

Burton Hospitals
NHS Foundation Trust

Prognosis, Follow-up and Recurrence for Endometrial Cancer

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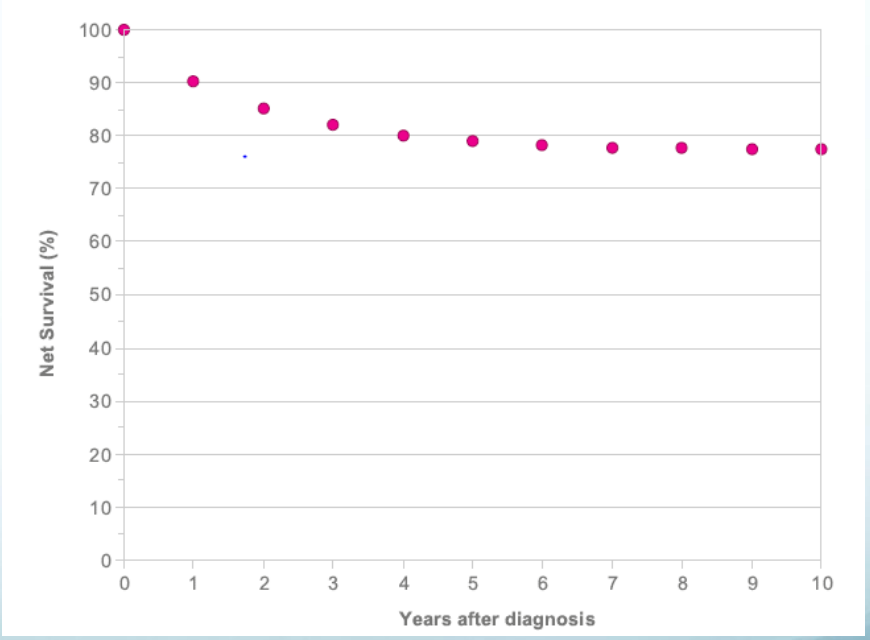
Prognosis

Prognosis

- Overall 5-year survival is 77% *

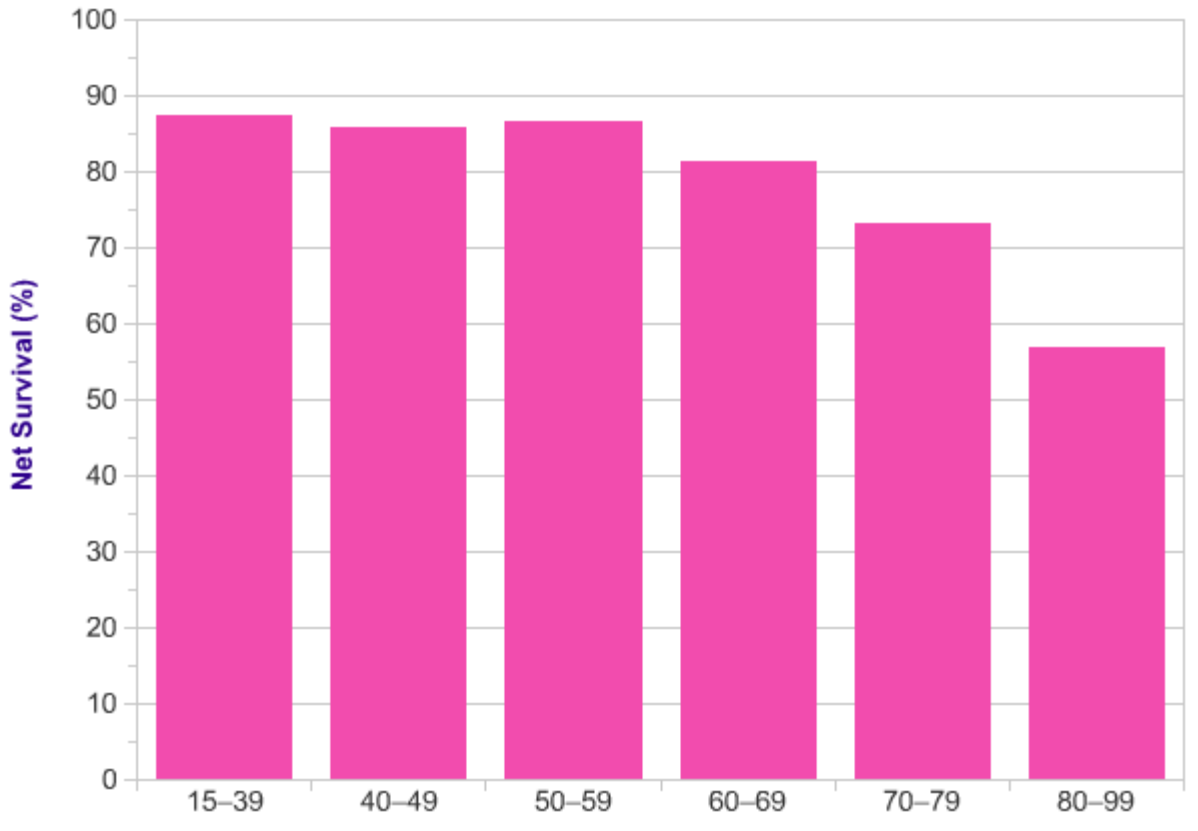
- This depends on:
  - Patient's Age
  - Staging
  - Histological Grading
  - Type of Tumour



* Office for National Statistics – Cancer Survival in England: Adults Diagnosed 2010-2014, followed up to 2015 and Adults Diagnosed 2011-2015, followed-up to 2016 (released 29/06/2017)

