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Prediction of preterm pre-eclampsia according to NICE and ACOG criteria: descriptive study of 597 492 Danish births from 2008 to 2017

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KEYWORDS: American College of Obstetricians and Gynecologists; National Institute for Health and Care Excellence; pre-eclampsia; screening

CONTRIBUTION

What are the novel findings of this work?
Based on Danish national data including 597 492 births, we have demonstrated that the incidence of preterm pre-eclampsia remained largely unchanged from 2008 to 2017, despite changes in the criteria for offering aspirin treatment according to maternal risk factors.

What are the clinical implications of this work?
The findings of this study highlight that screening for pre-eclampsia by maternal risk factors using the criteria of the National Institute for Health and Care Excellence or the American College of Obstetricians and Gynecologists should include both high- and moderate-risk factors.

ABSTRACT

Objective *The aim of this national study was to examine the incidence of preterm pre-eclampsia (PE) and the proportion of women with risk factors for PE, according to the criteria suggested by the National Institute for Health and Care Excellence (NICE) and the American College of Obstetricians and Gynecologists (ACOG), during a 10-year period in Denmark.*

Methods *Data from The Danish National Patient Registry and the Danish Medical Birth Registry were used to obtain the incidence of preterm PE with delivery < 37 weeks' gestation and risk factors for PE for all deliveries in Denmark from 1 January 2008 to 31 December 2017. The proportion of women with at least one high-risk factor and/or at least two moderate-risk factors for PE, according to the NICE and ACOG criteria, and the detection rate for preterm PE were examined. Race, socioeconomic status and the woman's weight at birth were not available from the registries used, and information on Type-2 diabetes was found to be invalid.*

Results *Of the 597 492 deliveries during the study period, any PE was registered in 3.2%, preterm PE < 37 weeks in 0.7% and early-onset PE < 34 weeks' gestation in 0.3%. These proportions remained largely unchanged from 2008 to 2017. Overall, the NICE criteria were fulfilled in 7.5% of deliveries and the ACOG criteria in 17.3%. In the total population, the NICE criteria identified 47.6% of those with preterm PE and the ACOG criteria identified 60.5%. The current criteria for offering aspirin treatment in Denmark largely correspond to having at least one NICE high-risk factor. In 2017, a total of 3.5% of deliveries had at least one NICE high-risk factor, which identified 28.4% of cases that later developed preterm PE.*

Conclusions *The incidence of preterm PE remained largely unchanged in Denmark from 2008 to 2017. Prediction of PE according to high-risk maternal factors could be improved by addition of moderate-risk factors.*

INTRODUCTION

Pre-eclampsia (PE) is one of the most frequent and severe pregnancy complications and has a strong association

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with preterm birth. The incidence of this obstetric syndrome has been reported to vary from 2% to 8% in different populations[1,2]. It is possible to prevent the development of preterm PE by treatment with low-dose aspirin in women who are at high risk, but the results of meta-analyses have demonstrated the importance of treatment onset before 16 weeks of gestation with a daily dose of at least 100 mg[3].

According to guidelines from the National Institute for Health and Care Excellence (NICE) and the American College of Obstetricians and Gynecologists (ACOG), women at high risk of developing PE should be offered 75–150 mg of aspirin daily from 12 weeks of gestation until birth, with high risk defined as having at least one high-risk factor or more than one moderate-risk factor[4,5]. The definitions of high- and moderate-risk factors differ slightly between the two guidelines. Current criteria for offering aspirin treatment in Denmark largely correspond to having at least one NICE high-risk factor.

It has been shown recently that a combination of maternal characteristics and medical history with measurement of mean arterial blood pressure, flow in the uterine artery and the biochemical markers pregnancy-associated plasma protein-A and placental growth factor (PlGF) improves markedly the prediction of preterm PE in the first trimester of pregnancy[6–8].

The aim of this national study was to examine the incidence of preterm PE during a 10-year period and the proportion of women with risk factors for PE according to the criteria suggested by NICE and ACOG, as well as the currently used criteria in Denmark, in the Danish population, which can be considered a low-risk population with regard to PE.

