



EVIDENCE SEARCH RESULTS

Question/subject of request:	Proliferative endometrium in post menopause management.
Date requested:	23 rd January 2025
Date completed:	3 rd March 2025
Compiled by:	Laetitia Delaleuf

CITING THIS SEARCH

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The citation format is:

- Delaleuf, L., (2025). *Evidence summary: proliferative endometrium in post menopause management* Taunton, UK: Somerset Foundation Trust Knowledge and Library Services.

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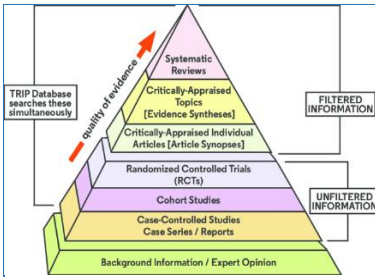
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The design of the study and the endpoints measured affect the strength of the evidence.

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Summary of search results:

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From the literature found, the debate is around evaluation and diagnosis as postmenopausal bleeding, or endometrial thickness can be a cause of concern and be symptoms of hyperplasia or even carcinoma ([Rotenberg, O. et al. 2020](#)). Other possible conditions could be fibroids polyps or adenomyosis ([Up to date 2024](#)).

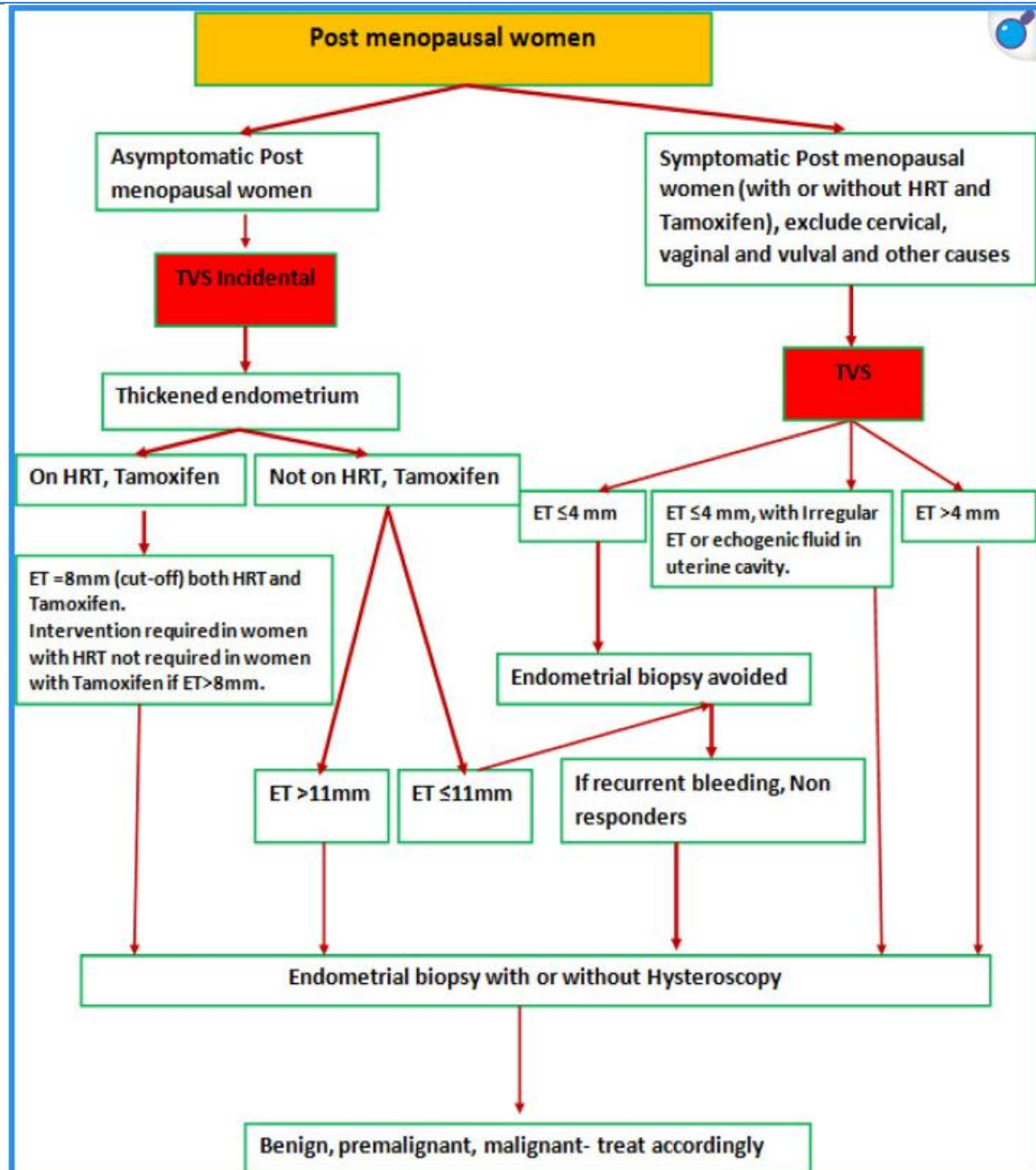
The best way to assess endometrial thickness is a high-resolution transvaginal ultrasonogram ([Giri, SK; Nayak, BL and Mohapatra, J 2021](#))

