Response to ACOG's Preeclampsia Screening Committee Opinion

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In the September issue of Obstetrics Gynecology, ACOG in a Committee Opinion statement endorsed by the Society of Maternal-Fetal Medicine does not recommend screening to predict early onset preeclampsia (EOP) beyond obtaining an appropriate medical history to evaluate for risk factors. Their criticisms of commercial preeclampsia multivariate screening tests employing medical history, demographics, biochemical analytes (PAPPA, P1GF) and biophysical parameters (uterine artery Doppler, maternal arterial blood pressure) included:

- a 7% positive predictive value PPV (Poon. 2009; Hypertension) is too small for screening purposes.
- ‘harm’ incurred by false positives.
- lack of predictive-intervention studies.
- lack of cost-effectiveness studies.

Background

ACOG's 2013 Hypertension in Pregnancy publication states –

- most cases of preeclampsia occur in healthy nulliparous women with no other obvious risks.

- ACOG references 2 studies with prediction of EOP using clinical risk factors achieved a 37% detection rate with false positive rates at 5% and 10%.

I. 7% Positive predictive value – but compared to what?

There is a paucity of published data on the statistical attributes of clinical history as a screening tool for early onset preeclampsia.

- Poon (2014. Prenatal Diagnosis) states there is no published data evaluating the positive predictive value of medical history alone as a screening methodology.

- Disease incidence is not synonymous with positive predictive value. U.S. Preventative Services Task Force states an 8% preeclampsia incidence for high-risk clinical criteria not including primiparity (LeFevre. Ann. Intern. Med. doi:10.7326/M14-1884.) Inclusion of primiparity, as suggested in ACOG's opinion, would significantly lower the incidence of preeclampsia as screened for by history alone.

A 7% PPV for multivariate EOP screening compares favorably to other commonly employed screening tests

Screening Protocol	PPV
First Trimester Screen T21 (1,2,3)	4.4%
First Trimester Screen with Nasal Bone, T21 (1,2,3)	10.5%
First Trimester Screen T18/13 (2,3,4)	9.6%
Quad Screen (2,3,5)	3.5%
Quad ScreenT18 (2,3,6)	7.8%
Open Spina Bifida (7)	1.9%
Breast Cancer Mammography 40-49 years old (8)	4.0%
Breast Cancer Mammography 50-59 years old (8)	9.0%

II. Inconsistencies between ACOG's 2013 Hypertension in Pregnancy monograph and current Committee Opinion.

In 2013, ACOG's Hypertension monograph acknowledges the following core components of commercial multivariate early onset preeclampsia screening –

- "In general, uterine artery Doppler studies are better in predicting early preeclampsia." pg 22
- "Biomarkers for the prediction of preeclampsia are integral to disease stratification and targeted therapy." Pg 22
- "Current evidence suggests that a combination of biomarkers along with uterine artery Doppler studies may provide the best predictive accuracy for the identification of early onset preeclampsia." Pg 23

III. ACOG's assertion of 'harm' incurred by false positives –

- ACOG's 2013 Hypertension monograph acknowledges "Low dose aspirin appears to be safe with no major adverse effects or evidence of increased bleeding or abruption." Pg 27

- As suggested by above detailed U.S. Preventative Task Force data, using medical history as the sole preeclampsia screening tool would expose equal if not greater – if primiparity was included – false positive screeners to unnecessary aspirin treatment.

- ACOG provides no reference as to published data on the cost-effectiveness of medical history screening strategies including the adverse effects of identifying women as high risk of preeclampsia, including parental anxiety, increased frequency of prenatal appointments, and additional surveillance testing.

IV. ACOG's current Committee Opinion states the need for prediction-intervention studies but does not reference the first of such validation studies

– Park. Prediction and prevention of early onset preeclampsia: The impact of aspirin after first trimester screening. (Ultrasound Obstet. Gynecol. Aug 2015.)

Park's multivariate screening identified EOP in 92% of 3066 pts screened (11 cases) and demonstrated a 90% reduction in EOP (1 case) in a separate cohort of 2717 pts that were screened and if screen positive treated with low dose aspirin begun <16 weeks. Positive predictive value 3.6% and a negative predictive value of 99.96%.

V. ACOG's advocacy of preeclampsia screening by history alone

- Seems at odds with the tenor and substance of its 2013 Hypertension monograph.

- Accepts the current paradigm of a 37% detection rate of early onset preeclampsia by clinical history alone. This has the potential consequence of denying the 63% of preeclampsia patients lacking any historical risk factors the proven benefit of safe aspirin treatment if found to be at high risk based on multivariate biochemical and biophysical screening methodology.

VI. Fundamental differences in the premise of what population should be screened for early onset preeclampsia limits meaningful statistical comparison.

- ACOG's advocacy of screening by history alone targets a limited population already at increased risk that contains only 37% of patients that will ultimately develop EOP. This is analogous to offering Down syndrome screening only to AMA patients.

- Commercially available multivariate preeclampsia screening targets the general obstetrical population. Its predictive value would likely be greater if targeted onto patients with positive clinical history.

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