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Review

Hormone replacement therapy following treatment of gynaecological malignancies

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Key content

- Approximately 21 000 women in the UK were diagnosed with a gynaecological malignancy in 2015; although most of these malignancies occurred in postmenopausal women, 30–40% present in premenopausal or perimenopausal women.
- Management typically involves surgery and/or chemotherapy and/or radiotherapy, which in younger women may result in an induced menopause.
- Many women struggle with both the immediate symptoms and the long-term consequences of estrogen deficiency, all of which are debilitating and compromise the quality and quantity of life, in addition to the cancer diagnosis and treatment.
- These patients represent a complex group and most units in the UK do not have easy access to menopause specialists.
- Gynaecologists may be reluctant to prescribe hormone replacement therapy (HRT) to these women; clinicians involved in the care of these women must appreciate when HRT is and is not contraindicated.

Learning objectives

- To understand the safety of HRT in women who have undergone treatment for endometrial, ovarian, cervical, vulval or vaginal malignancies, with particular emphasis on the type, stage and grade of cancer.
- To establish an evidence-based approach to the management of menopausal symptoms using HRT in women who have previously been treated for a gynaecological malignancy.
- To appreciate the role of non-hormonal alternatives to HRT in these women.

Ethical issues

- How to balance the known benefits of HRT against the potential risks, when evidence is limited in women who have undergone treatment for a gynaecological malignancy.

Keywords: cervical / endometrial / hormone replacement therapy / ovarian / malignancy

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Introduction

Approximately 21 000 women in the UK were diagnosed with a gynaecological malignancy in 2015.[1–5] Although most occurred in postmenopausal women, 30–40% of women with these cancers are premenopausal or perimenopausal.[6,7]

Management of a gynaecological malignancy typically involves surgery and/or chemotherapy and/or radiotherapy. In younger women, this may induce menopause. If menopause is left untreated, these women will experience all the typical symptoms of estrogen deficiency. Additionally, women who undergo a premature menopause are at increased risk of osteoporosis and cardiovascular disease in the future.[8] Prolonged estrogen deficiency prior to the age of natural menopause is therefore associated with a reduced quality and quantity of life.[9] Hormone replacement therapy (HRT) is the most effective way to treat the immediate symptoms of estrogen deficiency and prevent long-term sequelae. For most women experiencing an early or premature menopause, HRT presents minimal risks and there are very few absolute contraindications to its use.[10–12]

Women who were already postmenopausal at the time of their cancer diagnosis and treatment may also complain of menopausal symptoms – not as a consequence of their cancer treatment per se, but because of the increased contact with medical professionals that it affords.

For many gynaecological malignancies, survival rates are improving, hence quality of life is increasingly important. It

is crucial, therefore, that medical professionals involved in the care of these women appreciate whether there are additional cancer-related risks that would preclude the use of HRT when it may otherwise be recommended. It is equally important that HRT is not withheld from women because of doctors' (sometimes unjustified) anxiety.[13]

Women often receive conflicting information about their management from different specialists.[14] This article reviews the data regarding cancer-related risks of HRT in patients who have undergone treatment for ovarian, endometrial, cervical, vaginal and vulval malignancies and attempts to establish an evidence-based approach to the management of menopausal symptoms in these women (Table 1).

Endometrial cancer

Endometrial cancer is the most common malignancy of the female genital tract and the fourth most common female cancer in the UK.[1] It usually presents early, while still confined to the uterus, and is therefore associated with 5-year survival rates as high as 80–90%.[15] Although it most commonly affects women in their sixth decade, 5% of those affected are under the age of 40 years and 20–25% are premenopausal.[16,17] The mainstay of treatment involves hysterectomy and bilateral salpingo-oophorectomy (BSO).[18]

There are two different types of endometrial cancers: type 1, which are estrogen-dependent and account for the majority of cases,[19] and type 2, which are estrogen-independent. Unopposed estrogen in women with an intact uterus significantly increases the risk of endometrial cancer (odds ratio [OR] 6.2, 95% confidence interval [CI] 3.1–12.6),[20] which is largely avoided if progestogens are incorporated.[21,22] Historically, therefore, in the absence of any robust data, HRT was avoided in patients with a history of endometrial cancer because of the mutagenic effect of estrogen on endometrial tissue and the possible stimulatory effect on occult foci leading to recurrent disease.

