger's tests (20). Subgroup analysis by publication year (< 2016,  $\geq$  2016), study design, location, sample size (< 500,  $\geq$  500) and NOS score (< 7,  $\geq$  7) was performed to further evaluate the associations between HDP, PE, and GH and chronic hypertension.

### **Statistical Analysis**

We constructed forest plots to obtain pooled ORs and 95% CIs. We applied a fixed-effects model to calculate the combined effect estimate if  $I_2 \geq 50\%$ . Otherwise, we used a random-effects model.

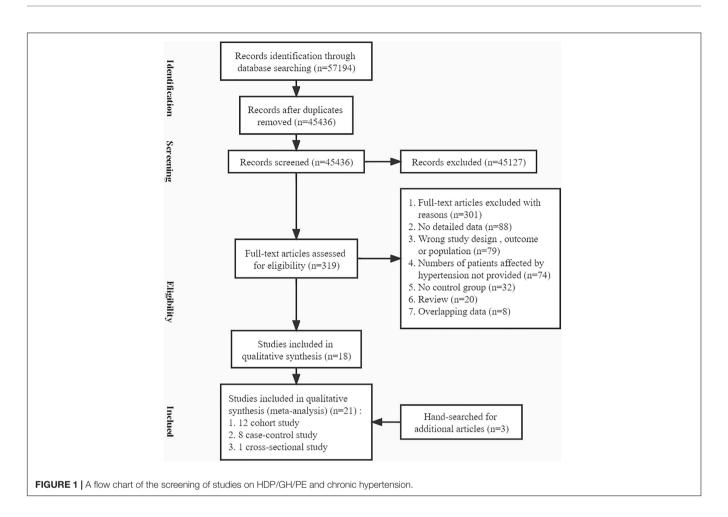


TABLE 2	Summar	v characteristics of the 2 <sup>-</sup>	1 studies included in the s	systematic review of pregnanc	v complications.
	Guinna			systematic review of program	y complication

Articles	Publication years	Country	Study design	Included population	Sample size	NOS score
Garrido-Gimenez et al. (21)	2020	France	Cohort study	PE	79	6
Moreira et al. (22)	2009	Brazil	Cross-sectional study	HDP	1,141	7
Drost et al. (23)	2011	Netherlands	Cohort study	PE	874	7
Watanabe et al. (24)	2020	Japan	Case-control study	HDP/GH/PE/OTHER	245	7
Nordén Lindeberg and Hanson (25)	2000	Sweden	Cohort study	HDP	115	8
Shammas and Maayah (26)	2000	Jordan	Case-control study	GH/PE	180	6
Garovic et al. (27)	2010	America	Case-control study	HDP	5,796	6
Wilson et al. (28)	2003	Britain	Cohort study	GH/PE	1,865	8
Mito et al. (29)	2018	Japan	Cohort study	HDP	796	7
Garovic et al. (30)	2020	America	Cohort study	HDP/PE	3,283	7
Edlow et al. (31)	2009	America	Case-control study	PE	248	7
Honigberg et al. (32)	2019	Britain	Cohort study	HDP	277,011	7
Marín et al. (33)	2000	Spain	Cohort study	HDP	463	8
Kuo et al. (34)	2018	China	Cohort study	PE/Eclampsia	7,050	7
Gastrich et al. (35)	2020	America	Case-control study	PE	331,707	6
White et al. (36)	2016	America	Cohort study	PE	112	8
Qasim et al. (37)	2016	Pakistan	Case-control study	HDP	527	7
Ghossein-Doha et al. (38)	2014	Netherlands	Cohort study	PE	28	6
Ehrenthal et al. (39)	2014	America	Case-control study	HDP	82	6
Shahul et al. (40)	2018	America	Case-control study	HDP/PE	137	6
Martelly et al. (41)	2021	America	Cohort study	PE	55	7

Sensitivity analysis was used to explore the robustness of the included literature. Publication bias was assessed by funnel plots and linear regression equations. If the funnel plot was obviously asymmetric, we further used the trim-and-fill method to adjust the data. In addition, meta-regression analysis was performed based on the publication year, NOS score, status, sample size, and study design to explore the sources of heterogeneity. All analyses were conducted *via* R version 3.6. The critical value for statistical significance was set as P < 0.05.

### RESULTS

#### Study Selection

To obtain relevant literature, we searched the PubMed, Embase and Cochrane Library databases from inception to August 20, 2021. A total of 57,194 studies were obtained (**Figure 1**). After removing duplicate articles, 45,436 articles remained. Then, we culled articles that were unrelated and lacked data by scanning the titles, abstracts, and full texts. In addition, three studies that were retrieved from the reference lists of previous relevant articles were included. Ultimately, 21 studies met all eligibility criteria (21–41).

### **Study Characteristics**

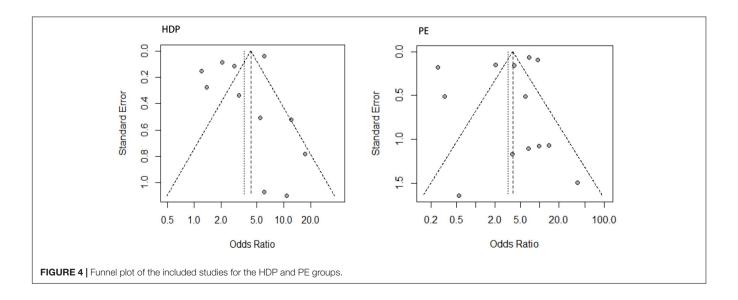
The 21 studies included in this systematic review and metaanalysis varied in study design, year of publication, NOS score, country, and sample size. All studies were observational; 12 were described as cohort studies, eight as case-control studies and one as a cross-sectional study. The publication dates of these articles ranged from 2000 to 2021. Among these articles, the study areas included Europe for seven studies, North and South America for nine studies, and other regions for five studies. The

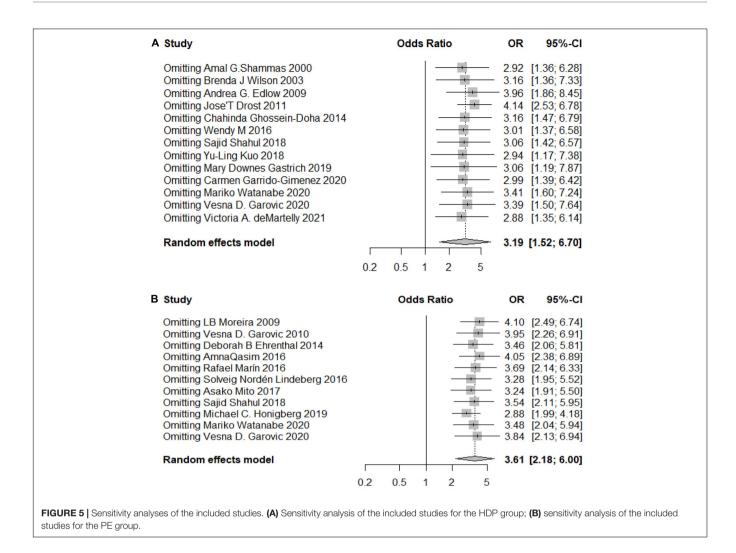
A Study	HI Events To		Control Total	Odds Ratio	OR 95%-0	Weight Weight I (fixed) (random)
LB Moreira 2009	131 2	53 242	515	<u> </u> ₽!	1.21 [0.90; 1.64	l] 9.0% 11.9%
Vesna D. Garovic 2010		43 1362	3421	-	2.05 [1.73; 2.43	
Deborah B Ehrenthal 2014		33 1	41		- 10.77 [1.25; 92.70	
AmnaQasim 2016		66 138	286		1.37 [0.80; 2.34	
Rafael Marín 2016		73 12	86		3.13 [1.62; 6.06	
Solveig Nordén Lindeberg 2016		46 2	47		- 17.31 [3.74; 80.06	
Asako Mito 2017		25 19	746		12.08 [4.34; 33.66	
Sajid Shahul 2018		60 1	25		- 6.00 [0.74; 48.90	
Michael C. Honigberg 2019	1889 28		217216		6.05 [5.59; 6.5	
Mariko Watanabe 2020		26 42	111		5.48 [2.04; 14.7;	
Vesna D. Garovic 2020		70 319	1120		2.78 [2.23; 3.48	
The definition of the						
Fixed effect model Random effects model	47	03	223614		4.27 [4.00; 4.58 3.61 [2.18; 6.00	
Heterogeneity: $l^2 = 96\%$ , $\tau^2 = 0.53$	90 n < 0.01				5.01 [2.10, 0.00	- 100.0%
$\frac{1}{1000} = \frac{1}{1000}, t = 0.35$	50, p < 0.01			0.1 0.51 2 10		
В	GH	Contr	ol			Weight Weight
Study Eve	ents Total E			Odds Ratio	OR 95%-CI	(fixed) (random)
-				1		
Amal G.Shammas 2000	21 54		16		28.64 [3.67; 223.73]	1.4% 21.5%
	215 428	76 27			2.67 [1.93; 3.69]	94.6% 46.4%
Mariko Watanabe 2020	14 17	42 1 <sup>·</sup>	11		7.67 [2.08; 28.26]	4.1% 32.1%
Fixed effect model	499	4:	34	\$	3.23 [2.38; 4.37]	100.0%
Random effects model				<u></u>	6.24 [1.73; 22.55]	100.0%
Heterogeneity: $I^2 = 73\%$ , $\tau^2 = 0$ .	0.0 = q . 3898	3				
5,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,			0.01	0.1 1 10 100		
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C	Events To		Control	Odda Batta	OR 95%	Weight Weig
Study	Events To	tal Events	Total	Odds Ratio	OR 95%	-CI (fixed) (randor
Amal G.Shammas 2000		47 1	46		13.75 [1.69; 111.	
Brenda J Wilson 2003		42 76	277		4.02 [2.94; 5.	
Andrea G. Edlow 2009		79 24	140		0.33 [0.12; 0.	
Jose'T Drost 2011		39 146	332		0.26 [0.18; 0.	
Chahinda Ghossein-Doha 2014		20 1	8	- <del>  <u> </u></del>	3.77 [0.38; 37.	
Wendy M 2016		40 8	40		6.00 [2.21; 16.	
		32 1	25	+	6.72 [0.77; 58.	
Sajid Shahul 2018					9.28 [7.68; 11.	22] 14.3% 10.5
Sajid Shahul 2018 Yu-Ling Kuo 2018	320 11		5180			
Sajid Shahul 2018			5180 325347		6.87 [6.06; 7.	79] 21.4% 10.6
Sajid Shahul 2018 Yu-Ling Kuo 2018	320 11 285 63 14	60 2206 43 1			6.87 [6.06; 7. 9.66 [1.17; 79.	79] 21.4% 10.6 42] 0.2% 5.7
Sajid Šhahul 2018 Yu-Ling Kuo 2018 Mary Downes Gastrich 2019	320 11 285 63 14 0	602206431142	325347		6.87 [6.06; 7.	79] 21.4% 10.6 42] 0.2% 5.7
Sajid Shahul 2018 Yu-Ling Kuo 2018 Mary Downes Gastrich 2019 Carmen Garrido-Gimenez 2020	320 11 285 63 14 0	60 2206 43 1	325347 21		6.87 [6.06; 7. 9.66 [1.17; 79.	79] 21.4% 10.6 42] 0.2% 5.7 69] 0.3% 3.5
Sajid Shahul 2018 Yu-Ling Kuo 2018 Mary Downes Gastrich 2019 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020	320 11 285 63 14 0 118 2	602206431142	325347 21 111		6.87 [6.06; 7. 9.66 [1.17; 79. 0.55 [0.02; 13.	79] 21.4% 10.6 42] 0.2% 5.7 69] 0.3% 3.5 79] 14.9% 10.4
Sajid Shahul 2018 Yu-Ling Kuo 2018 Mary Downes Gastrich 2019 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020 Vesna D. Garovic 2020	320 11 285 63 14 0 118 2	60         2206           43         1           1         42           58         169           21         0	325347 21 111 582		6.87 [6.06; 7. 9.66 [1.17; 79. 0.55 [0.02; 13. 2.06 [1.52; 2.	79]         21.4%         10.6           42]         0.2%         5.7           69]         0.3%         3.5           79]         14.9%         10.4           98]         0.1%         4.0
Sajid Shahul 2018 Yu-Ling Kuo 2018 Mary Downes Gastrich 2019 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020 Vesna D. Garovic 2020 Victoria A. deMartelly 2021	320 11 285 63 14 0 118 2 9	60         2206           43         1           1         42           58         169           21         0	325347 21 111 582 25		6.87 [6.06; 7. 9.66 [1.17; 79. 0.55 [0.02; 13. 2.06 [1.52; 2. — 38.76 [2.08; 720.	79]         21.4%         10.6           42]         0.2%         5.7           69]         0.3%         3.5           79]         14.9%         10.4           98]         0.1%         4.0           16]         100.0%         100.0%
Sajid Shahul 2018 Yu-Ling Kuo 2018 Mary Downes Gastrich 2019 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020 Vesna D. Garovic 2020 Victoria A. deMartelly 2021 Fixed effect model	320 11 285 63 14 0 118 2 9	60         2206           43         1           1         42           58         169           21         0	325347 21 111 582 25		6.87 [6.06; 7. 9.66 [1.17; 79. 0.55 [0.02; 13. 2.06 [1.52; 2. 38.76 [2.08; 720. <b>3.78 [3.43; 4.</b>	79]         21.4%         10.6           42]         0.2%         5.7           69]         0.3%         3.5           79]         14.9%         10.4           98]         0.1%         4.0           16]         100.0%         100.0%

FIGURE 2 | Forest plots of the risk of developing chronic hypertension. (A) Forest plots of the risk of developing chronic hypertension in the HDP group; (B) forest plots of the risk of developing chronic hypertension in the GH group; (C) forest plots of the risk of developing chronic hypertension in the PE group.

