**Patient-Initiated Follow-Up for Low-Risk Endometrial Cancer: An cost-analysis evaluation**

**Running title:** Economic evaluation of endometrial cancer follow-up

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**PRECIS:** Patient-initiated follow-up for low-risk endometrial cancer is associated with financial/time savings for both the patient and the health care economy compared to structured hospital follow-up.

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**KEY WORDS:** Endometrial cancer; follow-up; patient initiated; health economic analysis

**RESEARCH HIGHLIGHTS**

1)The number of follow-up appointments for low-risk endometrial cancer was reduced

with a patient-initiated follow-up

2) There was a 93.5% reduction in costs for hospital follow-up to patient-initiated followup.

3) The cost of follow-up for the patient is lower with patient-initiated compared to hospital follow-up

**ABSTRACT**

**Objective:** Risk stratification has resulted in patient-initiated follow-up being introduced for low-risk endometrial cancer in place of routine hospital follow-up. The financial benefit to the patient and the healthcare economy of patient-initiated follow-up, as compared to hospital follow-up, has yet to be explored. In this study, we explored the potential impact for both the healthcare economy and patients of patient-initiated follow up.

**Methods:** Women diagnosed with low-risk endometrial cancer enrolled on a patient-initiated follow-up scheme between November 2014 and September 2018 were included. Data on the number of telephone calls to the nurse specialists and clinic appointments attended were collected prospectively. The number of clinic appointments that would have taken place if the patient had continued on hospital follow-up, rather than starting on patient-initiated follow-up, was calculated and costs determined using standard NHS reference costs. The time/distance travelled by patients from their home address to the hospital clinic was calculated and used to determine patient-related costs.

**Results:** A total of 187 patients with a median of 37 months follow-up (range 2 to 62 months) after primary surgery were enrolled on the scheme. In total, the cohort were scheduled to attend 1,673 appointments with hospital follow-up, whereas they only attended 69 clinic appointments and made 106 telephone contacts with patient-initiated follow-up. There was a 93.5% reduction in costs from a projected £194,068.00 for hospital follow-up to £12,676.33 for patient-initiated follow-up. The mean patient-related costs were reduced by 95.6% with patient-initiated follow-up. The total mileage travelled by patients for hospital follow-up was 30,891.4 miles, which was associated with a mean travelling time per patient of 7.41 hours and clinic/waiting time of 7.5 hours compared to 1,165.8 miles and 0.46 hours and 0.5 hours; respectively for patient-initiated follow-up.

**Discussion:** The introduction of a patient self-management follow-up scheme for low-risk endometrial cancer was associated with financial/time saving to both the patient and the health care economy as compared to hospital follow-up.

**INTRODUCTION**

 The balance between clinical impact and cost effectiveness is under scrutiny in all aspects of healthcare in order to gain maximum cost benefit in financially finite systems. With growing cancer survivorship following successful treatment, attention is now turning on cancer follow-up, with the introduction of risk stratification with a view to variable follow-up schedules and models in order to reduce interventions that do not have a clinical impact.

 Low-risk endometrial cancer1 is a prime example of a malignancy with a typically excellent long-term survival, 10-year overall survival 94.1%, and a low risk of recurrence 6.0%2. The incidence of endometrial cancer has increased by over 50% in the UK in the past two decades3, with the rise attributed primarily to an increase in low-risk endometrial cancer4 and is reported to be as high as 56% of the total endometrial cancer population2. The value of routine scheduled hospital follow-up has long been called into question since studies have shown that overall survival when a recurrence is symptomatic at detection or asymptomatic is not significantly different5,6. The majority (up to 90%) of recurrences present with symptoms7, with an asymptomatic recurrence being identified in only 2.3% of the total population8. Furthermore, there is the concern that a proportion of patients who are symptomatic while on hospital follow-up, delay presentation until their next scheduled appointment rather than seeking an earlier appointment7.

 Various alternative follow-up schemes for low-risk endometrial cancer have been established with the aim of reducing the number of hospital follow-up appointments and their use is now supported by the British Gynaecological Cancer Society (BGCS)9. We have previously reported on the acceptability of a patient-initiated follow-up scheme in a multi-ethnic population10. In this study, we report the cost analysis of the first five years of the scheme and explore the potential impact for both the healthcare economy and patients should such a scheme be extended to the whole UK low-risk endometrial cancer population.