Between 1986 and 2001, several retrospective studies investigating the effects of HRT in women following treatment for endometrial cancer were undertaken – all of which reported no increase in recurrence or decrease in survival.[23–28] However, owing to considerable heterogeneity between the studies in terms of tumour characteristics, initiation time of therapy after surgery, treatment regimens and other factors, the findings were not considered robust enough to inform clinical practice.

Since then, there have been two large, prospective studies.[29,30] Between June 1997 and January 2003, a double-blind, randomised trial to investigate whether estrogen replacement therapy was detrimental for patients with a history of endometrial cancer was undertaken.[29] This study was the only one to be included in a recent systematic review.[31] Women were included who had undergone total hysterectomy and BSO (± pelvic and para-aortic lymphadenectomy) for stage I or II, grade 1, 2 or 3 endometrial adenocarcinoma. The aim was to recruit 2108 women, but the study closed prematurely following the announcement, in 2002, that the estrogen and progestogen arm of the Women's Health Initiative study was being stopped because of the risks of treatment[32] (conclusions that have since been retracted[33,34]). However, 1236 women were recruited and followed up for, on average, 30.8 months. The recurrence rate was 2.3% in women treated with estrogen and 1.9% in those who received placebo ($P > 0.05$).[29]

Although this study could not conclusively confirm the safety of exogenous estrogen with regard to risk of endometrial cancer recurrence, the absolute recurrence rate in this population was very low. Furthermore, given that unopposed estrogen was used, it is likely that many more recurrences would have been observed in the treatment arm if estrogen were indeed detrimental.

The second study incorporated 100 women who had undergone total simple/radical hysterectomy, BSO, peritoneal cytology, infracolic omentectomy and complete pelvic and para-aortic lymphadenectomy, and who had histologically confirmed stage I or II endometrioid endometrial cancer.[30] Case individuals, who were well-matched with control individuals in terms of clinical characteristics, were given continuous combined HRT, and both groups were followed up for at least 5 years. The mean duration of HRT use was 49.1 months (range 13–96 months). No case individuals and only one control individual developed recurrent disease. The authors concluded that HRT in women who had undergone treatment for endometrial cancer does not increase the risk of recurrence.

This is an important discovery, but it remains crucial for clinicians to exert caution. Most women in this study had stage I disease (only six had stage II disease) and all women had an endometrioid endometrial cancer. While this histopathology is typical of most women with endometrial cancer, the same conclusions may not necessarily apply to women with stage III or IV disease or non-endometrioid histology. Unfortunately, there are no data to guide the use of HRT in patients with advanced stage, high-grade or non-estrogen dependent endometrial cancers.[35]

Furthermore, the study by Ayhan and colleagues[30] did not incorporate a power calculation, so it is difficult to know whether the sample size was sufficient to detect a significant difference in recurrence rates between the cases and the controls. However, combined with the results from the study by Barakat et al.,[29] there is increasing evidence to suggest that the use of HRT is not associated with increased recurrence or decreased survival in patients with early stage, low-grade, endometrioid adenocarcinoma of the endometrium.

The women in the study by Ayhan and colleagues were given continuous combined HRT as opposed to an estrogen-only regimen that is more standard practice for women

Table 1. Summary of evidence and recommendations for practice

Malignancy	Type	Stage	Evidence	HRT recommendation
Ovarian	Epithelial		No evidence that HRT increases recurrence or decreases survival; may be beneficial but data are limited	Limited data
	Germ cell		Insufficient evidence	Avoid
	Sex cord stromal		Insufficient evidence	Avoid
	Borderline		Insufficient evidence	Avoid/use cautiously
Endometrial	Type 1 (Endometrioid)	I and II	No evidence that HRT increases recurrence or decreases survival	Estrogen only if no concerns of possible occult foci; otherwise continuous combined
		III and IV	Insufficient evidence	Avoid
	Type 2		Insufficient evidence	Avoid
Cervical	Squamous cell	I and II	No evidence that HRT increases recurrence or decreases survival	Estrogen only if previous hysterectomy; otherwise continuous combined
		III	Insufficient evidence	Avoid/use cautiously
		IV	Insufficient evidence	Avoid/use cautiously
	Adenocarcinoma		Insufficient evidence	Avoid/use cautiously
Vaginal	Squamous cell		No evidence that HRT increases risk of recurrence or decreases survival	Estrogen only if previous hysterectomy; otherwise continuous combined
	Non-squamous cell		Insufficient evidence	Avoid
Vulval	Squamous cell		No evidence that HRT increases risk of recurrence or decreases survival	Estrogen only if previous hysterectomy; otherwise continuous combined
	Non-squamous cell		Insufficient evidence	Avoid

HRT = hormone replacement therapy.

without a uterus. The addition of a progestogen is likely to abate fears regarding the possible stimulatory effect of estrogen on occult foci; however, it is also the progestogenic component of HRT that increases the risk of breast cancer.[33,36] Therefore, if women have been adequately staged, an estrogen-only preparation of HRT should suffice.

