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Effect of reduced follow-up care on patient satisfaction with care among patients with endometrial cancer: The ENSURE randomized controlled trial

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HIGHLIGHTS

- Reduced follow-up does not compromise satisfaction with care or worry.
- Patients prefer the schedule of reduced follow-up.
- Reduced follow-up care may be the new standard for endometrial cancer.
- Follow-up should be tailored to meet individual patient needs in case of worry.
- Findings may be relevant for other low-risk cancers.

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ABSTRACT

Background. Evidence on the optimal follow-up schedule after endometrial cancer is lacking. The study aim was to compare satisfaction with care between women who received reduced follow-up care and women who received usual guideline-directed follow-up care for three years after surgery.

Methods. The ENSURE (ENdometrial cancer SURvivors' follow-up carE) trial was a non-inferiority randomized controlled multicenter trial in 42 hospitals in the Netherlands. The intervention arm received reduced follow-up care (4 visits/3 years), while the control group received usual follow-up care (8–11 visits/3 years). Primary outcome was overall satisfaction with care, PSQIII score, over three years follow-up, with a non-inferiority margin of 6. Mixed linear regression, intention-to-treat and per-protocol analyses (presented below) were used.

Results. Among 316 women included, overall satisfaction with care was not lower in the reduced follow-up (mean 82; SD = 15) compared with the usual follow-up group (mean 80; SD = 15) group (B = 1.80 (−2.09;5.68)). At 6, 12 and 36 months, more women (93/94/90%) in the reduced follow-up group were satisfied with their follow-up schedule than in the usual follow-up group (79/79/82%; $p < 0.001$; $p < 0.001$; $p = 0.050$).

Conclusions and relevance. Women with low-risk, early-stage endometrial cancer who received reduced follow-up care were no less satisfied with their care than women receiving usual follow-up care. Compared with usual follow-up, women in the reduced follow-up group had fewer clinical visits and, at the same time,

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more often reported being satisfied with their follow-up schedule. Findings suggest that reduced follow-up care may be the new standard, but should be tailored to meet additional needs where indicated.

1. Introduction

Women with low-risk, early-stage endometrioid endometrial cancer, which accounts for 55% of all endometrial cancer diagnoses, are generally treated with surgery alone and have a favorable prognosis. The overall risk of recurrence in this group does not exceed 3–7% [1,2], and the majority (65–70%) of recurrences present with symptoms such as vaginal bleeding [1,2]. Treatment of early-stage endometrial cancer is associated with limited short- and long-term morbidity and a good quality of life [3]. The limited benefit of active surveillance to detect recurrence has led to beliefs that the current routine follow-up care may not be required for patients with low-risk endometrial cancer [1]. Hence, the benefits of the current 5-year or longer routine hospital-based follow-up in most parts of Europe and the United States may not justify the healthcare costs and effort [4–8]. However, there is no evidence on the optimal frequency of visits, and total follow-up time varies widely both on a national and international level [9].

As follow-up visits generally induce worry [9,10], patients may experience less fear and lower levels of illness perceptions with a reduced follow-up schedule [11–14]. The concept of illness perceptions refers to the beliefs a patient has about their illness, including its consequences, time course and controllability. These beliefs are related to quality of life, health care use and survival in cancer patients [15–17]. To date, only one randomized controlled trial, the OPAL trial, has been published that assessed the impact of a reduced follow-up schedule in low and intermediate risk endometrial cancer on fear of cancer recurrence [18]. In this trial among 156 Danish women, patient-initiated follow-up, with careful instruction on alarm symptoms and options for self-referral was compared with regular follow-up with scheduled visits at the hospital, at ten months after treatment. This patient-initiated follow-up, with a median of zero visits, did not alleviate fear of cancer recurrence as much as the more frequent hospital-based follow-up with a median of two visits. However, differences were small (6 points on a scale from 0 to 168) and occurred already in the first three months of follow-up [18]. These findings suggest that, at least in the early post-treatment period, patients may benefit from information provision and support to alleviate fear of recurrence [3,18]. Patients seem to find patient-initiated follow-up acceptable. An observational study in the United Kingdom of 129 women with early-stage endometrial cancer found that 97% of the women who were offered patient-initiated follow-up accepted it [19]. In this study, patients received a total of 264 visits over a median follow-up time of 5 years, compared with 1677 visits if they had received regular hospital-based follow-up. In light of these previous findings, a reduced follow-up schedule with sufficient information provision, and timely and adequate patient-initiated access to care may be an appropriate model of follow-up care for patients with low-risk endometrial cancer. Implementing a reduced follow-up schedule allows to provide support and information provision after end of treatment, without continuous and frequent visits that are generally focused on finding recurrences.

The aim of this randomized, controlled non-inferiority trial was to compare the impact of a reduced follow-up schedule (4 visits) among low-risk, early-stage endometrial cancer survivors, with the impact of a schedule according to the current Dutch guideline (8–11 visits) during three years of follow-up. The primary outcome was overall satisfaction with care and secondary outcomes included adherence to the indicated follow-up protocols, healthcare use, reasons for non-adherence, worry -including fear of recurrence-, anxiety, and depressive symptoms during the three years after diagnosis. We hypothesized that women with endometrial cancer in the reduced follow-up arm would not be less satisfied with care and would not report more worry, anxiety, and depressive symptoms than women in the usual follow-up arm [20].

2. Methods

2.1. Design

The ENSURE (ENdometrial cancer SURvivors' follow-up carE) trial was a Dutch national multicenter non-inferiority randomized controlled trial (RCT), which was conducted in 42 hospitals among low-risk, early-stage endometrial cancer survivors. This paper presents the primary outcomes over 3 years of follow-up. Details of the study have been published in a protocol paper [20]. The study was approved by a certified Medical Ethics Committee (METC Brabant, NL50713.028.14/P1457). The trial was registered in a clinical trials database, no. NCT02413606, ClinicalTrials.gov.

2.2. Randomization and masking

Patients were randomized 1:1 using a computer-generated list of random numbers. Block randomization (6 patients) was used (no stratification) to assure approximately equal numbers in both arms. Concealment of randomization allocation was guaranteed until after signing the informed consent. Doctors and patients could not be blinded for arm assignment.

2.3. Study population

Inclusion criteria were endometrioid type endometrial carcinoma with stage 1 (FIGO, 2009) low-risk disease, with the following combination of stage, age, and grade characteristics: stage 1 A, any age, grade 1 or 2; or stage 1B, < 60 years, grade 1 or 2 without lymphovascular space invasion (LVSI); and sufficient command of the Dutch language. Tumor stage, grade, and type had to be histologically confirmed by the pathologist before inclusion. Exclusion criteria included: receipt of radiotherapy for current endometrial carcinoma; previous malignancy (except for non-melanomatous skin cancer) <5 years; presence of metastases from other tumors; Lynch syndrome; and previous pelvic radiotherapy.

2.4. Procedures

Informed consent was obtained by the treating gynecologist at the second visit after surgery. The Netherlands Comprehensive Cancer Organization Trial Office performed the randomization. Patients were asked to complete paper questionnaires at baseline and at 6, 12, and 36 months. Patients received the baseline questionnaire in the hospital during the second visit after surgery. Follow-up questionnaires were sent by postal mail to their home address.

2.5. Reduced versus usual follow-up care

The usual follow-up arm received follow-up care according to the Dutch guideline, recommending follow-up visits every 3–4 months in the first/second year and every 4–6 months in the third year, irrespective of stage and grade, resulting in a total of 8–11 hospital visits over

three years. In the reduced follow-up arm, the follow-up schedule was limited to four follow-up visits at 3, 12, 24, and 36 months, provided that patients had easy and prompt access to care. The intervention schedule was the outcome of extensive discussion with health care providers throughout the Netherlands. The content of the follow-up visits was similar for both arms and included a specific medical history and a general and gynecologic examination, with imaging only performed if indicated. In both arms, a Survivorship Care Plan was provided, including information on diagnosis and signs of recurrence [21].

2.6. Patient and medical outcomes

We collected the following information from the medical records: date of birth, stage, grade, date of follow-up visits, date and localization of recurrence, and date and cause of death. Healthcare use included face-to-face and telephone-based visits to the gynecologist/nurse specialist or primary care physician.

2.7. Primary outcome and sample size

Overall satisfaction with follow-up care was assessed using the Patient Satisfaction Questionnaire (PSQ) III, which covers three healthcare domains: technical competence (10 items); interpersonal aspects (14 items); and access to care (12 items) [22]. The primary outcome was the one dimension construct of the questionnaire (PSQIII total score) that ranges from 0 to 100. Respondents were asked to indicate their level of agreement with the statements in the PSQ on a scale from 1 (strongly agree) to 5 (strongly disagree). Previously, the PSQ total score was well validated in a Dutch oncological sample [22].