A Study	TE seTE	Odds Ratio	OR	95%-CI	Weight (fixed)	Weight (random)	
Vesna D. Garovic 2010 AmnaQasim 2016 Rafael Marín 2016 Asako Mito 2017 Vesna D. Garovic 2020	0.79 0.3837 1.63 0.3837 1.96 0.6504		2.20 5.10 - 7.10	[1.25; 1.87] [1.04; 4.67] [2.40; 10.82] [1.98; 25.40] [1.94; 2.76]	2.9% 2.9% 1.0%	15.0% 15.0% 7.3%	
<b>Fixed effect model</b> <b>Random effects mode</b> Heterogeneity: <i>I</i> <sup>2</sup> = 79%, ·		1 0.1 0.5 1 2 10		[1.78; 2.30] [1.67; 3.64]		 100.0%	
B Study	TE seTE	Odds Ratio	OR	95%-CI	Weight (fixed)	Weight (random)	
LB Moreira 2009 AmnaQasim 2016 Asako Mito 2017 Vesna D. Garovic 2020	0.47 0.1723 0.34 0.2803 2.49 0.5252 0.90 0.0881		1.40 12.10	[1.14; 2.24] [0.81; 2.42] [4.32; 33.87] [2.06; 2.91]	18.8% 7.1% 2.0% 72.0%	29.4% 24.1% 13.9% 32.7%	
Fixed effect model Random effects model Heterogeneity: $l^2 = 83\%$ , $\tau^2$	$^{2} = 0.1901, p < 0.01$	0.1 0.5 1 2 10		[1.94; 2.60] [1.43; 3.88]	100.0% 	 100.0%	
C Study	TE seTE	Odds Ratio	OR	95%-CI	Weight (fixed)	Weight (random)	
Brenda J Wilson 2003 Andrea G. Edlow 2009 Jose'T Drost 2011 Vesna D. Garovic 2020	1.38 0.1755 2.63 0.5033 1.28 0.1889 0.56 0.1254	<b></b>	13.92 3.59	[2.82; 5.61] [5.19; 37.33] [2.48; 5.20] [1.37; 2.24]	25.4% 3.1% 21.9% 49.7%	27.4% 16.9% 27.1% 28.6%	
Fixed effect model Random effects model Heterogeneity: $I^2 = 90\%$ , $\tau^2$		0.1 0.5 1 2 10		[2.26; 3.20] [2.05; 6.98]	100.0% 	 100.0%	

FIGURE 3 | Forest plots of the risk of developing chronic hypertension in the adjusted group. (A) Forest plots of the risk of developing chronic hypertension in the HDP-adjusted group; (B) forest plots of the risk of developing chronic hypertension in the HDP-unadjusted group; (C) forest plots of the risk of developing chronic hypertension in the HDP-unadjusted group; (C) forest plots of the risk of developing chronic hypertension in the HDP-unadjusted group; (C) forest plots of the risk of developing chronic hypertension in the HDP-unadjusted group; (C) forest plots of the risk of developing chronic hypertension in the HDP-unadjusted group; (C) forest plots of the risk of developing chronic hypertension in the HDP-unadjusted group; (C) forest plots of the risk of developing chronic hypertension in the HDP-unadjusted group; (C) forest plots of the risk of developing chronic hypertension in the HDP-unadjusted group; (C) forest plots of the risk of developing chronic hypertension in the HDP-unadjusted group; (C) forest plots of the risk of developing chronic hypertension in the HDP-unadjusted group; (C) forest plots of the risk of developing chronic hypertension in the HDP-unadjusted group; (C) forest plots of the risk of developing chronic hypertension in the HDP-unadjusted group; (C) forest plots of the risk of developing chronic hypertension in the HDP-unadjusted group; (C) forest plots of the risk of developing chronic hypertension in the HDP-unadjusted group; (C) forest plots of the risk of developing chronic hypertension in the HDP-unadjusted group; (C) forest plots of the risk of developing chronic hypertension; (C) forest plots of the risk of developing chronic hypertension; (C) forest plots of the risk of developing chronic hypertension; (C) forest plots of the risk of developing chronic hypertension; (C) forest plots of the risk of developing chronic hypertension; (C) forest plots of the risk of developing chronic hypertension; (C) forest plots of the risk of developing chronic hypertension; (C) forest





smallest sample size was 28 (38), and the largest sample size was 331,707 (35). Eleven studies researched HDP, 3 researched GH, and 13 researched PE. There were five studies that included more than one disease. The research characteristics are summarized in **Table 2**.

## **Total Pooled Effect**

As shown in **Figure 2A**, the heterogeneity among the eligible articles about HDP was  $I^2 = 96\%$  (*P* < 0.01), so we chose

Study level variables	HDP Grou	р	PE Gro	up
	Coefficient (95% CI)	P-value	Coefficient (95% CI)	P-value
Publication year	(0.0077, 0.2026)	0.03	(-0.07, 0.16)	0.41
NOS score	(-1.28, 1.35)	0.96	(-3.10, 0.61)	0.19
Region	(-0.22, 0.82)	0.26	(-1.03, 1.28)	0.83
Sample size	(-1.31, 0.76)	0.6	(-1.78, 1.09)	0.64
Study design	(0.24, 1.17)	0.003	(-1.55, 2.19)	0.74

to use a random-effects model. The overall combined effect showed that HDP patients had a higher risk of developing chronic hypertension than healthy controls (OR 3.61, 95% CI 2.18–6.00). We also calculated the GH and PE results and chose to use random-effects models ( $I_{GH}^2 = 73\%$ , P = 0.03,  $I_{PE}^2 = 97\%$ , P < 0.01). Women with GH or PE were at higher risk of developing chronic hypertension than healthy controls (OR<sub>GH</sub> 6.24, 95% CI 1.73–22.55, OR<sub>PE</sub> 3.19, 95% CI 1.52–6.70) (**Figures 2B,C**).

Some articles reported adjusted OR values for age and BMI at recruitment, prepregnancy BMI, age at first delivery and other factors. We further evaluated the associations between HDP, GH, and PE and chronic hypertension based on the adjusted OR values.

The heterogeneity among the articles about HDP with adjusted OR values was 79% (OR 2.47, 95% CI 1.67–3.64) (**Figure 3A**), and the heterogeneity among those with unadjusted OR values was 83% (OR 2.36, 95% CI 1.43–3.88) (**Figure 3B**). The two results were similar, showing that patients with HDP are at higher risk of developing chronic hypertension than healthy controls. The same trend in the risk of chronic hypertension was observed in the PE group, and the OR

values were adjusted ( $I^2 = 90\%$ , OR = 3.78, 95% CI 2.05–6.98) (**Figure 3C**).

# Publication Bias, Sensitivity Analysis and Risk Analysis

Through linear regression and funnel plots, we found that studies on HDP (P = 0.4639) and PE (P = 0.5380) had no publication bias (**Figure 4**). **Figure 5A** shows that when omitting one of these studies (22), the sensitivity analysis of the HDP group showed an OR of 4.10 (95% CI 2.49–6.74), which was nearly the same outcome as the total pooled effect (OR 3.61, 95% CI 2.18–6.00). Similarly, when omitting other studies, women with HDP were at higher risk for developing chronic hypertension than healthy controls. Sensitivity analysis of the PE group showed similar results after omitting other studies, and women with PE were at higher risk of developing chronic hypertension than those in the healthy control group (**Figure 5B**).

The quality assessment and risk of bias analysis of each included study are shown in **Table 2**.

### **Meta-Regression Analysis**

In the total pooled effect, the heterogeneity of the HDP group was  $I^2 = 96\%$ , and the heterogeneity of the PE group was  $I^2 = 97\%$ . Thus, we conducted meta-regression analysis based on the publication year, NOS score, country, sample size and study

design. The results confirmed that the publication year and study design had a significant effect on the heterogeneity in the HDP group ( $P_{\text{publication year}} = 0.03$ ,  $P_{\text{study design}} = 0.003$ ). Other factors showed no significant effect on the heterogeneity in the HDP group. The publication year and study design may be the sources of heterogeneity for the experimental results. None of the factors showed a significant effect on the heterogeneity in the PE group (**Table 3**).

### **Subgroup Analysis**

We conducted subgroup analyses based on the year of publication (< 2016,  $\geq$  2016), study design, region (North America, South America, Europe, etc.), sample size (< 500,  $\geq$  500) and NOS score (< 7,  $\geq$  7) to further evaluate the correlations between HDP, GH, and PE and the risk of chronic hypertension. The subgroup analyses showed some inconsistencies; some of them seemed reasonable, while others did not.

An overall OR value of 5.75 (95% CI 3.92–8.44;  $I^2 = 49\%$ ) was found for the risk of developing postpartum hypertension among women with a history of HDP. According to the subgroup analysis, the risk of chronic hypertension in patients with HDP increased for different continents, but there were differences among the continents (P = 0.03). The increased risk in North and South America was the lowest (OR 2.11, 95% CI 1.42–3.14), and the risk in Europe was the highest (OR 5.52, 95% CI 3.01–10.14),

Study	l Events 1	HDP Total E		Control Total	Odds Rati	D	OR		95%-CI	-	Weight (random)
Country2 = 1 LB Moreira 2009 Vesna D. Garovic 2010 Deborah B Ehrenthal 2014 Sajid Shahul 2018 Vesna D. Garovic 2020 Fixed effect model Random effects model Heterogeneity: $J^2 = 82\%$ , $\tau^2 = 0.118$	7 12 247	253 643 33 60 470 1459	242 1362 1 1 319	515 3421 41 25 1120 5122			1.21 2.05 10.77 6.00 2.78 2.08 2.11	[0.90; [1.73; [1.25; [0.74; [2.23; [1.84; [1.42;	1.64] 2.43] 92.70] 48.90] 3.48] 2.35] 3.14]	9.0% 21.5% 0.1% 0.1% 10.5% 41.2%	11.9% 12.2% 3.8% 4.0% 12.1%
Country2 = 3 AmnaQasim 2016 Asako Mito 2017 Mariko Watanabe 2020 Fixed effect model Random effects model Heterogeneity: $J^2 = 88\%$ , $\tau^2 = 1.326$	37 6 20 7, p < 0.01	66 25 26 117	138 19 42	286 746 111 1143	+ - • V		1.37 12.08 5.48 2.29 4.26	[0.80; [4.34; [2.04; [1.49; [1.05;	2.34] 33.66] 14.73] 3.52] 17.21]	2.7% 0.1% 0.4% 3.2%	10.9% 8.2% 8.4%  27.5%
Country2 = 2 Rafael Marin 2016 Solveig Nordén Lindeberg 2016 Michael C. Honigberg 2019 Fixed effect model Random effects model Heterogeneity: $J^2 = 64\%$ , $\tau^2 = 0.174$	20 1889 2	3127		86 47 217216 217349	-	•	3.13 	[1.62; [3.74; [5.59; [5.54; [3.01;	6.06] 80.06] 6.55] 6.49] 10.14]	1.4% 0.1% 54.0% 55.6% 	10.3% 5.8% 12.4%  28.4%
Fixed effect model Random effects model Heterogeneity: $I^2 = 96\%$ , $\tau^2 = 0.539$ Test for subgroup differences (fixed Test for subgroup differences (rand	0, <i>p</i> < 0.01 effect): χ <sup>2</sup>	<b>4703</b>	.13, df =	<b>223614</b> 2 ( <i>p</i> < 0.01) = 2 ( <i>p</i> = 0.03)	0.1 0.51 2	10	4.27 3.61	[4.00; [2.18;	4.55] 6.00]	100.0% 	 100.0%