With regard to adequate staging, however, the women in the study by Ayhan et al. underwent hysterectomy, BSO, peritoneal cytology, infracolic omentectomy and complete pelvic and para-aortic lymphadenectomy. The fact that the women in this study were extremely well staged adds weight to the conclusions drawn. However, this is not standard practice for low-grade, presumed early stage endometrial cancer in the UK, where women with grade 1 or 2 endometrioid endometrial cancer confined to the uterus typically undergo hysterectomy and BSO.[18]

A 2008 study[37] reported that, in women with presumed stage I endometrioid endometrial cancer, there were no positive lymph nodes in women with grade 1 disease. However, 10.4% (19/182) of women with grade 2 disease were found to have positive nodes (and were therefore actually stage IIIc1).[37] There is therefore the possibility that, in standard UK practice, a small proportion of women with presumed early-stage endometrioid endometrial cancer actually have more advanced disease – it is these women who might suffer if estrogen-only preparations of HRT were used instead of continuous combined preparations.

Furthermore, the participants of all these studies were perimenopausal or postmenopausal. There are no specific studies investigating the safety of HRT in young women rendered prematurely menopausal by treatment of their endometrial cancer. Several retrospective studies have demonstrated that ovarian preservation in premenopausal women with early-stage endometrial cancer does not increase

cancer-related mortality[38,39] and while this evidence may be used to support the use of HRT in young women, ovarian conservation is not equivalent to HRT.

Finally, a small proportion of women treated for endometrial cancer will develop recurrent disease. Most recurrences occur within 3 years of treatment and are located at the vaginal vault.[40] Although studies have shown that the use of unopposed topical vaginal estrogen is not associated with increased risk of endometrial hyperplasia or cancer,[41] the effect of low-dose vaginal estrogen therapy on endometrial cancer recurrence is unknown.[42]

Ovarian cancer

Ovarian cancer is the sixth most common type of cancer in women. In 2015, nearly 7300 women in the UK were diagnosed with the condition.[2] Ovarian cancer itself is highly heterogeneous. Epithelial ovarian cancer (EOC) accounts for more than 90% of ovarian malignancies, while germ call tumours and sex cord stromal tumours account for 5% and 1.2%, respectively.[2]

Although most ovarian malignancies develop in postmenopausal women, 20–25% occur in younger women.[2] The median age for diagnosis of EOC is 63 years, but it can affect women as young as 40.[19] Germ cell tumours commonly affect those aged between 10 and 30 years.[43] Nearly 60% of women with sex cord stromal tumours present between the ages of 30 and 59 and 12% are under the age of 30.[35]

For all but the most comorbid of patients, treatment of EOC consists of cytoreductive surgery and platinum-based chemotherapy. For most women with germ cell tumours, fertility preserving surgery is followed by platinum-based combination chemotherapy.[44] A hysterectomy and BSO is recommended for most women with sex cord stromal tumours.[45]

The overall 5-year survival rate for ovarian cancer is approximately 46.2%, but this is dependent on, among other things, age at diagnosis and the type, stage and grade of cancer.[2] Five-year survival rates for women under the age of 40, those with stage I disease or those with a germ cell or sex cord stromal tumour exceed 90%.[2]

The role of estrogen and/or progestogen in the pathogenesis of ovarian cancer remains unclear. Epithelial ovarian cancers, especially serous and endometrioid subtypes, have been shown to express both estrogen and progesterone receptors[46,47] and anti-estrogens have been used with variable success to treat ovarian cancer in patients who cannot tolerate or have not responded to cytotoxic therapy.[48,49] Clinically, the oral contraceptive pill protects against development of ovarian cancer,[50] but data for HRT are conflicting. A meta-analysis incorporating 52 epidemiological studies and 21 488 postmenopausal women suggests that taking HRT, even if just for a few years, is associated with an increased risk of serous (relative risk [RR] 1.53, 95% CI 1.40–1.66; $P < 0.0001$) and endometrioid (RR 1.42, 95% CI 1.20–1.67; $P < 0.0001$) ovarian cancer.[51] The absolute risk, however, remains small.[10] Conversely, randomised data from a post-hoc analysis of the Women's Health Initiative failed to demonstrate any association.[52]

