

Management of postmenopausal bleeding by general practitioners in a community setting: an observational study

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ABSTRACT

AIM: To evaluate the safety and effectiveness of a clinical pathway for investigation of postmenopausal bleeding (PMB), managed primarily by general practitioners. Women with an endometrial thickness (ET) ≥ 5 mm on transvaginal ultrasound (TVUS) require either a pipelle biopsy in primary care or referral for specialist care.

METHOD: Data on 241 women with PMB were reviewed retrospectively over a 5-year follow-up period. Twenty-five women were excluded as they did not satisfy PMB clinical pathway criteria.

RESULTS: TVUS showed 121 women had an ET < 5 mm, 83 an ET ≥ 5 mm, and 12 an endometrial polyp. In the women with ET ≥ 5 mm, 38 had a pipelle biopsy performed in primary care, 36 were referred directly to secondary care, and 9 declined further investigations. Only 17 pipelle biopsies provided sufficient tissue, with the remaining 21 women referred to secondary care. Seven cases of endometrial cancer were identified, 4 by pipelle biopsy and 3 by hysteroscopy. Of the study cohort, 68% were managed solely by their general practitioner to the point of diagnosis, while 81% with an ET ≥ 5 mm required management in secondary care at some stage. No further cases of endometrial cancer were identified in reviews of patient medical records and cancer registries.

CONCLUSION: Community-based investigation of PMB is an alternative model of care with no evidence of additional risks to the patient. Targeted education of general practitioners on pipelle biopsies is essential to maximise the effectiveness of the pathway.

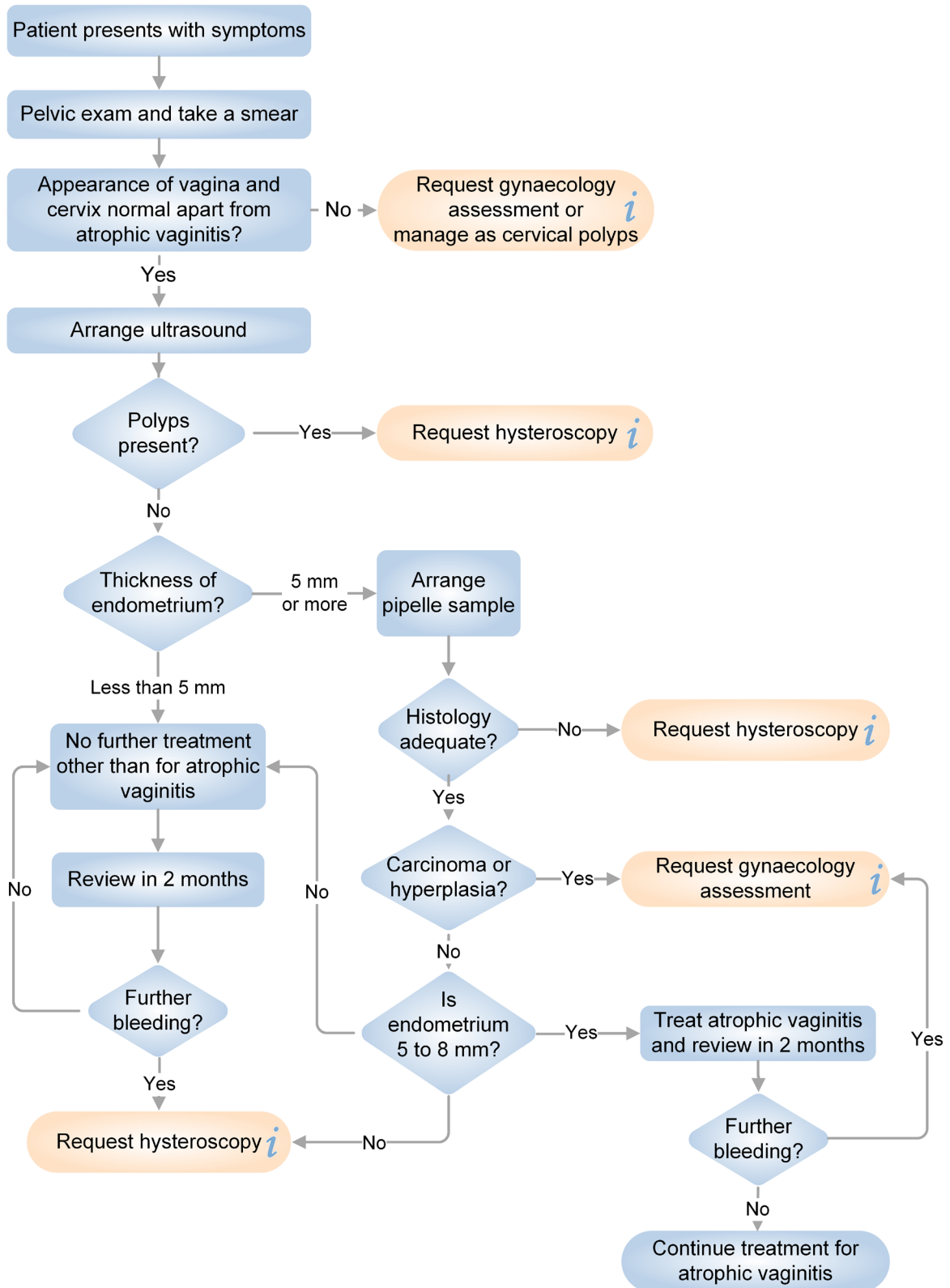
Post-menopausal bleeding (PMB) represents an absolute indication for specialist gynaecological investigation because of the underlying risk of endometrial cancer, estimated at 10%.¹ The aim of clinical management of PMB is to achieve an accurate diagnosis without over-investigation.