**METHODS**
 No ethical approval was required for this study however, approval was granted by the University Hospitals of Leicester Clinical Audit Team. A patient-initiated follow-up scheme was instigated at University Hospitals of Leicester in September 2014 for women with low-risk endometrial cancer (FIGO stage 1A grade 1 and 2 endometrioid endometrial carcinoma). It replaced a 5-year hospital follow-up scheme based on the European Society for Medical Oncology (ESMO) guidelines11 (Year 1: 3-monthly; Year 2: 4-monthly; Year 3: 6-monthly; Year 4: 6-monthly; Year 5: 12 monthly). All patient contacts with the gynaecological oncology team, telephone, emails, and/or clinic visits, were recorded prospectively and collated along with the patient demographics (age and ethnicity) and location of residence. During the first 18 months after the introduction of patient-initiated follow-up, women were mailed quality of life (EORTC QLQ-C30) and patient satisfaction questionnaires at 6 and 12 months following enrolment to assess the utility of the scheme10. Subsequent patients were sent a letter at 6 months and then 12 monthly from the Clinical Nurse Specialist reminding the patient of the symptoms that should prompt them to telephone and the contact details of the team. There was no other contact from the clinical team with the patients.

 The cost of a clinic appointment was £116/appointment (NHS Reference costs 2017/2018) and telephone calls or email contact was calculated as £43.67/telephone call, assuming 20 minutes duration and nurse time of £131/hour12. The return distance between the patients’ home address and the hospital clinic was calculated using an online mapping tool, along with estimated travelling time by car. The time for the appointment was calculated to be 20 minutes. The cost of patient travel by car was calculated at £0.45per mile13 plus £2.50 car parking charge. Patient time was calculated as £12.21/hour14.

 The time from the patient starting on the patient-initiated follow-up scheme was calculated and the number of appointments that would have been scheduled during that time period if the patient had been on hospital follow-up. Clinic visits or investigations arising as a result of a patient-initiated follow-up clinic appointment were not included since it was not possible to calculate the number of additional follow-up appointments that would have occurred with hospital follow-up should further investigations have been required, instead it was assumed that these would be the same for the two groups.

 In order to extrapolate the potential financial impact of extending a patient-initiated follow-up to the whole UK low-risk endometrial cancer population, the total number of endometrial cancer cases and the European age-standardised incidence rates per 100,000 females in 1996, 2006 and 2016 were used15. The projected 2026 female population was calculated to be 34,947,14516 and the incidence of endometrial cancer of 34.6/100,000 in 2026, assuming a further 5/100,000 rise incidence in keeping with the 5/100,000 increase per 10 years that has been reported in the UK over the past two decades15.

**RESULTS**

 In total 187 women with a new diagnosis of low-risk endometrial cancer were enrolled on patient-initiated follow-up between 2014 and 2018. The median follow-up from primary surgery was 37 months (range; 2 to 62). Median participant age was 61 years (range; 35 to 88), 150 participants were of White British ethnicity (80.2%), and 33 (17.6%) patients were of South Asian heritage. No UK address was available for one patient and therefore it was not possible to calculate time or distance travelled and so this case was excluded from the patient-related cost analysis.

 Twelve women were removed from the patient-initiated follow-up scheme during the follow-up period. Five patients were transferred back to hospital follow-up due to patient request (7, 9, 12, 25 and 39 months). There were three cases of endometrial cancer recurrence and all cases presented with symptoms (vaginal bleeding or abdominal pain); one patient had a vaginal vault recurrence at 30 months after primary surgery and was successfully treated with radiotherapy; the other two patients were diagnosed with distant metastases (2 months and 39 months after primary surgery) and died of their disease. Three patients died of a non-endometrial cancer related cause, another developed second primary malignancy and one patient transferred her care due to moving out of area. The mean travelling distance to the hospital was 18.4 miles (maximum 74 miles). There was no public transport option for two patients due to their rural location.

