Patient-initiated follow up affects fear of recurrence and healthcare use
a randomised trial in early-stage endometrial cancer
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Patient-initiated follow-up affects fear of recurrence and health care use: A randomized trial in early-stage endometrial cancer

Running title: Patient-initiated follow-up of endometrial cancer

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Abstract

Objective: To test the hypothesis that patient-initiated follow-up reduces fear of cancer recurrence (FCR) and health care use when compared to traditional hospital-based follow-up.

Design: Pragmatic, multi-centre randomized trial.

Setting: Four Danish departments of gynaecology between May 2013 and May 2016.

Population: 156 women diagnosed with International Federation of Gynaecology and Obstetrics (FIGO) stage I low-intermediate risk endometrial carcinoma.

Methods: Women allocated to the control group attended hospital-based follow-up consisting of regular out-patient visits for three years after primary treatment. Women in the intervention group were instructed in patient-initiated follow-up, which included careful instruction in alarm symptoms and options for self-referral rather than a schedule of examinations.

Main outcome measures: The primary endpoint was FCR as measured by the Fear of Cancer Recurrence Inventory (FCRI) after 10 months’ follow-up. Secondary endpoints included cancer-related use of primary and secondary health care during the first 10 months after treatment.

Results: In the primary analysis, FCR decreased significantly more in the control group from baseline to 10-months follow-up (difference -5.9, 95% CI: -10.9 to -0.9). The majority of this improvement happened after only 3 months’ follow-up. Women receiving the intervention had fewer examinations at the department compared to the control group (0 vs. 2 median visits, p < 0.01) and 58% of these examinations were scheduled due to vaginal bleeding.

Conclusions: Hospital-based follow-up alleviates FCR significantly more than patient-initiated follow-up, though the estimated difference was small. Patient-initiated follow-up is a feasible, potentially cost-reducing follow-up approach in a population of endometrial cancer survivors with low risk of recurrence. The decision to use patient-initiated follow-up should balance these benefits and harms.
**Funding:** Danish Cancer Society; National Research Center for Cancer Rehabilitation, University of Southern Denmark; Region of Southern Denmark; Odense University Hospital.

**Keywords:** patient-initiated follow-up, endometrial carcinoma, gynaecological malignancy, post-treatment surveillance, alarm symptoms, recurrence, cancer, uterus.

**Clinicaltrials.gov:** NCT01853865, **URL:** https://clinicaltrials.gov/ct2/show/NCT01853865

**Tweetable abstract:**

Patient-initiated follow-up reduces health care use but maintains fear of recurrence in endometrial cancer.

**Lay summary**

**Why and how was the study carried out?**

Follow-up of women with endometrial cancer is resource consuming and previous research suggests it is not effective. Even though the women benefit from reassurance at follow-up, routine examinations may also remind the women of the disease and induce fear of cancer recurrence. Furthermore, routine follow-up may delay recurrence diagnosis, because the women do not report their symptoms until the next scheduled visit. In the research explained in this article, patient-initiated follow-up was evaluated as an alternative to traditional follow-up. The women were randomly assigned to one of two follow-up programs; regular gynaecologic examinations at the department of gynaecology or self-referral with careful instruction in alarm symptoms, i.e. patient-initiated follow-up. The level of fear of cancer recurrence in the two groups was obtained by questionnaires. Health care use was obtained by questionnaires and a chart review.

**What were the main findings?**

Regular examinations at the department of gynaecology reduced fear of cancer recurrence significantly more than patient-initiated follow-up, though the difference was small. Women who were instructed in alarm symptoms, under self-referral, were able to monitor their symptoms, and this approach significantly reduced the number of examinations at the department of gynaecology.
What are the limitations of the work?
Participants in the self-referral group knew that they were examined less than other women, and this may have induced fear of cancer recurrence. Similarly, the regular completion of questionnaires regarding fear of cancer recurrence may have reminded the women of the disease and diminished the difference between the two groups.

What are the implications for patients
Patient-initiated follow-up reduced health care use but maintained fear of cancer recurrence in early stage endometrial cancer survivors. Future analyses on quality of life and cost-effectiveness are needed to balance the benefits and harms of patient-initiated follow-up.

