# Ultrasound in Obstet Gyne 2023 Golob Interim analysis of serum placental growth factor values for use in

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# Interim analysis of serum placental growth factor values for use in pre-eclampsia screening

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Screening for pre-eclampsia (PE) using the Fetal Medicine Foundation (FMF) algorithm identifies higher risk pregnancies that could benefit from increased surveillance and primary prevention with aspirin. The FMF algorithm incorporates serum placental growth factor (PlGF) and pregnancy-associated plasma protein-A (PAPP-A), mean arterial blood pressure and uterine artery pulsatility index to calculate an individualized risk for PE. It has been shown to be superior to screening by maternal characteristics alone in prediction of PE[1].

The FMF algorithm has been part of general antenatal care in our center since January 2022. Serum samples are analyzed by Thermo Fisher Scientific BRAHMS Kryptor analyzers to provide serum PlGF and PAPP-A values. The variables collected are then inputted into Astraia software, which provides a risk estimate as a ratio. In the ASPRE trial, a predicted risk of 1:100 for preterm PE was used to define patients as high risk and offer prophylaxis with low-dose aspirin. This resulted in a screen-positive rate (SPR) of 10.5%[2]. In our center, a wider cut off of 1:150 has been in use since the start of screening with the intention of increasing the detection rate.

PlGF values vary widely across the population and are influenced by a variety of maternal characteristics. The FMF algorithm adjusts serum PlGF values to give a figure in the form of multiples of the median (MoM). Adjustments are based on reference values for different maternal characteristics, so in principal the demographics of different cohorts should not skew the results[3]. Technical issues such as time of transfer for samples, storage of blood and variability in analyzers can also have an impact[4].

Figures 1 and 2 show the distribution of 3031 PlGF results from our center. There is a positive bias in the results with the median figure for MoM being 1.16, i.e. +16%. This would have the effect of underestimating risk and lowering the SPR. A risk of 1:150 in our population therefore only yielded an SPR of 7.5%. A risk of 1:100 would have resulted in an SPR of 5.4%.

The screen positive rate of 7.5% is less than the rate of 10.5% reported by the ASPRE trial. Two recent studies looking at general antenatal populations in Denmark and Spain used a fixed rate of 10%[4,5]. The lower SPR would be expected to result in a lower detection rate.

From our cohort of 3031 patients, so far 2351 have pregnancy outcomes. The incidence of preterm PE with onset <34 weeks was 0.13% (3/2351). The total incidence of all PE was 1.5% (36/2351). The detection rate for preterm PE with onset <34 weeks was 66% (2/3). At a SPR of 7.5% the algorithm is still superior to screening by maternal characteristics for the detection of preterm PE[1].

This demonstrates in a real world setting the possibility for median values to drift from reference values and the importance of regular audit when implementing screening in a new population. These results demonstrate the need to perform adjustments to PlGF MoM which are appropriate for the population in which the algorithm is being used. Correction of this bias in the PlGF MoM would increase the screen positive rate. At present, a fixed SPR of 10% would not have resulted in additional cases being detected but we would expect to see an impact with a larger sample.