The power calculation was performed on overall satisfaction with follow-up care as measured by the PSQIII over three years of follow-up (at 6, 12 and 36 months combined, analysed using mixed methods). The maximum difference between the arms that we considered acceptable (non-inferiority margin) was 6 points on a scale of 0 to 100, based on previous findings using the PSQIII in a Dutch oncological sample [22]. A sample size of 282 patients was required to evaluate the 6-point non-inferiority margin with a power of 0.80, 30–50 centers to account for clustering of patients within hospitals and an expected loss to follow-up of 20% and patients dying (16%) during five-years of follow-up.

2.8. Secondary outcomes

Worry was assessed using a single scale from the validated Impact Of Cancer Questionnaire (IOCv2) [23]. The scale consists of six items, including worry about the future, worry about health because of the cancer, and worry about recurrence. Respondents were asked to indicate their level of agreement with the statements on a five-point scale ranging from 1 (strongly agree) to 5 (strongly disagree). The scale showed good reliability and validity [23].

Anxiety and depressive symptoms were assessed using the 14-item Hospital Anxiety and Depression Scale (HADS) [24]. A total score was calculated for both anxiety and depressive symptoms by summing the scores on 7 items. These total scores range from 0 to 21, with higher scores indicating more symptoms. A cut-off score of 8 or higher is used to indicate symptoms of anxiety or depression [24].

Satisfaction with the follow-up schedule was measured with a single item that has been used in previous studies [25]: “Do you feel comfortable with the follow-up schedule?“, with the following response options: “yes”, “no, I prefer more contacts”, “no, I prefer less contacts”, and “no, I prefer no contacts”.

Sociodemographic characteristics were assessed using questionnaires, including educational level, marital status and employment status. Comorbidities at the time of questionnaire completion were measured using the Self-administered Comorbidity Questionnaire (SCQ) [26].

2.9. Statistical analysis

Recent evidence has urged that in non-inferiority trials, both intention-to-treat (analyses according to the arm to which they were assigned) and per-protocol (patients who received FU care according to the study protocol) analyses must be reported and should produce similar results [27]. So, in contrast to our protocol, where the main analysis was intention-to-treat, we also report per-protocol analyses.

Protocol adherence was evaluated by calculating visits per year and over the three-year follow-up period. In the reduced follow-up group, per-protocol was defined as four visits in three years; in the usual follow-up group 8 to 11 visits. Allowing for plus or minus one visit resulted in 3–5 and 7–12 visits, respectively. The number of visits to the gynecologist/nurse specialist and to the primary care physician were compared between trial arms. Only patients with complete data on number of follow-up visits were included.

Mixed model linear regression analyses were used to compare outcomes between arms. These models can handle (at random) missing data. Outcomes were analysed as non-inferiority, meaning that the lower bound of the 95% confidence interval did not exceed our predefined non-inferiority margin of −6 points for the primary outcome and 0.5 SD for all secondary outcomes [28]. Only the outcome satisfaction with the follow-up schedule, was tested for superiority. Analyses included relevant prespecified covariates, including age, partner status, education level, number of comorbidities, type of surgery, and FIGO stage.

To assess potential selection bias within our study sample, and thus the generalizability of the findings, we conducted three additional analyses, which are reported in more detail in Appendix D. These include: A comparison between the ENSURE study population and the background population of patients registered in the Netherlands Cancer Registry (NCR) during the study period and who met the ENSURE inclusion criteria; An analysis of a short non-responder questionnaire administered to those who were eligible and invited to participate in the ENSURE trial, but declined to do so; Within the reduced follow-up care arm, a comparison of the participants who received more follow-up care than scheduled (‘high consumers’) with the participants who received follow-up care according schedule or less than scheduled.

Analyses were performed using the SAS software package version 4.2.

3. Results

3.1. Participants

Enrolment was from 1 September 2015 to 28 February 2018. A total of 316 participants were enrolled; 160 were randomized to the reduced follow-up arm and 156 to the usual follow-up arm (Fig. 1). The following number of patients completed questionnaires: after surgery 299 (95%), after 6 months 291 (92%), after 12 months 272 (86%) and after 36 months 222 (70%). The mean age of the participants was 65 years and 96% had FIGO stage 1 A disease (Table 1).

During the 36 months of follow-up, 7 patients died in the reduced follow-up arm and 4 in the usual follow-up arm ($p = 0.38$; Appendix A). There were 14 recurrences, 9 in the reduced and 5 in the usual follow-up arm (Appendix A). Nine of the 14 recurrences were detected during extra visits (8 presented with symptoms; 1 without (distant metastasis)) and 5 during regular visits (3 patients presented with symptoms and 2 without (both a vaginal recurrence)). Most recurrences occurred in the first two years (93%). Characteristics of patients with and without a recurrence are shown in Appendix B.

3.2. Protocol adherence

101 (71%) women in the reduced follow-up arm and 82 (56%) in the usual follow-up arm adhered to the follow-up schedule (Appendix C)

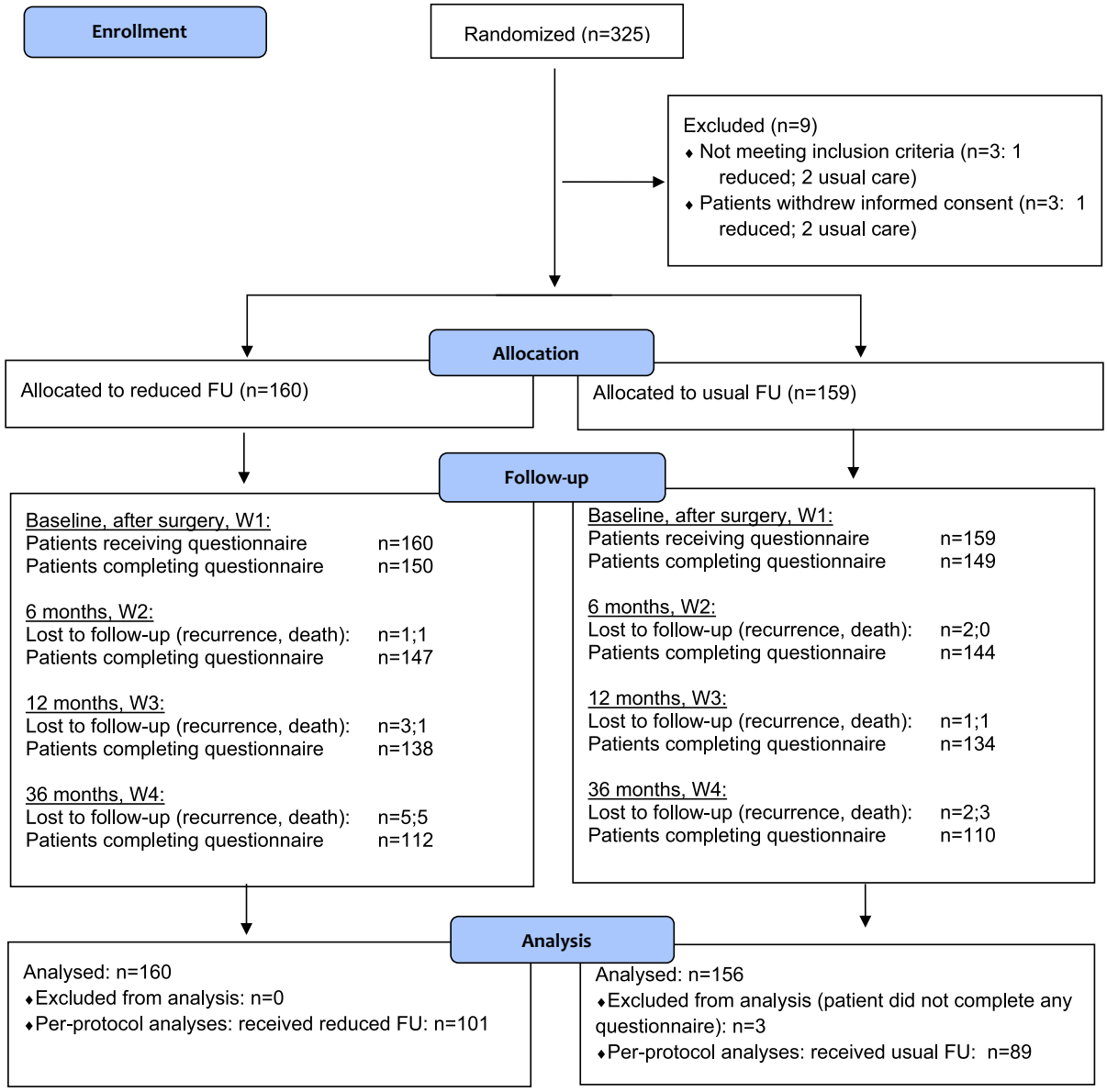

Fig. 1. Flowchart of study enrolment, follow-up and analyses. FU: follow-up.

and were included in the per-protocol analysis. Protocol adherence did not differ between trial arms ($p = 0.40$; Fig. 2). During the second and third year of follow-up, particularly in the usual follow-up arm, a substantial proportion of women received fewer consultations with the gynecologist or nurse specialists than recommended by the guidelines. Women contacted the primary care physician a median of 11 times (IQR 6.5–26.0) in the reduced follow-up arm and 14 times (IQR 8.0–25.0) in the usual follow-up arm (Fig. 2). This difference was not statistically significant (p = 0.40).