Introduction
The need for routine, hospital-based follow-up of early-stage endometrial cancer has been questioned, because little is known of its possible benefits and harms. In general, cancer survivors consider early detection of recurrence to be the primary purpose of post-treatment surveillance and associate follow-up with reassurance. However, an upcoming examination can cause distress and may remind the women of their cancer diagnosis, cause them to question their health status, and induce fear of cancer recurrence (FCR). FCR is common among cancer survivors and can be considered a rational response to the threat of recurrence; however, it is associated with psychological distress, impaired functioning, lower quality of life, and increased use of health care. Thus, it is essential to balance post-treatment surveillance with the women’s desire to return to normal life.

Current knowledge on the effect of follow-up on survival and recurrence detection relies on retrospective studies. The majority of studies conclude that follow-up does not improve survival. In a nationwide, population-based cohort study, we found that recurrence was symptomatic in the majority of the included women (65.5%) and could thus be detected outside of regular follow-up. Of
the recurrences, 53% were extra-vaginal with poor options for treatment, and early detection would most likely not improve survival.

Women with FIGO stage I low-intermediate risk disease have a recurrence risk of 1 to 3%. Hence, the majority of these women would never experience recurrence and it is estimated that only 2 in 1000 would potentially benefit from follow-up. In addition, routine follow-up could delay recurrence diagnosis, because patients postpone seeking help until the next scheduled visit. Consequently, follow-up care is subject to a paradigm shift, in which alternative strategies, including follow-up by general practitioners (GP), specialist nurses or the patients themselves are considered.

In patient-initiated follow-up, patients are instructed in self-referral, based on knowledge of alarm symptoms. They are given a direct access to secondary health care, rather than receiving a schedule of examinations. Hence, the approach is expected to reduce the number of unnecessary visits and diagnostic delay caused by patients not reacting to their symptoms.

Here, we present the first multi-centre randomized trial on patient-initiated follow-up in endometrial cancer. The objective of the trial was to compare traditional follow-up to patient-initiated follow-up regarding FCR and health care use in early-stage, low-intermediate risk endometrial cancer. We hypothesized that patient-initiated follow-up would reduce FCR and reduce cancer-related health care use.

**Methods**

**Study design**

The study design was a pragmatic, multi-centre, parallel-group randomized superiority trial. Participants were included from four Danish departments of gynaecology at: Odense University Hospital (May 2013 - May 2016), Aalborg University Hospital (July 2013 - May 2015), Roskilde Hospital (November 2014 - June 2015) and Aarhus University Hospital (March 2015 - December 2015). The study was conducted in accordance with the Declaration of Helsinki and was approved by the Regional Scientific Ethical Committees for Southern Denmark (S-20120223, approval date: 21.03.2013) and the Danish Data Protection Agency (12/25796).
Participants

Women eligible for participation were treated with curative intent for FIGO stage I, grades 1 and 2 endometrial carcinoma. Exclusion criteria were treatment with adjuvant chemotherapy or radiation therapy, participation in a project with follow-up examinations or follow-up for other gynaecological malignancy, tumours with high risk histology (clear cell, serous, squamous, non-differentiated adenocarcinoma), and inability to complete questionnaires, due to mental impairment, or insufficient literacy in Danish.

Written study information was administered at the department of gynaecology prior to initial surgery and was repeated verbally by a specialist in gynaecological cancer surgery before discharge. This information included a description of the study design, implications for participants, a description of the most important alarm symptom (vaginal bleeding/discharge) and contact information for the department of gynaecology. Participants gave informed written consent.

Randomisation and masking

The women were randomly assigned (1:1) to hospital-based or patient-initiated follow-up care at the time of final FIGO staging following surgery, using a computer-based system stratified according to health care centre. Randomization was performed centrally with a block size of 10 within each hospital. Health care providers and data analysts were blinded to the block size during recruitment. Neither patients nor health care providers could be blinded to the enrolment. However, data analysts were blinded to the group assignment until all the analyses were completed, by labelling the groups with non-identifying terms (1 and 2).

Procedures

The intervention consisted of patient-initiated follow-up without a schedule of examinations at the respective department of gynaecology. The women were thoroughly instructed in alarm symptoms that required examination, i.e. vaginal bleeding/discharge or other newly emerged symptoms including: pelvic pain/heaviness, distended abdomen, dyspnoea, gastrointestinal symptoms, fatigue, weight loss, and swelling of the leg(s). This information was provided verbally by a doctor specialized in gynaecological cancer surgery.
in gynaecologic oncology immediately after randomization. If they felt worried about the risk of recurrence, they could ask for a consultation. Self-referral was made easy by providing the telephone number of a designated project nurse at the department of gynaecology or, if preferred, they could contact their GP. In most cases, the women were seen within a week after contacting the department. The woman’s GP was informed of the study and the woman’s allocation through the discharge summary.

