Outpatient versus inpatient uterine polyp treatment for abnormal uterine bleeding: randomised controlled non-inferiority study

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ABSTRACT

OBJECTIVE

To compare the effectiveness and acceptability of outpatient polypectomy with inpatient polypectomy.

DESIGN

Pragmatic multicentre randomised controlled non-inferiority study.

SETTING

Outpatient hysteroscopy clinics in 31 UK National Health Service hospitals.

PARTICIPANTS

507 women who attended as outpatients for diagnostic hysteroscopy because of abnormal uterine bleeding and were found to have uterine polyps.

INTERVENTIONS

Participants were randomly assigned to either outpatient uterine polypectomy under local anaesthetic or inpatient uterine polypectomy under general anaesthesia. Data were collected on women's self reported bleeding symptoms at baseline and at 6, 12, and 24 months. Data were also collected on pain and acceptability of the procedure at the time of polypectomy.

MAIN OUTCOME MEASURES

The primary outcome was successful treatment, determined by the women's assessment of bleeding at six months, with a prespecified non-inferiority margin of 25%. Secondary outcomes included generic (EQ-5D) and disease specific (menorrhagia multi-attribute scale) quality of life, and feasibility and acceptability of the procedure.

RESULTS

73% (166/228) of women in the outpatient group and 80% (168/211) in the inpatient group reported successful treatment at six months (intention to treat relative risk 0.91, 95% confidence interval 0.82 to 1.02; per protocol relative risk 0.92, 0.82 to 1.02). Failure to remove polyps was higher (19% *v* 7%; relative risk 2.5, 1.5 to 4.1) and acceptability of the procedure was lower (83% *v* 92%; 0.90, 0.84 to 0.97) in the outpatient group Quality of life did not differ significantly between the groups. Four uterine perforations, one of which necessitated bowel resection, all occurred in the inpatient group.

CONCLUSIONS

Outpatient polypectomy was non-inferior to inpatient polypectomy. Failure to remove a uterine polyp was, however, more likely with outpatient polypectomy and acceptability of the procedure was slightly lower.

TRIAL REGISTRATION

International Clinical Trials Registry 65868569.

WHAT IS ALREADY KNOWN ON THIS TOPIC

A systematic review identified just two small comparative studies that evaluated outpatient versus inpatient polypectomy and found no difference in improvement of symptoms

The available data do not provide precise estimates of relative effectiveness, and the rates of technical failure, patient acceptability, and cost effectiveness are uncertain

WHAT THIS STUDY ADDS

In this study outpatient polypectomy was not inferior to inpatient polypectomy for the relief of abnormal bleeding associated with uterine polyps, confirming the provisional findings from earlier small, comparative studies

The overall safety, feasibility, and acceptability of outpatient polypectomy support the implementation of outpatient hysteroscopic services

Introduction

Abnormal uterine bleeding affects women of all ages and is the commonest gynaecological reason for referral to secondary care.[1 2] Uterine polyps are focal outgrowths of the endometrium and are often found in association with uterine bleeding in both premenopausal and postmenopausal women.[3 4] Such polyps are detected in an estimated 20–40% of women with abnormal uterine bleeding[3–7] following outpatient investigation with pelvic ultrasonography or hysteroscopy. The available evidence supports the current practice of surgically removing uterine polyps to help alleviate the symptoms of bleeding.[8 9] Conventional practice is to undertake this procedure under general anaesthesia in hospital. However, with advances in endoscopic technology it is now possible to perform uterine polypectomy under hysteroscopic guidance in an outpatient setting without the need for hospital admission and anaesthesia.[10–12] Furthermore, treatment can be carried out at the same time as diagnosis; the "see and treat" approach.[13]

The convenience and immediacy of outpatient treatment may seem advantageous over traditional practice. However, the limitations of operating in the genital tract using miniature equipment in a conscious patient may offset any apparent benefits. We carried out a multicentre, pragmatic, non-inferiority, randomised controlled trial (the Outpatient Polyp Treatment trial) to evaluate the effectiveness and acceptability of outpatient polyp treatment compared with traditional inpatient surgical treatment.

Methods

Population

All women with abnormal uterine bleeding and a uterine polyp diagnosed at outpatient hysteroscopy[13] were eligible to be recruited into the trial. Abnormal uterine

bleeding included heavy menstrual bleeding, intermenstrual bleeding, and postmenopausal bleeding. Women were excluded before randomisation if outpatient polypectomy was considered not feasible, malignancy was suspected, or another surgical uterine intervention was needed. All participants provided written informed consent. In clinics that provided a "see and treat" service, consent was obtained and the patient was registered on the online randomisation system before the diagnostic hysteroscopy, so that if a uterine polyp was diagnosed, randomisation could be performed quickly, without a lengthy interruption, should outpatient polypectomy be allocated.