PATIENTS AND METHODS

In Denmark, all individuals are registered with a personal identification number, which is used for all contacts with the Danish healthcare system and forms the basis for registration of diagnosis codes in the Danish healthcare registries. We used data from The Danish National Patient Registry, which was established in 1976, and the Danish Medical Birth Registry, which was established in 1973, to obtain the registry-based incidence of preterm PE as well as the incidence of high- and moderate-risk factors for PE according to the NICE and ACOG criteria (Table S1)[4,5], for all Danish women with a delivery between 1 January 2008 and 31 December 2017. All diagnoses in the registries were made by clinicians and coded using the International Classification of Diseases (ICD), 8th and 10th revisions. For women with more than one delivery during the study period, all pregnancies were included. The study was approved by the Danish Data Protection Agency (P-2020-213).

Pre-eclampsia

The diagnosis of PE was based on ICD diagnosis codes DO11, DO140, DO141, DO142, DO149, DO150, DO151, DO152 and DO159. Preterm PE was defined as a PE diagnosis and gestational age at delivery less than 37 weeks, and early-onset PE was defined as a diagnosis of PE and gestational age at delivery less than 34 weeks. Until 2017, the Danish national guideline (https://www.dsog.dk/obstetrik) defined PE as gestational hypertension accompanied by proteinuria and/or specific signs or symptoms of significant end-organ dysfunction (for example, thrombocytopenia, evidence of kidney dysfunction, impaired liver function, pulmonary edema or neurological complications). Gestational hypertension was defined as blood pressure $\geq$ 140 mmHg systolic or $\geq$ 90 mmHg diastolic on three separate readings after 20 weeks' gestation in a woman with previously normal blood pressure. Proteinuria was defined as $\geq$ 0.3 g in 24 h or at least ++ on dipstick analysis of midstream urine specimens if no 24-h collection was available. In the revision of the Danish guideline in 2017, uteroplacental dysfunction, defined as estimated fetal weight below the 10th percentile, was added to the list of signs or symptoms of significant end-organ dysfunction.

Risk factors

For this study, information regarding risk factors was based on diagnosis codes in The Danish National Patient Registry and the Danish Medical Birth Registry. PE during a previous pregnancy was based on the diagnosis code DZ358Q, as well as through registration of previous deliveries with a PE diagnosis in the Danish Medical Birth Registry. Chronic kidney disease was based on the diagnosis code DN10-16. Autoimmune disease was based on diagnosis codes DM32, DO991D and D686. Pregestational diabetes was based on a diagnosis code of Type-1 diabetes (DE10 and 249) before the onset of pregnancy. Since information regarding Type-2 diabetes was found not to be valid in the registries, this risk factor was omitted in this study. Chronic hypertension was based on diagnosis codes DI10, DI15, DO119 and DO13. First pregnancy was defined as nulliparity (i.e. first delivery) and was based on registered deliveries for all women in the Danish Medical Birth Registry. Maternal age was defined as the age of the woman at the date of delivery. Interpregnancy interval of more than 10 years was based on previous deliveries registered in the Danish Medical Birth Registry from 1997 onwards and was defined as at least 10 years since the last recorded delivery for each woman. Family history of PE was defined as women from same mother having a history of PE (i.e. having a sister with a history of PE) based on the Danish Medical Birth Registry and the Danish Civil Registration System. Multifetal pregnancy was based on registration in the Danish Medical Birth Registry. Body mass index has been reported in the Danish Medical Birth Registry from 2003 onwards and is based on self-reported prepregnancy weight and height. Information about race, socioeconomic status and the woman's weight at birth was not available from the used registries.

Statistical analysis

The incidence of preterm PE was calculated overall and annually from 2008 to 2017, including all deliveries. The proportion of women who had at least one high-risk factor and/or at least two moderate-risk factors was reported based on the NICE and ACOG criteria (Table S1), corresponding to the screen-positive rates for these screening criteria. High-risk factors did not include Type-2 diabetes in this study. Moderate ACOG risk factors did not include race, socioeconomic status and the woman's weight at birth. Prediction of preterm PE was calculated according to the NICE and ACOG criteria, respectively, and was reported as the observed detection rate (sensitivity) and positive predictive value. The proportion of deliveries that fulfilled the NICE and ACOG criteria, as well as the prediction of preterm PE according to these criteria, were also reported separately for singleton deliveries. The chi-square test for trend was used to test for a potential increase or decrease in the incidence of PE, screen-positive rates and detection rates during the period 2008 to 2017.