Women in the control group received conventional follow-up care, in accordance with Danish guidelines. This was a three-year follow-up period, consisting of scheduled visits every four-six months in the first two years and every six months during the third year. Because of the pragmatic study approach, variation in the frequency of follow-up visits was allowed, as each of the four centres were instructed to provide care as usual. The follow-up visits included clinical and gynaecological examinations with vaginal ultrasound, supplemented with biopsies in case of suspicious findings and imaging in case of symptoms or histologically verified recurrence.

Outcomes
Data were sampled by questionnaires administered at 1, 3, 6, and 10-months follow-up and chart review. Questionnaires were primarily administered online, although a paper version was sent in case the women preferred the paper version. Sociodemographic characteristics were collected from questionnaires. From the chart review, we obtained data on primary surgery, FIGO stage, grade, histological type, comorbidities and BMI at baseline, date of recurrence diagnosis, and date of death.

This report is focused on the primary endpoint, FCR after 10 months’ follow-up, as the majority of changes in FCR are expected to occur early after treatment. Additional endpoints collected in the trial included quality of life, unmet needs, post-traumatic growth after 10 months. Finally, a long-term assessment of the abovementioned endpoints and a cost-utility will be conducted after three years’ follow-up.

FCR was assessed using the Fear of Cancer Recurrence Inventory (FCRI). It is a multi-dimensional, 42-item questionnaire with a time frame of one month. It is comprised of seven subscales measuring different aspects associated with FCR: triggers, severity, psychological distress, reassurance-seeking,

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coping strategies, functioning impairments and insight (self-criticism towards FCR intensity). Each question is scored on a 5-point Likert scale from 0 “not at all” to 4 “a great deal”. A total summary score is obtained by summing all items (with item no. 13 reversed). The score ranges from 0-168, with a higher score indicating higher levels of FCR. A cut-off value for clinical FCR is defined as a score of 16 or greater on the Severity subscale (range 0-36)\(^\text{15}\). This instrument was chosen because it comprises a comprehensive assessment of FCR with a proposed cut-off score for clinically significant FCR\(^\text{16}\). The English version of the FCRI has demonstrated sound psychometric properties, including high internal consistency (Cronbach \(\alpha = 0.71-0.94\)), test-retest reliability (\(r = 0.56-0.87\)), and construct validity\(^\text{17}\). Before study start, the English version of the questionnaire was translated into Danish, inspired by the guidelines for cross-cultural adaptation of self-report measures by Beaton et al.\(^\text{18}\), involving a forward-backward translation approach. The translated version was pilot-tested in accordance with the guidelines of the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Group\(^\text{19}\) in a population of eleven women attending follow-up for endometrial cancer.

Information on primary care use was obtained from two questions regarding the number of cancer-related visits to a GP or a privately-practising gynaecologist since the last questionnaire completion. Information on number of telephone contacts and examinations at the department of gynaecology were obtained by chart review. Any symptoms reported by the women at the examination were registered.

**Statistical methods**

The power calculation was based on pilot study data from 22 endometrial cancer patients supplemented with unpublished data derived from a study on FCR in breast cancer patients. Corresponding to these data, the expected standard deviation was set at 22. A difference in decline of at least 10 points was considered of clinical relevance, based on experiences from scoring of quality of life measures\(^\text{20}\). To detect a difference of 10 in the change of total FCRI score with 80% power at the 5% level, 76 women were required in each group. To ensure that complete data were obtained for
152 women, the 10-month completion rate was estimated after 18 months of inclusion. This gave a completion rate of 72%, and thus 211 women were needed for the study.

The flowchart was constructed according to the CONSORT guidelines. Baseline characteristics of non-participants vs, participants as well as responders vs. non-responders were compared using t-tests for continuous variables, Pearson chi2 for categorical variables, and Mann Whitney U-test for non-parametric variables.