Randomisation and blinding

Patients were randomised in a 1:1 ratio to removal of uterine polyps in either an outpatient or an inpatient setting using a web based central randomisation service at the University of Birmingham Clinical Trials Unit. Blinding of the patients and clinicians was not possible owing to the nature of the interventions. Minimisation was used to achieve balance between groups for predominant bleeding (heavy, intermenstrual, or postmenopausal), location (fundal or non-fundal), and type of polyp (glandulocystic or fibrous).

Procedures

After the diagnostic hysteroscopy, we randomised eligible women. Those allocated outpatient polypectomy in most instances underwent the procedure immediately after diagnosis, although some participants had their treatment scheduled, depending on local circumstances, within the next eight weeks. Outpatient polypectomies were performed in the outpatient hysteroscopy clinic and inpatient procedures were performed in operating theatres, under general or regional anaesthesia. Polyp removal was carried out under direct hysteroscopic vision using miniature mechanical or electrosurgical instruments, with or without the need for minor degrees of cervical dilatation and local anaesthesia (direct cervical infiltration or paracervical injection). Blind avulsion with small polypectomy forceps was also allowed. In addition, women allocated inpatient polypectomy could have traditional dilatation and curettage or polyp removal under vision using a resectoscope. Clinicians were free to choose the technique for polypectomy post-randomisation. Endometrial biopsy and medical treatments were permitted when indicated.

Outcome measures and follow-up

The primary outcome was successful treatment, determined by the women's assessment of their bleeding at six months using a dichotomous (success or fail) outcome measure. For women with heavy menstrual bleeding, we considered treatment to be a success if bleeding had reduced to acceptable levels. For women with intermenstrual or postmenopausal bleeding the definition was cessation of bleeding. We considered this outcome to be the most clinically relevant and it was assessed using a non-inferiority framework with a prespecified margin of 25%.

Secondary measures of bleeding outcome included women's subjective assessment of their bleeding using visual analogue scales (0 for no bleeding to 100 heaviest imaginable and 0 for no days bleeding to 100 for bleeding every day) and response to the question "compared to before your treatment, would you say your bleeding is?" on an ordered Likert scale (much better, little better, same, worse). We measured health related quality of life using the generic EuroQol EQ-5D-3L[14] and the disease specific menorrhagia multi-attribute scale.[15] All clinical data were collected at baseline and then by post at 6, 12, and 24 months post-randomisation.

We also evaluated patient experience by asking the women to rate their level of pain one hour after the procedure and on discharge from hospital using a visual analogue scale (0 no pain to 100 worst imaginable pain). Women undergoing outpatient polypectomy also rated the level of pain during the procedure. Acceptability of the procedure was assessed using Likert scales and structured questions. This was supplemented by a series of semistructured qualitative telephone interviews in a purposive sample of women one week after the procedure. We collected perioperative and postoperative data and included rates of successful polyp removal, complications, adverse events, and further treatment.

Study oversight

An independent trial steering committee and an independent data monitoring and ethics committee provided oversight for the study; on the basis of three reviews of interim data there was no reason to stop or modify the trial on the basis of pragmatic stopping criteria.[16]

Statistical analysis

The sample size was based on data suggesting that patient rated success of treatment at six months would be 90% for inpatient polypectomy and 80% for outpatient polypectomy.[12] We determined that to show with 90% power (two sided $P<0.05$) that success rates with outpatient polypectomy were no lower than 68% (a 25% non-inferiority margin) required 400 women. This was increased to 480 to allow for 15% loss to follow-up. The prespecified non-inferiority margin of 25% (relative reduction) was based on the assumptions that outpatient polypectomy would be more convenient for women and cheaper, permitting it to be considered the treatment of choice even if fewer women had alleviation of bleeding symptoms.

Primary analyses were by intention to treat, but we also carried out per protocol sensitivity analyses for the primary outcome as protection against any theoretical increase in the risk of type I error.[17] The per protocol analysis included only those women who received their allocated treatment. For the primary outcome we calculated point estimates and two sided 95% confidence intervals from unadjusted risk ratios; the study could only declare non-inferiority if the lower band of the confidence interval was not lower than 0.75. We performed

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extensive sensitivity analysis on the primary outcome, particularly for missing responses.

Using analysis of covariance we analysed secondary endpoints measured on continuous scales at each time point, adjusting for baseline score, along with a further repeated measures analysis including all assessment time points.[18] Models here included variables allowing for group, time, and baseline score. To test for differences in efficacy between prespecified subgroups for the primary outcome, we included treatment by subgroup interaction variables in the linear model. We calculated adjusted estimates of difference for the primary and main patient reported secondary outcomes through the addition of the minimisation variables to the corresponding linear models. Output here was similar to the unadjusted results. We used paired *t* tests to analyse changes from baseline score within groups. Standard tests were used for other outcome measures: Cochran-Armitage test for trend for ordinal responses, *t* tests for continuous data, and χ^2 tests for binary responses. The non-inferiority hypothesis did not apply for these other end points; we present 95% confidence intervals and P values from two sided superiority tests. SAS version 9.2 was used for analyses.

