OBJECTIVES
To investigate if preterm preeclampsia prediction can be improved with metabolite biomarkers in three screening resource scenarios:
1. availability of Placental Growth Factor (PIGF),
2. availability of PIGF + Mean Arterial Pressure (MAP)
3. availability of PIGF, MAP + Uterine Artery Pulsatility Index (UTA-PI),

DISCUSSION
➢ Preeclampsia (PE) screening is a key component of antenatal care.
➢ Current benchmark for PE screening1 (Figure 1) is performed at 11th-13th weeks gestation.
➢ Detects 75% of women developing PE with a delivery <37 weeks (preterm PE).
➢ Allows for timely initiation of aspirin prophylaxis, i.e., <16 weeks.1
➢ Universal implementation is hampered by insufficient availability of and access to prenatal care experts.
➢ To improve PE screening further additional biomarkers are required.

BACKGROUND
➢ Recent findings:
  ➢ Early pregnancy metabolite levels associate with preterm PE.
  ➢ Metabolite associations with preterm PE prediction can vary according to maternal body mass index (BMI).5

Hypothesis: Use of patient classification enables a more effective combination of biomarkers and thus improved preterm PE risk prediction (Figure 2).

RESULTS
➢ Metabolite biomarkers can be combined with the established biomarkers PIGF, MAP and UTA-PI to improve the detection of preterm PE risk in a clinically useful way. Pivotal to achieving improved prediction was the classification of pregnant women according to the maternal characteristics of BMI and/or race. This suggests that maternal phenotyping can have a role in improving the prediction of obstetric syndromes like PE.

CONCLUSIONS
➢ Modelling methodology validation: Splitting the patient set into a training (2/3) and a test (1/3) set showed developed models were not overfitted.
➢ 3 Prediction models were developed using the complete data set in accordance with the three resource scenarios investigated.
➢ 26 Metabolites were used across the 3 prediction models; 21 contributed to at least 2 out of 3 prediction models developed.
➢ Detection rates were markedly higher with the prediction models than with the respective reference models (Figure 4), whereby the largest improvements were observed in scenario 2, with a 15% increase over the detection rate estimated for the reference PIGF + MAP.
➢ Prediction was improved in Black (14%) and White (19%).
➢ Prediction was improved in the normal weight (18.5≤BMI<25) and the obese groups (BMI≥30), but not in the overweight group (25≤BMI<30).

STUDY DESIGN
➢ Metabolite data were normalized using multiples of medians.
➢ Model development: (1) in all patients, (2) BMI and/or race patient strata.
➢ Modelling methodology to generate prediction model:
  1. z-score conversion of predictors.
  2. combinatorial modelling of single predictive models.
  3. selection of single sparse models, and
  4. aggregation of the selected models into final prediction model.
➢ Model Prediction performance evaluation: detection rate at 10% FPR.