RESULTS

The cohort included data from 597 492 deliveries between 1 January 2008 and 31 December 2017. Overall, during the 10-year period, the incidence of any PE was 3.2%, with an incidence of preterm PE with delivery < 37 weeks and early-onset PE with delivery < 34 weeks' gestation of 0.7% and 0.3%, respectively. The incidence of preterm PE and early-onset PE remained largely unchanged over the 10-year period (Figure 1), although the characteristics of the population changed slightly (Table 1). For example, the rate of smoking during pregnancy decreased significantly from 11.0% in 2008 to 6.2% in 2017 and multifetal gestations became significantly less frequent during the 10-year period. Conversely, the rate of fertility treatment increased significantly from 6.3% to 8.5% and the rate of nulliparity increased from 43.0% to 48.5%.

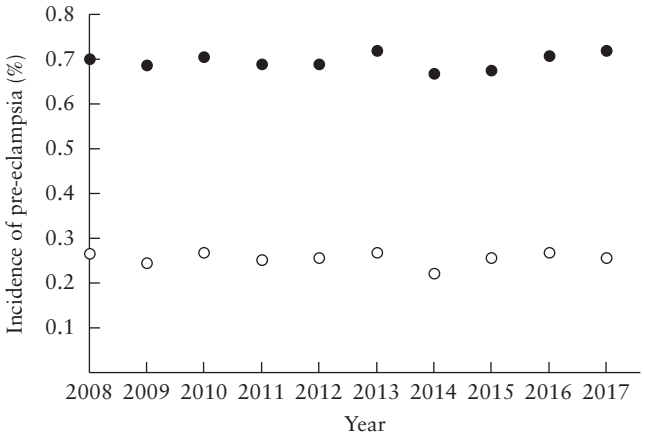

Figure 1 Incidence of preterm pre-eclampsia < 37 weeks (*P*-value for trend, 0.83) (●) and early-onset pre-eclampsia < 34 weeks (*P*-value for trend, 0.90) (○) among deliveries in Denmark from 2008 to 2017.

The proportion of deliveries with at least one high-risk factor and/or at least two moderate-risk factors increased significantly during the 10-year period according to both the NICE and ACOG criteria (Table 2). In 2008, 6.8% of all deliveries fulfilled the NICE criteria for aspirin treatment, while the proportion was 8.1% in 2017. The corresponding proportions were 15.4% and 18.2% for the ACOG criteria. The proportion of deliveries with at least one NICE high-risk factor, which corresponds largely to the current Danish criteria for offering aspirin treatment, increased significantly from 3.2% in 2008 to 3.5% in 2017.

Table S2 shows the incidence of preterm PE among deliveries that fulfilled the NICE or ACOG criteria from 2008 to 2017, i.e. the positive predictive value. Overall, 5.4% of pregnancies with at least one high-risk factor according to NICE criteria and 5.6% of pregnancies with at least one high-risk factor according to ACOG criteria developed preterm PE. For pregnancies with at least one high-risk factor and/or at least two moderate-risk factors, the corresponding proportions were 4.4% and 2.4%. Preterm PE occurred in 0.4% of deliveries that did not fulfill the NICE criteria and in 0.3% of deliveries that did not fulfil the ACOG criteria for aspirin treatment.

The detection rate of preterm PE did not change significantly from 2008 to 2017 (Table 3). Using the NICE high-risk factors alone, corresponding to the Danish criteria, yielded an overall detection rate of preterm PE of 26.6%. There were only minor differences between the detection rates of preterm PE and early-onset PE (Table S3). Figure 2 shows the screen-positive rate and detection rate for preterm PE in 2017 according to the Danish criteria, the NICE criteria and the ACOG criteria.

