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# Shared follow-up and survivorship care for women with low-risk endometrial cancer: summary of evidence

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# Summary

Cancer Australia has undertaken a body of work that identified shared follow-up care for women with low-risk endometrial cancer as a model that assists in providing holistic care, addresses the increasing demand for specialist services and facilitates equity of access to best practice care. This summary of evidence outlines the evidence base that supports and informs Cancer Australia's *Shared follow-up and survivorship care model for women with low-risk endometrial cancer*. The purpose is to provide the context, evidence base and, where applicable, the consensus base for Cancer Australia's shared follow-up care model and resources. The primary audience is health professionals and other stakeholders involved in the uptake and implementation of a shared model of follow-up care for women with low-risk endometrial cancer. This summary of evidence is based on systematic searches of the literature undertaken to March 2019.

## Background on endometrial cancer

- Endometrial cancer is the most common gynaecological cancer in Australian women.[1]
- Endometrial cancer is mostly diagnosed at an early stage and has a high survival rate compared to many other cancers. [23,1,*]
- Due to the relatively high survival rate, there is an increasing number of endometrial cancer survivors.[1]
- Surgery is the primary treatment for endometrial cancer.[2]
- Many women with endometrial cancer have co-morbidities including obesity-related issues, hypertension, diabetes and cardiovascular disease.[3-5] Co-morbidity rates reported for women with uterine cancer include: 59% with hypertension, 34% with obesity, 26% with diabetes and 12% with chronic pulmonary disease.[4] Cardiovascular disease is the leading cause of death for women with localised or low grade endometrial cancer.[21, 22]

## Endometrial cancer recurrence

- Definitions of low-risk endometrial cancer vary, but low-risk groups commonly include International Federation of Gynecology and Obstetrics (FIGO) stage IA or IB endometrial cancers that are histological grade 1 or grade 2.[6]
- Endometrial cancer has a low recurrence rate overall of approximately 13% and for patients considered low-risk, recurrence rates range from 1% - 3%.[6-8]
- Most endometrial cancer recurrences are detected within the first three years after treatment and the vaginal vault is a common site of recurrence.[6, 9, 10]
- The majority (approximately 65% - 70%) of endometrial cancer recurrences are symptomatic.[6, 11]
- Symptoms of endometrial cancer recurrence include vaginal bleeding, pain, abdominal/pelvic pain or distension, and cough.[6, 12] It is important that women are educated about these symptoms and the need to report them to their healthcare team without delay.[6]

* Currently Australian statistics on incidence by stage at diagnosis and on survival by stage at diagnosis for endometrial cancer are not available.

## Principles and purpose of follow-up and survivorship care for women with endometrial cancer

- Peak cancer organisations including Cancer Australia have identified key principles to guide follow-up and survivorship care for people living with and beyond cancer.[13]
- Observational studies of women with endometrial cancer have identified supportive care needs and unmet needs, including dealing with late effects of treatment, psychosocial needs (such as depression, anxiety, stress and fear of recurrence) and psychosexual needs.[14-18] Information needs include information on symptoms of recurrence and on late effects of treatment.[10, 19]
- The purpose of follow-up and survivorship care for women with endometrial cancer includes:
  - Early detection of recurrence.[6, 20]
  - Identification, monitoring and management of treatment-related side effects and co-morbidities.[2, 6, 20] Screening, assessment and management of supportive care needs.[14, 16, 19]
  - Reviewing and updating family history information.[20, 23]
  - Providing holistic care.[13]
  - Exploring and managing the woman's expectations.[24]

## Follow-up care for endometrial cancer

- As most endometrial cancer recurrences occur within three years of treatment, follow-up of endometrial cancer is generally undertaken for up to five years after treatment with more frequent visits in the first two to three years.[2, 6, 20, 25]
- There is currently a lack of evidence from randomised controlled trials on the frequency and duration of follow-up visits for endometrial cancer. Recommended schedules are based on the evidence on endometrial cancer recurrence from retrospective studies and on expert consensus.[6, 20, 25]
- Guidelines for women with low-risk endometrial cancer recommend a reduced frequency of follow-up visits compared to higher-risk patients.[6, 20, 26]
- Guidelines recommend that follow-up visits for women with low-risk endometrial cancer include a thorough clinical history with review of symptoms and a physical examination including pelvic examination and if feasible, vaginal speculum examination, based on retrospective evidence indicating that most recurrences are symptomatic or detected by physical examination.[6, 20, 26, 27]
- Other tests such as vaginal cytology and imaging (such as abdominal ultrasound or computed tomography (CT) scan) should only be undertaken for women with low-risk endometrial cancer if symptoms or findings from a physical examination suggest a recurrence.[6, 20, 26]

## Models of follow-up care for endometrial cancer including shared follow-up care

- Studies of follow-up care models for endometrial cancer have indicated that a GP-based model can be feasible and acceptable to women and their GPs (one small non-randomised Australian study)[28] and that nurse-led follow-up is non-inferior to standard hospital-based follow-up care (one randomised trial and one comparative cohort study).[29, 30] A randomised trial reported that patient-initiated follow-up for women with early stage endometrial cancer was inferior to hospital-based

follow-up for the outcome of fear of cancer recurrence[31], and a non-comparative cohort study of women with early stage endometrial cancer reported satisfaction with patient-initiated follow-up by the majority of women.[32] These trials did not investigate the impact of these models of care on recurrence rates or survival outcomes.

- Randomised trials of GP-based models of follow-up care for early breast cancer and colon cancer have indicated similar patient satisfaction, quality of life and recurrence outcomes compared to hospital-based specialist care.[33-35]
- Shared follow-up care between specialist and primary care teams has potential benefits such as improved access to follow-up care and to person-centred holistic care, including management of co-morbidities and supportive care needs, and strengthened care coordination.[8, 36, 37]
- Enablers of shared follow-up care include strong clinical leadership and partnerships between GPs and cancer specialists, a multidisciplinary approach, use of shared care plans and treatment summaries for GPs and patients, education and training for GPs, availability of rapid access to specialist consultation and high-quality supporting resources.[2, 28, 37-39]
- Ongoing trials of endometrial cancer follow-up are investigating telephone follow-up care, different intensities of follow-up visits, and surveillance tests.[40-44]

## Conclusion

Shared follow-up and survivorship care for women with low-risk endometrial cancer, involving the joint participation of primary and specialist health teams, is supported by evidence from retrospective studies that endometrial cancer recurrence rates are low (1% - 3% for women considered low-risk), that most endometrial cancer recurrences are detected within the first three years after treatment, and that the majority of recurrences are symptomatic. Evidence on recurrence supports a risk-stratified approach to follow-up, with less frequent visits and less intensive surveillance tests for women at lower risk. Follow-up of endometrial cancer is generally undertaken for up to five years after treatment with more frequent visits in the first two to three years, based on the evidence of low recurrence rates.

Co-morbidities such as cardiovascular disease and their underlying risk factors should be identified and managed in follow-up, since cardiovascular disease is a greater cause of death than endometrial cancer for women treated for localised or low grade endometrial cancer. There is evidence from observational studies of supportive care and information needs, and of unmet needs, for women with endometrial cancer that should be addressed in follow-up care. Shared follow-up care can help improve access to person-centred holistic care, improve management of co-morbidities and supportive care needs, and strengthen care coordination.

Results of randomised trials in early breast cancer and colon cancer indicate similar patient satisfaction, quality of life and recurrence outcomes for GP-based follow-up care compared to hospital-based specialist follow-up care, supporting use of a similar model for the follow-up of women with low-risk endometrial cancer. Studies indicate that enablers of shared follow-up care include strong clinical leadership and partnerships between GPs and cancer specialists, a multidisciplinary approach, use of shared care plans, education and training for GPs, availability of rapid access to specialist consultation, and high-quality supporting resources.

# 1. Introduction

## 1.1 Purpose

Cancer Australia has undertaken a body of work that identifies shared follow-up care for women with low-risk endometrial cancer as a model that assists in providing holistic care, addresses the increasing demand for specialist services and facilitates equity of access to best practice care. Cancer Australia worked with key stakeholders, including staff of gynaecological oncology units across Australia, general practitioners (GPs) and patients over several years (2015-2020) to develop a shared follow-up and survivorship care model for women with low-risk endometrial cancer. Resources to support this model of care and its implementation, including evidence-based guidance material for GPs and a Guidance toolkit, have been developed with input from key stakeholders by Cancer Australia.

This summary of evidence outlines the evidence base that supports and informs Cancer Australia's *Shared follow-up and survivorship care model for women with low-risk endometrial cancer*. The purpose of this summary of evidence is to provide the context, evidence base and, where applicable, the consensus base for Cancer Australia's shared care model and resources. The audience for this summary of evidence includes health professionals and other key stakeholders involved in the uptake and implementation of a shared model of follow-up care for women with low-risk endometrial cancer. This summary is based on systematic searches of literature databases and of the grey literature undertaken to March 2019.