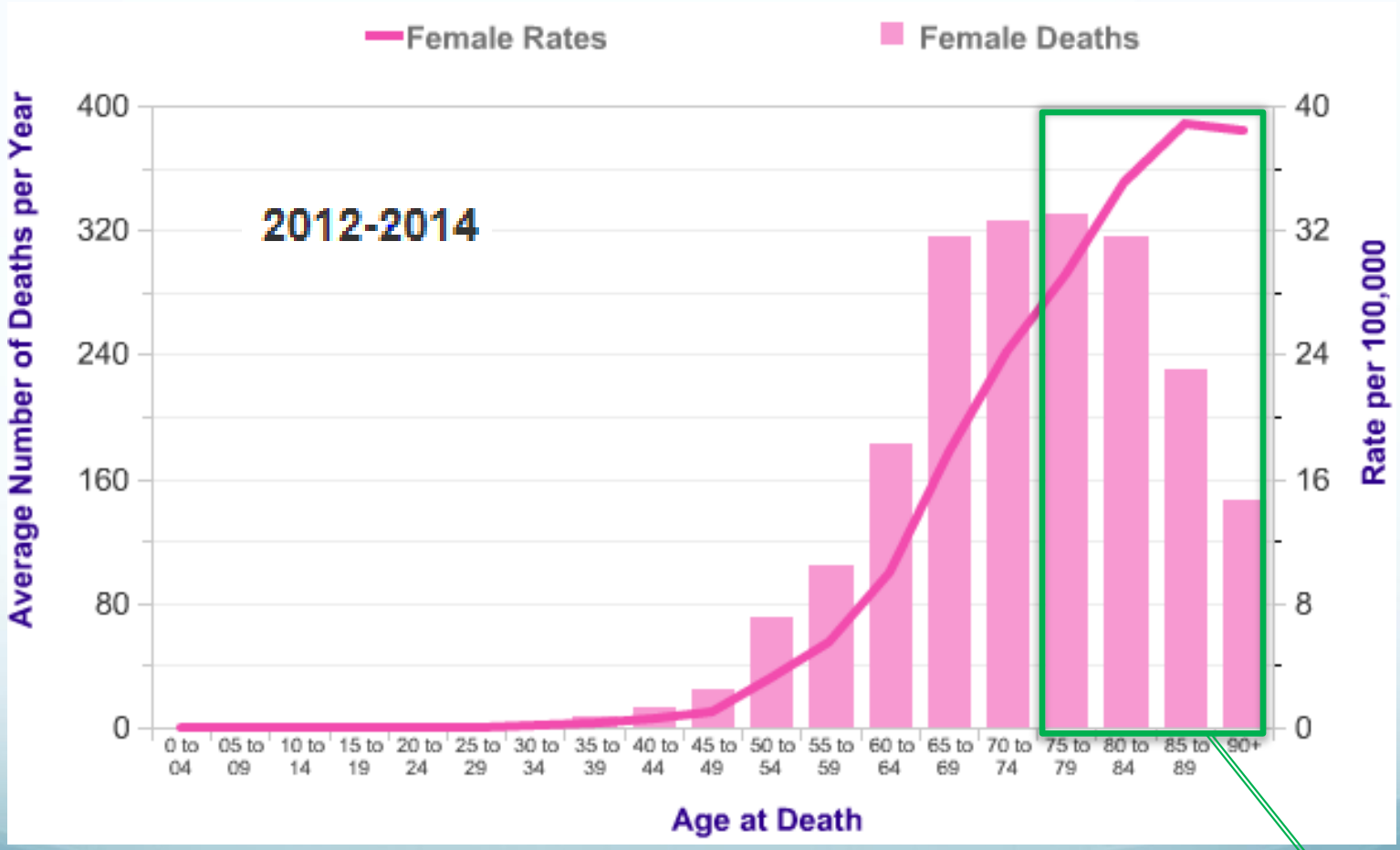
Prognosis based on Age

- **Five year survival by Age, England 2009-2013**



Cancer Research UK: data for 2009-2014

Mortality by Age

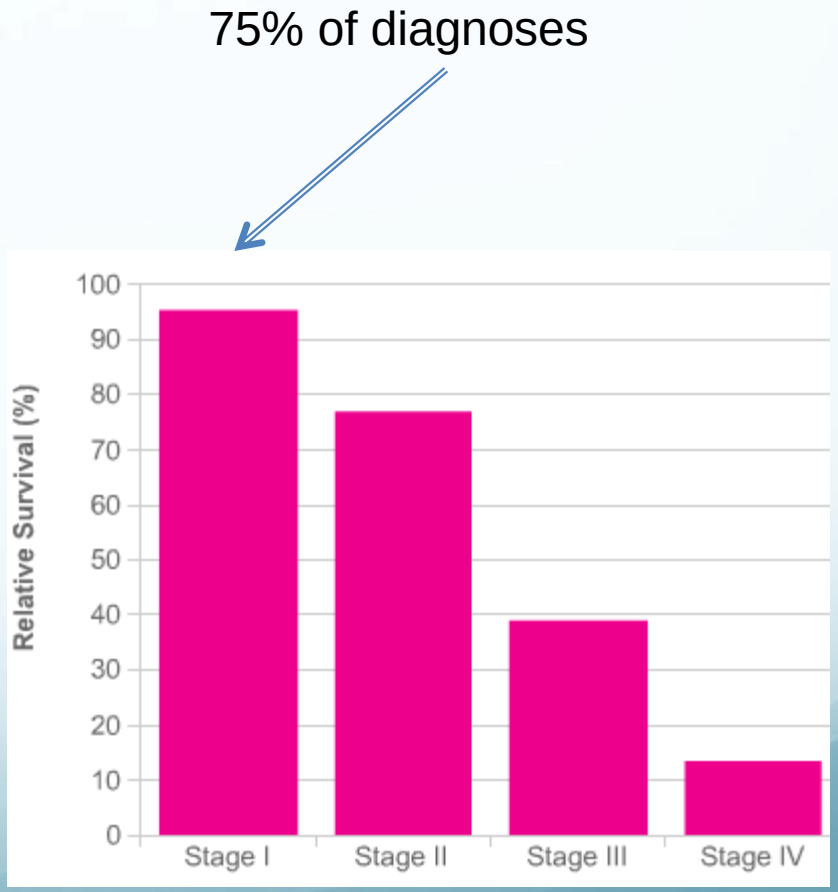


49% of patients ≥75 years

Cancer Research UK: data for 2012-2014

Prognosis based on Staging

FIGO Stage	5-year survival (%)
I	95
II	77
III	40
IV	15



Cancer Research UK: data for 2002-2006

Prognosis based on Grading

- Grade = degree of histologic differentiation

Grade	5-year survival (%)
1	94
2	84
3	72

In ♀ with stage I or occult stage II endometrioid adenocarcinoma

Levine DA, De los Santos J, Fleming G. Handbook for principles and practice of Gynaecologic Oncology, 2010; Lippincott Williams & Wilkins: USA.

