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ORIGINAL ARTICLE

Maternal educational level and risk of gestational hypertension: the Generation R Study

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We examined whether maternal educational level as an indicator of socioeconomic status is associated with gestational hypertension. We also examined the extent to which the effect of education is mediated by maternal substance use (that is smoking, alcohol consumption and illegal drug use), pre-existing diabetes, anthropometrics (that is height and body mass index (BMI)) and blood pressure at enrolment. This was studied in 3262 Dutch pregnant women participating in the Generation R Study, a population-based cohort study. Level of maternal education was established by questionnaire at enrolment, and categorized into high, mid-high, mid-low and low. Diagnosis of gestational hypertension was retrieved from medical records using standard criteria. Odds ratios (OR) of gestational hypertension for educational levels were calculated, adjusted for potential confounders and additionally adjusted for potential mediators. Adjusted for age and gravidity, women with mid-low (OR: 1.52; 95% CI: 1.02, 2.27) and low education (OR: 1.30; 95% CI: 0.80, 2.12) had a higher risk of gestational hypertension than women with high education. Additional adjustment for substance use, pre-existing diabetes, anthropometrics and blood pressure at enrolment attenuated these ORs to 1.09 (95% CI: 0.70, 1.69) and 0.89 (95% CI: 0.50, 1.58), respectively. These attenuations were largely due to the effects of BMI and blood pressure at enrolment. Women with relatively low educational levels have a higher risk of gestational hypertension, which is largely due to higher BMI and blood pressure levels from early pregnancy. The higher risk of gestational hypertension in these women is probably caused by pre-existing hypertensive tendencies that manifested themselves during pregnancy.

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Introduction

Gestational hypertension is associated with perinatal morbidity, including preterm birth and foetal growth retardation.[1,2] It is characterized by *de novo* hypertension after the twentieth week of pregnancy without proteinuria, and complicates about 7–18% of first pregnancies and 4–9% of all pregnancies.[1,3–5]

Although little is known about the pathophysiology of gestational hypertension, studies have shown that it is associated with features of the metabolic syndrome[6] and with later development of essential hypertension and cardiovascular disease.[7,8] This suggests that these conditions may have similar pathological mechanisms.

Known risk factors for gestational hypertension are high maternal age, twin pregnancy, pre-existing diabetes, obesity and high-normal blood pressure in early pregnancy.[2,9] In some studies, smoking during pregnancy has been associated with a lower risk of gestational hypertension.[10,11]

Because low socioeconomic status is a marked risk factor for obesity, metabolic syndrome, hypertension and cardiovascular disease,[12–14] socioeconomic status is also likely to be associated with gestational hypertension. As early as the 1950s, researchers described associations between measures of socioeconomic status and hypertension during pregnancy.[15–19] However, most earlier studies

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focused primarily on pre-eclampsia, which is characterized by hypertension and proteinuria, and which is thought to have a different aetiology than gestational hypertension.[20] The results of these studies also conflict. For example, in 1955 Nelson studied maternal social class as measured by the husband's occupation in relation to the incidence of pre-eclampsia, and found no association.[17] In contrast, Davies *et al.*,[15] and, more recently, Haelterman *et al.*[16] found that, relative to women with a higher educational level, those with a low educational level had a higher risk of pre-eclampsia. We found only two studies that evaluated socioeconomic status in relation to isolated gestational hypertension.[18,19] Surprisingly, these found no associations, but this may have been due to the study design or to the chosen measures of socioeconomic status. For example, while these two studies used occupation of the woman's partner[18] and the woman's area of residence[19] as measures of socioeconomic status, such measures may not reflect all aspects of a pregnant woman's individual socioeconomic circumstances.

Given the adverse health consequences for the offspring of mothers with gestational hypertension, it is important for clinical practice and for public health policy to know whether socioeconomically disadvantaged women run a higher risk of gestational hypertension. Studying the association between socioeconomic status and gestational hypertension might also improve our insight into the causes of socioeconomic inequalities in women's cardiovascular health.

Working within the framework of the Generation R Study, a large birth-cohort study recruited prenatally,[21] we studied the association between maternal educational level as an indicator of maternal socioeconomic status and gestational hypertension. We also examined whether such an association can be explained by the mediating effects of substance use (that is smoking, alcohol consumption and illegal drug use), pre-existing diabetes, and maternal anthropometrics and blood pressure at enrolment. We used level of maternal education as it has been found to be the strongest and most consistent socioeconomic predictor of cardiovascular health.[22] As the literature indicates that socioeconomic disparities in hypertensive complications of pregnancy may differ between ethnic groups, the present study was restricted to an ethnically homogeneous population.[23]

Materials and methods

The Generation R Study

The present study was embedded within the Generation R Study, a population-based prospective cohort study from foetal life until young adulthood. The Generation R Study has previously been described in detail.[21,24] Briefly, the cohort includes 9778 (response rate 61%) mothers and children of various ethnicities living in Rotterdam, the Netherlands.[24] Although enrolment ideally took place in early pregnancy, it was possible until the birth of the child. All children were born between April 2002 and January 2006.

Assessments during pregnancy included physical examinations, ultrasound assessments and questionnaires, and took place in early pregnancy (gestational age <18 weeks), mid-pregnancy (gestational age 18–25 weeks) and late pregnancy (gestational age $\geqslant 25$ weeks). The study was conducted in accordance with the guidelines proposed in the World Medical Association Declaration of Helsinki, and has been approved by the Medical Ethical Committee at the Erasmus MC, University Medical Centre Rotterdam (Erasmus MC). Written consent was obtained from all participating parents.