3.3. Overall satisfaction with care (primary outcome)

Women in the reduced follow-up arm did not report lower overall satisfaction with care: the estimated between-arm difference was 1.07 (CI -1.82; 3.96) in the intention-to-treat analysis and 1.80 (CI -2.09; 5.68) in the per-protocol analysis (on a scale of 0–100) (Fig. 3; Table 2). The CIs for both analyses were above the non-inferiority margin of −6, indicating non-inferiority of the reduced follow-up arm. Similar results were found for the subscales on satisfaction with care, i.e. interpersonal aspects, technical competence, access to care, and general satisfaction with care (Fig. 3; Table 2). Descriptive numbers and results per year of follow-up are presented in Appendix D.

3.4. Satisfaction with follow-up schedule (secondary outcome)

In the per-protocol analysis, women in the reduced follow-up arm were more than four times more likely to be satisfied with the follow-up schedule than women in the usual follow-up arm (OR 4.27 CI 1.81; 10.05, $p < 0.05$), with the percentage of patients satisfied at 6/12/36 months in the reduced follow-up arm being 95/94/88%, compared with 75/75/82% in the usual follow-up arm (Table 3). Between 11% (post-surgery) and 25% (at 6 months) of women in the usual follow-up arm reported preferring less or no scheduled follow-up (per-protocol group), compared with 1% (12 months) and 16% (post-surgery) in the reduced follow-up arm.

3.5. Illness perceptions, worry, anxiety and depressive symptoms (secondary outcomes)

For illness perceptions, worry, anxiety and depressive symptoms the estimated between-arm differences did not exceed the non-inferiority

Table 1
Baseline sociodemographic and clinical characteristics of study participants, N (%).

	Reduced FU (N = 160)	Usual FU (N = 156)
SOCIODEMOGRAPHIC		
Age at time of diagnosis (M, SD)	65.1 (9)	64.6 (9)
Partner, yes	136 (85)	118 (76)
Employed, yes	46 (29)	50 (32)
Education		
Lower/ primary education	20 (13)	10 (6)
Secondary education (high school)	50 (31)	48 (31)
Secondary vocational education	58 (36)	64 (41)
Higher (vocational) education, university	32 (20)	34 (22)
CLINICAL		
Comorbidity		
0	22 (15)	15 (10)
1	43 (29)	43 (28)
>1	85 (57)	97 (63)
FIGO stage		
IA	153 (96)	149 (96)
IB	7 (4)	7 (4)
FIGO grade		
I	133 (83)	124 (79)
II	27 (17)	32 (21)
Type of surgery		
TAH-BSO	8 (5)	15 (10)
TAH-BSO with lymphadenectomy	0 (0)	1 (1)
Laparoscopic TLH-BSO or LAVH-BSO	147 (92)	134 (86)
Laparoscopic TLH-BSO or LAVH-BSO with lymphadenectomy	1 (1)	2 (1)
TAH	2 (1)	0 (0)
Other	2 (1)	4 (3)
Complications of surgery		
No complications	148 (93)	146 (94)
Wound infection	0 (0)	1 (1)
Other	3 (2)	1 (1)
Combination	9 (5)	8 (5)

FU: follow-up; TAH: Total abdominal hysterectomy; BSO: Bilateral salpingo oophorectomy; TLH: Total laparoscopic hysterectomy; LAVH: Laparoscopically assisted vaginal hysterectomy.

margin of +/− 0,5 standard deviation, meaning that the reduced follow-up arm did not do worse than the usual follow-up arm (Fig. 3; Table 2).

3.6. Post-hoc analyses of selection bias and generalizability (Appendix E)

Through comparison of the ENSURE study population with the total eligible background population sampled from the NCR, we estimated that approximately 65% of the eligible population has participated in the ENSURE trial (Appendix E1). Trial participants and the eligible population, as sampled from the Netherlands Cancer Registry, were comparable in age, but stage and grade were slightly lower in the participant group compared to the total eligible population (stage 1 A, 96% vs. 90%; grade I, 82 vs. 75%).

Non-participants who completed a non-participant questionnaire (n = 59) were somewhat younger than the participants (Mean (M) = 62 vs. M = 65 years) (Appendix E2). In addition, non-participants reported more cancer worry (M = 2.8 vs. M = 2.4 on a scale 1–5)), were more emotionally affected (M = 3.4 vs. M = 2.6 on a scale 0–10), and reported less understanding of their illness (M = 5.2 vs. 6.5 on a scale 0–10). Self-reported reasons for non-participation included wanting to receive usual follow-up care because they believed it was important for their health (41%), and worrying about receiving less follow-up care (28%).

Patients in the reduced follow-up arm with more visits than protocolized (>5 in 3 years; n = 27), the 'high consumers', reported more worry compared with patients that received follow-up according schedule or received fewer visits (≤5 in 3 years; n = 135)(M = 2.7 vs. M = 2.3 on a scale of 1–5, p = 0.03) (Appendix E3) than patients in the reduced follow-up arm who received scheduled or less follow-up. In addition, 'high consumers' in the reduced follow-up arm had a higher tumor grade, more often received 'other' treatments, and more often experienced complications from primary surgery.

4. Discussion

In line with our hypothesis, this multicenter, non-inferiority RCT showed that women with low-risk, early-stage endometrial cancer who received reduced follow-up care (i.e. 4 visits) were no less satisfied with their care compared to women receiving follow-up care according to Dutch guidelines (i.e. 8–11 visits) over three years of follow-up. Compared with usual follow-up, women in the reduced follow-up arm had fewer medical visits and, at the same time, more often reported being satisfied with this reduced frequency.

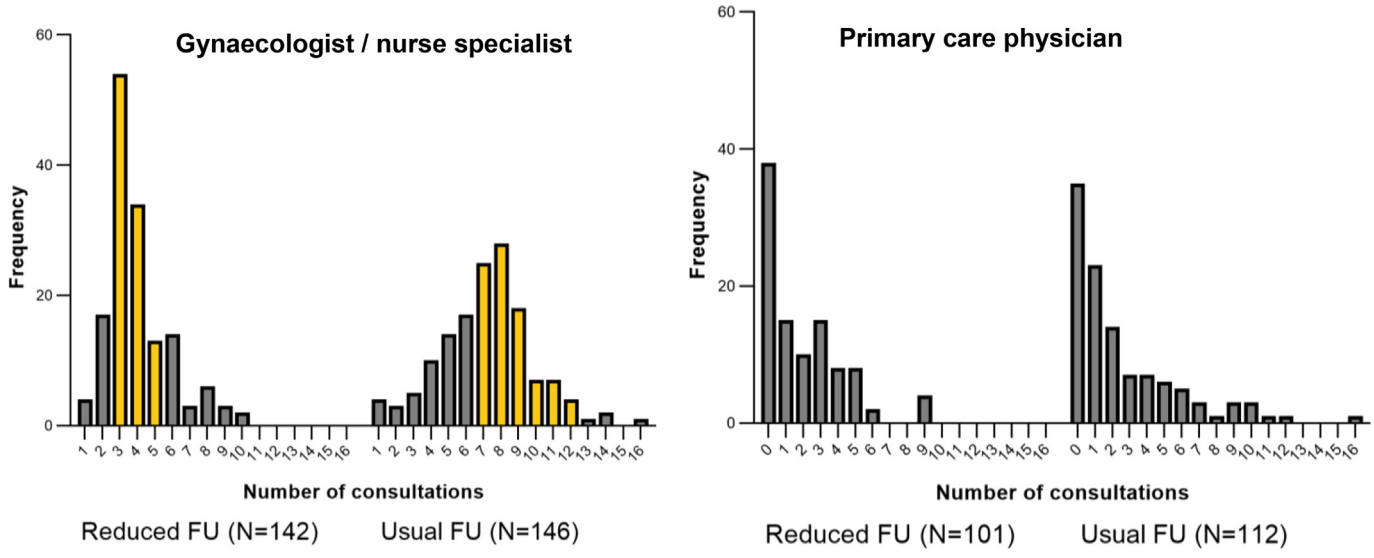

Fig. 2. Total number of follow-up consultations by trial arm with gynecologist/nurse specialist and consultations with the primary care physician (PCP) over three years of follow-up. Yellow bars indicate that the number of follow-up consultations was per-protocol. For this graph, only patients with complete data on number of follow up visits in year 1–3 were included. FU: follow-up. Protocol adherence and number of PCP consultations were not significantly different between trial arms (p = 0.40 based on Chi-Square test; p = 0.40 based on Mann Whitney U tests, respectively). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

