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Date of request: October 29, 2019
NCCN Guidelines Panel: Survivorship

Specific Changes:

On page SURV-3, modify bullet points 7 thru 9 as follows, including the addition of a new bullet point:

- Regular updating of family cancer history is recommended to reassess hereditary risk, based on new family diagnoses, as well as broader genetic risk assessment and testing criteria recommended by NCCN and other professional societies. Many current cancer survivors were not assessed at the time of their initial diagnosis, which may have occurred prior to the recent expansion in knowledge about hereditary cancer risk.
- Genetic risk assessment and/or testing should be considered for appropriate candidates to identify those with an increased risk for subsequent malignancies, as well as to identify individuals for whom hormonal therapies may be contraindicated (see SMP-B). Genetic testing may also provide opportunities to identify and reduce risks in relatives of cancer survivors.
- Based on guidelines from NCCN, the US Preventative Services Task Force (USPSTF) and the
 American Association of Breast Surgeon (ASBS), genetic risk assessment/testing is appropriate
 for all breast cancer survivors, all survivors of epithelial ovarian cancer, survivors of colorectal or
 endometrial cancer diagnosed at age 50 or younger, high-grade prostate cancer, or pancreatic
 cancer. Many other survivors of rare cancers, cancers diagnosed at young ages, multiple primary
 cancers, or those with one or more relatives with the same or related cancers are also
 candidates for testing per guidelines from NCCN and other expert groups.
- Criteria for genetic risk assessment and testing, and for management of patients with known germline mutations linked to an increased risk for cancer, can be found in the following NCCN guidelines:
 - (Add NCCN Guidelines for Prostate Cancer and NCCN Guidelines for Melanoma to the list)

Rationale: Guidelines for genetic risk assessment and testing from NCCN expert panels, as well as other professional societies (i.e., US Preventative Services Task Force, American Society of Breast Surgeons), been steadily expanded and now include many individuals who would not have been considered appropriate candidates just a few years ago. Many current cancer survivors have not been evaluated using current guidelines, which are based on recent evidence demonstrating the high prevalence and significant clinical relevance of germline mutations in a wider selection of patients than previously thought. These individuals may have significant risks for new cancers that could be mitigated through increased screening, preventative surgeries or risk reducing agents. Additionally, the identification of a

germline mutation in a survivor has profound implications for risk reduction in relatives. Studies have repeatedly documented under-identification of appropriate candidates for genetic testing among newly diagnosed individuals, a problem that is particularly acute in under-served populations. Therefore, this represents an important opportunity in the survivorship setting.

The NCCN Prostate Cancer and Melanoma panels have added content regarding criteria for genetic risk assessment/testing, and some management recommendations for mutation carriers, and should be added to the list of resources.

References:

Carlo MI, et al. Prevalence of germline mutations in cancer susceptibility genes in patients with advanced renal cell carcinoma. JAMA Oncol. 2018 4:1228-1235. PMID: 29978187.

Garcia C, et al. Genetic counseling referral for ovarian cancer patients: a call to action. Fam Cancer. 2019 18:303-309. PMID: 30993488.

Hinchcliff EM, et al. Disparities in gynecologic cancer genetics evaluation. Gynecol Oncol. 2019 153:184-191. PMID: 30711300.

Kehl KL, et al. Rates of BRCA1/2 mutation testing among young survivors of breast cancer. Breast Cancer Res Treat. 2016 155:165-73. Erratum in: Breast Cancer Res Treat. 2016 159:201. PMID: 26706041.

Manahan ER, et al. Consensus guidelines on genetic testing for hereditary breast cancer from the American Society of Breast Surgeons. Ann Surg Oncol. 2019 26:3025-3031. PMID: 31342359.

Neben CL, et al. Multi-Gene panel testing of 23,179 individuals for hereditary cancer risk identifies pathogenic variant carriers missed by current genetic testing guidelines. J Mol Diagn. 2019 21:646-657. PMID: 31201024.

Rosenthal ET, et al. Clinical testing with a panel of 25 genes associated with increased cancer risk results in a significant increase in clinically significant findings across a broad range of cancer histories. Cancer Genet. 2017 218-219:58-68. PMID: 29153097.

Ruddy KJ, et al. Cancer Survivorship Care: An opportunity to revisit cancer genetics. J Clin Oncol. 2016 34:539-41. PMID: 26712228.

Runowicz CD, et al. American Cancer Society/American Society of Clinical Oncology breast cancer survivorship care guideline. CA Cancer J Clin. 2016 66:43-73. PMID: 26641959.

Silver MI, et al. Concordance with BRCA1/2 testing guidelines among women in The Health of Women (HOW) Study(®). Breast Cancer Res Treat. 2019 173:719-726. PMID: 30413980.

Tian W, et al. Screening for hereditary cancers in patients with endometrial cancer reveals a high frequency of germline mutations in cancer predisposition genes. Int J Cancer. 2019 145:1290-1298. PMID: 31054147.

US Preventive Services Task Force, Owens DK, et al. Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer: US Preventive Services Task Force recommendation statement. JAMA. 2019 322:652-665. PMID: 31429903.

Wiggins J, et al. Germline BRCA1 and BRCA2 testing for breast cancer survivors. J Med Ger	et. 2019 Sep
[Epub ahead of print] PMID: 31511339.	

Sincerely,

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