## 1.2 Background on endometrial cancer

Endometrial cancer is cancer that arises from the lining of the uterus (the endometrium). Endometrial cancer is the most common type of cancer of the uterus, and uterine cancer is the most common gynaecological cancer diagnosed in Australian women.[1] Most statistics are reported for uterine cancer overall, which includes endometrial cancer (approximately 95%) and uterine sarcoma, rather than for endometrial cancer. The numbers of women diagnosed with uterine cancer in Australia have increased from 942 in 1982 to an estimated 3,224 in 2020, and the age-standardised incidence rate has increased from 14 cases per 100,000 women in 1982 to an estimated 21 cases per 100,000 women in 2020.[1] The increased incidence rate is likely due to demographic factors such as population ageing and to increases in prevalence of risk factors such as obesity. The incidence rate for uterine cancer increases with age and peaks at age 65-69 years, with approximately 90% of women at diagnosis of uterine cancer aged over 50 years.[1]

Endometrial cancer is commonly diagnosed at an early stage where it is localised to the uterus (stage I or stage II endometrial cancer).[2,3] Approximately 70% of uterine cancers are diagnosed at an early stage, based on statistics from the USA.[τ,7] Diagnosis of most cases at an early stage is associated with a high survival rate for endometrial cancer compared with other cancers. In Australia, the five-year relative survival rate for women diagnosed with uterine cancer overall was 83% in 2012-2016.[1] For women diagnosed with early stage uterine cancer, survival rates are higher. For example in the USA, five-year relative survival rates were 95% for localised (early) uterine cancer, compared to 69% for regional and 17% for distant uterine cancer, for 2009-2015.[7]

[τ]Currently Australian statistics on incidence by stage at diagnosis and on survival by stage at diagnosis for endometrial cancer are not available.



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Due to the relatively high survival rate, especially for the majority of women diagnosed with early stage endometrial cancer, there is an increasing number, or prevalence, of endometrial cancer survivors. The number of women in Australia living with uterine cancer at the end of 2015 who had been diagnosed in the previous five years was 10,763 and the number of women diagnosed in the previous 34 years was 30,791.[1]

Surgery is the primary treatment for endometrial cancer.[2] Surgery for early stage endometrial cancer usually involves hysterectomy and bilateral salpingo-oophorectomy, with or without lymph node dissection.[2] Most women with early stage endometrial cancer do not require adjuvant treatment with radiation therapy or chemotherapy. Adjuvant radiation therapy such as vaginal brachytherapy or pelvic external-beam radiation therapy may be offered for women with higher risk factors, and adverse effects of radiotherapy should be monitored in follow-up of women receiving this therapy.[2, 6]

Many women with endometrial cancer experience a range of co-morbidities including obesity-related issues, hypertension, diabetes and cardiovascular disease.[3-5] Co-morbidity rates of 59% with hypertension, 34% with obesity, 26% with diabetes and 12% with chronic pulmonary disease have been reported among women with uterine cancer in a large recent US study.[4] The high prevalence of co-morbidities indicates the need during follow-up to consider their identification and management, and address underlying risk factors.

## Key points: Background on endometrial cancer

- Endometrial cancer is the most common gynaecological cancer in Australian women.[1]
- Endometrial cancer is mostly diagnosed at an early stage and has a high survival rate compared to many other cancers. [23,1, τ]
- Due to the relatively high survival rate, there is an increasing number of endometrial cancer survivors.[1]
- Surgery is the primary treatment for endometrial cancer.[2]
- Many women with endometrial cancer have co-morbidities including obesity-related issues, hypertension, diabetes and cardiovascular disease.[3-5] Co-morbidity rates reported for women with uterine cancer include: 59% with hypertension, 34% with obesity, 26% with diabetes and 12% with chronic pulmonary disease.[4] Cardiovascular disease is the leading cause of death for women with localised or low grade endometrial cancer.[21, 22]

[τ] Currently Australian statistics on incidence by stage at diagnosis and on survival by stage at diagnosis for endometrial cancer are not available.



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# 2. Endometrial cancer recurrence

While there are ongoing studies (see section 5.5), there are currently no data available from randomised controlled studies on endometrial cancer follow-up that have recurrence detection or overall survival as primary endpoints.[6, 24] The available evidence on rates and detection of endometrial cancer recurrence is based on retrospective studies which have inherent risks of bias. In addition to limitations due to their retrospective design, many studies on recurrence have small sample sizes and were published over a decade ago.[24] A systematic review of the evidence by Cancer Care Ontario (CCO) in 2006 included 12 non-comparative retrospective studies (published 1990-2001) and an update of the review in 2017 included one additional retrospective study (published 2014) on recurrence.[6] Since this systematic review, a Danish population-based cohort study by Jeppesen et al has been published (2016, 2017) that reported recurrence among 2,612 women with early stage endometrial cancer, which is the largest cohort reported to date.[9, 11]

## 2.1 Definition of low-risk endometrial cancer

Low-risk endometrial cancer is variously defined for different purposes. Some clinical practice guidelines, for example the ESMO-ESGO-ESTRO Consensus 2017[27] and National Comprehensive Cancer Network Guidelines 2020 (NCCN)[25], define risk groups for the purpose of guiding the use of adjuvant therapy for endometrial cancer. Other guidelines, such as CCO and the Society of Gynecological Oncology (SGO), have defined risk of recurrence groups for the purpose of guiding suitable follow-up care.[6, 20]

There is variation in the criteria used for the definitions of low-risk endometrial cancer. In assessing endometrial cancer recurrence risk, International Federation of Gynecology and Obstetrics (FIGO) stage determined by surgical staging (which incorporates depth of myometrial invasion and cervical involvement)[23] and histological grade (according to World Health Organization/International Society of Gynecological Pathology classification) are often used (Refer Appendix A). Definitions of low-risk endometrial cancer groups commonly include FIGO stage IA or IB cancers that are histological grade 1 or 2, whereas high-risk groups include stage IA or IB cancers that are histological grade 3; stage IC; or advanced stage endometrial cancers.[6, 27]

In addition to histological grade and stage, there is evidence for the prognostic value of the features 'lymphovascular space invasion' and 'histopathological type' for endometrial cancer.[27] These features are included in the ESMO-ESTRO-ESGO criteria for classification of low-, intermediate- and high-risk groups for the purpose of guiding adjuvant therapy use for endometrial cancer.[27] The addition of other factors such as age, tumour size and molecular characteristics (e.g. TP53 gene mutation, oestrogen receptor, progesterone receptor, L1 cell adhesion molecule) are being investigated for inclusion in risk prediction models for endometrial cancer recurrence.[27, 45-47]

In clinical practice the definition of 'low-risk endometrial cancer' may vary from one cancer service to another, and depending on the purpose for defining risk level. One guideline from BC (British Columbia) Cancer has stratified endometrial cancer follow-up groups according to the adjuvant treatment received.[48] Women who have received adjuvant therapy may have particular needs during follow-up due to the effects of the adjuvant treatment.

For the purposes of guiding follow-up care, 'low-risk endometrial cancer' should be determined by the treating multidisciplinary team, which may consider features such as stage and histological grade, treatment received, and other individual factors.



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## 2.2 Recurrence rate, timing and site of recurrence

Studies have shown that endometrial cancer has a favourable prognosis with a low risk of recurrence. In the CCO systematic review of 12 non-comparative retrospective studies (published 1990 – 2001), recurrence rates for patients with endometrial cancer overall ranged from 8% - 19% (12 studies, mean 13%; 95%CI: 11% - 14%) and for patients with low-risk of recurrence ranged from 1% - 3% compared to 5% - 16% for high-risk patients (four studies).[6] The recent large population-based cohort study by Jeppesen et al of 2,616 women with early stage (stage I or stage II) endometrial cancer diagnosed 2005 - 2009, which is the largest cohort to date, reported an average of 7% (183/2612) recurrence within three years. [9] Three-year recurrence was 4.4% for stage IA; 9.2% for stage IB; and 13.7% for stage II.[9]

The majority of endometrial cancer recurrences are detected within three years of treatment. In the CCO review, 68% - 82% of recurrences were detected within two years of primary treatment (three studies) and 70% - 89% of recurrences were detected within three years of primary treatment (five studies).[6] In the Danish study by Jeppesen et al, the median time to recurrence was 12 months (interquartile range 7.2 - 20.6 months).[9]

Common sites of endometrial cancer recurrence are the vaginal vault, pelvis, intra-abdominal region and lungs.[6] The CCO review reported pooled data indicating that 39% (95%CI: 35% - 44%) of recurrences were local and 61% of recurrences were distant (95%CI: 56% - 65%) (11 studies).[6] In the Danish study by Jeppesen et al, the most frequent site of endometrial cancer recurrence was the vaginal vault (48.1%, 88/183 of women); followed by pelvic lymph nodes/sidewall (17.5%, 32/183 of women); and distant metastases (33.3%, 61/183 of women).[9] Recurrence in the vaginal vault was associated with better five-year survival than distant endometrial cancer recurrence: vaginal 64.8% vs distant 17.5%.[9]

## 2.3 Symptomatic and asymptomatic recurrence

The majority of endometrial cancer recurrences are symptomatic at the time of recurrence. The CCO systematic review reported that approximately 70% of all endometrial cancer recurrences were symptomatic (range 41% - 100%, 12 studies).[6] In the Danish cohort study by Jeppesen et al of 2,616 women with early stage endometrial cancer, 65.5% (116/177) of the recurrences were symptomatic.[11]