In recent years, newer methods of investigation of PMB, such as transvaginal ultrasonography (TVUS), endometrial biopsy, and hysteroscopy, have superseded dilation and curettage (D&C).² Most guidelines³⁻⁷ use an endometrial thickness (ET) of ≥ 5 mm measured by TVUS to indicate an increased risk of endometrial cancer in post-menopausal women, with conservative management recommended for those with

an ET < 5 mm. Further invasive diagnostic testing is indicated in all women with a 'thin' endometrium on TVUS and ongoing or recurrent bleeding.

Women with an ET ≥ 5 mm need an endometrial biopsy. This can usually be carried out as an office procedure as it requires minimal or no cervical dilation and no anaesthesia. In addition to being more convenient and less stressful for patients, the cost of the biopsy is considerably less than a hospital D&C. Evidence from a meta-analysis⁸ showed outpatient endometrial biopsies reduced the time to treatment and had a high diagnostic accuracy for endometrial cancer when an adequate specimen was obtained.

Figure 1: Postmenopausal bleeding pathway in HealthPathways.



Until 2008, women with PMB in the Canterbury region of New Zealand were referred directly for specialist gynaecological investigation that included a TVUS with or without a D&C. Around that time, the Canterbury District Health Board—through a proactive group called the Canterbury Initiative (<http://www.canterburyinitiative.org.nz/>)—introduced several programmes to integrate health services, and to transfer some services to the community that had traditionally been carried out by hospital specialists.⁹ This involved developing clinical pathways for various conditions, including PMB. These pathways provided locally relevant patient-centred models of care in line with international best practice guidelines. For dissemination, these pathways were placed on a local clinical guidance website called HealthPathways (<http://www.cdhb.health.nz/Hospitals-Services/Health-Professionals/Pages/Health-Pathways.aspx>).

As shown in Figure 1, the Canterbury District Health Board clinical pathway for PMB involves an initial examination followed by TVUS. If ET is ≥ 5 mm, an endometrial biopsy, performed by an appropriately trained general practitioner, is organised. Depending on the histology report of the biopsy the patient either remains on the pathway (ie, normal report) or is referred for specialist review (ie, abnormal histology or inadequate sample). Women with findings suggestive of focal endometrial abnormalities, such as polyps, are referred directly for specialist management. The pathway recommends general practitioners review the patient after 2 months and, should symptoms persist, arrange for specialist review. Failure to identify any further investigations in women with an ET ≥ 5 mm in ongoing clinical safety audits leads to the general practitioner being contacted to determine the reason for the lack of follow-up.

Because the PMB pathway represented a substantial change from historical practice, it was considered necessary to review the practicability, effectiveness and safety of the management protocol. This paper describes the findings of a review of 241 women with PMB investigated according to the pathway over a 1-year period, with a 5-year

follow-up period to check for the presence of subsequent endometrial carcinoma.