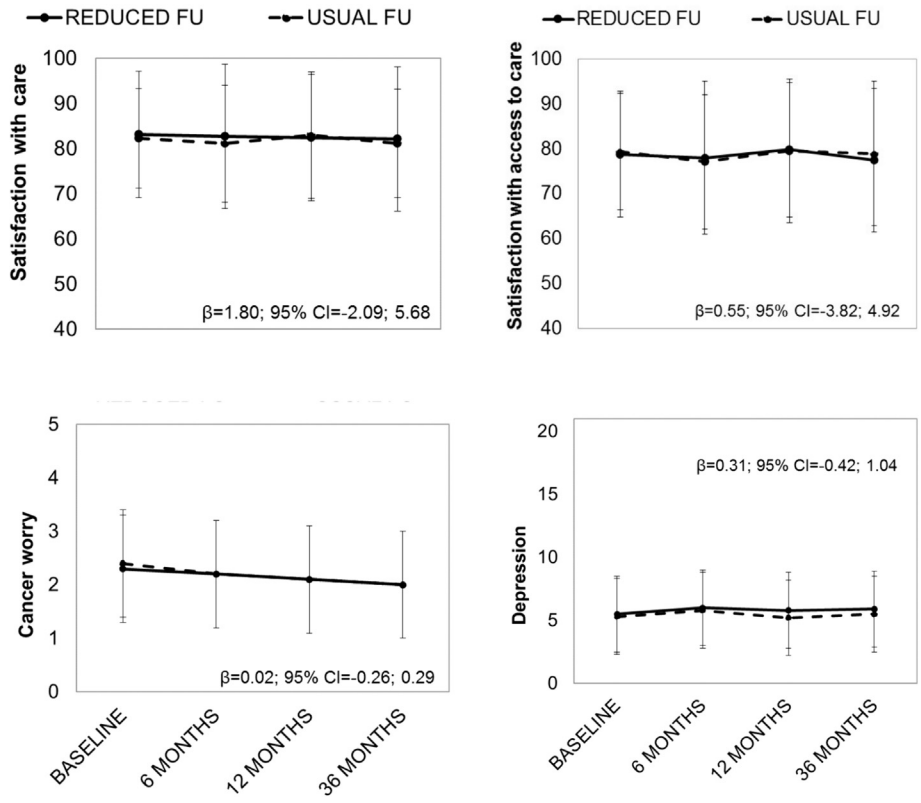

Fig. 3. Graphical representations of outcomes over time for reduced and usual follow-up (FU). Crude means are shown. Error bars show +/− one standard deviation. Multilevel linear regression analyses (per-protocol) assessed outcomes of 6–36 months FU (reduced FU: $N = 101$, usual FU: $N = 87$).
Numbers included: at baseline-reduced FU: $N = 95$, usual FU N = 87; at 6 months-reduced FU $N = 89$, usual FU $N = 81$; 12 months-reduced FU $N = 85$, usual FU $N = 78$; at 36 months-reduced FU $N = 67$, usual FU $N = 62$.

The reduction in the follow-up visits did not lead to additional visits to the primary care physician. There was no increase in cancer worry, anxiety, depressive symptoms or illness perceptions in the reduced follow-up arm compared to the usual follow-up arm. Similar results were found in both the intention-to-treat and per-protocol analyses.

The higher satisfaction with the follow-up schedule in patients who received reduced follow-up care, is in line with the observational study from the UK [19]. Also in line with our findings, the MELFO trial which evaluated the effect of a stage-adjusted reduced versus regular follow-up schedule in melanoma patients, showed no increase in cancer worry after reduced follow-up care (Cancer Worry Scale) [29]. So, as

Table 2
Overall beta and confidence intervals (month 6–36) for satisfaction with care (PSQ), illness perceptions (BIPQ), cancer worry (IoC V2), and distress (HADS). Multilevel linear regression analysis, both intention-to-treat ($n = 315$) and per-protocol ($n = 190$). Unstandardized beta's of reduced follow-up care vs usual follow-up care as reference condition.

	Intention-to-treat (ITT)	Per-protocol (PP)	
	Overall beta 6–36 months* (95%CI)	Overall beta 6–36 months* (95%CI)	Non-inferiority margin**
Satisfaction with care (0–100)			
Overall satisfaction	1.07 (−1.82; 3.96)	1.80 (−2.09; 5.68)	−6.00
Interpersonal aspects	1.24 (−1.97; 4.45)	2.70 (−1.54; 6.95)	−6.00
Technical competence	0.80 (−2.41; 4.00)	1.45 (−2.78; 5.68)	−6.00
Access to care	1.72 (−1.50; 4.94)	0.55 (−3.82; 4.92)	−6.00
General satisfaction	1.52 (−1.72; 4.76)	1.17 (−3.79; 6.14)	−6.00
Illness perceptions (0–10)			
How much illness affects life	0.01 (−0.50; 0.52)	−0.06 (−0.73; 0.62)	−1.22
How long illness will continue	−0.17 (−0.75; 0.42)	−0.35 (−1.11; 0.42)	−1.07
How much control over illness	−0.13 (−0.74; 0.47)	−0.54 (−1.34; 0.25)	−1.43
How much treatment helps to cure	0.28 (−0.44; 1.00)	0.55 (−0.40; 1.50)	−1.87
How much follow-up care helps to cure	−0.41 (−0.99; 0.17)	−0.38 (−1.14; 0.39)	−1.58
How much symptoms experienced	−0.01 (−0.50; 0.47)	−0.28 (−0.91; 0.35)	−1.23
How concerned about illness	−0.06 (−0.61; 0.49)	−0.16 (−0.87; 0.55)	−1.38
How well understand illness	0.14 (−0.46; 0.75)	0.18 (−0.62; 0.98)	−1.59
How much affects emotionally	−0.13 (−0.68; 0.41)	−0.40 (−1.11; 0.32)	−1.40
Cancer worry scale (1–5)			
Cancer worry	0.03 (−0.18; 0.23)	0.02 (−0.26; 0.29)	−0.51
Distress (0–21)			
Anxiety	−0.09 (−0.69; 0.50)	−0.02 (−0.79; 0.75)	−1.52
Depressive symptoms	0.06 (−0.48; 0.60)	0.31 (−0.42; 1.04)	−1.31

* Analyses were adjusted for age, partner status, education level, number of comorbidities, type of surgery, and FIGO stage.
** Based on −6.00 for satisfaction with care, and −0.5 SD of overall score in usual care group for all other scales.

Table 3
Number and percentages of responses on satisfaction with the follow-up *schedule* and multilevel logistic regression analysis of satisfied vs. not satisfied with the follow-up schedule (reduced FU arm versus usual FU arm (reference), intention-to-treat (ITT) and per-protocol (PP).

Overall (6–36 months)		After surgery		At 6 months		At 12 months		At 36 months	
Satisfaction with follow-up schedule		Reduced FU N (%)	Usual FU N (%)	Reduced FU N (%)	Usual FU N (%)	Reduced FU N (%)	Usual FU N (%)	Reduced FU N (%)	Usual FU N (%)
Intention-to-treat (ITT)									
Yes		104 (80)	99 (77)	129 (93)	107 (79)	123 (94)	102 (78)	65 (90)	78 (82)
No, I prefer more contacts		5 (4)	7 (5)	6 (4)	0 (0)	5 (4)	0 (0)	4 (6)	3 (3)
No, I prefer less contacts		21 (16)	21 (16)	2 (2)	27 (20)	1 (1)	23 (18)	0 (0)	9 (9)
No, I prefer no contacts		0 (0)	1 (0)	1 (1)	2 (2)	2 (2)	3 (2)	3 (4)	5 (5)
Per-protocol (PP)									
Yes		66 (80)	56 (80)	81 (95)	60 (75)	81 (94)	58 (75)	46 (88)	54 (82)
No, I prefer more contacts		3 (4)	6 (9)	2 (2)	0 (0)	4 (5)	1 (1)	3 (6)	1 (2)
No, I prefer less contacts		13 (16)	7 (10)	1 (1)	19 (24)	0 (0)	16 (21)	0 (0)	8 (12)
No, I prefer no contacts		0 (0)	1 (1)	1 (1)	1 (1)	1 (1)	2 (3)	3 (6)	3 (5)
Multilevel logistic regression	**OR (95% CI)***	**OR (95% CI)***		**OR (95% CI)***		**OR (95% CI)***		**OR (95% CI)***	
Intention-to-treat (ITT)	**3.20 (1.65; 6.17)****	1.13 (0.55; 2.30)		**3.65 (1.49; 8.91)****		**3.79 (1.49; 9.67)****		2.03 (0.69; 6.03)	
Per-protocol (PP)	**4.27 (1.81; 10.05)****	0.95 (0.35; 2.59)		**7.55 (2.08; 27.4)****		**5.89 (1.73; 20.0)****		1.87 (0.52; 6.78)	

FU: follow-up.
* Analyses were adjusted for age, partner status, education level, number of comorbidities, type of surgery, and FIGO stage.
** $p < 0.05$, two-sided, superiority testing.

patient-initiated follow-up care may add to increased fear of cancer recurrence [3,18], it appears important to find an optimal balance in reducing scheduled follow-up visits to alleviate sickness identity, while maintaining sufficient visits to provide psychosocial support [11–14].