 The 187 patients who enrolled on the patient-initiated follow-up scheme would have been scheduled to attend 1,673 appointments with hospital follow-up, whereas only 53 patients attended for a total of 69 clinic appointments with patient-initiated follow-up. Forty women attended one appointment, ten attended two appointments and three women attended three appointments. The majority of patient-initiated follow-up appointments occurred in year 1 (58.0%), with 24.6% in year 2, 15.9% in year 3 and only one appointment in year 4. In addition to the patient-initiated follow-up clinic appointments, there were 106 telephone calls; 43 women had one telephone contact, 12 women had two contacts, and 10 women telephoned three times and two patients had phoned 4 and 5 times. This resulted in a 95.9% reduction in the number of appointments (clinic and telephone) with patient-initiated follow-up, giving a mean of 0.95 appointments per patient as compared to 9.0 appointments that would have been scheduled with hospital follow-up. Adding the cost of the clinic appointments and telephone calls resulted in a 93.5% reduction in costs from a projected £194,068.00 for hospital follow-up to £12,676.33 (£8,004.00 clinic appointments and £4,672.33 telephone calls) for patient-initiated follow-up. Considering all the patients with completed years of follow-up, excluding five patients who had less than 1 year follow-up, gave a cumulative cost of £1,357.34 per patient for 4 years of hospital follow-up versus £67.69 for patient-initiated follow-up over the same time period; thus equating to an annual cost of patient-initiated follow-up of £16.92 per patient (Figure 1).

 The mean patient-related costs were reduced by 95.6% with patient-initiated follow-up compared to hospital follow-up. (Table 2) The total mileage travelled by patients for hospital follow-up would have been 30,891.4 miles, which was associated with a mean travelling time per patient of 7.41 hours and a clinic/waiting time of 7.50 hours compared to 1,165.8 miles and 0.46 hours and 0.50 hours; respectively for patient-initiated follow-up.

 The cost of a 5-year hospital follow-up scheme (12 appointments) and patient-initiated follow-up scheme based on the costs determined in our cohort (£16.92/patient/year) were calculated for the whole UK endometrial cancer population. The cost of hospital follow-up rose from £5,568,000 in 1996 to £12,806,400 in 2016 and was projected to rise to £16,831,663 by 2026. Transfer of 20% of the endometrial cancer population from hospital follow-up to patient-initiated follow-up in 2016 would have resulted in a cost saving of £2,405,599, rising to £3,608,398 if 30% were transferred and £4,811,198 for 40:60 patient-initiated/hospital follow-up divide. Further cost savings of £3,161,718, £4,742,578 and £6,323,437 were calculated for 2026 for 20%, 30% and 40% patient-initiated follow-up respectively (Table 3).

**DISCUSSION**

 In this study we have shown that the number of clinic appointments needed by women under follow-up for low-risk endometrial cancer through a patient-initiated follow-up scheme is a fraction of those that would be scheduled to take place as part of a standard hospital follow-up. Patient-initiated follow-up schemes10,17 and nurse-led telephone follow-up18 for low-risk endometrial cancer appear to show no clinical detriment to the patients in the short-term, however long-term data (over 5 years) is lacking. The recurrence rate in our study population was 1.6%, in keeping with the rates reported in low-risk endometrial cancer of 2.2-3.6% for local recurrence and <1-1.4% for distant metastases2,19. There is an argument that the cost of a delay in diagnosis of recurrence should be added to cost of patient-initiated follow-up; however, delays in diagnosis that occur due to patients under routine follow-up not expediting routine appointments should they become symptomatic must also be considered. Since the majority of patients are symptomatic at recurrence (90%) and the proportion of asymptomatic recurrences is less than 3%7,8 there should be greater emphasis on educating all women as to the potential signs/symptoms of recurrence and performing investigations in a timely manner when they are reported.