Patients and methods

All women in Canterbury referred through the publically-funded Community Referred Radiology programme between 1 October 2009 and 30 September 2010 for investigation of PMB by TVUS were identified (n=241). Ethical approval for review of the women's electronic and paper medical records was obtained from the regional Ethics committee. Data collected included age, ethnicity, time from LMP, TVUS reports (type of scan, duration from request to scan, gross findings and ET), pipelle biopsies (proportion of adequate biopsies and histology), and gynaecological investigations over the 1-year period following TVUS (conservative management, hysteroscopy or hysterectomy). A review of the National Cancer Registry was carried out 14 months after enrolment in the study to determine if any of the women had been subsequently diagnosed with endometrial or any other gynaecological cancer. This review was extended to a follow-up period of 5 years by searching the Local Cancer Registry in 2015 and reviewing the patient's electronic medical and laboratory records.

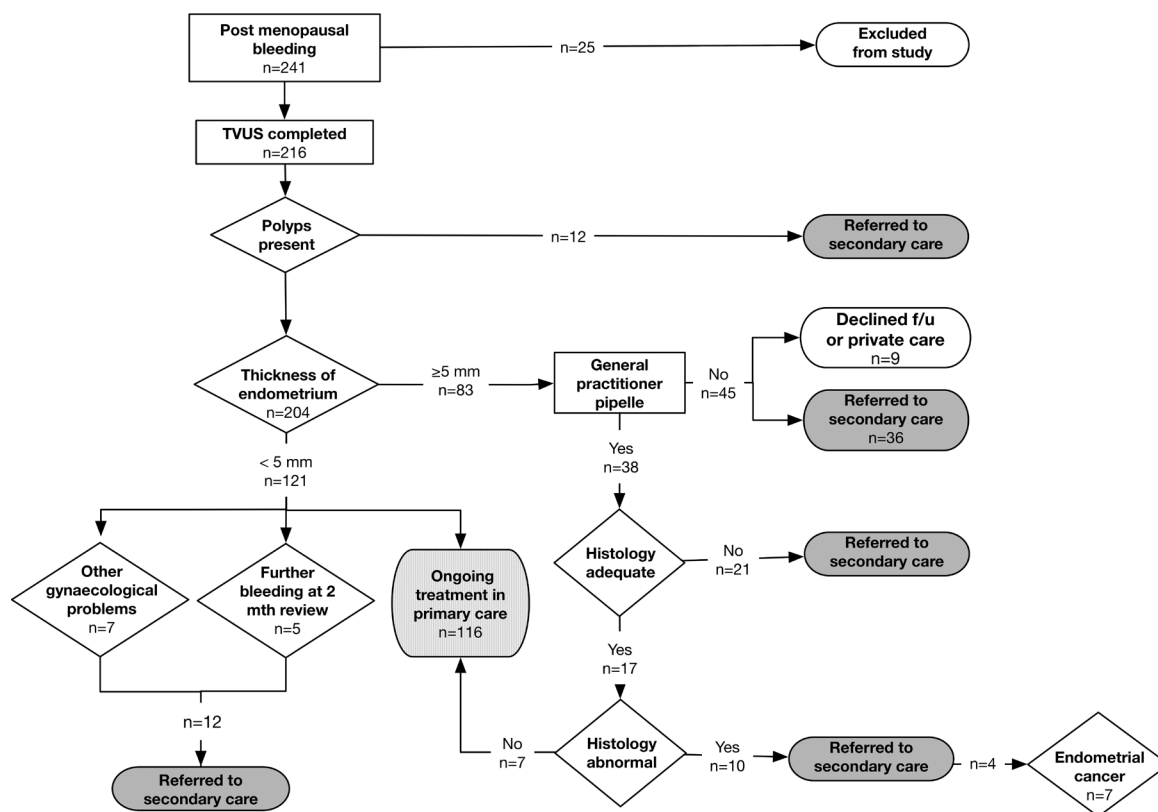
The data were anonymised and entered into a secure electronic spreadsheet for analysis. In accordance with the pathway, the data were examined as two groups using an ET cut-off value of ≥ 5 mm. The primary outcome measure used to assess the safety of the pathway was the number of cases of endometrial cancer missed in patients commenced on the pathway. The secondary outcomes used to assess the effectiveness of the pathway were the proportion of successful pipelle biopsies carried out by general practitioners, the proportion of women requiring specialist management and waiting times for the investigations of PMB.

Results

The gynaecological procedures and outcomes in the study cohort are shown in Figure 2.