The cohort included 585 465 singleton pregnancies, with an overall incidence of PE of 3.1%; 0.6% developed preterm PE and 0.2% developed early-onset PE. Omitting multifetal gestations from the overall population led to only a slight decrease in the proportion of deliveries that fulfilled the NICE or ACOG criteria, and prediction of preterm PE was largely unchanged (Tables S4–S6). In 2017, the incidence of preterm PE was 5.3% among singleton pregnancies with at least one high-risk factor according to the NICE criteria.

DISCUSSION

The most important finding of this large national study of births in Denmark from 2008 to 2017 is that the incidence of preterm PE remained largely unchanged, at a rate of 0.7%, despite the increased focus on preventing preterm PE. The incidence may have remained unchanged due to simultaneous changes in the incidence of different risk factors during the study period, i.e. a decrease in the rate of multiple pregnancy, but increases in the rates of fertility treatment and nulliparity.

Our data suggest a slight, although not statistically significant, increase in the detection rate for preterm

Table 1 Maternal background characteristics, obstetric history and chronic diseases in 597 492 deliveries in Denmark from 2008 to 2017

Variable	*Overall* (n = *597 492*)	*2008* (n = *64 414*)	*2009* (n = *62 292*)	*2010* (n = *62 904*)	*2011* (n = *58 556*)	*2012* (n = *57 493*)	*2013* (n = *55 378*)	*2014* (n = *56 451*)	*2015* (n = *57 890*)	*2016* (n = *61 271*)	*2017* (n = *60 843*)	P *for trend**
Maternal age												
< 25 years	12.6	12.6	12.5	12.8	12.9	13.0	12.9	12.6	12.4	12.3	11.8	—
25–29 years	32.3	31.2	31.2	30.8	30.8	31.5	31.7	32.9	33.5	34.4	34.7	—
30–34 years	36.0	37.9	37.6	37.2	36.7	36.0	35.8	34.8	34.9	34.4	34.7	—
35–39 years	15.6	15.1	15.6	16.1	16.3	16.1	15.9	15.9	15.4	15.3	14.9	—
≥ 40 years	3.5	3.1	3.2	3.1	3.3	3.5	3.7	3.8	3.8	3.7	3.9	< 0.001
BMI†												
< 18.5 kg/m^2	4.4	4.3	4.2	4.3	4.1	4.4	4.4	4.5	4.6	4.5	4.4	—
18.5–24.9 kg/m^2	61.5	62.1	62.3	61.8	61.0	61.3	61.7	62.1	61.7	61.4	59.9	—
25.0–29.9 kg/m^2	21.2	21.3	20.9	21.3	21.6	21.3	21.1	20.8	21.0	21.1	21.8	—
30.0–34.9 kg/m^2	8.3	7.8	8.2	8.2	8.7	8.4	8.4	8.3	8.2	8.6	8.8	—
≥ 35.0 kg/m^2	4.5	4.4	4.5	4.5	4.7	4.6	4.4	4.4	4.4	4.5	5.0	< 0.001
Smoker	8.4	11.0	10.2	9.6	9.0	8.6	7.8	7.7	7.3	6.5	6.2	< 0.001
Fertility treatment	7.6	6.3	6.3	7.1	8.3	7.2	7.9	7.9	8.0	8.3	8.5	< 0.001
Nulliparous	45.6	43.0	44.1	44.0	44.0	45.2	46.2	46.3	46.8	48.0	48.5	< 0.001
Multifetal gestation	2.0	2.3	2.2	2.1	2.2	2.2	2.1	1.9	1.7	1.7	1.8	< 0.001
Previous PE	2.4	2.2	2.3	2.3	2.4	2.3	2.4	2.4	2.5	2.3	2.4	0.001
Family history of PE‡	0.2	0.2	0.2	0.2	0.2	0.2	0.3	0.2	0.2	0.2	0.2	0.02
> 10 years since last pregnancy	1.4	0.9	1.1	1.3	1.4	1.5	1.6	1.6	1.5	1.4	1.5	< 0.001
Chronic hypertension	0.5	0.4	0.4	0.4	0.6	0.4	0.4	0.4	0.5	0.4	0.6	< 0.001
Chronic kidney disease	0.3	0.3	0.2	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.07
Type-1 diabetes	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.50
Autoimmune disease												
SLE	0.06	0.05	0.04	0.05	0.06	0.06	0.06	0.05	0.06	0.05	0.06	0.24
APS	0.04	0.03	0.03	0.03	0.03	0.02	0.03	0.03	0.06	0.04	0.07	< 0.001