There have been mixed findings from available studies, which have limitations due to their retrospective design, on the survival of women with symptomatic compared to asymptomatic endometrial cancer recurrence. The CCO systematic review reported five studies with no difference in survival between women with symptomatic and asymptomatic recurrence, and one study (with only 17 recurrences) that reported a survival advantage for women with asymptomatic recurrence.[6] A retrospective Australian study reported symptomatic recurrence in 71.1% (199/280) of women with recurrent uterine cancer.[49] In this study there was a survival advantage for asymptomatic recurrence patients among women with stage I or II endometrioid tumours: overall 5-year survival probability was 38.0% (asymptomatic) vs. 25.7% (symptomatic recurrence).[49] In the Danish cohort study by Jeppesen et al, women with an asymptomatic recurrence had a significantly improved three-year survival compared to those with a symptomatic recurrence (80.3% vs 54.3%, $p<0.01$), however the difference may have been influenced by lead-time and length-time biases.[11]

## 2.4 Symptoms of recurrence

Symptoms of possible endometrial cancer recurrence include unexplained vaginal bleeding or discharge, detection of a mass, abdominal distension, persistent pain especially in the abdomen or


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pelvic region, loss of appetite, fatigue, diarrhoea, nausea or vomiting, persistent cough, swelling or weight loss.[6, 20, 25] In the large Danish cohort study by Jeppesen et al, vaginal bleeding was the most common symptom (47% of symptomatic recurrences).[11]

A literature review of symptoms of recurrence in women with endometrial cancer indicated that the most commonly reported symptoms were vaginal bleeding, pain, abdominal pain and/or discomfort and swelling, and cough.[12] Based on these most commonly reported symptoms and on additional symptoms reported in the literature, an expanded symptom checklist has been developed by Australian researchers.[12] This checklist is being tested in a non-randomised prospective study in Queensland (the 'TEACUP' study, refer section 5.5) in which patients will be interviewed via telephone using the expanded symptom checklist 2 - 5 days prior to attending routine clinic follow-up visits.[41]

Since the majority of cancer recurrences are symptomatic, guidelines recommend that patients be educated and counselled about the most likely symptoms of recurrence, and to not delay in seeking prompt evaluation of symptoms until the next scheduled visit.[6, 20] An Australian study of 280 women with recurrence after treatment for uterine cancer (1990-2006) reported that 15.4% (43/280) of patients with symptoms waited until their next scheduled follow-up visit to consult with health care professionals.[49] The Danish study by Jeppesen et al, reported that women with symptoms of recurrence who had a higher education level more often sought medical attendance compared to those with a lower education level, suggesting the possible impact of factors such as health literacy on prompt reporting of symptoms.[11]

## Key points: Endometrial cancer recurrence

- Definitions of low-risk endometrial cancer vary, but low-risk groups commonly include International Federation of Gynecology and Obstetrics (FIGO) stage IA or IB endometrial cancers that are histological grade 1 or grade 2.[6]
- Endometrial cancer has a low recurrence rate overall of approximately 13% and for patients considered low-risk, recurrence rates range from 1% - 3%.[6-8]
- Most endometrial cancer recurrences are detected within the first three years after treatment and the vaginal vault is a common site of recurrence.[6, 9, 10]
- The majority (approximately 65%-70%) of endometrial cancer recurrences are symptomatic.[6, 11]
- Symptoms of endometrial cancer recurrence include vaginal bleeding, pain, abdominal/pelvic pain or distension, and cough.[6, 12] It is important that women are educated about these symptoms and the need to report them to their healthcare team without delay.[6]



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# 3 Principles and purpose of follow-up and survivorship care for women with endometrial cancer

## 3.1 Principles of cancer survivorship

Key principles to guide follow-up and survivorship care for people living with and beyond cancer have been identified by peak health organisations including the Institute of Medicine in the USA *(From cancer patient to cancer survivor: lost in transition, 2006)*,[50] the Clinical Oncology Society of Australia[51] and Cancer Australia.[13] Cancer Australia's *Principles of Cancer Survivorship* (2017) were developed through a process of consultation and engagement with national leaders in survivorship care, including people affected by cancer, and are supported by available evidence on cancer survivorship.[13]

Cancer Australia's *Principles of Cancer Survivorship* (Refer Appendix B) are:[13]

1. Consumer involvement in person-centred care
2. Support for living well
3. Evidence-based pathways
4. Co-ordinated and integrated care
5. Data-driven improvements and investment in research.

## 3.2 Needs of women with endometrial cancer during follow-up

Evidence from survey-based observational studies on the concerns, needs and unmet needs of women with endometrial cancer after treatment informs the purpose of follow-up and supportive care specifically for endometrial cancer.

A systematic review in 2018 reported evidence on patient-reported outcomes in survivors of endometrial cancer from 27 observational studies (published 2005 - 2017; included 19 cross-sectional studies and eight longitudinal studies that evaluated changes over time; sample sizes ranged from 38 – 666 women).[14] Population-based surveys by the Australian National Endometrial Cancer Study Group of Australian women three to five years after endometrial cancer diagnosis have reported on supportive care needs (study with n=629, diagnosed 2005 – 2007; 85% stage I at diagnosis) (2015)[17] and on sexual well-being (study with n=395, diagnosed 2005 – 2007) (2014).[18] A Canadian study of endometrial cancer survivors surveyed within two years of active treatment (n=169 survey responses and n=14 women in focus groups) reported on late effects and psychosocial issues.[10] For gynaecological cancer patients generally, supportive care needs were reported in an Australian observational study of women one to eight years after primary treatment (46% (91/199) women with endometrial cancer) (2007),[16] and a review in 2013 reported on psychosocial needs.[15]

Supportive care needs and unmet needs of women with endometrial cancer reported from these studies include:

- dealing with late effects of treatment, including menopausal symptoms, pain, lymphoedema, poor sleep quality, fatigue and neurocognitive issues.[10, 14] These needs were reported often several years after diagnosis, indicating the importance of ongoing monitoring of late effects during follow-up.[14]
- psychosocial needs, including emotional distress and social functioning,[14] depression and anxiety,[10, 16] and dealing with stress and coping with others not acknowledging the impact of cancer on them.[17]



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Ongoing psychosocial assessment is required, as distress or need levels may not necessarily decline over time.[16]

- fear of cancer recurrence, which was reported in many studies of patients with gynaecological/endometrial cancer.[15-17] Help in dealing with and living with fear of cancer recurrence was a frequently reported unmet need.[15-17]
- psychosexual needs including sexual dysfunction.[10] Positive sexual well-being was associated with having fewer symptoms of anxiety.[18] Addressing problems with their sex lives was identified as an unmet need by endometrial cancer patients.[17]

Information needs for women following endometrial cancer have been reported in observational survey studies including a population-based survey of endometrial cancer survivors (mean 4.9 years from diagnosis) from the Netherlands (n=742, diagnosed 1998 - 2007, 93% stage I at diagnosis) (2012)[19] and a Canadian study of endometrial cancer survivors (n=169) surveyed within two years of active treatment (2012).[10]

Information needs and unmet needs of women with endometrial cancer identified from these studies include:

- information on risk and symptoms of recurrence. Women in the Canadian study reported that they were not aware of their risk of recurrence or how to monitor for this, and they were not provided with clear information.[10]
- information on late effects of treatment. Women have reported being unsure about, or receiving insufficient information on late effects, including expected results of the treatment on their social and sexual life; where to go for additional information, help or psychosocial support; and things to do to improve their health.[10, 19]
- Women may differ in their information needs, as while some women indicated they had wanted to receive more information, others indicated they had wanted to receive less.[19] In the Dutch study, women who had received written information, indicated they had received more information and were more satisfied than women who did not receive written information.[19]

## 3.3 Purpose of follow-up and survivorship care for endometrial cancer

The transition from active treatment to post-treatment care and beyond is a critical time that can impact long-term health, and patients may experience particular issues after treatment that are different to those during active treatment.[2] The *Principles of Cancer Survivorship*[13] and evidence on the needs of women with endometrial cancer have informed the components of the purpose of follow-up and supportive care.