Missing values on the FCRI were handled according to the scoring manual provided by the developer\textsuperscript{13}: Questionnaires were discarded if 1) more than half of the data were missing, 2) two or more subscales were completely missing, 3) a “0”-response pattern for the entire FCRI was used. Otherwise, missing data were imputed by the mean subscale score on a person level. Mean scores and standard deviations (SD) were calculated, and the change in total FCRI score from treatment to 10-months follow-up was compared between the two trial arms using linear regression analysis adjusted for hospital and baseline score. Based on the severity subscale, the proportion of women with clinical FCR was estimated and the odds ratio for clinical FCR was estimated in a multiple logistic regression analysis adjusted for hospital and baseline.

Median number of cancer-related visits to the GP, privately-practising gynaecologist, and telephone contacts and follow-up visits to the department of gynaecology within the first 10 months following treatment were estimated for both trial arms, and compared using Mann-Whitney U tests, because the data did not meet the assumption of normal distribution.

For all analyses, a modified intention-to-treat approach was applied, as only women who completed the first and fourth questionnaires were included in the analyses. A two-sided p-value below 0.05 was considered statistically significant. Analyses were performed using Stata/IC 14.0 for Windows. The CONSORT-criteria (www.equator-network.org) were followed in the reporting of the study. The trial is registered at clinicaltrials.gov, identifier: NCT01853865.
Patient involvement

The patient association “Women with reproductive cancers” was consulted during the design phase of the trial. This resulted in changes made to the written study information as well timing for when oral and written information was presented to eligible women.

Funding

Danish Cancer Society; National Research Center for Cancer Rehabilitation, University of Southern Denmark; Region of Southern Denmark; Odense University Hospital.

Results

A total of 549 women were assessed for eligibility between May 1st 2013 and June 1st 2016 and 307 women were eligible for participation. Of these, 214 women were randomized for the trial (Fig. 1). Two of these women were subsequently excluded due to high-risk disease. Baseline characteristics of participants are summarised in Table 1. Complete data were obtained for 156/212 (74%) (Fig. 1). No evidence of a difference was found in baseline and disease characteristics between women with complete datasets and non-responders (Table S1). More non-participants had cardiovascular disease compared to participants (73% vs. 54%, p = 0.03).

No deaths were observed within the 10-month follow-up period. Disease recurrence was detected in two of the women allocated to the intervention. One 79-year-old woman contacted the department of gynaecology due to a painful palpable tumour in her left hypogastric region, whereas the other woman, 84 years old, was diagnosed at a department of general medicine due to general fatigue and pain in her right side, and a CT scan revealed peritoneal carcinomatosis.

At baseline, women in the control group had a mean FCR total score of 48.5 (SD: 28.8). At 10-months follow-up, this score had improved by 8.0, and the majority of this improvement happened after 3-months follow-up with a reduction in overall score of 6.6 (Table 2). In the intervention group, the baseline score was 44.8 (SD: 27.3), and this score was kept on a more constant level with an improvement of 1.4 at 10-months follow-up (Table 2). In the linear regression, FCR decreased

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significantly more in the control group with an estimated difference of -5.9 (95% CI: [-10.9; -0.9], p= 0.02).

The proportion of women with clinical FCR as derived from the Severity subscale did not differ between the groups at 10-months follow-up when adjusting for baseline score and hospital (odds ratio= 0.9, p= 0.89). The estimated proportions indicated that one in five women struggled with clinical FCR ten months after their primary treatment, regardless of allocation (Table 2).

All subscales improved in the control group from baseline to 10-months follow-up (Table 2). The greatest improvement was seen in coping strategies, which suggested that, because of their reduced level of FCR, the women depended less on coping strategies to deal with their FCR.

Twenty-six of the women who declined participation (27% of non-participants) completed the baseline questionnaire. No evidence of a difference was found in the mean total FCR score when compared to participants (47.5 vs. 46.6, p= 0.88).

No evidence of a difference was found between the two groups in the number of cancer-related visits to the GP (p= 0.77), privately-practising gynaecologist (p= 0.31), or telephone contacts to the departments of gynaecology (p= 0.15) (Table 3). However, women in the intervention group had significantly fewer examinations at the gynaecology departments compared to the control group (p < 0.01) (Table 3). Reasons for the 19 examinations in the intervention group were: vaginal bleeding or discharge (n= 11), pain in the pelvic or inguinal region (n= 4), palpable tumour (n= 1), worry (n= 1), and dropout from allocated intervention (n= 2, 1 woman).

Discussion

Main findings

This is the first study to examine the use of patient-initiated follow-up in endometrial cancer.