According to Giri, SK; Nayak, BL and Mohapatra, J ([2021](#)), there is a clinical conundrum:

In post-menopausal women with bleeding, the cut-off of ET that warrants investigation is almost defined. However, the cut-off value of ET in asymptomatic postmenopausal women; beyond which intervention is required, is still debated. A dilemma also exists about the cut-off of ET in both symptomatic and asymptomatic women on HRT and Tamoxifen.

Additionally, in this article, there is a decision tree to support evaluation for postmenopausal women that may be useful for patient management:





GIRI, S.K., NAYAK, B.L. and MOHAPATRA, J., 2021. Thickened Endometrium: When to Intervene? A Clinical Conundrum. *Journal of Obstetrics and Gynaecology of India*, 71(3), pp. 216–225.

In the discussion about endometrial thickness cut-offs for postmenopausal bleeding, the previous threshold for symptomatic women was set at 5mm. However, using a threshold of 3mm may offer higher sensitivity but can result in more false positives, which could increase stress levels for patients.

The British Medical Ultrasound Society and the Society of Radiographers advise in their Guidelines for Professional Ultrasound Practice (2023) to “agree on endometrial thickness cut-offs and PMB protocols locally with clinicians.” According to Kaur, H. et al. (2024) this is still uncertain for postmenopausal women without bleeding.

In terms of management, there are no clear guidelines for proliferative endometrium. Guidelines are available for other conditions such as endometrial cancer.

From UpToDate:

Patients with proliferative/secretory endometrium — Proliferative/secretory endometrium is not a form of endometrial hyperplasia but suggests active estradiol secretion (eg, by adipose tissue; an estrogen-producing tumour) or exposure to exogenous estrogens and should be evaluated further. This is



discussed in detail separately. (See "[Endometrial hyperplasia or endometrial intraepithelial neoplasia: Management and prognosis](#)", section on 'Proliferative endometrium'.)

For postmenopausal patients proliferative/secretory endometrium is an excess of **estrogen** which could place them at a higher risk of EH (Endometrial Hyperplasia) or endometrial cancer.

Treatment of proliferative endometrium should be solely based on the nature of the patient's symptoms that prompted the biopsy and the effect of such symptoms on quality of life. For postmenopausal patients, consideration can be given to either the LNG 52 mg IUD or oral progestins; however, the LNG 52 mg IUD is favoured in postmenopausal patients with a history of EH.

The frequency and duration of follow-up for such patients is uncertain. For postmenopausal patients, we perform endometrial sampling every three to six months for one year, and longer if the source of estrogen exposure (eg, obesity) has not been corrected.