### Early detection of recurrence

Early detection of local, regional or distant recurrence is an important aim of follow-up after treatment for endometrial cancer. Early detection of recurrence may allow earlier treatment, with the overall aim of improved survival or decreased morbidity secondary to the recurrence.[6, 52] Patients should be educated and counselled about the most likely symptoms of recurrence since the majority of endometrial cancer recurrences are symptomatic (refer to section 2), hence women should not delay seeking prompt evaluation of symptoms until the next scheduled visit.[6, 20]

## Identification, monitoring and management of treatment-related side effects and co-morbidities

Treatment-related side effects should be identified, monitored and managed during follow-up. Effects of treatment for endometrial cancer depend on the type of treatment received and can include effects on menopause, bladder and bowel function and lymphoedema.[14, 53] Late effects may occur months or years later.[53] Special consideration may need to be given to premature menopause following surgical or radiation therapy to the pelvic organs or chemotherapy for endometrial cancer.[2] Adverse effects associated with radiotherapy for endometrial cancer can include complications with the rectum, urinary bladder, vagina, skin, subcutaneous tissues, bone and other sites.[6]

Many women with endometrial cancer have co-morbidities including obesity-related issues, hypertension, diabetes and cardiovascular disease.[3-5] A large retrospective cohort study of 23,227 women with uterine cancer in the USA (2010-2014) reported a prevalence of 59% with hypertension, 34% with obesity, 26% with diabetes and 12% with chronic pulmonary disease.[4] For women with uterine cancer the age-adjusted odds ratios (ORs) of these co-morbidities compared to women who did not have uterine cancer were: obesity OR = 3.26, 95%CI: 3.15–3.37; diabetes OR = 2.14, 95%CI: 2.07–2.22; hypertension OR = 1.70, 95%CI: 1.65–1.76; pulmonary circulation disorders OR = 1.69, 95%CI: 1.52–1.89; and congestive heart failure OR = 1.48, 95%CI: 1.35–1.61.[4]

Cardiovascular disease is a major co-morbidity for women with endometrial cancer. In a study from the US population-based Surveillance, Epidemiology and End Results (SEER) database (of patients diagnosed 1973-1988), cardiovascular disease was the leading cause of death in endometrial cancer survivors overall after a minimum potential 20 years of follow-up.[21] In the first five years after diagnosis endometrial cancer was the most frequent cause of death, however after five years and for every subsequent five-year interval after diagnosis, cardiovascular disease was the most frequent cause of death.[21] Similar results were reported from the SEER database in endometrial cancer survivors (diagnosed 1988-2012), namely higher cardiovascular deaths than endometrial cancer deaths for survivors more than five years after diagnosis of endometrial cancer, and cardiovascular death as the dominant cause of mortality overall for women with localised or low-grade endometrial cancer.[22] In another study of over 3 million cancer survivors (28 cancer sites) from the SEER database (patients diagnosed 1973–2012) that included over 100,000 women with uterine cancer, the risk of mortality from heart disease was greatest for endometrial cancer compared to the average for all 28 cancer sites at all time points following diagnosis, and especially in the first year following diagnosis.[54]

Co-morbidities should be identified and managed during follow-up and lifestyle changes encouraged to reduce risk factors, such as stopping smoking, exercising, healthy nutrition and maintaining a healthy weight.[20] Management to reduce cardiovascular disease risk factors such as obesity in women with endometrial cancer can include counselling on lifestyle, and interventions to increase physical activity and achieve a healthy weight.[55]

## Screening, assessment and management of supportive care needs

There is evidence of ongoing supportive care needs, such as psychological and psychosexual needs, and of unmet needs for women after treatment for endometrial cancer (see section 3.2). Emotional and psychological issues can include distress, anxiety, depression, cognitive changes and fear of cancer recurrence.[2, 14, 17] There should be ongoing assessment and management of women's supportive care needs during follow-up, as they may change over time and may differ for each individual.[14, 16, 19]



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## Reviewing and updating family history information

Follow-up provides an opportunity to review and update personal and family history in relation to endometrial cancer and other cancers. There is a risk of a second cancer following endometrial cancer, for example, due to Lynch syndrome.[23] Review of personal and family history may help to identify women for consideration of referral for genetic assessment and counselling.[20]

## Providing holistic care

There is a need for a holistic approach that identifies and addresses a woman's individual supportive care needs and includes managing co-morbidities, that may be appropriate for the woman.[13] Holistic care involves a person-centred approach that looks at the whole person, with consideration of their needs such as physical, emotional, social, economic and spiritual needs. Care should be integrated and coordinated between health and other service providers to enable seamless holistic person-centred care for cancer patients.[13]

## Exploring and managing the woman's expectations

Follow-up provides the opportunity to explore and manage the woman's expectations, and to support her to openly discuss her care, support and information needs. Patient empowerment may result in fewer unmet needs, improved quality of life and reduced fear of cancer recurrence.[24]

## Key points: Principles and purpose of follow-up and survivorship care for women with endometrial cancer

- Peak cancer organisations including Cancer Australia have identified key principles to guide follow-up and survivorship care for people living with and beyond cancer.[13]
- Observational studies of women with endometrial cancer have identified supportive care needs and unmet needs, including dealing with late effects of treatment, psychological needs (such as depression, anxiety, stress and fear of recurrence) and psychosexual needs.[14-18] Information needs include information on symptoms of recurrence and on late effects of treatment.[10, 19]
- The purpose of follow-up and survivorship care for women with endometrial cancer includes:
  - Early detection of recurrence.[6, 20]
  - Identification, monitoring and management of treatment-related side effects and co-morbidities.[2, 6, 20]
  - Screening, assessment and management of supportive care needs.[14, 16, 19]
  - Reviewing and updating family history information.[20, 23]
  - Providing holistic care.[13]
  - Exploring and managing the woman's expectations.[24]



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# 4 Follow-up care for endometrial cancer

Evidence on the optimal schedules and duration of follow-up visits and tests undertaken for endometrial cancer follow-up is not currently available from randomised controlled trials that have overall survival and recurrence detection as primary endpoints.[6, 24] There are ongoing randomised controlled trials investigating different intensities of follow-up visits and tests for endometrial cancer, including the randomised controlled trials ENSURE and TOTEM (refer section 5.5), but findings from these studies have not yet been published.

Available evidence on follow-up for endometrial cancer has been reviewed in a systematic review by Cancer Care Ontario (CCO) in 2006 that included 12 non-comparative retrospective studies (published 1990-2001) and an update of the review in 2017 included one additional retrospective study (published 2014) on recurrence.[6]

## 4.1 Schedules for endometrial cancer follow-up visits

### Follow-up of women with endometrial cancer overall

There is no evidence currently available to indicate whether more intensive follow-up schedules (with more frequent visits) compared to less intensive schedules for endometrial cancer follow-up result in survival benefits.[6] The intensity of follow-up visits reported in studies varies. In the CCO systematic review (12 non-comparative retrospective studies, published 1990-2001), follow-up visits in the first five years after primary treatment for endometrial cancer ranged from eight to 32 visits.[6] There were fewer than 12 follow-up visits reported in four studies; 12 to 14 visits (six studies); 15 visits (one study) and 20-32 visits (one study).[6] From the 12 studies that reported results for specific follow-up schedules, no differences in outcomes were detected between the follow-up programs.[6] Based on the evidence that the majority of recurrences of endometrial cancer occur within three years and on expert consensus, most guidelines for follow-up of endometrial cancer recommend a higher frequency of follow-up visits in the first two to three years after diagnosis.[2, 6, 20, 25]

While follow-up for three to five years after treatment is supported by the evidence that the majority of recurrences of endometrial cancer occur within three years, there is no randomised evidence available on the total duration of follow-up. In the CCO systematic review of non-comparative retrospective studies, the duration of follow-up visits for endometrial cancer at a gynaecology clinic varied from: completion five years after primary treatment (four studies); continued for an additional five or eight years (two studies); annual ongoing from the sixth year (four studies); or semi-annual ongoing from the sixth year (one study).[6] Based on consensus, the CCO guidelines recommend follow-up visits for five years then a return to annual population-based general physical and pelvic examination.[6] SGO and NCCN guidelines recommend follow-up visits for five years then ongoing annual follow-up.[20, 25]

Expert consensus also indicates that individual patient preferences for follow-up schedule should be considered.[6] While there is currently no evidence that more frequent follow-up leads to improved recurrence detection, women may derive psychological and supportive care benefits with more frequent follow-up.[6] Based on expert consensus, a clear and mutually agreed follow-up plan should be offered to women who have been treated for endometrial cancer.[2]



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### Follow-up of women with low-risk endometrial cancer.

Several guidelines suggest that follow-up schedules for endometrial cancer should be stratified according to risk,[2, 6, 20, 48] based on the evidence of recurrence rates of 1% - 3% for patients with low-risk of recurrence, compared to 5% - 16% for high-risk patients.[6] For women at a low-risk of recurrence of endometrial cancer, several guidelines recommend a reduced frequency of follow-up visits compared to the frequency for higher-risk patients,[6, 20, 48] including the suggestion by one guideline that low-risk women might be reviewed only if symptoms develop.[2]

The SGO (2017)[20] and CCO (2017)[6] risk-stratified guidelines have recommended follow-up schedules based on the available retrospective evidence on endometrial cancer recurrence and on expert consensus opinion. The CCO and SGO recommended schedule for women with low-risk endometrial cancer after completion of primary treatment is for Years 1 - 3: six-monthly or 12-monthly visits, and for Years 4 - 5: annual visits.[6, 20]

Cancer Australia's suggested follow-up schedule for women with low-risk endometrial cancer is based on expert consensus and endorsed by relevant Australian professional Colleges.[26] For asymptomatic women following treatment for early stage low-risk endometrial cancer, Cancer Australia's suggested follow-up schedule is: [26]

- Years 1 - 2: every 3 - 6 months
- Year 3: every 6 - 12 months
- Years 4 - 5: every 12 months.