Traditional follow-up alleviated FCR more effectively than patient-initiated follow-up. The intervention group had significantly fewer hospital examinations (p <0.01) and these examinations...
were primarily scheduled because of symptoms, with vaginal bleeding/discharge being the most prevalent symptom.

**Strengths and limitations**

Study strengths include the randomized design, the fact that the required sample size was reached, and the blinding of data analysts. The pragmatic design ensured that the intervention was evaluated in real-life settings, thus maximizing the generalizability of the study. The baseline questionnaire was completed after randomization, as the FCRI would neither have made sense to complete nor been ethical to give out at the time of primary treatment. Responses could thus be affected by the allocation. Even so, the 1-month questionnaire was considered a credible baseline score, because it covered the experience of FCR during the past month (prior to randomization). Blinding of participants for this trial was not possible. Women who received the intervention knew that they were examined less than the control group, and we cannot rule out that this bias in part explains the constant level of FCR in the intervention group.

The regular completion of questionnaires may have served as a reminder of disease, and may have attenuated the differences between the control and intervention group. As the women in the intervention did not receive reassurance from an examination, the questionnaire may have induced FCR in this group.

The analyses were limited to a modified intention-to-treat approach. However, complete datasets were obtained from the majority of the women (73.6%), and there were no significant differences in baseline characteristics or questionnaire scores between responders and non-responders. The participation rate was 69%, and non-participants could possibly represent a group that preferred hospital-based follow-up. Reasons for non-participation were only available for five of the women, but only two of these women refused participation due to a wish for traditional follow-up.
Interpretation:

Only four randomized trials have compared patient-initiated follow-up to traditional follow-up, and these were conducted in breast and colorectal cancer survivors. No evidence of a difference was found with regard to quality of life, anxiety or depression in breast cancer, or on survival in colorectal cancer. These studies differed from the present study in two important aspects: i) Women in the intervention groups attended annual mammograms or conducted faecal examinations at regular intervals; ii) General anxiety was measured using the Hospital Anxiety and Depression Scale, and even though some correlation exists between anxiety, depression and FCR measures, they represent different constructs.

Our trial demonstrated a superior effect of traditional follow-up on FCR compared to patient-initiated follow-up with an estimated significant difference in total score of -5.9. Hence, we reject our hypothesis that patient-initiated follow-up would reduce FCR. Women in the control group may have achieved medical reassurance at the scheduled examinations that outweighed any potential distress prior to examinations. Furthermore, in the intervention group, detection of recurrence relied on the woman’s ability to detect signs of recurrence. For some women, this responsibility might have led to distress, and the complete absence of a scheduled visit might have been too drastic.

No study has validated a cut-off for the minimal clinically-important difference (MID) on the total FCRI score. A common approach to interpreting quality of life data is to choose a cut-off of 5-10% of the scale width. To ensure sufficient power to detect a difference and considering the paucity of knowledge on MID on the FCRI, we decided on a cut-off of 10 points, corresponding to 6% of the scale width. Based on the confidence interval, we are 95% confident that the true difference between the groups lies between -0.9 and -10.9. Hence, the intervention may have been clinically inferior to the control group.

In this study the mean total score on the FCRI ranged from 40 – 48.5. In comparison, the mean total FCRI score was found to be 66.3 in survivors from lung cancer, indicating an association between the actual risk of recurrence and FCR. Nonetheless, our findings revealed a large variation in scores with standard deviations between 26.5 and 29.5, suggesting that a subgroup of endometrial cancer survivors...
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Conclusion

Traditional follow-up reduced FCR significantly more than patient-initiated follow-up, though the estimated difference was small. The population of cancer survivors is growing, which has resulted in an increasing strain on health care resources. Women treated for stage I low-intermediate risk endometrial cancer have a low risk of recurrence, and patient-initiated follow-up represents a feasible alternative, with the potential of reducing the use of health care. The decision of whether the benefits of patient-initiated follow-up outweigh the harms will be supported by future long-term analyses on quality of life and cost-utility.

Acknowledgements

We thank the women who participated in this trial. This study was made possible by the collaborative efforts of physicians and nurses at the recruiting hospitals. We sincerely appreciate your time. In particular, we wish to thank Rikke Maria Iversen and Camilla Vestergaard Jensen (Odense University Hospital), Marianne Mulle Jensen (Aalborg University Hospital), Jan Blaakær, Lotte Dahl, Ulla Margrethe Kehlet, and Malene Kjærgaard Larsen (Aarhus University Hospital), Rie Rosgaard, and Aviaja Siegstad Roos (Roskilde Hospital). Finally, we thank Lorna Campbell for editing the manuscript.