Study	Events	HDP Total	Events	Control Total	Odds Ratio	OR	95%-CI	Weight (fixed)	Weight (random)
Year_group = 1									
B Moreira 2009	131	253	242	515		1.21	[0.90; 1.64]	9.0%	11.9%
Vesna D. Garovic 2010	370	643	1362	3421		2.05	[1.73; 2.43]	21.5%	12.2%
Deborah B Ehrenthal 2014	7	33	1	41		- 10.77	[1.25; 92.70]	0.1%	3.8%
Fixed effect model		929		3977	•	1.83	[1.58; 2.12]	30.6%	
Random effects model					$\diamond$	1.78	[1.04; 3.04]		27.9%
Heterogeneity: $I^2 = 83\%$ , $\tau^2 = 0.145$	60, p < 0.(	01							
Year_group = 2 AmnaQasim 2016	37	66	138	286	I	1.37	[0.80; 2.34]	2.7%	10.9%
Rafael Marín 2016	92	273	12			3.13	[1.62; 6.06]		10.3%
Solveig Nordén Lindeberg 2016	20	46	2		· · · · · · · · · · · · · · · · · · ·	17.31	[3.74; 80.06]		5.8%
Asako Mito 2017	6	25	19			12.08	[4.34; 33.66]		8.2%
Sajid Shahul 2018	12	60	1	25		6.00	[0.74; 48.90]		4.0%
Michael C. Honigberg 2019		2808		217216	+	6.05	[5.59; 6.55]		12.4%
Mariko Watanabe 2020	20	26	42			5.48	[2.04; 14.73]		8.4%
Vesna D. Garovic 2020	247		319			2.78	[2.23; 3.48]		12.1%
Fixed effect model	241	3774	010	219637	\$	5.34	[4.97: 5.75]		12.170
Random effects model		0114		210001		4.33	[2.62: 7.16]		72.1%
Heterogeneity: $I^2 = 91\%$ , $\tau^2 = 0.346$	67, p < 0.0	01				4.00	[2.02, 1.10]		12.170
Fixed effect model		4703		223614	0	4.27	[4.00; 4.55]	100.0%	
<b>Random effects model</b> Heterogeneity: <b>Ι</b> <sup>2</sup> = 96%, τ <sup>2</sup> = 0.539	0 0 0 0	11				3.61	[2.18; 6.00]		100.0%
Test for subgroup differences (fixed	1  effect	$v^2 = 16^{\circ}$	3.52 df =	1 (n < 0.01)	0.1 0.51 2 10				
Test for subgroup differences (rand	long offer	(1 = 10) to): 2	- E 62 df	= 1 (n = 0.01)	0.1 0.012 10				

**FIGURE 7** | Subgroup analysis by publication year of the risk of developing chronic hypertension in the HDP group (Group 1 = years < 2016, Group 2 = years  $\geq 2016$ ).

Study	Events	HDP Total	Events	Control Total	Odds Ratio	OR	95%-CI	-	Weight (random)
Design = Cross-sectional									
LB Moreira 2009	131	253	242	515	-	1.21	[0.90; 1.64]	9.0%	11.9%
Fixed effect model		253		515		1.21	[0.90; 1.64]	9.0%	
Random effects model Heterogeneity: not applicable					\$	1.21	[0.90; 1.64]		11.9%
Design = Case-control									
Vesna D. Garovic 2010	370		1362	3421			[1.73; 2.43]		12.2%
Deborah B Ehrenthal 2014	7	33	1	41		- 10.77	[1.25; 92.70]	0.1%	3.8%
AmnaQasim 2016	37	66	138	286	+ <b>-</b>		[0.80; 2.34]		10.9%
Sajid Shahul 2018	12		1	25			[0.74; 48.90]		4.0%
Mariko Watanabe 2020	20		42	111			[2.04; 14.73]	0.4%	8.4%
Fixed effect model		828		3884	•		[1.78; 2.44]	24.8%	
<b>Random effects model</b> Heterogeneity: $I^2 = 57\%$ , $\tau^2 = 0.154$	12, p = 0.0	05				2.47	[1.47; 4.13]		39.3%
Design = Cohort study									
Rafael Marín 2016	92	273	12	86		3.13	[1.62; 6.06]	1.4%	10.3%
Solveig Nordén Lindeberg 2016	20	46	2	47	· · · · · · · · · · · · · · · · · · ·	- 17.31	[3.74; 80.06]	0.1%	5.8%
Asako Mito 2017	6	25	19	746	<u> </u> − + −−−	12.08	[4.34; 33.66]	0.1%	8.2%
Michael C. Honigberg 2019	1889	2808	55098	217216	+	6.05	[5.59; 6.55]	54.0%	12.4%
Vesna D. Garovic 2020	247	470	319	1120	-	2.78	[2.23; 3.48]	10.5%	12.1%
Fixed effect model		3622		219215	0	5.50	[5.11; 5.92]	66.2%	
<b>Random effects model</b> Heterogeneity: $I^2 = 92\%$ , $\tau^2 = 0.275$	52, p < 0.(	D1				5.19	[2.99; 9.01]		48.8%
Fixed effect model		4703		223614	0	4.27	[4.00; 4.55]	100.0%	
Random effects model Heterogeneity: $I^2 = 96\%$ , $\tau^2 = 0.539$	0.0 < 0.0	01				3.61	[2.18; 6.00]		100.0%
Test for subgroup differences (fixed	effect):	$v_{a}^{2} = 19$	0.20. df =	2(p < 0.01)	0.1 0.51 2 10				
Test for subgroup differences (rand		2 2	- 00 40 -	4-0/ 0/					

FIGURE 8 | Subgroup analysis by the study design of the risk of developing chronic hypertension in the HDP group.

A Study	Events	HDP Total		Control Total	Odds Ratio	OR	95%-CI	Weight (fixed)	Weight (random)
NOS_group = 2 LB Moreira 2009 AmnaQasim 2016 Rafael Marin 2016 Solveig Nordén Lindeberg 2016 Asako Mito 2017 Michael C. Honigberg 2019 Mariko Watanabe 2020	131 37 92 20 6 1889 20	253 66 273 46 25 2808 26	242 138 12 2 19 55098 42	515 286 86 47 746 217216 111		1.21 1.37 3.13 17.31 12.08 6.05 5.48	[0.90; 1.64] [0.80; 2.34] [1.62; 6.06] [3.74; 80.06] [4.34; 33.66] [5.59; 6.55] [2.04; 14.73]	9.0% 2.7% 1.4% 0.1% 0.1% 54.0% 0.4%	11.9% 10.9% 10.3% 5.8% 8.2% 12.4% 8.4%
Vesna D. Garovic 2020 Fixed effect model Random effects model Heterogeneity: $I^2 = 96\%$ , $\tau^2 = 0.599$ NOS_group = 1	247	470 3967	319	1120 220127	*	2.78 4.86 3.68	[2.23; 3.48] [4.53; 5.22] [2.03; 6.66]	10.5% 78.3%	12.1%  80.0%
Vesna D. Garovic 2010 Deborah B Ehrenthal 2014 Sajid Shahul 2018 Fixed effect model Random effects model Heterogeneity: $l^2 = 39\%$ , $\tau^2 = 0.375$	370 7 12	643 33 60 <b>736</b>	1362 1 1	3421 41 25 3487	*	2.05 - 10.77 6.00 2.11 3.21	[1.73; 2.43] [1.25; 92.70] [0.74; 48.90] [1.78; 2.49] [1.19; 8.66]	21.5% 0.1% 0.1% 21.7%	12.2% 3.8% 4.0%  20.0%
Fixed effect model Random effects model Heterogeneity: $I^2 = 96\%$ , $\tau^2 = 0.539$ Test for subgroup differences (fixed Test for subgroup differences (rand	d effect): ;	$c_1^2 = 80$	.19, df = 1 = 0.05, df	<b>223614</b> ( <i>p</i> < 0.01) = 1 ( <i>p</i> = 0.82	0.1 0.51 2 10	4.27 3.61	[4.00; 4.55] [2.18; 6.00]	100.0% 	 100.0%
B Study	Events	HDF Tota	l Event	Control s Total	Odds Ratio	OR	95%-CI	Weight (fixed)	Weight (random)
Samle_size_group = 2 LB Moreira 2009 Vesna D. Garovic 2010 Asako Mito 2017 Michael C. Honigberg 2019 Vesna D. Garovic 2020 Fixed effect model Random effects model Heterogeneity: $I^2$ = 98%, $\tau^2$ = 0.55	131 370 6 1889 247	1 253 0 643 0 2808 7 2808 7 470 4199	3 242 3 1362 5 19 3 55098 0 319	2 515 2 3421 9 746 8 217216	*	1.21 2.05 12.08 6.05 2.78 4.33	[0.90; 1.64] 5 [1.73; 2.43] 3 [4.34; 33.66] 5 [5.59; 6.55] 3 [2.23; 3.48]	9.0% 21.5% 0.1% 54.0% 10.5% 95.1%	11.9% 12.2% 8.2% 12.4% 12.1%
Samle_size_group = 1 Deborah B Ehrenthal 2014 AmnaQasim 2016 Rafael Marín 2016 Solveig Nordén Lindeberg 2016 Sajid Shahul 2018 Mariko Watanabe 2020	37 92 5 20 12 20	7 66 2 273 0 46 2 60 0 26	6     130       3     12       3     12       5     12       5     12       6     12       6     12       7     12       8     12       9     12       10     12	2 86 2 47 1 25		1.37 3.13 - 17.31 - 6.00 5.48		0.1% 2.7% 1.4% 0.1% 0.1% 0.4% 4.9%	3.8% 10.9% 10.3% 5.8% 4.0% 8.4%
Fixed effect model Random effects model Heterogeneity: $l^2 = 69\%$ , $\tau^2 = 0.56$	55, p < 0	.01	•	590			5 [1.94; 9.33]		43.2%

**Random effects model** Heterogeneity:  $I^2 = 96\%$ ,  $\tau^2 = 0.5390$ , p < 0.01Test for subgroup differences (fixed effect):  $\chi_1^2 = 4.49$ , df = 1 (p = 0.03) Test for subgroup differences (random effects):  $\chi_1^2 = 0.28$ , df = 1 (p = 0.59)

**FIGURE 9 | (A)** Subgroup analysis by NOS score of the risk of developing chronic hypertension in the HDP group (Group 1 = NOS < 7, Group  $2 = NOS \ge 7$ ). **(B)** Subgroup analysis by the sample size of the risk of developing chronic hypertension in the HDP group (Group 1 = sample size < 500, Group  $2 = \text{sample size} \ge 500$ ).

0.1 0.51 2

10

while the risk in Asia was similar to the overall assessment (OR 4.26, 95% CI 1.05–17.21) (**Figure 6**). According to the analysis of publication years, when the publication year was before 2016, the increase in the risk of developing chronic hypertension among

patients with HDP was significantly lower than that among patients included in studies with a publication year of 2016 or later (P = 0.02, OR<sub><2016</sub> 1.78, 95% CI<sub><2016</sub> 1.04–3.04, OR<sub>>2016</sub> 4.33, 95% CI<sub>>2016</sub> 2.62–7.16) (**Figure** 7). Grouped by study

design, the OR value of the case–control group was 2.47 (95% CI 1.47–4.13), that of the cohort control group was 5.19 (95% CI 2.99–9.01), and that of the cross-sectional group was 1.21 (95% CI 0.90–1.64) (**Figure 8**). According to the NOS score and sample size, the increased risk of developing chronic hypertension among HDP patients was similar to that of the overall evaluation ( $OR_{NOS \ge 7}$  3.68, 95%  $CI_{NOS \ge 7}$  2.03–6.66;  $OR_{NOS < 7}$  3.21, 95%  $CI_{NOS < 7}$  1.19–8.66;  $OR_{>500}$  3.21, 95%  $CI_{>500}$  1.62–6.35;  $OR_{\le 500}$  4.26, 95%  $CI_{<500}$  1.94–9.33) (**Figure 9**).

