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Early pregnancy maternal blood pressure and risk of preeclampsia: Does the association differ by parity? Evidence from 14,086 women across 7 countries

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ABSTRACT

Objective: To determine if the relationship between blood pressure (BP) before 16 weeks' gestation and subsequent onset of preeclampsia differs by parity, and by history of hypertensive disorders of pregnancy (HDP) in parous women.

Study design: Data from two studies were pooled. First, routinely collected clinical data from three metropolitan hospitals in Sydney, Australia (2017–2020), where BP was measured as part of routine clinical care using validated mercury-free sphygmomanometers. Second, prospectively collected research data from the INTERBIO-21st Study, conducted in six countries, investigating the epidemiology of fetal growth restriction and preterm birth, where BP was measured by dedicated research staff using an automated machine validated for use in pregnancy.

Main outcome: Adjusted odds ratios (aOR) (95% confidence interval (CI)) for the association of systolic BP (SBP), diastolic BP (DBP) and mean arterial pressure (MAP) with preeclampsia were obtained from logistic regression models. Models were adjusted for age, smoking, body mass index, previous hypertension, previous diabetes, and previous preeclampsia. Interactions for parity, and history of HDP in parous women were included.

Results: There were 14,086 pregnancies (Sydney = 11008, INTERBIO-21st = 3078) in the pooled analyses, 6914 (49 %) were parous, of which 414 (6.0 %) had a history of HDP. Nulliparous women had a higher risk of preeclampsia (2.6 %) compared with parous women (1.5 %): [aOR (95 %CI) 3.61 (2.67, 4.94)], as did parous women with a history of HDP (15.0 %) compared with no history (0.7 %) [12.70 (8.02, 20.16)]. MAP before 16 weeks' gestation (mean [SD] 78.8[8.6] mmHg) was more strongly associated than SBP or DBP with development of preeclampsia in parous women [2.22 (1.81, 2.74)] per SD higher MAP] compared with nulliparous women [1.58 (1.34, 1.87)] (p for interaction 0.013). There were no significant differences on the effect of blood pressure on preeclampsia in parous women by history of HDP (p for interaction 0.5465).

Conclusion: The risk of preeclampsia differs according to parity and history of HDP in a previous pregnancy. Blood pressure in early pregnancy predicts preeclampsia in all groups, although more strongly associated in parous than nulliparous women, but no different in parous women by history of HDP.

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1. Introduction

Hypertensive disorders of pregnancy (HDP) encompasses pre-eclampsia, gestational hypertension, chronic hypertension, and pre-eclampsia superimposed on chronic pre-pregnancy hypertension, and affect approximately 5–10 % of pregnancies [22,36]. HDP are associated with increased risk of severe maternal and fetal morbidity and mortality [14], and preeclampsia is a leading cause of maternal mortality globally [34], leading to approximately 70,000 annual direct maternal deaths worldwide [11,25].

Preeclampsia is a multisystem disorder characterised by hypertension plus evidence of maternal organ dysfunction, including renal, haematological, hepatic and neurological dysfunction, and/or fetal growth restriction [5]. It is associated with increased risk of stillbirth, neonatal death, placental abruption and preterm birth. Preeclamptic women are at higher risk of cardiovascular, cerebrovascular, renal disease and diabetes in later life [3].

The risk of preeclampsia and its complications can be reduced by using low-dose aspirin [13]. There is heterogeneity in the timing of aspirin commencement studied. However, *meta*-analyses have shown that preeclampsia risk reduction is greater when aspirin is commenced before 16 weeks' gestation [26,27]. Thus, identifying women at high risk of preeclampsia before 16 weeks' gestation is vitally important, as it allows timely commencement of prophylactic aspirin [22,30]. Additionally, closer monitoring of high-risk women should facilitate earlier diagnosis and treatment of preeclampsia, thereby potentially improving maternal and perinatal outcomes [12,17,21].

Over the last two decades, there has been a plethora of preeclampsia prediction models [8]. However, those that only use maternal characteristics perform poorly, and comprehensive models using ultrasound measures and biomarkers are expensive and not universally accessible [16,32].