Several epidemiological studies have investigated the safety of HRT in women with a history of ovarian cancer.[53–57] These focus largely on the use of HRT in women with EOC after surgical treatment. While they should be interpreted with caution (since most were relatively small and had methodological limitations), none report an increased risk of recurrence or decreased survival in women treated with HRT for 2–4 years after surgery. One even suggests that HRT improves survival (hazard ratio [HR] 0.57, 95% CI 0.42–0.78).[54] This latter study was a prospective nationwide cohort, incorporating 649 women with predominantly stage I–II EOC.

There have also been two randomised trials.[58,59] The first incorporated 130 women aged between 50 and 74 years, who had undergone surgery for EOC.[58] It was powered to detect a 20% difference in progression-free survival. Conjugated estrogens or placebo were commenced and no significant effect of HRT on survival (44 versus 33 months; $P = 0.3$) or recurrence (34 versus 27 months; $P = 0.8$) was observed after 5 years of follow-up, but a non-significant trend towards improved outcomes with HRT is evident.

The second was a randomised, non-blinded, phase III study, which incorporated 150 women with EOC from across 19 centres in the UK, Spain and Hungary.[59] Patients in both cohorts were well matched for clinical characteristics. Most, but not all, were postmenopausal (77% versus 23%) and 63% had stage III disease. Statistical analysis was based on the intention to treat. The conclusions drawn were that both overall survival (HR 0.63; 95% CI 0.44–0.90; $P = 0.011$) and progression-free survival (HR 0.67; 95% CI 0.47–0.97; $P = 0.032$) were significantly improved in the women who received HRT. The choice of HRT in this study was at the discretion of the prescribing clinician and was therefore not standardised.

The results from both of these randomised trials[58,59] have been combined and the HR for overall survival is 0.68 (95% CI 0.51–0.90) in favour of HRT.[59]

A major limitation of all of the studies incorporating women with EOC is that EOC is itself highly variable. There are four main histological subtypes (serous, endometrioid, clear cell and mucinous), which are all distinct in terms of their origin, molecular pathogenesis, pathology, immunohistochemistry, clinical features, response to treatment and outcome. None of the studies differentiated between the types of EOC; hence, conclusions made may be true for some but not all of the different subtypes.

As a consequence of variations in stage, histology and HRT regimes, the decision for HRT in patients with EOC after

surgery remains problematic on the basis of current evidence. More robust data are needed before advising HRT for women with ovarian cancer for relief of menopausal symptoms. While the studies that have been undertaken have all reported the safety of HRT in patients with EOC, most have methodological limitations. Furthermore, the answers to fundamental clinical questions remain lacking: namely, what type of HRT should be recommended, for how long and for whom?

With respect to non-epithelial ovarian cancers, currently, there are unfortunately no data regarding the safety of HRT after treatment for ovarian germ cell tumours or sex cord stromal tumours of the ovary. For granulosa cell tumours, the consensus is that HRT should be avoided because it is an endocrinologically active and hormone-dependent disease.[35,45]

Data regarding the safety of HRT in women treated for borderline ovarian tumours are also scarce. One study incorporating 150 women demonstrated that the use of HRT before or after diagnosis and treatment had no effect on overall survival.[54] However, since some borderline tumours may also be treated with anti-estrogenic agents and, given the limited data available, hormone therapy in these patients may not be appropriate.[35]

Cervical cancer

Cervical cancer is the 13th most common cancer in women in the UK, with 3100 UK women being diagnosed with this cancer in 2015.[3] Infection with high-risk strains of the human papilloma virus (HPV) is responsible for most cervical cancers.

