Supplemental Digital Content 2. Aim, statistical analysis and main findings of the reviewed studies.

ID	Objective	Main results	Control for nutritional status	Estimators (Statistical tests)
1	To investigate whether a 1st trimester elevation of serum CRP is associated with PE.	1st trimester CRP levels were significantly higher among women who subsequently developed PE than controls (4.6 *vs.* 2.3 mg/L, p = 0.04). The highest quartile of CRP was associated with PE (OR = 3.2, 95% CI: 1.1–9.3; p = 0.02).	Association of CRP and PE lost significance after inclusion of BMI in the MLRM (OR=1.1, 95% CI: 0.3–4.3; p=0.94).	Median group difference (Wilcoxon rank-sum test), OR (MLRM).
2	To investigate whether a maternal inflammatory response at the 18th week precedes the development of PE.	No statistically significant difference in 2nd trimester levels of micro-CRP were observed between controls and women who subsequently developed PE, whether it was early-onset [< 37 weeks] (4.54 mg/L, range: 0.56–32.00 *vs.* 4.00 mg/L, range: 0.15–27.20; p = 0.96) or late-onset [≥ 37 weeks] (4.30 mg/L, range: 0.62–34.20 *vs.* 4.10 mg/L, range: 0.89–20.20; p = 0.46), respectively.	Case and control groups comparable with respect to BMI.	Median (range) group difference (Paired two-tailed Wilcoxon signed rank test).
3	To investigate whether a maternal inflammatory response precedes the development of PE.	The 2nd trimester levels of highly sensitive CRP were similar in women who subsequently developed PE and in women who experienced healthy pregnancies (1.56 mg/L, IQR: 0.55–3.12 *vs.* 1.28 mg/L, IQR: 0.75–2.08; p = 0.95).	Case and control groups comparable with respect to BMI.	Median (IQR) group difference (ANOVA).
4	To investigate whether CRP levels are elevated during the 1st trimester in women from a low-risk population who subsequently developed PE or delivered a growth-restricted offspring.	1st trimester mean CRP levels were significantly higher in the PE group (0.158 g/L ± 0.029) when compared to the control group (0.067 g/L ± 0.004); p = 0.002. The results remained statistically significant when parity, gravidity, age at delivery and gestational age matched controls (0.0072 g/L ± 0.0019) were employed in comparison to PE group (0.0158 g/L ± 0.0029); p = 0.041.	Did not adjust for nutritional status	Mean (± SD) group difference (Mann Whitney U-test).
5	To examine weather lipid abnormalities and other features related to the "metabolic syndrome" predict the development of PE in GDM women.	3rd trimester CRP levels were significantly higher in GDM-PE (approx. 12.5 mg/L) compared to GDM-N (approx. 6.5 mg/L); $p < 0.05$[1]. In logistic regression, CRP (OR = 1.13, 95% CI: 1.05–1.21) was a significant independent predictor for the development of PE in GDM women.	Mean BMI significantly higher in PE group compared to normotensive women. MLRM not adjusted for BMI.	Group difference; OR (MLRM).
6	To compare baseline and changes in plasma inflammatory markers prospectively among healthy pregnant women and PE.	There were no significant differences in 1st trimester CRP level between controls and women who subsequently developed PE (3.18 mg/L ± 2.60 *vs.* 4.18 mg/L ± 3.75, respectively; p = 0.23). There were significantly higher 3rd trimester CRP levels in women with PE when compared with controls (5.84 mg/L ± 5.38 vs. 3.34 mg/L ± 3.40, respectively; p = 0.0091). This difference lost significance after adjustment for BMI, smoking and gestational age at 3rd trimester.	Case and control groups comparable with respect to BMI.	Mean (± SD) group difference (Two-sample t-test).

Supplemental Digital Content 2. Aim, statistical analysis and main findings of the reviewed studies.