Prognosis base on Type

Tumour Type	Incidence	Oestrogen Dependent	Prognosis
Endometrioid adenocarcinoma	77%	Yes	Good
Serous carcinoma	5%	No	Poor
Clear cell	1-2%	No	Poor
Mixed epithelial and mesenchymal	6%	No	Poor
Leiomyosarcoma	2%	Yes	Poor

National Cancer Intelligence Network (NCIN 2013): 2009 data

Follow-up

Follow-up

- **Aim**
  - To detect recurrence and improve patient survival chances
  - To assess morbidity due to treatment
    - eg. sexual dysfunction, psychological distress

Follow up

- As:
  - most patients with endometrial cancer do well
  - there is no clear evidence that early detection of disease recurrence improves outcomes

- **Debate**
  - frequency of follow-up visits
  - extent of surveillance tests
  - cost-effectiveness

Literature Review

Gynecologic Oncology 101 (2006) 520–529

Follow-up after primary therapy for endometrial cancer: A systematic review

Michael Fung-Kee-Fung [a,*], Jason Dodge [b], Laurie Elit [c], Himu Lukka [c], Alex Chambers [d], Tom Oliver [d]
On behalf of the Cancer Care Ontario Program in Evidence-based Care Gynecology Cancer Disease Site Group

[a] *Ottawa Regional Cancer Centre, Ontario, Canada*

2955 patients

Abstract

Objective. To determine the optimum follow-up of women who are clinically disease-free following potentially curative treatment for endometrial cancer.

Methods. A systematic search of MEDLINE, EMBASE and the Cochrane Library databases (1980 to October 2005) was conducted. Data were pooled across trials to determine overall estimates of recurrence patterns.

Results. Sixteen non-comparative retrospective studies were identified. The overall risk of recurrence was 13% for all patients and 3% or less for patients at low risk. Approximately 70% of all recurrences were symptomatic, and 68% to 100% of recurrences occurred within approximately the first 3 years of follow-up. No reliable differences in survival were detected between patients with symptomatic or asymptomatic recurrences nor were differences in patient outcomes reported by type of follow-up strategy employed. Detection of asymptomatic recurrences ranged from 5% to 33% of patients with physical examination, 0% to 4% with vaginal vault cytology, 0% to 14% with chest X-ray, 4% to 13% with abdominal ultrasound, 5% to 21% with abdominal/pelvic CT scan, and 15% in selected patients with CA 125.

Conclusions. There is limited evidence to inform whether intensive follow-up schedules with multiple routine diagnostic interventions result in survival benefits any more or less than non-intensive follow-up schedules without multiple routine diagnostic interventions. Routine testing seems to be of limited benefit for patients at low risk of disease. Most recurrences tend to occur in high risk patients within 3 years, and most recurrences involve symptoms. The most appropriate follow-up strategy is likely one based upon the risk of recurrence and the natural history of the disease. Counseling on the potential symptoms of recurrence is extremely important because the majority of patients with recurrences were symptomatic. A proposed routine follow-up schedule is offered.

Results – systematic review

Recurrences

- Overall 13%
- 70% symptomatic
- 61% involved distant metastasis – poor prognosis
- 68-100% occurred within 3 years