Elevated blood pressure (BP) in the first trimester of pregnancy identifies women at higher risk of preeclampsia [15,24], although mean arterial pressure (MAP) in the first and second trimester may be the more predictive measure. Studies on the predictive accuracy of BP measure type (systolic BP (SBP), diastolic BP (DBP) or some combination) have reported conflicting results [6,9]. Primiparity is associated with a higher risk of preeclampsia [11], although, to our knowledge, there is little evidence as to whether BP's effect on the risk of pre-eclampsia is different in nulliparous and parous women.

In the present study, we therefore aimed to determine: (i) the association between three BP measures (SBP, DBP and MAP at less than 16 weeks' gestation) and subsequent preeclampsia development and (ii) whether any association between those BP measures and risk of pre-eclampsia development differs by parity and by history of HDP in parous women.

2. Methods

2.1. Study population

Data from two studies were pooled. The first dataset comes from a multi-ethnic cohort of women who received antenatal care and gave birth from 20 weeks' gestation at one of three metropolitan hospitals in Sydney, Australia (March 2017- June 2020) (Sydney Study). Data were extracted from the 'eMaternity' database, which holds the records of maternal history, antenatal visits, delivery details, and maternal and neonatal complications. Patient information in the 'eMaternity' database was entered by midwives and doctors with prompting and standard definitions for clinical measures ensuring high quality data. Microsoft Office Excel was used to compile extracted data. Data were de-identified prior to statistical analysis.

The second dataset comes from the INTERBIO-21st Fetal Study (Phase II of the INTERGROWTH-21st Project). A detailed description of the INTERBIO-21st study is provided elsewhere [9]; (Kennedy et al., 2018; Villar et al., 2021). In brief, the study, conducted in six sites, Pelotas (Brazil), Nairobi (Kenya), Karachi (Pakistan), Soweto (South Africa), Mae Sot (Thailand) and Oxford (UK), aimed to improve the functional classification of the highly heterogenous preterm birth and fetal growth restriction syndromes. The women were enrolled irrespective of their risk profile for adverse pregnancy/neonatal outcomes but included many at high risk for fetal growth and preterm birth, especially in the resource-poor settings because of malnutrition and/or infection (HIV and malaria). The only inclusion criteria at study entry were: maternal age $\geq$ 18 years, body mass index (BMI) $<$ 35 kg/m^2 (to facilitate ultrasound scanning of the fetus), natural conception, and singleton pregnancy.

2.2. Blood pressure measurements

Sydney Study: SBP and DBP were measured and recorded in the 'eMaternity' database at booking visit as part of routine clinical care. All three hospitals use validated mercury-free sphygmomanometers for BP measurement, with varied cuff sizes available for use as appropriate. INTERBIO-21st Study: SBP and DBP were measured at booking visit by dedicated research staff using an automated machine validated for use in pregnancy (Microlife Blood Pressure Monitor for Pregnant Women, Microlife USA, Inc., Florida, USA) with an appropriately sized cuff on the right arm. In the present study inclusion criteria were singleton pregnancy and for women to have their booking visit with a BP recording before 16 weeks' gestation.

2.3. Outcome

Sydney Study: Preeclampsia was defined as BP $\geq$ 140/90 mmHg after 20 weeks' gestation accompanied by at least one of: renal, liver, haematological or neurological dysfunction, pulmonary oedema, and/or fetal growth restriction as per the SOMANZ Hypertension in Pregnancy Guideline [31]. Pregnancy induced hypertension (PIH) was diagnosed in women with de novo hypertension, BP $\geq$ 140/90 mmHg, after 20 weeks' gestation without maternal or fetal features of preeclampsia [31].

INTERBIO 21st Study: Preeclampsia was broadly defined as BP $\geq$ 140/90, or an increase of 30 mmHg systolic or 15 mmHg diastolic over baseline values, on at least two occasions $\geq$ 6 h apart after 20 weeks' gestation, combined with proteinuria (defined as $\geq$ 2 + on dipstick or $\geq$ 300 mg/dL), in a previously normotensive pregnancy. PIH was defined as BP $\geq$ 140/90 mmHg measured on at least two occasions after 20 weeks' gestation in a previously normotensive pregnancy.

2.4. Statistical analyses

Baseline (booking visit) maternal and pregnancy characteristics were summarised by parity status, where women were defined as (1) as nulliparous (primigravidae) if they had not previously given birth, or (2) parous if they had previously given birth, where birth was defined as delivery of a baby (alive or dead) at $\geq$ 20 weeks' gestation.

