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Bioidentical hormone therapy

The conclusion of the July Tools for Practice, "that there is no convincing evidence that bioidentical hormones are safer or more effective than synthetic HRT [hormone replacement therapy],"¹ is contradicted by a meta-analysis that concluded "physiological data and clinical outcomes demonstrate that bioidentical hormones are associated with lower risks, including the risk of breast cancer and cardiovascular disease, and are more efficacious than their synthetic and animal-derived counterparts. Until evidence to the contrary, bioidentical hormones remain the preferred method of HRT. Further randomized controlled trials are needed to delineate these differences more clearly."² I wonder if the authors of the Tools for Practice have reviewed the papers that made up this meta-analysis.

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Competing interests

None declared

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Response

Thank you for your comments regarding the Tools for Practice on bioidentical hormones.¹ As you mentioned, there is a commonly referred to review published in *Postgraduate Medicine* that comes to very different conclusions regarding the efficacy and safety of bioidentical hormones.² We are very familiar with this review.

First, we would point out that this is not a systematic review or meta-analysis, but rather a general review of the literature.² Of the 196 references listed in this review, we found only 2 randomized controlled trials that compared progesterone to medroxyprogesterone acetate (MPA) with regard to symptoms and tolerability.³⁻⁵ One of these involved only 23 women.³ The other, published as 2 papers looking at different symptoms, was discussed in our Tools for Practice and demonstrated no significant benefit of progesterone compared with MPA.^{4,5} The conclusion for harm reduction with regard to breast cancer was based largely on 1 cohort study (2 publications), which we also reviewed and found to contain a number of potential biases.^{6,7} No studies comparing progesterone with MPA looked at clinical outcomes for cardiovascular harm reduction.

The largest trial cited in this review assessed surrogate outcomes and reported a statistically significant increase in high-density lipoprotein cholesterol with progesterone (Bonferroni $P < .004$).⁸ We know from previous data that increases in high-density lipoprotein cholesterol do not always correlate positively with improved clinical outcomes.⁹ The other articles refer mainly to in vitro data, observational data, or data from primates. We believe that one cannot make reliable conclusions with regard to human outcomes from these data. Our opinion is that the conclusion presented in this review is in stark contrast to the evidence that is presented. Of note, while Dr Holtorf reported no conflict of interest in the writing of the paper, he is Medical Director of Holtorf Medical Group Inc, which is a centre for "hormone balance, hypothyroidism and fatigue" and is self-reported to provide physicians a "turn-key program for a successful cash-based anti-aging practice."¹⁰

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