Our results showed a clear need for more frequent follow-up of those who were worried. Patients who did not participate in the ENSURE trial and those in the reduced arm who were 'high consumers' were more worried. These findings call for follow-up care that addresses the elevated needs of worried patients.

An indication of a discrepancy between the perceived need for follow-up and the follow-up provided by the hospital would be an increase in the number of consultations with the general practitioner. Both our study and the previous Danish RCT of patient-initiated follow-up showed no such substitution [18,30].

Our finding that reduced follow-up did not induce anxiety or depressive symptoms is encouraging and is also consistent with findings from the MELFO-study showing similar levels of mental health (i.e., component summary score of the RAND-36 health-related quality of life measure) in both trial arms [29].

Our study was not powered to assess differences in recurrence or overall survival. A recent Cochrane review of follow-up care after cancer in general found that less intensive follow-up had no effect on overall survival, but was likely to increase the time to detect a recurrence (longer recurrence-free survival) [31]. However, no trials of follow-up care after endometrial cancer were included in this review. The only trial in endometrial cancer that assessed recurrence-free and overall survival is the TOTEM trial, comparing more intensive follow-up (13 visits over 5-years follow-up with regular serological and vaginal cytological testing and CT scans) with minimalistic follow-up (11 visits over 5-years follow-up with no testing/imaging) in 1847 patients [32]. Additional testing did not lead to improved survival or earlier detection of recurrence [32]. Notably, the minimal follow-up in the TOTEM trial is comparable to the usual follow-up in the ENSURE trial. Therefore, no conclusions can be drawn from the TOTEM study about the effect of reduced or patient-initiated follow-up on survival.

Our findings suggest that a reduced follow-up schedule can be implemented without compromising patient satisfaction with care, cancer worry, anxiety, or depressive symptoms. In fact, patients were more satisfied with fewer hospital visits. At the same time, about a third of all eligible patients did not want to be included in this trial, mostly because they wanted usual follow-up care, but sometimes also because they wanted reduced follow-up care. Worry was the main reason for wanting usual follow-up and declining trial participation. Worry was also an important factor associated with high care use in those randomized to the reduced follow-up care arm, demonstrating the necessity to tailor follow-up care to the individual needs of patients. Hence, addressing and reducing worry should be an important element of follow-up care.

Study strengths include the individually randomized design, adequate sample size, inclusion of almost two-thirds of the eligible population, both intention-to-treat and per-protocol analyses, the inclusion of several relevant outcomes, a limited attrition over time for the patient-reported outcome measures, and extensive analyses of selection bias and generalizability of the results. Limitations include that the counselling may have affected the results, as blinding of patients and/or health care providers was not possible. Healthcare providers were generally supportive about introducing reduced follow-up, which may have biased the trial counselling in favor of the reduced follow-up. Therefore, patients may have felt that usual follow-up care was not beneficial, leading to lower satisfaction in this arm. Likewise, it may have led to lower compliance in the usual follow-up care arm.

In conclusion, our results show that a reduced follow-up schedule of four visits over three years does not compromise overall satisfaction with care, cancer worry, anxiety or depressive symptoms compared with the usual follow-up schedule with 8–11 visits over three years. Patients were even more satisfied with the reduced follow-up *schedule*. As a negative impact on survival is very unlikely based on previous literature, the reduced follow-up schedule can be implemented in survivorship care for patients with early-stage endometrial cancer. However, the trial findings may not reflect the preferences of all women with early-stage endometrial cancer, such as those who are more worried. This group may benefit from personalized follow-up care, where follow-up is tailored to the patient's needs. This results in reduced follow-up care as the new standard, but tailored to meet additional needs where indicated.

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Data sharing

After publication, deidentified individual participant data and syntax files will be shared upon request, for scientific purposes, after approval of the proposal, with a signed data access agreement and with investigator support. Contact information can be found at the PROFILES registry webpage: www.profilesregistry.nl/contact. In addition, study protocol can be accessed at: www.nvog.nl/specialismen/oncologie/dgog/gesloten-studies/. Metadata on variables and data collection will be provided.

CRediT authorship contribution statement

Nicole P.M. Ezendam: Writing – review & editing, Writing – original draft, Project administration, Methodology, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Belle H. de Rooij:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Carien L. Creutzberg:** Writing – review & editing, Funding acquisition, Data curation, Conceptualization. **Roy F.P.M. Kruitwagen:** Writing – review & editing, Funding acquisition, Data curation, Conceptualization. **Luc R.P.M. van Lonkhuijzen:** Writing – review & editing, Data curation. **Mirjam J.A. Apperloo:** Writing – review & editing, Data curation. **Kees Gerestein:** Writing – review & editing, Data curation. **Astrid Baalbergen:** Writing – review & editing, Data curation. **Dorry Boll:** Writing – review & editing, Funding acquisition, Data curation, Conceptualization. **M. Caroline Vos:** Writing – review & editing, Funding acquisition, Data curation, Conceptualization. **Lonneke V. van de Poll-Franse:** Writing – review & editing, Writing – original draft, Methodology, Funding acquisition, Formal analysis, Conceptualization.

Declaration of competing interest

Authors have no conflict of interests.

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Appendix A. Deaths and recurrences during study follow-up, N (%)

	Reduced FU ($N = 160$)	Usual FU ($N = 156$)	p-value
DEATHS			
Total number of deaths	7 (4)	4 (3)	0.38
Cause of death*			
Pelvic disease progression	1 (1)	0 (0)	
Distant metastases	3 (2)	0 (0)	
Intercurrent death, second cancer	1 (1)	0 (0)	
Intercurrent death, other	1 (1)	2 (1)	
Other or uncertain	1 (1)	2 (1)	
RECURRENCES			
Total number of recurrences	9 (6)	5 (3)	0.33
Symptomatic			
No, asymptomatic	2 (22)	1 (20)	
Yes, symptomatic	7 (78)	4 (80)	
Location of recurrence - vaginal			
No tumor	2 (22)	0 (0)	
Proximal 1/3 vagina	3 (33)	4 (80)	
Mid 1/3 vagina	0 (0)	0 (0)	
Distal 1/3 vagina	2 (22)	1 (20)	
Multiple vaginal sites	2 (22)	0 (0)	
Location of recurrence – pelvis (up to L5-S1)			
No tumor	5 (56)	5 (100)	
Central recurrence	1 (11)	0 (0)	
Side wall	0 (0)	0 (0)	
Multiple	3 (33)	0 (0)	
Location of recurrence – abdominal/ distant			
No tumor	4 (44)	5 (100)	
Lower para-aortic lymph node metastases (L5-S1 to L3–4)	2 (22)	0 (0)	
Peritonitis carcinomatosa	2 (22)	0 (0)	
Lung	2 (22)	0 (0)	
Bone	1 (11)	0 (0)	
Other	3 (33)	0 (0)	
Time between diagnosis and first recurrence, years			
<1 year	4 (44)	3 (60)	
1–2 years	5 (56)	1 (20)	
2–3 years	0 (0)	1 (20)	

The p-value is based on t-test, tested as a superiority t, two-sided with an alpha on 0.05.

* Causes of death in the reduced follow-up arm included pelvic disease progression (n = 1), distant metastasis ($n = 3$), second cancer (n = 1), gastric perforation ($n = 1$), and ileus bowel obstruction due to a sigmoid tumor ($n = 1$). Causes of death in the usual follow-up arm were urosepsis (n = 2), complications after laparoscopic surgery for cholecystectomy (n = 1), and unknown (n = 1).