Study population

Of the 9778 women, 91% ($n=8880$) were enrolled during pregnancy.[24] Women of Dutch ethnicity ($n=4057$) comprised the largest ethnic subgroup, and were selected for the analyses described below. A woman was classified as Dutch if she reported that both her parents had been born in the Netherlands.[25] Of the women who participated in this study with more than one pregnancy (8.3%), data on the second ($n=332$) or third pregnancy ($n=5$) were excluded from analyses to avoid clustering. Women who had been included after 25 weeks of gestation ($n=77$) were also excluded, because we were mainly interested in the effects of maternal anthropometrics and blood pressure early in pregnancy. To restrict the study to adult pregnant women, women younger than 20 years of age ($n=63$) were excluded. We also excluded twin pregnancies ($n=51$), cases of induced abortion, foetal deaths before 20 weeks of gestation and women lost to follow-up ($n=23$), and women lacking information on their educational level ($n=20$), diagnosis of gestational hypertension ($n=65$), gravidity ($n=5$), anthropometrics ($n=17$) or blood pressure at enrolment ($n=29$). Finally, as this study focused on *de novo* and isolated hypertension in pregnancy, we excluded women with pre-existing hypertension and those who developed pre-eclampsia, eclampsia or haemolysis, elevated liver enzyme and low platelet syndrome ($n=108$). This left 3262 women for analysis.

Educational level

On the basis of a questionnaire used at enrolment, we established the highest education achieved by each mother. This was categorized into four levels: (1) high (university degree), (2) mid-high (higher vocational training), (3) mid-low (more than 3 years general secondary school, intermediate vocational training or first year of higher vocational training) and (4) low (no education, primary school, lower

vocational training, intermediate general school or 3 years or less at general secondary school).[26]

Gestational hypertension
After each participant had given birth, the attending community midwife or obstetrician completed a delivery report. The reports on those participants who had given birth under the medical supervision of an obstetrician were selected and screened by a trained medical-record abstractor.

On the basis of documentation on the delivery report of any kind of hypertensive complication or foetal growth retardation, 398 women were suspected of having gestational hypertension. To confirm the presence of gestational hypertension, the same abstractor conducted detailed reviews of these women's hospital charts. Gestational hypertension was defined according to the criteria described by the International Society for the Study of Hypertension in Pregnancy:[27] development of systolic blood pressure $\geqslant 140$ mm Hg and/or diastolic blood pressure $\geqslant 90$ mm Hg without proteinuria after 20 weeks of gestation in previous normotensive women.

Potential mediators and confounders
Level of maternal education cannot directly affect the risk of gestational hypertension, but is likely to act through more proximal risk factors, so-called mediators.[28] We considered the following factors to be potential mediators in the pathway between maternal education and gestational hypertension: factors involving substance use, that is smoking, alcohol consumption and illegal drug use; pre-existing diabetes; maternal anthropometrics and blood pressure at enrolment (Figure 1). Categories are indicated below in parentheses.

Substance use. Smoking, alcohol consumption and illegal drug use, including marijuana, hashish, cocaine, heroin and ecstasy (never, before conception, until pregnancy was known, continued in pregnancy) were established using questionnaires in early, mid and late pregnancy.

Pre-existing diabetes. Presence of pre-existing diabetes (no, yes, unknown) was established by questionnaire at enrolment. Because we could not assume that women who answered 'no' to this question had actually been tested for diabetes, we recoded 'no' into 'unknown'.

Anthropometrics and blood pressure at enrolment. Maternal anthropometrics and blood pressure were measured at enrolment in one of the research centres. Height and weight were measured without shoes and heavy clothing, and body mass index (BMI) was calculated from height and weight (weight/height^2). BMI was categorized according to WHO standards into normal weight (<25 kg m^{-2}), overweight (25–30 kg m^{-2}) and obese ($\geqslant 30$ kg m^{-2}). Systolic and diastolic blood pressure were measured using an Omron 907 Automated Blood Pressure Monitor (OMRON Healthcare Europe BV, Hoofddorp, the Netherlands).[29]

Gestational age at enrolment varied from 5.1 to 24.9 weeks, and was correlated with level of education. We therefore adjusted BMI and blood pressure values for gestational age at time of measurement. First, we performed a separate linear regression analysis with gestational age at time of enrolment as predictor and BMI/blood pressure as outcome. Next, per woman, we added the difference between the fitted BMI/blood pressure value at the individual's gestational age at enrolment and the actual BMI/blood pressure observation to the fitted value at the population median gestational age at enrolment (14 weeks).

All models were adjusted for age and gravidity, treating them as potential confounders, because the effects of these factors in the association between maternal education and gestational hypertension were not of primary interest in this study, and as they cannot be considered indisputable mediators (Figure 1). Maternal age was assessed at enrolment in one of the research centres and categorized into four groups (20–25, 25–30, 30–35 and $\geqslant 35$ years). Gravidity (first pregnancy, $\geqslant$second pregnancy) was obtained through questionnaires at enrolment in the study.

Statistical analyses
We assessed the frequency distribution of potential confounders and mediators according to educational level. χ^2-Tests for trend were used for categorical factors, and Spearman's correlation coefficients were used for continuous factors.

Multivariate logistic regression was used to calculate the odds ratios (OR) of gestational hypertension and their 95% confidence intervals (CI) for levels of education after adjustment for the potential confounders (model 1), and after additional

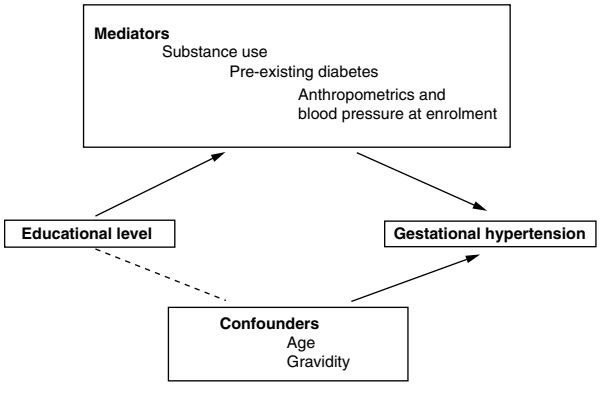

Figure 1 Simplified conceptual framework for the association between maternal educational level and gestational hypertension.

adjustment for potential mediators. The highest educational level was set as reference. Missing data on categorical factors were included as separate categories.

