Detection of false positives from first-trimester screening for preeclampsia at the second trimester of pregnancy (STOP-PRE trial)

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Objective
Preeclampsia (PE) can be screened at different times during pregnancy, but first-trimester screening is the most useful since salicylic acid (ASA) can be started before 16 SG, and 85% of early-onset PE (<34 weeks) and 60% of preterm PE (<37 weeks) can be detected. The biggest drawback of this screening is the high number of false positives. Approximately 10% of the population screened is classified to be at high risk for PE and, therefore, will be treated with ASA. Of this 10%, only around 10% will have preterm PE, even if they are not treated with ASA. Therefore, up to 90% of the remaining patients classified as high risk, will be taking daily ASA unnecessarily throughout their pregnancy. The sFlt-1/PlGF ratio <38 has a high negative predictive value (NPV) for PE, so it could be useful for ruling out patients who have been erroneously classified as being at high risk in the first-trimester screening.

Methods
This was a multicenter, randomized, open-label, parallel-group clinical trial. Routine screening for PE in the first trimester was performed in the 9 participating sites. Screening was made by the Gaussian algorithm with the combination of maternal history, maternal characteristics, pregnancy-associated plasma protein (PAPP-A), placental growth factor (PIGF) and uterine artery Doppler pulsatility index. Women at high risk were treated with 150mg of ASA daily. Women who accepted to participate, signed the informed consent and sFlt-1/PlGF was measured at 24th to 28th weeks of gestation. Participants with sFlt-1/PlGF <38 were randomized (1:1) in two groups. In the control group, ASA was continued until 36 weeks, as in clinical practice. In the intervention group, ASA was stopped at randomization (24th to 28th weeks of gestation). Monthly follow up was performed in both groups and perinatal outcomes were compared. The main outcome was the rate of preterm PE (requiring delivery <37 weeks).

Results
Between May 2019 and June 2021, 971 screened women were at high risk for PE and accepted to participate in this study. A total of 485 women were assigned to the intervention group and 486 to the control group. 32 (3.3%) of them were excluded for the following reasons: being lost to follow up (n=26), for retiring their consent (n=3), and for being erroneously enrolled (n=3). Finally, 474 (50.5%) women in the intervention group and 465 (49.5%) women in the control group were analyzed. In the intervention group, 7 (1.48%) preterm PE were diagnosed and 8 (1.72%) in the control group (OR=0.86, 95% CI: 0.31-2.38). No cases of early-onset PE were found in the intervention group and only one case was diagnosed in the control group.

Conclusion
Women at high risk for PE in the first-trimester screening, which started ASA treatment before 16 weeks of gestation, and with sFlt-1/PlGF ratio <38 at 24th-28th weeks of gestation, can safely stop ASA treatment at 24th-28th weeks without increasing their incidence of preterm PE, which could reduce the risks of iatrogenic complications due to unnecessary ASA treatment.