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Response

Response to Nahshon and Lavie

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We thank Nahshon and Lavie (1) for their interest in our article. But most of all, we are pleased with their support of our statement that, given the increased risks of *gBRCA1/2* mutation carriers to develop p53-abnormal (11- to 12-fold) and serous-like endometrial cancer (8- to 10-fold) presented in our article, endometrial cancer (EC) and especially p53-abnormal and serous-like EC should be considered part of the hereditary breast and ovarian cancer syndrome caused by a *gBRCA1/2* mutation. Broad support of that statement is of utmost importance for *gBRCA1/2* mutation carriers because this will result in numerous improvements in the quality and outcome of care for *gBRCA1/2* mutation carriers, their relatives, and EC patients.

The question is how to proceed from here. In our opinion, we should start today to consider EC and especially p53-abnormal EC and serous-like EC part of the hereditary breast and ovarian cancer syndrome caused by *gBRCA1/2* mutations. Having said that, among other issues, mutation carriers should be counseled with regard to their increased risk to develop EC. It is important to take mutation type into account; according to our results, *BRCA1* mutation carriers are at higher lifetime risk compared with *BRCA2* mutation carriers (2). Consequently, risk-reducing hysterectomy (RRH) should be considered. However, the following issues should be taken into careful account in this consideration: 1) the small absolute risks to develop EC (3.0% and 1.1% for EC and serous-like histology, respectively), 2) the majority of EC cases concern the endometrioid subtype with excellent survival after hysterectomy, 3) the uncertain effect of RRH on (EC specific) mortality, and 4) the complications and long-term morbidity caused by hysterectomy (2). In their correspondence, Nahshon and Lavie (1) add a specific argument to the discussion on RRH in favor of preventive surgery: future tamoxifen treatment because of breast cancer (BC) which we take the opportunity to comment on. It is well known that patients with EC after at least 5 years tamoxifen use are at increased EC mortality risk compared with never users (hazard ratio = 1.59, 95% confidence interval = 1.13 to 2.25) (3). However, again the absolute risk of developing EC after BC is, even after the use of tamoxifen, extremely low at 0.36% in 27 034 BC patients who used tamoxifen with a follow-up of more than 110 000 person-years (4).

Whether the benefits of preventive surgery outweigh the disadvantages should be weighed for patients based on their individual health situation. As argued above, we doubt whether future tamoxifen treatment as suggested by Nahshon and Lavie (1) is a relevant additional argument to be taken into account in this consideration. In the meantime, the effects of RRH with regard to (long-term) complications and cancer-specific survival should be studied. Lastly and most importantly, as suggested by Sherman (5), detailed viewpoints of *gBRCA1/2* mutation carriers should be collected to provide women facing decisions about preventive surgery with well informed choices.

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Data Availability

All data in this response can be found in the original article. No new data are presented.

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