Table 1 | Baseline characteristics of women receiving polypectomy for abnormal uterine bleeding. Values are numbers (percentages) unless stated otherwise

Characteristics	Outpatient polypectomy (n=254)	Inpatient polypectomy (n=253)
Mean (SD) age (years)	50 (10)	51 (11)
Ethnicity:		
White	207 (88)	179 (87)
Asian	17 (7)	16 (7)
Black	11 (5)	9 (4)
Other	1 (<1)	1 (<1)
Not given/not known	18	48
Predominant bleeding complaint at randomisation*:		
Postmenopausal†	113 (44)	114 (45)
Heavy menstrual‡	77 (30)	76 (30)
Intermenstrual§	64 (25)	63 (25)
Site of uterine polyp*:		
Fundal	99 (39)	99 (39)
Non-fundal	155 (61)	154 (61)
Type of uterine polyp*:		
Glandular	190 (75)	188 (74)
Fibrous	64 (25)	65 (26)
No of polyps:		
1	193 (76)	201 (79)
2	40 (16)	43 (17)
≥3	21 (8)	9 (4)
Other benign disease:		
None	251 (99)	250 (99)
Submucosal fibroid, adhesion, and septum	0	1 (<1)
Adhesion and septum	0	1 (<1)
Submucosal fibroid	2 (1)	0
Septum	1 (<1)	1 (<1)

10 women (2%) had a history of taking tamoxifen (five allocated to each group). Five of these were currently taking the treatment (two in inpatient group, three in outpatient group).
*Minimisation variable and predefined subgroup.
†29 of these women (13%) were currently taking a continuous combined "no bleed" hormone replacement therapy (14 allocated inpatient, 15 allocated outpatient).
‡Includes one postmenopausal woman (1%) taking sequential hormone replacement therapy (allocated inpatient).
§Includes six postmenopausal women (5%) taking a sequential hormone replacement therapy (two allocated inpatient, four allocated outpatient).

Results

Patients and follow-up

Overall, 507 women with abnormal uterine bleeding and uterine polyps from 31 UK National Health Service centres were randomised between April 2008 and July 2011. Baseline characteristics of the women in both groups were similar (table 1). For 45% (227/507) of those randomised, the initial problem was postmenopausal bleeding, 30% (153/507) had heavy menstrual bleeding, and 25% (127/507) had intermenstrual bleeding. In total, 230/254 (91%) women in the outpatient group received their randomised allocation compared with 206/253 (81%) in the inpatient group (fig 1). Seventy two per cent (174/242, 12 dates missing) of the women allocated to outpatient polypectomy were treated in see and treat clinics. Primary outcome responses were available from 439/507 (87%) participants at six months. Twenty eight women underwent qualitative telephone interviews.

Primary outcome: treatment success

Overall, 73% (166/228) of women in the outpatient polypectomy group and 80% (168/211) in the inpatient polypectomy group reported a successful response to surgery at six months (intention to treat relative risk 0.91, 95% confidence interval 0.82 to 1.02; per protocol relative risk 0.92, 95% confidence interval 0.82 to 1.02). The lower ends of the confidence intervals showed that outpatient polypectomy was at most 18% worse than inpatient treatment and was within the 25% margin of non-inferiority (fig 2). In absolute terms this translated to a number needed to treat to harm of 15 with outpatient treatment (95% confidence interval number needed to treat to harm of 6 to number needed to benefit of 39). By one and two years the corresponding proportions were similar between groups, producing relative risks close to unity (see supplementary table A1). Treatment effect did not seem to differ according to any of the predefined subgroups; predominant bleeding complaint, polyp site and type, or through the various sensitivity analyses performed (see supplementary tables A2-A4).

Operative results

Partial or failed removals occurred in 46/242 (19%) of the outpatient group and 18/233 (7%) in the inpatient group (relative risk 2.5, 95%confidence interval 1.5 to 4.1; P<0.001). The most common reason for incomplete removal in the outpatient group was patient discomfort (table 2). Overall, 25/46 (54%) of the failed outpatient removals were immediately scheduled for reoperation, usually as an inpatient (23/25, 92%). Over the two year follow-up period, 43 women in the outpatient group and 21 in the inpatient group had a further polyp removal (2.0, 1.2 to 3.3, P=0.003, fig 1).