Data are given as %. *A *P*-value < 0.004 was considered significant after Bonferroni adjustment (0.05/14 = 0.004). †Body mass index (BMI) was not reported in 4.2% of all pregnancies (in 4.3% of women who did not develop pre-eclampsia (PE) and in 2.2% of women who developed PE). ‡Defined as having a sister with a PE diagnosis. APS, antiphospholipid syndrome; SLE, systemic lupus erythematosus.

Table 2 Proportion of pregnancies that fulfilled NICE or ACOG risk criteria for pre-eclampsia (i.e. screen-positive rate), delivered in Denmark from 2008 to 2017

Variable	*Overall* (n = 597 492)	*2008* (n = 64 414)	*2009* (n = 62 292)	*2010* (n = 62 904)	*2011* (n = 58 556)	*2012* (n = 57 493)	*2013* (n = 55 378)	*2014* (n = 56 451)	*2015* (n = 57 890)	*2016* (n = 61 271)	*2017* (n = 60 843)	P *for trend**
NICE criteria												
≥ 1 high-risk factor†	3.4	3.2	3.3	3.3	3.6	3.3	3.5	3.5	3.6	3.5	3.5	< 0.001
≥ 2 moderate-risk factors‡	4.3	3.8	4.0	4.0	4.3	4.6	4.5	4.4	4.2	4.5	4.9	< 0.001
≥ 1 high-risk and/or ≥ 2 moderate-risk factors	7.5	6.8	7.1	7.2	7.7	7.6	7.7	7.8	7.6	7.7	8.1	< 0.001
ACOG criteria§												
≥ 1 high-risk factor†	5.4	5.4	5.4	5.4	5.7	5.4	5.5	5.3	5.2	5.1	5.2	0.002
≥ 2 moderate-risk factors‡	12.8	10.9	11.8	12.3	13.1	13.2	13.3	13.3	13.2	13.6	13.9	< 0.001
≥ 1 high-risk and/or ≥ 2 moderate-risk factors	17.3	15.4	16.3	16.8	17.8	17.6	17.8	17.7	17.5	17.8	18.2	< 0.001

Data are given as %. *A *P*-value < 0.008 was considered significant after Bonferroni adjustment (0.05/6 = 0.008). †The group with at least one high-risk factor also includes women with moderate-risk factors. ‡The group with at least two moderate-risk factors also includes women with high-risk factors. §Modified ACOG criteria were used as information about the moderate-risk criteria of race, socioeconomic status and the woman's weight at birth was not available from the registries used, and information on the high-risk criterion of Type-2 diabetes was found to be invalid.

Table 3 Detection rate for preterm pre-eclampsia < 37 weeks using NICE or ACOG risk criteria for pre-eclampsia in pregnancies delivered in Denmark from 2008 to 2017

Variable	*Overall* (n = 4158)	*2008* (n = 451)	*2009* (n = 427)	*2010* (n = 444)	*2011* (n = 404)	*2012* (n = 396)	*2013* (n = 398)	*2014* (n = 377)	*2015* (n = 391)	*2016* (n = 433)	*2017* (n = 437)	P *for trend**
NICE criteria												
≥ 1 high-risk factor†	26.6	27.3	24.8	26.1	29.5	23.5	27.6	24.4	30.2	23.8	28.4	0.78
≥ 2 moderate-risk factors‡	25.9	21.5	26.0	22.5	24.0	31.6	26.1	28.9	26.1	26.6	26.5	0.04
≥ 1 high-risk and/or ≥ 2 moderate-risk factors	47.6	43.2	46.1	45.0	48.8	50.3	49.0	49.3	52.4	46.0	47.4	0.10
ACOG criteria§												
≥ 1 high-risk factor†	42.9	39.5	40.7	41.9	45.3	43.9	46.2	43.0	47.6	39.5	42.1	0.38
≥ 2 moderate-risk factors‡	30.6	25.3	28.1	29.3	30.0	35.6	30.4	32.6	33.0	30.7	32.5	0.009
≥ 1 high-risk and/or ≥ 2 moderate-risk factors	60.5	54.8	58.8	59.5	61.4	63.9	63.6	63.9	65.0	56.6	59.5	0.15

