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# Contraception



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Society of Family Planning Clinical Recommendation: Contraceptive considerations for individuals with cancer and cancer survivors part 3 – Skin, blood, gastrointestinal, liver, lung, central nervous system, and other cancers: *Joint with the Society of Gynecologic Oncology*<sup>\*,\*\*</sup>



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# ABSTRACT

This Clinical Recommendation provides evidence-informed, person-centered, and equity-driven recommendations to facilitate the management of and access to contraception care for individuals who are diagnosed with, being actively treated for, or who have previously been treated for skin, blood, gastrointestinal, liver, lung, central nervous system, and other cancers. For individuals with a history of nonmelanoma skin cancers, we recommend clinicians provide access to all available contraceptive methods utilizing a person-centered approach (GRADE 1B). Based on expert opinion, for individuals with a history of melanoma who are considering hormonal contraception, we suggest shared decision-making with the individual and their oncologist (GRADE 2C). For individuals with a history of myeloproliferative neoplasms, lymphatic or hematopoietic cancer, and hematopoietic stem cell transplantation, we recommend clinicians provide access to all contraceptive methods (GRADE 1B); we suggest shared decision-making in those with follicular lymphoma subtype of non-Hodgkin lymphoma who are considering hormonal contraception (GRADE 2C). For individuals with a history of colorectal, pancreatic, esophageal, and gastric cancer, we recommend clinicians provide access to all available contraceptive methods (GRADE 1C). We recommend clinicians provide access to all available contraceptive methods in individuals with a history of primary hepatocellular carcinoma with normal liver function (GRADE 1C); with severely altered liver function, we recommend nonhormonal and progestin-only contraceptives as first-line contraceptive methods (GRADE 1B). For individuals with a history of glioma, we recommend clinicians provide access to all available contraceptives (GRADE 1B). For individuals with a history of meningioma who request hormonal contraception, we recommend shared decision-making with the individual and their oncologist (GRADE 2B). We recommend clinicians provide access to all available contraceptive options for individuals with a history of or active bladder, kidney, thyroid, head and neck squamous cell, and soft tissue sarcomas (GRADE 1B). This document is part 3 of a three-part series that updates the Society of Family Planning's 2012 Cancer and contraception clinical guidance. It builds upon the considerations outlined in the Society of Family Planning Committee Statement: Contraceptive considerations for individuals with cancer and cancer survivors part 1 - Key considerations for clinical care and parallels recommendations outlined in the Society of Family Planning Clinical Recommendation: Contraceptive considerations for individuals with cancer and cancer survivors part 2 - Breast, ovarian, uterine, and cervical cancer. Readers are encouraged to review parts 1 and 2 for this additional context.

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### 1. Background

This Clinical Recommendation provides evidence-informed, person-centered, and equity-driven recommendations to facilitate the management of and access to contraception care for individuals who are diagnosed with, being actively treated for, or who have previously been treated for skin, blood, gastrointestinal, liver, lung, central nervous system, and other cancers. It builds upon the considerations outlined in the *Society of Family Planning Committee Statement: Contraceptive considerations for individuals with cancer and cancer survivors part 1 – Key considerations for clinical care and parallels recommendations outlined in the <i>Society of Family Planning Clinical Recommendation: Contraceptive considerations for individuals with cancer and cancer survivors part 2 – Breast, ovarian, uterine, and cervical cancer.* Readers are encouraged to review parts 1 and 2 for this additional context [1,2].

When literature regarding the safety and efficacy of specific contraceptive methods in individuals with a history of a particular type of cancer was not available, literature from the general population was used to inform recommendations. No well-designed studies assessing contraceptive risks in those actively undergoing cancer treatment were available. Thus, recommendations for those with a history of a specific cancer type also apply to those who are actively being treated for that cancer. However, active cancer is often associated with higher risks of thrombosis, which needs to be taken into consideration during shared decision-making if contraceptives that increase thrombotic risks are considered while the individual is receiving treatment.