A total of 25 women were excluded from the study cohort. The reasons for exclusion were: 9 did not attend the TVUS

Figure 2: Flow diagram of clinical outcome in the study cohort.



appointment; 7 were not post-menopausal; 7 were on hormone replacement therapy (none on tamoxifen); and 2 with recurrent PMB were considered to be perimenopausal and had a mirena inserted. The mean age of the remaining 216 women was 59 years (range 40–91 years), 88% of whom were New Zealand European, 5% Asian, 4% Māori, and 3% Pacific Islander. Information on the time since the LMP was included in only 65 (30%) of the referrals (mean, 4.0 years; range, 1–30 years).

TVUS showed that of the 216 women, 83 (38%) had an ET ≥ 5 mm, 121 (56%) had an ET < 5 mm, while 12 (6%) were found to have polyps and were referred directly for a hysteroscopy. Other endometrial abnormalities identified by TVUS included fibroids (n=70), cysts (n=28), and adenomyosis (n=8).

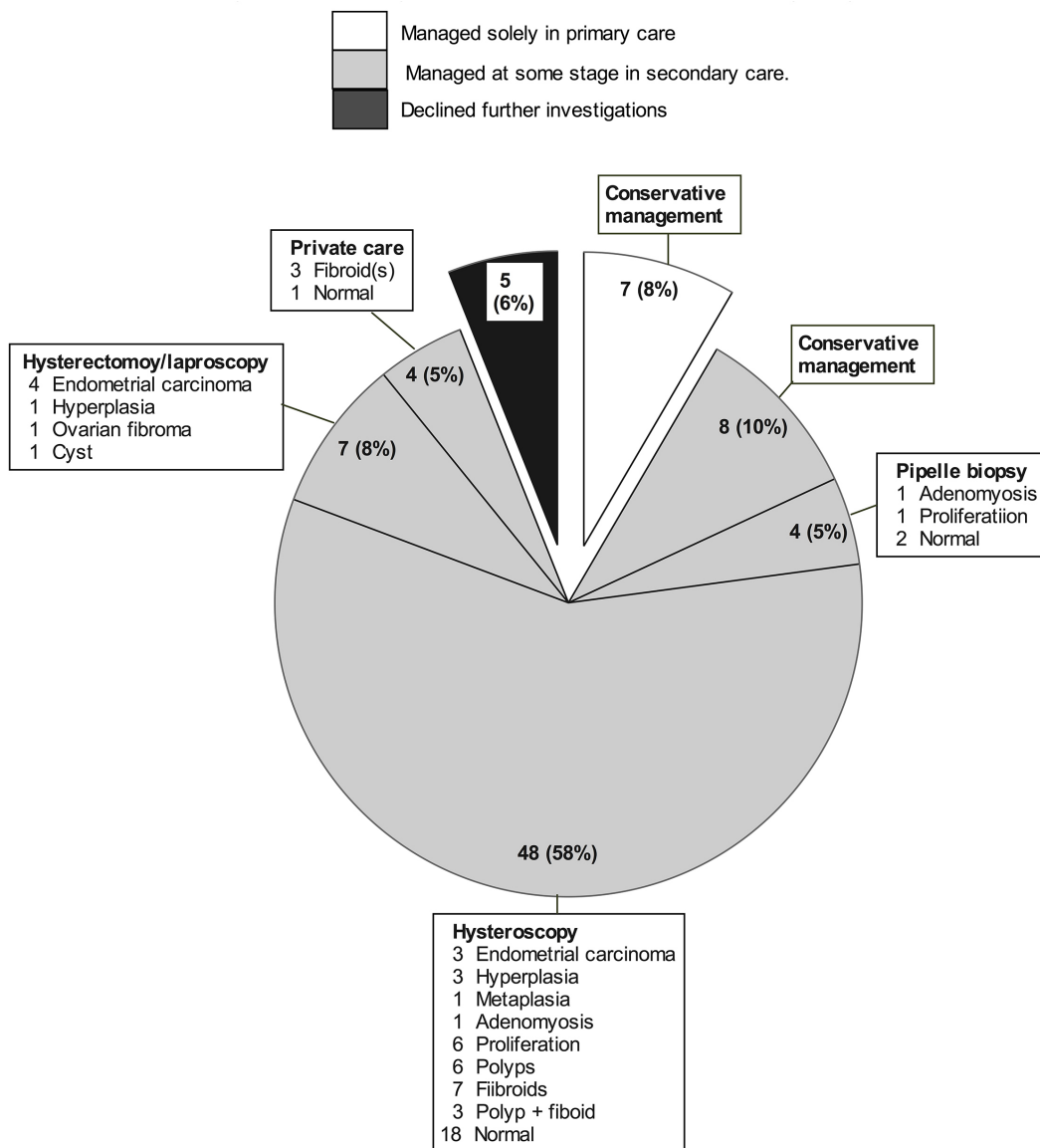
In accordance with the clinical pathway, the 83 women with an ET ≥ 5 mm required further investigation, with 38 (46%) having a pipelle carried out by a general practitioner. Only 17 of these pipelle biopsies (45%) provided sufficient tissue for histological diagnosis. Four cases of carcinoma, 2 of hyperplasia, and 4 of endometrial proliferation were identified, with these 10 women