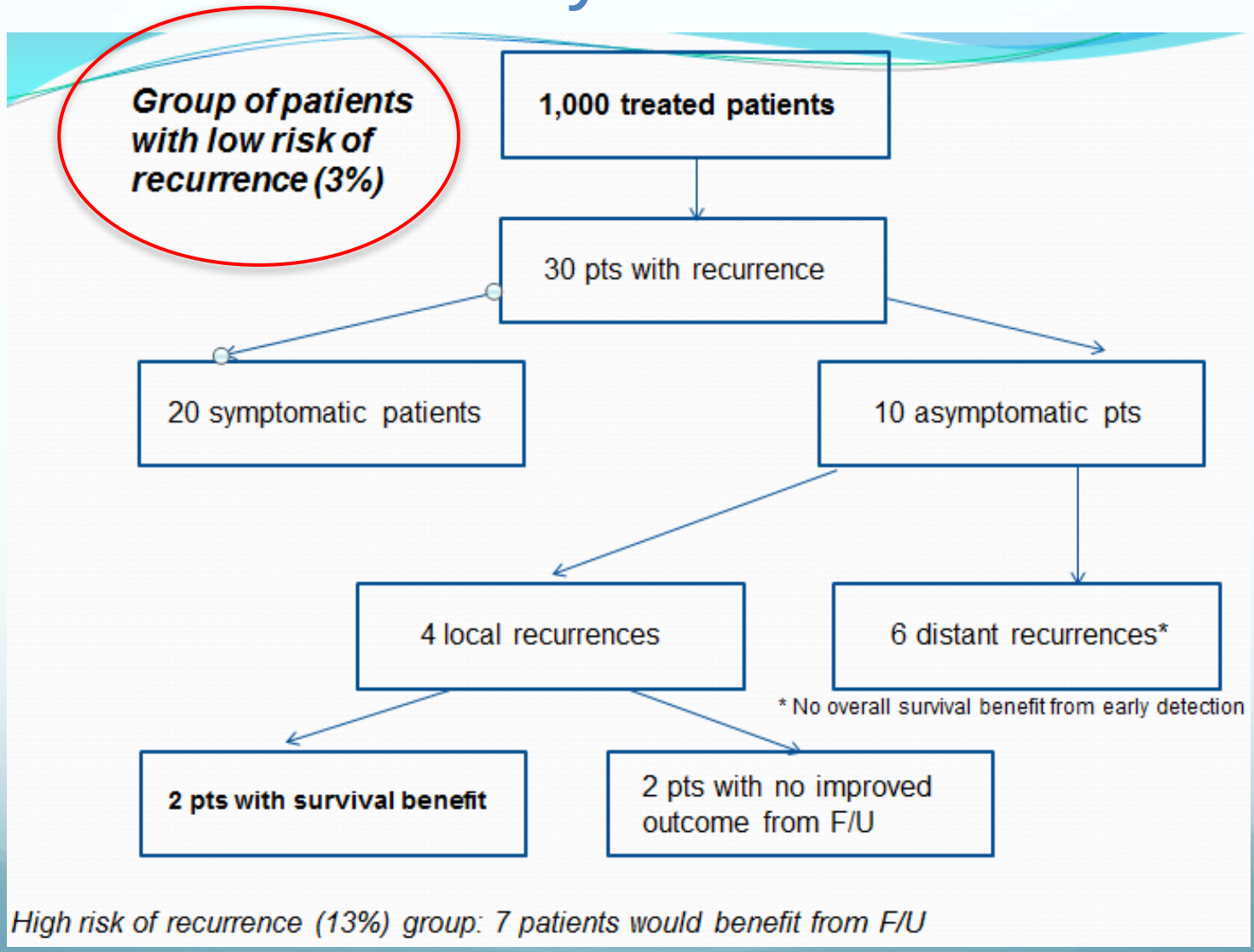
Detection of asymptomatic disease

- On physical examination: 5-33%

Survival rate

- Same between symptomatic and asymptomatic patients
- Same with different F/U strategies

Results – systematic review



Conclusions – systematic review

- Limited evidence for intensive F/U schedule
- Recurrences occurred mainly:
  - in high risk patients
  - within 3 years
  - involved symptoms
- Therefore F/U should be based on risk of recurrence
- Counselling on the potential symptoms of recurrence essential

Role of hospital follow-up - studies

Int J Gynecol **Cancer**. 2010 Nov;20(8):1307-20.

The value of gynecologic cancer follow-up: evidence-based ignorance?

Lajer H, Jensen MB, Kilsmark J, Albæk J, Svane D, Mirza MR, Geertsen PF, Reerman D, Hansen K, Milter MC, Mogensen O.

Department of Gynecology and Obstetrics, Copenhagen University Hospital Rigshospitalet, Copenhagen, Denmark. lajer@dadlnet.dk

Int J Gynecol Cancer. 2014 Mar;24(3):556-63. doi: 10.1097/IGC.0000000000000088.

Why routine clinical follow-up for patients with early stage endometrial cancer is not always necessary: a study on women in South Wales.

Aung L[1], Howells RE, Lim KC, Hudson E, Jones PW.

Cancer Nurs. 2015 May-Jun;38(3):232-8. doi: 10.1097/NCC.0000000000000177.

Nurse-Led Telephone Follow-up: Improving Options for Women With Endometrial Cancer.

Smits A[1], Lopes A, Das N, Bekkers R, Kent E, McCullough Z, Galaal K.

Role of hospital follow-up - studies

BJOG An International Journal of Obstetrics and Gynaecology

DOI: 10.1111/1471-0528.14000
www.bjog.org

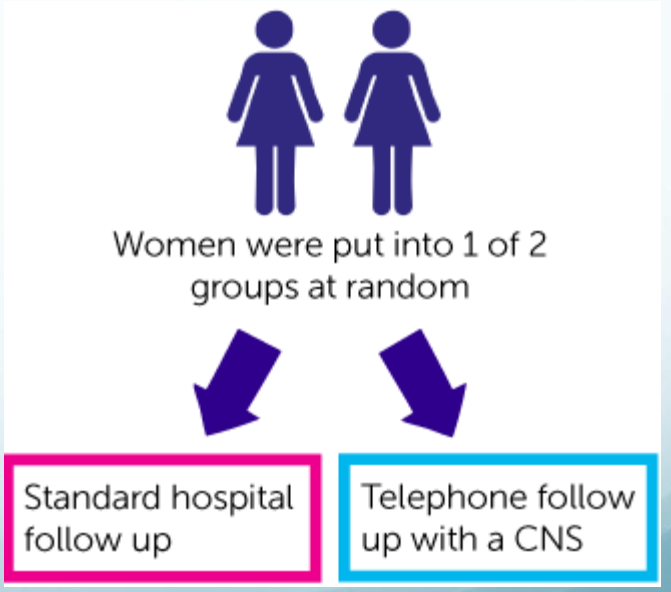
Gynaecological oncology

Comparing hospital and telephone follow-up for patients treated for stage–I endometrial cancer (ENDCAT trial): a randomised, multicentre, non-inferiority trial

K Beaver,[a] S Williamson,[a] C Sutton,[b] W Hollingworth,[c] A Gardner,[d] B Allton,[e] M Abdel-Aty,[f] K Blackwood,[g] S Burns,[g] D Curwen,[h] R Ghani,[e] P Keating,[i] S Murray,[i] A Tomlinson,[j] B Walker,[f] M Willett,[f] N Wood,[i] P Martin-Hirsch[i]

ENDCAT study

- Published in 2016
- Five hospitals in North West England
- Patients randomised:
  - Standard hospital follow-up
  - Telephone F/U with a CNS
  - 130 women in each group



ENDCAT study

- Five recurrences in both groups and similar time to diagnosis
- Patients found telephone F/U more convenient
- Quality of life and satisfaction scores were high in both groups
- Conclusion: telephone F/U by CNS is effective and can be used instead of hospital F/U in patients at low risk of recurrence