ID	Objective	Main results	Control for nutritional status	Estimators (Statistical tests)
7	To explore the hypothesis that placental debris and systemic inflammation could cause PE.	There were no differences in CRP levels between women who subsequently developed PE and controls at 8 to 20, 23 to 32 and 33 to 39 weeks of gestation[1].	Mean BMI was significantly higher in PE group compared to normotensive women.	MD
8	To examine the independent and joint associations of CRP levels and pre-pregnancy overweight with the risk of PE.	PE group had significantly higher 1st trimester CRP levels than controls (6.5 vs. 3.0 mg/L; $p < 0.001$). Lean women with 1st trimester CRP levels ≥ 4.9 mg/L had increased risk of PE (OR = 2.5, 95% CI: 1.1–5.5) compared to lean with CRP <4.9 mg/L. Overweight women with 1st trimester CRP levels ≥ 4.9 mg/L (OR =5.5, 95% CI: 2.6-11.4) and <4.9 mg/L (OR = 4.9, 95% CI: 2.0–11.7) had increased risk of PE compared to lean women with CRP <4.9 mg/L.	Association lost significance after adjustment for BMI (OR =1.8, 95% CI: 0.8–4.1; p =0.160). When stratified by BMI, the risk differed for lean and overweight women.	Median group difference (Mann-Whitney two-sample statistics), OR (MLRM).
9	To quantify the mediating role of inflammation and triglycerides in the association between pre-pregnancy BMI and PE.	2nd trimester CRP levels were significantly higher in PE women (0.49 mg/dl, 95% CI: 0.37–0.64) than in controls (0.33 mg/dl, 95% CI: 0.30–0.38); $p < 0.01$. The proportion of women with markedly elevated 2nd trimester CRP level (> 1.0 mg/dl) was also significantly higher in PE group (23.6%) than in controls (10.3%); $p < 0.05$.	PE group had significantly more women with BMI ≥ 25.0 kg/m², who tended to have higher CRP levels at ≤20 weeks' gestation. Estimated that ≈69% of BMI effect was directly mediated by pathways, not involving inflammation ($p = 0.08$).	Geometric mean (95% CI) and proportions group difference (Student t-test and chi-squared test, respectively); MLRM.
10	To investigate the variation of CRP in women with normal pregnancy and those with subsequent PE	CRP levels were significantly higher in women with PE than in controls at week 32 (5.1 mg/L ± 2.5 vs. 3.2 mg/L ± 2.2; $p = 0.0007$) and 36 (5.9 mg/L ± 2.2 vs. 4.3 mg/L 2.5; $p = 0.001$), but not at week 16 (4.1 mg/L ± 3.8 vs. 2.9 mg/L ± 2.5; $p = 0.07$).	Did not adjust for nutritional status.	Mean (± SD) group difference.
11	To investigate whether FDM impaired and inflammation precedes clinical PE.	CRP level at study entry were significantly higher among women who subsequently developed PE (8.7 mg/L ± 5.5) when compared to controls ($p = 0.022$).	Case and control groups comparable with respect to BMI (matched).	Mean (± SD) group difference (Two-sample t-test).
12	To test the hypothesis of altered sCD163 levels in predicting PE, compared to neopterin and CRP.	CRP increased during pregnancy in both the control and PE group. CRP was higher at week 38 in PE (159 nmol/L, IQR: 73-741) than in the control group (91 nmol/L, IQR: 48-230); $p=0.0189$.	Did not adjust for nutritional status	Median (IQR) group difference (Student t-test)

Supplemental Digital Content 2. Aim, statistical analysis and main findings of the reviewed studies.

ID	Objective	Main results	Control for nutritional status	Estimators (Statistical tests)
13	To investigate the association of serum markers measured in the 1st trimester and nuchal translucency thickness with the risk of PE.	There were no significant differences in median values give values of CRP in PE and the control group. Women with CRP ≥6.32μg/L (median) were not more likely to develop PE when compared to women with CRP < median (OR=1.51, 95% CI: 0.72-3.17).	Case and control groups comparable with respect to maternal weight.	Median (range) group difference (Wilcoxon rank-sum test) and OR (Conditional logistic regression model).
14	To test the screening and predictive abilities of the CRP test in order to detect and diagnose pregnant women prone to PE prior to onset of symptoms.	Mean serum CRP were significantly different comparing preeclamptic patients (6.18 mg/L) with normal patients (4.12 mg/L), p=0.003. Patients whose CRP level was ≥4.0 mg/L were six times more likely to have PE than those with CRP ≤4.0 mg/L (k=9.4; p=0.002; OR=6.15; 95%CI=0.69-22.28).	MD	Mean group difference. Chi-square test.
15	To determine whether *Chlamydia pneumoniae* antibodies and hsCRP levels in maternal sera are associated with PE or GH.	hsCRP (median [IQR]) were 2.4 [0.9-4.3] mg/L in women that developed preeclampsia and 1.8 [0.8-3.8] among those that remain normotensive (p>0.05).	Mean BMI was significantly higher in PE and GH group compared to normotensive women.	Median (IQR) group difference (Mann Whitney *U* test)
16	To investigate the relationship between maternal periodontal disease, maternal systemic inflammation and PE risk.	Women with CRP ≥75th percentile at enrolment were more likely to develop PE (RR=2.2, 95% CI: 1.1-4.4) than those with CRP <75th percentile. After adjustment for gestational age at delivery and smoking history, the likelihood for PE significantly increased for women with periodontal disease and CRP ≥75th percentile (RR=5.8, 95% CI: 1.2-26.9) in relation to those with the absence of periodontal disease and CRP <75th percentile.	Case and control groups comparable with respect to maternal weight.	RR (MLRM)
17	To compare 1st trimester level of PTX-3 and CRP in women who subsequently developed pre-term PE to those requiring preterm delivery for FGR or with a normal pregnancy outcome.	There were no significant differences in 1st trimester CRP levels between women with a normal pregnancy outcome (0.30 mg/dL; IQR: 0.17–1.37), preterm PE (0.37 mg/dL, IQR: 0.20–1.21), and preterm FGR (0.24 mg/dL, IQR: 0.18–0.65); p = 0.26.	Case and control groups comparable with respect to BMI.	Median (IQR) group difference (Kruskal-Wallis test)

Supplemental Digital Content 2. Aim, statistical analysis and main findings of the reviewed studies.