referred to secondary care for further management. The remaining 7 women had normal histology and were returned to their general practitioner for management.

The 45 women with an ET ≥ 5 mm who did not have a general practitioner pipelle, and the 21 women with inadequate histology, were referred to secondary care for further investigations and management. A further 3 cases of endometrial carcinoma were identified in the women referred directly to secondary care, and 2 cases of hyperplasia (1 simple and 1 atypical) in the women with inadequate GP pipelle biopsies.

A summary of clinical management carried out in primary or secondary care during the 1-year follow-up period and the histological findings of the 83 women with an ET ≥ 5 mm is shown in Figure 3. Of the 83 women, 7 (8%) were managed solely in primary care, 67 (81%) in secondary care at some stage during the follow-up period, while 9 (11%) women either declined further investigations or were seen by a private gynaecologist. Twelve women had a pipelle as the first line of ongoing investigation in secondary care, 8 of whom subsequently had a hysteroscopy.

Figure 3: Management in women with an ET ≥5mm (n=83).



All 121 women with an ET <5mm were managed initially in general practice. As shown in Figure 4, 15 of these women were referred to secondary care for further management within the next year. This included 8 hysteroscopies (5 recurrent PMB and 3 abnormal findings on a repeat prolapse) and 7 hysterectomies (1 hyperplasia, 4 prolapse, 1 multiple fibroids, and 1 ovarian mucinous tumour). The remaining 106 women continued to be managed conservatively in general practice, with a record of repeat TVUS or routine cytology in 79 cases.

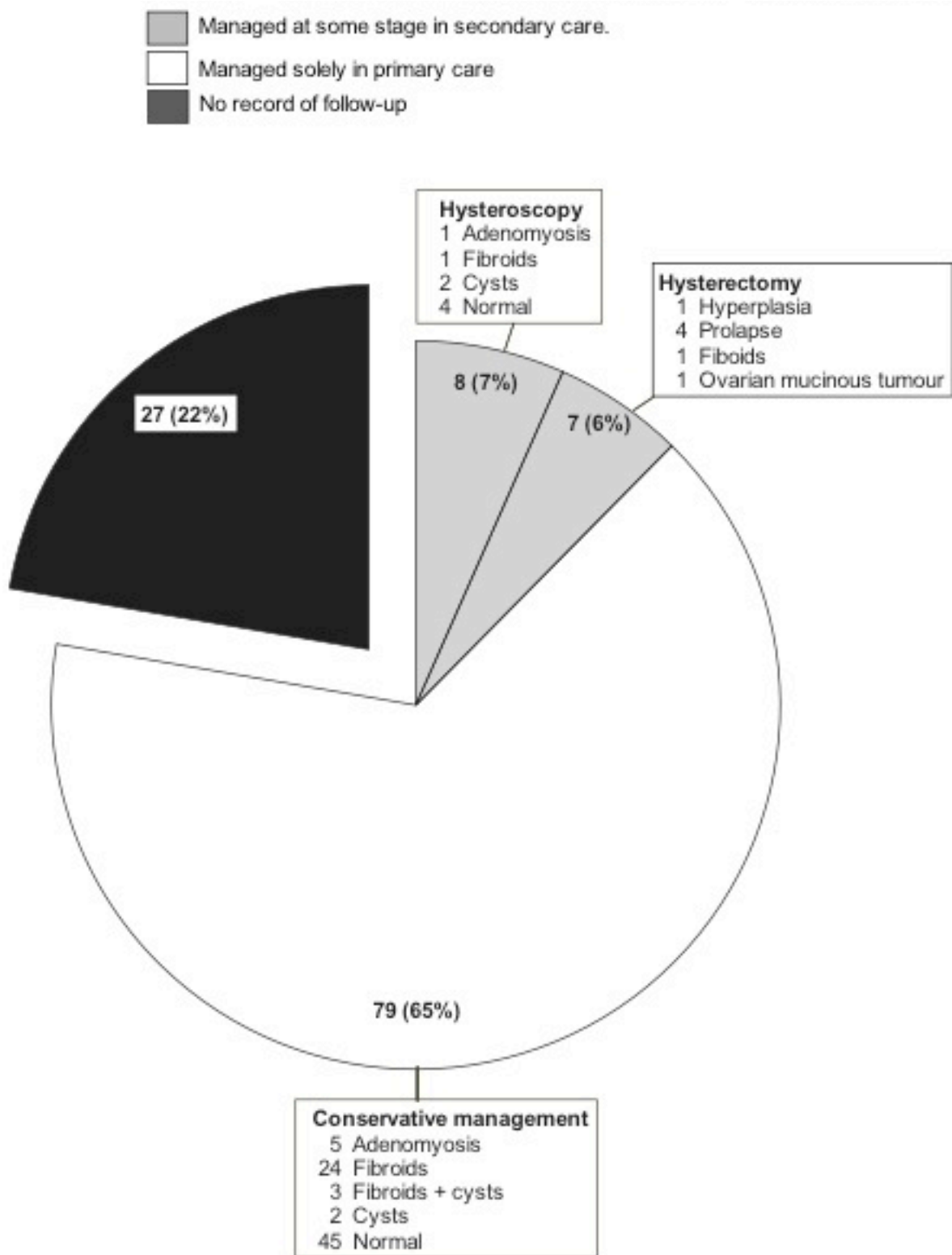
Therefore, of the 204 women in the study, 138 (68%) avoided referral to secondary care and were managed entirely by their general practitioner to the point of diagnosis. This included the 10 women with an