1	Study	Events	PE Total	Events	Total	Odds Ratio	OR		95%-CI	Weight (fixed)	Weigh (random
	Country2 = 3 Amal G Shammas 2000	11	47	1	46		13 75	[1.69;	111.56)	0.2%	5.89
Ì	Yu-Ling Kuo 2018	320	1144	208	5180		9.28	[7.68]	11.22]	14.3%	10.59
1	Mariko Watanabe 2020	0	1	42	111		0.55	0.02;	13.69]	0.3%	3.59
1	Fixed effect model Random effects model Heterogeneity: $I^2 = 36\%$ , $\tau^2 = 0.4478$	8 0 = 0.2	1192		5337	\$	9.17 7.54	[7.59; [2.49;	11.08] 22.81]	14.8% 	19.8%
1	Country2 = 2										
	Brenda J Wilson 2003 Jose'T Drost 2011	327 57	542 339	76 146	277 332		4.02 0.26	[2.94; [0.18;	5.51] 0.37]	10.5% 32.4%	10.4% 10.4%
	Chahinda Ghossein-Doha 2014	7	20	1	8		3.77	[0.38;	37.14]	0.2%	5.39
	Carmen Garrido-Gimenez 2020 Fixed effect model	14	43 944	1	21 638	0	9.66	[1.17;	79.42]	0.2%	5.79
j	Random effects model Heterogeneity: $I^2 = 98\%$ , $\tau^2 = 3.5734$	4, <i>p</i> < 0.0			038	÷	2.19	[0.30;	16.02]	40.0%	31.8%
1	Country2 = 1 Andrea G. Edlow 2009	5	79	24	140		0.33	[0.12;	0.891	4.3%	8 99
1	Andrea G. Edlow 2009 Wendy M 2016	24	40	8	40		6.00	[2 21:	16.311	0.8%	8.99
ł	Sajid Shahul 2018	7	32	1	25		6.72	0.77;	58.79	0.2%	5.6%
ļ	Mary Downes Gastrich 2019 Vesna D. Garovic 2020	285 118	6360 258	2206 :	325347 582	100	6.87 2.06	[6.06]	7.79] 2.79]	21.4%	10.69 10.49
1	Victoria A. deMartelly 2021	9	21	0	25		- 38.76	[2.08;	720.98	0.1%	4.09
1	Fixed effect model Random effects model		6790		326159	2	4.51	[3.97; [1.26;	5.13] 8.74]	41.7%	48.4%
	Heterogeneity: $I^2 = 95\%$ , $\tau^2 = 1.0656$	δ, <i>p</i> < 0.0	1			Ť	3.32	[1.20;	0.74]		40.47
	Fixed effect model Random effects model		8926		332134		3.78 3.19	[3.43; [1.52;	4.16] 6.70]	100.0% 	100.0%
	Random effects model Heterogeneity: $I^2 = 97\%$ , $\tau^2 = 1.3473$ Test for subgroup differences (fixed Test for subgroup differences (rando	3, p < 0.0 effect): χ om effect	$x_2^2 = 202$ s): $\chi_2^2 =$	.26, df = 2 1.71, df =	2 (p < 0.01) 0. 2 (p = 0.43)	01 0.1 1 10 100					
			PE	Events	Control	Odds Ratio	OR	9	5%-CI	Weight (fixed)	Weight (random)
	Year_group = 1 Amal G.Shammas 2000	11	47	1	46		13 75	[1.69; 1	111 561	0.2%	5.8%
	Brenda J Wilson 2003	327	542	76	277	+	4.02	[2.94:	5.51] 0.89]	10.5%	10.4%
ļ	Andrea G. Edlow 2009	5	79	24	140		0.33	0.12	0.89]	4.3%	8.9%
1	Jose'T Drost 2011	57			332	■	0.26	[0.18;	0.37]	32.4%	10.4%
1	Chahinda Ghossein-Doha 2014 Fixed effect model	7	20	1	8 803	•	3.77	[0.38; [0.96;	37.14]	0.2%	5.3%
1	Random effects model Heterogeneity: $I^2 = 97\%$ , $\tau^2 = 3.280$	17 0 < 0			000	+	1.54	[0.28;	8.44]		40.7%
		u, p < 0.									
ļ	Year_group = 2 Wendy M 2016	24	40	8	40		0.00	10.04	40.041	0.8%	8.9%
ł	Sajid Shahul 2018	24	40	0	25		6.00 6.72	[0.77;	16.31] 58.79]	0.8%	5.6%
1	Yu-Ling Kuo 2018	320		208	5180		9.28	[7.68:	11.22]	14.3%	10.5%
1	Mary Downes Gastrich 2019	285					6.87	[6.06	7.79]	21.4%	10.6%
1	Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020	14		42	21 111		9.66 0.55	[1.17;	79.42] 13.69]	0.2%	5.7% 3.5%
1	Vesna D. Garovic 2020	118	258	169	582	-	2.06	[1.52]	2.79	14.9%	10.4%
1	Victoria A. deMartelly 2021	9		0	25		38.76	[2.08; 7	20.98]	0.1%	4.0%
į	Fixed effect model Random effects model Heterogeneity: $l^2 = 91\%$ , $\tau^2 = 0.313$		7899		331331	• •	6.17 5.53	[5.55; [3.21;	6.85] 9.53]	52.3%	59.3%
		15, p < 0.	8926		332134		3.78	[3.43:	4.16]	100.0%	-
	Fixed effect model					-	3.19	11 52	6.70]		100.0%
ļ	Fixed effect model Random effects model Heterogeneity: $l^2 = 97\%$ , $\tau^2 = 1.347$	3, p < 0.	01	0.00 #-	4 / 0.040			[1.02,			
	Fixed effect model Random effects model Heterogeneity: $t^2 = 97\%$ , $\tau^2 = 1.347$ Test for subgroup differences (fixed Test for subgroup differences (rand	73, p < 0. d effect): lom effec	:ts): χ <sub>1</sub>	= 1.97, df	= 1 (p = 0.16	0.01 0.1 1 10 10 )	00	[1.02,	-		
	Random effects model Heterogeneity: 1 <sup>2</sup> = 97%, x <sup>2</sup> = 1.347 Test for subgroup differences (fixed Test for subgroup differences (rand Study	forn effec	ts): χ <sub>1</sub> : PE	= 1.97, df	1 (p < 0.01) ( = 1 (p = 0.16 Control Total	0.01 0.1 1 10 10	0 00 0R			Weight (fixed)	Weight (random)
	Random effects model Heterogeneity: I <sup>2</sup> = 07%, I <sup>2</sup> = 1.347 test for subgroup differences (fixed Test for subgroup differences (rand Study Design = Case-control Amal G.Shammas 2000	tom effect Events	rts): χ <sub>1</sub> PE Total 47	= 1.97, df Events	= 1 (p = 0.16 Control Total 46	)	OR 13.75	5	95%-CI	(fixed)	(random)
	Random effects model Heterogeneity, "7 e 97%, c? = 1.347 Test for subgroup differences (foec Test for subgroup differences (rand Study Design = Case-control Amal G. Shammas 2000 Amdrea G. Edlow 2009	tom effect Events	rts): χ <sub>1</sub> PE Total 47	= 1.97, df Events 1 24	= 1 (p = 0.16 Control Total 46 140	)	OR 13.75 0.33	[1.69; [0.12;	95%-CI 111.56] 0.89]	(fixed) 0.2% 4.3%	Weight (random) 5.8%
	Random effects model Heterogeney, <sup>72</sup> = 39%, <sup>22</sup> = 132 Test for subgroup differences (fixed Test for subgroup differences (rand Study Design = Case-control Amal G Shammas 2000 Andrea G, Edlow 2009 Said Shahul 2018	Events	ts): χ <sub>1</sub> PE Total 47 79 32	= 1.97, df Events 1 24 1	<sup>46</sup> 140 25	) Odds Ratio	OR 13.75 0.33 6.72	[1.69; [0.12; [0.77;	95%-CI 111.56] 0.89] 58.79]	(fixed) 0.2% 4.3% 0.2%	(random) 5.8% 8.9% 5.6%
	Random effects model Heterogenety: 7 e 97%, c? = 1.347 Test for subgroup differences (foec Test for subgroup differences (rand Study Design = Case-control Amal G. Shammas 2000 Amdrea G. Edlow 2009	Events	ts): χ <sub>1</sub> PE Total 47 79 32 6360 1	= 1.97, df Events 1 24 1	= 1 (p = 0.16 Control Total 46 140	) Odds Ratio	OR 13.75 0.33	[1.69; [0.12; [0.77; [6.06;	95%-CI 111.56] 0.89] 58.79]	(fixed) 0.2% 4.3%	(random) 5.8% 8.9%
	Random effects model Heterogenety, <sup>77</sup> = 97%, <sup>47</sup> = 1.3 Test for subgroup differences (fixed Test for subgroup differences (fixed Study Design = Case-control Arnal G Shammas 2000 Andrea G: Educy 2009 Sajd Shahul 2018 Mary Downes Castrich 2019 Mariko Watanabe 2020 Fixed effect model	Events	ts): χ <sub>1</sub> PE Total 47 79 32 6360	= 1.97, df Events 1 24 1 2206	= 1 (p = 0.16 Control Total 46 140 25 325347	) Odds Ratio	OR 13.75 0.33 6.72 6.87 0.55 5.79	[1.69; [0.12; [0.77; [6.06; [0.02; [5.06;	95%-CI 111.56] 0.89] 58.79] 7.79] 13.69] 6.62]	(fixed) 0.2% 4.3% 0.2% 21.4%	5.8% 8.9% 5.6% 10.6% 3.5%
	Random effects model Heterogenety, <sup>72</sup> = 97%, <sup>4</sup> , <sup>42</sup> = 134 Test for subgroup differences (fixed Study Design = Case-control Amal G.Shammas 2000 Andrea G. Edlow 2009 Sajid Shahi 2018 Mary Downes Gastrich 2019 Marko Watanabe 2020	tom effect Events 11 5 7 285 0	ts): χ <sub>1</sub> PE Total 47 79 32 6360 1 6519	= 1.97, df Events 1 24 1 2206	= 1 (p = 0.16 Control Total 46 140 25 325347 111	) Odds Ratio	OR 13.75 0.33 6.72 6.87 0.55	[1.69; [0.12; [0.77; [6.06; [0.02;	95%-Cl 111.56] 0.89] 58.79] 7.79] 13.69]	(fixed) 0.2% 4.3% 0.2% 21.4% 0.3%	(random) 5.8% 8.9% 5.6% 10.6%
	Random effecta model Heregreneyt, <sup>2</sup> – 1978, <sup>2</sup> – 1.347 Tes for staggroup differences (sea Ers for staggroup differences (sea Study Danigen – Classa control Andrea G. Editors 2000 Andrea G. Editors 2000 Andrea G. Editors 2000 Andrea G. Editors 2000 Fixed effect model Random effects model, Heatongeneyt, <sup>2</sup> – 50%, <sup>2</sup> = 3.232 Dealem – Cohott	tom effect Events 11 5 7 285 0 285 0 26, <i>p</i> < 0.	47 79 32 6360 1 6519	= 1.97, df Events 1 24 1 2206 42	= 1 (p = 0.16 <b>Control</b> <b>Total</b> 46 140 25 325347 111 325669	Odds Ratio	OR 13.75 0.33 6.72 6.87 0.55 5.79 2.68	[1.69; [0.12; [0.77; [6.06; [0.02; [5.06; [0.45;	<b>95%-CI</b> 111.56] 0.89] 58.79] 7.79] 13.69] 6.62] 15.86]	(fixed) 0.2% 4.3% 0.2% 21.4% 0.3% 26.4%	5.8% 8.9% 5.6% 10.6% 3.5% 34.3%
	Random effects model Heterogeney, I <sup>-</sup> o 1978, s <sup>2</sup> = 1.347 Test for subgroup differences (text Test for subgroup differences (text Study Design = Case-control Arnal G. Sharmmas 2000 Arnala G. Eduka 2009 Sajd Shahul 2018 Marko Watanabe 2020 Text effects model Heterogeney I <sup>-</sup> = 3.252 Design = Cohort Brenda J Wilson 2003	tom effect Events 11 5 7 285 0 26, p < 0. 327	(ts): x <sub>1</sub> PE Total 47 79 32 6360 1 6519 01 542	= 1.97, df Events 1 24 1 2206 42 76	= 1 (p = 0.16 Control Total 46 140 25 325347 111 325669 277	Odds Ratio	OR 13.75 0.33 6.72 6.87 0.55 5.79 2.68 4.02	[1.69; [0.12; [0.77; [6.06; [0.02; [5.06; [0.45; [0.45;	95%-Cl 111.56] 0.89] 58.79] 7.79] 13.69] 6.62] 15.86] 5.51]	(fixed) 0.2% 4.3% 0.2% 21.4% 0.3% 26.4% 	(random) 5.8% 8.9% 5.6% 10.6% 3.5% 34.3%
	Random effecta model Heregrenety, <sup>2</sup> – 9 (39%, <sup>2</sup> – 1.347) Test for subgroup differences (sub Ers for subgroup differences (sub Study Design – Classe confrol Andra G Sherman 2000 Andra G Sherman 2000 Andra G Ledwa 2000 Ers de effect model Random effects model Heregrenety, <sup>2</sup> = 10%, <sup>2</sup> = 3.222 Design – Chohrt Breda 7 USA, <sup>3</sup> = 3.222 Design – Chohrt Breda 7 USA, <sup>3</sup> = 3.222 Design – Chohrt Breda 7 USA, <sup>3</sup> = 3.222 Design – Chohrt Breda 7 USA, <sup>4</sup> = 3.222 Design – Chohrt	tom effect Events 11 5 7 285 0 285 0 26, <i>p</i> < 0.	(ts): x <sub>1</sub> PE Total 47 79 32 6360 1 6519 01	= 1.97, df Events 1 24 1 2206 42 76 146	= 1 (p = 0.16 Control Total 46 140 25 325347 111 325669 277 332	) Odds Ratio	OR 13.75 0.33 6.72 6.87 0.55 5.79 2.68 4.02 0.26	[1.69; [0.12; [0.77; [6.06; [0.02; [5.06; [0.45; [0.45;	95%-Cl 111.56] 0.89] 58.79] 7.79] 13.69] 6.62] 15.86] 5.51] 0.37]	(fixed) 0.2% 4.3% 0.2% 21.4% 0.3% 26.4% 	(random) 5.8% 8.9% 5.6% 10.6% 3.5% 34.3%
	Random effecta model Heterogeney, I <sup>-</sup> = 0 Nyr, C <sup>-</sup> = 1.347 Tes for subgroup differences (sea Ers for subgroup differences (sea Study Design = Case-control Arral G. Saharman 2000 Arral G. Saharman 2000 Arral G. Saharman 2000 Find effect model Near Downes Gastrich 2019 Mary Downes Gastrich 2019 Mary Downes Gastrich 2019 Mary Downes Gastrich 2019 Radom effects model Heterogeney, I <sup>-</sup> = 00%, I <sup>-</sup> = 3.322 Design = Cahort Design C. Chort Design C. Schort Design	tom effect Events 11 5 7 285 0 26, p < 0. 327 57	(ts): x <sub>1</sub> PE Total 47 79 32 6360 1 6519 01 542 339 20	= 1.97, df Events 1 24 1 2206 42 76	= 1 (p = 0.16 Control Total 46 140 25 325347 111 325669 277	Odds Ratio	OR 13.75 0.33 6.72 6.87 0.55 5.79 2.68 4.02	[1.69; [0.12; [0.77; [6.06; [0.02; [5.06; [0.45; [0.45; [0.45; [0.38; [0.38; [2.21;	95%-Cl 111.56] 0.89] 58.79] 7.79] 13.69] 6.62] 15.86] 5.51]	(fixed) 0.2% 4.3% 0.2% 21.4% 0.3% 26.4% 	(random) 5.8% 8.9% 5.6% 10.6% 3.5% - 34.3% 10.4% 10.4% 5.3% 8.9%
	Random effects model Heregreney, I <sup>-</sup> = 978, r <sup>2</sup> = 1.347 Test for subgroup differences (best Test for subgroup differences (best Test for subgroup differences (best Study Design = Case-control Amal G. Shammas 2000 Amal G. Shammas 2000 Amal G. Shammas 2000 Shards a. E. divo Shards a. divo Shards	tom effect Events 11 5 7 285 0 26, p < 0. 327 57 7 24 320	tts): x <sub>1</sub> PE Total 47 79 32 6360 1 6519 01 542 339 20 40 1144	= 1.97, df Events 1 24 1 2206 42 76 146 1 8 208	= 1 ( <i>p</i> = 0.16 <b>Control</b> <b>Total</b> 46 140 25 325347 111 325669 2777 332 8 40 5180	Odds Ratio	OR 13.75 0.33 6.87 0.55 5.79 2.68 4.02 0.26 3.77 6.00 9.28	[1.69; [0.12; [0.77; [6.06; [0.45; [0.45; [2.94; [0.18; [0.38; [2.21; [7.68;	5.51] 0.37] 0.37] 0.37] 0.37] 0.37] 37.14] 16.31]	(fixed) 0.2% 4.3% 0.2% 21.4% 0.3% 26.4% 	(random) 5.8% 8.9% 5.6% 10.6% 3.5% - 34.3% 10.4% 5.3% 8.9% 10.5%
	Random effecta model Heterogeney, I <sup>-</sup> o 1978, C <sup>-</sup> a 1347 Test for subgroup differences (sec Test for subgroup differences (sec Study Design = Case-control Arnal G Shamma 2000 Arnal G Shamma 2000 Arnal G Shamma 2000 Arnal G Shamma 2000 Fixed effect model Heterogeney, I <sup>-</sup> = 05%, C <sup>+</sup> = 3222 Design = Cohort Design 2 Cohort Design 2 Cohort Design 2 Cohort Design 4 Cohort Design 2 Cohort Design 4 Cohort Design	tom effect Events 11 5 7 285 0 26, p < 0 327 57 7 24 320 14	tts): x1 PE Total 47 79 32 63600 1 6519 01 542 339 20 0 1144 43	= 1.97, df Events 1 244 1 2206 42 76 146 1 8 208 1	= 1 ( <i>p</i> = 0.16 Control Total 46 140 25 325347 111 325669 277 332 8 40 5180 21	Odds Ratio	OR 13.75 0.33 6.72 6.87 0.55 5.79 2.68 4.02 0.26 3.77 6.00 9.28 9.66	[1.69; [0.12; [0.77; [6.06; [0.02; [5.06; [0.45; [0.45; [2.944; [0.18; [0.38; [2.21; [7.68; [2.24;	95%-CI 111.56] 0.89] 58.79] 7.79] 13.69] 6.62] 15.86] 5.51] 0.37] 37.14] 16.31] 11.22 79.42]	(fixed) 0.2% 4.3% 0.2% 21.4% 0.3% 26.4% 0.3% 32.4% 0.2% 0.2% 0.8% 14.3% 0.2%	(random) 5.8% 8.9% 5.6% 10.6% 3.5% 34.3% 10.4% 5.3% 8.9% 10.5% 5.7%
	Random effects model Heregrenky, 1 <sup>-</sup> = 93%, 2 <sup>-</sup> = 1.34% Test for subgroup differences (theor Test for subgroup differences (theor Study Design = Case-control Amai G Shammas 2000 Amai G Shammas 2000 Amai G Shammas 2000 Amai G Shammas 2000 Sharda S. Ledu 2009 Sajid Shahul 2018 Marko Walanabe 2020 Frade effect model Random effects model Breada J Wilson 2003 Design = Cohort Breada J Wilson 2003 Design = Cohort Design = Cohort	26, p < 0. 26, p < 0. 26, p < 0. 327 5 7 24 320 14 118	tts): x1 PE Total 47 79 72 6360 16519 01 542 339 20 40 414 43 258	= 1.97, df Events 1 24 1 2206 42 76 146 146 1 8 208 208 1 169	2777 3322 840 5180 2180 225 325347 1111 325669 2777 332 8 40 5180 21 21 562	Odds Ratio	OR 13.75 0.33 6.72 6.87 0.55 5.79 2.68 4.02 0.26 3.77 6.00 9.28 9.66 2.06	(1.69; [0.12; [0.77; [6.06; [0.02; [5.06; [0.18; [0.18; [0.18; [0.18; [0.18; [1.17; [1.52]	95%-Cl 111.56] 0.89] 58.79] 7.79] 13.62] 15.86] 5.51] 0.37] 37.14] 16.31] 11.22] 79.42] 2.79]	(fixed) 0.2% 4.3% 0.2% 21.4% 0.3% 26.4% 0.3% 32.4% 0.2% 0.8% 14.3% 0.2% 0.2%	(random) 5.8% 8.9% 5.6% 10.6% 3.5% 10.4% 5.3% 8.9% 10.5% 5.7% 10.4%
	Random effecta model Herogrenky, <sup>2</sup> – 1978, <sup>2</sup> – 1347 Ters for subgroup differences (see Ters for subgroup differences (see Study Danigon – Class control Randi G Sharmano 2000 Andras G Edinar 2000 Saydi Shahu 2018 Mary Downes Gastrich 2019 Mary Downes Gastrich 2019 Mary Downes Gastrich 2019 Mary Downes Gastrich 2019 Rade diffect model Random effecta model Nearing Control Beaging – Cchott Bendar J, Wilson 2003 Joart Thoot 2014 Charlinda Ghossein-Doha 2014 Wordy M 2016 Charma Gamodo-Gamoez 2020 Victora A, deMantely 2021 Victora A, deMantely 2021 Victora A, deMantely 2021	tom effect Events 11 5 7 285 0 26, p < 0 327 57 7 24 320 14	tts): x1 PE Total 47 79 32 6360 16519 01 542 339 20 40 414 43 258	= 1.97, df Events 1 244 1 2206 42 76 146 1 8 208 1	= 1 ( <i>p</i> = 0.16 Control Total 46 140 25 325347 111 325669 277 332 8 40 5180 21	Odds Ratio	OR 13.75 0.33 6.72 6.87 0.55 5.79 2.68 4.02 0.26 3.77 6.00 9.28 9.66	[1.69; [0.12; [0.77; [6.06; [0.02; [5.06; [0.45; [0.45; [2.944; [0.18; [0.38; [2.21; [7.68; [2.24;	95%-Cl 111.56] 0.89] 58.79] 7.79] 13.62] 15.86] 5.51] 0.37] 37.14] 16.31] 11.22] 79.42] 2.79]	(fixed) 0.2% 4.3% 0.2% 21.4% 0.3% 26.4%  10.5% 32.4% 0.2% 14.3% 0.2% 14.3% 0.2% 14.3% 0.2%	(random) 5.8% 8.9% 5.6% 10.6% 3.5% - 34.3% 10.4% 5.3% 8.9% 10.5% 5.7% 10.4% 4.0%
	Random effecta model Heregreney, F. – 9187, C. – 1347 Test for subgroup differences (bes Test for subgroup differences (bes Test for subgroup differences) Study Design = Case-control Arnal G. Sharmmas 2000 Arnal G. Sharmmas 2000 Arnal G. Sharmas 2000 Sayd Shahu 2018 Marko Watanaba 2020 Prote diffect model Hernda J. Wilson 2003 JoseT Drost 2011 Camino Lamido-Gimenez 2020 Victora A. deMantely 2021 Victora A. deMantely 2021 Victora A. deMantely 2021	26, p < 0: 26, p < 0: 26, p < 0: 327 57 24 320 14 118 9	47 79 32 6360 1 6519 01 542 339 20 40 01 1144 43 258 21 2407	= 1.97, df Events 1 24 1 2206 42 76 146 146 1 8 208 208 1 169	2777 32569 2777 325347 325669 2777 32569 2777 32569 2777 32569 2777 277 277 277 277 277 277 277 277 2	Odds Ratio	OR 13.75 0.33 6.72 6.87 2.68 4.02 0.26 0.26 0.26 9.268 9.66 9.206 	[1.69; [0.12; [0.77; [6.06; [0.45; [0.45; [0.45; [0.45; [0.38; [2.21; [7.68; [1.17; [1.52; [2.08;	95%-Cl 111.56] 0.89] 58.79] 7.79] 13.69] 6.62] 15.86] 15.86] 15.86] 15.85] 15.85] 15.85] 16.37] 27.42] 16.31] 17.942] 2.79] 720.96] 3.47]	(fixed) 0.2% 4.3% 0.2% 21.4% 0.3% 26.4% 0.3% 32.4% 0.2% 0.8% 14.3% 0.2% 0.2%	(random) 5.8% 8.9% 5.6% 10.6% 3.5% 10.4% 5.3% 8.9% 10.5% 5.7% 10.4%
	Random effecta model Herogrenky, <sup>2</sup> – 1978, <sup>2</sup> – 1347 Ters for subgroup differences (see Ters for subgroup differences (see Study Danigon – Class control Randi G Sharmano 2000 Andras G Edinar 2000 Saydi Shahu 2018 Mary Downes Gastrich 2019 Mary Downes Gastrich 2019 Mary Downes Gastrich 2019 Mary Downes Gastrich 2019 Rade diffect model Random effecta model Nearing Control Beaging – Cchott Bendar J, Wilson 2003 Joart Thoot 2014 Charlinda Ghossein-Doha 2014 Wordy M 2016 Charma Gamodo-Gamoez 2020 Victora A, deMantely 2021 Victora A, deMantely 2021 Victora A, deMantely 2021	26, p < 0: 26, p < 0: 26, p < 0: 327 57 24 320 14 118 9	47 79 32 6360 1 6519 01 542 339 20 40 01 1144 43 258 21 2407	= 1.97, df Events 1 24 1 2206 42 76 146 146 1 8 208 208 1 169	2777 32569 2777 325347 325669 2777 32569 2777 32569 2777 32569 2777 277 277 277 277 277 277 277 277 2	Odds Ratio	OR 13.75 0.33 6.72 6.87 0.55 5.79 2.68 4.02 0.26 3.77 6.00 9.28 9.66 2.06 2.06 2.06 3.876 3.06	[1.69; [0.12; [0.77; [6.06; [0.02; [5.06; [0.45; [0.18; [0.38; [2.21; [7.68; [1.17; [1.52] [2.08;	5.51] 0.37 7.79 13.69 7.79 13.69 6.52 15.86 15.86 15.86 15.86 15.86 15.86 15.86 15.86 15.86 15.86 15.86 15.86 15.86 15.86 15.86 16.31 16.31 16.31 11.22 79.42 2.79 72.08 13.47 11.22	(fixed) 0.2% 4.3% 0.2% 21.4% 0.3% 26.4% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 14.3% 0.2% 14.9% 0.2% 14.9% 0.2% 14.3% 0.2% 14.3% 0.2% 0.2% 26.4% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2% 0.2	(random) 5.8% 8.9% 5.6% 10.6% 3.5% - 34.3% 10.4% 5.3% 8.9% 10.5% 5.7% 10.4% 4.0%