This is also the conclusion made by Rotenberg, o. et al. (2023) "Medical management targeted to negate estrogenic activity and associated risks may be considered in these cases". Due to the risk of endometrial polyp, hyperplasia or even cancer (Rotenberg, O. et al. 2020 also suggest long-term monitoring)

Abraham, C. (2023) highlights the same course of action but warned about four factors:

- 1) *histologic patterns between proliferative endometrium and endometrial hyperplasia may portend differing risks of progression to endometrial cancer*
- 2) *evidence assessing observation as a management option is lacking,*
- 3) *the number of patients to treat with progestins to prevent one case of progression of proliferative endometrium to endometrial cancer is currently unknown, and*
- 4) *recommendations for treatment with progestins and surveillance after treatment initiation (which can be invasive) are drawn from studies on the treatment of endometrial hyperplasia. There is currently no evidence supporting medical intervention for proliferative endometrium*

O'Connor E. et al. (2021) performed a retrospective review on postmenopausal women at NHS Lanarkshire from January 2018 to April 2019 and identified 77 women and a wide variety of their management including "recommending weight loss, hysteroscopic guided biopsy, repeat pipelle biopsy, progesterone, departmental ultrasound of ovaries or reassure and discharge depending upon the patient's risk factors".

There is a need for a unified approach to this to avoid unnecessary treatment, tests and stress for patients.

I hope this is helpful. Please do let us know if you need any further information.



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UP TO DATE (be aware you may need to login to view the full text. If you have issues accessing it, please contact us)

[Approach to the patient with postmenopausal uterine bleeding](#) (Last updated 10TH October 2024)

Author: Goodman, A.

Date retrieved: 14th February 2025

Relevant extract: see highlight summary

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GUIDELINES

[Guideline No. 447: Diagnosis and Management of Endometrial Polyps.](#)

Authors: Bougie, Olga;Randle, Elizabeth;Thurston, Jackie;Magee, Bryden;Warshafsky, Chelsie and Rittenberg, David

Publication Date: Mar ,2024

Journal: Journal of Obstetrics & Gynaecology Canada: JOGC 46(3), pp. 102402

Abstract: Objective: The primary objective of this clinical practice guideline is to provide gynaecologists with an algorithm and evidence to guide the diagnosis and management of endometrial polyps. Target Population: All patients with symptomatic or asymptomatic endometrial polyps. Options: Options for management of endometrial polyps include expectant, medical, and surgical management. These will depend on symptoms, risks for malignancy, and patient choice. Outcomes: Outcomes include resolution of symptoms, histopathological diagnosis, and complete removal of the polyp. Benefits, Harms, And Costs: The implementation of this guideline aims to benefit patients with symptomatic or asymptomatic endometrial polyps and provide physicians with an evidence-based approach toward diagnosis and management (including expectant, medical, and surgical management) of polyps. Evidence: The following search terms were entered into PubMed/Medline and Cochrane: endometrial polyps, polyps, endometrial thickening, abnormal uterine bleeding, postmenopausal bleeding, endometrial hyperplasia, endometrial cancer, hormonal therapy, female infertility. All articles were included in the literature search up to 2021 and the following study types were included: randomized controlled trials, meta-analyses, systematic reviews, observational studies, and case reports. Additional publications were identified from the bibliographies of these articles. Only English-language articles were reviewed. Validation Methods: The authors rated the quality of evidence and strength of recommendations using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. See Appendix A (Tables A1 for definitions and A2 for interpretations of strong and weak recommendations).

[Endometrial Thickening](#)

Authors: Schick, M.

Publication Date: December ,2024

Abstract: this is from Cornwall and Isles of Scilly Trust - RMS Clinical Referral Guidelines for endometrial thickening: Asymptomatic Endometrial Thickening in Postmenopausal Women. This is primarily aim at GPs use. Decisions about further investigations should be made on a case-by-case basis in asymptomatic women with increased endometrial thickness.

[Guideline No. 451: Asymptomatic Endometrial Thickening in Postmenopausal Women.](#)

Authors: Wolfman, Wendy;Bougie, Olga;Chen, Innie;Tang, Yale;Goldstein, Susan and Bouteaud, Jeanne

Publication Date: Jul ,2024

Journal: Journal of Obstetrics & Gynaecology Canada: JOGC 46(7), pp. 102591

Abstract: Objective: To formulate strategies for clinical assessments for endometrial thickening on



