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## Accuracy of mean arterial pressure and blood pressure measurements in predicting pre-eclampsia: systematic review and meta-analysis

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### ABSTRACT

**Objective** To determine the accuracy of using systolic and diastolic blood pressure, mean arterial pressure, and increase of blood pressure to predict pre-eclampsia.

**Design** Systematic review with meta-analysis of data on test accuracy.

**Data sources** Medline, Embase, Cochrane Library, Medion, checking reference lists of included articles and reviews, contact with authors.

**Review methods** Without language restrictions, two reviewers independently selected the articles in which the accuracy of blood pressure measurement during pregnancy was evaluated to predict pre-eclampsia. Data were extracted on study characteristics, quality, and results to construct 2×2 tables. Summary receiver operating characteristic curves and likelihood ratios were generated for the various levels and their thresholds.

**Results** 34 studies, testing 60 599 women (3341 cases of pre-eclampsia), were included. In women at low risk for pre-eclampsia, the areas under the summary receiver operating characteristic curves for blood pressure measurement in the second trimester were 0.68 (95% confidence interval 0.64 to 0.72) for systolic blood pressure, 0.66 (0.59 to 0.72) for diastolic blood pressure, and 0.76 (0.70 to 0.82) for mean arterial pressure. Findings for the first trimester showed a similar pattern. Second trimester mean arterial pressure of 90 mm Hg or more showed a positive likelihood ratio of 3.5 (95% confidence interval 2.0 to 5.0) and a negative likelihood ratio of 0.46 (0.16 to 0.75). In women deemed to be at

high risk, a diastolic blood pressure of 75 mm Hg or more at 13 to 20 weeks' gestation best predicted pre-eclampsia: positive likelihood ratio 2.8 (1.8 to 3.6), negative likelihood ratio 0.39 (0.18 to 0.71). Additional subgroup analyses did not show improved predictive accuracy.

**Conclusion** When blood pressure is measured in the first or second trimester of pregnancy, the mean arterial pressure is a better predictor for pre-eclampsia than systolic blood pressure, diastolic blood pressure, or an increase of blood pressure.

### INTRODUCTION

Blood pressure measurement is routinely used in antenatal care to detect or predict hypertensive disease.<sup>1</sup> The results from studies on the predictive accuracy of such measurements have conflicted and it is therefore uncertain whether blood pressure measurement should be used routinely as a predictive test or used only to diagnose suspected hypertensive disorders in pregnancy. We carried out a systematic review to investigate the accuracy of blood pressure measurement for prediction of pre-eclampsia in pregnant women.

### METHODS

We included studies that reported on any technique to measure blood pressure in pregnant women in any healthcare setting and of any level of risk for pre-eclampsia (see [bmj.com](http://bmj.com) for search strategy). We

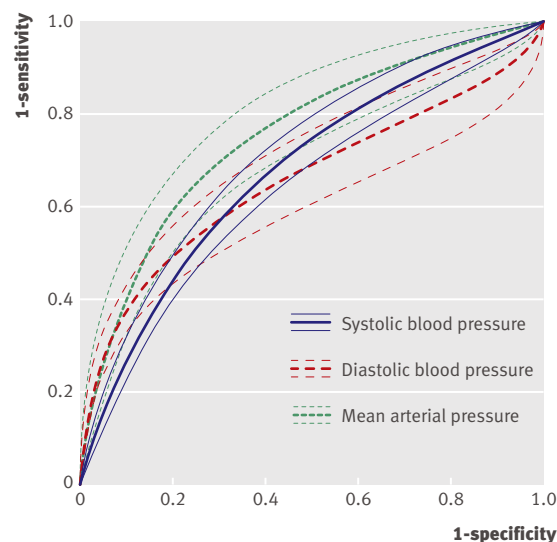
included test accuracy studies allowing generation of 2×2 tables.

Potentially eligible studies were assessed by one reviewer (JSC) for methodological quality against the quality assessment of diagnostic accuracy studies criteria<sup>2</sup> and randomly checked by a second reviewer (NdV). For multiple publications of one dataset we included the most recent or complete study.