**FIGURE 10 | (A)** Subgroup analysis by region of the risk of developing chronic hypertension in the PE group (1 = North and South America, 2 = Europe, 3 = Asia). **(B)** Subgroup analysis by publication year of the risk of developing chronic hypertension in the PE group (Group 1 = years < 2016, Group 2 = years  $\geq$  2016). **(C)** Subgroup analysis by the study design of the risk of developing chronic hypertension in the PE group.

The overall OR was 3.19 (95% CI 1.52–6.70;  $I_2 = 97\%$ ), and women with a history of PE had a greater risk of developing postpartum hypertension than women without PE. The increased risks in the Americas and Europe were similar to the overall risk (OR<sub>Americas</sub> 3.32, 95% CI<sub>America</sub> 1.26-8.74; OR<sub>Europe</sub> 2.19, 95% CI<sub>Europe</sub> 0.3-16.02), while the risk of developing chronic hypertension in Asia was significantly increased (OR 7.54, 95% CI 2.49-22.81) (Figure 10A). According to the analysis of the publication years, when the publication year was before 2016, the increase in the risk of developing chronic hypertension among patients with PE was significantly lower than that among patients included in studies with a publication year of 2016 or later (OR<sub><2016</sub> 1.54, 95% CI<sub><2016</sub> 0.28-8.44, OR<sub>>2016</sub> 5.53, 95% CI>2016 3.21-9.53) (Figure 10B). Grouped by study design, the OR value of the case-control group was 2.68 (95% CI 0.45, 15.86) and that of the cohort control group was 2.70 (95% CI 1.22, 11.22) (**Figure 10C**). The OR value of the NOS score  $\geq$  7 group was 2.15 (95% CI 0.7-6.64), and the OR of the other group was 6.88 (95% CI 6.07-7.80) (Figure 11A). According to sample size, the increase in the risk of developing chronic hypertension among PE patients was similar to that of the overall evaluation  $(OR_{<500} 4.05, 95\% CI_{<500} 1.12-14.69; OR_{\geq 500} 2.69, 95\% CI_{\geq 500}$ 0.97, 7.45) (Figure 11B).

## DISCUSSION

### **Principal Findings**

Our systematic review and meta-analysis comprehensively explored the associations of HDP, GH, and PE with chronic hypertension. We included 21 articles with a total of 634,293 patients. The results of this systematic review and meta-analysis suggested that women with a history of HDP are almost 3.6 times more likely to develop chronic hypertension than those without a history of HDP, women with a history of GH are almost 6.2 times more likely to develop chronic hypertension than those without a history of GH, and women with a history of PE are almost 3.2 times more likely to develop chronic hypertension than those without a history of PE. In addition, we further calculated the probability of developing chronic hypertension among patients with HDP or PE after adjusting for age and BMI at recruitment, prepregnancy BMI, age at first delivery and other factors. The results suggested that women with a history of HDP were almost 2.47 times more likely to develop chronic hypertension than those without a history of HDP and that women with a history of PE were almost 3.78 times more likely to develop chronic hypertension than those without a history of PE (Figure 12). The above results show that women with HDP are more likely to develop chronic hypertension and that those with GH are more likely to have PE. Therefore, patients with HDP should monitor their blood pressure more actively in the future and choose a healthy lifestyle, such as a low-salt and low-fat diet, to reduce the possibility of hypertension. One meta-analysis showed that subclinical hypothyroidism during pregnancy is associated with an increased risk of developing HDP, and this association is present regardless of the gestational period (42). Some studies have shown that BMI or maternal prepregnancy obesity and