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ultrasound in a postmenopausal woman without bleeding. Target Population: Postmenopausal women of any age. Outcomes: To reduce unnecessary invasive interventions and investigations in women with asymptomatic endometrial thickening while selectively investigating women at risk for endometrial cancer. Benefits, Harms, And Costs: It is anticipated that the adoption of these recommendations would save postmenopausal women unnecessary anxiety, pain, and risk of procedural complications. It is also expected to decrease the cost to the health care system by eliminating unnecessary interventions. Evidence: English language articles from Medline, Cochrane, and PubMed databases for relevant peer-reviewed articles dating from 1995 to 2022 (e.g., asymptomatic endometrial thickness, endometrial cancer, postmenopausal bleeding, transvaginal ultrasound, endometrial biopsy, cervical stenosis, hormone therapies and the endometrium, tamoxifen, tibolone, aromatase inhibitors). Results were restricted to systematic reviews and meta-analyses, randomized controlled trials/controlled clinical trials, and observational studies. Validation Methods: The authors rated the quality of evidence and strength of recommendations using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. See Appendix A (Tables A1 for definitions and A2 for interpretations of strong and conditional [weak] recommendations).

[Guidelines for Professional Ultrasound Practice](#)

Author: The Society of Radiographers and British Medical Ultrasound Society

Publication Date: December, 2023

Publication Details: Eighth edition,

Extract: p.63 *There is no agreed consensus on reference values for predicting endometrial cancer (Saccardi et al., 2021). Some centres use a threshold of 4mm in symptomatic postmenopausal women and 11mm in asymptomatic postmenopausal women (Alcázar et al., 2018; Wolfman 2018 and Morrison et al., 2022). Therefore, it is important to agree endometrial thickness cut-offs and PMB protocols locally with clinicians.*

[Green-top Guidelines No. 67: Management of Endometrial Hyperplasia](#)

Authors: The Royal College of Obstetricians and Gynaecologists and British Society for Gynaecological Endoscopy

Publication Date: February , 2016

Extract: *Progestogens have been advocated to treat endometrial hyperplasia because they modify the proliferative effects of estrogen on the endometrium. Treatment with progestogens was originally limited to oral progestogens such as norethisterone, medroxyprogesterone acetate and megestrol acetate. Oral progestogens can have significant adverse effects and norethisterone at a high dose has similar contraindications to combined contraceptive pills.⁴⁸ More recently, intrauterine delivery of progestogens via the LNG-IUS has been successfully used for this purpose.⁴⁶ The intrauterine release of the levonorgestrel minimises the systemic absorption of the hormone and aids compliance by reducing adverse effects. The LNG-IUS achieves a higher concentration of levonorgestrel at the level of the endometrium compared with oral progestogens.*

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REVIEWS

[New Light on Endometrial Thickness as a Risk Factor of Cancer: What Do Clinicians Need to Know?](#)

Authors: Saccardi, Carlo; Spagnol, Giulia; Bonaldo, Giulio; Marchetti, Matteo; Tozzi, Roberto and Noventa, Marco

Publication Date: 2022

Journal: Cancer Management and Research 14, pp. 1331–1340

Abstract: Transvaginal ultrasound (TVUS) represents an accurate and noninvasive technique to investigate endometrial thickness (ET) in the early diagnosis of endometrial cancer (EC). In the



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literature, for maximum ET there is no consensus on the cutoff value for normal ET in postmenopause for either symptomatic or asymptomatic women. Most patients with EC present with postmenopausal bleeding (PMB) and in these patients is necessary to perform TVUS to evaluate ET as an indicator for endometrial biopsy. On the contrary, if ET is incidentally detected in postmenopausal patients without bleeding, endometrial sampling for a postmenopausal woman without bleeding should not be routinely performed, although it is estimated that up to 15% of EC occurs in women without vaginal bleeding. The aim of our review was to give clinicians necessary and useful knowledge on the role of TVUS and ET for early detection of EC in their daily routine practice. Based on the most important studies in the literature, we summarized that in premenopausal woman with abnormal uterine bleeding, an optimal cutoff for ET has not yet been established. For postmenopausal women with PMB, at low risk, and ET < 4 mm, a follow-up scan could be offered, and for women with ET ≥ 4 mm, office hysteroscopy–guided endometrial sampling is recommended independently of ET results. On the other hand, in postmenopausal women with PMB and at high risk of EC, office hysteroscopy–guided endometrial sampling is necessary. In postmenopausal women without PMB and ET ≥ 4 mm, arbitrary endometrial sampling is not recommended, but evaluated case by case based on risk factors. In conclusion, there is broad consensus on the importance of TVUS and the need for further investigation based on risk factors of EC.