This guidance series uses shared decision-making to refer to a collaborative process in which individuals and clinicians work together to make healthcare decisions informed by evidence, the care team's knowledge and experience, and the individual's values, goals, preferences, and circumstances. It uses person-centered care to refer to care that is respectful of and responsive to the individual's preferences, needs, and values, ensuring that these elements guide all clinical decisions. These principles are fundamental to contraceptive care, and all recommendations in this guidance series should be interpreted in this context. This guidance discusses providing a method to an individual with a US Centers for Disease Control and Prevention (CDC) medical eligibility criteria (MEC) condition or characteristic with an unacceptable risk (category 4). Typically, this should occur in rare circumstances and when no safer alternative or acceptable method exists. Ultimately, the acceptability of risk should be determined by the individual. Clinicians can support an individual's understanding of risk through shared decision-making.

### 2. Clinical questions

# 2.1. Skin

2.1.1. Does the use of hormonal contraception increase the risk of skin cancer recurrence?

For individuals with a history of nonmelanoma skin cancer, we recommend clinicians provide access to all available contraceptive methods utilizing a person-centered approach (GRADE 1B) (Table 1).

# Based on expert opinion, for individuals with a history of melanoma who are considering hormonal contraception, we suggest shared decision-making with the individual and their oncologist (GRADE 2C).

Estrogens, and to a lesser extent progestins, play a role in increasing melanocytes and melanin content in the skin, with a potential impact on skin cancer risks [3,4]. Studies of exogenous hormone use after malignant melanoma diagnosis are limited and show mixed results, including a possible protective effect, potentially due to differential cancer expression of the estrogen receptor (ER)  $\alpha$ , which may have a stimulatory effect compared to ER $\beta$  which can have a suppressive effect [5,6]. Overall, hormone exposure or pregnancy-associated melanoma has not been associated with a poorer prognosis [7].

Given the limited evidence regarding hormonal contraceptive use by skin cancer survivors, studies of cancer risk in the general population can also inform decision-making. Older observational studies have suggested that oral contraception users have a twofold melanoma risk compared to nonusers and that this risk was over threefold among those who used oral contraception for more than 10 years [8]. However, updated meta-analyses show either no increased melanoma risks with exogenous hormone use or a much lesser magnitude of increased risk, with 5 or more years of oral contraception use having a risk ratio (RR) of 1.18 (95% CI 1.07-1.31), while 10 years or more had a RR of 1.25 (95% CI 1.06-1.48) [9,10]. A prospective cohort study of 98,995 French, pregnancy-capable individuals also showed no strong association between oral contraception use and melanoma; the risk increases were related to older high-dose formulations and other confounders, including increased rates of sunburns and tanning bed use in contraceptive users [11]. In many studies, sun exposure and reproductive factors that are independent risk factors for melanoma, such as decreased parity or first live birth after age 20 years, were unknown, making it difficult to draw definitive conclusions [10]. Regarding other types of skin cancer, a meta-analysis and prospective study have shown no association between hormonal contraception and basal cell or squamous cell carcinomas [12,13].

#### 2.2. Blood

# 2.2.1. Does the use of hormonal contraception impact blood cancer treatment effectiveness or the risk of cancer recurrence?

For individuals with a history of myeloproliferative neoplasms, lymphatic or hematopoietic cancer, and hematopoietic stem cell transplantation, we recommend clinicians provide access to all contraceptive methods utilizing a person-centered approach (GRADE 1B). For individuals with follicular lymphoma subtype of non-Hodgkin lymphoma who are considering hormonal contraception, we suggest shared decision-making with the individual and their oncologist (GRADE 2C).

Hormonal contraception has been shown to have a protective effect on the diagnosis of acute myeloid leukemia and neutral or protective effects on the risks of non-Hodgkin lymphoma. However, a potential increase in follicular lymphoma subtype is possible given multiple pregnancies are protective for the latter [14–17]. Overall, lymphatic and hematopoietic cancer risk is lower among hormonal contraception users compared to nonusers, with an incidence rate

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**Disclaimer**: This publication is designed as a resource to assist clinicians in providing family planning care. It should not be considered inclusive of all proper treatments or serve as the standard of care. It is not intended to substitute for the independent professional judgment of the treating clinician. Variations, taking into account individual circumstances, may be appropriate. This publication reflects the best-available evidence at the time of publication, recognizing that continued research or major changes in the practice environment may impact future recommendations and should be evaluated for incorporation into care. Clinical guidance, grounded in evidence-based research, are distinct from legal requirements and restrictions governing family planning care. Medical recommendations do not vary based on practice location. However, abortion is not legal in all states and circumstances, and this document is not intended to aid in or otherwise advocate for unlawful care. Any updates to this document can be found on https:// societyfp.org/clinical-guidance-library/. The Society and its contributors provide the information contained in this publication "as is" and without any representations or warranties, express or implied, of any kind, whether of accuracy, reliability, or otherwise.