We first modelled the association of booking SBP, DBP and MAP in women overall in the two studies, per standard deviation (SD) higher, with preeclampsia. MAP was calculated as: DBP + 1/3(SBP – DBP) [10]. Estimates per SD higher in each BP parameter were obtained by dividing the respective BP measure by its SD and fitting models with the BP per SD measures. Odds ratios (OR) with 95 % confidence intervals (CIs) were obtained from logistic regression models. Three sets of model adjustment were applied: (1) unadjusted models, (2) adjusted for parity only, (3) multiple adjusted for preselected covariates parity, age, smoking, BMI, previous hypertension, previous diabetes, previous pre-eclampsia (in parous women), week of first BP measurement and study. The BP parameter that yielded the 'best fitting' models was determined using the model with the lowest Akaike Information Criterion (AIC) [1]. AIC is used for model selection based on assessing goodness of fit and parsimony in the model structure relative to other models in the same

data. From the multiple adjusted models, we also extracted the coefficients for risk of preeclampsia by parity (nulliparous vs parous), and also age, smoking, BMI, previous hypertension, previous diabetes, and previous preeclampsia (in parous women).

The association of BP with preeclampsia was then explored by parity status, where an interaction for parity was included (in contrast to models adjusted for parity as described above) to enable comparison of BP coefficients between parous and nulliparous women via (parous vs nulliparous) ratio of ORs (ROR) (95 %CI) [35]. Two model specifications were applied: (1) unadjusted and (2) multiple adjusted for: age, smoking, BMI, previous hypertension, previous diabetes, previous preeclampsia (in parous women), week of first BP measurement and study. The effect of the aforementioned covariates on preeclampsia were also presented by parity status.

2.5. Sensitivity analyses

A series of sensitivity analyses were conducted. First, we conducted the analyses for association of BP and risk of preeclampsia in parous women with and without a history of HDP, and tested for an interaction effect to determine if the effect of BP on preeclampsia was different in women by history of HDP, models were adjusted for age, smoking, BMI, previous diabetes, week of first BP measurement and study. Next, baseline characteristics and the analyses for association of BP and preeclampsia by parity were conducted separately by study (Sydney and INTERBIO-21st). As a further sensitivity analysis, we also adjusted for aspirin status in the INTERBIO 21st study and compared to the results unadjusted for aspirin status. This information was not collected in the Sydney study.

Furthermore, two specifications were considered for the outcome: women with PIH were either excluded from the analysis (primary outcome), or were included as no event (secondary outcome). For the secondary outcome, the association of BP parameters, overall and by parity status, on new onset preeclampsia were run as a sensitivity analyses.

Finally, post hoc analyses were conducted to account for the small percentage (2.7 %) of women that appear in the dataset for multiple different pregnancies during the study. Two different approaches were used to extract the multiple adjusted OR's (95 %CI's) for BP parameters overall and by parity status. First generalized linear mixed effects models under maximum likelihood using adaptive Gaussian quadrature were used to account for multiple different pregnancies within women during the study. Second, women with multiple different pregnancies during the study were excluded and logistic regression models were fit as previously described. All analyses were performed in R Studio Version 4.3.1 (R Core Team, 2023).

3. Results

3.1. Baseline characteristics

A total of 14,086 singleton pregnancies (13710 women) (49 % parous) were included in the analysis of the pooled datasets, (INTERBIO-21st = 3078 pregnancies (3053 women), Sydney = 11008 pregnancies (10657 women)). The mean (SD) age of participants was 31.1 (5.0) years for nulliparous women and 33.3 (4.8) years for parous women (Table 1). Of the 6914 parous women 414 (6.0 %) had a history of HDP, comprising a previous diagnosis of chronic hypertension and/or prior preeclampsia, eclampsia or HELLP. Timing of first visit BP measurements (median (min, max)) were similar between parous 13 (5,15) and nulliparous 14 (5,15) women. Overall mean (SD) first visit BP measurements were: SBP 105.7 (11.5) mmHg, DBP 65.3 (8.3), MAP 78.8 (8.6). Of the 14,086 pregnancies, 295 (2.1 %) developed new onset preeclampsia (nulliparous = 2.6 %, parous = 1.5 %) and 616 (4.4 %) developed PIH (nulliparous = 5.0 %, parous = 3.7 %). In parous women with a history of HDP 15 % developed new onset preeclampsia and 23 % pregnancy induced hypertension, compared with parous women with no history of HDP in which 0.7 % developed new onset preeclampsia and 2.5 % pregnancy induced hypertension (Supplementary Table 1).

