estrogen-alone menopausal hormone therapy. Importantly, though, menopausal hormone therapy has both benefits and harms, and when assessing the totality of outcomes, the USPSTF concluded that the use of menopausal hormone therapy has no net benefit for the primary prevention of chronic conditions in postmenopausal persons.1

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In Reply Regarding our systematic review on hormone therapy for the primary prevention of chronic conditions in postmenopausal persons,1 Dr Anderson and Dr Chlebowski and Mr Aragaki express concern about our assessment of the methodological quality of the WHI, which we rated as fair quality or moderate risk of bias.2,3 Bias, in general terms, is a systematic error in study design, conduct, or analysis that can overestimate or underestimate the true intervention effect.4 However, quantifying bias and assessing the extent of the impact of bias on study results are usually impossible. Therefore, systematic reviews determine the risk of bias using validated tools based on empirical evidence demonstrating that particular methodological shortcomings can lead to bias. A rating of fair quality indicates that some risk exists that observed treatment effects could deviate from the true effects because of some methodological limitations. In the case of the WHI, our main concerns were high attrition and low adherence to medication.

An important aspect of risk-of-bias assessment is that risk of bias can vary by outcome. This explains why we rated outcomes from some ancillary studies of the WHI as low risk of bias, as Anderson notes. Higher risk of bias due to attrition occurs when events are rare (such as breast cancer mortality). When outcomes are frequent or determined on a continuous scale in most participants (such as cognitive function), risk of bias due to attrition is less of a concern. Nevertheless, risk-of-bias assessment is not an exact science and always includes an element of subjective judgment. For this reason and for the sake of transparency, in the Evidence Report we presented detailed judgments of our risk-of-bias ratings in eTable 3 in the Evidence Report Supplement.1

Chlebowski and Aragaki also express concern about our assessment that participants of the WHI were unmasked. This judgment in eTable 3 in the Evidence Report Supplement referred only to outcomes of long-term follow-up when participants were aware of their original assignments. In the case of breast cancer mortality, however, lack of masking of participants would not have had an effect on risk of bias.

We believe it is important to emphasize that the WHI was a groundbreaking study and that it was able to provide the best and most applicable information for our research questions.

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CORRECTION

Incomplete Information in Table: In the US Preventive Services Task Force Updated Evidence Report and Systematic Review titled “Hormone Therapy for the Primary Prevention of Chronic Conditions in Postmenopausal Persons: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force,”1 published in the November 1, 2022, issue of JAMA, information in a table was incomplete. In Table 2, in the second column of the “Breast cancer mortality” row, the sentence that read “During cumulative follow-up, 63 events in 10 739 persons contributed to effect estimate” should have read “During cumulative follow-up, 63 events in 10 739 persons at 17.7 years and 76 events in 10 739 persons at 20.7 years contributed to the effect estimates.” This article was corrected online.