Table 1

Key for GRADE recommendations<sup>a</sup>

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Symbol	Meaning	
1	Strong recommendation	
2	Weaker recommendation	
Α	High quality evidence	
В	Moderate quality evidence	
С	Low quality evidence, clinical experience, or expert consensus	
Best Practice	A recommendation in which either (1) there is an enormous amount of indirect evidence that clearly justifies a strong recommendation; direct evidence	
	would be challenging and an inefficient use of time and resources to bring together and carefully summarize, or (2) a recommendation to the contrary	
	would be unethical	

<sup>a</sup> Society of Family Planning Clinical Recommendations use a modified GRADE system. The GRADE system is described in several publications, with a comprehensive set of articles in the Journal of Clinical Epidemiology (J Clin Epidemiology, (2011) 64:383–394, 64:395–400, 64:401–406, 64:407–415, 64:1277–1282, 64:1283–1293, 64:1294–1302, 64:1303–1312, 64:1311–1316, (2013) 66:140–150, 66: 151–157, 66:158–172, 66:173–183, 66:719–725, 66:726–735).

ratio of 0.74 (99% CI 0.58-0.94) [18]. Myeloproliferative neoplasms, including polycythemia vera and essential thrombocythemia, are not impacted by hormonal contraception use [19]. Importantly, hematopoietic stem cell transplantation causes hypoestrogenism symptoms in approximately 86% of individuals and premature ovarian insufficiency in 74%, necessitating conversations about contraceptive need as well as ways to manage the symptoms and long-term risks of hypoestrogenism [20-22]. Those with a history of blood dyscrasias, such as leukemia, or those suffering from thrombocytopenia due to myelosuppressive therapy often experience abnormal uterine bleeding, requiring the use of hormonal contraception to manage symptoms [23]. Individuals with a history of hematologic malignancies may safely use hormonal contraception. However, myeloproliferative neoplasms and hematopoietic stem cell transplantation can significantly increase thrombotic risks, which should be considered in shared decision-making.

## 2.3. Gastrointestinal (GI)

# 2.3.1. Does the use of hormonal contraception impact gastrointestinal cancer treatment effectiveness or the risk of cancer recurrence?

For individuals with a history of colorectal, pancreatic, esophageal, and gastric cancer, we recommend clinicians provide access to all available contraceptive methods utilizing a personcentered approach (GRADE 1C). For individuals with malabsorption, nonoral methods may be more effective.

Although multiple studies have examined associations between hormonal contraception use and GI cancers, including colorectal, pancreas, esophageal, and gastric cancer, information on how use may impact individuals who have been diagnosed with GI cancer is limited. Overall, hormonal contraception use is associated with either no or decreased risk of colorectal cancer in the general population [24–30]. While risk reductions have been hypothesized for individuals with a high risk of GI cancer, such as those with Lynch syndrome, these have not been clearly documented. Similarly, individuals with inflammatory bowel disease (IBD) have a higher risk of GI cancers and often need to plan for pregnancy while on immunomodulator therapies. There are no studies evaluating the impact of contraceptives on cancer risk in those with IBD.

The majority of studies investigating hormonal contraception use and subsequent pancreatic cancer found either no or decreased risk of cancer [31–37]. Though two prospective cohort studies suggested exogenous hormone use is associated with a small increased risk of pancreatic cancer, methodologic limitations prevent their generalizability [38,39]. Two meta-analyses report reduced risk of esophageal cancer with oral contraception use; one meta-analysis focused on gastric cancer found no association with hormonal contraception [40–42]. Given these findings, clinicians should not limit the contraceptive options offered to individuals being treated for or with a history of colorectal, pancreatic, esophageal, and gastric cancer. However, pancreatic and gastric cancer can significantly increase thrombotic risks, which should be considered in shared decisionmaking. Certain GI cancers or cancer therapies can impair medication absorption, leading to theoretical concerns for decreased effectiveness of oral formulations. Therefore, individuals who are experiencing malabsorption should consider nonoral contraceptives.