Appendix B. Baseline characteristics of patients with and without recurrence over the 3-years follow-up period, N(%)

	Patients with recurrence ($N = 14$)	Patients without recurrence ($N = 302$)
Sociodemographic		
Age at time of diagnosis (M, SD)	68.6 (8)	64.6 (9)
Partner, yes	12 (86)	242 (80)
Employed, yes	3 (21)	93 (31)
Education		
Lower/ primary education	0 (0)	30 (10)
Secondary education (high school)	6 (43)	92 (30)
Secondary vocational education	5 (36)	117 (39)
Higher (vocational) education, university	3 (21)	63 (21)

(*continued*)

	Patients with recurrence ($N = 14$)	Patients without recurrence ($N = 302$)
Clinical		
Comorbidity		
0	2 (14)	37 (12)
1	3 (21)	84 (28)
>1	9 (64)	180 (60)
FIGO stage		
IA	13 (93)	289 (96)
IB	1 (7)	13 (4)
FIGO grade		
I	11 (79)	246 (81)
II	3 (21)	56 (19)
Type of surgery		
TAH-BSO	1 (7)	22 (7)
TAH-BSO with lymphadenectomy	0 (0)	1 (0)
Laparoscopic TLH-BSO or LAVH-BSO	12 (86)	269 (89)
Laparoscopic TLH-BSO or LAVH-BSO with lymphadenectomy	0 (0)	3 (1)
TAH	0 (0)	2 (1)
Other	1 (7)	5 (2)
Complications of surgery		
No complications	14 (100)	280 (93)
Wound infection	0 (0)	1 (0)
Bowel obstruction	0 (0)	4 (1)
Other	0 (0)	17 (6)
Deaths		
Total number of deaths	3 (21)	8 (3)
Cause of death		
Pelvic disease progression	1 (33)	0 (0)
Distant metastases	2 (67)	1 (13)
Intercurrent death, second cancer	0 (0)	1 (13)
Intercurrent death, other	0 (0)	3 (38)
Other or uncertain	0 (0)	3 (38)

TAH: Total abdominal hysterectomy; BSO: Bilateral salpingo oophorectomy; TLH: Total laparoscopic hysterectomy; LAVH: Laparoscopically assisted vaginal hysterectomy.

Appendix C. Number of follow-up visits

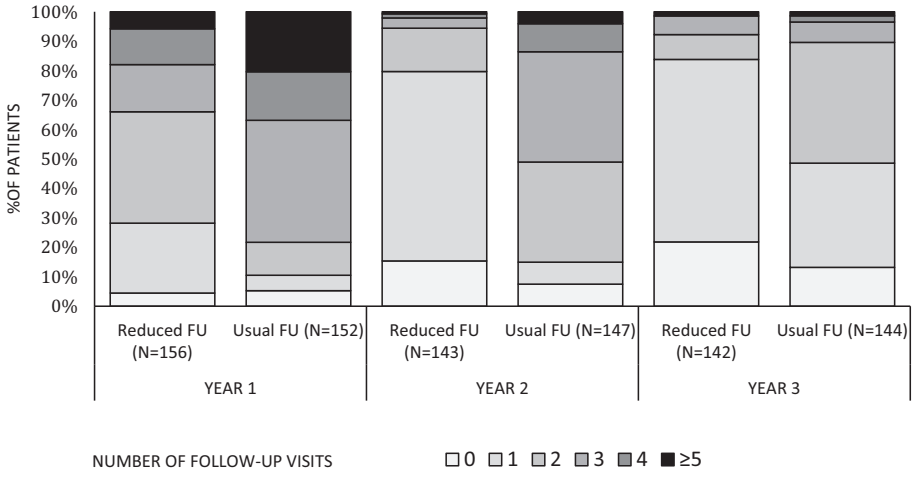

Figure Number of follow-up visits to the gynecologist/nurse specialist by trial arm and follow-up year. FU: follow-up.

Appendix D. Means with standard deviations (SD) at all time points for satisfaction with care (PSQ), illness perceptions (BIPQ), cancer worry (IoC V2), and distress (HADS). Multilevel linear regression analysis, both intention-to-treat and per-protocol; Unstandardized beta's of reduced follow-up care vs. usual follow-up care as reference condition

	After surgery			At 6 months			At 12 months			At 36 months		
Intention-to-treat (ITT)	Reduced FU M (SD) ($N = 150$)	Usual FU M (SD) ($N = 149$)	Beta (95% CI)*	Reduced FU M (SD) ($N = 144$)	M (SD) Usual FU ($N = 143$)	Beta (95% CI)*	Reduced FU M (SD) ($N = 133$)	Usual FU M (SD) ($N = 130$)	Beta (95% CI)*	Reduced FU M (SD) (=104)	Usual FUl M (SD) ($N = 102$)	Beta (95% CI)*
Satisfaction with care (0–100)												
Overall satisfaction	83.9 (10.8)	82.1 (12.7)	1.71 (−1.25; 4.66)	81.9 (13.0)	80.4 (15.0)	1.36 (−1.66; 4.38)	82.7 (13.4)	82.3 (13.0)	0.60 (−2.48; 3.67)	81.7 (12.4)	80.3 (15.0)	1.42 (−1.98; 4.82)
Interpersonal aspects	88.6 (12.6)	87.0 (13.9)	1.48 (−1.87; 4.83)	86.4 (14.8)	85.2 (16.1)	1.67 (−1.77; 5.11)	86.8 (14.5)	87.2 (14.6)	0.12 (−3.40; 3.64)	86.6 (14.8)	84.4 (16.3)	2.66 (−1.37; 6.69)
Technical competence	82.4 (12.7)	80.2 (15.0)	2.30 (−1.11; 5.70)	80.1 (14.2)	79.0 (16.3)	1.20 (−2.27; 4.66)	80.2 (15.5)	80.7 (15.4)	0.21 (−3.35; 3.76)	79.1 (15.2)	79.1 (17.6)	0.46 (−3.51; 4.43)
Access to care	79.6 (12.7)	78.1 (14.2)	1.24 (−2.16; 4.64)	77.9 (14.7)	76.7 (16.1)	0.55 (−2.91; 4.01)	80.5 (15.0)	78.1 (14.6)	1.81 (−1.75; 5.36)	78.1 (15.5)	75.2 (19.6)	2.14 (−1.82; 6.11)
General satisfaction	84.3 (15.0)	82.0 (17.2)	2.16 (−1.78; 6.11)	83.2 (16.4)	80.7 (20.2)	1.89 (−2.13; 5.91)	83.1 (16.5)	81.9 (18.6)	0.95 (−3.18; 5.09)	81.0 (18.5)	79.9 (20.9)	0.46 (−4.19; 5.11)
Illness perceptions (0–10)												
How much illness affects life	2.7 (2.3)	3.3 (2.8)	−0.47 (−1.04; 0.10)	2.7 (2.5)	2.6 (2.5)	0.10 (−0.48; 0.68)	2.3 (2.4)	2.2 (2.5)	0.16 (−0.43; 0.75)	1.7 (2.2)	2.5 (2.8)	−0.64 (−1.28; 0.00)
How long illness will continue	1.8 (2.1)	2.4 (2.9)	−0.42 (−1.04; 0.21)	2.2 (2.7)	2.2 (2.9)	0.10 (−0.53; 0.73)	1.9 (2.6)	2.2 (2.9)	−0.36 (−1.02; 0.30)	1.6 (3.2)	2.0 (2.8)	−0.13 (−0.84; 0.58)
How much control over illness	2.2 (2.7)	2.8 (3.2)	−0.38 (−1.10; 0.34)	2.7 (3.0)	3.0 (3.4)	−0.12 (−0.86; 0.62)	2.1 (3.0)	2.7 (3.2)	−0.48 (−1.23; 0.28)	2.9 (3.2)	2.9 (3.2)	0.23 (−0.62; 1.08)
How much treatment helps to cure	7.2 (3.4)	6.7 (3.8)	0.68 (−0.18; 1.53)	6.4 (3.6)	6.2 (3.7)	0.43 (−0.45; 1.30)	6.3 (3.9)	6.0 (3.8)	0.50 (−0.39; 1.40)	6.0 (3.9)	6.4 (3.7)	−0.16 (−1.16; 0.83)
How much follow-up care helps to cure	2.4 (2.8)	3.0 (3.1)	−0.45 (−1.15; 0.26)	2.7 (3.0)	3.3 (3.2)	−0.53 (−1.24; 0.19)	2.4 (2.9)	2.6 (3.0)	−0.14 (−0.88; 0.59)	2.1 (2.7)	2.8 (3.3)	−0.63 (−1.45; 0.19)
How much symptoms experienced	1.82 (2.2)	2.37 (2.7)	−0.35 (−0.90; 0.20)	2.03 (2.5)	1.87 (2.4)	0.20 (−0.36; 0.76)	1.6 (2.4)	1.8 (2.6)	−0.18 (−0.75; 0.40)	1.2 (1.8)	1.6 (2.5)	−0.35 (−0.98; 0.28)
How concerned about illness	2.84 (2.7)	3.20 (3.0	−0.13 (−0.73; 0.47)	2.45 (2.5)	2.56 (2.7)	0.03 (−0.58; 0.64)	2.2 (2.5)	2.3 (2.8)	0.14 (−0.48; 0.76)	1.5 (2.1)	2.3 (2.9)	−0.54 (−1.21; 0.13)
How well understand illness	6.3 (3.3)	6.7 (3.1)	−0.27 (−1.00; 0.46)	6.1 (3.3)	6.5 (3.1)	−0.32 (−1.06; 0.42)	6.1 (3.3)	6.5 (3.1)	0.43 (−0.33; 1.20)	6.2 (3.3)	6.0 (3.4)	0.10 (−0.76; 0.95)
How much affects emotionally	2.32 (2.6)	3.0 (2.9)	−0.52 (−1.12; 0.09)	2.26 (2.5)	2.57 (2.8)	−0.26 (−0.88; 0.35)	2.0 (2.6)	2.1 (2.1)	0.06 (−0.57; 0.68)	1.4 (2.1)	2.2 (2.9)	−0.44 (−1.12; 0.25)
Cancer worry scale (1–5)												
Cancer worry	2.3 (0.9)	2.4 (1.1)	−0.01 (−0.23; 0.22)	2.3 (1.0)	2.3 (1.0)	0.03 (−0.19; 0.26)	2.1 (1.0)	2.1 (1.0)	−0.00 (−0.20; 0.20)	2.0 (0.9)	2.1 (1.0)	−0.03 (−0.27; 0.22)
Distress (0–21)												
Anxiety	5.9 (2.8)	5.9 (2.8)	0.04 (−0.63; 0.70)	6.1 (2.8)	6.1 (2.9)	0.20 (−0.47; 0.88)	5.8 (2.8)	6.1 (2.9)	−0.04 (−0.73; 0.65)	6.0 (2.8)	6.5 (3.4)	−0.11 (−0.85; 0.62)
Depressive symptoms	5.2 (2.5)	5.1 (2.3)	−0.00 (−0.58; 0.57)	5.4 (2.6)	5.2 (2.4)	0.11 (−0.47; 0.70)	5.5 (2.9)	5.3 (2.7)	0.02 (−0.58; 0.62)	5.6 (2.8)	5.5 (2.8)	0.09 (−0.55; 0.73)
Per-protocol (PP)	**M (SD) reduced FU (N = 95)**	**M (SD) Usual FU (N = 87)**	**Beta (95% CI)***	**M (SD) reduced FU (N = 89)**	**M (SD) Usual FU (N = 81)**	**Beta (95% CI)***	**M (SD) reduced FU ($N = 85$)**	**M (SD) Usual FU ($N = 78$)**	**Beta (95% CI)***	**M (SD) reduced FU (=62)**	**M (SD) Usual FU (N = 67)**	**Beta (95% CI)***
Satisfaction with care (0–100)												
Overall satisfaction	83.1 (11.3)	82.3 (13.7)	1.68 (−2.37; 5.73)	82.7 (13.0)	81.1 (15.5)	2.52 (−1.60; 6.65)	82.4 (13.8)	83.0 (14.0)	0.82 (−3.35; 4.99)	82.2 (12.0)	81.2 (15.7)	1.54 (−2.86; 5.95)