Data are given as %. *A *P*-value < 0.008 was considered significant after Bonferroni adjustment (0.05/6 = 0.008). †The group with at least one high-risk factor also includes women with moderate-risk factors. ‡The group with at least two moderate-risk factors also includes women with high-risk factors. §Modified ACOG criteria were used as information on the moderate-risk criteria of race, socioeconomic status and the woman's weight at birth was not available from the registries used, and information on the high-risk criterion of Type-2 diabetes was found to be invalid.

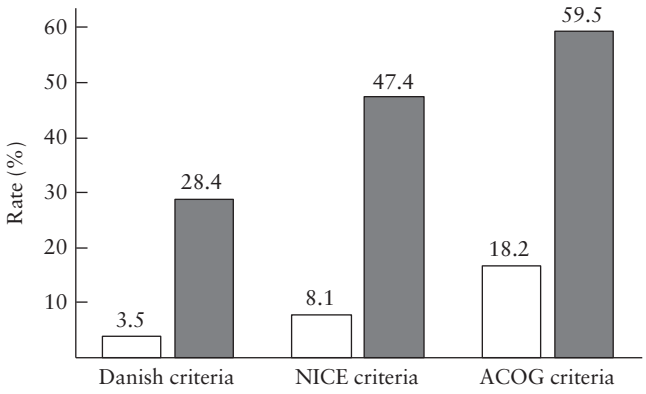

Figure 2 Screen-positive rate (□) and detection rate (■) for preterm pre-eclampsia < 37 weeks in deliveries in Denmark in 2017, according to Danish criteria, NICE criteria and ACOG criteria (modified ACOG criteria were used as information on the moderate-risk criteria of race, socioeconomic status and the woman's weight at birth was not available from the registries used, and information on the high-risk criterion of Type-2 diabetes was found to be invalid).

PE according to maternal risk factors from 2010 to 2011 (Table 3). This could be explained by the greater focus on screening by risk factors and the importance placed on commencing aspirin treatment in the first trimester, following the publication of the meta-analysis by Bujold *et al.*[9] in 2010, in which a greater effect of aspirin was shown when treatment was started before 16 weeks' gestation in high-risk patients. Until 2017, the Danish national PE guideline recommended giving 75 mg of aspirin daily from 12 to 37 weeks to high-risk women, the definition of which corresponds to having at least one NICE high-risk factor. In 2015, Park *et al.*[10] showed that using a strategy of first-trimester screening for early-onset PE and administration of 150 mg of aspirin to the high-risk group reduced effectively the incidence of preterm PE. This might explain, at least in part, the observed drop in the prediction of preterm PE in Denmark from 2015 to 2016, as studies have suggested a greater benefit of aspirin for doses > 100 mg/day[3]. In 2017, the Danish guideline was amended, recommending 150 mg of aspirin.

These national data indicate that, using the present Danish strategy, approximately 3.5% of pregnant women will be offered aspirin treatment, with a detection rate of preterm PE of less than 30%. Applying the combination of high- and moderate-risk factors according to the NICE criteria would increase the screen-positive rate and detection rate to 8.1% and 47.4%, respectively. However, there is evidence to suggest that the most significant change in the performance of first-trimester screening for PE would be the introduction of a first-trimester screening algorithm combining maternal characteristics and medical history with measurements of mean arterial blood pressure, flow in the uterine arteries and PlGF. The Combined Multimarker Screening and Randomized Patient Treatment with Aspirin for Evidence-Based Preeclampsia Prevention (ASPRE) trial showed that this first-trimester screening algorithm would increase the detection rate for preterm PE to 76.7% at a 10.5% screen-positive rate, with the benefit of a 60% reduction in the rate of preterm PE when high-risk women are treated with 150 mg of aspirin[6,11].