## 4.2 Surveillance methods for endometrial cancer follow-up visits

As the majority of endometrial cancer recurrences are symptomatic at the time of recurrence, a thorough history with a review of symptoms is important in follow-up visits.[6] In women without symptoms, physical examination has the greatest efficacy compared to other surveillance methods in detecting endometrial cancer recurrence, detecting 5% - 33% of recurrences in seven studies from the CCO systematic review.[6]

Evidence on the use of other methods to detect endometrial cancer recurrence is limited due to the retrospective study design, inconsistent reporting of outcomes, and small number of studies.[6] Detection rates of endometrial cancer recurrence in women without symptoms reported in the CCO systematic review of 12 retrospective studies (published 1990-2001) were: vaginal vault cytology from 0% - 4% (four studies); chest X-ray from 0% - 14% (six studies); abdominal ultrasound from 4% - 13% (two studies); abdominal/pelvic Computed Tomography (CT) from 5% - 21% (two studies); and 15% in selected patients with CA-125 (one study).[6]

Further retrospective studies have indicated limited utility of vaginal cytology in detection of endometrial cancer recurrence at the vaginal vault, in comparison to clinical assessment of symptoms and performance of a physical examination, which detect most recurrences (2011, 2017).[20, 56] Elevated levels of CA-125 did not consistently indicate disease recurrence (two studies) and high rates of false positives were reported (two studies) in the four retrospective studies in the CCO systematic review.[6] A more recent retrospective study reported that elevated CA-125 levels at diagnosis were associated with endometrial cancer recurrence in patients with uterine papillary serous carcinoma, which is a high-risk histology (2013).[57] However elevated CA-125 levels may also be secondary to other conditions.[20]

Low detection rates of endometrial cancer in asymptomatic patients have been reported for imaging methods such as chest X-rays, CT scans, positron emission test (PET)/CT scans and pelvic ultrasounds.[20, 24]

Based on available retrospective evidence and on expert consensus opinion, the risk-stratified guidelines from CCO (2017)[6], the SGO (2017)[20] and Cancer Australia (2020)[26] recommend that follow-up visits for women with low-risk endometrial cancer include:

- a thorough clinical history with review of symptoms
- physical examination including pelvic examination and if feasible, vaginal speculum
- educating women about the symptoms and signs of recurrence of endometrial cancer and encouraging them to report any symptoms to their healthcare team without delay.

The CCO, SGO and Cancer Australia recommend that vaginal cytology and imaging (such as chest X-ray, abdominal ultrasound or CT scan) are not used routinely in asymptomatic women and are undertaken only if recurrence is suspected.[6, 20, 26] The CCO and SGO guidelines do not recommend routine use of CA-125, based on insufficient evidence.[6, 20]

## Key points: Follow-up care for endometrial cancer

- As most endometrial cancer recurrences occur within three years of treatment, follow-up of endometrial cancer is generally undertaken for up to five years after treatment with more frequent visits in the first two to three years.[2, 6, 20, 25]
- There is currently a lack of evidence from randomised controlled trials on the frequency and duration of follow-up visits for endometrial cancer. Recommended schedules are based on the evidence on endometrial cancer recurrence from retrospective studies and on expert consensus.[6, 20, 25]
- Guidelines recommend a reduced frequency of follow-up visits for women with low-risk endometrial cancer compared to higher-risk patients.[6, 20, 26]
- Guidelines recommend that follow-up visits for women with low-risk endometrial cancer include a thorough clinical history with review of symptoms and a physical examination including pelvic examination and if feasible, vaginal speculum examination, based on retrospective evidence indicating that most recurrences are symptomatic or detected by physical examination.[6, 20, 26, 27]
- Other tests such as vaginal cytology and imaging (such as abdominal ultrasound or CT scan) should only be undertaken for women with low-risk endometrial cancer if symptoms or findings from a physical examination suggest a recurrence.[6, 20, 26]



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# 5 Models of follow-up care

## 5.1 Trials of different models of follow-up care for endometrial cancer

Table 1 Summary of trials reporting on different models of follow-up for endometrial cancer

| Author (study name) | Follow-up model | Study design | Participants | Main findings |
|---|---|---|---|---|
| Rio and McNally 2017[28]<br><br>Australia | GP-based follow-up | Non-randomised, single centre study | FIGO stages IA or IB, Grades 1 and 2 endometrial cancer n=73 | ▸ 73 of 81 eligible women participated and all their GPs agreed<br>▸ Most women found the GP consultation useful<br>▸ All GPs reported being confident in providing follow-up care<br>▸ Model implemented as standard care at the Melbourne hospital |
| Beaver et al 2017[29]<br>Dixon et al 2018[58]<br>(ENDCAT trial)<br><br>England | Nurse-led telephone follow-up vs. hospital outpatient follow-up | Randomised controlled trial, multicentre | Stage I endometrial cancer<br>n=259<br>(129 telephone; 130 hospital-based) | ▸ No significant differences in psychological morbidity or satisfaction with the information provided<br>▸ No significant differences in patient satisfaction with service and quality of life<br>▸ No difference in total health services costs to the National Health Service per patient at six or 12 months |
| Smits at al 2015[30]<br><br>England | Nurse-led telephone follow-up vs. hospital-based care | Comparative cohort, single centre | Endometrial cancer<br>n=296 | ▸ No significant differences in quality of life outcomes, or in patient satisfaction<br>▸ 98% women in telephone-led follow-up stated that they would like to continue in this telephone follow-up |
| Morrison et al. 2018[59]<br>(TOPCAT-G trial<br><br>Wales | Nurse-led telephone follow-up vs. hospital-based follow up | Feasibility study, multicentre | Cervical, endometrial, epithelial ovarian, or vulval cancer n=24 (12 hospital-based; 12 telephone based) | ▸ All outcome measure completion rates exceeded 96%<br>▸ Analyses of outcome measures indicated positive changes in quality of life and well-being<br>▸ Exploratory cost consequence analysis indicated that the nurse-led intervention had a mean total service use cost lower than the standard care group |
| Jeppesen et al 2018[31]<br><br>Denmark | Patient-initiated follow-up vs. hospital-based outpatient follow-up | Randomised trial | FIGO stages IA or IB, Grades 1 and 2 endometrial cancer<br>n=156<br>(79 patient-initiated; 77 hospital-based) | ▸ Fear of cancer recurrence decreased more in the hospital-based group than in the patient-initiated group<br>▸ Patient-initiated group had fewer examinations at the hospital department and reduced healthcare use than the control group |
| Kumarakulasingam et al 2019[32]<br><br>England | Patient-initiated follow-up | Non-comparative prospective study | Early stage endometrial cancer<br>n=228 | ▸ Follow-up contacts made by women were for physical symptoms and for psychological support<br>▸ Quality of life was higher than cancer patient reference ranges after 6 and 12 months<br>▸ Approximately 60% patient satisfaction with patient-initiated follow-up |



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Follow-up care for women after endometrial cancer has traditionally been provided by a specialist clinician such as a gynaecological oncologist in a hospital-based setting.[24] Different models for follow-up of endometrial cancer are being developed and investigated, including shared follow-up care with GPs, specialist nurse-led follow-up and patient-initiated follow-up. Studies on different models of follow-up for endometrial cancer that have been reported (Table 1) include a non-randomised study of GP-based care[28], two studies on nurse-led telephone follow-up (one randomised trial and one comparative cohort)[29, 30] and two studies on patient-initiated follow-up (one randomised trial and one prospective non-comparative cohort study).[31, 32]

A GP-based model of follow-up after treatment for early endometrial cancer (FIGO stages IA or IB, Grades 1 and 2) has been reported in a non-randomised Australian study from the Royal Women's Hospital in Melbourne (2017).[28] Women with early endometrial cancer who had a regular GP were eligible and 73 of the eligible 81 women and all the GPs involved in their care (n=72) agreed to participate.[28] Patients attended a consultation with a hospital nurse where a structured care plan was developed with follow-up information provided, including possible side effects of treatment, symptoms of recurrence, psychosocial and supportive care needs and suggested lifestyle changes.[28] Care plans were sent to the GP and the women instructed to see their GP in approximately one month. Questionnaires sent to women and their GPs one month after the nurse consultation indicated that most patients found the appointments with the nurse and with the GP useful or very useful, and the majority of GPs found the care plans useful.[28] All GPs indicated they were confident in providing follow-up cancer care, with 91% reporting that the care plan and hospital processes improved their confidence.[28] Comparison to a pre-model cohort (n=20 women) indicated higher rates of communication with GPs, more referrals and a projected decrease in hospital doctor appointments.[28] The study reported that the model has been implemented as standard care at the hospital.[28] Limitations of the study included the survey response rate of only about 50% from patients and GPs, the short time frame of the survey assessment (one month after the nurse consultation) and lack of longer-term assessment of adherence to the care plan and of patient outcomes.

A randomised controlled trial in England, the ENDCAT trial, compared nurse-led telephone follow-up for endometrial cancer to standard hospital outpatient follow-up in stage 1 endometrial cancer patients (2017).[29] Women were randomised during follow-up (median 12 months after diagnosis) to continued hospital-based follow-up (n=130), or to the telephone intervention (n=129) delivered by a gynaecological oncology nurse specialist, at intervals consistent with the usual hospital-based follow-up.[29] There were no significant differences between the telephone and hospital follow-up in the primary outcomes of psychological morbidity or satisfaction with the information provided, or in the outcomes of patient satisfaction with service and quality of life.[29] There were 10 recurrences which were all symptomatic and were all interval events reported by patients between scheduled appointments.[29] In cost-consequence analysis, there was no difference in total health services costs to the National Health Service per patient at six months or at 12 months, however patient travel and productivity costs were lower in the telephone follow-up group.[58]

A comparative cohort study in England compared nurse-led telephone follow-up (n=118) to conventional hospital-based care (n=178) (2015).[30] Women with endometrial cancer were given the option to participate in nurse-led follow-up, at times varying from initial follow-up visit to >5 years after diagnosis.[30] A questionnaire indicated no significant differences in quality of life outcomes, or in patient satisfaction between women in the nurse-led group (n=78 responses) and the conventional follow-up group (n=112 responses).[30]

A feasibility study in Wales (TOPCAT-G) randomised 24 women after gynaecological cancer (71% (17/22) with endometrial cancer) to specialist nurse-led telephone follow-up or to standard hospital-based follow-up (2018).[59] The study reported that eligibility, recruitment and retention rates, and outcome measure completion indicated the intervention was feasible[59] Further trials of nurse-led follow-up for gynaecological cancer patients that are underway include the NEMO study[44] in Denmark and the LETSGO study[43] in Norway (refer to section 5.5).