Disclosure of interests

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work. Completed disclosure of interest forms are available to view online as supporting information.

Contribution to authorship

MMJ was involved in all phases of the literature search, design, data collection and cleaning, design of tables and figures, interpretation and writing of the manuscript. PTJ, DGH and OM acted as supervisors and were thus actively involved in the study design, data collection, and interpretation and

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writing of the journal manuscript. RDC performed the sample size calculations and the statistical analyses and took part in writing of the journal manuscript with specific emphasis on sections regarding statistics and results.

**Details of ethics approval**

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Regional Scientific Ethical Committees for Southern Denmark (S-20120223, approval date: 21.03.2013) and the Danish Data Protection Agency (12/25796).

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**References**


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Figure title and legend

Figure 1. Trial profile

Legend: CONSORT flow chart of the progress of patients with endometrial cancer through the phases of the trial.
Table 1 - Sociodemographic and disease characteristics of the modified intention-to-treat population

<table>
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<th>Patient-initiated follow-up N = 79 (%)</th>
<th>Hospital-based follow-up N = 77 (%)</th>
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<td>• Odense</td>
<td>54 (68)</td>
<td>52 (68)</td>
</tr>
<tr>
<td>• Aalborg</td>
<td>11 (14)</td>
<td>11 (14)</td>
</tr>
<tr>
<td>• Aarhus</td>
<td>6 (8)</td>
<td>7 (9)</td>
</tr>
<tr>
<td>• Roskilde</td>
<td>8 (10)</td>
<td>7 (9)</td>
</tr>
</tbody>
</table>
TAH = Total abdominal hysterectomy, TLH = Total laparoscopic hysterectomy, RALH = Robotically-assisted laparoscopic hysterectomy, RARH = Robotically-assisted radical hysterectomy

Table 2 – Mean summary scores and standard deviations for the Fear of Cancer Recurrence Inventory for both trial arms at 1, 3, 6, and 10-months follow-up

<table>
<thead>
<tr>
<th>Subscales</th>
<th>Range</th>
<th>1 Month</th>
<th>3 Months</th>
<th>6 Months</th>
<th>10 Months</th>
<th>Effect size [95 % CI]</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total FCRI score</td>
<td>0-168</td>
<td>44.8 (27.3)</td>
<td>43.8 (28.5)</td>
<td>42.8 (26.9)</td>
<td>43.4 (26.5)</td>
<td>-5.9 [-10.9; -0.9]*</td>
<td>0.02</td>
</tr>
<tr>
<td>- intervention</td>
<td></td>
<td>48.5 (28.8)</td>
<td>41.9 (28.4)</td>
<td>40.4 (29.5)</td>
<td>40.5 (28.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- control</td>
<td></td>
<td>44.8 (27.3)</td>
<td>43.8 (28.5)</td>
<td>42.8 (26.9)</td>
<td>43.4 (26.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% with clinical FCR</td>
<td></td>
<td>16.5</td>
<td>22.8</td>
<td>20.3</td>
<td>17.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- intervention</td>
<td></td>
<td>26.0</td>
<td>24.7</td>
<td>24.7</td>
<td>22.1</td>
<td>0.9** [0.32;2.67]</td>
<td>0.89</td>
</tr>
<tr>
<td>- control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychological distress</td>
<td>0-32</td>
<td>9.6 (6.8)</td>
<td>10.2 (7.0)</td>
<td>10.2 (6.6)</td>
<td>9.7 (6.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- intervention</td>
<td></td>
<td>10.0 (6.8)</td>
<td>9.2 (7.0)</td>
<td>9.2 (7.0)</td>
<td>9.1 (6.7)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>- control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severity</td>
<td>0-36</td>
<td>9.9 (6.5)</td>
<td>10.4 (7.0)</td>
<td>9.8 (6.6)</td>
<td>10.1 (6.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- intervention</td>
<td></td>
<td>10.9 (7.9)</td>
<td>10.3 (7.8)</td>
<td>10.7 (7.3)</td>
<td>9.8 (7.2)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>- control</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coping strategies</td>
<td>0-16</td>
<td>2.9 (3.6)</td>
<td>2.7 (3.5)</td>
<td>2.8 (3.7)</td>
<td>3.2 (3.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- intervention</td>
<td></td>
<td>3.2 (3.6)</td>
<td>2.9 (3.4)</td>
<td>2.7 (3.2)</td>
<td>2.9 (3.4)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>- control</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Functioning impairments</td>
<td>0-24</td>
<td>15.7 (9.4)</td>
<td>15.3 (9.3)</td>
<td>14.6 (9.1)</td>
<td>14.9 (9.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- intervention</td>
<td></td>
<td>17.0 (8.5)</td>
<td>14.2 (9.0)</td>
<td>12.8 (9.1)</td>
<td>13.0 (9.2)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>- control</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insight</td>
<td>0-12</td>
<td>3.4 (5.0)</td>
<td>2.9 (4.4)</td>
<td>2.7 (4.2)</td>
<td>2.5 (3.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- intervention</td>
<td></td>
<td>3.9 (5.0)</td>
<td>3.5 (4.9)</td>
<td>2.9 (4.6)</td>
<td>3.1 (4.7)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>- control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reassurance</td>
<td>0-12</td>
<td>1.2 (2.2)</td>
<td>1.2 (2.3)</td>
<td>1.0 (2.1)</td>
<td>1.2 (2.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- intervention</td>
<td></td>
<td>1.4 (2.5)</td>
<td>1.1 (2.3)</td>
<td>1.4 (2.7)</td>
<td>1.1 (2.2)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>- control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Standard deviations are given in parentheses. The percentage of women with clinical FCR is based on the Severity subscale score.  
* Linear regression analysis adjusted for hospital and baseline score  
** Odds ratio from logistics regression analysis adjusted for hospital and baseline score