Reference standards for pre-eclampsia were a persistent systolic blood pressure of 140 mm Hg or more or a persistent diastolic blood pressure of 90 mm Hg or more, or both, with proteinuria of 0.3 g/day or more or a dipstick result of + or more, or both, new after 20 weeks of gestation. Severe pre-eclampsia was a systolic blood pressure of 160 mm Hg or more or diastolic blood pressure of 110 mm Hg, or more, or both, with proteinuria 2.0 g/day or more or a dipstick result of ++ or more, or both, of early onset (<34 weeks) gestation. Chronic hypertension was hypertension before pregnancy or before 20 weeks' gestation and not resolving within three months after delivery.<sup>3</sup>

#### Data synthesis

From the 2×2 tables we calculated sensitivity and specificity and plotted their results in receiver operating characteristic plots. We pooled results among groups of studies measuring similar blood pressure variables and similar outcome. We used a bivariate regression model that takes into account the negative correlation between sensitivity and specificity. This is recommended for meta-analysis of diagnostic tests.<sup>4,5</sup> The model acknowledges the difference in precision of measurements for sensitivity and specificity in each study. Studies with a larger number of women with pre-eclampsia receive more weight in the calculation of the pooled estimate of sensitivity, whereas studies with more women without pre-eclampsia are



**Fig 1** Summary receiver operating characteristic curves with 95% confidence intervals for systolic blood pressure, diastolic blood pressure, and mean arterial pressure for women in population at low risk of pre-eclampsia tested in second trimester

more influential in the pooling of specificity. To estimate a summary receiver operating characteristic curve and an area under that curve, we used the results of the model with the smallest Akaike's information criterion (a measure of the goodness of fit of an estimated model).<sup>6</sup> This model best accounts for heterogeneity between studies. We calculated areas under the curves in the first trimester for the complete summary receiver operating characteristic curve. We also calculated pooled sensitivities and specificities and derived likelihood ratios.<sup>7</sup>

We carried out subgroup analyses for outcome (severe pre-eclampsia), population (low risk *v* high risk), number of readings (multiple *v* single), and gestational age at testing (first *v* second trimester). Sensitivity analyses were done for preventive treatment and study quality. We considered studies of high quality when they scored positive on at least four of the items: prospective design with consecutive recruitment, appropriate reference standard, follow-up greater than 90%, adequate description of the index test, and reporting of preventive treatment.

#### RESULTS

Overall, 34 studies<sup>w1-w34</sup> screening 60 599 women (3341 pre-eclamptic women) were included (see [bmj.com](http://bmj.com)). Twenty eight studies were prospective and six retrospective. Sample sizes ranged from 22-22 582 women. The incidence rates for pre-eclampsia ranged from 0.8% to 40.8% (median 6.3%; case-control studies excluded). Seven studies reported on "high risk" women (incidence rates 2.0-28.7%). Fourteen studies reported exclusion of women with chronic hypertension and four reported inclusion of women with chronic hypertension. Twenty eight studies reported on blood pressure measurement in the second trimester. Eighteen studies reported on mean arterial pressure. Six studies reported on systolic blood pressure; 11 on diastolic blood pressure; and three on increases of systolic or diastolic blood pressure, or both. As both randomised controlled trials in women at low risk investigated calcium supplementation, of unproved effectiveness,<sup>8</sup> and one only included a placebo group, we analysed the trials with the cohort studies. Four studies were excluded from the meta-analysis (three case-control studies<sup>w2 w15 w20</sup> to further enhance validity and one study without a threshold for the index test<sup>w26</sup>).

#### Quality assessment

More than 70% of studies met the items for quality assessment: period between tests, avoidance of partial and differential verification, independent reference test, blind assessment of index test, and clinical data available (see [bmj.com](http://bmj.com)). Less than 30% of studies scored positive on the items for adequate patient spectrum; adequate descriptions of selection criteria, index test, and reference test; and blind assessment of reference test.