First, to evaluate the individual mediating effects of all potential mediators, these factors were added separately to model 1. For each adjustment, we calculated the percentage change in OR for the educational levels with a higher risk of gestational hypertension compared to the reference ($100 \times (OR_{model1} - OR_{+mediator})/(OR_{model1} - 1)$). When the OR attenuated to lower than 1, the change was set at 100%. Factors that caused an attenuation of the OR were defined as mediators in the association between maternal education and gestational hypertension.[30]

In the subsequent analyses, hierarchical logistic models[31] were built for two reasons: (1) to evaluate the mediating effects of substance use, pre-existing diabetes, anthropometrics and blood pressure at enrolment in the association between maternal education and gestational hypertension and (2) their own effects on gestational hypertension, taking due account of the conceptual hierarchical relationships between these factors. We hypothesized that, as an indicator of socioeconomic status, maternal education was the factor most distal to gestational hypertension that might influence risk of gestational hypertension through substance use, pre-existing diabetes, anthropometrics and blood pressure at enrolment. In turn, substance use might influence gestational hypertension risk directly, or indirectly through diabetes[32] or changes in anthropometrics.[33] Finally, we hypothesized that pre-existing diabetes, height and BMI at enrolment might influence gestational hypertension risk directly, or indirectly through blood pressure changes.[9]

For the logistic hierarchical models, we started with model 1, then added smoking, alcohol consumption and illegal drug use (model 2). To this model, we then added pre-existent diabetes, height and BMI at enrolment (model 3). In the final model (model 4), additional adjustment was made for systolic and diastolic blood pressure at enrolment.

All analyses were performed using the Statistical Package of Social Sciences version 11.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

Of the 3262 women in the study, mean age was 31.3 years (s.d. 4.3), 8.9% were between 20 and 25 years old, 17.6% were 35 years or older and 53.6% were primigravida. The median gestational age at enrolment was 13.6 weeks (90% range: 10.9, 21.2). Participants gave birth at a median gestational age of 40.3 weeks (90% range: 37.1, 42.1); their children had a mean birth weight of 3492 g (s.d. 547.9).

Of all women, 16.3% had a low educational level and 32.6% had a high educational level (Table 1). Gestational hypertension developed in 180 women (5.5%); the respective percentages for women with high, mid-high, mid-low and low education were 5.1, 4.4, 7.2 and 5.6% (χ^2: 6.77; degrees of freedom: 3; *P*-value: 0.08).

Age, alcohol consumption in pregnancy and height were positively associated with level of education (*P* for trend <0.001). Gravidity, smoking and illegal drug use during pregnancy, BMI, systolic and diastolic blood pressure at enrolment were negatively associated with level of education (*P* for trend <0.05). Women with a mid-low educational level had the highest systolic and diastolic blood pressure values at enrolment (Table 1).

Compared with women with high education, those with a mid-low and low education had a higher risk of gestational hypertension after adjustment for age and gravidity; those with a mid-low education had the highest risk (OR: 1.52; 95% CI: 1.02, 2.27; model 1; Tables 2 and 3). The OR for women with a low educational level did not reach statistical significance (OR: 1.30; 95% CI: 0.80, 2.12).

Individual adjustment for each potential mediator resulted in $+2$ to -71% changes in the OR for mid-low education and $+10$ to -100% change in the OR for low education (Table 2). The largest attenuations were caused by BMI, systolic and diastolic blood pressure at enrolment.

Table 3 presents the hierarchical logistic models fitted on gestational hypertension. Part of the effect of a mid-low and low educational level on gestational hypertension was mediated by substance use. When added to model 1, substance use, in particular alcohol consumption, attenuated the ORs by 21 and 63% to 1.39 (95% CI: 0.92, 2.11) and 1.11 (95% CI: 0.64, 1.92), respectively (model 2). Although alcohol consumption tended to reduce the risk of gestational hypertension in this model, this effect was not significant. In contrast, smoking before conception was associated with a higher risk of gestational hypertension than never smoking was (OR: 1.68; 95% CI: 1.14, 2.46).

Pre-existing diabetes, height and BMI at enrolment further mediated more than half the effect of mid-low education (OR: 1.12; 95% CI: 0.73, 1.71; model 3) and all of the remaining effect of low education (OR: 0.83; 95%: 0.48, 1.44). This mediation was due mainly to BMI at enrolment. After adjustment for the other factors in model 3, overweight (OR: 2.43; 95% CI: 1.70, 3.46) and obesity (OR: 5.15; 95% CI: 3.34, 7.95) were significant risk factors for gestational hypertension. Systolic and diastolic blood pressure at enrolment, when added in model 4, further mediated the effect of mid-low education with 25% (in relation to model 3) to an OR of 1.09 (95% CI: 0.70, 1.69). This final OR for mid-low education corresponded with a total attenuation of 83% relative to model 1.