(*continued*)

Per-protocol (PP)	M (SD) reduced FU (N = 95)	M (SD) Usual FU (N = 87)	Beta (95% CI)*	M (SD) reduced FU (N = 89)	M (SD) Usual FU (N = 81)	Beta (95% CI)*	M (SD) reduced FU (*N* = 85)	M (SD) Usual FU (*N* = 78)	Beta (95% CI)*	M (SD) reduced FU (=62)	M (SD) Usual FU (N = 67)	Beta (95% CI)*
Interpersonal aspects	87.7 (13.4)	86.1 (15.2)	2.41 (−2.15; 6.98)	87.7 (14.3)	85.3 (16.8)	3.67 (−1.01; 8.36)	86.7 (15.0)	87.3 (15.6)	0.95 (−3.78; 5.68)	87.0 (15.4)	84.0 (17.6)	4.17 (−0.96; 9.29)
Technical competence	81.9 (13.1)	80.4 (16.1)	2.65 (−1.90; 7.21)	80.5 (13.9)	80.1 (17.2)	1.19 (−3.46; 5.83)	79.8 (15.5)	81.1 (15.6)	0.44 (−4.26; 5.15)	80.2 (14.9)	79.7 (18.1)	1.68 (−3.35; 6.70)
Access to care	78.8 (12.9)	79.4 (14.3)	0.03 (−4.45; 4.51)	78.0 (15.4)	77.1 (16.8)	1.27 (−3.29; 5.82)	79.8 (15.5)	79.6 (15.2)	0.62 (−3.99; 5.23)	77.5 (16.1)	79.0 (16.2)	−2.16 (−7.04; 2.72)
General satisfaction	83.7 (15.9)	80.8 (18.3)	4.12 (−1.24; 4.51)	83.9 (16.0)	81.2 (20.7)	3.28 (−2.19; 8.75)	82.6 (17.1)	82.9 (19.3)	0.61 (−4.93; 6.15)	80.7 (20.1)	81.6 (20.6)	−0.58 (−6.51; 5.36)
Illness perceptions (0–10)												
How much illness affects life	2.4 (2.2)	3.3 (2.9)	−0.96 (−1.71; −0.21)	2.6 (2.6)	2.7 (2.6)	−0.17 (−0.93; 0.60)	2.6 (2.5)	2.1 (2.4)	0.32 (−0.45; 1.09)	1.7 (2.4)	2.3 (2.6)	−0.65 (−1.46; 0.16)
How long illness will continue	1.8 (2.2)	2.5 (3.1)	−0.61 (−1.44; 0.22)	2.3 (2.8)	2.5 (3.0)	−0.13 (−0.96; 0.71)	1.9 (2.5)	2.1 (2.9)	−0.27 (−1.13; 0.59)	1.5 (2.5)	2.0 (2.9)	−0.49 (−1.38; 0.41)
How much control over illness	2.0 (2.7)	3.0 (3.4)	−0.93 (−1.89; 0.03)	2.7 (3.0)	3.4 (3.8)	−0.59 (−1.57; 0.39)	2.0 (2.9)	2.9 (3.3)	−0.90 (−1.89; 0.10)	3.0 (3.3)	3.1 (2.9)	−0.14 (−1.21; 0.92)
How much treatment helps to cure	7.0 (3.5)	7.2 (3.6)	0.15 (−0.94; 1.25)	6.5 (3.6)	6.2 (3.7)	0.66 (−0.45; 1.78)	6.1 (4.0)	6.0 (3.9)	0.64 (−0.50; 1.77)	6.2 (3.8)	6.2 (3.8)	0.15 (−1.06; 1.35)
How much follow-up care helps to cure	2.2 (2.7)	3.1 (3.2)	−0.83 (−1.75; 0.09)	2.8 (3.2)	3.2 (3.3)	−0.37 (−1.30; 0.56)	2.5 (3.0)	2.5 (3.0)	−0.08 (−1.04; 0.87)	2.0 (2.5)	2.7 (3.3)	−0.78 (−1.80; 0.24)
How much symptoms experienced	1.6 (2.1)	2.5 (2.8)	−0.82 (−1.53; −0.11)	1.9 (2.5)	2.1 (2.5)	−0.17 (−0.90; 0.55)	1.6 (2.3)	1.8 (2.5)	−0.32 (−1.06; 0.41)	1.2 (1.8)	1.5 (2.3)	−0.45 (−1.22; 0.33)
How concerned about illness	2.6 (2.7)	3.3 (3.0)	−0.57 (−1.35; 0.20)	2.3 (2.5)	2.6 (2.6)	−0.35 (−1.13; 0.44)	2.4 (2.6)	2.2 (2.7)	0.17 (−0.63; 0.96)	1.5 (2.3)	1.9 (2.5)	−0.52 (−1.35; 0.31)
How well understand illness	6.1 (3.4)	6.8 (3.0)	−0.31 (−1.26; 0.64)	6.1 (3.2)	6.7 (3.1)	−0.17 (−1.14; 0.80)	6.2 (3.2)	6.3 (3.1)	0.29 (−0.70; 1.27)	6.2 (3.4)	5.9 (3.5)	0.23 (−0.84; 1.30)
How much affects emotionally	2.1 (2.5)	3.2 (3.1)	−1.09 (−1.89; −0.29)	2.3 (2.6)	2.9 (2.9)	−0.67 (−1.49; 0.14)	2.1 (2.5)	2.1 (2.7)	−0.11 (−0.94; 0.71)	1.5 (2.2)	2.1 (2.7)	−0.53 (−1.40; 0.34)
Cancer worry scale (1–5)												
Cancer worry	2.3 (0.9)	2.4 (1.1)	−0.07 (−0.36; 0.22)	2.2 (1.0)	2.2 (1.0)	−0.01 (−0.31; 0.28)	2.1 (1.0)	2.1 (1.0)	−0.04 (−0.30; 0.23)	2.0 (1.0)	2.0 (0.9)	−0.00 (−0.31; 0.31)
Distress (0–21)												
Anxiety	6.0 (2.9)	6.2 (3.0)	−0.25 (−1.12; 0.62)	6.1 (2.8)	6.1 (2.7)	0.06 (−0.82; 0.95)	6.0 (2.8)	5.8 (2.6)	0.31 (−0.59; 1.20)	6.3 (3.1)	6.4 (3.2)	−0.01 (−0.93; 0.92)
Depressive symptoms	5.5 (2.7)	5.3 (2.3)	0.03 (−0.74; 0.80)	5.6 (2.7)	5.3 (2.6)	0.15 (−0.63; 0.92)	5.8 (3.0)	5.2 (2.6)	0.26 (−0.53; 1.05)	5.9 (3.0)	5.5 (2.7)	0.35 (−0.47; 1.17)

* Analyses were adjusted for age, partner status, education level, number of comorbidities, type of surgery, and FIGO stage.

