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Progesterone in Women with Recurrent Miscarriages: Author Reply

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DOI:

[10.1056/NEJMc1600491](https://doi.org/10.1056/NEJMc1600491)

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Document Version

Publisher's PDF, also known as Version of record

Citation for published version (Harvard):

Coomarasamy, A, Williams, H & Rai, R 2016, 'Progesterone in Women with Recurrent Miscarriages: Author Reply', *New England Journal of Medicine*, vol. 373, pp. 894. <https://doi.org/10.1056/NEJMc1600491>

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Checked for eligibility: 03/03/2016

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Progesterone in Women with Recurrent Miscarriages

TO THE EDITOR: In summarizing their well-executed randomized trial, Progesterone in Recurrent Miscarriages (PROMISE), Coomarasamy et al. (Nov. 26 issue)¹ state that there is no evidence of benefit from progesterone supplementation “in the first trimester” of pregnancy among women who have had three or more miscarriages. We wish to clarify three points. First, the trial did not address progesterone supplementation in women with coexisting subfertility. Nearly 33% of the women screened for the trial were excluded because of subfertility (515 of 1568 women). Second, because progesterone plays a key role in the implantation of the embryo, benefit from supplementation may be realized if progesterone is administered before and at the time of implantation. In women undergoing fertility treatments, it is common to administer progesterone before and at the time of implantation,² but in the trial by Coomarasamy et al., administration began after implantation. Third, a short luteal phase (<10 days) is associated with a lower probability of clinical pregnancy, and it may also be associated with miscarriage.^{3,4} The correction of a luteal-phase defect before implantation may improve the chance of ongoing pregnancy. The initiation of progesterone supplementation before pregnancy testing in women with subfertility, luteal-phase defect, or both deserves further investigation to determine whether it would increase the chance of successful implantation and ongoing pregnancy.

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No potential conflict of interest relevant to this letter was reported.

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DOI: 10.1056/NEJMc1600491

THE AUTHORS REPLY: The purpose of the PROMISE trial was to examine the effects of progesterone supplementation in women who have had unexplained recurrent miscarriages. We did not include women with subfertility, and in fact women who did not conceive naturally within 1 year after recruitment were ineligible for randomization.

Our study focused on the use of progesterone in the first trimester of pregnancy and not in the luteal phase. The use of progesterone in the first trimester of pregnancy in women who have a history of unexplained recurrent miscarriages is widespread, although progesterone use in the luteal phase is rare. Our trial was designed to test current common practice. However, we agree that the question of whether to use progesterone in the luteal phase in women with unexplained recurrent miscarriages is important and requires further research. Such research will first require an improved understanding of luteal-phase defect; currently there are no accepted histologic, biochemical, proteomic, genomic, or other systems-biology-based techniques to identify luteal-phase defect, and a short cycle is only a crude marker of luteal-phase defect.

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Since publication of their article, the authors report no further potential conflict of interest.

DOI: 10.1056/NEJMc1600491