Prevention of recurrence

Cochrane Review 2012

Cochrane Library

Cochrane Database of Systematic Reviews

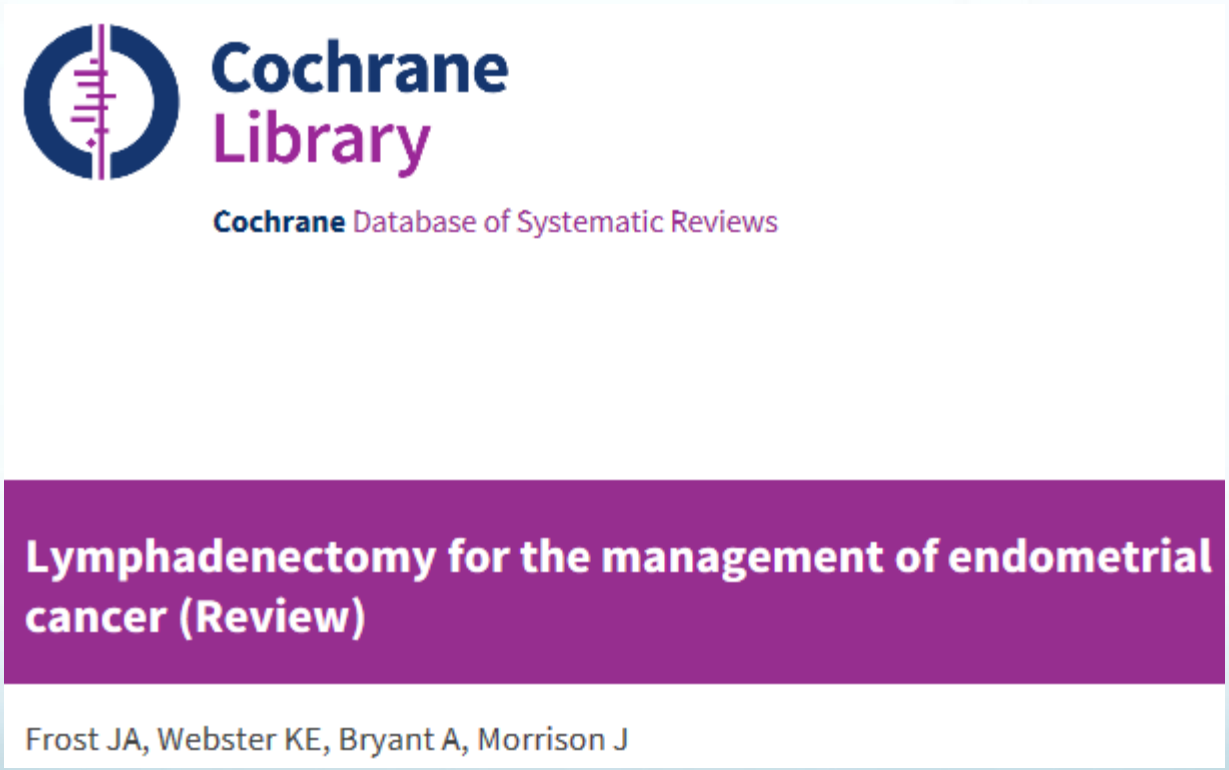
Laparoscopy versus laparotomy for the management of early stage endometrial cancer (Review)

Galaal K, Bryant A, Fisher AD, Al-Khaduri M, Kew F, Lopes AD

Laparoscopic Treatment

- All RCTs comparing laparoscopy *vs*. laparotomy for early stage endometrial cancer (up to Apr 2012)
- Eight trails (3644 women)
- Conclusions:
  - For early stage endometrial cancer, laparoscopy is associated with similar overall and disease-free survival
  - Laparoscopy is associated with reduced operative morbidity and hospital stay
  - No difference in severe post-op morbidity (death, blood transfusion, bladder/ureteric/bowel/vascular injury)

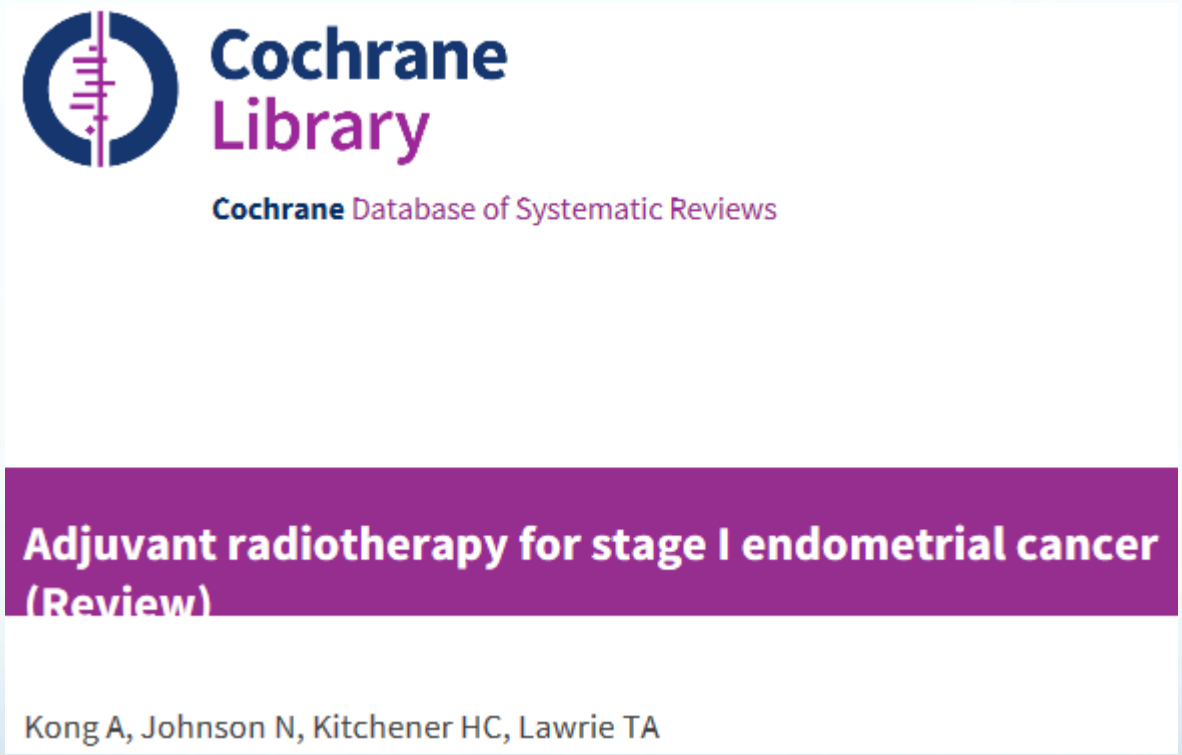
Cochrane Review 2017



Lymphadenectomy

- All RCT comparing lymphadenectomy *vs*. no lymphadenectomy in women diagnosed with endometrial cancer (up to March 2017)
- Two trails (1945 women)
- Conclusion:
  - No evidence that lymphadenectomy decreases the risk of death or disease recurrence in women with presumed stage I disease
  - Lymphadenectomy group had higher serious adverse events (surgically related morbidity and lymphoedema)