Additionally, blood pressure mediated half the effect of overweight (OR: 1.70; 95% CI: 1.17,

Table 1 Distribution of general characteristics, substance use, pre-existing diabetes, anthropometrics and blood pressure at enrolment in total study population and by educational level

	Level of maternal education					
	Total (n = *3262*)	*High* (n = *1063*) *(32.6%)*	*Mid-high* (n = *843*) *(25.8%)*	*Mid-low* (n = *823*) *(25.2%)*	*Low* (n = *533*) *(16.3%)*	P *for trend*[a]
General characteristics						
Age, in years mean (s.d.)	31.3 (4.3)	32.9 (3.2)	31.9 (3.8)	30.0 (4.5)	29.2 (5.0)	<0.001
Age, categorical						
20–25 years (%)	8.9	0.1	3.3	15.9	24.2	
25–30 years (%)	25.1	16.2	27.5	31.2	29.6	<0.001
30–35 years (%)	48.4	62.1	49.3	39.9	33.2	
⩾35 years (%)	17.6	21.6	19.9	13.0	13.0	
Gravidity						
First pregnancy (%)	53.6	56.4	56.1	55.3	41.3	<0.001
Parity						
Nulliparous (%)	64.6	64.9	67.9	67.1	55.0	0.004
Substance use						
Smoking						
Never (%)	49.4	59.7	52.9	45.8	29.1	
Before conception (%)	19.4	20.1	21.1	19.1	15.8	
Until pregnancy was known (%)	8.3	7.7	8.9	9.5	6.5	<0.001
Continued in pregnancy (%)	16.4	5.1	10.3	19.9	43.3	
Missing (%)	6.5	7.4	6.8	5.7	5.3	
Alcohol consumption						
Never (%)	13.1	3.4	9.9	17.8	30.0	
Before conception (%)	19.0	13.9	15.9	23.6	27.0	
Until pregnancy was known (%)	15.2	13.0	16.1	17.9	14.1	<0.001
Continued in pregnancy (%)	49.4	67.3	54.8	36.2	25.7	
Missing (%)	3.3	2.4	3.3	4.5	3.2	
Illegal drug use						
Never (%)	86.7	90.5	86.7	85.0	81.8	
Before conception (%)	4.4	1.8	5.0	5.8	6.7	
Until pregnancy was known (%)	2.1	0.6	1.8	1.7	6.2	<0.001
Continued in pregnancy (%)	0.8	0.1	0.3	1.3	1.9	
Missing (%)	6.0	7.0	6.2	6.2	3.4	
Pre-existing diabetes						
Unknown (%)	92.4	91.6	92.1	92.4	94.7	
Yes (%)	0.2	0.1	0	0.4	0.4	0.097
Missing (%)	7.4	8.3	7.9	7.2	4.9	
Anthropometrics and BP at enrolment						
Height, in cm mean (s.d.)	170.7 (6.4)	171.4 (6.0)	171.3 (6.3)	170.6 (6.5)	168.9 (6.7)	<0.001
BMI[b], in kg m^{-2} mean (s.d.)	24.2 (4.0)	23.3 (3.1)	23.5 (3.3)	24.9 (4.5)	25.7 (5.0)	<0.001
BMI[b], categorical						
Normal weight (%)	68.2	77.6	73.8	60.8	52.4	
Overweight (%)	23.3	18.8	21.9	26.1	29.8	<0.001
Obese (%)	8.5	3.6	4.3	13.1	17.8	
SBP[b], in mm Hg mean (s.d.)	117.4 (11.9)	116.0 (11.2)	116.3 (9.1)	119.1 (12.5)	118.6 (12.3)	<0.001
DBP[b], in mm Hg mean (s.d.)	68.5 (9.2)	68.0 (8.6)	68.3 (9.1)	69.4 (9.8)	68.5 (9.5)	0.017

Abbreviations: BMI, body mass index; BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure.
[a]*P*-values are for χ^2-test for trend (categorical factors) or Spearman's correlation coefficient (continuous factors).
[b]Values of BMI and SBP and DBP at enrolment are adjusted for gestational age at enrolment.

2.45) and 72% of the effect of obesity (OR: 2.13; 95% CI: 1.31, 3.47) on gestational hypertension risk. Adjusted for all other factors in model 4, the risk of gestational hypertension increased with increasing systolic (OR per mm Hg increase: 1.02; 95% CI: 1.00, 1.04) and diastolic blood pressure (OR per mm Hg increase: 1.07; 95% CI: 1.04, 1.09). The effect of smoking hardly changed after adjustment for BMI and blood pressure at enrolment.

Discussion

This study showed that women with relatively low levels of education had a higher risk of gestational

Table 2 Odds ratios and change in odds ratios of gestational hypertension for the different levels of maternal education after individual adjustment for each potential mediating factor

Maternal education	*High (n = 1063) OR*	*Mid-high (n = 843) OR (95% CI)*	*Mid-low (n = 823) OR (95% CI)*	*Change a*[a] (%)	*Low (n = 533) OR (95% CI)*	*Change b*[a] (%)
Model 1 (includes maternal education, age and gravidity)	1.00	0.87 (0.56, 1.34)	1.52 (1.02, 2.27)		1.30 (0.80, 2.12)	
Substance use						
Model 1+smoking	1.00	0.86 (0.55, 1.32)	1.51 (1.01, 2.25)	−2	1.26 (0.76, 2.11)	−13
Model 1+alcohol consumption	1.00	0.85 (0.55, 1.31)	1.44 (0.95, 2.16)	−15	1.19 (0.71, 1.98)	−37
Model 1+illegal drug use	1.00	0.87 (0.56, 1.34)	1.52 (1.02, 2.27)	−0	1.33 (0.81, 2.18)	+10
Pre-existing diabetes						
Model 1+pre-existing diabetes	1.00	0.87 (0.56, 1.34)	1.52 (1.02, 2.27)	−0	1.30 (0.79, 2.11)	−0
Anthropometrics and BP at enrolment						
Model 1+height	1.00	0.87 (0.56, 1.34)	1.53 (1.02, 2.27)	+2	1.31 (0.80, 2.14)	+3
Model 1+BMI (categorical)	1.00	0.83 (0.54, 1.28)	1.15 (0.76, 1.74)	−71	0.87 (0.53, 1.45)	−100
Model 1+SBP	1.00	0.81 (0.52, 1.26)	1.26 (0.84, 1.90)	−50	1.10 (0.66, 1.81)	−67
Model 1+DBP	1.00	0.83 (0.53, 1.29)	1.31 (0.87, 1.98)	−40	1.18 (0.70, 1.96)	−40

Abbreviations: BMI, body mass index; BP, blood pressure; CI, confidence interval; DBP, diastolic blood pressure; OR, odds ratio; SBP, systolic blood pressure.
[a]Change a and change b represent the respective changes in OR for mid-low and low education relative to model 1 after individual adjustment for potential mediators $(100 \times (OR_{model\,1} - OR_{+mediator})/(OR_{model\,1} - 1))$. Since the subgroup with mid-high education did not have a higher risk of gestational hypertension than the subgroup with high education, changes in OR for mid-high education are not presented.

hypertension than women with a high level. This higher risk was explained by unequal distributions of known risk factors for gestational hypertension across educational levels, particularly by the higher rates of overweight and obesity and the relatively high blood pressure levels at enrolment found in lower educated women.