Patient-initiated follow-up has been compared with hospital-based outpatient follow-up of women with early stage endometrial cancer in a pragmatic randomised trial in Denmark (2018).[31] Women in the patient-initiated group (n=79) were given careful instruction by a gynaecological oncologist in symptoms of recurrence and on options for self-referral with open access, but no regular appointments were made; whereas women in the hospital-based group (n=77) attended regular outpatient visits for three years.[31] The primary endpoint of fear of cancer recurrence decreased more in the hospital-based group than in the patient-initiated group (difference -5.9, 95%CI: -10.9 to -0.9), although bias due to lack of blinding may have contributed.[31] Women in the patient-initiated group had fewer examinations at the hospital department than the control group, and reduced healthcare use.[31]

A prospective non-comparative study in England of patient-initiated follow-up included 228 women with early stage endometrial cancer (2019).[32] At the end of treatment, a clinical nurse specialist provided women with written information including symptoms and signs that should prompt a medical review, and contact information; and telephone calls were scheduled at six and 12 months to check the patient was happy to continue.[32] The median time in patient-initiated follow-up for the study was 14 months and in this time 20% (45/228) of women contacted the nurse at least once.[32] Women who made contact were younger than those who did not (57 years vs 65 years, $p<0.001$).[32] The primary reason for contact was vaginal bleeding or discharge (42%) and the next most common reason was that women wanted psychological support or reassurance.[32] Questionnaires at six and 12 months indicated quality of life higher than cancer patient reference ranges, and patient satisfaction of approximately 60% with patient-initiated follow-up.[32] A strong theme from semi-structured interviews (n=21) was that women understood their risk of recurrence was low and they did not want to keep being reminded of their diagnosis by attending hospital-based follow-up.[32]

In summary:

- A small non-randomised Australian study at a single centre reported that a GP-based model of follow-up care for early endometrial cancer is feasible and acceptable to patients and their GPs.[28]
- Two studies from England (one randomised trial and one comparative cohort) indicated that nurse-led telephone follow-up was non-inferior to standard hospital-based follow-up for psychological morbidity, quality of life and patient satisfaction outcomes.[29, 30]
- A randomised trial in Denmark reported patient-initiated follow-up was inferior to hospital-based follow-up for the outcome of fear of cancer recurrence.[31]
- A non-comparative study in England reported satisfaction with patient-initiated follow-up by the majority of women and indicated that while many contacts made by women were related to physical symptoms, many were for psychological support and reassurance.[32]
- None of these reported studies of follow-up models have investigated outcomes such as recurrence or survival and were not powered with sufficiently large numbers of participants to detect changes in these outcomes.

## 5.2 GP-based follow-up care for other cancers

A number of randomised trials have compared GP-based models of follow-up care to hospital-based, specialist follow-up care for early breast cancer and for colon cancer. A Cochrane review of follow-up strategies for women treated with early breast cancer[60] included two randomised controlled trials of GP-based follow-up compared to hospital-based specialist care in England (1996)[34] and in Canada (2006).[33] There were no significant differences between the groups in overall survival (HR 1.07, 95%CI: 0.64-1.78, one study, 968 participants, moderate-quality evidence), time to detection of recurrence (HR 1.06, 95%CI: 0.76-1.47, two studies, 1264 participants, moderate-quality evidence), and quality of life (one study, 356 participants, high-quality evidence).[60] Patient satisfaction was higher among patients treated by GPs.[60]

An Australian randomised controlled trial of follow-up of colon cancer patients compared GP-based (n=76) to specialist-based follow-up by surgeons (n=81) (2006).[35] There were no significant differences between the groups for the primary outcomes of quality of life, depression, anxiety or patient satisfaction.[35] The study was not powered to detect differences in rates of recurrence or survival, but the data did not suggest any trends.[35]

The evidence from these randomised trials in patients with early breast cancer and colon cancer therefore indicates that outcomes such as patient satisfaction, quality of life and recurrence are similar for GP-based models of care compared to hospital-based specialist care.[33-35] In these three randomised controlled trials (1996 – 2006), the interventions of GP-based follow-up were not explicitly described as 'shared follow-up care'. In all three trials, patient's GPs were provided with guidelines on recommended follow-up schedules, however there was variation between the trials in the availability of additional information or resources, and of any arrangement for rapid referral back to specialists.[33-35]

## 5.3 Shared follow-up care and its potential benefits

Shared follow-up care has been defined generally as 'the joint participation of primary and specialist health teams in the planned delivery of patient care'.[61] Shared care may be informed by enhanced information exchange between primary care and specialist teams, over and above routine discharge and referral notices.[61] It has been suggested that shared follow-up care has the potential to improve patient management compared to primary or specialty care alone.[61]

In a shared follow-up care model for cancer, depending on the risk of recurrence, follow-up after active treatment may be transferred back to the patient's GP who assumes responsibility for ensuring that the physical and emotional needs of patients are met.[62] The GP refers patients back to the specialist team for any recurrence or other specific problems and consults in areas of uncertainty.[62] Information may be provided in a shared care plan and there can be ongoing communication between the primary care physician and specialist team.[62]

The American Society of Clinical Oncology (ASCO) Statement on achieving high-quality cancer survivorship care (2013) notes that, ideally, a shared-care model using a risk-stratified approach can take advantage of the expertise of the cancer team and the primary care team in coordinating survivor follow-up.[36] The ASCO Statement (2013) includes the following recommendations for models of cancer survivorship care.[36]

- Promote successful models of survivorship care and tools that optimise the transition process between oncology and primary care providers.

- Promote a shared-care model for survivorship care that includes communication between the oncology specialist and primary care provider and successful transition of the patient from the oncology setting to primary care setting post treatment, using a risk-stratified approach as part of the survivorship care plan.
- Partner with other organisations to support demonstration programs to test models of coordinated, interdisciplinary survivorship care in diverse communities and across systems of care.

A retrospective study from the USA of cancer survivors using the SEER database (cancer diagnosis in 2004) reported positive associations between care provided by primary care providers and quality indicators for co-morbid conditions, indicating the central role of primary care providers in care quality of co-morbid conditions (2015).[63]

In the Australian setting, a national demonstration project by Cancer Australia of shared follow-up care for early breast cancer reported that nearly 80% of patients agreed to participate, suggesting that shared care was an acceptable model of care (2014).[64] In the Cancer Australia demonstration project, the majority of specialists (68%, n=26) and GPs (68%, n=36) surveyed reported confidence in delivering shared follow-up care (2019).[8] Cancer Australia's evaluation project of shared follow-up care for early breast cancer reported adherence to best practice for follow-up schedules and tests by patients and GPs in the shared model of care, and higher documentation of clinician checks for psychosocial issues, review of family history, menopausal status and other health conditions for GP visits compared to specialist visits.[8] Economic evaluation indicated that shared follow-up care for early breast cancer was more cost-effective than specialist-led follow-up care.[8]

Potential benefits of shared follow-up care identified from Cancer Australia's evaluation project of shared follow-up care for early breast cancer (2019)[8], from the ASCO *Statement on achieving high-quality cancer survivorship care* (2013)[36] and from learnings reported on models of follow-up care for cancer in Victoria that included engagement with GPs (2015)[37] include: improved access to holistic and patient-centred care, including management of co-morbidities and patients' supportive care needs; increased capacity for specialist teams to manage and support high-risk patients; strengthened care coordination between specialist and primary care teams, and improved access to follow-up care closer to home and to community-based services for patients.

