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# Pre-pregnancy blood pressure and offspring sex in the HUNT Study, Norway

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**Conflict of Interest:** The authors declare that they have no conflict of interest.

1 Dear Ernesto L. Schiffrin,

2 We read with great interest the recent paper by Retnakaran et al.<sup>1</sup> describing an  
3 association between higher maternal pre-pregnancy systolic blood pressure and increased  
4 probability of delivering a boy. As the authors suggested this finding needs replication, which  
5 we aimed to do using the Norwegian HUNT Study.

6 In the HUNT Study, the entire adult population of Nord-Trøndelag county, Norway  
7 has been invited to health surveys since the 1980s.<sup>2</sup> By linking HUNT Study data with the  
8 Medical Birth Registry of Norway,<sup>3</sup> which has prospectively recorded all births in Norway  
9 since 1967, we identified 2427 women with blood pressure recorded in the HUNT2 (1995-97)  
10 or HUNT3 (2006-08) surveys prior to a singleton first pregnancy. Blood pressure was  
11 measured at rest by trained staff three times at 1-minute intervals using an automatic  
12 oscillometric method (Dinamap, Critikon, Florida). We used the mean of the second and third  
13 measurements, or the second measurement for women (n=163) who did not have a third  
14 measurement. Associations between pre-first pregnancy systolic blood pressure and sex of the  
15 offspring of first pregnancy were analyzed with logistic and linear regression models using  
16 Stata. In a very similar fashion to Retnakaran et al. we adjusted for the highest obtained  
17 education level, age, current smoking, body mass index, waist circumference, non-fasting  
18 serum glucose, high-density and non-high-density lipoprotein cholesterol and triglycerides.  
19 We also adjusted for HUNT survey occasion (HUNT2 or HUNT3).

20 Overall, mean (SD) pre-pregnancy blood pressure among the 2427 women was 121  
21 (11) mm Hg systolic and 70 (9) mm Hg diastolic. There were 1267 (52%) boys and 1160  
22 (48%) girls (sex ratio 1.09). Median time from blood pressure recording to pregnancy was 3  
23 years. Unadjusted pre-pregnancy systolic and diastolic blood pressure was similar before  
24 pregnancies with male (121/70 mm Hg) and female (121/70 mm Hg) offspring. The adjusted

1 differences in pre-pregnancy systolic and diastolic blood pressure between mothers of male  
2 and female offspring were 0.2 mm Hg (95% CI, -0.6 to 1.1) and -0.1 mm Hg (95% CI, -0.8 to  
3 0.5), respectively.

4 We found no meaningful association of systolic blood pressure with the probability of  
5 male offspring. Overall, each one mm Hg higher systolic blood pressure was associated with  
6 an adjusted odds ratio of male offspring of 1.002 (95% CI, 0.994–1.010). The predicted  
7 probabilities of having a boy by quintiles of systolic blood pressure are shown in Figure 1. As  
8 time from blood pressure measurement to pregnancy was shorter (median: 26.3 weeks) in the  
9 study by Retnakaran et al., we repeated the analysis in a sub-group of females with blood  
10 pressure measurements taken less than 3 years before pregnancy (n=1210); the odds ratio of  
11 having a boy per one mm Hg higher systolic blood pressure was 1.005 (95% CI 0.994–1.015).  
12 Findings were similar for diastolic blood pressure and sex of offspring.

13 The blood pressure measurement protocol did not substantially differ between our  
14 study and the study by Retnakaran et al. Retnakaran et al. studied a Chinese population whilst  
15 our study population was predominantly Caucasian, included both planned and unintended  
16 pregnancies, and was restricted to first births. However, we do not expect that any causal  
17 effect of maternal blood pressure on offspring sex would differ by these characteristics.

18 In summary, these results from a Norwegian population-based cohort of greater size  
19 than that of Retnakaran et al., do not support the suggestion that maternal pre-pregnancy  
20 blood pressure influences the probability of delivering a boy.

21

Yours sincerely,

Eirin B. Haug, Julie Horn, Abigail Fraser, Amanda R. Markovitz, Janet Rich-Edwards,

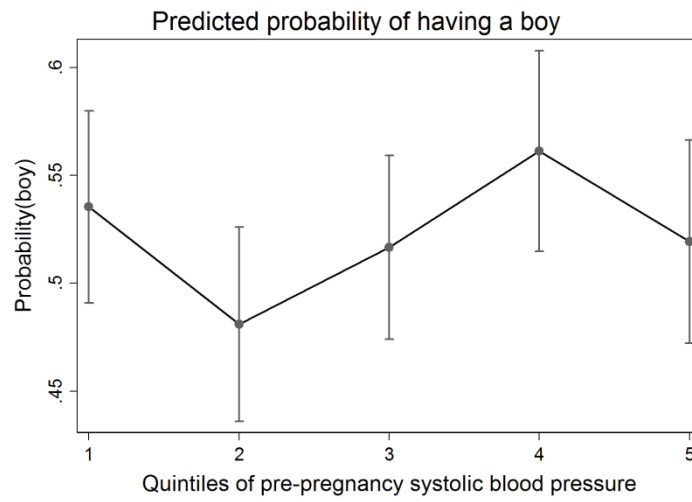
George Davey Smith, Pål R. Romundstad, Bjørn O. Åsvold

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1  
2

## Figure



3

## Figure legend

4 **Figure 1. Predicted probability (with 95% CI) of having a boy by quintiles of pre-**  
5 **pregnancy systolic blood pressure calculated at means of other covariates.** Quintile  
6 categories: 1=88-111, 2=112-117, 3=118-123, 4=124-130 and 5=131-168 mm Hg.