both in the groups of smokers and nonsmokers.1 Concerning this finding, we believe that the smokers population who receive antioxidant supplementation is relatively small (64/851 women); therefore, the statistical power of the study could have been limited by the small sample size. In contrast with the findings in this study, in the literature, the positive association is well known between the oxidative damage caused by maternal smoke and the increased incidence of neonatal complications, such as bronchopulmonary dysplasia (BPD), intraventricular hemorrhage, and retinopathy of prematurity.2 On this regard, several clinical studies showed that the maternal supplementation of vitamin A, which exerts antioxidant activity, during the late phase of pregnancy is effective in decreasing BPD incidence in newborn infants.3 Moreover, in line with these findings, Sharma et al4 found in the rat model that the maternal supplementation with polyunsaturated fatty acids ω-3 significantly decreases the neonatal onset of BPD, especially protecting the reduction of alveolarization caused by the hyperoxia-induced oxidative damage.

Given these assumptions, we deem that omega-3 fatty acid supplementation should be investigated more thoroughly for at least 2 reasons: first, their efficacy in reducing significantly the preterm delivery rate in smoker mothers and, second, through the already proven protective effect during pregnancy. Thus, further larger scale studies should be performed to better understand the potential effect of antioxidant agent administration in the pregnancy of smoker women.

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REFERENCES

REPLY

We thank Dr Ferro Desideri et al for their interest in our article.1 As stated in the article, our study was a secondary analysis of a previously performed multicenter randomized controlled study that randomly assigned women with a history of spontaneous preterm birth to omega-3 supplementation vs placebo.2 All women in the original trial received intramuscular 17 alpha-hydroxyprogesterone caproate. We acknowledged that the small number of smokers in the original study for the subgroup analyses left us underpowered for some of the secondary outcomes. Findings from subgroup analyses, particularly those that are unplanned, are frequently likely to be due to chance. Therefore, we agree that adequately powered primary trials are needed to further investigate our findings that suggest the potential benefits of omega-3 fatty acid supplementation in smokers.

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Genitourinary syndrome of menopause: corrections and comments by a gynecologist

TO THE EDITORS: Thank you for choosing the topic genitourinary syndrome of menopause (GSM) for Expert Review, and to the authors for their efforts.1 I am concerned that the article contains some misstatements, and information is presented in a way that could give an incorrect impression. While a gynecologist will have no difficulty
sorting through the article for its pearls, a junior reader or other practitioner could be misled. Therefore, I would like to offer some observations and clinical perspective gained from 2 decades in academic medicine focusing on gynecologic care of older women.

There is confusion about signs and symptoms throughout the article. The authors state, “Additionally, 50% of post-menopausal women with mild or moderate GSM are asymptomatic...”1 In fact, the Vulvovaginal Atrophy Terminology Consensus Conference Panel stated that “women may present with some or all of the signs and symptoms, which must be bothersome...”2 Therefore, GSM cannot be asymptomatic.

The authors state, “GSM-related incontinence is a key cause of recurrent UTI in postmenopausal women...”1 This is not supported by the cited reference or other literature I can find. GSM is called “a chronic, progressive...condition...” for which “life-long management” is “essential.” A more accurate characterization from my perspective would be that GSM is waxing and waning. I posit that periodic management for bothersome symptoms is more appropriate.

The authors recommend adding topical estrogen if GSM persists despite systemic estrogen therapy. However, often the problem is a dermatosis or dermatitis and not simple atrophy. Benefit from local treatment would more likely be due to the vehicle than the estrogen. The authors should provide clinical guidance, preferably with supporting evidence.

Tables contain information not typically used in evaluation and management of GSM. The first heading in Table 1 would more correctly be “genital,” rather than “external genital” as some structures listed are proximal to the hymen. Table 4 would benefit from including causes of chronic pelvic pain such as pelvic floor tension myalgia,3 rather than just stating that “pelvis floor abnormalities” are a “risk factor.” While it is true that there are physical findings associated with GSM (Table 5), it is important to note that neither cystoscopy nor laparoscopy is indicated in the evaluation of GSM. Similarly, while some diagnostic tests, such as rectal exam and imaging, may be warranted after initial GSM evaluation, they are not routinely indicated, as implied in the text.

Use of this article for teaching purposes should include careful review.

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The preterm labor associated ADAMTS2 gene is induced by glucocorticoids

TO THE EDITORS: In their study of the maternal blood leukocyte transcriptome at the time of preterm labor, Paquette et al1 report on a 5-fold increase of the ADAMTS2 transcripts as compared to term labor and go on to suggest it may be a clinically useful biomarker for this condition. The authors considered the possible impact of glucocorticoids (GC), which are given before preterm but not term delivery and they addressed this by analyzing the GSE61881 GEO data set, which we published alongside an article on the response of macrophages to GC.2 In their analysis of our data, Paquette et al1 do not mention the response of ADAMTS2 under “Results” but they imply that ADAMTS2 does not change with GC. However, in their Table S4, which compiles FDR values, ADAMTS2 is listed as a responder gene and our published analysis of the same data (GSE61881) also clearly demonstrates that ADAMTS2 is strongly induced as given in the table below:

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Log2 fold change</th>
<th>Adjusted P value (Benjamini-Hochberg)</th>
<th>Time, h</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADAMTS2</td>
<td>2.019</td>
<td>4.67E-04</td>
<td>10</td>
</tr>
<tr>
<td>ADAMTS2</td>
<td>4.836</td>
<td>4.52E-09</td>
<td>24</td>
</tr>
</tbody>
</table>

Furthermore, looking at human blood monocytes in another in vitro study we reported earlier on a >100-fold induction of ADAMTS2 by GC in a dose- and time-dependent manner.3 Incidentally this study was based on the observation of an induction of ADAMTS2 mRNA expression in monocyte-derived macrophages obtained from patients who had received oral treatment with GC (GEO GSE8608) before donating blood.

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