Table 1
Baseline (booking visit) characteristics of women/pregnancies by parity status.

	Nulliparous	Parous	Overall
N pregnancies*	***7172***	***6914***	***14,086***
INTERBIO-21st study n(%)	*1257*	*1821*	*3078*
Sydney study n(%)	*5915*	*5093*	*11,008*
Age (years), mean (SD)	31.1 (5.0)	33.3 (4.8)	32.2 (5)
Smokers, n(%)	325 (4.5)	347 (5.0)	672 (4.8)
BMI (kg/m^2), mean (SD)	23.5 (4.2)	24.5 (4.8)	24.0 (4.5)
Parity, median (min, max)	NA	1 (1,11)	0 (0, 11)
History of HDP**	NA	414 (6.0)	414 (2.9)
Previous diagnosis of chronic hypertension, n(%)	*67 (0.9)*	*155 (2.2)*	*222 (1.6)*
Prior preeclampsia, eclampsia or HELLP (if parous), n(%)	*NA*	*300 (4.3)*	*300 (2.1)*
Previous diagnosis of type 1 or type 2 diabetes, n(%)	33 (0.5)	85 (1.2)	118 (0.8)
Prior gestational diabetes, (if parous) n (%)	NA	588 (8.5)	588 (4.2)
Booking visit blood pressure			
Systolic (mmHg), *mean (SD)*	105.7 (11.2)	105.7 (11.8)	105.7 (11.5)
Diastolic (mmHg), *mean (SD)*	65.0 (8.0)	65.35 (8.5)	65.3 (8.3)
Mean arterial pressure (mmHg), mean (SD)	78.6 (8.3)	78.9 (8.8)	78.8 (8.6)
Timing (week), median (min, max)	14 (5,15)	13 (5,15)	13 (5,15)

Footnote: min – minimum, max – maximum, SD standard deviation, HELLP (haemolysis, elevated liver enzymes, low platelet count) syndrome.
* The dataset comprises 14,086 pregnancies in 13,710 women (13335 had one pregnancy and 375 women had multiple pregnancies – 374 had two pregnancies and 1 had three pregnancies).
**We define a history of HDP as: previous diagnosis of chronic hypertension and/or prior preeclampsia, eclampsia or HELLP (n = 414), whereby 155 parous women had a previous diagnosis of chronic hypertension and 300 had prior preeclampsia, eclampsia or HELLP – such that 114 had a previous diagnosis of chronic hypertension (alone), 259 had prior preeclampsia, eclampsia or HELLP (alone) and 41 parous women had both.

3.2. Association of BP at booking and preeclampsia

Higher BP at booking was associated with increased risk of preeclampsia. In unadjusted models the OR (95 %CI) for MAP per SD higher was 2.35 (2.12, 2.61); corresponding results for SBP and DBP were 2.16 (1.94, 2.40) and 2.21 (1.99, 2.45), respectively (Fig. 1).

After adjustment for parity, age, smoking, BMI, previous hypertension, previous diabetes, previous preeclampsia (in parous women), week of first BP measurement and study. MAP yielded the best fitting model according to the AIC compared to SBP and DBP: MAP (per SD higher) was associated with a more than 70 % higher risk of preeclampsia: aOR (95 %CI) 1.77 (1.56, 2.01); corresponding results for SBP and DBP were 1.63 (1.44, 1.85) and 1.67 (1.48, 1.89), respectively (Fig. 1).

3.3. Association of parity and other covariates with preeclampsia

Nulliparous women were over three times as likely to develop preeclampsia compared to parous women (aOR (95 %CI)) 3.61 (2.67, 4.94) (adjusted for MAP, age, smoking, BMI, previous hypertension, previous diabetes, previous preeclampsia (in parous women), week of first BP measurement and study). However, parous women with previous preeclampsia had a higher risk of new onset preeclampsia compared with women without previous preeclampsia aOR (95 %CI) 6.17 (3.72, 10.01) (Supplementary Fig. 1).