[Endometrium at Menopause: The Pathologist's View](#)

Authors: Swain, Meenakshi and Kulkarni, Aditya D.

Publication Date: 2021

Journal: Journal of Mid-Life Health 12(4), pp. 310–315

Abstract: Endometrium at menopause is inactive and free of cyclical changes that are characteristics of the reproductive age. At the same time, menopausal endometrium is subject to a variety of disease processes, the most sinister of which are the endometrial malignancies. In the present pictorial review, we briefly discuss the various morphologic patterns of diseases affecting the menopausal endometrium. With an aim to provide insights from the pathologists' point of view, multiple pictures for each of the disorders are shared. We highlight the finer points a pathologist looks for, to ensure proper treatment and welfare of postmenopausal women.

[Clinical management of vaginal bleeding in postmenopausal women](#)

Authors: Carugno, J.

Publication Date: 2020

Journal: Climacteric 23(4), pp. 343–349

Abstract: Menopause is characterized by permanent cessation of menstrual periods and is clinically diagnosed after 12 months of complete amenorrhea. It occurs at a median age of 51 years alongside the physiological process of aging, although it can happen at an earlier age for other medical conditions or after surgery (surgical menopause). Due to reduced circulating estrogens and progesterone, the reproductive organs undergo progressive atrophy. This physiologic process of aging is also present at an endometrial level; without the cyclic hormonal actions of the menstrual cycle, the endometrium during menopause becomes atrophic. Postmenopausal bleeding (PMB) is a common gynecologic complaint encountered by the clinician. Endometrial cancer is present in about 10% of patients with PMB. Nevertheless, many other conditions, such as endometrial or cervical polyps, genital atrophy, or non-gynecologic conditions, may also be present. Historically, dilation and curettage (D&C) was the main diagnostic procedure in patients with PMB; however, newer methods of investigation have replaced D&C. The aim of this review is to present an up-to-date analysis of the current evidence for the clinical management of vaginal bleeding in postmenopausal women.

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STUDIES

[The optimal endometrial thickness threshold for prediction of endometrial cancer in postmenopausal women without bleeding remains uncertain-Systematic review and meta-analysis.](#)

Authors: Kaur H.;Qadri S.;Nevill A.M. and Ewies, A. A. A.

Publication Date: 2024

Journal: Journal of Gynecology Obstetrics and Human Reproduction 53(10) (pagination), pp. Article Number: 102831. Date of Publication: 01 Dec 2024

Abstract: The incidental finding of endometrial thickness (ET) >4 mm in the absence of postmenopausal bleeding (PMB) is a common cause of referring women to secondary care. However, there is lack of consensus amongst gynecologists as regards the management. It is estimated that up to 15 % of endometrial cancers occur in women without PMB. The aim this study was to determine the optimal ET threshold, on trans-vaginal ultrasound scan, that discriminates normal endometrium from endometrial hyperplasia and cancer in this cohort. On using a thorough search strategy, a total 16 studies including 4088 women were deemed eligible. However, the data were not amenable to meta-analysis. There were wide variations in the thresholds reported with potential bias given the retrospective nature of the majority of the studies. Despite contacting authors, we could not obtain the primary data to generate a Receiver Operating Characteristic (ROC) Curve. No linear or curvilinear association was found between ET thresholds and the percentage of women diagnosed with endometrial hyperplasia and cancer using either Pearson's correlation, linear or curvilinear regression, or a simple visual scan/scatter diagram. The result of this study reveals the lack of evidence to inform clinical practice in this area, and there is a need for a well-designed multi-center prospective study.

