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Primary Care Endometrial Sampling for Abnormal Uterine Bleeding: A Pilot Study

Jon M Dickson[1]*, Brigitte Delaney[1], Mary E Connor[2]

* Corresponding author, Dr Jon M Dickson, j.m.dickson@sheffield.ac.uk

1 The University of Sheffield, The Academic Unit of Primary Medical Care, Samuel Fox House, Northern General Hospital, Herries Road, Sheffield , UK S5 7AU.

2 Sheffield Teaching Hospitals NHS Foundation Trust, Department of Obstetrics and Gynaecology Sheffield, UK

Background
Most cases of abnormal uterine bleeding (AUB) could potentially be managed in primary care but lack of access to endometrial sampling leads to avoidable referrals to hospital to rule out endometrial hyperplasia and cancer.

Aims
To design and evaluate a pilot service for primary care endometrial sampling (PCES).

Design
Retrospective analysis of data from two service evaluations.

Setting
General practices and the gynaecology department in a large city in the United Kingdom.

Methods
1) To design the new service we identified all the endometrial samples taken in the city's gynaecology department in 2012/13 and estimated the proportion of these with AUB that would be suitable for PCES. 2) To evaluate the new PCES service we analysed data from the first year of activity.

Results
1) 1894 endometrial samples were taken in hospital in 2012/13. An estimated 424 (22.4%) of these were from patients with AUB who fitted the criteria for PCES. 2) In the first year of the PCES service 108 samples were taken by GPs. Initial management of these patients was exclusively in primary care in 97.2% (104/108), most patients were treated with Mirena IUS (79/109; 73.1%) and there were no cases of hyperplasia or cancer.

Conclusions
Most pre-menopausal patients with AUB could potentially be managed in primary care without referral to hospital if ES was made available to appropriately trained and supported GPs. However, this study was limited by it's retrospective non-interventional design and more research is required to demonstrate safety and cost-effectiveness.

Key Message Points

Primary care is a crucial part of the care pathway for patients with abnormal uterine bleeding.

In the first instance, the majority of patients with AUB can be managed exclusively in primary care without referral to hospital.

Primary care management of AUB may be cost effective but an economic model of the care pathway is required to make accurate comparisons between primary care and secondary care.

Introduction

Abnormal uterine bleeding (AUB) affects 14-25% of women of reproductive age (1) (2) and one in 20 women aged 30-49 consults a GP for AUB each year (3). Most cases of AUB could potentially be managed in primary care without referral to hospital. Careful history and examination is required to diagnose AUB by excluding other causes of abnormal vaginal bleeding such as vaginal pathology, cervical pathology and pregnancy (4) (5). AUB is a syndrome defined as 'bleeding from the uterine corpus that is abnormal in volume, regularity and/or timing that has been present for the majority of the last six months' (5) (irregular bleeding associated with hormonal contraception is often referred to as breakthrough bleeding). This definition of AUB includes heavy menstrual bleeding (HMB) (6) and prolonged vaginal bleeding and overlaps with the term unscheduled vaginal bleeding, which is bleeding that occurs outside the normal menstrual period (or the regular withdrawal bleed associated with oral contraception) (7) i.e. irregular bleeding, inter-menstrual bleeding (IMB), post-coital bleeding (PCB). Dysfunctional uterine bleeding (DUB) is AUB in the absence of organic disease (8) and is the most common cause of menstrual complaints (4) especially towards the end of reproductive life (9) (10).

The causes of AUB can be summarised using the PALM-COEIN acronym: polyps, adenomyosis, leiomyoma/fibroids, malignancy (and hyperplasia), coagulopathy, ovulatory disorders, endometrial, iatrogenic and not otherwise classified (5). Endometrial cancer is the most common gynaecological malignancy in the Western world and rates of endometrial cancer are rising with the increasing prevalence of obesity and diabetes (11). Most women with endometrial cancer are post-menopausal, the incidence rises steeply with age after 45 (7) with the peak incidence over 55 years. However, endometrial cancer can occur in young women. 7% of women with endometrial cancer are under 50 years of age and 2-5% are under 40 years of age (6).