The incidence of cervical cancer is highest in 25–29 year-olds, and most cases in the UK are diagnosed in women under the age of 45.[3]

It is usually detected at an early stage, such that 54% of women diagnosed with cervical cancer have stage I disease, while only 8% have stage IV disease.[3] The overall 5-year survival rate is 67%, but this depends on stage: women with stage I disease have a 5-year survival rate of 95.9%, while in women with stage IV cervical cancer it is only 5.3%.[3]

Treatment depends on stage. Surgery, ranging in extent from conisation to radical hysterectomy, is generally reserved for earlier stage disease, while primary chemo-radiotherapy is recommended for disease more advanced than FIGO (International Federation of Gynecology and Obstetrics) 2018 stage IB3. Women who are considered at intermediate or high risk of recurrence after surgery (depending on various pathological factors) will also receive adjuvant radiotherapy, with or without chemotherapy.

There are two main histological subtypes of cervical cancer: squamous cell carcinoma (SCC), which accounts for more than 70% of cases, and adenocarcinoma, which accounts for approximately 25% of cases.

For women with SCC, the incidence of ovarian metastasis is very low (0.2% for stage IB and 2% for stage IIB disease). As such, the ovaries can be preserved in women undergoing surgery.[60] The incidence of ovarian metastasis is higher for women with adenocarcinoma (4% for stage IB disease); hence, if these women are to undergo surgery, most gynaecological oncologists recommend BSO.[45,60]

Young women who undergo BSO will inevitably be rendered menopausal by their treatment. Those who receive chemotherapy and/or radiotherapy are also at risk of an induced menopause. While preserved ovaries can be transposed out of the pelvis to avoid the direct field of irradiation, the effect of scatter alone can induce ovarian failure and menopausal symptoms.[61,62] Whether or not chemotherapy induces menopausal symptoms largely depends on the type(s) of chemotherapeutic agents administered and the cumulative dose(s), as well as the ovarian reserve prior to treatment.

Like ovarian cancer, the relationship between hormone exposure and cervical cancer is unclear. While cervical cancer is generally not considered to be hormone-dependent, several studies have demonstrated the presence of estrogen and progesterone receptors in the cervix.[63] These receptors are overexpressed in approximately one-third of adenocarcinomas (but not SCC).[63] Furthermore, a systematic review reported that the RR of cervical cancer increased with increasing duration of use of the combined oral contraceptive pill.[64] This risk persisted even after adjusting for number of sexual partners, smoking, histology, HPV status and use of barrier methods. Another, albeit small study,[65] has suggested that noncontraceptive estrogens, especially unopposed estrogens, are positively associated with adenocarcinomas (but not SCC) of the cervix (OR 2.7; 95% CI 1.1–6.8).

Unfortunately, randomised data evaluating the safety of HRT in patients following treatment for cervical cancer are lacking. An epidemiological study from 1987, which incorporated 120 women under the age of 45 treated with either surgery and adjuvant radiotherapy (n = 79) or primary radiotherapy (n = 41) for stage I (n = 94) or II (n = 26) cervical cancer, is frequently cited to purport the safety of HRT in survivors of cervical cancer.[66] This study compared 80 women who received combined HRT following treatment, with 40 women who did not. Their results suggest that the overall 5-year survival was significantly higher (80% versus 65%) and recurrence rates lower (20% versus 32%) in women who received HRT. While these data may appear to be reassuring, the study did not differentiate between women with SCC or adenocarcinoma. It is likely, given the relative infrequency of adenocarcinomas, that fewer than 20 women included in the study had an adenocarcinoma. The same conclusions may therefore not be true for both SCCs and adenocarcinomas of the cervix.

A recent, albeit small and retrospective, case-control study, has attempted to investigate the safety of HRT following

treatment of cervical adenocarcinomas specifically.[67] This study, which incorporated women with stage IA–IB adenocarcinoma, compared the survival of 38 women who had received tibolone following surgery (in the form of radical hysterectomy, BSO and retroperitoneal lymph node dissection) with or without adjuvant chemo-radiotherapy, with 32 women who received no hormonal therapy. Although this study reported that the overall survival rate appeared not to be affected by the use of tibolone, the Kaplan–Meier curves presented suggest a non-significant survival benefit in the non-users. Larger studies are therefore required to substantiate these findings.

While the use of HRT in women who have undergone treatment for SCC of the cervix appears to be safe, there are, in the presence of evidence suggesting a role of estrogen in the pathogenesis of adenocarcinoma of the cervix, insufficient data regarding the safety of HRT in women who have undergone treatment for adenocarcinomas. HRT should therefore be used cautiously, if at all, in these women.