Methodological considerations

The main strength of this study lies in its population-based prospective design, in which a large number of women were enrolled early in pregnancy. The detailed information available on known risk factors for gestational hypertension enabled us to explain much of the association we observed between maternal education and gestational hypertension. Furthermore, the use of a conceptual hierarchical framework afforded insight into the interrelationships between maternal education and mediators, and their combined effects on gestational hypertension.

An additional strength was the use of medical chart review and applied standard international criteria for a consistent definition of gestational hypertension.

Although other measures of socioeconomic status exist, such as income level and occupational class;[34] for our study we selected maternal educational level as a main indicator of socioeconomic status. We did this for two reasons: (1) not only does educational level partly reflect material resources because it structures occupation and income, it also reflects non-economic social characteristics, such as general and health-related knowledge, literacy, problem-solving skills and prestige[35,36] and (2) educational level has also been shown to be the strongest and most consistent socioeconomic predictor of cardiovascular health.[22]

To various extents, our results may have been influenced by the following limitations.

First, the response rate among pregnant Dutch women in the Generation R Study was relatively high (68%),[37] but there was some selection towards a relatively high educated and healthier study population.[24]

Second, review of delivery reports and hospital charts was restricted to women who had been referred for delivery under medical care. However, in Dutch practice, community midwives often remain responsible for the care of women with a diastolic blood pressure between 90 and 100 mm Hg, provided that proteinuria does not develop. In the event of a diastolic blood pressure between 95 and 100 mm Hg, they are required to consult an obstetrician. All women with gestational hypertension with a diastolic blood pressure over 100 mm Hg should receive antenatal care and give birth in the hospital under the supervision of an obstetrician. Our study may therefore have missed mild cases of gestational hypertension with a diastolic blood pressure up to 100 mm Hg.

Third, in all logistic models, we adjusted for gravidity, to take account of the protective effect of a previous pregnancy, including those that ended in spontaneous abortions. Although a woman's risk of gestational hypertension is highest during her first pregnancy, the literature indicates that a change of partner between pregnancies may cause the risk to revert towards the same level as a primigravida.[38] Unfortunately, in this study we had no information on change of partners between pregnancies.

Table 3 Hierarchical logistic regression models fitted on gestational hypertension

	Model 1 OR (95% CI)	*Model 2 OR (95% CI)*	*Model 3 OR (95% CI)*	*Model 4 OR (95% CI)*
Maternal education				
High (reference)	1.00	1.00	1.00	1.00
Mid-high	0.87 (0.56, 1.34)	0.83 (0.54, 1.29)	0.81 (0.52, 1.25)	0.79 (0.50, 1.24)
Mid-low	1.52 (1.02, 2.27)	1.39 (0.92, 2.11)	1.12 (0.73, 1.71)	1.09 (0.70, 1.69)
Low	1.30 (0.80, 2.12)	1.11 (0.64, 1.92)	0.83 (0.48, 1.44)	0.89 (0.50, 1.58)
Substance use				
Smoking				
Never (reference)		1.00	1.00	1.00
Before conception		1.68 (1.14, 2.46)	1.63 (1.10, 2.40)	1.70 (1.14, 2.53)
Until pregnancy was known		1.20 (0.67, 2.16)	1.20 (0.66, 2.16)	1.41 (0.77, 2.58)
Continued in pregnancy		1.28 (0.79, 2.09)	1.21 (0.74, 1.97)	1.35 (0.81, 2.24)
Missing		1.41 (0.48, 4.11)	1.53 (0.48, 4.85)	1.58 (0.46, 5.48)
Alcohol consumption				
Never (reference)		1.00	1.00	1.00
Before conception		0.89 (0.53, 1.49)	1.01 (0.59, 1.70)	1.02 (0.60, 1.76)
Until pregnancy was known		0.85(0.49, 1.48)	1.00 (0.56, 1.76)	1.07 (0.59, 1.91)
Continued in pregnancy		0.68 (0.41, 1.13)	0.86 (0.52, 1.45)	0.97 (0.57, 1.64)
Missing		0.50 (0.15, 1.70)	0.59 (0.17, 2.08)	0.71 (0.20, 2.54)
Illegal drug use				
Never (reference)		1.00	1.00	1.00
Before conception		1.11 (0.56, 2.20)	1.36 (0.68, 2.72)	1.39 (0.68, 2.81)
Until pregnancy was known		0.48 (0.11, 2.01)	0.59 (0.14, 2.52)	0.67 (0.16, 2.91)
Continued in pregnancy		0.66 (0.09, 5.06)	0.59 (0.07, 4.68)	0.68 (0.08, 5.47)
Missing		1.13 (0.37 (3.47)	1.45 (0.39, 5.43)	1.54 (0.37, 6.35)
Pre-existing diabetes				
Unknown (reference)			1.00	1.00
Yes			1.49 (0.16, 14.13)	1.27 (0.13, 12.67)
Missing			0.69 (0.20, 2.34)	0.60 (0.17, 2.19)
Anthropometrics and BP at enrolment				
Height			1.01 (0.99, 1.04)	1.00 (0.98, 1.03)
BMI				
Normal weight (reference)			1.00	1.00
Overweight			2.43 (1.70, 3.46)	1.70 (1.17, 2.45)
Obese			5.15 (3.34, 7.95)	2.13 (1.31, 3.47)
SBP				1.02 (1.00, 1.04)
DBP				1.07 (1.04, 1.09)

Abbreviations: BMI, body mass index; CI, confidence interval; DBP, diastolic blood pressure; SBP, systolic blood pressure.
Model 1: Adjusted for age and gravidity.
Model 2: Model 1+smoking, alcohol consumption and illegal drug use.
Model 3: Model 2+pre-existing diabetes, height and BMI at enrolment.
Model 4: Model 3+SBP and DBP at enrolment (full model).