Ultrasound scans (USS), which are readily available to GPs in the UK, cannot exclude the presence of endometrial atypical hyperplasia or malignancy. In pre-menopausal women, none of the symptoms of AUB are in themselves criteria for urgent referral for suspected cancer (12) but national guidelines in the UK recommend that endometrial sampling should be performed for AUB in women >40 (13) (14) or >45 (6) to exclude atypical hyperplasia and cancer. It is not specified if ES should be performed in primary care or secondary care. Despite being a safe and relatively simple investigation ES has not traditionally be undertaken in primary care in the UK. A recent study looked at diagnostic strategies for management of AUB and concluded that hysteroscopy with or without ES was cost-effective but this was based on a secondary care population and included patients with post-menopausal bleeding (15). Local GPs felt that primary care ES may be a safe and cost effective way of managing AUB without referral to hospital. A new pilot primary care endometrial sampling (PCES) service was set-up to facilitate primary care management of AUB. In this paper we present the results of two service evaluations which were used to plan and evaluate the new service.

Methods

<u>Context</u>

Sheffield is a large city in the United Kingdom with a single Clinical Commissioning Group (CCG). CCGs are clinically led statutory National Health Service (NHS) bodies responsible for the planning and commissioning of healthcare services for their local area. Sheffield has a population of 451,100 adults (551,756 adults and children) (16) and is served by a single acute adult hospital trust (Sheffield Teaching Hospitals NHS Foundation Trust) (STH) which includes a specialised gynaecology department. General Practice (GP) is provided in the city by 88 GP partnerships and 113 GP practices (GP partnerships often have more than one building/practice). The total of the registered list size for all the practices in Sheffield is 580,263.

The Clinical Guideline

A PCES clinical guideline was drawn-up as part of preparations for the proposed pilot. AUB was defined as heavy menstrual bleeding, irregular bleeding and/or change in bleeding pattern. The inclusion criteria were AUB in women ≥45 years old or <45 with risk factors (obesity, polycystic ovarian syndrome, diabetes mellitus, tamoxifen use, hereditary nonpolyposis colorectal cancer). Exclusion criteria were: post-menopausal bleeding, post-coital bleeding, inter-menstrual bleeding, active infection, pregnancy. The guideline specified full clinical assessment including examination and USS for all patients. The full clinical guideline is available as additional online content (See Supplementary 1).

Hospital Service Evaluation

We undertook a service evaluation at STH to establish the number of endometrial samples undertaken each year, the proportion of these with AUB that would be suitable for PCES, and the clinical characteristics of the cohort. We requested the following data from the histopathology laboratory 1) the total number of samples taken in 2012/13 and 2) histopathology reports for all endometrial samples taken during a sample month. A data collection tool was created by JMD and MEC which was used to extract relevant information from a combination of sources: histopathology request forms and reports, USS request forms and reports and medical records. Data extracted were: age, indication for biopsy, AUB which fits the criteria for PCES, endometrial biopsy result and initial management plan. All data was extracted by MEC and borderline cases were discussed with JMD.

Calculation of Costs

Secondary Care Costs

We used Secondary Uses Service (SUS) data from Hospital Episode Statistics (HES) (17) and reviewed clinical notes to define the care pathway and tariff for those patients with AUB identified in he hospital service evaluation. STH supplied Yorkshire and Humber Commissioning Support Unit (YHCSU) with the NHS numbers of patients identified from the hospital service evaluation as suitable for the LCS. The data were processed by the DMIC (Data Management and Integration Centre) of YHCSU. The processing was carried out by using a pseudonymised data set. Data processing and data sharing agreements were already in place to support the process which comply with data protection legislation and Information Governance requirements. The only data released to the study team was fully pseudonymised and identified only by the research ID number. For each suitable patient the SUS database was searched. We searched using NHS number for outpatient attendances six months before and twelve months after the sample month and filtered by speciality codes 502 (Gynaecology) and 503 (Gynaecological Oncology). This allowed identification, on a case-by-case basis, of procedure codes, number of outpatient attendances, HRG (Health Resources Group) codes and the tariff per attendance. A second analysis of CCG-level anonymised data was undertaken for gynaecology referrals in 2013/14 with relevant HRG codes. The data from these two sources, combined with the clinical opinion of MEC and JMD on the usual care pathway, were discussed by the costs analysis group (JMD, SA, DM, RS, AE) and a consensus view on the usual patient pathway and tariff for a simple case of AUB was determined. We were not able to check with the provider (STH) if the correct procedure code was applied, only which code was actually applied. The cost of USS in primary care and secondary care was not included because this was part of routine care before the LCS and shouldn't have differed between the two groups.