Cochrane Review 2012



Adjuvant Radiotherapy

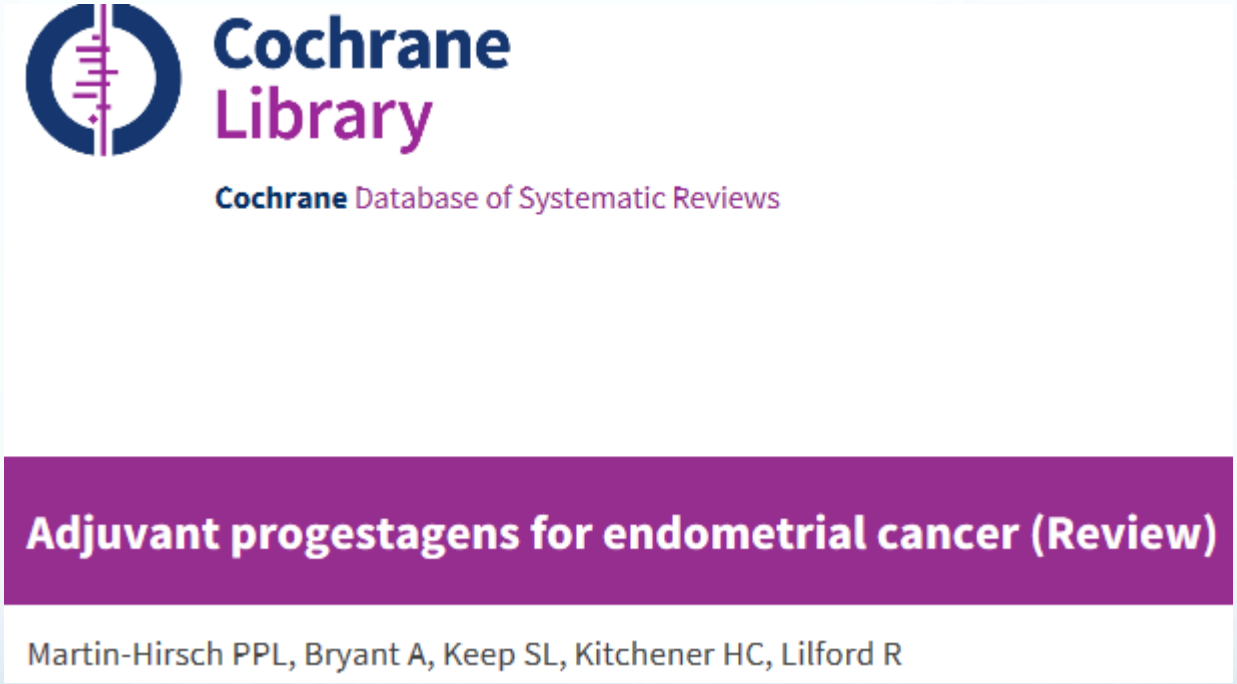
- All RCT comparing post-op adjuvant radiotherapy (both pelvic external beam radiotherapy and vaginal intracavity brachytherapy) *vs*. no radiotherapy (up to Jan 2012)
- Eight trails (3628 women) included
- Trials included:
  - ASTEC/EN5: EBRT vs. no radiotherapy
  - PORTEC-1
  - PORTEC-2
  - GOG 99
  - Aalders 1980, Soderini 2003, Sorbe 2009, Sorbe 2011

Adjuvant Radiotherapy

- Conclusions:
  - EBRT* reduces risk of loco-regional recurrence but has no impact on cancer-related deaths or overall survival
  - EBRT* is associated with significant morbidity (toxicity, rectal and bladder dysfunction) and reduction in quality of life
  - EBRT* may have an adverse effect on endometrial cancer survival in uncomplicated low-risk group
  - VBT** alone appears adequate in ensuring vaginal control for the intermediate-high risk group