In terms of other covariates, per unit higher BMI aOR (95 %CI) (1.04

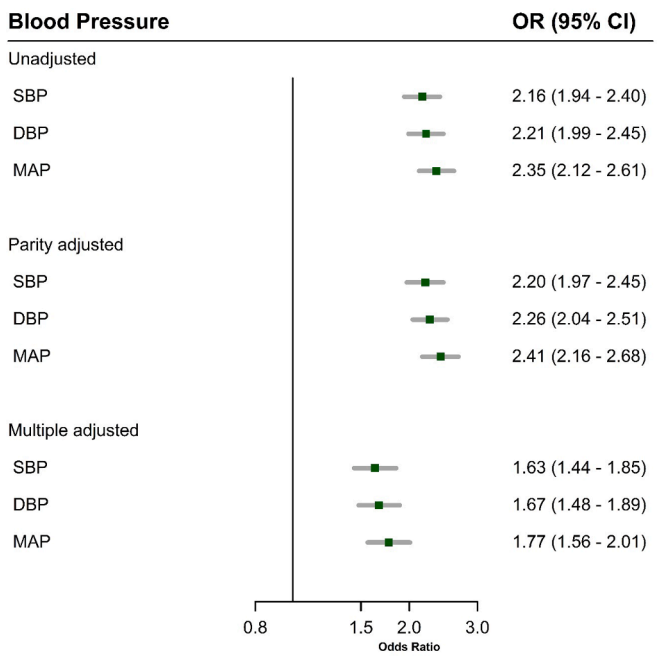

Fig. 1. Association of blood pressure (SBP, DBP and MAP) per standard deviation higher with preeclampsia. Footnote: Multiple adjusted models adjusted for parity, age, smoking, BMI, previous hypertension, previous diabetes, and previous preeclampsia (for parous women), week of first BP measurement and study. Akaike Information Criterion (AIC) for multiple adjusted models were: 2406.25 for SBP model, 2401.20 for DBP model, and 2388.45 for MAP model. OR: Odds Ratio, CI: Confidence interval, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP).

(1.01, 1.07)) and previous hypertension (10.54 (6.81, 10.01)) were associated with a higher risk of new onset preeclampsia. Age, smoking and diabetes were not associated with new onset preeclampsia.

3.4. Association of BP and preeclampsia by parity

Whilst parous women were at lower risk of preeclampsia overall, in those with higher BP at first visit the risk of preeclampsia was greater than in nulliparous women, ROR (95 %CI) 1.40 (1.08, 1.83) (p for interaction = 0.013). For every SD higher in MAP at booking, the aOR (95 %CI) for preeclampsia was 2.22 (1.81, 2.74) in parous and 1.58 (1.34, 1.87) in nulliparous women (Fig. 2). Furthermore, there were no differences in the association of other covariates (age, smoking, BMI, previous hypertension, or previous diabetes) and new onset pre-eclampsia between parous and nulliparous women (Supplementary Table 2).

3.5. Sensitivity analyses

3.5.1. Association of MAP and preeclampsia in parous women by history of HDP

In parous women, a history of HDP was associated with a greater risk of preeclampsia than in parous women with no history of HDP (aOR (95 %CI) 12.70 (8.02, 20.16). In parous women with no history of HDP the adjusted OR (95 %CI) per SD higher in MAP was 2.36 (1.72, 3.25) compared with 2.08 (1.60, 2.75) in women with a history of HDP (p for interaction 0.5465).

3.5.2. Stratified analysis by study

There were some differences in baseline characteristics by study, such that women from the Sydney study were older, mean (SD) 33 years (4.6) compared with 29.3 years (4.3) in INTERBIO-21st. Women in INTERBIO-21st had a higher (mean (SD)) baseline SBP mmHg (111.0 (12.4)) than women in the Sydney study 104.2 (10.8). (Supplementary Table 3). The median week of first BP measurement was 14 weeks in the Sydney study, and 12 weeks in INTERBIO-21st (Supplementary Fig. 2). However, the results for the association of BP and preeclampsia by parity were similar when conducted separately by study (Supplementary Table 4). Furthermore, results from INTERBIO-21st were much the same from models with and without aspirin prescription as an adjustment covariate.