### Data analysis

The area under the curve was 0.68 (95% confidence interval 0.64 to 0.72) for systolic blood pressure, 0.66 (0.59 to 0.72) for diastolic blood pressure, and 0.76 (0.70 to 0.82) for mean arterial pressure (fig 1). For a specificity of 90% the sensitivities of diastolic blood pressure and mean arterial pressure were both 35%, whereas for systolic blood pressure the sensitivity was only 24%. For the six studies with a mean arterial pressure threshold of 85 mm Hg or more the pooled sensitivity was 52% (95% confidence interval 28% to 75%) and pooled specificity 84% (95% confidence interval 75% to 94%); derived positive likelihood ratio 3.3 (95% confidence interval 2.2 to 4.3) and negative likelihood ratio 0.57 (95% confidence interval 0.35 to 0.80). A mean arterial pressure of 90 mm Hg or more showed a pooled sensitivity of 62% (35% to 89%) and a pooled specificity of 82% (72% to 92%); derived positive likelihood ratio 3.5 (2.0 to 5.0) and negative likelihood ratio 0.46 (0.16 to 0.75). The three studies on increase of systolic blood pressure or increase of diastolic blood pressure, or both, showed poor predictive accuracy (fig 2). Poor predictive accuracy was shown for an increase in either blood pressure type compared with baseline<sup>w16 w27</sup> and an increase of blood pressure compared with later gestational ages.<sup>w32</sup>

### Subgroup and sensitivity analysis

Severe pre-eclampsia was reported by only one cohort study<sup>w25</sup> and one case-control study.<sup>w2</sup>

In high risk populations a diastolic blood pressure of 75 mm Hg or more at 13-20 weeks' gestation best predicted pre-eclampsia (positive likelihood ratio 2.8,

1.8 to 3.6; negative likelihood ratio 0.39, 0.18 to 0.71).<sup>w26</sup>

In 24 studies it was unclear whether single or multiple readings were reported. When it was assumed that these studies carried out single measurements, the areas under the curves for testing low risk populations in the second trimester remained 0.68 for systolic blood pressure, 0.66 for diastolic blood pressure, and 0.76 for mean arterial pressure. Areas under the curves for measurements in the first trimester were 0.66 for systolic blood pressure, 0.67 for diastolic blood pressure, and 0.79 for mean arterial pressure.

Sensitivity analysis on preventive treatment was considered impractical because 25 studies (80%) did not report on it.

### DISCUSSION

Mean arterial pressure predicted pre-eclampsia fairly well whereas systolic blood pressure; diastolic blood pressure; and an increase of systolic blood pressure or increase of diastolic blood pressure, or both, predicted pre-eclampsia poorly. In low risk populations a mean arterial pressure in the second trimester best predicted pre-eclampsia. An increased mean arterial pressure of 90 mm Hg or more in the second trimester, however, showed a small increase in the likelihood of developing pre-eclampsia. In high risk populations a diastolic blood pressure of 75 mm Hg or more at 13-20 weeks' gestation best predicted pre-eclampsia, although the accuracy of prediction was modest. Subgroup analyses were limited and did not improve predictive accuracy.

We carried out extensive searches without language restrictions, assessed the quality of the studies and reporting, and used contemporary statistical methods. Many studies did not distinguish between pre-eclampsia and other hypertensive disorders in pregnancy, nor did many report sufficient information to construct a 2×2 table. Quality assessment and subgroup analyses were hindered by unclear reporting in many studies. As a result of unclear reporting it was not possible to carry out multivariate subgroup analysis on the basis of individual quality criteria, therefore we reported the overall results. Poor reporting occurred in details of the index test and reference standard, patient selection criteria, and blinding. The measurement of blood pressure was poorly reported, underestimating the importance of recording diastolic blood pressure with Korotkoff phase V.<sup>9-11</sup> Poor reporting of the device used underestimates the importance of its validation for blood pressure measurement during pregnancy.<sup>12-13</sup> Poor reporting of patient selection criteria may partly explain the great variability of incidence rates of pre-eclampsia not only between but within the categories of populations. Large cohort studies (>300 000 women) reflecting unselected populations, however, showed incidence rates of pre-eclampsia between 0.8% and 5.1%.<sup>14-16</sup>

A published review evaluated risk factors for pre-eclampsia at the first antenatal visit.<sup>17</sup> It included four studies on blood pressure and concluded that the risk of pre-eclampsia was increased in women with a raised