* EBRT= external beam radiotherapy **VBT= vaginal brachytherapy

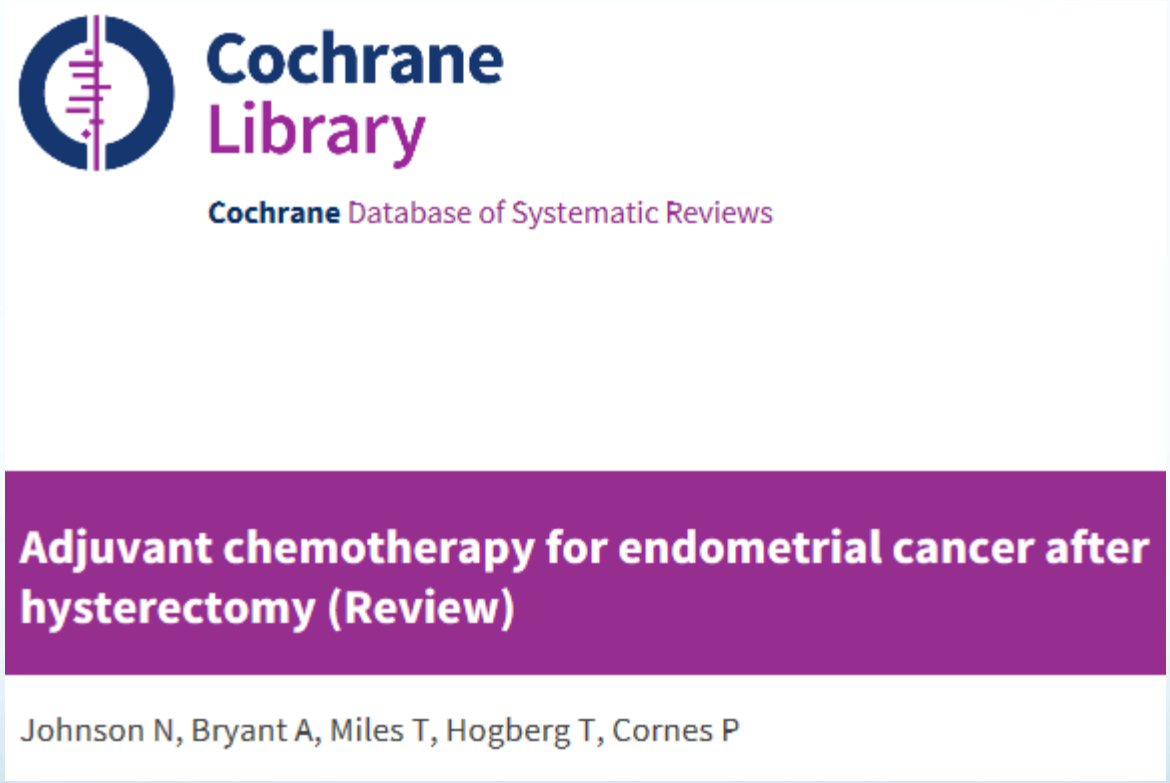
Cochrane Review 2011



Adjuvant Progestagens

- All RCT of progestagen therapy in women who have had surgery for endometrial cancer (up to April 2009)
- Seven trials (4556 women)
- Conclusion:
  - No evidence to support the use of adjuvant progestagen therapy following primary surgery to reduce the risk of recurrence

Cochrane Review 2011



Adjuvant Chemo

- All RCTs comparing adjuvant chemotherapy with any other adjuvant treatment or no other treatment (up to Aug 2010)
- Five trials (2197 women treated surgically with *curative intent*)
- Conclusion:
  - Post-op platinum-based chemotherapy offers a small benefit in progression-free survival and overall survival irrespective of radiotherapy
  - It reduces the risk of developing metastases

Cochrane Review 2014

Adjuvant Chemo

- All RCTs of adjuvant chemotherapy *vs*. radiotherapy or *vs*. chemo-radiation in women with FIGO stage III and IV endometrial cancer (up to Nov 2013)
- Four trials (1269 women)
- Conclusion:
  - Moderate evidence that chemotherapy increases survival time after primary surgery by 25% compared to radiotherapy in stage III and IV endometrial cancer
  - It may be associated with more adverse effects

Prevention of Recurrence

- **Offer advantages**
  - Laparoscopic treatment
  - Vaginal brachytherapy for intermediate-high risk groups only
  - Platinum-based chemotherapy for stage III and IV
- **No advantages**
  - Lymphadenectomy in early stage disease
  - External beam radiation of pelvis for stage I disease
- **No evidence**
  - Adjuvant progestagens

Recurrence

Recurrence

How they present

70 % symptomatic

vaginal bleeding and pelvic pain

O/E: mass at vaginal vault

When they occur

34% within 1 year

76% within 3 years

10% after 5 years

Berek J.S. Hacker N.F. Practical Gynaecologic Oncology, 2005; Lippincott Williams & Wilkins.

Recurrence

Where they occur

Local recurrence: 50%

Distant metastases: 29%

Simultaneous local and distant metastases: 21%

NB: these patients have an ↑ risk of developing cancer of the ovary, colon and breast

Berek J.S. Hacker N.F. Practical Gynaecologic Oncology, 2005; Lippincott Williams & Wilkins.

Recurrence - Investigation

To diagnose lesion & detect associated metastatic foci

- CXR
- CT
- MRI
- FNA cytologic testing of suspicious nodules
- Serum CA-125:
  - usually elevated in patients with intra-peritoneal recurrence

Berek J.S. Hacker N.F. Practical Gynaecologic Oncology, 2005; Lippincott Williams & Wilkins

Recurrence - Management

Isolated vaginal metastases:

- most amenable to therapy with curative intent
  [75% PORTEC trial]
  - Surgery: isolated lesions
    surgical debulking / exenteration
  - *Radiotherapy*:
    local recurrence if not previously irradiated

Berek J.S. Hacker N.F. Practical Gynaecologic Oncology, 2005; Lippincott Williams & Wilkins

Survival After Relapse

Survival after relapse

PRESS Gynecologic Oncology 89 (2003) 201–209 www.elsevier.com/locate/ygyno

Survival after relapse in patients with endometrial cancer: results from a randomized trial☆

Carien L. Creutzberg, M.D.,[a,*] Wim L.J. van Putten, M.Sc.,[b] Peter C. Koper, M.D.,[a] Marnix L.M. Lybeert, M.D.,[c] Jan J. Jobsen, M.D.,[d] Carla C. Wárlám-Rodenhuis, M.D.,[e] Karin A.J. De Winter, M.D.,[f] Ludy C.H.W. Lutgens, M.D.,[g] Alfons C.M. van den Bergh, M.D.,[h] Elzbieta van der Steen-Banasik, M.D.,[i] Henk Beerman, M.D.,[j] and Mat van Lent, M.D.,[k] for the PORTEC Study Group

[a] *Department of Radiation Oncology, Erasmus MC-Daniel den Hoed Cancer Center, Rotterdam, The Netherlands*

Relapse in patients with stage I endometrial cancer

Survival after relapse

- Survival after relapse was better in the patient group without previous radiotherapy treatment