Finally, our study may have been vulnerable to misclassification, particularly with regard to substance-use factors, which were measured using questionnaires. Similarly, in accordance with the Dutch Standard Classification,[25] we assigned a Dutch ethnicity to a participant if both her parents had been born in the Netherlands. However, when identifying immigrant descent in Dutch residents, this classification goes no further than the second generation. The number of third-generation immigrants is nonetheless likely to have been very small and not to have affected our conclusions.

Comparison with other studies

Socioeconomic differences in blood pressure and prevalence of hypertension have been consistently reported among the general, adult population.[14,39] According to a review by Colhoun *et al.*[39] most studies performed in developed countries associate indicators of low socioeconomic status with higher blood pressures; these associations are stronger in women than in men, and are largely explained by socioeconomic differences in BMI.

Hypertension during pregnancy, particularly pre-eclampsia, has also been associated with level of education as a measure of socioeconomic status.[15,16] However, two studies that evaluated the association between indicators of socioeconomic status and isolated gestational hypertension[18,19] did not find an association. Although this contrasts with our own findings, the discrepancy in both cases is probably due to differences in study design or in exposure definition. One study[18] depended on retrospective data and had to deal with a large amount of missing data. The same study also

primarily used occupation of the women's partners as an indicator of maternal socioeconomic status—which, because it reflects other aspects of socioeconomic status, may therefore influence risk of gestational hypertension differently than maternal education does. The second study[19] examined an area-based measure of socioeconomic status in relation to occurrence of gestational hypertension. However, an area-based measure of socioeconomic status is unlikely to fully capture health risks that are associated with socioeconomic status at an individual level.

Educational level and risk of gestational hypertension

Relative to women with a high educational level, those with a low educational level and those with a mid-low educational level had, respectively, a 30 and 52% higher risk of gestational hypertension. The finding that the highest risk was not found in women with the lowest educational level somewhat weakens the evidence for a firm conclusion that maternal education level is negatively associated with gestational hypertension risk. However, this finding was probably attributed to chance; women with low education comprised the smallest subgroup, and the difference in gestational hypertension incidence between mid-low and low-educated women was not statistically significant (7.2 versus 5.6%; χ^2: 1.25; degrees of freedom: 1; *P*-value: 0.263).

Another hypothetical explanation for this finding is that women with a low education received better medical care, due for example to their coverage under social medicine schemes. However, this is unlikely: in the Netherlands, obligatory health insurance ensures equal primary prenatal care for everyone.

Referral bias is a third possible explanation. As previously discussed, mild cases of gestational hypertension were not necessarily referred to an obstetrician. If women with a low education with gestational hypertension were more likely to remain under a midwife's care, these cases may have been selectively missed in our study.

The last possible explanation is the selection bias that would have resulted if low-educated women who did not participate in this study had a higher risk of gestational hypertension than low-educated women who did participate. However, among the participants we found a clear linear trend across educational levels in a variety of other factors, such as smoking, alcohol consumption and BMI. This makes selection bias less likely.

Mediating mechanisms

Most of the higher risk of gestational hypertension in women with mid-low and low education was mediated by relatively high rates of overweight and obesity at enrolment in these subgroups. Although obesity is an important risk factor for gestational hypertension, the underlying biological mechanism is not completely clear. A recent study suggested that obesity mostly increases the risk of gestational hypertension through higher blood pressure levels.[9] Our results indeed suggest that at least half the effect of overweight and obesity acts through relative increases in blood pressure early in pregnancy. In women with a mid-low education, relatively high blood pressure levels at enrolment further contributed independently of BMI to the explanation of their increased risk of developing gestational hypertension.

Blood pressure in early pregnancy has been shown to be positively associated with the risk of gestational hypertension, even when it is within the normal range.[9] Normal pregnancy is characterized by haemodynamic changes, which cause a steady decrease in blood pressure in the first half of pregnancy, followed by a rise in blood pressure in the second half until delivery.[40] It is plausible that the higher the blood pressure is at the start of pregnancy, the higher the blood pressure will be when haemodynamic demands increase in the second half of pregnancy, and the sooner blood pressure will cross the threshold level of hypertension.

The higher risk of gestational hypertension in women with mid-low and low education was explained to a lesser extent by lower rates of alcohol consumption before and during pregnancy. This was due to a trend shown in our data towards a protective effect on gestational hypertension of alcohol consumption, which seemed to act through changes in BMI and blood pressure. Moderate alcohol consumption is known to lower blood pressure and to reduce the risk of development of essential hypertension in the non-pregnant population.[41] It is unknown whether moderate alcohol consumption during pregnancy has a similar effect on gestational hypertension.

Maternal smoking and illegal drug use did not contribute an explanation of the effects of a mid-low and low educational level. Remarkably, we observed that smoking before conception and during pregnancy tended to increase the risk of gestational hypertension, significantly so for smoking before conception. This is in contrast with many other studies which reported that women who smoke during pregnancy have a lower risk of gestational hypertension than women who have never smoked.[11] However, with regard to the effect of smoking before conception, studies have shown conflicting results. Zhang *et al.*[42] found that past smoking was associated with a lower risk of gestational hypertension, whereas a more recent study by England *et al.*[10] showed that women who smoked before pregnancy did not have a lower risk.