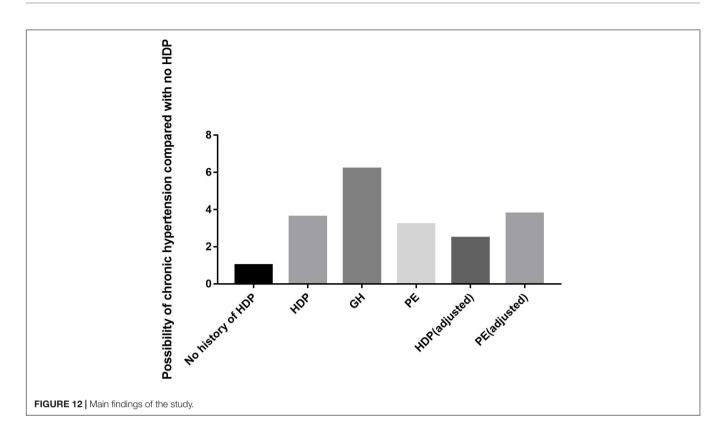
A Study	Events	PE Total	Events	Control Total	Odds Ratio	OR	95%-CI		Weight (random)
NOS_group = 1									
Amal G.Shammas 2000	11	47	1	46		13.75	[1.69; 111.56]	0.2%	5.8%
Chahinda Ghossein-Doha 2014	7	20	1	8			[0.38; 37.14]	0.2%	5.3%
Sajid Shahul 2018	7			25	<u> </u>	6.72		0.2%	5.6%
Mary Downes Gastrich 2019		6360		325347	+	6.87		21.4%	10.6%
Carmen Garrido-Gimenez 2020	14		1	21		9.66	[1.17; 79.42]	0.2%	5.7%
Fixed effect model	14	6502		325447	0	6.93	[6.09; 7.88]	22.3%	5.170
Random effects model		0002		323447	¢	6.88	[6.07; 7.80]	22.370	32.9%
Heterogeneity: $I^2 = 0\%$ , $\tau^2 = 0$ , $p = 0$	94				v	0.00	[0.07, 7.00]		32.970
notorogonouj., ovo, e o, p									
NOS_group = 2	007	540	70	077		1.00	10.04 E E 41	40 50/	40.40
Brenda J Wilson 2003	327			277	_ 1	4.02		10.5%	10.4%
Andrea G. Edlow 2009	5	79	24	140		0.33		4.3%	8.9%
Jose'T Drost 2011	57	339	146	332	+	0.26		32.4%	10.4%
Wendy M 2016	24	40	8	40			[2.21; 16.31]	0.8%	8.9%
Yu-Ling Kuo 2018		1144	208	5180	•		[7.68; 11.22]	14.3%	10.5%
Mariko Watanabe 2020	0		42	111			[0.02; 13.69]	0.3%	3.5%
Vesna D. Garovic 2020	118		169	582	+	2.06	[1.52; 2.79]	14.9%	10.4%
Victoria A. deMartelly 2021	9		0	25			[2.08; 720.98]	0.1%	4.0%
Fixed effect model		2424		6687	¢	2.88	[2.55; 3.26]	77.7%	
Random effects model					$\frown$	2.15	[0.70; 6.64]		67.1%
Heterogeneity: $I^2 = 98\%$ , $\tau^2 = 2.217$	7, p < 0.0	)1							
Fixed effect model		8926		332134		3.78	[3.43; 4.16]	100.0%	-
Random effects model					\	3.19	[1.52; 6.70]		100.0%
Heterogeneity: $I^2 = 97\%$ , $\tau^2 = 1.3475$		2 - 02	66 df - 1	(n < 0.01)	0.01 0.1 1 10 100				
Test for subgroup differences (fixed Test for subgroup differences (rand	om effec	$\chi_1 = \frac{93}{2}$ ts): $\chi_1^2$	= 4.04, df	= 1 (p = 0.01)	04)				
Test for subgroup differences (fixed Test for subgroup differences (rand B Study	om effec	ts): χ <sub>1</sub> <sup>2</sup> : <b>PE</b>	= 4.04, df	= 1 (p = 0. Control Total	Odds Ratio	OR	95%-CI		Weigh (random
Test for subgroup differences (rand B Study Samle_size_group = 1	om effec Events	ts): χ <sub>1</sub> = PE Total	= 4.04, df Events	= 1 (p = 0. Control Total	04)			(fixed)	(random
Test for subgroup differences (rand B Study Samle_size_group = 1 Amal G.Shammas 2000	om effec Events 11	ts): χ <sub>1</sub> <sup>2</sup> : PE Total 47	= 4.04, df <b>Events</b> 1	= 1 (p = 0. Control Total 46	04)	13.75	[1.69; 111.56]	(fixed)	(random 5.8%
Test for subgroup differences (rand B Study Samle_size_group = 1 Amal G.Shammas 2000 Andrea G. Edlow 2009	om effec Events 11 5	ts): χ <sub>1</sub> <sup>2</sup> = <b>PE</b> <b>Total</b> 47 79	= 4.04, df Events 1 24	= 1 (p = 0. Control Total 46 140	04)	13.75 0.33	[1.69; 111.56] [0.12; 0.89]	(fixed) 0.2% 4.3%	(random 5.8% 8.9%
Test for subgroup differences (rand B Study Samle_size_group = 1 Amal G.Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014	om effec Events 11 5 7	ts): χ <sub>1</sub> <sup>2</sup> = <b>PE</b> <b>Total</b> 47 79 20	= 4.04, df Events 1 24 1	= 1 ( <i>p</i> = 0. <b>Control</b> <b>Total</b> 46 140 8	04)	13.75 0.33 3.77	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14]	(fixed) 0.2% 4.3% 0.2%	(random 5.8% 8.9% 5.3%
Test for subgroup differences (rand B Study Samle_size_group = 1 Amal G.Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016	om effec Events 11 5 7 24	ts): χ <sub>1</sub> <sup>2</sup> <b>PE</b> <b>Total</b> 47 79 20 40	= 4.04, df Events 1 24 1 8	= 1 ( <i>p</i> = 0. <b>Control</b> <b>Total</b> 46 140 8 40	04)	13.75 0.33 3.77 6.00	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31]	(fixed) 0.2% 4.3% 0.2% 0.8%	(random 5.8% 8.9% 5.3% 8.9%
Test for subgroup differences (rand B Study Samle_size_group = 1 Amal G.Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018	om effec Events 11 5 7 24 7	ts): χ <sub>1</sub> <sup>2</sup> <b>PE</b> <b>Total</b> 47 79 20 40 32	= 4.04, df Events 1 24 1 8 1	= 1 (p = 0. <b>Control</b> <b>Total</b> 46 140 8 40 25	04)	13.75 0.33 3.77 6.00 6.72	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31] [0.77; 58.79]	(fixed) 0.2% 4.3% 0.2% 0.8% 0.2%	(random 5.8% 8.9% 5.3% 8.9% 5.6%
Test for subgroup differences (rand B Study Samle_size_group = 1 Amal G.Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018 Carmen Garrido-Gimenez 2020	om effec Events 11 5 7 24 7 14	ts): χ <sub>1</sub> <sup>2</sup> <b>PE</b> <b>Total</b> 47 79 20 40 32 43	= 4.04, df Events 1 24 1 8 1 1	= 1 (p = 0. <b>Control</b> <b>Total</b> 46 140 8 40 25 21	04)	13.75 0.33 3.77 6.00 6.72 9.66	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31] [0.77; 58.79] [1.17; 79.42]	(fixed) 0.2% 4.3% 0.2% 0.8% 0.2% 0.2%	(random 5.8% 8.9% 5.3% 8.9% 5.6% 5.7%
Test for subgroup differences (rand B Study Samle_size_group = 1 Amal G.Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020	0m effec Events 11 5 7 24 7 14 0	ts): χ <sub>1</sub> <sup>2</sup> <b>PE</b> <b>Total</b> 47 79 20 40 32 43 1	= 4.04, df Events 1 24 1 8 1 1 42	= 1 (p = 0. Control Total 46 140 8 40 25 21 111	Odds Ratio	13.75 0.33 3.77 6.00 6.72 9.66 0.55	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31] [0.77; 58.79] [1.17; 79.42] [0.02; 13.69]	(fixed) 0.2% 4.3% 0.2% 0.8% 0.2% 0.2% 0.2% 0.3%	(random 5.8% 8.9% 5.3% 8.9% 5.6% 5.6% 5.7% 3.5%
Test for subgroup differences (rand B Study Samle_size_group = 1 Amal G.Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020 Victoria A. deMartelly 2021	om effec Events 11 5 7 24 7 14	ts): χ <sub>1</sub> <sup>2</sup> <b>PE</b> <b>Total</b> 47 79 20 40 32 43 1 21	= 4.04, df Events 1 24 1 8 1 1	= 1 (p = 0. <b>Control</b> <b>Total</b> 46 140 8 40 25 21 111 25	Odds Ratio	13.75 0.33 3.77 6.00 6.72 9.66 0.55 — 38.76	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31] [0.77; 58.79] [1.17; 79.42] [0.02; 13.69] [2.08; 720.98]	(fixed) 0.2% 4.3% 0.2% 0.8% 0.2% 0.2% 0.3% 0.1%	(random 5.8% 8.9% 5.3% 8.9% 5.6% 5.7%
Test for subgroup differences (rand <b>B</b> <b>Study</b> <b>Samle_size_group = 1</b> Amal G. Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020 Victoria A. deMartelly 2021 Fixed effect model	0m effec Events 11 5 7 24 7 14 0	ts): χ <sub>1</sub> <sup>2</sup> <b>PE</b> <b>Total</b> 47 79 20 40 32 43 1	= 4.04, df Events 1 24 1 8 1 1 42	= 1 (p = 0. Control Total 46 140 8 40 25 21 111	04)	13.75 0.33 3.77 6.00 6.72 9.66 0.55 — 38.76 2.64	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31] [0.77; 58.79] [1.17; 79.42] [0.02; 13.69] [2.08; 720.98] [1.69; 4.11]	(fixed) 0.2% 4.3% 0.2% 0.8% 0.2% 0.2% 0.2% 0.3%	(random 5.8% 8.9% 5.3% 8.9% 5.6% 5.7% 3.5% 4.0%
Test for subgroup differences (rand B Study Samle_size_group = 1 Amal G.Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020 Victoria A. deMartelly 2021	000 effect Events 11 5 7 24 7 14 0 9	ts): χ <sub>1</sub> <sup>2</sup> PE Total 47 79 20 40 32 43 1 21 283	= 4.04, df Events 1 24 1 8 1 1 42	= 1 (p = 0. <b>Control</b> <b>Total</b> 46 140 8 40 25 21 111 25	Odds Ratio	13.75 0.33 3.77 6.00 6.72 9.66 0.55 — 38.76 2.64	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31] [0.77; 58.79] [1.17; 79.42] [0.02; 13.69] [2.08; 720.98]	(fixed) 0.2% 4.3% 0.2% 0.8% 0.2% 0.2% 0.3% 0.1% 6.4%	(random 5.8% 8.9% 5.3% 8.9% 5.6% 5.6% 5.7% 3.5%
Test for subgroup differences (rand B Study Samle_size_group = 1 Amal G. Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020 Victoria A. deMartelly 2021 Fixed effect model Random effects model Heterogeneity: J <sup>2</sup> = 75%, τ <sup>2</sup> = 2.3278	000 effect Events 11 5 7 24 7 14 0 9	ts): χ <sub>1</sub> <sup>2</sup> PE Total 47 79 20 40 32 43 1 21 283	= 4.04, df Events 1 24 1 8 1 1 42	= 1 (p = 0. <b>Control</b> <b>Total</b> 46 140 8 40 25 21 111 25	Odds Ratio	13.75 0.33 3.77 6.00 6.72 9.66 0.55 — 38.76 2.64	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31] [0.77; 58.79] [1.17; 79.42] [0.02; 13.69] [2.08; 720.98] [1.69; 4.11]	(fixed) 0.2% 4.3% 0.2% 0.8% 0.2% 0.2% 0.3% 0.1% 6.4%	(random 5.8% 8.9% 5.3% 8.9% 5.6% 5.7% 3.5% 4.0%
Test for subgroup differences (rand <b>B</b> <b>Study</b> <b>Samle_size_group = 1</b> Amal G. Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020 Victoria A. deMartelly 2021 Fixed effect model Random effects model Heterogeneity: $I^2 = 75\%$ , $\tau^2 = 2.3278$ <b>Samle_size_group = 2</b>	000 effect Events 11 5 7 24 7 14 0 9	ts): χ <sub>1</sub> <sup>2</sup> = <b>PE</b> <b>Total</b> 47 79 20 40 32 43 1 21 283 01	= 4.04, df Events 1 24 1 8 1 1 42	= 1 (p = 0. <b>Control</b> <b>Total</b> 46 140 8 40 25 21 111 25 416	Odds Ratio	13.75 0.33 3.77 6.00 6.72 9.66 0.55 — 38.76 2.64	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31] [0.77; 58.79] [1.17; 79.42] [0.02; 13.69] [2.08; 720.98] [1.69; 4.11] [1.12; 14.69]	(fixed) 0.2% 4.3% 0.2% 0.2% 0.2% 0.3% 0.1% 6.4%	(random 5.8% 8.9% 5.3% 8.9% 5.6% 5.7% 3.5% 4.0%
Test for subgroup differences (rand <b>B</b> <b>Study</b> Samle_size_group = 1 Amal G.Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020 Victoria A. deMartelly 2021 Fixed effect model Random effects model Heterogeneity: $l^2 = 75\%$ , $\tau^2 = 2.3278$ Samle_size_group = 2 Brenda J Wilson 2003	24 5 7 24 7 14 0 9 8, ρ < 0.0	ts): χ <sub>1</sub> <sup>2</sup> = <b>PE</b> <b>Total</b> 47 79 20 40 32 43 1 21 283 01 542	= 4.04, df Events 1 24 1 8 1 1 42 0	= 1 (p = 0. <b>Control</b> <b>Total</b> 46 140 8 40 25 21 111 25	Odds Ratio	13.75 0.33 3.77 6.00 6.72 9.66 0.55 — 38.76 2.64 4.05	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31] [0.77; 58.79] [1.17; 79.42] [0.02; 13.69] [1.69; 4.11] [1.12; 14.69] [2.94; 5.51]	(fixed) 0.2% 4.3% 0.2% 0.2% 0.2% 0.3% 0.1% 6.4%	(random 5.8% 8.9% 5.3% 8.9% 5.6% 5.7% 3.5% 4.0% 4.0% 47.6%
Test for subgroup differences (rand <b>B</b> <b>Study</b> <b>Samle_size_group = 1</b> Amal G. Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020 Victoria A. deMartelly 2021 Fixed effect model Random effects model Heterogeneity: $I^2 = 75\%$ , $\tau^2 = 2.3278$ <b>Samle_size_group = 2</b>	om effec <b>Events</b> 11 5 7 24 7 14 0 9 B, p < 0.0 327 57	ts): χ <sub>1</sub> <sup>2</sup> = <b>PE</b> <b>Total</b> 47 79 20 40 32 43 1 21 283 01 542	= 4.04, df <b>Events</b> 1 24 1 8 1 42 0 76	= 1 (p = 0. <b>Control</b> <b>Total</b> 46 140 8 40 25 21 111 25 416 277	Odds Ratio	13.75 0.33 3.77 6.00 6.72 9.66 0.55 - 38.76 2.64 4.05	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31] [0.77; 58.79] [1.17; 79.42] [0.02; 13.69] [2.08; 720.98] [1.69; 4.11] [1.12; 14.69] [2.94; 5.51] [0.18; 0.37]	(fixed) 0.2% 4.3% 0.2% 0.2% 0.2% 0.2% 0.1% 6.4% 	(random 5.8% 8.9% 5.3% 8.9% 5.6% 5.6% 5.6% 3.5% 4.0% - 47.6%