Serious adverse events

Four uterine perforations (4/233, 2%) occurred in the inpatient group. One of these involved a bowel injury, requiring laparotomy and a small bowel resection. One woman needed an indwelling catheter after inpatient

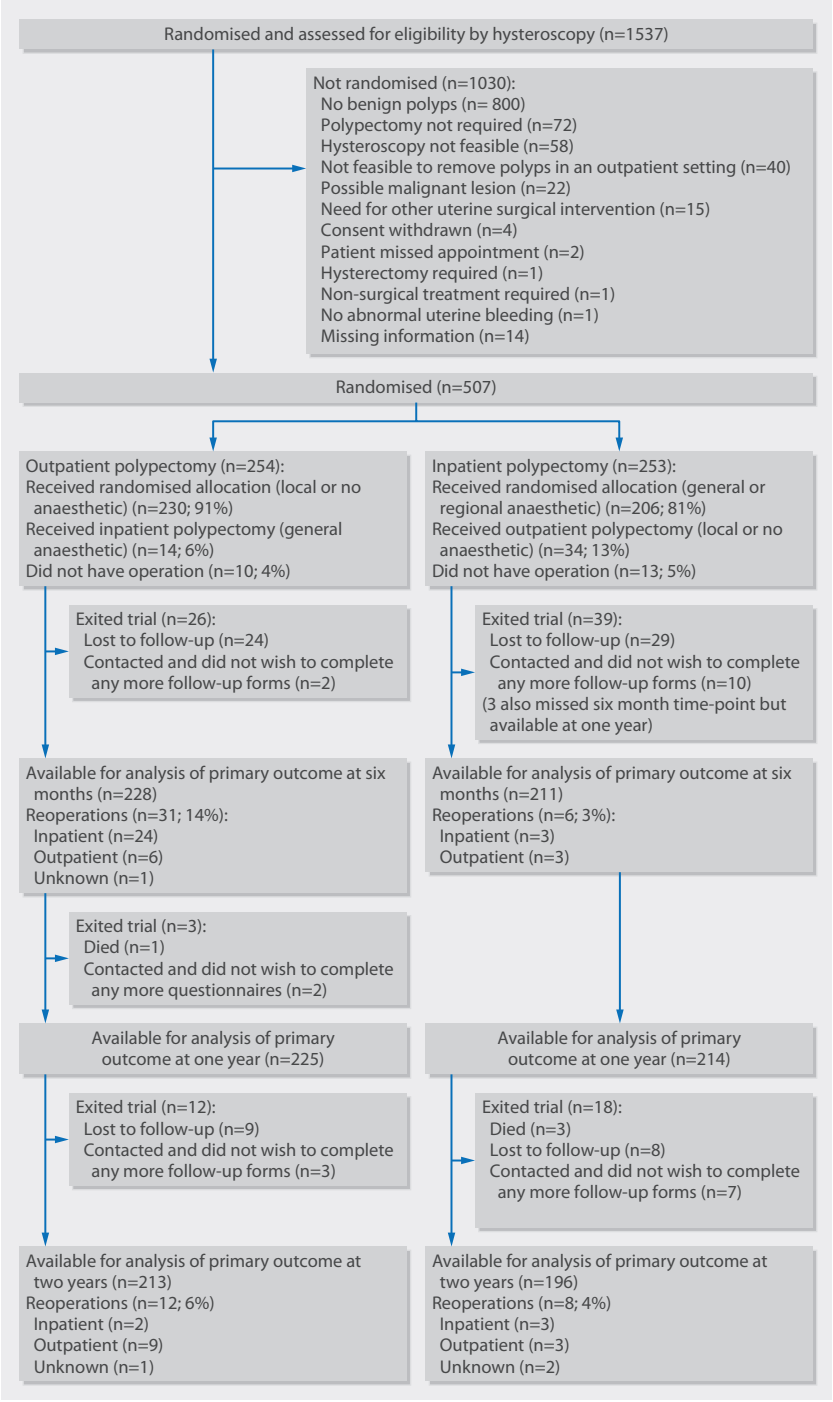

Fig 1 | **Flow chart showing enrolment, randomisation, and follow-up of participants. A small number of women had more than one reoperation**

polypectomy and one woman was admitted to a high dependency unit for the period of her outpatient procedure as she had recently experienced a myocardial infarction. No serious adverse events occurred in the outpatient group.

Quality of life and bleeding scores

Condition specific and generic quality of life scores were significantly improved from baseline at all time points in both groups, with no differences between them (table 3) (see also supplementary table A5).