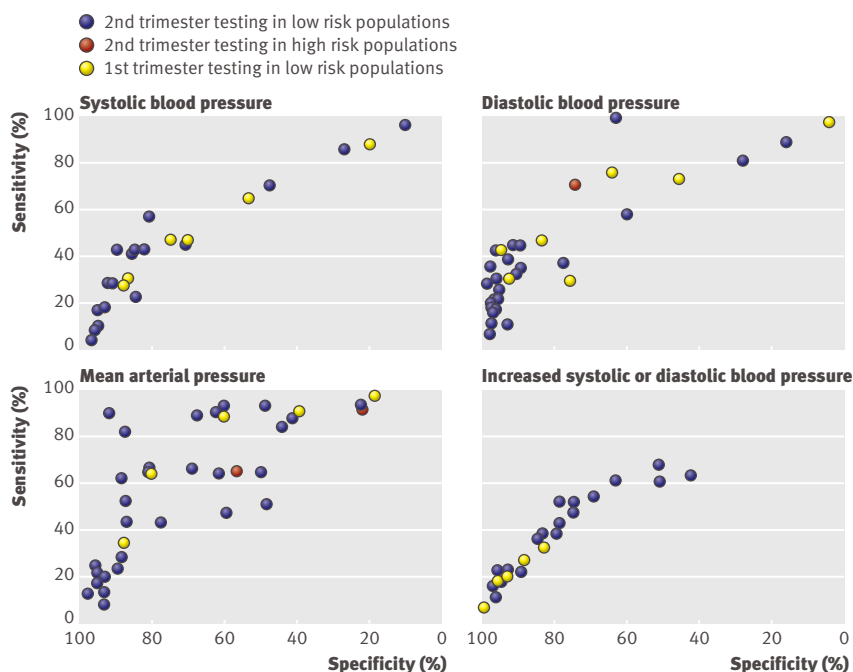


Fig 2 | Receiver operating characteristic plots for all results according to timing of test during gestation

## WHAT IS ALREADY KNOWN ON THIS TOPIC

Pre-eclampsia is an important disorder in pregnancy, with potentially severe consequences for mother and child

Blood pressure measurement is routinely used in antenatal care to predict or detect hypertensive disorders

## WHAT THIS STUDY ADDS

Mean arterial pressure is a better predictor for pre-eclampsia than systolic blood pressure, diastolic blood pressure, or increased blood pressure

Blood pressure measurements at the first antenatal visit for healthy normotensive women in the first and second trimester does not help predict pre-eclampsia

diastolic blood pressure ( $>80$  mm Hg): relative risk 1.48 (95% confidence interval 1.0 to 1.9). Other reviews did not apply appropriate methods for systematic reviews of screening tests or did not distinguish between different hypertensive disorders.<sup>18-23</sup> Some of these reviews concluded that an increased mean arterial pressure ( $\geq 85$  mm Hg or  $\geq 90$  mm Hg) predicted transient hypertension rather than pre-eclampsia<sup>18-20</sup> and that pregnant women with diastolic blood pressures of 70 mm Hg or more or mean arterial pressures of 80 mm Hg or more in the second trimester have a small risk of developing pre-eclampsia.<sup>22</sup>

Before predictive tests are applied in clinical practice consideration needs to be given to the prevalence of the disease, predictive accuracy of the test, cost of the test, acceptability to patients, and treatments available. Pre-eclampsia is of relatively low prevalence. From the results of this review mean arterial pressure still shows the greatest predictive accuracy in the first and second trimesters. In clinical practice measurement of mean arterial pressure at the first antenatal visit may improve the accuracy for estimating risk of pre-eclampsia. Our data cannot rationalise current obstetrical practice of repeated blood pressure measurements during the first and second trimester in healthy women with a normal blood pressure at the first antenatal visit.

At present no pharmacological treatment or management strategy has been shown to effectively prevent pre-eclampsia. Early antihypertensive treatment only prevents severe hypertension. Research into aspirin has, however, shown a modest preventive effect<sup>24</sup> in the absence of any serious side effects.

It is imperative to differentiate between mild and severe disease because early or severe pre-eclampsia is associated with raised rates of maternal morbidity and mortality and has pronounced risks for the fetus.<sup>1-25</sup> Research should also concentrate on the development of algorithms that combine biochemical and biophysical markers, including blood pressure measurement.

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