Test for subgroup differences (rand <b>B</b> <b>Study</b> <b>Samle_size_group = 1</b> Amal G. Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018 Carmen Garrido-Gimenez 2020 Victoria A. deMartelly 2021 Fixed effect model Random effects model Heterogeneity: $t^2 = 75\%$ , $\tau^2 = 2.3276$ <b>Samle_size_group = 2</b> Brenda J Wilson 2003 Jose'T Drost 2011 Yu-Ling Kuo 2018 Mary Downes Gastrich 2019	events 11 5 7 24 7 14 0 9 8, p < 0.0 327 57 320	ts): χ <sub>1</sub> <sup>2</sup> = <b>PE</b> <b>Total</b> 47 79 20 40 32 40 32 41 21 283 1 542 339	= 4.04, df Events 1 24 1 8 1 4 20 76 146 2206	= 1 (p = 0. <b>Control</b> <b>Total</b> 46 140 8 40 25 21 111 111 25 416 277 332 5180 325347	Odds Ratio	13.75 0.33 3.77 6.00 6.72 9.66 0.66 2.64 4.05 4.05	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31] [0.77; 58.79] [1.17; 79.42] [0.02; 13.69] [2.08; 720.98] [1.69; 4.11] [1.12; 14.69] [2.94; 5.51] [0.18; 0.37] [7.68; 11.22] [6.06; 7.79]	(fixed) 0.2% 4.3% 0.2% 0.2% 0.2% 0.3% 0.1% 6.4% 10.5% 32.4% 14.3%	(random 5.8% 8.9% 5.3% 8.9% 5.7% 3.5% 4.0% 47.6%
Test for subgroup differences (rand <b>B</b> <b>Study</b> Samle_size_group = 1 Amal G.Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020 Victoria A. deMartelly 2021 Fixed effect model Random effects model Heterogeneity: $l^2 = 75\%$ , $\tau^2 = 2.3278$ Samle_size_group = 2 Brenda J Wilson 2003 JoseT Drost 2011 Yu-Ling Kuo 2018 Mary Downes Gastrich 2019 Vesna D. Garovic 2020	om effec <b>Events</b> 111 57 24 7 14 0 9 8, p < 0.0 327 57 320 285	τs): χ1         τ           PE         Total           47         79           20         40           32         43           1         21           283         11           542         339           114         6360           6360         258	= 4.04, df Events 1 24 1 8 1 42 0 76 146 208	= 1 (p = 0. <b>Control</b> <b>Total</b> 46 140 8 40 25 21 111 25 416 277 332 5180 325347 582	Odds Ratio	13.75 0.33 3.77 6.00 9.66 0.55 - 38.76 2.64 4.05 4.02 0.26 9.28	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31] [0.77; 58.79] [1.17; 79.42] [0.02; 13.69] [1.08; 720.98] [1.69; 4.11] [1.12; 14.69] [2.94; 5.51] [0.18; 0.37] [7.68; 11.22] [6.06; 7.79] [1.52; 2.79]	(fixed) 0.2% 4.3% 0.2% 0.2% 0.2% 0.3% 0.1% 6.4% 	(random 5.8% 8.9% 5.3% 8.9% 5.6% 5.7% 3.5% 4.0% - 47.6%
Test for subgroup differences (rand <b>B</b> <b>Study</b> Samle_size_group = 1 Amal G.Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020 Victoria A. deMartelly 2021 Fixed effect model Heterogeneity: $I^2 = 75\%$ , $\tau^2 = 2.3276$ <b>Samle_size_group = 2</b> Brenda J Wilson 2003 Jose'T Drost 2011 Yu-Ling Kuo 2018 Mary Downes Gastrich 2019 Vesna D. Garovic 2020 Fixed effect model	om effec <b>Events</b> 111 57 24 7 14 0 9 8, p < 0.0 327 57 320 285	s): χ1         τ           PE         Total           47         79           20         43           41         21           283         11           542         339           1144         6360	= 4.04, df Events 1 24 1 8 1 4 20 76 146 2206	= 1 (p = 0. <b>Control</b> <b>Total</b> 46 140 8 40 25 21 111 111 25 416 277 332 5180 325347	Odds Ratio	13.75 0.33 3.77 6.00 6.72 9.66 0.55 2.64 4.05 4.05 4.02 0.26 9.28 6.87 2.06 3.86	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31] [0.77; 58.79] [1.17; 79.42] [0.02; 13.69] [2.08; 720.98] [1.69; 4.11] [1.12; 14.69] [2.94; 5.51] [0.18; 0.37] [7.68; 11.22] [6.06; 7.79] [1.52; 2.79] [3.50; 4.26]	(fixed) 0.2% 4.3% 0.2% 0.2% 0.2% 0.2% 0.3% 0.1% 3.4% 10.5% 32.4% 14.3% 21.4%	(random 5.8% 8.9% 5.3% 8.9% 5.6% 5.7% 3.5% 4.0% 47.6% 10.4% 10.4% 10.5% 10.6%
Test for subgroup differences (rand <b>B</b> <b>Study</b> <b>Samle_size_group = 1</b> Amal G.Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020 Victoria A. deMartelly 2021 Fixed effect model Random effects model Heterogeneity: $J^2 = 75\%$ , $\tau^2 = 2.3276$ <b>Samle_size_group = 2</b> Brenda J Wilson 2003 Jose'T Drost 2011 Yu-Ling Kuo 2018 Mary Downes Gastrich 2019 Vesna D. Garovic 2020 Fixed effect model Random effects model	om effec Events 11 5 7 24 7 14 0 9 8, p < 0.0 327 57 320 285 118	si:         χ1           PE         Total           47         79           20         40           32         41           21         21           283         11           542         339           1144         6360           258         8643	= 4.04, df Events 1 24 1 8 1 4 20 76 146 2206	= 1 (p = 0. <b>Control</b> <b>Total</b> 46 140 8 40 25 21 111 25 416 277 332 5180 325347 582	Odds Ratio	13.75 0.33 3.77 6.00 6.72 9.66 0.55 2.64 4.05 4.05 4.02 0.26 9.28 6.87 2.06	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31] [0.77; 58.79] [1.17; 79.42] [0.02; 13.69] [1.08; 720.98] [1.69; 4.11] [1.12; 14.69] [2.94; 5.51] [0.18; 0.37] [7.68; 11.22] [6.06; 7.79] [1.52; 2.79]	(fixed) 0.2% 4.3% 0.2% 0.2% 0.2% 0.3% 0.1% 6.4% 	(random 5.8% 8.9% 5.3% 8.9% 5.6% 5.7% 3.5% 4.0% 47.6%
Test for subgroup differences (rand <b>B</b> <b>Study</b> Samle_size_group = 1 Amal G.Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020 Victoria A. deMartelly 2021 Fixed effect model Random effects model Heterogeneity: $l^2 = 75\%$ , $\tau^2 = 2.3278$ <b>Samle_size_group = 2</b> Brenda J Wilson 2003 Jose'T Drost 2011 Yu-Ling Kuo 2018 Mary Downes Gastrich 2019 Vesna D. Garovic 2020 Fixed effect model Random effects model Heterogeneity: $l^2 = 99\%$ , $\tau^2 = 1.3268$	om effec Events 11 5 7 24 7 14 0 9 8, p < 0.0 327 57 320 285 118	ts): $\chi^{4}$ ; <b>PE</b> <b>Total</b> 47 79 20 40 32 43 1 283 11 283 11 542 339 114460 258 8643 11	= 4.04, df Events 1 24 1 8 1 4 20 76 146 2206	= 1 (p = 0. <b>Control</b> <b>Total</b> 46 140 8 40 25 21 111 25 416 277 332 5180 325347 582 331718	Odds Ratio	13.75 0.33 3.77 6.00 6.72 9.66 0.55 2.64 4.05 4.05 4.02 0.26 9.28 6.87 2.06 3.86	$      \begin{bmatrix} 1.69; 111.56 \\ [0.12; 0.89] \\ [0.38; 37.14] \\ [2.21; 16.31] \\ [0.77; 58.79] \\ [1.02; 13.69] \\ [1.02; 13.69] \\ [1.02; 13.69] \\ [1.02; 13.69] \\ [1.02; 13.69] \\ [1.12; 14.69] \\ \hline \\ \hline \\ \begin{bmatrix} 2.94; 5.51 \\ [0.18; 0.37] \\ [7.68; 11.22] \\ [6.06; 7.79] \\ [1.52; 2.79] \\ [3.50; 4.26] \\ [0.97; 7.45] \\ \hline           \end{bmatrix}     $	(fixed) 0.2% 4.3% 0.2% 0.2% 0.2% 0.3% 0.1% 6.4% 14.3% 21.4% 93.6%	(random 5.8% 8.9% 5.3% 8.9% 5.6% 5.7% 3.5% 4.0% 47.6% 10.4% 10.4% 10.5% 10.6%
Test for subgroup differences (rand <b>B</b> <b>Study</b> Samle_size_group = 1 Amal G.Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020 Victoria A. deMartelly 2021 Fixed effect model Heterogeneity: $l^2 = 75\%$ , $t^2 = 2.3276$ <b>Samle_size_group = 2</b> Brenda J Wilson 2003 Jose'T Drost 2011 Yu-Ling Kuo 2018 Mary Downes Gastrich 2019 Vesna D. Garovic 2020 Fixed effect model Random effects model Heterogeneity: $l^2 = 99\%$ , $t^2 = 1.3266$ <b>Fixed effect model</b>	om effec Events 11 5 7 24 7 14 0 9 8, p < 0.0 327 57 320 285 118	si:         χ1           PE         Total           47         79           20         40           32         41           21         21           283         11           542         339           1144         6360           258         8643	= 4.04, df Events 1 24 1 8 1 4 20 76 146 2206	= 1 (p = 0. <b>Control</b> <b>Total</b> 46 140 8 40 25 21 111 25 416 277 332 5180 325347 582	Odds Ratio	13.75 0.33 3.77 6.00 6.72 9.66 0.55 2.64 4.05 4.05 4.02 0.26 9.28 6.87 2.06 3.86 2.69 3.86 2.69	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31] [0.77; 58.79] [1.17; 79.42] [0.02; 13.69] [2.08; 720.98] [1.69; 4.11] [1.12; 14.69] [2.94; 5.51] [0.18; 0.37] [7.68; 11.22] [6.06; 7.79] [1.52; 2.79] [3.50; 4.26] [0.97; 7.45] [3.43; 4.16]	(fixed) 0.2% 4.3% 0.2% 0.2% 0.2% 0.3% 0.1% 6.4% 14.3% 21.4% 93.6%	(random 5.8% 8.9% 5.3% 5.6% 5.7% 3.5% 4.0% 10.4% 10.4% 10.4% 10.5% 10.6% 10.6%
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Test for subgroup differences (rand <b>B</b> <b>Study</b> Samle_size_group = 1 Amal G.Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018 Carmen Garrido-Gimenez 2020 Mariko Watanabe 2020 Victoria A. deMartelly 2021 Fixed effect model Random effects model Heterogeneity: $I^2 = 75\%$ , $\tau^2 = 2.3276$ Samle_size_group = 2 Brenda J Wilson 2003 Jose'T Drost 2011 Yu-Ling Kuo 2018 Mary Downes Gastrich 2019 Vesna D. Garovic 2020 Fixed effect model Random effects model Heterogeneity: $I^2 = 99\%$ , $\tau^2 = 1.3266$ <b>Fixed effect model</b> Random effects model Heterogeneity: $I^2 = 97\%$ , $\tau^2 = 1.3475$	om effect Events 11 5 7 24 7 14 0 9 3, p < 0.0 327 57 320 285 118 3, p < 0.0 3, p < 0.0 285 118 3, p < 0.0 3, p <	ts):         x <sub>1</sub> <sup>2</sup> ;           PE         Total           47         79           20         40           32         43           1         21           283         11           542         339           1144         6360           6258         8643           8926         11           2         2           2         2	= 4.04, df Events 1 24 1 42 1 42 0 76 146 208 2206 169 9, df = 1	= 1 (p = 0. Control Total 46 140 8 40 25 21 111 25 416 277 332 5180 32537 582 331718 332134 (p = 0.10)	Odds Ratio	13.75 0.33 3.77 6.00 6.72 9.66 0.55 2.64 4.05 4.05 4.02 0.26 9.28 6.87 2.06 3.86 2.69 3.86 2.69	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31] [0.77; 58.79] [1.17; 79.42] [0.02; 13.69] [2.08; 720.98] [1.69; 4.11] [1.12; 14.69] [2.94; 5.51] [0.18; 0.37] [7.68; 11.22] [6.06; 7.79] [1.52; 2.79] [3.50; 4.26] [0.97; 7.45] [3.43; 4.16]	(fixed) 0.2% 4.3% 0.2% 0.2% 0.2% 0.3% 0.1% 6.4% 14.3% 21.4% 93.6%	(random 5.8% 8.9% 5.3% 5.6% 5.7% 3.5% 4.0% 10.4% 10.4% 10.4% 10.5% 10.6% 10.6%
Test for subgroup differences (rand <b>B</b> <b>Study</b> <b>Samle_size_group = 1</b> Amal G.Shammas 2000 Andrea G. Edlow 2009 Chahinda Ghossein-Doha 2014 Wendy M 2016 Sajid Shahul 2018 Carmen Garrido-Gimenez 2020 Wictoria A. deMartelly 2021 Fixed effect model Random effects model Heterogeneity: $l^2 = 75\%$ , $\tau^2 = 2.3276$ <b>Samle_size_group = 2</b> Brenda J Wilson 2003 Jose'T Drost 2011 Yu-Ling Kuo 2018 Mary Downes Gastrich 2019 Vesna D. Garovic 2020 Fixed effect model Random effects model Heterogeneity: $l^2 = 99\%$ , $\tau^2 = 1.3266$ Fixed effect model Random effects model	om effect Events 11 5 7 24 7 14 0 9 3, p < 0.0 327 57 320 285 118 3, p < 0.0 3, p < 0.0 285 118 3, p < 0.0 3, p <	ts):         x <sub>1</sub> <sup>2</sup> ;           PE         Total           47         79           20         40           32         43           1         21           283         11           542         339           1144         6360           6258         8643           8926         11           2         2           2         2	= 4.04, df Events 1 24 1 42 1 42 0 76 146 208 2206 169 9, df = 1	= 1 (p = 0. Control Total 46 140 8 40 25 21 111 25 416 277 332 5180 32537 582 331718 332134 (p = 0.10)	Odds Ratio	13.75 0.33 3.77 6.00 6.72 9.66 0.55 2.64 4.05 4.05 4.02 0.26 9.28 6.87 2.06 3.86 2.69 3.86 2.69	[1.69; 111.56] [0.12; 0.89] [0.38; 37.14] [2.21; 16.31] [0.77; 58.79] [1.17; 79.42] [0.02; 13.69] [2.08; 720.98] [1.69; 4.11] [1.12; 14.69] [2.94; 5.51] [0.18; 0.37] [7.68; 11.22] [6.06; 7.79] [1.52; 2.79] [3.50; 4.26] [0.97; 7.45] [3.43; 4.16]	(fixed) 0.2% 4.3% 0.2% 0.2% 0.2% 0.3% 0.1% 6.4% 14.3% 21.4% 93.6%	(random 5.8% 8.9% 5.3% 5.6% 5.7% 3.5% 4.0% 10.4% 10.4% 10.4% 10.5% 10.6% 10.6%