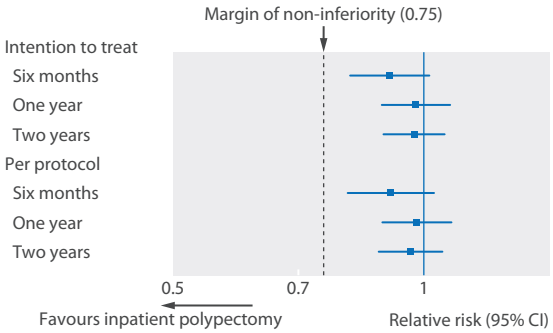

Fig 2 | **Primary outcome (successful treatment, determined by the women's assessment of their bleeding at six months) compared with margin of non-inferiority**

Procedure acceptability

Mean pain scores were higher in the outpatient group than in the inpatient group (table 3). Treatment was unacceptable for 2% of women in each group (5/225 inpatient; 3/197 outpatient, relative risk 0.7, 95% confidence interval 0.2 to 2.8; P=0.6), but women in the outpatient group were less likely to recommend the procedure to a friend or to have it again if necessary (see also supplementary table A6). In qualitative interviews, women in the outpatient group balanced pain, which they mainly experienced short term, with the convenience of a fast response to their problem.

Additional treatments

The groups did not differ for the number of women using additional medical treatments for their bleeding or consulting a healthcare provider during the two years of follow-up. An increased number of women in the outpatient group underwent further gynaecological surgery (excluding polypectomy); 61/230 (27%) *v* 36/219 (16%), relative risk 1.6 (95% confidence interval 1.1 to 2.3); P=0.01), see supplementary tables A7–10). Overall, 7/449 (1.6%, 95% confidence interval 0.6% to 3.2%) women developed endometrial cancer during the two years of follow-up, of whom four had been treated in the outpatient setting and three in the inpatient setting.

Discussion

The results of this trial show that outpatient polypectomy is non-inferior to inpatient polypectomy for the successful alleviation of uterine bleeding associated with uterine polyps. At six months 73% (166/228) of women who received outpatient treatment and 80% (168/211) who received inpatient treatment were successfully treated, and the treatment effects were maintained at 12 and 24 months. There was no evidence that successful resolution of symptoms varied by primary bleeding complaint, or polyp type and location. The duration and amount of bleeding were significantly reduced after both outpatient and inpatient treatment, with no difference between the groups. Similarly, a non-differential but significant improvement in generic and disease specific quality of life was seen after polypectomy. Over the two year follow-up period, women treated in the outpatient setting were twice as likely to

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Table 2 | Operative and postoperative details. Values are numbers (percentages) of women unless stated otherwise

Operative/postoperative variable	Outpatient polypectomy	Inpatient polypectomy	Mean difference or relative risk (95% CI), P value*
Median (interquartile range) largest polyp size (cm), No	1.0 (0.6–2.0), 230	1.2 (1.0–2.0), 217	−0.2 (−0.3 to 0.0), 0.04
Required cervical dilation (No/No in group (%))	76/241 (32)	178/232 (77)	0.41 (0.34 to 0.50), <0.001
Use of vaginal speculum (No/No in group (%))	126/236 (53)	193/224 (86)	0.62 (0.54 to 0.71), <0.001
Use of local anaesthetic (No/No in group (%))	91/244 (37)	15/240 (6)	6.0 (3.6 to 10.0), <0.001
Removal by hysteroscopy† (No/No in group (%))	175/225 (78)	122/217 (56)	1.4 (1.2 to 1.6), <0.001
Median (interquartile range) hysteroscope diameter (mm), No	4.0 (3.0–4.0), 148	5.0 (5.0–6.0), 136	−1.5 (−2.0 to −1.0), <0.001
Method for detachment:	n=228	n=222	1.6 (1.3 to 2.0)‡, <0.001
Electrode	124 (54)	75 (34)	
Mechanical	89 (39)	139 (63)	
Combination	15 (7)	8 (4)	
Method of retrieval:	n=227	n=223	2.2 (1.7 to 2.9)§, <0.001
None	37 (16)	15 (7)	
Hysteroscopic	127 (56)	56 (25)	
Mechanical	59 (26)	147 (66)	
Combination	4 (2)	5 (2)	
Surgeon grade: consultant¶ (No/No in group (%))	172/244 (70)	153/236 (65)	1.1 (1.0 to 1.2), 0.2
Median (interquartile range) time between randomisation and treatment (days), No	0 (0–14), 242	26 (14–42), 237	−20 (−22 to −18), <0.001
Mean (SD) time taken for polypectomy (mins), No	11 (8), 223	12 (8), 186	−1 (−3, 0 to 0.07)
Mean (SD) time in outpatient room/theatre (mins), No	29 (15), 225	29 (13), 216	−1 (−3.2 to 0.7)
Success of removal:	n=242	n=233	2.5 (1.5 to 4.1),** <0.001
Complete	196 (81)	215 (92)	
Partial	25 (10)	15 (6)	
Failed	21 (9)	3 (1)	
Planned reoperation	25 (10)††	1 (<1)††	
Reasons for partial/failed removal:	n=242	n=233	
Patient discomfort	22 (9)	1 (<1)	
Unable to locate blindly	7 (3)	5 (2)	
Unable to access under vision	4 (2)	2 (1)	
Inadequate visualisation	3 (1)	2 (1)	
Polyp/fibroid too large	6 (2)	0	
Uterine perforation	0	2 (1)	
Equipment failure	1 (<1)	0	
Missing reason	1 (<1)	0	
Other‡‡	2 (1)	6 (3)	
Operative complications:	n=241	n=233	
Vasovagal episode	17 (7)	3 (1)	
Nausea/pain	4 (2)	0	
Cervical trauma	0	3 (1)	
Uterine perforation	0	4 (2)	
Haemorrhage	0	3 (1)	
Other§§	2 (1)	1 (<1)	
Postoperative complications:	n=232	n=223	
Vasovagal episode	15 (6)	3 (1)	
Vomiting	6 (3)	4 (2)	
Dizziness/nausea	5 (2)	2 (1)	
Severe pain	3 (1)	0	
Other¶¶	2 (1)	2 (1)	
Further treatment/procedure given:	n=229	n=222	
Levonorgestrel intrauterine system	31 (14)	43 (19)	
Tranexamic acid	12 (5)	1 (<1)	
Progestins	8 (3)	0	
Endometrial destruction	4 (2)	1 (<1)	
Mefenamic acid	1 (<1)	1 (<1)	
Hysterectomy	1 (<1)	1 (<1)	
Goserelin acetate	2 (1)	0	
Missing reason	0	1 (<1)	
Other***	0	1 (<1)	