3.6. Alternative outcome specification

Including women with PIH as no events, rather than excluding them, yielded broadly similar, albeit attenuated, results (Supplementary Table 5 and 6).

3.7. Accounting for multiple different pregnancies within women during the study

Both the mixed effects estimates and analyses excluding 375 women with multiple different pregnancies during the study showed comparable results to the primary analyses (Supplementary Table 7).

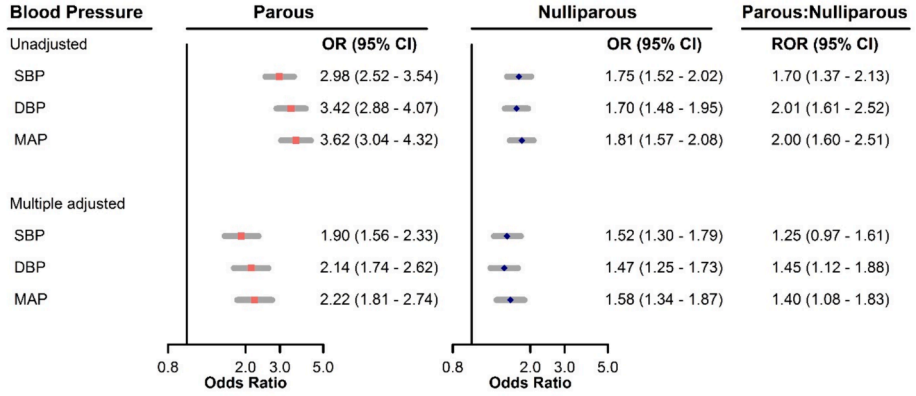

Fig. 2. Association of blood pressure (SBP, DBP and MAP) per standard deviation higher with preeclampsia, by parity. Footnote: Multiple adjusted models adjusted for age, smoking, BMI, previous hypertension, previous diabetes, and previous preeclampsia (for parous women), week of first BP measurement and study. Akaike Information Criterion (AIC) for unadjusted models were: 2605.15 for SBP, 2562.92 for DBP, and 2533.54 for MAP. Corresponding AIC values for multiple adjusted models were 2405.55, 2394.62, 2382.71. P values for interaction from unadjusted models between parous and nulliparous for all BP parameters were all < 0.001, and from multiple adjusted were 0.090, 0.005, and 0.013 for SBP, DBP and MAP respectively. OR: Odds Ratio, ROR: Ratio of odds ratios, CI: Confidence interval, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP) and Mean Arterial Pressure (MAP).

4. Discussion

In this multi-ethnic, multi-national cohort, we sought to quantify the effect of BP, whilst accounting for relevant confounders, on new onset preeclampsia and determine whether the effect of BP on the risk of preeclampsia was different by parity status and by history of HDP in parous women. We demonstrated that higher MAP, measured at the first antenatal visit before 16 weeks' gestation, was associated with subsequent development of preeclampsia, and this association was stronger in parous women. However, there were no differences on the effect of MAP on the risk of preeclampsia within parous women by history of HDP status. Furthermore, whilst the association of parity with preeclampsia is well recognised, to our knowledge, BP differences by parity have not been extensively investigated. Our findings suggest that parous women, who are often assumed to be at lower risk if they did not have preeclampsia in their first pregnancy, may have specific risk factors.

Understanding the mechanisms why BP predicts the onset of preeclampsia better in parous than nulliparous women is important. A recent study has revealed parity-specific differences in maternal haemodynamics including cardiac output and peripheral vascular resistance [19]. Parous women without history of preeclampsia and/or small for gestational age (SGA) had higher cardiac output and lower peripheral vascular resistance compared to nulliparous women. Meanwhile, compared to low-risk parous and nulliparous women, parous women with a history of preeclampsia and/or SGA had higher cardiac output and lower peripheral vascular resistance in the first trimester [19]. It is possible these underlying physiological differences may contribute to our findings.

