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REPLY

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We thank Drs Driul and Londero for their interest in our study.[1] We agree that thrombogenic mutations may be a contributing factor in migraine-related stroke. We did not adjust for known thrombogenic mutations; however, because combined hormonal contraceptives (CHCs) are not recommended for use by women with known thrombogenic mutations because of safety concerns,[2] we expect that there would be only a small number of women with those disorders who use CHCs. Our analysis adjusted for the important confounders mentioned by Drs Driul and Londero, namely age, hypertension, smoking, and obesity as well as others that included diabetes mellitus, ischemic heart disease, and valvular heart disease, while noting the potential for misclassification from the use of healthcare claims data. Because of the use of healthcare claims data, we could not assess migraine or aura frequency. Although there is some evidence that migraine frequency impacts stroke risk,[3] it is not clear whether aura frequency is related to stroke risk; these associations warrant further study.

We agree that the mechanism of ischemic stroke related to migraine with aura is not well understood and probably involves multiple mechanisms.[3] The pathways may include cerebral hypoperfusion related to the aura, arterial dissections, patent foramen ovale, or the presence of vascular risk factors.[3] Although these complex mechanisms need to be further clarified, migraine with aura is associated independently with an increased risk of ischemic stroke.[3] Given that CHCs are also associated with an elevated risk of ischemic stroke, even at lower doses of ethinyl estradiol (including 20 μg),[4] and that stroke is a devastating event, concerns remain about the use of CHCs in women who experience migraine with aura. Based on current understanding of mechanisms, it is not clear that there are subgroups of women with migraine with aura (eg, women without a thrombogenic mutation) for whom CHCs would not further elevate the risk of stroke to an unacceptable level.[2] In addition, the prevalence of thrombogenic mutations is low, and the cost of screening is high; therefore, screening is not recommended before considering whether to use CHCs.[2]

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The authors report no conflict of interest.

Future studies are needed on the pathophysiology and magnitude of risk of stroke related to migraine, hormonal contraceptives, and other stroke risk factors. Such research would contribute to better understanding the safety of hormonal contraceptive use among women with migraine. Healthcare providers should counsel women about risks, benefits, and alternatives so that women can make informed decisions about contraceptive method choice.

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The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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