[Risk of endometrial polyp and surgical intervention in postmenopausal women with proliferative endometrium](#)

Authors: Rotenberg, Ohad;Doulaveris, Georgios;Fridman, Dmitry;Renz, Malte;Kaplan, Julie;Xie, Xianhong;Goldberg, Gary L. and Dar, Pe'er

Publication Date: Dec ,2023

Journal: Maturitas 178, pp. 107847

Abstract: Objective: To study the long-term risks of postmenopausal women with proliferative endometrium developing benign uterine pathologies (endometrial polyps and uterine fibroids) and requiring future gynecological interventions, and to compare them with women with atrophic endometrium. Design: Retrospective cohort study of all women aged 55 or over who underwent endometrial biopsy between 1/1997 and 12/2008. Outcome data were available through to 2/2018. Women with proliferative endometrium were compared with those with atrophic endometrium for the presence of endometrial polyps, uterine fibroids, future endometrial biopsy for recurrent vaginal bleeding, and future hysteroscopy or hysterectomy. Logistic regression models were used to evaluate the association of endometrial histology and other covariates with the risk of morbidities. Main Findings: Postmenopausal women with proliferative endometrium are at higher risk of developing endometrial polyps, uterine fibroids and need for surgical intervention. Of 1808 women who underwent endometrial biopsy during the study period, 962 met inclusion criteria: 278 had proliferative and 684 had atrophic endometrium. Length of surveillance was similar in the two groups (11.9 vs. 11.5 years, $p = 0.2$). Compared with women with atrophic endometrium, women with proliferative endometrium had significantly higher rates of endometrial polyps (17.3 % vs 9.7 % $p = 0.001$). Multivariable logistic regression confirmed that women with proliferative endometrium had more fibroids on ultrasound (62.1 % vs 50.3 % $p = 0.02$), and had increased risks of developing endometrial polyps (aOR 1.9, 95 % CI 1.28-3.07, $p = 0.002$), repeat endometrial biopsy (34.9 % vs. 16.8% $p < 0.001$) and future hysterectomy or hysteroscopy (26.6 % vs 16.2 % $p < 0.001$). Conclusions: In addition to the long-term increased risk of cancer, postmenopausal women with proliferative





endometrium are more likely to have future bleeding, surgical interventions and diagnosis of endometrial polyps. Medical management to reduce estrogenic activity and associated risks may be considered in these cases.

[Significance of incidental thickness of endometrium echo on transvaginal ultra sound in asymptomatic postmenopausal women.](#)

Authors: Gupta P.;Sachdev P.;Paramhans R. and Dhawale, N.

Publication Date: 2022

Journal: European Journal of Molecular and Clinical Medicine 9(3), pp. 2543–2551

Abstract: Background-The World Health Organization defines natural menopause as the permanent cessation of menstruation resulting from the loss of ovarian follicular activity without an obvious intervening cause and is confirmed only after 12 consecutive months of amenorrhea. In asymptomatic postmenopausal women sonographically thickened endometrium (usually ≥ 5 mm) as an indication to proceed to further, more invasive investigations to find out endometrial pathology to reduce morbidity and mortality. AIM- To evaluate endometrial pathology in asymptomatic postmenopausal women with endometrial thickness ≥ 5 mm on transvaginal ultrasound. Methods- This was a Descriptive study done in All Asymptomatic Postmenopausal Women attending Gynecology OPD in the Department of Obstetrics and Gynecology Kasturba Hospital, BHEL, Bhopal, Madhya Pradesh, India between - MAY 2018 to AUGUST 2019. sample size 100 patients. In inclusion criteria, all asymptomatic postmenopausal women having endometrial thickness ≥ 5 mm and written informed consent. In exclusion criteria, women with abnormal pap smear report grossly abnormal cervix and diagnosed genital tract malignancy, bleeding diathesis, and cardiac diseases. Result-Out of 100 patients on which transvaginal sonography was performed Majority of the patients had endometrium thickness (mm) of 9 mm (23%) followed by 8 mm (22%) and 10 mm (14%). There were further taken hysteroscopy guided biopsy which shows 2% of women ca endometrium diagnosed and 19 % of the women endometrial polyp was diagnosed, 16% had endometrial hyperplasia without atypia and 1% patients had endometrial hyperplasia with atypia. Conclusion- The risk of cancer is high if the endometrium is thick (≥ 8 mm) in asymptomatic postmenopausal women. The results of our study highlight the need for routine use of transvaginal ultrasound as a screening test for endometrial cancer. We should consider though the rising incidence of endometrial cancer, and the requirement for more and larger prospective trials with surrogate criteria for the thickened endometrial stripe in postmenopausal women in TVS for both symptomatic and asymptomatic postmenopausal women.