In non-pregnant women, cessation of smoking has been associated with a higher risk of hypertension than continued smoking or never smoking,[43] a finding that appears to support our results. Further

study is needed to confirm a similar association between cessation of smoking and gestational hypertension.

Implications and conclusions

It has been postulated that gestational hypertension is a 'sign of latent hypertension unmasked by pregnancy'.[44] The present study supports this hypothesis. The educational subgroups with the highest risk of gestational hypertension had the highest blood pressure values at enrolment, and their increased risk of gestational hypertension was almost entirely explained by factors that are also associated with essential hypertension.[45] These findings suggest that the relatively high risk of gestational hypertension in women with relatively low levels of education may reflect pre-existing hypertensive tendencies that are disclosed by the physiological stress of pregnancy.

We conclude that a relatively low educational level is associated with a higher risk of gestational hypertension. The educational inequalities observed in gestational hypertension may represent an early manifestation of the socioeconomic differences in morbidity and mortality from cardiovascular disease in women.[13] Strategies to reduce educational inequalities in gestational hypertension should be aimed primarily at reducing the burden of overweight and obesity in lower socioeconomic groups.

What is known about this topic

- Gestational hypertension is associated with perinatal morbidity and with hypertension and cardiovascular disease later in the mother's life
- Socioeconomic disadvantage is associated with a higher prevalence of hypertension and cardiovascular disease, especially among women

What this study adds

- Women with a relatively low educational level have a higher risk of gestational hypertension, which is largely due to higher BMI and BP levels from early pregnancy
- This higher risk of gestational hypertension in women with a relatively low educational level probably reflects pre-existing hypertensive tendencies that are disclosed during pregnancy
- Our findings may represent an early manifestation of the marked socioeconomic gap in cardiovascular disease in women

Abbreviations: BMI, body mass index; BP, blood pressure.

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References

1 Hauth JC, Ewell MG, Levine RJ, Esterlitz JR, Sibai B, Curet LB *et al.* Pregnancy outcomes in healthy nulliparas who developed hypertension. Calcium for Preeclampsia Prevention Study Group. *Obstet Gynecol* 2000; **95**: 24–28.
2 Villar J, Carroli G, Wojdyla D, Abalos E, Giordano D, Ba'aqeel H *et al.* Preeclampsia, gestational hypertension and intrauterine growth restriction, related or independent conditions? *Am J Obstet Gynecol* 2006; **194**: 921–931.
3 Groom KM, North RA, Poppe KK, Sadler L, McCowan LM. The association between customised small for gestational age infants and pre-eclampsia or gestational hypertension varies with gestation at delivery. *BJOG* 2007; **114**: 478–484.
4 Alexander JM, McIntire DD, Leveno KJ, Cunningham FG. Selective magnesium sulfate prophylaxis for the prevention of eclampsia in women with gestational hypertension. *Obstet Gynecol* 2006; **108**: 826–832.
5 Xiong X, Demianczuk NN, Saunders LD, Wang FL, Fraser WD. Impact of preeclampsia and gestational hypertension on birth weight by gestational age. *Am J Epidemiol* 2002; **155**: 203–209.
6 Solomon CG, Seely EW. Brief review:hypertension in pregnancy. A manifestation of the insulin resistance syndrome? *Hypertension* 2001; **37**: 232–239.
7 Smith GC, Pell JP, Walsh D. Pregnancy complications and maternal risk of ischaemic heart disease: a retrospective cohort study of 129 290 births. *Lancet* 2001; **357**: 2002–2006.
8 Wilson BJ, Watson MS, Prescott GJ, Sunderland S, Campbell DM, Hannaford P *et al.* Hypertensive diseases of pregnancy and risk of hypertension and stroke in later life: results from cohort study. *BMJ* 2003; **326**: 845–849.
9 Ohkuchi A, Iwasaki R, Suzuki H, Hirashima C, Takahashi K, Usui R *et al.* Normal and high-normal blood pressures, but not body mass index, are risk factors for the subsequent occurrence of both pre-eclampsia and gestational hypertension: a retrospective cohort study. *Hypertens Res* 2006; **29**: 161–167.
10 England LJ, Levine RJ, Qian C, Morris CD, Sibai BM, Catalano PM *et al.* Smoking before pregnancy and risk of gestational hypertension and preeclampsia. *Am J Obstet Gynecol* 2002; **186**: 1035–1040.
11 Marcoux S, Brisson J, Fabia J. The effect of cigarette smoking on the risk of preeclampsia and gestational hypertension. *Am J Epidemiol* 1989; **130**: 950–957.

