**BMJ pico**

**Antenatal blood pressure for prediction of preeclampsia, preterm birth and small-for-gestational age: development and validation in two general population cohorts**

Corrie Macdonald-Wallis,1,2 Richard J Silverwood,3,4 Bianca L De Stavola,3,4 Hazel Inskip,5,6 Cyrus Cooper,5,6,7 Keith M Godfrey,5,6 Sarah Crozier,5 Abigail Fraser,1,2 Scott M Nelson,8 Debbie A Lawlor,\*1,2 Kate Tilling.\*1,2

1 MRC Integrative Epidemiology Unit at the University of Bristol, Oakfield House, Oakfield Grove, Bristol, UK, BS8 2BN

2 School of Social and Community Medicine, University of Bristol, Oakfield House, Oakfield Grove, Bristol, UK, BS8 2BN

3 Department of Medical Statistics, London School of Hygiene and Tropical Medicine, Keppel Street, London, UK, WC1E 7HT

4 Centre for Statistical Methodology, London School of Hygiene and Tropical Medicine, Keppel Street, London, UK, WC1E 7HT

5 MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton General Hospital, Southampton, UK, SO16 6YD

6 NIHR Southampton Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Tremona Road  
Southampton General Hospital, UK, SO16  6YD

7 National Institute for Health Research Musculoskeletal Biomedical Research Unit, University of Oxford, Oxford, UK, OX3 7LE

8 School of Medicine, University of Glasgow, University Avenue, Glasgow, UK, G12 8QQ

\* These authors contributed equally and are joint senior authors

**Corresponding author e-mail**: d.a.lawlor@bristol.ac.uk and C.Macdonald-Wallis@bristol.ac.uk

**Study question**: Can routine antenatal blood pressure measurements between 20 and 36 weeks gestation contribute to the prediction of preeclampsia and its associated adverse outcomes?

**Summary answer**: The addition of blood pressure measurements from 28 weeks onwards improved prediction models for preeclampsia compared with using early-pregnancy risk factors alone, but they contributed little to the prediction of preterm birth or small-for-gestational age.

**What is known and what this paper adds**: Blood pressure at booking is predictive of the risk of developing preeclampsia later in pregnancy. We have shown that sequential screening using blood pressure at subsequent appointments may enable a stratified approach to antenatal care scheduling.

**Participants and setting**: Prediction models were developed in 12996 women in the Avon Longitudinal Study of Parents and Children (ALSPAC; n=317 preeclampsia cases) and externally validated in 3005 women in the Southampton Women’s Survey (SWS; n=88 preeclampsia cases); both UK-based prospective cohort studies. Antenatal blood pressure measurements were abstracted from obstetric records.

**Design, size and duration**: We compared a model based on early-pregnancy clinical risk factors (BMI, height, age, parity, smoking, existing and previous gestational hypertension and diabetes, ethnicity and initial mean arterial pressure (MAP); Model 1) with a model additionally including the later gestational age measures of MAP (Model 2), a model including the deviation of later gestational age MAP from a stratified normogram (Model 3) and a model including both (Model 4) for gestational ages 20, 25, 28, 31, 34 and 36 weeks.

**Main results and the role of chance**: The area under the ROC curve for Model 2 was higher compared with Model 1 at all gestational ages in ALSPAC, and from 28 weeks onwards in SWS. Models 3 and 4 performed similarly to Model 2. When we applied a threshold that provides a sensitivity of 99%, our results suggest that if women were screened sequentially using risk factors at the first antenatal clinic followed by repeat blood pressure from 20 weeks onwards, 360 per 1000 women to be classified as at low-risk of preeclampsia and could be transferred to a reduced antenatal care schedule. The **Figure** shows a proposed care schedule for a nulliparous woman screening as low-risk at 20 weeks. This illustrates how our model could be used to stratify women into different levels of antenatal care.

**Bias, confounding and other reasons for caution**: We used multiple imputation of missing data to increase the sample size and minimise selection bias. Still, the validation sample may have been slightly underpowered as the number of preeclampsia cases in SWS was just below the recommended 100. Several risk factors were self-reported, potentially introducing measurement error, but this reflects how information would be obtained in clinical practice.

**Generalisability to other populations**: The risk factors included are widely available in low and middle income as well as high income settings. However, recalibration of the prediction model was required for use in SWS, possibly due to different definitions of preeclampsia in the two cohorts. This suggests that further recalibration may be required for use in other populations with differing criteria for preeclampsia.

**Study funding/potential competing interests**: The work was supported by the UK Wellcome Trust [grant number WT087997MA], US National Institutes of Health [grant number R01 DK077659] and UK Medical Research Council [grant number MR/J011932/1]. Other funding sources for authors are detailed in the full on-line paper. With the exceptions of CM-W, HMI and KMG (see details in online paper) there were no competing interests.

**Figure:** Proposed care schedule for a nulliparous woman who screens below the threshold of the risk prediction score for preeclampsia from 20 weeks onwards compared with the usual schedule of appointments for all nulliparous women (Booking, 16 weeks, 20 weeks, 25 weeks, 28 weeks, 31 weeks, 34 weeks, …)

Booking

20 weeks

28 weeks

31 weeks

34 weeks

25 weeks

16 weeks

…

ABOVE threshold – continue with usual schedule

BELOW threshold – transfer to reduced schedule and skip next appointment

BELOW threshold -remain on reduced schedule and skip next appointment

BELOW threshold -continue with standard appointment schedule post-34 weeks

SCREENED

(MODEL 1)

SCREENED

(MODEL 1)

SCREENED (MODEL 2)

SCREENED

(MODEL 2)

SCREENED

(MODEL 2)

ABOVE threshold – continue with usual schedule