*P values from two sided tests for superiority where given. Mean differences and relative risks <0 indicate lower with outpatient polypectomy. For skewed variables presented with medians, differences in location between groups were calculated using Hodges-Lehmann estimates and Moses' confidence intervals. Complication rates and reason for failure were not formally analysed.
†Versus blind removal.
‡Relative risk calculated from electrode versus any other category.
§Relative risk calculated from hysteroscopic versus any other category.
¶Versus staff grades less than consultant.
**Relative risk calculated from partial or failed versus complete.
††23/25 (92%) planned reoperations in outpatient group were to be as inpatient. The single planned reoperation in the inpatient group was to be as a further inpatient.
‡‡Outpatient polypectomy: polyp biopsied and ablated (n=1), difficult procedure (n=1); inpatient polypectomy: actually a fibroid (n=2), broad stem (n=1), removal by forceps (n=1), difficult procedure (n=1), failure by diathermy (n=1).
§§Outpatient polypectomy: perineal numbness (n=1), diclofenac suppository given postoperatively (n=1); inpatient polypectomy: false passage (n=1).
¶¶Outpatient polypectomy: not given (n=1), complication from entonox (n=1); inpatient polypectomy: antibiotics required owing to uterine perforation (n=1), intravenous cannula site pain (n=1).
***Transcervical resection of fibroids.

Table 3 | Results of quality of life assessments, bleeding, pain scores, and acceptability of procedure. Values are means (standard deviations), (number) unless stated otherwise