[Evaluation of endometrial thickness by transvaginal ultrasound and baseline risk factors as a predictor for endometrial abnormalities in postmenopausal women.](#)

Authors: Yerrisani J.;Collins K.;Ballard E. and Kothari, A.

Publication Date: 2022

Journal: Australasian Journal of Ultrasound in Medicine 25(4), pp. 186–194

Abstract: Introduction/Purpose: To evaluate the endometrial thickness (ET) as a predictor of endometrial abnormalities in postmenopausal women and whether consideration of baseline risk factors increases diagnostic accuracy. Methods: This is a retrospective observational study of postmenopausal women presenting with bleeding or thickened endometrium (≥ 4 mm) on ultrasound, between 2003 and 2012. Risk factors for endometrial abnormality were analysed using logistic regression. Of 301 women, 220 were symptomatic and 81 were asymptomatic. The median ET was 6 mm (IQR 4–9) for symptomatic women and 9 mm (IQR 6–12) for asymptomatic women. Results: Abnormal pathology was found in 35 symptomatic (15.9%) and 6 asymptomatic women (7.4%). For each 1 mm increase in ET, the odds of an abnormal diagnosis increased by 16.3% (95% CI 9.6–23.5) for symptomatic and 19.9% (95% CI 3.1–39.3) for asymptomatic women. The Youden's index method identified an ET threshold of ≥ 7.1 mm for symptomatic and ≥ 14.5 mm for asymptomatic women. In symptomatic women the sensitivity was 88.6% (95% CI 72.3–96.3) and specificity 69.2% (95% CI 61.9– 75.6), while in asymptomatic women the sensitivity was 50.0% (95% CI 13.9–86.1) and specificity was 89.3% (95% CI 79.5–95.0). The addition of age in the symptomatic women model reduced the sensitivity (82.9% (95% CI 65.7–92.8)) but increased the specificity (72.4% (95% CI 65.3–78.6)). Conclusion: ET is a significant predictor of abnormality. In the absence of risk factors, our





study suggests that invasive procedures may be withheld until the ET is ≥ 7.1 mm with bleeding and ≥ 14.5 mm in asymptomatic women with no bleeding.

[Long-term outcome of postmenopausal women with non-atypical endometrial hyperplasia on endometrial sampling](#)

Authors: Rotenberg, O.;Fridman, D.;Doulaveris, G.;Renz, M.;Kaplan, J.;Gebbs, J.;Xie, X.;Goldberg, G. L. and Dar, P.

Publication Date: Apr ,2020

Journal: Ultrasound in Obstetrics & Gynecology : The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology 55(4), pp. 546–551

Abstract: Objective: To assess the long-term outcome of postmenopausal women diagnosed with non-atypical endometrial hyperplasia (NEH). Methods: This was a retrospective study of women aged 55 or older who underwent endometrial sampling in our academic medical center between 1997 and 2008. Women who had a current or recent (< 2 years) histological diagnosis of NEH were included in the study group and were compared with those diagnosed with atrophic endometrium (AE). Outcome data were obtained until February 2018. The main outcomes were risk of progression to endometrial carcinoma and risk of persistence, recurrence or new development of endometrial hyperplasia (EH) ('persistent EH'). Logistic regression analysis was used to identify covariates that were independent risk factors for progression to endometrial cancer or persistent EH. Results: During the study period, 1808 women aged 55 or older underwent endometrial sampling. The median surveillance time was 10.0 years. Seventy-two women were found to have a current or recent diagnosis of NEH and were compared with 722 women with AE. When compared to women with AE, women with NEH had significantly higher body mass index (33.9 kg/m²) vs 30.6 kg/m² ; $P = 0.01$), greater endometrial thickness (10.00 mm vs 6.00 mm; $P = 0.01$) and higher rates of progression to type-1 endometrial cancer (8.3% vs 0.8%; $P = 0.0003$) and persistent NEH (22.2% vs 0.7%; $P < 0.0001$). They also had a higher rate of progression to any type of uterine cancer or persistent EH (33.3% vs 3.5%; $P < 0.0001$). Women with NEH had a significantly higher rate of future surgical intervention (51.4% vs 15.8%; $P < 0.0001$), including future hysterectomy (34.7% vs 9.8%; $P < 0.0001$). On multivariable logistic regression analysis, only NEH remained a significant risk factor for progression to endometrial cancer or persistence of EH. Conclusions: Postmenopausal women with NEH are at significant risk for persistent EH and progression to endometrial cancer, at rates higher than those reported previously. Guidelines for the appropriate management of postmenopausal women with NEH are needed in order to decrease the rate of persistent disease or progression to cancer.