Primary Care Costs

The costs of consumables and histopathology services for PCES were established from commercial suppliers and the histopathology laboratory at STH. These costs were already included in the tariff price for patients managed in secondary care but needed calculating separately for patients

managed in primary care. The basic price for providing a histopathology report for an ES is £55.67, but additional immunohistochemistry tests are required for some samples which cost around £30 each (as many as ten of these may be necessary in some cases). If 1/200 endometrial samples actual cost £350 then the average cost of each sample is £57. GP practices were paid £40 for each sample taken. The total average cost to the CCG for each PCES undertaken was therefore £97. Additional costs to the GP practice were: speculum (£0.84), tenaculum (£4.26), Instillagel (£1.62) and endometrial sampler (£1.08).

Primary Care Endometrial Sampling Service Evaluation

Once the hospital service evaluation was completed and the business case was approved by the CCG, the primary care endometrial sampling (PCES) service was set-up as a locally commissioned service (LCS) (a contract between the CCG and individual GP practices). GPs who wished to provide the service were required to hold the DFSRH plus the Letter of Competence for Intra-Uterine Techniques. In addition, they were required to attend a two-hour training session led by MEC which outlined the clinical guideline (available in full as additional online content) which was drawn-up by JMD and MEC based on feedback from local clinicians and key stakeholders. Endometrial sample results taken as part of the LCS were processed by the laboratory in the same way as samples taken in secondary care and the result was returned to the requesting GP. GP practices were required to complete a service evaluation form for each sample completed which was submitted to the CCG. The data from each service evaluation form were extracted and entered into an SPSS database. We used standard descriptive statistics to analyse the data.

Results

Hospital Service Evaluation

There were 1894 endometrial samples processed in the histopathology laboratory in the financial year 2012/13. 111 were taken in the sample month, 11 were excluded (these were incorrectly labelled as ES e.g. sample of peritoneal endometriosis) which left a total of 100 cases where a full set of data were extracted (we present the results using a denominator or 111 so that percentages generated can be applied to the total group of 1894). The most common indications for endometrial samples taken in hospital were heavy menstrual bleeding (18.0%, 20/111), irregular menstrual bleeding (9.9%, 11/111), change in bleeding pattern (0.9%, 1/111), inter-menstrual bleeding (7.2%, 8/111), post-menopausal bleeding (41.4%, 46/111) and other (18.0%, 20/111). There were 25/111 (22.4%) samples from patients with AUB who fitted the criteria for PCES.

Of those with AUB that fitted the criteria for PCES, the mean age was 46 years (SD 6.15), 16/25 (64%) were over 45 years and 9/25 (36%) were under 45. The most numerically important indications were heavy menstrual bleeding 12/29 (38%) and irregular bleeding 9/29 (31%) (note that patients may have more than one indication hence the denominator of 29). The majority of ES results were normal and there were no cases of endometrial cancer; see Table 1. The initial management plan for these patients is shown in Table 2.

The usual care pathway for a patient with uncomplicated AUB after referral to hospital begins with a gynaecology outpatient clinic appointment. After clinical assessment, USS (which may be undertaken in primary or secondary care) and endometrial sampling, most patients are discharged from the clinic with a plan to write to the GP and patient with the histology result. A small proportion of these patients, estimated at 20%, are seen in a follow-up outpatient clinic. STH routinely used the procedure code (OPCS) Q181 (diagnostic endoscopic examination of the uterus) for patients with AUB who underwent endometrial sampling. The HRG (Health Resources Group) code for a new outpatient gynaecology clinic appointment, plus the procedure code (OPCS) Q181 (diagnostic endoscopic examination of the uterus) is MA21Z which, based on the 2013/14 tariff,

generates a price of £486. A single follow-up outpatient gynaecology clinic appointment generates a tariff of £82/£91 (mean of £87 used for subsequent calculations) for gynaecology/gynaecological oncology and so the average patient pathway generates a bill to the CCG of £503 (£486 + (0.2 x £87)).