## 2.4. Liver

# 2.4.1. Does the use of hormonal contraception impact the effectiveness of liver cancer treatment or increase the risk of liver cancer recurrence?

For individuals with a history of primary hepatocellular carcinoma with normal liver function, we recommend clinicians provide access to all available contraceptive methods utilizing a person-centered approach (GRADE 1C). For individuals with severely altered liver function, we recommend nonhormonal and progestin-only contraceptives as first-line contraceptive methods, given the increased risk of thrombosis in this population (GRADE 1B). Given the risk associated with combined hormonal contraceptives in individuals with a history of hepatocellular adenoma, these individuals may prefer methods that avoid or minimize systemic hormone levels.

Given the limited evidence on the impact of hormonal contraceptive use in individuals with liver cancer or a history of liver cancer, studies of cancer risk in the general population are used to inform decision-making. The 2024 CDC Medical Eligibility Criteria (MEC) categorizes combined hormonal contraceptive (CHC) use for individuals with hepatocellular carcinoma as an unacceptable risk (category 4) [43]. Research on whether the use of hormonal contraception impacts the risk of liver cancer, specifically hepatocellular carcinoma, focuses exclusively on contraception and its relationship to developing cancer, with none providing information on the potential impact of hormonal contraceptive use on cancer outcomes. In 2018, the International Agency for Research on Cancer (IARC) concluded that existing evidence supports the idea that oral contraceptives containing a combination of estrogen and progestin can lead to the development of liver cancer [44]. This document did, however, acknowledge that no association was found in cohort studies, and most of these included a small number of cases. A meta-analysis and a pooled cohort of observational data from 799,500 US participants suggested that oral contraceptives are not associated with a risk of liver cancer; few studies control for important confounders such as chronic hepatitis infection or alcohol consumption [45,46]. Individuals with liver dysfunction related to primary or metastatic malignancy have an elevated thrombosis risk, and therefore estrogen-containing contraceptives are not recommended.

Hepatocellular adenomas are benign lesions that primarily occur in pregnancy-capable individuals of reproductive age. The 2024 CDC MEC categorizes hepatocellular adenoma as an unacceptable risk (category 4) for CHC use because oral contraceptive use is associated with the development and growth of hepatocellular adenoma [43]. However, this risk has significantly declined with the use of lower doses of estrogen in current formulations [47,48]. Whether other forms of hormonal contraception have similar effects is unknown. For individuals with a history of hepatocellular adenoma, it is important to balance the risk associated with hormonal contraceptive use with its benefits for anemia, a common complication for individuals with liver disease; these individuals may want to consider methods that reduce menstrual bleeding, such as an levonorgestrel intrauterine device (IUD). For individuals who prefer higher-dose hormonal contraceptives, discussion of whether follow-up imaging is necessary can be considered.

### 2.5. Lung

2.5.1. Does the use of hormonal contraception impact the effectiveness of lung cancer treatment or increase the risk of lung cancer recurrence?

For individuals with a history of lung cancer, we recommend clinicians provide access to all available contraceptive methods utilizing a person-centered approach (GRADE 1B).

There is limited evidence on the impact of hormonal contraceptive use in individuals with lung cancer or a history of lung cancer. Reports on hormonal contraception and lung cancer risk are sparse and consist of meta-analyses, case-control, and prospective observational cohort studies, which are also limited by recall bias; only one reported on the possible effect on lung cancer outcomes [49]. Several studies indicate that the majority of nonsmall cell lung cancers express ER<sub>β</sub>, and its prevalence is higher among never-smokers when compared to smokers [50-52]. Studies examining the possible effects of post-menopausal hormone therapy on lung cancer risk have had inconsistent results [53,54]. Two studies, including the large Women's Health Initiative study, concluded that oral contraceptive use had little to no impact on lung cancer risk [55,56]. Three smaller studies demonstrated a decreased risk of lung cancer associated with oral contraceptive use [57–59].

# 2.6. Central nervous system (CNS)

2.6.1. Does the use of hormonal contraception impact the effectiveness of CNS cancer treatment or increase the risk of CNS cancer recurrence?