## 5.4 Barriers and enablers to shared follow-up care

Barriers and enablers to shared follow-up care have been indicated by studies on endometrial cancer follow-up in Australia and USA, although these studies have involved only small numbers of participants.[28, 38] An Australian study (2017) of a GP-based model of follow-up care for early endometrial cancer incorporated enablers identified from high-quality models of survivorship care and from studies of follow-up for various cancers, into the model.[28] An observational study (2017) in a rural population in the USA (focus groups including 53 patients and 16 primary care providers) on views of shared follow-up care for endometrial cancer, identified barriers and enablers.[38] The *Optimal care pathway for women with endometrial cancer* (2016) also provides relevant guidance on follow-up.[2]

In the settings of shared follow-up care for early breast cancer and for cancer generally, barriers and enablers of shared follow-up care have also been reported in additional Australian studies including: Cancer Australia's demonstration and evaluation projects on shared follow-up care for early breast cancer (2019),[8] reported learnings on models of follow-up care for cancer that included engagement with GPs in Victoria (2015),[37] and views of cancer survivors and clinicians on shared care from a forum in South Australia (2017).[39]

Barriers for shared follow-up care identified from these studies in endometrial cancer and other cancers include:

- the need for effective communication and engagement between specialist care and primary care teams, and engagement with community-based organisations.[8, 28, 38, 39]
- limited confidence, information and training to deliver shared care among some GPs.[8, 38, 39] Patients may have perceptions of deficits in knowledge of cancer surveillance by primary care providers and not all patients are confident in their GP's ability to deliver follow-up care.[38 8, 39]
- issues with survivorship care plans, such as the time to develop and complete forms and available IT support.[37]
- lack of valid assessment and prediction tools, including tools for risk stratification and assessment of supportive care needs.[37]

Enablers for shared follow-up care identified from these studies in endometrial cancer and other cancers include:

- strong clinical leadership to promote buy-in from clinical teams, with a multidisciplinary approach.[8, 28, 37]
- partnerships with consumers, primary care and community organisations, including continued engagement with GPs by specialists.[8, 28, 37]
- education and training for primary care providers, building GPs' skills and confidence.[8, 37-39]
- patients being at the centre of follow-up and having active involvement, ensuring accurate communication, ownership, and access to their medical records, and shared decision making, and established relationships between patients and GPs.[8, 39]
- coordination of a patient's care (by a specialist nurse, nurse coordinator or administrative staff) and ongoing coordination between acute, rehabilitative and community-based care.[8, 37, 39]
- IT systems to support communication between specialist and primary care teams, including shared electronic health records.[37, 39]
- providing a treatment summary to the woman and her GP that includes details of her diagnosis and tumour characteristics, treatments and interventions from other health professionals and supportive care services.[2]
- use of shared care plans to help ensure care coordination between specialist and primary care teams.[28, 38] An agreed care plan should include required medical follow-up (surveillance for cancer spread, recurrence or secondary cancers, and screening and assessment for medical and psychosocial effects), and plans from other health professionals to manage consequences of cancer and treatment.[2]
- early provision of information to patients and early preparation for survivorship and shared follow-up care. Early information about expected care after treatment can provide patients with the time needed to prepare for follow-up care and can strengthen their receptivity to shared follow-up care.[8, 37]
- workforce education and training, including reorientating health professionals from traditional disease-focused follow-up, to delivering wellness-focused survivorship care.[37]
- multidisciplinary stratification of patients and agreed risk-stratified pathways to guide the different levels of intensity and settings for follow-up care based on recurrence risk.[28, 37]
- availability of rapid access to specialist consultation.[8, 28, 37]
- availability of high-quality supporting resources, including clinical practice guidelines.[8]

Cancer Australia has developed *Principles of shared follow-up and survivorship care for low-risk endometrial cancer* (Refer Appendix C) (2020) to guide shared follow-up and survivorship care by multidisciplinary teams:

1. Person-centred care
2. Care is delivered according to best practice
3. Co-ordination of care
4. Support for living well
5. Support for primary care providers
6. Support for specialist treatment team
7. Care is informed and improved by data.

## 5.5 Ongoing trials of follow-up care for endometrial and gynaecological cancer

Table 2 Summary of ongoing trials on different models of follow-up for endometrial and gynaecological cancer

| Study name *NCT number | Description | Study design | Participants | Outcomes |
|---|---|---|---|---|
| TEACUP[41]<br>NCT01610375<br>Australia | Telephone interview using symptom checklist before follow-up visit | Non-randomised, single arm study | Endometrial cancer | ▸ Sensitivity, specificity and overall accuracy of the telephone follow-up compared to clinic-based follow-up<br>▸ Patient satisfaction |
| ENSURE[40, 65]<br>NCT02413606<br>The Netherlands | Standard vs. less frequent hospital-based follow-up schedule | Randomised controlled trial<br>Multicentre | Stage I endometrial cancer | ▸ Primary: Patient satisfaction with follow-up care and cost-effectiveness<br>▸ Secondary: health care use, adherence to schedule, health-related quality of life, fear of recurrence, anxiety and depression, information provision, recurrence, survival |
| TOTEM[42]<br>NCT00916708<br>Italy | Comparison of 'minimalist' vs. 'intensive' follow-up schedules and tests, within low- and high-risk groups | Randomised controlled trial (4 arms)<br>Multicentre | Endometrial cancer, stratified into low-risk and high-risk groups | ▸ Primary: Overall survival<br>▸ Secondary: Progression-free survival, proportion of complications, second cancers, co-morbidity, proportion of asymptomatic patients with diagnosis of relapse, proportion of subjects who complete the two different regimes follow up |
| NEMO[44]<br>NCT03838861<br>Denmark | Nurse-led follow-up vs standard follow-up in doctors setting | Randomised trial | Endometrial cancer<br>and cervical cancer | ▸ Primary: Patient Empowerment using the Health Education Impact Questionnaire<br>▸ Secondary: Quality of life, fear cancer recurrence, patient empowerment |
| LETSGO[43]<br>NCT03453788<br>Norway | Nurse-led follow-up with a mobile App | Pilot study<br>Prospective cohort study with reference group | Gynaecological cancer | ▸ Primary: Satisfaction with LETSGO app<br>▸ Secondary: Recruitment rate, acceptability of goal setting |

*NCT number: a unique identification code given to each clinical study record registered on ClinicalTrials.gov.

## Trials that include telephone follow-up for endometrial cancer

**TEACUP** (NCT01610375): Telephone follow-up after treatment for endometrial cancer.

TEACUP is a non-randomised observational study in Queensland in which endometrial cancer patients (in first to third year after treatment) are interviewed via telephone by the researchers using a checklist of symptoms and signs of recurrence, 2-5 days prior to attending routine hospital clinic follow-up visits.[41] The checklist was developed based on symptoms of recurrence reported in the literature.[12] In the telephone interview, patients are also asked about their wellbeing, and resources on physical activity, quality of life, diet, anxiety and depression and supportive care, are provided when needed prior to each clinic visit. Recruitment was completed by 2019.[41]

Further trials of nurse-led follow-up for gynaecological cancer patients that are underway include the NEMO study [44] in Denmark and the LETSGO study [43] in Norway (refer Table 2).

## Trials comparing intensities of follow-up schedules for endometrial cancer

**ENSURE** (NCT02413606): ENdometrial Cancer SURvivors' Follow-up carE (ENSURE): Less is More? Randomised Controlled Trial to Evaluate Patient Satisfaction and Cost-effectiveness of a Reduced Follow-up Schedule.

ENSURE is a randomised controlled trial in the Netherlands comparing a less frequent hospital-based follow-up schedule for women with stage I endometrial cancer to the standard hospital-based follow-up schedule (according to the Dutch guidelines), with a 5-year follow-up.[40, 65] Patients (n=282) are randomised to an intervention group with four follow-up visits during three years, or to a control group with 10-13 follow-up visits during five years.[40, 65] Primary outcomes are patient satisfaction with follow-up care and cost-effectiveness between groups. The estimated study completion date is 2023.[40, 65]

**TOTEM** (NCT00916708): Multicentre Randomised Controlled Clinical Trial Between Two Follow up Regimens With Different Tests Intensity in Endometrial Cancer Treated Patients.

TOTEM is a randomised controlled trial in Italy comparing a more intense schedule of follow-up visits and tests to a less intense 'minimalist' schedule of visits and tests, in women following endometrial cancer, with five years of follow-up visits.[42] Patients are stratified into low or high risk of recurrence groups, and within each group are randomised to an 'intensive' or 'minimalist' follow-up schedule.[42] The intensive schedules involve more frequent follow-up visits and more tests at each visit, compared to the minimalist schedules.[42] The primary outcome is overall survival, and secondary outcomes include progression-free survival, asymptomatic recurrence and complications/co-morbidities. The estimated study completion date is December 2020.[42]

## Key points: Models of follow-up care for endometrial cancer including shared follow-up care

- Studies of follow-up care models for endometrial cancer have indicated that a GP-based model can be feasible and acceptable to women and their GPs (one small non-randomised Australian study)[28] and that nurse-led follow-up is non-inferior to standard hospital-based follow-up care (one randomised trial and one comparative cohort study).[29, 30] A randomised trial reported that patient-initiated follow-up for women with early stage endometrial cancer was inferior to hospital-based follow-up for the outcome of fear of cancer recurrence [31] and a non-comparative cohort study of women with early stage endometrial cancer reported satisfaction with patient-initiated follow-up by the majority of women.[32] These trials did not investigate the impact of these models of care on recurrence rates or survival outcomes.