Primary Care Service Evaluation

Of the GP partnerships in Sheffield 34/88 (39%) confirmed that they would like to provide the LCS starting from April 2014. By the end of March 2015, 19/88 had undertaken at least one endometrial sample as part of the LCS. The total of the registered list size for these 19 GP partnerships is 157,423 (27.1% of the Sheffield total list size). There were a total of 108 primary care endometrial samples were taken in the 12 months between April 2014 and March 2015.

The most frequent indications for the samples were HMB 82/108 (75.9%), irregular bleeding 31/108 (28.7%) and change in bleeding pattern 34/108 (31.5%). The median age of the patients was 46 (range 25-58), 76/108 (70.4%) were over 45 years old and 32/108 (29.6%) were under 45. Of the 32/108 patients who were under 45 years old, 31/32 (97%) had risk factors for endometrial hyperplasia/cancer. The most common risk factors were obesity 19/32 (59.4%), PCOS 3/32 (9.4%) and diabetes mellitus 3/32 (6.3%). The majority of patients 98/108 (92.5%) had an USS. Of these 48/98 (44.9%) women had normal scans ('no abnormality detected'), fibroids were detected in 40/98 (37.4%) and 10/98 (10.2%) had other abnormalities such as adenomyosis and simple ovarian cysts. The majority of ES results were normal (see Table 1), there were no cases of endometrial cancer, 2/108 (1.9%) samples were inadequate and there were no failed procedures (although this data wasn't specifically collected).

Initial management was exclusively in primary care in 104/108 (97.2%), 3/108 (2.8%) women were referred routinely to gynaecology and no patients were referred to the fast track service for suspected cancer ('two week wait'). Formal advice on management from the hospital gynaecology department or the gynaecology triage service was taken in 7/67 (6.5%) cases. The most common primary care management plans were Mirena coil 79/108 (73.1%), oral medication 13/108 (12.0%) and continued observation without treatment 16/108 (14.8%).

Discussion

Our results demonstrate that GPs are able to assess and manage most cases of AUB in the first instance without referral to hospital and without advice from specialists. The cost of managing each case in primary care was £97 and the average hospital cost for each case of AUB was £503. Feedback from GPs after the first year of the pilot was that £40 was insufficient and the fee was increased to £75 but even including this increase, the LCS generates a cost saving of 74% per case. The primary care costs that we calculated were based on the fee paid by the CCG to the GP practice per ES not the actual amount of time spent by the GP, and other members of the primary care team, managing each case. There is no formula for calculating the costs of activity in general practice based on time aliquots, appointment duration or type of appointment e.g. with a GP or a nurse. The hospital cost per case of AUB of £503 was generated by STH by applying the procedure code Q181 (diagnostic endoscopic examination of the uterus) despite the fact that none of these patients had undergone hysteroscopy. We were unable to establish if this code was applied deliberately or erroneously by STH and we are not aware of any rules used by hospital coders to guide them in correctly applying procedure codes. A proper health economic model is required to draw more accurate and robust conclusions but our data show that PCES may be a cost-effective strategy.

The majority of ES results in both the primary care and hospital cohorts were normal and there were no cases of endometrial cancer. This raises the question of whether endometrial sampling is necessary in all cases of AUB; current national guidance is ambiguous on this issue. Further research

on the epidemiology of AUB in primary care populations especially the predictive value of risk factors and individual symptoms for hyperplasia/cancer would allow risk stratification of patients and may allow identify groups of patients sampling in the >45 age group that can be managed without endometrial sampling. The ES results and initial management plans were comparable in the GP and hospital cohorts. The only major difference was the use of Mirena IUS which was much more common in primary care (79/108; 73.1%) than in hospital (7/25; 28%). Mirena IUS is an effective treatment and is the first line treatment in the UK (18) (19) (20) (6). We do not have data on what percentage of these patients were not satisfied with the initial treatment and eventually required referral to gynaecology.

