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NCCN Guidelines Panel:	Genetic/Familial High Risk Assessment: Breast and Ovarian

Specific Changes: Add a "Familial Risk Management" table addressing management for patients negative for genetic testing but with a family history of cancer that includes the following. (See similar table in NCCN CRC Screening guidelines, page CSCR-6)

- Women with 1-2 first degree relatives with ovarian cancer have a 4-11% lifetime risk of ovarian cancer and should be managed by a multidisciplinary team to offer risk reducing options including oral contraceptives or bilateral salpingo-oophorectomy.
- Women with a greater than 20% lifetime risk of breast cancer due to family history should be managed by a multidisciplinary team to offer enhanced screening options such as clinical breast exam every 6-12m at 30, MRI annually at 30. This would include outputs from appropriate risk models or histories such as the following:
  - Women with two first degree relatives with breast cancer at any age
  - Women with three relatives with breast cancer at any age
  - Women with one first degree relative who had breast cancer under age 60

FDA Clearance: Not applicable.

Rationale: Given the demonstrated inefficiency of current ovarian cancer screening methods and the fact that family history of 1-2 first degree relatives with ovarian cancer confers a level of risk similar to that associated with Lynch syndrome, the same risk reducing options such as bilateral salpingo-oophorectomy would equally be a reasonable option for women with 1 first degree relative with ovarian cancer.

Current guidelines support enhanced screening considerations when a patient meets >20% lifetime risk based on genetic (BRCA1/2, CHEK2, *ATM*, *PALB2*, etc.) and familial risk models (Claus, TC, etc.). Women with a strong family history of breast cancer who do not have access to risk models would benefit from guidelines that are more specific as to how to manage their increased risk.

The following articles are submitted in support of this proposed change. We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of some of these publications.

Metcalfe KA[1], Finch A, Poll A, Horsman D, Kim-Sing C, Scott J, Royer R, Sun P, Narod SA. Breast cancer risks in women with a family history of breast or ovarian cancer who have tested negative for a BRCA1 or BRCA2 mutation. *Br J Cancer*. 2009 Jan 27;100(2):421-5.

Pharoah PDP, Ponder BA. The genetics of ovarian cancer. *Best Pract Res Clin Obstet Gynaecol*. 2002 Aug;16(4):449-68.

Sutcliffe S, Pharoah PD, Easton DF, Ponder BA. Ovarian and breast cancer risks to women in families with two or more cases of ovarian cancer. *Int. J. Cancer:* 87, 110–117 (2000).

Tavani A[1], Ricci E, La Vecchia C, Surace M, Benzi G, Parazzini F, Franceschi S. Influence of menstrual and reproductive factors on ovarian cancer risk in women with and without family history of breast or ovarian cancer. *Int J Epidemiol*. 2000 Oct;29(5):799-802.

Walker GR, Schlesselman JJ, Ness RB. Family history of cancer, oral contraceptive use, and ovarian cancer risk. *Am J Obstet Gynecol*. 2002 Jan;186(1):8-14.

Collaborative Group on Hormonal Factors in Breast Cancer. Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast cancer and 101,986 women without the disease. *Lancet.* 2001 Oct 27;358(9291):1389-99.

Sincerely,

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