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Table 3 - Number of cancer-related visits to primary and secondary health care providers within the first 10 months after treatment for both trial arms

<table>
<thead>
<tr>
<th></th>
<th>Patient-initiated follow-up</th>
<th>Hospital-based follow-up</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>median (IQR)</td>
<td>total number</td>
<td>median (IQR)</td>
</tr>
<tr>
<td>Cancer-related visits to GP</td>
<td>1 (0-4)</td>
<td>213</td>
<td>1 (0-3)</td>
</tr>
<tr>
<td>Cancer-related visits to privately-practising gynaecologist</td>
<td>0 (0-0)</td>
<td>17</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Telephone contacts with the departments of gynaecology</td>
<td>0 (0-0)</td>
<td>20</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Examinations performed at the departments of gynaecology</td>
<td>0 (0-0)</td>
<td>19</td>
<td>2 (1-2)</td>
</tr>
</tbody>
</table>

* Mann Whitney U test
Figure 1 - Trial profile

Assessed for eligibility (n= 549)
- Excluded (n= 240)
  - Disease stage > 1 (n= 91)
  - High risk histology/ENGOT candidate (n= 62)
  - Undergoing palliative care (n= 8)
  - Limited Danish or cognitive impairment (n= 54)
  - Not invited to participate (administrative failure) (n= 25)*
- Declined (n= 95)
  - Refused randomization, but completed questionnaires (n= 26)
  - Declined to participate (n= 69)

Randomized (n= 214)
- Excluded (n= 2)
  - High risk histology (n= 2)

Randomized (n= 212, 69%)

Intervention (n= 105)
- Received allocated intervention (n= 104)
- Did not receive allocated intervention, due to dropout (n= 1)

Control (n= 107)
- Received allocated intervention (n= 106)
- Did not receive allocated intervention, due to administrative failure (n= 1)

Completion of questionnaires:
- 1 month: (n= 79)
- 3 months: (n= 78)
- 6 months: (n= 77)
- 10 months: (n= 79)
- Deceased (n= 0)
- Disease recurrence (n= 2)

Completion of questionnaires:
- 1 month: (n= 77)
- 3 months: (n= 76)
- 6 months: (n= 71)
- 10 months: (n= 77)
- Deceased (n= 0)
- Disease recurrence (n= 0)

Analysed (n= 79, 75.2%)
- Excluded from analysis (1 and/or 10 month data missing) (n= 26)

Analysed (n= 77, 72.0%)
- Excluded from analysis (1 and/or 10 month data missing) (n= 30)

CONSORT flow chart of the progress of patients with endometrial cancer through the phases of the trial.

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