adequate pipelle sample who were diagnosed with either endometrial carcinoma or abnormal histology.

The median waiting times for the procedures were general practitioner referral to TVUS 13 days (interquartile range [IQR] 8–21 days), and for women with an ET ≥5mm, referral to general practitioner pipelle biopsy 29 days (IQR 15–59 days), and referral to first specialist assessment 54 days (IQR 35–80 days). For the women with a confirmed cancer diagnosis, the median time from referral to hysterectomy was 55 days (range 42–90 days) for those who had a general practitioner pipelle biopsy, and 88 days (range 81–98 days) for those who had a hysteroscopy in secondary care.

No additional cases of endometrial cancer were identified in the study cohort

Figure 4: Management in women with an ET <5mm (n=121).



in the 1-year review of the National Cancer Registry, and 5-year follow-up of the Local Cancer Registry and medical and laboratory records.

Discussion

The advent of simple devices for obtaining endometrial biopsies without general anaesthesia has resulted in an increasing number of biopsies being carried out in primary care.^{10,11} The current study evaluated a clinical pathway for PMB that included the option of an endometrial biopsy carried out by a general practitioner based on the results of TVUS. Because low grade and early stage endometrial cancers have an indolent natural history, we used a relatively long period of follow-up to evaluate the safety of the clinical pathway.

The study showed that the pathway was a safe model of care. Follow-up over a 14-month period using the National Cancer Registry, and 5-year period using the Local Cancer Registry and medical and laboratory records showed no cancer diagnosis was missed in the study cohort. The importance of ongoing monitoring of symptoms and repeat investigation in the PMB clinical pathway was emphasised by the finding of endometrial hyperplasia in a small number of women investigated in secondary care. The incidence of cancer in the study group (3.2%) was considerably lower than the established rate of 10%.¹ This low rate may have been attributable to the fact that all women referred for community TVUS for investigation of PMB were enrolled in the study. Because information on LMP was provided in only one-third of the women, it is possible peri- and pre-menopausal women may have been included in the study cohort.