Variables	Mean (SD), No		Mean difference or relative risk (95% CI), P value*
	Outpatient polypectomy	Inpatient polypectomy	
Quality of life and bleeding scores			
Menorrhagia multi-attribute scale†:			
Baseline	52 (27), 134	58 (24), 124	
Six months	78 (22), 115‡	79 (23), 99‡	−1 (−7 to 5), 0.68
One year	82 (23), 110‡	83 (21), 101‡	−1 (−7 to 5), 0.78
Two years	84 (21), 93‡	85 (21), 83‡	−2 (−8 to 4), 0.47
Overall§			−1 (−6 to 4), 0.65
EuroQol EQ-5D¶:			
Baseline	0.78 (0.25), 242	0.78 (0.27), 232	
Six months	0.87 (0.23), 230‡	0.87 (0.20), 211‡	−0.01 (−0.04 to 0.03), 0.70
One year	0.86 (0.25), 227‡	0.86 (0.24), 219‡	0.00 (−0.04 to 0.04), 0.85
Two years	0.85 (0.25), 213‡	0.84 (0.27), 196	0.03 (−0.02 to 0.07), 0.28
Overall§			0.00 (−0.03 to 0.03), >0.99
EuroQol health thermometer**:			
Baseline	77 (18), 233	78 (18), 225	
Six months	79 (18), 227‡	80 (17), 212	0 (−3 to 3), 0.89
One year	80 (17), 228‡	82 (16), 219‡	−1 (−4 to 2), 0.50
Two years	79 (18), 207	83 (16), 194‡	−2 (−5 to 1), 0.19
Overall§			−1 (−3 to 1), 0.28
Bleeding duration visual analogue scale††:			
Baseline	46 (28), 68	53 (28), 67	
Six months	35 (30), 64	28 (26), 56‡	−10 (−21 to 1), 0.07
One year	18 (21), 58‡	24 (28), 62‡	5 (−5 to 14), 0.32
Two years	16 (22), 61‡	15 (25), 53‡	−2 (−12 to 8), 0.65
Overall§			−3 (−10 to 4), 0.39
Bleeding amount visual analogue scale‡‡:			
Baseline	58 (28), 70	66 (26), 68	
Six months	29 (29), 68‡	29 (29), 58‡	−1 (−12 to 9), 0.82
One year	23 (26), 66‡	19 (22), 66‡	−4 (−12 to 5), 0.36
Two years	19 (24), 63‡	18 (27), 57‡	−2 (−12 to 8), 0.66
Overall§			−3 (−10 to 4), 0.40
Operation pain scores:			
During procedure§§	45 (26), (217)	Not applicable	Not applicable
60 minutes after procedure§§	28 (23), (176)	23 (22), (191)	−5 (−10 to 0), 0.03
On discharge§§	23 (21), (200)	15 (17), (186)	−8 (−12 to −4), <0.001
Operation acceptability			
Procedure acceptable (No, %):			
Totally	136 (60)	152 (77)	
Generally	51 (23)	30 (15)	0.90 (0.84 to 0.97), <0.001¶¶
Fairly	33 (15)	12 (6)	
Unacceptable	5 (2)	3 (2)	
Exposure embarrassing (No, %):			
Extremely	5 (2)	4 (2)	
Moderately	17 (8)	24 (12)	1.45 (0.86 to 2.46), 0.24***
A little	79 (35)	35 (18)	
No	123 (55)	133 (68)	
Would recommend to a friend, No/No in group (%)	205/222 (92)	190/196 (97)	0.95 (0.91 to 1.00), 0.04
Would have same treatment again, No/No in group (%)	200/223 (90)	186/193 (96)	0.93 (0.88 to 0.98), 0.009
Prefer alternative treatment, No/No in group (%)	47/218 (22)	39/190 (21)	0.95 (0.65 to 1.39), 0.80

*P values from two sided tests for superiority. Estimates of differences >0 favour outpatient polypectomy, <0 favour inpatient polypectomy (for continuous responses), similarly estimates of relative risk >1 favour outpatient polypectomy, <1 favour inpatient polypectomy (for dichotomous responses). When baseline scores were available, difference between groups at each time point was adjusted for baseline score.
†Menorrhagia multi-attribute scale questionnaire: scores range from 0 (severely affected) to 100 (not affected); restricted to those with heavy menstrual and intermenstrual bleeding only. and time (see statistical analysis section for details).
‡P<0.05 when compared with baseline score within group (by paired *t* test).
§Overall estimate is mean difference over all time points using a repeated measures model including variables adjusting for group, baseline score and time (see statistical analysis section for details).
¶Health related quality of life questionnaire: scores range from −0.59 (health state worse than death) to 1.0 (perfect health state).
**Health related quality of life questionnaire: scores range from 0 (worst imaginable health state) to 100 (best imaginable health state).
††Visual analogue scale score: scores range from 0 (no days of bleeding in past month) to 100 (bleeding every day in past month); restricted to those with heavy menstrual bleeding only.
‡‡Visual analogue scale score: scores range from 0 (no bleeding in past month) to 100 (heaviest imaginable bleeding in past month); restricted to those with heavy menstrual bleeding only.
§§Visual analogue scale score; scores range from 0 (no pain at all) to 100 (worst imaginable pain). *t* test used for analysis.
¶¶Cochran-Armitage test for trend used for analysis; totally acceptable/generally acceptable versus fairly acceptable/unacceptable combined categories used to calculate relative risk.
***Cochran-Armitage test for trend used for analysis; extremely/moderately versus a little/no combined categories used to calculate relative risk.

undergo at least one further polyp removal and 1.6 times more likely to have further gynaecological surgery. These observations may imply reduced effectiveness of outpatient compared with inpatient polypectomy. However, the increased rates of further gynaecological surgery in women undergoing treatment as an outpatient could be because they were more willing to seek referral and treatment for ongoing or new gynaecological problems because of the perceived convenience of their initial experience.

Despite fewer serious complications and avoiding hospital admission and general anaesthesia, the outpatient procedure was associated with more technical failures, increased postoperative pain, and reduced acceptability to patients. Over 90% of uterine polyps were considered feasible to remove in an outpatient setting, but failure to completely remove polyps was higher in conscious women owing to the limitations of miniature endoscopic equipment and patient tolerability. Ongoing technological advances and refinement of treatment protocols may further improve feasibility. The clinical importance of differences in pain experience should be interpreted cautiously. Average pain scores during the outpatient procedure were of moderate intensity but low postoperatively,[19] and our qualitative research suggested that women believed that the discomfort of outpatient treatment was outweighed by convenience. Moreover, the differences may reflect the shorter interval between intervention and pain assessment before leaving the outpatient clinic. The clinical importance of differences in acceptability should be interpreted in light of the high overall levels of patient acceptability and the convenience of outpatient treatment. Practitioners may require additional training to become competent in therapeutic outpatient procedures. However, proficiency should be quickly acquired given the familiarity of diagnostic outpatient hysteroscopy and the relative simplicity of uterine polypectomy.