- Randomised trials of GP-based models of follow-up care for early breast cancer and colon cancer have indicated similar patient satisfaction, quality of life and recurrence outcomes compared to hospital-based specialist care.[33-35]
- Shared follow-up care between specialist and primary care teams has potential benefits such as improved access to follow-up care and to person-centred holistic care, including management of co-morbidities and supportive care needs, and strengthened care coordination.[8, 36, 37]
- Enablers of shared follow-up care include strong clinical leadership and partnerships between GPs and cancer specialists, a multidisciplinary approach, use of shared care plans and treatment summaries for GPs and patients, education and training for GPs, availability of rapid access to specialist consultation and high-quality supporting resources.[2, 28, 37-39]
- Ongoing trials of endometrial cancer follow-up are investigating telephone follow-up care, different intensities of follow-up visits, and surveillance tests.[40-44]

# 6 Conclusion

Cancer Australia's Shared *follow-up and survivorship care model for women with low-risk endometrial cancer* is supported by evidence from retrospective studies that endometrial cancer recurrence rates are low (1% - 3% for women considered low-risk), that most endometrial cancer recurrences are detected within the first three years after treatment and that the majority of recurrences are symptomatic. Definitions of low-risk endometrial cancer vary, but commonly include FIGO stage IA or IB endometrial cancers that are histological grade 1 or grade 2. The evidence on recurrence provides support for a risk-stratified approach to follow-up for women with endometrial cancer with less frequent visits and less intensive surveillance tests for women at lower risk. Based on the evidence on endometrial cancer recurrences, follow-up of endometrial cancer is generally undertaken for up to five years after treatment with more frequent visits in the first two to three years. Recommended schedules for the frequency and duration of follow-up for endometrial cancer visits are based on the evidence on the recurrence of endometrial cancer and on expert consensus. While there are ongoing trials, there is currently a lack of evidence from randomised controlled trials on the optimal frequency and duration of follow-up visits for endometrial cancer.

Shared follow-up care with the joint participation of primary and specialist health teams can address the purpose of follow-up and survivorship care for endometrial cancer. Co-morbidities such as cardiovascular disease and their underlying risk factors should be identified and managed in follow-up, since cardiovascular disease is a greater cause of death than endometrial cancer for women treated for localised or low grade endometrial cancer. There is evidence from observational studies that women with endometrial cancer can have supportive care needs and information needs that should be addressed in follow-up care. Shared follow-up care can help improve access to person-centred holistic care, improve management of co-morbidities and supportive care needs, and strengthen care coordination.

A shared care model for follow-up of women with low-risk endometrial cancer is supported by evidence from randomised trials in early breast cancer and colon cancer for similar patient satisfaction, quality of life and recurrence outcomes for GP-based follow-up care, compared to hospital-based specialist follow-up care. Cancer Australia's *Shared follow-up and survivorship care model for women with low-risk endometrial cancer* incorporates enablers of shared follow-up care identified from studies, including strong clinical leadership and partnerships between GPs and cancer specialists, a multidisciplinary approach, use of shared care plans, education and training for GPs, availability of rapid access to specialist consultation and high-quality supporting resources.



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# Appendix A
# International Federation of Gynecology and Obstetrics (FIGO) stages and histopathologic grades for endometrial cancer

## FIGO staging classification

International Federation of Gynecology and Obstetrics (FIGO) stage is determined by surgical staging.[23]

Cancer of the corpus uteri is usually referred to as endometrial cancer, which arises from the epithelial lining of the uterine cavity.

| FIGO Stage | Description |
|---|---|
| I[a] | Tumour confined to the corpus uteri |
| IA[a] | No or less than half myometrial invasion |
| IB[a] | Invasion equal to or more than half of the myometrium |
| II[a] | Tumour invades cervical stroma, but does not extend beyond the uterus[b] |
| III[a] | Local and/or regional spread of the tumour |
| IIIA[a] | Tumour invades the serosa of the corpus uteri and/or adnexae[c] |
| IIIB[a] | Vaginal involvement and/or parametrial involvement[c] |
| IIIC[a] | Metastases to pelvic and/or para-aortic lymph nodes[c] |
| IIIC1[a] | Positive pelvic nodes |
| IIIC2[a] | Positive para-aortic nodes with or without positive pelvic lymph nodes |
| IV[a] | Tumour invades bladder and/or bowel mucosa, and/or distant metastases |
| IVA[a] | Tumour invasion of bladder and/or bowel mucosa |
| IVB[a] | Distant metastasis, including intra-abdominal metastases and/or inguinal nodes |

[a] either G1, G2 or G3.
[b] Endocervical glandular involvement only should be considered as stage I and no longer as stage II.
[c] Positive cytology has to be reported separately without changing the stage.

## Histopathological grades (G)

The histopathologic grades of endometrial carcinomas are:[23]

1. GX: Grade cannot be assessed
2. G1: Well differentiated
3. G2: Moderately differentiated
4. G3: Poorly or undifferentiated

## Histopathological types

The histopathologic types of endometrial carcinomas are:[23]

1. Endometrioid carcinoma: adenocarcinoma; adenocarcinoma-variants (with squamous differentiation; secretory variant; villoglandular variant; and ciliated cell variant)
2. Mucinous adenocarcinoma
3. Serous adenocarcinoma
4. Clear-cell adenocarcinoma
5. Undifferentiated carcinoma
6. Neuroendocrine tumours
7. Mixed carcinoma (carcinoma composed of more than one type, with at least 10% of each component).


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# **Appendix B** Principles of Cancer Survivorship

**Cancer Australia's *Principles of Cancer Survivorship* are supported by intended outcomes and underpinned by elements to achieve personalised care, opportunities for self-management and an emphasis on recognising and incorporating patient experiences.[13] They incorporate a focus on the ongoing management, recovery, health and wellbeing during and after cancer treatment.[13]**

**Cancer Australia's Principles of cancer survivorship and their intended outcomes are:[13]**

## Principle 1. Consumer involvement in person-centred care

**People affected by cancer are enabled to be involved in shared decision-making and supported to self-manage according to their preferences.**

**Informed and engaged consumers lead to better health outcomes and improved safety.**

## Principle 2. Support for living well

**The supportive care needs* of people affected by cancer are assessed and they receive appropriate referrals to promote optimal health and quality of life outcomes.**

**People affected by cancer are supported to make informed lifestyle choices to promote wellness, manage treatment related side effects and co-morbidities, and reduce risk of second and recurrent cancers.**

## Principle 3. Evidence-based pathways

**People affected by cancer receive consistent, safe, high-quality evidence-based cancer care in line with Optimal Cancer Care Pathways, according to their individual circumstances and needs.**

## Principle 4. Co-ordinated and integrated care

**People affected by cancer receive holistic patient-centred care which is coordinated and integrated across treatment modalities, providers and health settings, including public and private sectors; and specialist, primary, community based and not-for-profit services.**

**Care is delivered in a logical, connected and timely manner for optimal continuity and to meet the individual needs of people affected by cancer.**

## Principle 5. Data-driven improvements and investment in research

**National collection and reporting of key cancer data, including consumer experience and outcome data, provides an indicator for high quality care, influences health service improvements and informs investment in research.**

**Published research in cancer survivorship enriches the evidence base and informs improvements to enhance the care and outcomes of people affected by cancer.**

* Includes physical, psychological, social (including educational, financial and occupational issues), cultural, information and spiritual needs.

# Appendix C
## Principles of shared follow-up and survivorship care for low-risk endometrial cancer

**Cancer Australia has developed *Principles of shared follow-up and survivorship care for low-risk endometrial cancer* (2020). Shared follow-up and survivorship care for low-risk endometrial cancer by multidisciplinary teams should be guided by the following principles:**

### 1. Person-centred care

**The woman is the focus for all care providers**

Care is respectful and responsive to the woman's needs, preferences, circumstances and values. The woman is supported to participate in shared decision making and self-management.

### 2. Care is delivered according to best practice

**Provision of care is in accordance with nationally-agreed standards and is outcome-focused**

Individual follow-up care includes identified pathways for timely access to specialist providers as required.

### 3. Coordination of care

**Care coordination is enhanced through timely and effective communication, and clarification of the roles and responsibilities of the care providers**

The collection and sharing of appropriate clinical data and information supports continuity of care integration across treatment providers and health settings.

### 4. Support for living well

**Women are supported to make positive lifestyle choices which promote health, reduce risk of disease and prevent distress**

The woman's supportive care needs (physical, psychological, social, cultural, informational and spiritual) are assessed with appropriate referrals and management to promote optimal health and quality of life.

### 5. Support for primary care providers

**The role of primary care in the delivery of safe and effective follow-up care is supported**

Primary care providers are supported in the delivery of shared follow-up and survivorship care through early involvement, and through the provision of education, resources, information for people affected by cancer and pathways for access to specialist advice.

### 6. Support for specialist treatment team

**The role of specialist care providers in the delivery of safe and effective follow-up care is supported**

Specialist care providers are supported in the delivery of shared follow-up care and survivorship care through the provision of resources, information for people affected by cancer and pathways for communication with primary care providers.

### 7. Care is informed and improved by data

**Improvements in shared care are data driven**

The collection and utilisation of key cancer data, including consumer experience and outcome data, supports the delivery of holistic patient care and continuous improvement in care.



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# Abbreviations

| | |
|---|---|
| **ASCO** | American Society of Clinical Oncology |
| **CA-125** | Cancer Antigen 125 |
| **CCO** | Cancer Care Ontario |
| **CT scan** | Computed Tomography scan |
| **ESMO-ESGO-ESTRO** | European Society for Medical Oncology - European Society of Gynaecological Oncology - European Society of Radiotherapy and Oncology |
| **FIGO** | International Federation of Gynecology and Obstetrics |
| **GP** | General practitioner |
| **NCCN** | National Comprehensive Cancer Network |
| **SEER** | Surveillance, Epidemiology and End Results |
| **SGO** | Society of Gynecologic Oncology |
| **TP53** | Tumour Protein 53 |



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