The overall performance of the NICE criteria in this study is comparable to results reported from the Screening ProgRamme for prE-Eclampsia (SPREE) study and ASPRE trial[12,13]. We found a screen-positive rate of 7.2% and a detection rate of 39.3% for preterm PE in singleton pregnancies in 2017 when using the NICE criteria including both high- and moderate-risk factors, while Tan *et al.*[12] reported a screen-positive rate of 10.3% and a detection rate of 40.8%. Poon *et al.*[13] found that 4% of the 34 573 women screened in the ASPRE trial fulfilled at least one of the NICE high-risk criteria, and this proportion was 3.5% in the Danish singleton population in 2017.

The main strength of this study is the large nationwide register-based study population with information about preterm PE and risk factors for PE. The study also has some limitations. First, the incidence of PE was based solely on diagnosis codes, and the validity of such diagnoses could be questioned. However, a former Danish study found acceptable agreement between registry-based and chart-review incidences[14]. In addition, in the current study, we focused on preterm and early-onset PE, which further increases the validity, as the most severely complicated pregnancies are the most likely to have been coded by specialist doctors and midwives[15]. Second, we were not able to include all the relevant risk factors as prepregnancy Type-2 diabetes was not coded routinely, which could be explained by these women being seen and followed in the primary healthcare system, in which diagnoses are not reported to the national registries. Furthermore, having a family history of PE was based on information from sisters only and did not include information on the mothers' obstetric history. However, this information on family history was based on registered deliveries as opposed to being self-reported. Information regarding ethnicity and socioeconomic status was not available from our registries. Although this may be important for other populations, it is likely to have little impact on the estimated screening performance in a Danish setting, in which the proportion of non-Caucasian women is relatively small and distributed across all social groups, and all women are offered equal and universal access to the healthcare system, including antenatal care, free of charge. Overall, missing data may be an issue when dealing with register-based data and particularly with diagnosis codes, with it only being possible to see if the given diagnosis code has been registered or not. Third, information on use of aspirin treatment was not available, and we were therefore not able to adjust for the potential preventive effect of this treatment in our cohort. Our reported detection rates may therefore be underestimated due to aspirin treatment, resulting in cases that would otherwise have developed PE being classified as a false-positive screening result[16]. It would, however, not be possible to obtain this information in a register-based study as aspirin is given as an over-the-counter medicine in many countries and,

thus, it could not be extracted from the Danish National Prescription Registry. Including this information in analyses would therefore be best achieved in a study with prospective registration of aspirin treatment.

In conclusion, the incidence of preterm PE remained largely unchanged from 2008 to 2017 in Denmark despite changes in the criteria for offering aspirin treatment, although it cannot be ruled out that the changes to the Danish guidelines in 2017 have had an effect on the rate of preterm PE, which might become evident only after a few years. Prediction of preterm PE according to high-risk maternal factors could be improved by addition of moderate-risk factors.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Table S1 High- and moderate-risk factors for pre-eclampsia, according to the guidelines from the National Institute for Health and Care Excellence (NICE) and the American College of Obstetricians and Gynecologists (ACOG)

Table S2 Incidence of preterm pre-eclampsia < 37 weeks in pregnancies that fulfilled NICE or ACOG risk criteria for pre-eclampsia (i.e. positive predictive value) delivered in Denmark from 2008 to 2017

Table S3 Detection rate for early-onset pre-eclampsia < 34 weeks using NICE or ACOG risk criteria for pre-eclampsia in pregnancies delivered in Denmark from 2008 to 2017

Table S4 Proportion of singleton pregnancies that fulfilled NICE or ACOG risk criteria for pre-eclampsia (i.e. screen-positive rate) delivered in Denmark from 2008 to 2017

Table S5 Incidence of preterm pre-eclampsia < 37 weeks in singleton pregnancies that fulfilled NICE or ACOG risk criteria for pre-eclampsia (i.e. positive predictive value) delivered in Denmark from 2008 to 2017

Table S6 Detection rate for preterm pre-eclampsia < 37 weeks using NICE or ACOG risk criteria for pre-eclampsia in singleton pregnancies delivered in Denmark from 2008 to 2017