 The importance of psychological support19 in the survivorship phase must be remembered since fear of cancer recurrence with patient-initiated follow-up is reportedly higher as compared to hospital follow-up17. We have previously shown that a proportion of the patient contacts are not related to symptoms but due to other issues, for example help with applying for benefits or psychological support, and do not require a clinic appointment with a gynaecological oncologist to resolve10. There is growing support for a reduced duration of follow-up in low-risk endometrial cancer to 3 years, as compared to the 5 years advised in the ESMO guidelines11. Although many studies report that the majority of endometrial cancer recurrences occur within the first 3 years, categorising cases by risk shows that the peak incidence of low-risk endometrial cancer relapse appears to be later, 4-6 years after diagnosis as compared to 1-3 years with intermediate and high-risk endometrial cancer2. This has led to calls to extend, as opposed to reduce, the period of follow-up for low-risk endometrial cancer. The low recurrence rate in the low-risk endometrial cancer population however, would mean that extending hospital follow-up would incur increasing costs with very few recurrences detected. Circulating tumour DNA (ctDNA) to monitor endometrial cancer activity appears to have very high sensitivity to identify recurrent disease, detected in 8 out of 8 (100%) recurrences, and with a lead-time compared to radiology of up to 10 months and up to 18 months compared to patient symptoms21. Should the sensitivity of circulating tumour DNA be confirmed in larger populations it could be combined with patient-initiated follow-up in order to develop a remote monitoring scheme, since the additional cost of circulating tumour DNA analysis would be offset by the cost savings from reducing the number of hospital clinic appointments.

 The economic benefit of follow-up for gynaecological cancers, in particular endometrial cancer, has long been raised as an issue20-22. Nurse-led telephone follow-up compared to hospital follow-up (ENDCAT study) showed no difference in cost to the NHS23, whereas we have shown large potential cost savings with patient-initiated follow-up. Several clinical trials are ongoing in Europe evaluating the role of patient-initiated follow-up (OPAL: NCT01853865) and reduced hospital follow-up schedules (ENSURE: NCT0241360624) but have yet to report on the cost outcomes. A successful patient-initiated follow-up scheme does still require resources, initially to support and train the clinical nurse specialists in developing the skills to manage this patient cohort and subsequently flexibility in the nurses’ timetable to be able to speak to patients when they contact. In addition, there needs to be availability for ad hoc clinic appointments at short notice, in order to respond to patient issues in a timely manner. Patients also need to be educated in the signs/symptoms that should prompt referral and consideration needs to be given as to the requirements of minority populations that are at risk of isolation, for example non-English speakers.

 In this study we have demonstrated large cost savings for the patient with patient-initiated follow-up as compared to hospital follow-up. The cost of cancer care to the patient is an issue that is often forgotten by the clinician since these expenses are hidden; however, the financial burden can create significant distress. Nearly 40% of the endometrial cancer population are under the UK retirement age at diagnosis (67 years)15 and therefore many women are likely to return to paid employment following their diagnosis, necessitating them to take time away from work in order to attend hospital follow-up. In addition, women may take a supporting relative or friend to a hospital follow-up appointment, again resulting time away from work, which would also have a cost implication. It is therefore likely that the patient-related costs we have attributed in our study are only a fraction of those actually incurred.

 The proportion of UK endometrial cancer cases that fall within the low-risk endometrial cancer category is estimated to be between 20 and 40%, although it has been reported that low-risk endometrial cancer cases are responsible for the steady rise in incidence4. Despite support for less intensive follow-up, the establishment of such schemes is sporadic25,26 and depends on the willingness of local gynaecological cancer centres and commissioners to instigate changes.

The calculated travelling times and distances were limited to travel by car and it was not possible to calculate public transport costs. It was also not possible to determine the true cost to the patient since we were not able to capture the real-world duration and waiting times of the appointments or account for the time of any accompanying relative/friend. The record of appointments/telephones calls for patients on patient-initiated follow-up was kept prospectively and contemporaneously; however, there is always the potential that a patient contact was not recorded.

 We have demonstrated a large reduction in the number of clinic appointments with patient-initiated as compared to hospital follow-up for low-risk endometrial cancer. This was associated with large cost savings for both the patient and the health care economy. Patients appear to be managed well by having open access to clinical nurse specialist support who are able to triage queries, organise appointments or signpost to other specialities as indicated.

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**AUTHOR CONTRIBUTION**

EM, LB and NP conceived the idea for the study. IQ, PK and R W-J performed the data collection. NC performed the analysis. EM wrote the manuscript and all the authors approved the final version.