If HRT is to be used following treatment of cervical cancer, patients who have undergone hysterectomy and BSO only require estrogen. Patients receiving primary radiotherapy are treated with a combination of external beam radiation and vaginal brachytherapy. Although patients are generally treated with radiation doses that ablate the endometrium, several studies have demonstrated that some endometrial tissue may survive usual doses.[68] Hence, if HRT is being considered for these women, a continuous combined preparation should be prescribed. Brachytherapy is associated with significant radiation toxicity to the vagina, causing partial stenosis or even complete occlusion in approximately 27% and 11% of cases, respectively.[69] This inevitably contributes to the development of dyspareunia and sexual dysfunction, for which local estrogens may be beneficial. There is no evidence that use of vaginal estrogens has an adverse effect on the course of a cervical cancer.[45]

Vaginal cancer

Vaginal cancer accounts for approximately 3% of gynaecological malignancies.[6] There were 232 new cases of vaginal cancer in the UK in 2015.[4] Most occur in postmenopausal women and are of squamous histology, occurring mainly as a consequence of HPV-related vaginal intraepithelial neoplasia. These tumours are not estrogen-dependent, hence the use of HRT, if required, appears to be safe.[45]

Melanomas, sarcomas and adenocarcinomas of the vagina also occur, albeit rarely.[6] Adenocarcinomas of the vagina account for almost all vaginal cancers diagnosed in women under the age of 20.[70] Clear-cell vaginal cancer is most commonly seen in patients exposed to diethylstilboestrol in utero.[71] A small increase in the risk of breast cancer has been reported in the mothers of these children.[72] This risk may also extend to the female patients exposed in utero.[73–75] Research on the safety of hormone therapy in female patients exposed to diethylstilboestrol in utero is limited,[45] hence HRT should be used cautiously, if at all, in these women.

Vulval cancer

Vulval cancer accounts for approximately 5% of gynaecological malignancies.[6] Approximately 1300 cases are diagnosed in the UK each year.[5] The incidence is highest in women over the age of 90 years.[6] HPV-related vulval intraepithelial neoplasia is, however, becoming more prevalent in young women and this may lead to more vulval cancers being diagnosed at a younger age in the future.[76]

The most common type of vulval cancer, accounting for 85–90% of cases, is non-estrogen dependent SCC.[45] Other vulval malignancies are rare. Estrogen use after the menopause is not associated with vulval intraepithelial neoplasia or vulval cancer[77–79] and there is no evidence that HRT increases the risk of recurrence after treatment for vulval cancer.[77,78] Systemic and topical estrogens can therefore be used safely after an SCC of the vulva.

Non-hormonal approaches to the management of menopausal symptoms

Survivors of gynaecological malignancies for whom HRT is inadvisable may still experience troublesome vasomotor symptoms. These should be managed in the same way as they would in women who have any other contraindication to HRT, incorporating lifestyle modifications and non-hormonal medications including venlafaxine, fluoxetine, paroxetine, citalopram, clonidine or gabapentin.[33] Guidance on the use of these medications is available from the British Menopause Society.[80]

Complementary medicines such as isoflavones, black cohosh or St John's wort may relieve vasomotor symptoms, but their safety is uncertain and they should not be recommended.[33] Acupuncture is also often advised for the treatment of hot flushes and while there is some evidence supporting its efficacy, it is generally of poor quality.[81] Cognitive behavioural therapy can be used to alleviate low mood or anxiety that may arise as a consequence of the menopause.[33]

Conclusion

Maintaining quality of life is important in gynaecological oncology, particularly since many women are living longer following improvements in cancer care. In the general population, the benefits of HRT for the treatment of the immediate symptoms of estrogen deficiency (and, in young women, the prevention of the associated long-term sequelae)

are incontrovertible. For women with a history of gynaecological malignancy, there are cancer-related risks that must also be considered. A multi-disciplinary, individualised, patient-centred, evidence-based approach to management is essential for women to make an informed decision when considering the use of HRT for the treatment of menopausal symptoms following treatment of gynaecological malignancies.

Disclosure of interests

AR is a Trainee Representative on the Editorial Board of *The Obstetrician & Gynaecologist*. She was excluded from editorial discussions regarding the paper and had no involvement in the decision to publish.

Author contributions

AR researched the literature and wrote the manuscript. JA, MC and AP contributed to the content and reviewed the draft manuscript. All authors approved the final version.

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