Our study reaffirmed that higher early pregnancy BP is associated with greater risk of preeclampsia, as reported previously [6,7]. Varied gestational age ranges within early pregnancy have been explored. We focused on BP before 16 weeks' gestation to apply the results clinically, i.e. to maximise the opportunity to prescribe prophylactic aspirin for optimal prevention of early onset preeclampsia [22,28]. However, within the present study we were unable to stratify analyses by prophylactic aspirin prescription since data were not consistently collected between the Sydney study and INTERBIO-21st. Furthermore, the median week of first BP measurement was 14 weeks in the Sydney study, and 12 weeks in INTERBIO-21, which may suggest that the potential for prophylactic aspirin prescription could be earlier than 16 weeks [30,33].

There were also differences between studies in terms of the device used to measure BP, such that validated mercury-free sphygmomanometers were used in the Sydney study, and an automated machine validated for use in pregnancy was used in INTERBIO-21st which may bring in some bias since automatically vs manually measured blood pressures cannot be used interchangeably [20,29]. However, both methods and devices were validated for measurement of BP in pregnancy [22,31], and after adjusting for study and week of first BP measurement, as well as conducting stratified analyses by study, the association of BP with new onset preeclampsia remained consistent.

We found that MAP before 16 weeks' gestation was the better predictor of preeclampsia in both crude and multiple adjusted models, supporting Cnossen et al.'s conclusions from their *meta*-analysis of 34 studies. They showed that MAP in the first and second trimester was the superior predictor for preeclampsia compared to SBP or DBP among "low-risk" women. However, in contrast to our findings, DBP was deemed the better predictor for preeclampsia among the widely defined group of "high-risk" women [6].

Consistent with existing literature [2,4], our study also demonstrated that the risk of preeclampsia was higher in nulliparous women compared with parous women, with a higher risk after multiple adjustment compared to the crude estimate. We also showed that the risk of preeclampsia was higher in women with a history of HDP, compared with women with no history, these results are also consistent with existing literature [18,23].

5. Strengths and limitations

A major strength of this study is that it is based on a large multinational, diverse cohort of women improving the applicability of our results to different population groups. Furthermore, use of BP measures prior to 16 weeks' gestation as discussed above, facilitates translation of our results to clinical practice. A further strength is that our study population included women at low and high risk for developing preeclampsia as classified by known preeclampsia risk factors [31]. However, a limitation is that we did not perform subgroup analyses by low versus high risk for PIH, as in other studies, since our primary aim was to examine the relationship of early BP and preeclampsia by parity. A further limitation is that we did not adjust for prophylactic aspirin prescription at any point during the pregnancy in the pooled analyses, nor autoimmune disorders such as systemic lupus erythematosus, as this information was not consistently available between our pooled datasets. However, we did consider important confounding factors in our analyses since we adjusted for known preeclampsia risk factors, e.g.: parity, age, BMI, previous hypertension, previous diabetes and previous preeclampsia. Finally, there was slight variation in definitions of preeclampsia and PIH between the Sydney and INTERBIO-21st studies, and timing of preeclampsia onset and earlier delivery due to preeclampsia was not available in the Sydney data. However, the rates of preeclampsia and PIH were similar to those reported worldwide.

6. Conclusion

The risk of preeclampsia risk differs according to parity and history of HDP in a previous pregnancy. Blood pressure in early pregnancy predicts preeclampsia in all groups, although more strongly associated in parous than nulliparous women, but no different in parous women by history of HDP. Further research is needed on whether serial BP measures during pregnancy are useful in developing a model for preeclampsia prediction that is affordable and accessible and provide guidance on monitoring those at high risk, including consideration of the role of aspirin.

7. Declarations

Details of ethical approval: Ethical approval for the INTERBIO-21st Study was granted by the Oxfordshire Research Ethics Committeee "C" (reference 08/H0606/139), the research committees of the individual participating institutions, and the corresponding regional or national health authorities where the project was done. All women provided written informed consent for the use of their clinical data. Ethical approval for the Sydney Study was granted by the South Eastern Sydney Local Health District HREC LNR Committee **(**project identifier: 2020/ETH00671).

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9. Authors' contributions

AH, MW, ADK, XZ, JH contributed to the study concept and design. KH and LX wrote the first draft of the manuscript. KH performed statistical analysis with support from LX, ADK and MW. All authors contributed to the interpretation of results, critical revision of the manuscript for intellectual content. All authors approved submission of the paper for the publication.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.preghy.2024.101136.

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