abnormal gestational glucose metabolism are independently associated with an increased risk of HDP. Controlling these factors may reduce the occurrence of HDP (43, 44). Preventing or reducing the occurrence of HDP in pregnant women will inevitably reduce the probability of developing hypertension in the future. In terms of countries, women in Asian countries are more likely to develop chronic hypertension after HDP or PE,

while the relative risk in the Americans is not high. This may be related to race, medical level and economic conditions. We look forward to future research.

## **Comparison With Other Studies**

Our systematic review illustrates the risk of developing chronic hypertension among pregnant women with HDP, GH and PE.



Although the evidence linking pregnancy-induced hypertension with the development of hypertension has been recognized, there are still many outstanding problems in a number of specific aspects (45).

In 2007, a systematic review and meta-analysis showed that preeclampsia patients had more than three times the risk of developing hypertension (OR 3.70, 95% CI 2.70-5.05) than those without preeclampsia; the follow-up time was adjusted to 14.1 years (46). Subsequent studies did not adjust the followup years. A systematic review and meta-analysis in 2013 showed that women with a history of preeclampsia or eclampsia had more than three times the risk of developing hypertension (RR 3.13, 95% CI 2.51, 3.89) (14) than those without a history of preeclampsia or eclampsia. In 2016, Mayri Sagady Leslie reviewed 48 unique studies from 20 countries that included a total of 3,598,601 women, and found similar results (47). This outcome was consistent with ours. In 2018, L Brouwers' team found that recurrent preeclampsia was consistently associated with an increased pooled risk ratio for hypertension (RR 2.3; 95% CI 1.9-2.9) (48). The above articles all studied the relationship between preeclampsia and chronic hypertension, and few meta-analyses have directly studied the relationship between HDP or GH and chronic hypertension.

The advantage of our study is that a large number of articles were selected, and the sample size was large. We not only studied the possibility of HDP leading to chronic hypertension but also accounted for the relevant data on various types of HDP and finally chose to analyze the large amount of relevant data for PE and GH. We also performed subgroup analysis (publication year, study design, country, sample size and NOS score) to analyze the sources of heterogeneity and the probability of developing chronic hypertension in each subgroup. In addition, we further calculated the probability of developing chronic hypertension for patients with HDP or PE after adjusting for age and BMI at recruitment, prepregnancy BMI, age at first delivery and other factors. In general, we carried out statistical analysis on all aspects of the obtained data that could be analyzed.

However, there are still some limitations of this study, which need further study. There are few studies with high scores. The ages of patients with HDP and chronic hypertension were not statistically analyzed because the data were seriously lacking, which may be the reason for the high heterogeneity. The published literature is insufficient to determine the best screening period for postpartum detection of hypertension. We could not determine an observation age or follow-up period to limit the screening of the articles. The heterogeneity of the population and hypertension definitions and the failure to obtain sufficient details make the results of the metaanalysis misleading, and they could not be adjusted using statistical tests.

### CONCLUSION

HDP, GH, and PE increase the likelihood that patients will develop chronic hypertension. After adjustment for age and BMI at recruitment, prepregnancy BMI, age at first delivery and other factors, patients with HDP or PE were still more likely to develop chronic hypertension. HDP, GH, and PE may be risk factors for chronic hypertension, independent of other risk factors.

#### DATA AVAILABILITY STATEMENT

The original contributions presented in this study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

#### **AUTHOR CONTRIBUTIONS**

JX, TL, and YW: study design, data extraction, statistical analysis, and manuscript writing. LX, ZM,

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WL, and KX: study design, data extraction, and verification. CH and HD: study design, statistical analysis, manuscript editing and reviewing, and funding. All authors contributed to the article and approved the submitted version.

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