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## Evidence-based Series #4-9: Section 1

# Follow-up after Primary Therapy for Endometrial Cancer: A Clinical Practice Guideline

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### Question

What is the most appropriate strategy for the follow-up of patients with endometrial cancer who are clinically disease free after receiving potentially curative primary treatment? Specifically, do differences in follow-up intervals, diagnostic interventions, clinical setting, or specialty influence patient outcomes related to local or distant recurrence, survival, or quality of life?

### Target Population

Women without evidence of disease after primary potentially curative treatment for any stage of endometrial cancer comprise the target population. Of particular interest are outcomes from follow-up strategies reported for patients at a lower risk of recurrence (i.e., stage IA or IB, grade 1 or 2) and those at a higher risk of recurrence (i.e., stage IA or IB, grade 3, or stage IC or advanced stage).

### Recommendations

There is a lack of randomized controlled trial evidence related to the clinical questions. Based on the interpretation of evidence from retrospective studies and expert consensus opinion, the Gynecology Cancer Disease Site Group recommends the following:

- It is recommended that all patients receive counselling about the potential symptoms of recurrence of endometrial cancer, because the majority of recurrences in the identified studies were symptomatic.
  - Symptomatic signs of possible recurrence can include, but are not limited to, unexplained vaginal bleeding or discharge, detection of a mass, abdominal distension, persistent pain, especially in the abdomen or pelvic region, fatigue, diarrhea, nausea or vomiting, persistent cough, swelling, or weight loss.

- The most appropriate follow-up strategy is likely one based upon the risk of recurrence, with individual patient preferences for more or less follow-up taken into account.
  - For patients at a surgically or pathologically confirmed low risk of recurrence (i.e., stage IA or IB, grade 1 or 2): A general examination, including a complete history and a pelvic-rectal examination, conducted semi-annually or annually for the first three years and annually for the next two years.
  - For patients at high risk of recurrence (i.e., stage IA or IB, grade 3, or stage IC or advanced stage). A general examination, including a complete history and a pelvic-rectal examination, every three to six months for the first three years and semi-annually for the next two years.
- Since the majority of patients with recurrence were symptomatic and virtually all recurred within five years, it seems reasonable that patients return to annual population-based general physical and pelvic examination after five years of recurrence-free follow-up.
- There is insufficient evidence to inform the optimum clinical setting or type of specialist required for follow-up; however, it is recommended that all patients be followed by a health care professional who is knowledgeable about the natural history of the disease, and who is comfortable performing speculum and pelvic exams, in order to diagnose or detect a local (vaginal) recurrence.
  - If a patient is initially followed by a specialist, it seems reasonable that they be followed by a qualified general practitioner after three to five years of recurrence-free follow-up.
- It is recommended that all patients undergo a targeted investigation to rule out recurrence if symptomatic, since patients with local recurrence are potentially curable with further therapy.
- There is insufficient evidence to inform the routine use of Pap smear, chest x-ray, abdominal ultrasound, computed tomography (CT) scan or CA 125 testing to detect asymptomatic recurrences.
- Where treatment with radiotherapy is involved, it is recommended that patients be counselled on the potential adverse effects of radiotherapy. Adverse effects associated with radiotherapy can include complications with the rectum, urinary bladder, vagina, skin, subcutaneous tissue, bones, and other sites.

### **Key Evidence**

- Sixteen non-comparative retrospective studies provided the evidence basis for this report. Twelve studies evaluated follow-up programs, while four studies evaluated the role of the tumour-marker cancer antigen (CA) 125 in detecting disease recurrence.
- In 12 studies, overall (local and distant) recurrence rates ranged from 8% to 19%, with a weighted mean of 13% (95% confidence interval [CI]; 11%-14%). In four studies that categorized patients by risk of recurrence, recurrence rates ranged from 1% to 3% for low-risk patients and 5% to 16% for high-risk patients.
- In 12 studies, 41% to 100% of all recurrences were symptomatic, the weighted mean being 77% (95% CI; 74%-81%).
- In 9 studies, 68% to 100% of recurrences occurred within approximately three years of follow-up.
- The number of asymptomatic patients with recurrences detected by a routine follow-up test alone was not consistently reported; however, with the available data, as a percentage of total recurrences:
  - Seven studies reported 5% to 33% of recurrences were detected by physical examination,
  - Four studies reported 0% to 4% of recurrences were detected by Pap smear,
  - Six studies reported 0% to 14% of recurrences were detected by chest x-ray,

- Two studies reported 4% and 13% of recurrences were detected by abdominal ultrasound,
- Two studies reported 5% and 21% of recurrences were detected by CT scan, and
- One study reported 15% of recurrences in selected patients were detected by CA-125 level.

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