Strengths and limitations of this study

The strengths of this trial include strict randomisation, size, the multicentre design, low rates of losses to follow-up, and use of outcome measures appropriate to the primary outcome. Some limitations of the study should be noted. These include variation in the practice of polypectomy, with several techniques and forms of instrumentation being utilised. Although we allowed flexibility for pragmatic reasons, there was greater variation in technique in the outpatient group. Not all women received the treatment to which they were originally allocated. However, per protocol analysis did not significantly alter the results, supporting the robustness of the findings. The non-inferiority level of 25% might be considered large by some and hence a limitation of the study; however, this was selected based on the perceived advantages of outpatient treatment. These advantages include avoiding a general anaesthetic, being treated immediately after diagnosis, taking only half a day's leave from work, not having to arrange for childcare, and fewer hospital appointments. Ultimately, the results of this study showed that outpatient polypectomy was at worst only 18% less effective than inpatient treatment.

Comparison with other studies

To our knowledge, this is the first large prospective, randomised controlled trial of outpatient compared with inpatient polypectomy for abnormal uterine bleeding. However, two small controlled studies that evaluated the two treatment settings have been published.[12 20] The first, an observational study from 2002, evaluated symptomatic improvement after polypectomy in the outpatient compared with inpatient setting and found no difference in success of treating bleeding symptoms between the two groups; however, only 26 patients were evaluated in the study.[12] In the second study, a randomised controlled trial, outpatient polypectomy was as successful as the inpatient procedure, with good patient tolerability and low pain scores as well as faster recovery.[20] The study did not, however, evaluate the effect of polypectomy on alleviation of patients' symptoms.

Previously published studies of polypectomy for treating abnormal uterine bleeding have reported success rates of 60–100%,[12 21–28] which are similar to the 73% and 80% reported in this study. However, these were mainly small, cohort studies of patients undergoing inpatient polypectomy with general anaesthesia.

Owing to the large study population and the rigorous methodology of this trial, the results presented in this paper provide accurate data, confirming that outpatient treatment is non-inferior to inpatient treatment.

Conclusions and policy implications

By evaluating all types of uterine bleeding the generalisability of the findings in this study has been enhanced. Although the procedural approaches studied represent options available in the United Kingdom, outpatient polypectomy is not available in all healthcare systems. Despite this caveat, outpatient, ambulatory, or office based interventions are becoming increasingly common across all medical disciplines, driven by advances in technology and a desire to enhance recovery.[29–31] The simplicity of outpatient based interventions may encourage these treatments to be moved from hospital based environments to community settings. Thus the Outpatient Polyp Treatment trial is timely, novel, and relevant to contemporary clinical practice. Further randomised controlled trials will be needed to evaluate the merits of innovative outpatient interventions against conventional inpatient practices across all surgical specialties.

In summary, this study found that outpatient polypectomy was non-inferior to inpatient polypectomy in alleviating abnormal uterine bleeding. Therapeutic outpatient hysteroscopic services should be established in light of this finding and the overall safety, feasibility, and acceptability of the procedure. The relative advantages and disadvantages of available treatment settings should be discussed with women so that they can make an informed decision.

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Contributors: TJC, LM, ED, TR, SJ, and JD designed the study as co-applicants. TJC oversaw the running of the trial and all the authors contibuted to the ongoing management of the trial. NAMC, TJC, and the Outpatient Polyp Treatment trial collaborative group recruited patients to the trial. NAMC, TJC, LD, PS, ED, LS, and the Outpatient Polyp Treatment trial collaborative group collected data for the trial. LM performed the statistical analysis. TR, SJ, and LD performed the parallel cost efectiveness analysis. ED and LS evaluated the qualitative data. The mansucript was drafted by NAMC and TJC with contributions from LM (statistics) and ED (qualitative study). All the authors contributed to the interpretation of the results of the study and revised and reviewed the paper. They are the guarantors. The Birmingham Clinical Trials Unit did the randomisation and data management and monitoring. Neither the funder nor sponsor had any role in study design, data collection, interpretation or analysis, or in writing the report for publication. The authors had full access to all the data from the study. The authors vouch for the accuracy and completeness of the data and analyses.

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Data sharing: The full dataset is available from the corresponding author (Justin.clark@bwhct.nhs.uk).

Transparency: The corresponding author (TJC) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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