Appendix E. Analysis of selection bias

Selection bias of our study sample may affect the generalizability of the findings. Trial participants may have had a preference for reduced follow-up and therefore the participants in the control condition may have been less satisfied. According to Rogers' diffusion of innovations theory [33] (a model of adaptation of innovations), participants could be innovators, early adopters and the early majority. In addition, those who chose not to participate in the trial may reflect people who preferred the usual follow-up care. This group may actually consist of two sub-groups. i.e. 1) a group that may just not be ready for reduced follow-up care and/or 2) a group that has specific reasons for not participating. Using Rogers' theory of adoption, the first group is likely to change over time, when a decreased follow-up schedule would become the new standard of care, in which case more and more patient are expected to find this new schedule of follow-up care acceptable (the late majority and the laggards). The second group may have had specific reasons for not participating, such as patient (e.g. worry) and tumor characteristics (high grade/stage). This group is important because they may need a more personalized follow-up that takes into account their specific needs.

To better understand the degree of selection bias and generalizability we conducted three post hoc analyses:

1. A comparison between the ENSURE study population and the background population, as registered in the Netherlands Cancer Registry (NCR).

Within the NCR we selected patients who would have been eligible for the ENSURE trial, based on the eligibility criteria. We selected on: inclusion period per hospital, tumor type, FIGO stage, grade, no clear cell or papillary serous histology, no radiotherapy, no previous tumor, still alive 3 months after diagnosis. We compared the following characteristics between ENSURE participants and the sample population: age, FIGO stage, grade, and lymphadenectomy.

2. An analysis of a short non-participant questionnaire.

If patients did not wish to participate in the ENSURE trial, we asked them to complete a short questionnaire about the reason for non-participation. For this purpose, they also completed an informed consent form. This short questionnaire was completed by 56 women.

3. Within the reduced follow-up care arm, a comparison of participants who had more follow-up care than protocolized ('high consumers') with the participants who had follow-up care according schedule or less than scheduled. The following characteristics of participants were compared using chi-square and *t*-tests: sociodemographic (age, partner status, employment status, educational level), clinical (comorbidity, stage, grade, type of surgery, complications), psychological (cancer worry, anxiety, depressive symptoms).

Appendix E1

Characteristics of the background population selected from Netherlands Cancer Registry (including the ENSURE study sample) and the ENSURE study sample, N(%).

	Background population selected from NCR*	ENSURE study sample
	N = 484	*N* = 316
Age at time of diagnosis (M, SD)	64.6 (11)	64.8 (9)
FIGO stage		
IA	435 (90)	302 (96)
IB	49 (10)	14 (4)
TNM grade		
I	364 (75)	133 (83)
II	120 (25)	27 (17)
Lymphadenectomy		
Yes	8 (2)	4 (1)
No	476 (98)	312 (99)

* Patients with a diagnosis within inclusion period of ENSURE trial within ENSURE hospital who met inclusion criteria (endometrial cancer; age ≥ 18 years; FIGO stage 1 A or 1B, TNM grade 1 or 2, no clear cell or papillary serous histology, no radiotherapy, no other primary tumor) and being alive >90 days after diagnosis were selected from the Netherlands cancer registry (NCR).

Appendix E2

Results of non-participant survey and baseline questionnaire in ENSURE study sample, N(%).

	Non-participant N = 59	ENSURE study sample (N = 316)	P-value
Sociodemographic			
Age, M (SD)	62.1 (9)	64.8 (9)	**0.04**
Partner	44 (75)	254 (80)	0.52
Education			
Lower/ primary education	7 (12)	30 (9)	0.17
Secondary education (high school)	13 (22)	98 (31)	
Secondary vocational education	25 (42)	122 (39)	
Higher (vocational) education, university	13 (22)	66 (21)	
Reasons for non-participation			
Don't want to be randomized, wants usual care	18 (32)	NA	
Don't want to be randomized, wants reduced care	6 (11)	NA	
Usual care is important for my health	23 (41)	NA	
It is a difficult choice to decide to participate or not	8 (14)	NA	
I am worried to receive less follow-up care than usual	15 (28)	NA	
I am worried that I will not receive immediate help for symptoms or questions	8 (14)	NA	
Satisfaction with care (0–100)			
Access to care	76.5 (16)	78.8 (13)	0.31
General satisfaction	82.5 (17)	83.1 (16)	0.78
Cancer worry			
Cancer worry	2.8 (0.8)	2.4 (1.0)	**<0.01**
Illness perceptions (0–10)			
How much illness affects life	3.3 (2.7)	3.0 (2.6)	0.37
How long illness will continue	2.5 (2.2)	2.1 (2.6)	0.23
How much control over illness	2.2 (2.6)	2.5 (3.0)	0.44
How much treatment helps to cure	6.4 (3.4)	6.9 (3.6)	0.33
How much follow-up care helps to cure	3.0 (3.0)	2.7 (3.0)	0.51
How much symptoms experienced	1.9 (2.0)	2.1 (2.5)	0.58
How concerned about illness	3.6 (2.8)	3.0 (2.8)	0.16
How well understand illness	5.2 (3.3)	6.5 (3.2)	**<0.01**
How much affects emotionally	3.4 (2.7)	2.6 (2.8)	**0.046**

NA = Not applicable.

Appendix E3

Comparison of patients of the reduced follow-up care arm of the ENSURE trial who had more visits than per protocol (>5 in 3 years; 'high consumers') vs. per protocol or less (≤ 5 in 3 years).

	Visits per protocol or fewer (N = 135)	More visits than protocol (N = 27)	P-value
Sociodemographic			
Age at time of diagnosis (M, SD)	64.9 (9)	65.6 (9)	0.70
Partner, yes	111 (83)	25 (93)	0.23
Employed, yes	94 (71)	20 (74)	0.72
Education			
Lower/ primary education	16 (12)	4 (15)	0.69
Secondary education (high school)	43 (32)	7 (26)	
Secondary vocational education	46 (35)	12 (44)	
Higher (vocational) education, university	28 (21)	4 (15)	
CLINICAL			
Comorbidity			
0	21 (16)	3 (11)	0.57
1	38 (29)	6 (22)	
>1	74 (56)	18 (67)	
FIGO stage			
IA	127 (95)	26 (96)	0.85
IB	6 (5)	1 (4)	
TNM grade			
I	117 (88)	16 (59)	**<0.01**
II	16 (12)	11 (41)	
Type of surgery			
TAH-BSO	6 (5)	2 (7)	**0.01**
TAH-BSO with lymphadenectomy	0 (0)	0 (0)	
Laparoscopic TLH-BSO or LAVH-BSO	125 (94)	22 (81)	
Laparoscopic TLH-BSO or LAVH-BSO with lymphadenectomy	1 (1)	0 (0)	
TAH	1 (1)	1 (4)	
Other	0 (0)	2 (7)	
Complications of surgery			
No complications	126 (95)	22 (81)	**0.04**
Wound infection	1 (1)	2 (7)	
Other	5 (5)	3 (11)	
Combination	1 (1)	0 (0)	
Satisfaction			
Baseline satisfaction with care (0–100)			
Overall satisfaction	83.8 (11)	84.1 (12)	0.92
Interpersonal aspects	88.7 (13)	87.8 (12)	0.74
Technical competence	82.3 (13)	83.1 (14)	0.78
Access to care	79.4 (12)	80.6 (14)	0.69
General satisfaction	84.4 (15)	83.9 (15)	0.90
Baseline satisfaction with follow-up scheme			
Yes	88 (80)	16 (80)	0.24
No, I prefer more contacts	3 (3)	2 (10)	
No, I prefer less contacts	19 (17)	2 (10)	
No, I prefer no contacts	0 (0)	0 (0)	
Baseline cancer worry	2.3 (0.9)	2.7 (0.9)	**0.03**
Baseline anxiety	5.8 (2.8)	6.3 (2.9)	0.41
Baseline depressive symptoms	5.3 (2.6)	4.6 (2.3)	0.20

TAH: Total abdominal hysterectomy; BSO: Bilateral salpingo oophorectomy; TLH: Total laparoscopic hysterectomy; LAVH: Laparoscopically assisted vaginal hysterectomy.

Appendix F. Collaborators ENSURE study group

Initials	First name	Last name	Center
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(continued on next page)

(*continued*)

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M.	Majoie	Hemelaar	NA
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