For individuals with a history of glioma, we recommend clinicians provide access to all available contraceptive methods utilizing a person-centered approach (GRADE 1B). For individuals with a history of meningioma who request hormonal contraception, we recommend shared decision-making with the individual and their oncologist (GRADE 2B). The hormone receptor status of a meningioma may influence decisions to initiate or continue hormonal contraceptives or consider increased monitoring while on hormonal therapy.

Data regarding hormonal contraceptive use and primary CNS tumors can be divided into two main histologic categories: glioma and meningioma. Sex hormones are hypothesized to play a role in both the development and progression of these tumors, albeit with opposite effects. Gliomas are a heterogeneous group of CNS tumors and are more common in men than women [60–62]. No clinical studies report on the effects of hormonal contraceptives on existing gliomas, and studies of glioma risk in the general population can, therefore, inform decision-making. Meta-analyses, case-control, and prospective observational cohort studies consistently demonstrate either no association or decreased risk of glioma with oral contraception use [63–69]. However, one case-control Danish registry study that utilized prescription data to ascertain hormonal contraception exposure in individuals younger than 50 years of age

demonstrated an increased risk of glioma that increased with duration of hormonal contraception use (OR 1.5; 1.2–2.0 for everusers) [70]. However, this study did not control for body mass index or reproductive factors other than parity, which may also affect glioma risk.

Meningiomas, the most common primary brain tumor, occur more frequently in women compared to men. Although 95% of meningiomas are benign, their size and location can cause significant morbidity and may require surgical excision. Hormonal factors may have a role in meningioma development as progesterone receptors are present in approximately 75% of tumors, androgen receptors in just under 50%, and estrogen receptors have been identified in approximately 10% of cases [71,72]. There are case reports describing the growth of meningiomas during pregnancy and the decrease or regression of tumors following delivery [73-76]. Multiple observational studies and meta-analyses examining a possible relationship between the risk of meningioma with low-dose estrogen and progestin exposure, either related to menopausal hormone therapy or hormonal contraception use, showed mixed results. Some demonstrated a small increased risk of meningioma (OR 1.24; 1.01-1.51 and OR 1.8; 1.1-2.9). This includes one small Swedish case-control study that suggested an increased risk (OR 2.7; 95% CI 0.9-7.5) with subdermal contraceptive implants, injections, or hormonal intrauterine devices (IUDs). Several studies indicate no association with oral contraceptive use and meningioma risk [64,69,77-83]. A recent casecontrol study raises concerns about the relationship between injection medroxyprogesterone acetate and meningioma [83]. However, the study has significant limitations, including the failure to assess important confounders such as exposure to ionizing radiation. According to the European Medicines Agency, cyproterone acetate, a drug used in combination with ethinyl estradiol as a CHC, has been associated with an increased risk of meningioma, is contraindicated in people with a history of meningioma, and should be discontinued if meningioma is diagnosed [84,85]. However, cyproterone acetate is not approved by the Food and Drug Administration for use in the US.

2.7. Does the use of hormonal contraception impact the effectiveness of treatments for other common cancers or increase the risk of cancer recurrence for these cancer types?

For individuals with a history of or active bladder, kidney, thyroid, head and neck squamous cell, and soft tissue sarcomas, we recommend clinicians provide access to all available contraceptive options utilizing a person-centered approach (GRADE 1B).

Large observational studies show no association of hormonal contraception use with bladder cancer [86], and mixed results about whether there may be a protective versus neutral effect on cancers of the kidney [87–89]. Many, though not all, studies suggest a protective effect on thyroid cancer, with increased protection from longer duration of use [90–95]. Similarly, hormonal contraception does not seem to impact the risk of head and neck squamous cell cancers and may have a protective role in soft tissue sarcoma [96,97].

### 3. Summary of recommendations

Please see Table 1 for a key to interpreting GRADE.