**Table 1.** Table of unit costs

|  |  |  |  |
| --- | --- | --- | --- |
|  | Cost year 2017 | Cost year of source | Year of source |
| Average earnings/hour (time cost of working person) (£/hour)14  | £12.21 | £12.21 | 2017 |
| Car/mile (£/mile)13 | £0.45 | £0.45 | 2017 |
| Car parking charge (£/visit) | £2.50 | £2.50 | 2017 |
| Telephone call – length in minutes (hours)12 | 0.33 | 0.33 |  |
| Clinic visit (£/appointment)12 | £116.00 | £116.00 | 2018 |
| Clinic appointment time (hours) | 0.33 | 0.33 |  |
| Clinic visit waiting time (hours) | 0.5 | 0.5 |  |

**Table 2.** Patient related costs of hospital follow-up and patient-initiated follow up (n=187)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Patient-related resource use and costs** | **HOSPITAL FOLLOW-UP** | **PATIENT-INITIATED FOLLOW-UP** | **HOSPITAL FOLLOW-UP-PATIENT-INITIATED FOLLOW-UP** | **Percentage difference** |
| Total miles travelled by patients (car) | 30,891.40 | 1165.8 | -29,725.6 | -96.23% |
| *Mean miles travelled per patient (car)* | 166.08 | 0.58 | -165.51 |  |
| Total costs of travel (car + parking) | £18,083.63 | £524.61 | -£17,559.02 | -97.10% |
| Total travel time (hours) by patients (car) | 1377.00 | 51.97 | -1325.40 | -96.23 % |
| *Mean travel time (hours) per patient (car)* | 7.41 | 0.46 | -6.94 |  |
| Total costs of time travelling (car) | £16,810.85 | £634.26 | -£16,176.60 | -96.23% |
| Total time in or waiting for appointments (hours)  | 1394.17 | 93.17 | -1301.00 | -93.32% |
| *Mean time in or waiting for appointments (hours)* | 7.50 | 0.50 | -6.99 |  |
| Total costs of time in appointments or waiting | £17,015.90 | £1137.11 | -£15878.79 | -93.32% |
| Total patient-related costs (travel and time) | £51,910.38 | £2,295.97 | -£49,614.41 | -95.58% |
| ***Mean patient-related costs per patient*** | *£279.09* | *£12.34* | *-£266.74* |  |

**Table 3.** Cost of follow-up for the UK endometrial cancer population. Hospital follow-up 12 appointments. Patient-initiated follow-up calculated based on appointment costs £16.92 per patient per year (from our cohort data)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **1996** | **2006** | **2016** | **2026** |
| Number of new cases | 4000 | 6600 | 9200 | 12092 |
| **5 year follow-up** |  |  |  |  |
| Total appointment costs |  |  |  |  |
| 100% Hospital follow-up | £5,568,000 | £9,187,200 | £12,806,400 | £16,831,663 |
| 100% Patient-initiated follow-up | £338,437 | £558,421 | £778,405 | £1,023,071 |
|  |  |  |  |  |
| 80% Hospital follow-up | £4,454,400 | £7,349,760 | £10,245,120 | £13,465,331 |
| 20% Patient-initiated follow-up | £67,687 | £111,684 | £155,681 | £204,614 |
| Total appointment costs 80:20 follow-up | £4,522,087 | £7,461,44 | £10,400,801 | £13,669,945 |
|  |  |  |  |  |
| 70% Hospital follow-up | £3,897,600 | £6,431,040 | £8,964,480 | £11,782,164 |
| 30% Patient-initiated follow-up | £101,531 | £167,526 | £233,522 | £306,921 |
| Total appointment costs 70:30 follow-up | £3,999,131 | £6,598,566 | £9,198,002 | £12,089,086 |
|  |  |  |  |  |
| 60% Hospital follow-up | £3,340,800 | £5,512,320 | £7,683,840 | £10,098,998 |
| 40% Patient-initiated follow-up | £135,375 | £223,368 | £311,362 | £409,228 |
| Total appointment costs 60:40 follow-up | £2,091,825 | £3,451,512 | £4,811,198 | £6,323437 |

Figure 1. Mean cost per patient of Hospital follow-up (HFU) and Patient-Initiated follow-up (PIFU) over time, n=182