12 Loucks EB, Rehkopf DH, Thurston RC, Kawachi I. Socioeconomic disparities in metabolic syndrome differ by gender: evidence from III NHANES. *Ann Epidemiol* 2007; **17**: 19–26.
13 Mackenbach JP, Cavelaars AE, Kunst AE, Groenhof F. Socioeconomic inequalities in cardiovascular disease mortality; an international study. *Eur Heart J* 2000; **21**: 1141–1151.
14 Vargas CM, Ingram DD, Gillum RF. Incidence of hypertension and educational attainment: the NHANES I epidemiologic followup study. First National Health and Nutrition Examination Survey. *Am J Epidemiol* 2000; **152**: 272–278.
15 Davies AM, Czaczkes JW, Sadovsky E, Prywes R, Weiskopf P, Sterk VV. Toxemia of pregnancy in Jerusalem. I. Epidemiological studies of a total community. *Isr J Med Sci* 1970; **6**: 253–266.
16 Haelterman E, Qvist R, Barlow P, Alexander S. Social deprivation and poor access to care as risk factors for severe pre-eclampsia. *Eur J Obstet Gynecol Reprod Biol* 2003; **111**: 25–32.
17 Nelson TR. A clinical study of pre-eclampsia. I. *J Obstet Gynaecol Br Emp* 1955; **62**: 48–57.
18 Lawlor DA, Morton SM, Nitsch D, Leon DA. Association between childhood and adulthood socioeconomic position and pregnancy induced hypertension: results from the Aberdeen children of the 1950s cohort study. *J Epidemiol Community Health* 2005; **59**: 49–55.
19 Clausen T, Oyen N, Henriksen T. Pregnancy complications by overweight and residential area. A prospective study of an urban Norwegian cohort. *Acta Obstet Gynecol Scand* 2006; **85**: 526–533.
20 Saftlas AF, Logsden-Sackett N, Wang W, Woolson R, Bracken MB. Work, leisure-time physical activity, and risk of preeclampsia and gestational hypertension. *Am J Epidemiol* 2004; **160**: 758–765.
21 Hofman A, Jaddoe VW, Mackenbach JP, Moll HA, Snijders RF, Steegers EA *et al.* Growth, development and health from early fetal life until young adulthood: the Generation R Study. *Paediatr Perinat Epidemiol* 2004; **18**: 61–72.
22 Winkleby MA, Jatulis DE, Frank E, Fortmann SP. Socioeconomic status and health: how education, income, and occupation contribute to risk factors for cardiovascular disease. *Am J Public Health* 1992; **82**: 816–820.
23 Tanaka M, Jaamaa G, Kaiser M, Hills E, Soim A, Zhu M *et al.* Racial disparity in hypertensive disorders of pregnancy in New York State: a 10-year longitudinal population-based study. *Am J Public Health* 2007; **97**: 163–170.
24 Jaddoe VW, Mackenbach JP, Moll HA, Steegers EA, Tiemeier H, Verhulst FC *et al.* The Generation R Study: design and cohort profile. *Eur J Epidemiol* 2006; **21**: 475–484.
25 Statistics Netherlands. Migrants in the Netherlands 2004 (Allochtonen in Nederland 2004). *Voorburg/Heerlen* 2004. http://www.cbs.nl.
26 Statistics Netherlands. Standard classification of education 2003 (Standaard onderwijsindeling 2003). *Voorburg/Heerlen* 2004. http://www.cbs.nl.
27 Brown MA, Lindheimer MD, de Swiet M, Van Assche A, Moutquin JM. The classification and diagnosis of the hypertensive disorders of pregnancy: statement from the International Society for the Study of Hypertension in Pregnancy (ISSHP). *Hypertens Pregnancy* 2001; **20**: IX–XIV.
28 McNamee R. Confounding and confounders. *Occup Environ Med* 2003; **60**: 227–234; quiz 164, 234.
29 El Assaad MA, Topouchian JA, Darne BM, Asmar RG. Validation of the Omron HEM-907 device for blood pressure measurement. *Blood Press Monit* 2002; **7**: 237–241.
30 MacKinnon DP, Krull JL, Lockwood CM. Equivalence of the mediation, confounding and suppression effect. *Prev Sci* 2000; **1**: 173–181.
31 Victora CG, Huttly SR, Fuchs SC, Olinto MT. The role of conceptual frameworks in epidemiological analysis: a hierarchical approach. *Int J Epidemiol* 1997; **26**: 224–227.
32 Patja K, Jousilahti P, Hu G, Valle T, Qiao Q, Tuomilehto J. Effects of smoking, obesity and physical activity on the risk of type 2 diabetes in middle-aged Finnish men and women. *J Intern Med* 2005; **258**: 356–362.
33 Omvik P. How smoking affects blood pressure. *Blood Press* 1996; **5**: 71–77.
34 Lynch J, Kaplan GA. Socioeconomic position. In: Berkman LF, Kawachi I (eds). *Social Epidemiology*, 1st edn. Oxford University Press: Oxford, 2000, pp 13–35.
35 Braveman PA, Cubbin C, Egerter S, Chideya S, Marchi KS, Metzler M *et al.* Socioeconomic status in health research: one size does not fit all. *JAMA* 2005; **294**: 2879–2888.
36 Galobardes B, Shaw M, Lawlor DA, Lynch JW, Davey Smith G. Indicators of socioeconomic position (part 1). *J Epidemiol Community Health* 2006; **60**: 7–12.
37 Center for Research and Statistics, Rotterdam (COS), . 2005:Center for Research and Statistics, Rotterdam (COS) http://www.cos.rotterdam.nl; 2005.
38 Tubbergen P, Lachmeijer AM, Althuisius SM, Vlak ME, van Geijn HP, Dekker GA. Change in paternity: a risk factor for preeclampsia in multiparous women? *J Reprod Immunol* 1999; **45**: 81–88.
39 Colhoun HM, Hemingway H, Poulter NR. Socioeconomic status and blood pressure: an overview analysis. *J Hum Hypertens* 1998; **12**: 91–110.
40 Hermida RC, Ayala DE, Iglesias M. Predictable blood pressure variability in healthy and complicated pregnancies. *Hypertension* 2001; **38**: 736–741.
41 Gillman MW, Cook NR, Evans DA, Rosner B, Hennekens CH. Relationship of alcohol intake with blood pressure in young adults. *Hypertension* 1995; **25**: 1106–1110.
42 Zhang J, Klebanoff MA, Levine RJ, Puri M, Moyer P. The puzzling association between smoking and hypertension during pregnancy. *Am J Obstet Gynecol* 1999; **181**: 1407–1413.
43 Janzon E, Hedblad B, Berglund G, Engstrom G. Changes in blood pressure and body weight following smoking cessation in women. *J Intern Med* 2004; **255**: 266–272.
44 Chesley LC. Hypertension in pregnancy: definitions, familial factor, and remote prognosis. *Kidney Int* 1980; **18**: 234–240.
45 Franklin SS, Pio JR, Wong ND, Larson MG, Leip EP, Vasan RS *et al.* Predictors of new-onset diastolic and systolic hypertension: the Framingham Heart Study. *Circulation* 2005; **111**: 1121–1127.