How do the outcomes of the clinical pathway on HealthPathways compare with other services described in the literature? The median time from referral to final diagnosis was 42 days (referral to scan = 13 days and scan to pipelle = 29 days). The waiting times for hysterectomy for 3 of the 4 women with endometrial cancer identified by a general practitioner pipelle biopsy were within the 62-day guideline of the Faster Cancer Treatment Programme of the Ministry of Health, New Zealand,¹² and were of shorter duration than for women

who required specialist management. However, of the 38 pipelles attempted by general practitioners, 21 (55%) did not allow histological diagnosis due to 7 technical failures and 14 yielding insufficient tissue, thereby requiring referral to secondary care and a small delay in diagnosis. This relatively high rate of inadequate biopsies is greater than that reported by other studies for primary care clinicians which range between 13–31%.^{8,13-15} This high rate may reflect, in part, the fact that biopsies are often more difficult to obtain in post-menopausal women, mainly because of endometrial atrophy. It is relevant to note that specialist clinicians also had difficulty obtaining diagnostic samples in a small number of women in our study cohort. Clinical audits of the PMB clinical pathway carried out annually since the study period have shown similar inadequacy rates for the general practitioner biopsies, although there has been a trend towards a reduced rate in recent years (2011, 47%; 2012, 54%; 2013, 38%; 2014, 35%). Our results indicate targeted education programs for general practitioners on endometrial biopsy techniques may be necessary to reduce the rate of failed or inadequate biopsies.

In our study, approximately one-half (45%) of the women suitable for a general practitioner pipelle were referred directly to secondary or private care. The reasons for these direct referrals may include sampling being limited by a high body mass index (BMI) or another gynaecological problem, while 4 women declined a pipelle, requesting hysteroscopy instead. It is possible this relatively high rate of referral for secondary care may have affected the results of our analysis and the perceived benefits of the pathway. Notwithstanding this possibility, approximately two-thirds of the study cohort were managed entirely in the community by their general practitioner, equivalent to a potential saving of about 140 first specialist appointments. In comparison, an earlier 'in-house' safety audit of hospital-based services showed approximately 63% of women with PMB who had a pipelle biopsy required referral to secondary care, with about 50% requiring a hysteroscopy as they had an ET >8mm.

Despite numerous studies comparing the effectiveness, safety and acceptability

of methods for investigating PMB and detecting malignant pathology, there is still no consensus on the most accurate and efficient diagnostic clinical pathway. An important finding of the current study was the relative contributions of TVUS and endometrial biopsy towards the diagnostic process. Although a large number of women were able to be managed without referral to secondary care, it is clear that this benefit was attributable mainly to the initial TVUS. The additional information provided by a pipelle carried out in the community was of less benefit. Although pipelle biopsies carried out in the community appeared to be a safe and time efficient method for investigation of PMB, the fact that over three-quarters of the women with a thickened endometrium required referral to a specialist gynaecologist raises questions as to the effectiveness of this approach. It is possible a pathway that includes specialist referral for all women with PMB and an ET ≥ 5 mm may be more appropriate, or alternately, that the resources required to support such a pathway may be better utilised to establish a 'one-stop' PMB clinic, as suggested in other papers.^{16,17} However, in a constrained health system with limited access to specialist gynaecology, the pathway described in this paper reduced the demand on secondary services. Another advantage of a clinical pathway involving a pipelle biopsy in primary care is that access to geographically convenient specialist care may not always be available in rural or smaller communities.

This study had several limitations. Because it was a retrospective design it is possible some selection bias may have occurred. The study cohort was relatively

small, although because withdrawals from the pathway were low at approximately 10% and follow-up data was available for the majority of women, we consider the conclusions are applicable to current practice. The study did not, however, evaluate the cost effectiveness of the pathway—suffice it to say, that the cost of TVUS and a pipelle biopsy is considerably less than a hysteroscopy. TVUS should cost the same in a community setting as in a hospital, and therefore any additional costs are incurred downstream. Our review also did not evaluate the cost and time involved to carry out a safety audit to ensure all women with a thickened endometrium receive adequate follow-up.

Conclusions

The findings of this study suggest that the clinical pathway disseminated on HealthPathways is a safe and promising alternative model of care for women with PMB that does not expose them to the risk of undue delay or missed diagnoses of endometrial cancer. The pathway enables women with potentially serious gynaecological problem to receive specialist care, and for those with a endometrial cancer diagnosed by pipelle, the potential to fast track care.

However, there are potential concerns regarding the efficiency of this pathway, mainly regarding the high inadequacy rate of pipelle biopsies carried out in primary care, requiring further investigations in secondary care. This indicates that targeted education of general practitioners on pipelle biopsies is necessary. The issues of cost effectiveness and patient satisfaction of the pathway also warrant further study.

Competing interests:

Nil

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