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## FIGURE LEGENDS

**Figure 1** Distribution of serum PlGF values in antenatal screening.

**Figure 2** PlGF values in antenatal screening expressed as MoM.

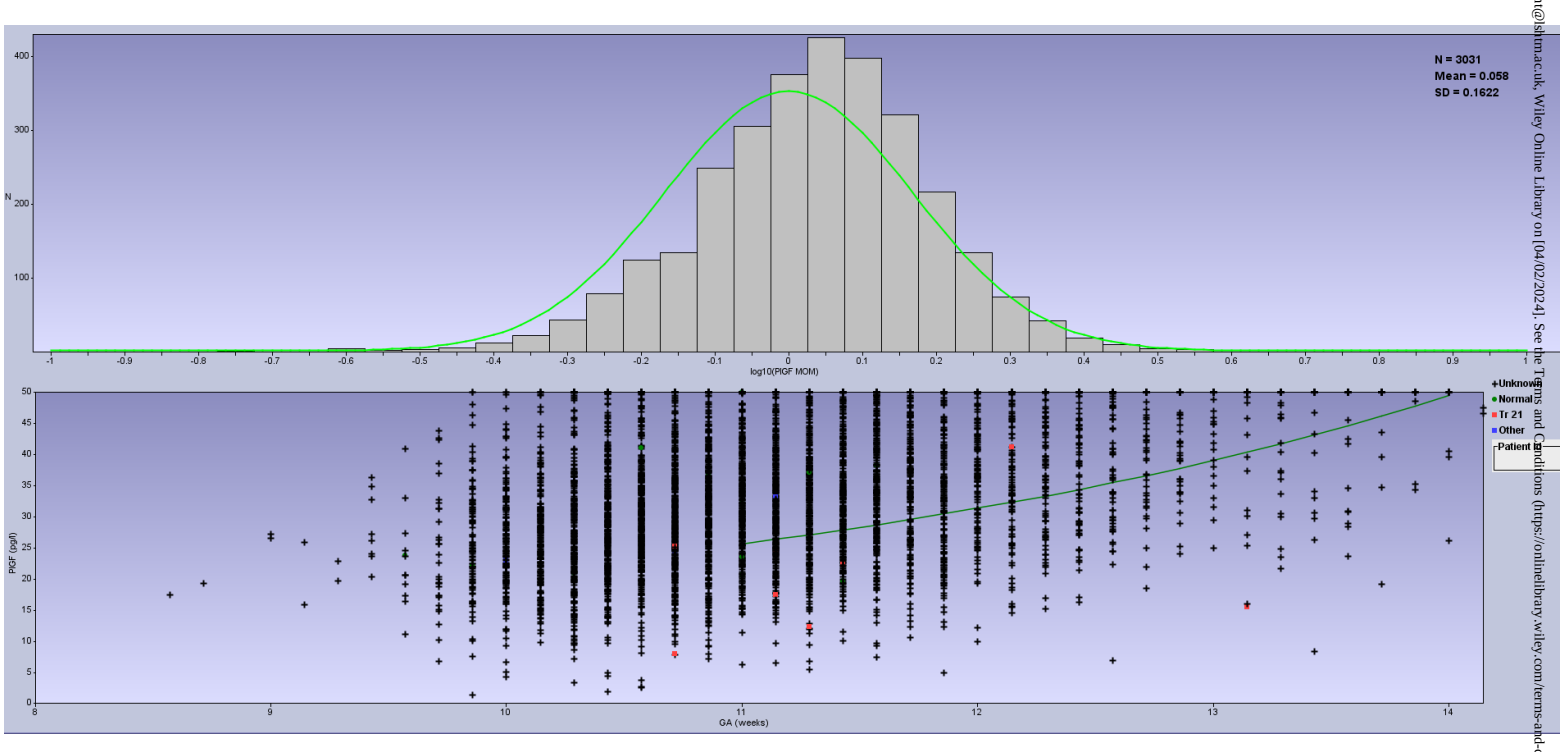


Figure 1.tif

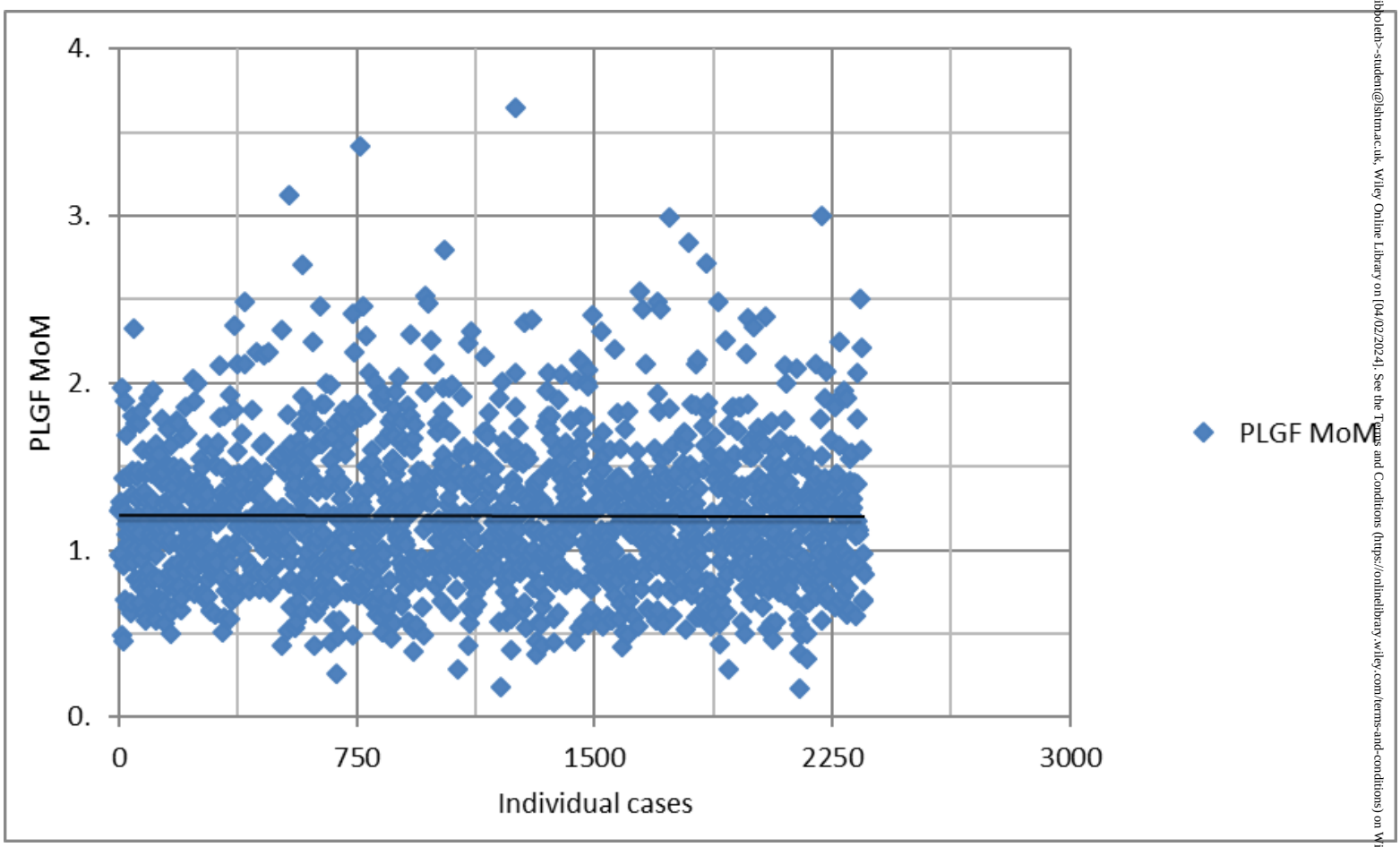


Figure 2.png