Personal cancer history <sup>a,b</sup>	Recommendation <sup>c</sup>	
Skin Nonmelanoma	Provide access to all available contraceptive methods for history of nonmelanoma skin cancers (1B).	
Melanoma	SDM <sup>d</sup> for HC use (2C).	
<b>Blood</b> Myeloproliferative neoplasms, lymphatic or hematopoietic canc- er, and hematopoietic stem cell transplantation	Provide access to all available contraceptive methods (1B).	
Follicular lymphoma subtype of non-Hodgkin lymphoma	SDM for HC use (2C).	
<b>Gastrointestinal</b> Colorectal, pancreatic, esophageal, and gastric cancer	Provide access to all available contraceptive methods (1C). For individuals with malabsorption, nonoral methods may be more effective.	
Liver Primary hepatocellular carcinoma with normal liver function	Provide access to all available contraceptive methods (1C).	
Severely altered liver function	Nonhormonal and progestin-only contraceptives as first-line option given thrombosis risk (1B).	
Hepatocellular adenoma	Individuals may prefer methods which avoid or minimize systemic levels of hormone.	
Lung Lung cancer	Provide access to all available contraceptive methods (1B).	
<b>CNS</b> Glioma	Provide access to all available contraceptive methods (1B).	
Meningioma	SDM for HC use (2B). The hormone receptor status of a meningioma may influence decisions to initiate or continue HC or consider increased monitoring while on hormonal therapy.	
Other Bladder, kidney, thyroid, head and neck squamous cell, and soft	Provide access to all available contraceptive methods (1B).	

tissue sarcomas

CNS, central nervous system; HC, hormonal contraception; IUD, intrauterine device; SDM, shared decision-making,

<sup>a</sup> Active cancer treatment (as opposed to past cancer history) may increase the risk of thrombosis, and should be included in clinical decision-making.

<sup>b</sup> Statements made in these recommendations for those with a history of a specific cancer type also apply to those who are actively being treated for that cancer.

<sup>c</sup> Clinicians should provide person-centered contraceptive care that supports autonomy in decision-making for the individual receiving care and counseling directly tailored to

the individual's expressed preferences and values.

<sup>d</sup> Shared decision-making with the individual and their oncologist.

### 4. Recommendations for future research

- Effect of hormonal contraception on inflammatory bowel disease and cancer risk.
- Effects of combined vs progestin-only hormonal contraception on meningioma development.
- Effects of hormonal contraception on bladder, kidney, thyroid, head and neck squamous cell, and soft tissue sarcomas cancer outcomes based on expression of estrogen receptor subtypes.
- Effects of different contraceptive methods on cancer treatment and outcomes in individuals with active cancer or a history of cancer.

#### 5. Sources

A series of clinical questions were developed by the authors and representatives from the Society of Family Planning's Clinical Affairs Committee. With the assistance of medical librarians, we searched the databases of Medline, Embase, Cochrane reviews and registered clinical trials to identify any relevant articles related to cancer and contraception, published between January 1, 2012 and June 29, 2023. The initial search yielded over 16,000 results, which were further limited to those relevant to hormonal contraception. We reviewed 5484 references for relevance and to use in drafting the recommendations. The search was restricted to articles published in English. We also identified studies by reviewing the references of relevant articles and clinical guidelines published by organizations or institutions with related recommendations, such as the Centers for Disease Control and Prevention, the American College of Obstetricians and Gynecologists, and the Society of Family Planning. The content of and references cited in relevant product labels and Food and Drug Administration prescribing information were also considered when developing clinical critical statements on topics involving medication. When relevant evidence was not available or too limited to inform practice, the expert opinion of clinicians with complex family planning expertise was used to develop the critical statements.

# 6. Intended audience

This Clinical Recommendation is intended for Society of Family Planning members, family planning and reproductive health service clinicians, oncologists and clinicians who care for cancer survivors, family planning and reproductive health researchers, consumers of family planning care, and policymakers.

#### Authorship

This Clinical Recommendation was prepared by Pelin Batur, MDD; Ashley Brant, DO, MPH; Carolyn McCourt, MD; and Eleanor Bimla Schwarz, MD, MS, with the assistance of Anitra Beasley, MD, MPH; Jessica Atrio, MD, MSc; Danielle Gershon, MD; and Neil A. Nero, MLIS, AHIP. It was reviewed and approved by Clinical Affairs Committee members on behalf of the Board of Directors of the Society of Family Planning, the Society of Gynecologic Oncology's (SGO's) Publication Committee, and SGO's Board of Directors.

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