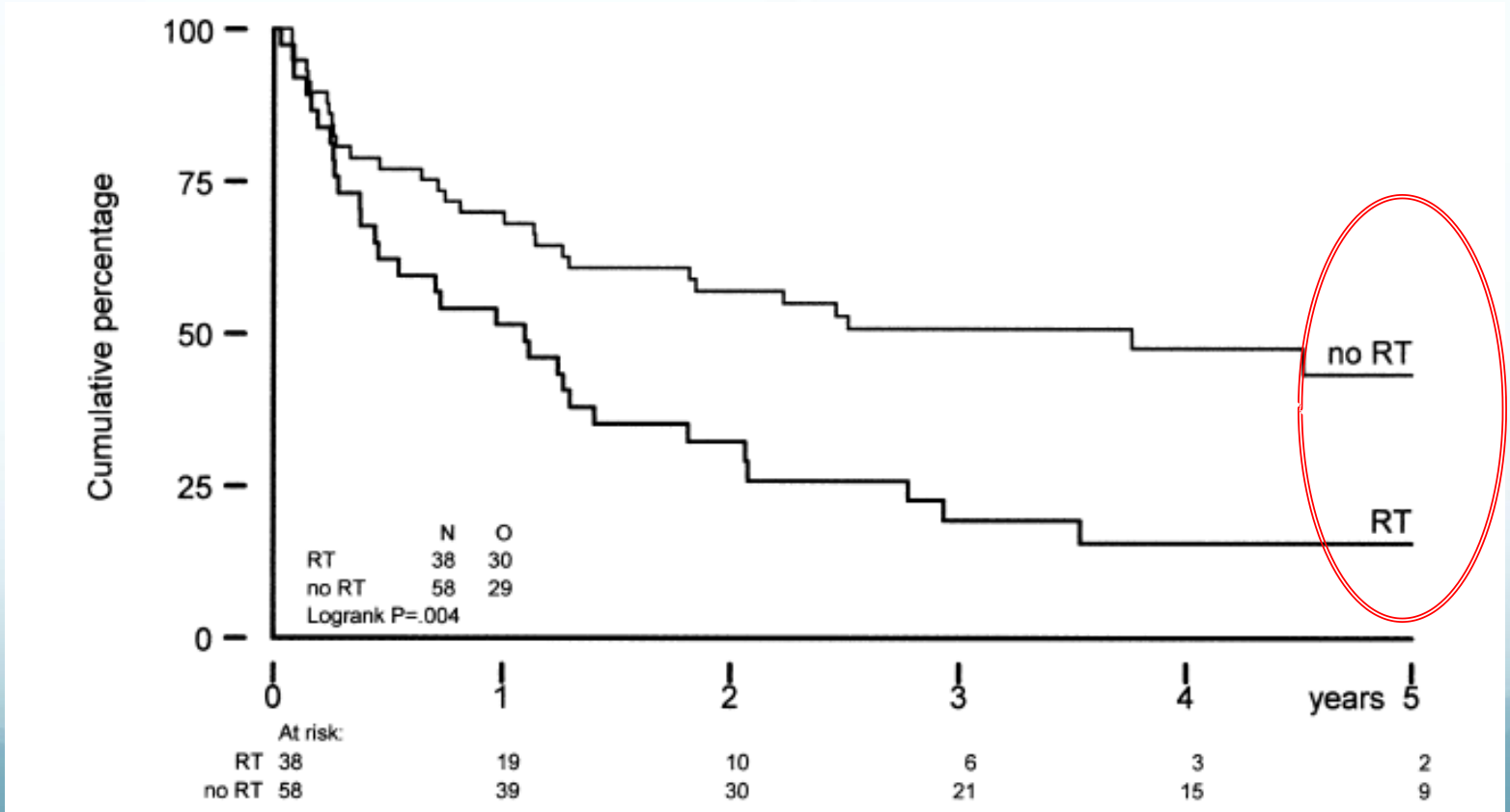


Fig. 1. Probability of survival after first relapse for patients assigned to postoperative radiotherapy (RT) or no further treatment (no RT).

Survival after relapse

- Treatment for vaginal relapse was effective (radiotherapy or surgery):
  - 89% complete remission
  - 65% 5-year survival
- No difference in survival in patients with pelvic relapse or distant metastases
  - Therefore pelvic radiotherapy improved local control but not survival

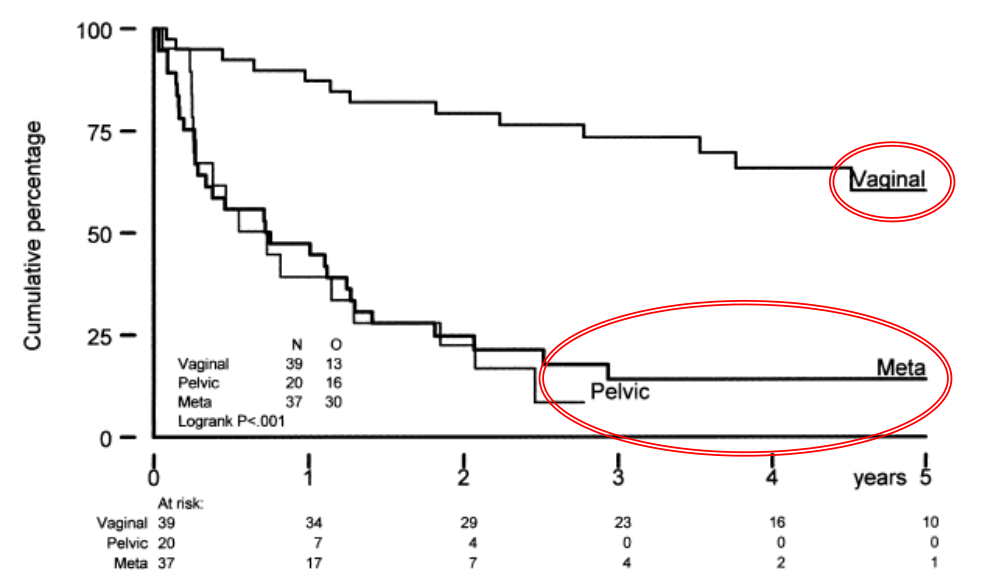


Fig. 2. Probability of survival after relapse by site of relapse: vaginal, pelvic, and distant relapse (both study groups combined).

Cochrane Review 2012

Chemotherapy

- All RCTs comparing chemotherapy *vs*. another intervention in advance disease (up to Jan 2012)
- Fourteen trails (1519 women)
- Conclusion:
  - More intense chemotherapy may improve overall survival and progression-free survival for women with advanced or recurrent endometrial cancer
  - The optimum regime is still to be found

Cochrane Review 2010

Hormonal Treatment

- All RCTs that studies hormonal therapy in adult women diagnosed with advanced or recurrent endometrial cancer (up to May2009)
- Six trials (542 women)
- Conclusion:
  - Insufficient evidence that hormonal treatment in any form, dose or part of combination therapy improves survival of patients with advanced or recurrent endometrial cancer

Conclusion

Conclusion

- Survival good
- Recurrence:
  - usually in first 3 years
  - symptomatic in 70% of cases
  - 50% at vaginal cuff = potentially curable
- Recurrence Treatment:
  - Radiotherapy = first line
  - Chemo = palliative

Conclusion

- F/U
  - Questions remain as to who should carry this out
    - ? Hospital, nurse, telephone, GP
  - Follow-up recommended for at least 2 years
  - Patients should be educated about possible symptoms of recurrence