ID	Objective	Main results	Control for nutritional status	Estimators (Statistical tests)
18	To assess the relationship between CRP in early pregnancy and its change with the subsequent development of PE in a high risk population.	Maternal CRP levels were not different at baseline between women who later developed PE (1.17 mg/dL, IQR: 0.09–5.72) and controls (1.01 mg/dL, IQR: 0.01–4.97); $p > 0.05$. There was no association of baseline CRP level (OR: 1.0; 95% CI: 1.00–1.00) or the change in CRP level across pregnancy (OR: 0.99; 95% CI: 0.98–1.00) with development of PE.	Case and control groups comparable with respect to BMI. The MLRM was adjusted for BMI and found no association (OR: 1.0; 95% CI: 1.00–1.00)	Median (IQR) group difference (Wilcoxon rank-sum test) and OR (MLRM).
19	Evaluate whether the maternal serum proteomic profile for patients with clinical PE differs from those with normotensive pregnancies.	In pairwise comparison, CRP level was significantly higher between mild PE vs. normotense (fold change 6.50, p=0.0160); but not between severe PE and normotense (fold change 3.8, p=0.370).	Did not adjust for nutritional status.	ANOVA; MLRM; ROC curve
20	To estimate the ability of maternal serum biomarkers and uterine artery Doppler in predicting PE.	Crude analysis showed that 2nd trimester CRP level was significantly associated with the occurrence of PE (OR = 1.65; 95% CI: 1.13–2.43). In the adjusted analysis, only Doppler RI, cystatin C and CRP level (OR=2.19; 95% CI: 1.21-3.96) remained as independent predictors of PE. The AUC for 2nd trimester CRP level as a single marker in the screening for PE was 0.634 (95% CI: 0.536–0.732).	Mean BMI was significantly higher in PE group, when compared to normotensive women. The logistic regression was not adjusted for BMI.	OR (Univariable and MLRM); AUC (ROC curve)
21	To investigate hsCRP levels in early pregnancy and blood pressure in different periods of pregnancy and the risk of gestational hypertensive disorders.	No significant association was observed for the risk of PE in mothers with elevated CRP levels. The trend test showed an association of higher CRP levels with an increased risk of PE (P for trend <0.05). All effect estimates attenuated towards the null after adjustment for maternal BMI.	The association of CRP and PE lost significance after inclusion of BMI in the MLRM.	OR (MLRM) and tests for trends.
22	To examine the association of hsCRP with preeclampsia, to adverse pregnancy outcomes and to the maternal diet.	Lean women with high hsCRP had a greater likelihood (2.6- to 3.5-fold increases) of PE. In overweight women there were no significant associations of PE and hsCRP levels.	Before stratification for BMI, the chance for PE wasn't increased, but after the stratification, it became apparent that chance was specific to the lean.	OR (MLRM)

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ID	Objective	Main results	Control for nutritional status	Estimators (Statistical tests)
23	To investigate the association between hsCRP serum levels in early pregnancy with the severity of preeclampsia.	Mean±SD hsCRP levels in mild (7.2±2.2 mg/L) and severe (9.4±3.9 mg/L) PE were significantly higher than the normal group (2.5±2.7 mg/L). The ROC curve showed that hsCRP >4.5 and >5.0 mg/L could predict mild and severe PE, respectively. At this level, sensitivity and specificity for mild PE were 100% and 80.7%, and for severe PE were 93.9% and 75.7%, respectively.	The % of women with BMI≥25,0 were higher in PE groups. After adjustment for pre-pregnancy BMI, hsCRP levels remained higher in severe PE patients compared to mild PE and normotensive patients.	Mean (±SD) group difference (Mann Whitney U-test); MLRM; ROC curve

ID: Identification number, according to Table 1; **ANOVA:** Analysis of variance; **AUC:** Area under the curve; **BMI:** Body mass index; **CI:** Confidence interval; **CRP:** C-reactive protein; **hsCRP:** High-sensitive C-reactive protein; **FDM:** Flow-mediated dilatation; **FGR:** Fetal growth restriction; **GDM:** Gestational diabetes mellitus; **GDM-N:** Gestational diabetes mellitus with normal pregnancy; **GDM-PE:** Gestational diabetes mellitus with preeclampsia; **GH:** Gestational hypertension; **IQR:** Inter-quartile range; **MD:** Missing data; **OR:** Odds ratio; **PE:** Preeclampsia; **PTX-3:** Pentraxin-3; **RI:** Resistance index; **RR:** Risk ratio; **SD:** Standard deviation; **MLRM:** Multiple Logistic Regression Model.