Our data show that 426 of the patients who had an ES in hospital in 2012/13 (22.5% x 1894) had AUB which could have been managed in primary care (the 'annual demand' for PCES). In the first year of the pilot LCS, 25.4% (108/426) of the annual demand was met by GP practices. The 19 practices that actually delivered the service in the pilot year covered 27.1% of the Sheffield list size. So the practices that delivered the service seemed to meet the pro-rata needs of their population. The challenge of meeting 100% of the annual demand for PCES is to extend the service to patients registered with practices that do not currently deliver the service. There are a number of likely barriers to practices offering the service to their own patients: inadequate remuneration, lack of appropriately qualified staff, workload, medico-legal concerns, and justifying setting-up a service for a relatively small number of patients per practice per year. These factors probably explain the drop-out from those practices that signed-up for the LCS and those that actually delivered it. Training requirements for ES mean that many practices may not have clinical staff qualified to deliver the service. Innovative methods of primary care service delivery such as inter-practice referral or primary care specialist providers may be necessary to deliver this service to the entire population of the city and there is only limited evidence that this type of working at scale can be effective (21) (22).

Limitations

The retrospective design of our study was the major limitation, some variables such as precise symptoms are likely to have been incompletely recorded in the clinical notes, we found that data for some variables was missing in some cases and we did not collected data on failed procedures. A prospective study where these variables could have been specifically enquired about directly with the patient would have been more accurate. A prospective design would also allow collection of follow-up data to draw stronger conclusions on safety and to quantify adverse outcomes. The low prevalence of cancer and hyperplasia in our data confirm that the risk of these conditions is low but we do not have data on the potential of missed diagnoses in our cohorts. GPs have a responsibility to report significant events (23) but there was no formal requirement for these to be reported to the CCG during the study period (this has subsequently been changed). We did not collect any long-term follow-up data and therefore we cannot draw firm conclusions about the outcomes of our patients or the safety of the service. There are limitations in our method of estimating and comparing costs for the pathway in primary care and in secondary care. Further research using a health economic model, a larger sample size and a prospective design would provide stronger evidence for the conclusions in this paper.

Conclusions

Most pre-menopausal patients with AUB could potentially be assessed and managed in primary care without referral to hospital if ES was made available to appropriately trained and supported GPs. However, this study was limited by it's retrospective non-interventional design and more research is required to demonstrate safety and cost-effectiveness.

Ethics

NHS Research Ethics Committee permission was not required because data collection was deemed to be service evaluation by NHS Sheffield and STH. The project was reviewed and approved by the Ethics Committee of the University of Sheffield (reference number SMBRER323).

Competing Interests

MC reports personal fees from Bayer Medical and Smith & Nephew outside the submitted work. JMD and BC have declared no competing interests.

Licence for Publication

Contributorship Statement

JMD suggested undertaking the service evaluation, took overall responsibility for the planning, conduct and reporting of the work and is guarantor for the study. MC was involved in data collection, provided gynaecological expertise, was involved in preparation of the manuscript throughout and approved the final version. BD analysed the data, was involved in preparation of the manuscript throughout and approved the final version.

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Category	Hospital Results	GP Results	Description
1	23/25 (92%)	105/108 (97.2%)	Secretory changes, consistent/inconsistent with time of cycle. Proliferative changes, consistent/inconsistent with time of cycle. Inactive endometrium.
2	1/25 (4%)	2/108 (1.9%)	Inadequate as no endometrial tissue in the sample
3	0/25 (0%)	1/108 (0.9%)	Simple hyperplasia
4	1/25 (4%)	0/108 (0%)	Complex hyperplasia without atypia. Complex hyperplasia with atypia/Endometrial intraepithelial neoplasia.
5	0/25 (0%)	0/108 (0%)	Endometriod endometrial adenocarcinoma or other endometrial malignancy.

Table 1. Histopathology results from endometrial samples in the hospital cohort and the GP cohort.

Management	General Practice	Hospital
No treatment	16/108 (14.8%)	4/25 (17%)
Oral medication	13/108 (12.0%)	6/25 (24%)
Mirena IUS	79/108 (73.1%)	7/25 (28%)
Uterine artery embolisation	N/A	0/25 (00%)
Hysteroscopic procedure	N/A	2/25 (08%)
Endometrial ablation	N/A	2/25 (08%)
Hysterectomy	N/A	0/25 (00%)
Myomectomy	N/A	0/25 (00%)
Other/missing	N/A	4/25 (16%)

Table 2. The initial management of patients with AUB in the hospital cohort and in the GP cohort.

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