[Long-term outcome of postmenopausal women with proliferative endometrium on endometrial sampling](#)

Authors: Rotenberg, Ohad;Doulaveris, Georgios;Fridman, Dmitry;Renz, Malte;Kaplan, Julie;Xie, Xianhong;Goldberg, Gary L. and Dar, Pe'er

Publication Date: Dec ,2020

Journal: American Journal of Obstetrics and Gynecology 223(6), pp. 896.e1–896.e7

Abstract: Background: Proliferative endometrium has been reported in 15% of endometrial biopsies of women aged 50 years and older. Contrary to endometrial hyperplasia, proliferative endometrium has not been associated with the risk of endometrial cancer. Objective: This study aimed to report on the long-term outcome of postmenopausal women who received a diagnosis of proliferative endometrium. Study Design: This is a retrospective cohort study of 1808 women aged 55 years and older who underwent endometrial sampling between January 1997 and December 2008. Outcome data were available through February 2018. Women with a proliferative endometrium were compared with those with an atrophic endometrium for future development of endometrial hyperplasia or cancer. A subanalysis was performed for those who presented with postmenopausal bleeding. Uni- and multivariable logistic regression analyses were used to assess for confounders. Results: In this study, 297 women (16.4%) received a diagnosis of proliferative endometrium. Furthermore, 962 women met the inclusion criteria. Among those women, 278 had a proliferative endometrium, and 684 had an atrophic endometrium. Women with a proliferative endometrium were younger (61.2 vs 64.5 years; $P < 0.001$), had a higher body mass index (33.9 vs 30.6 kg/m²; $P = 0.01$), and had a higher rate of progression to endometrial cancer (8.3% vs 0.8%; $P = 0.0003$), and persistent proliferative endometrium (22.2% vs 0.7%; $P < 0.0001$). Women with a proliferative endometrium were younger (61.2 vs 64.5 years; $P < 0.001$), had a higher body mass index (33.9 vs 30.6 kg/m²; $P = 0.01$), and had a higher rate of progression to endometrial cancer (8.3% vs 0.8%; $P = 0.0003$), and persistent proliferative endometrium (22.2% vs 0.7%; $P < 0.0001$). On multivariable logistic regression analysis, only proliferative endometrium remained a significant risk factor for progression to endometrial cancer or persistence of proliferative endometrium. Conclusions: Postmenopausal women with proliferative endometrium are at significant risk for persistent proliferative endometrium and progression to endometrial cancer, at rates higher than those reported previously. Guidelines for the appropriate management of postmenopausal women with proliferative endometrium are needed in order to decrease the rate of persistent disease or progression to cancer.





kg/m²) (odds ratio, 2.3; 95% confidence interval, 1.09-4.83; P<.0001) remained significant risk factors for progression to cancer. Conclusion: One of the 6 postmenopausal women who underwent endometrial sampling had a proliferative endometrium. Furthermore, 11.9% of women developed endometrial hyperplasia or cancer, a 4-fold greater incidence than women with an atrophic endometrium. The findings of this study suggest that long-term monitoring is warranted for women with postmenopausal bleeding and a proliferative endometrium histology. Further studies are needed to examine if a treatment is required to negate the risk of unopposed estrogen.

[Clinicopathological Spectrum of Endometrial Changes in Peri-menopausal and Post-menopausal Abnormal Uterine Bleeding: A 2 Years Study](#)

Authors: Damle, Rajshri P.;David, N. V.;Suryawanshi, Kishor H.;Gadre, Arundhati S.;Bagale, Priya S. and Ahire, Neelam

Publication Date: Dec ,2013

Journal: Journal of Clinical and Diagnostic Research : JCDR 7(12), pp. 2774–2776

Abstract: Background: Abnormal uterine bleeding is the Common presenting complaint in Gynaecology Outpatient Department in all age groups. It is due to the anovulatory cycles which are commonly seen in adolescent and peri-menopausal women. Abnormal uterine bleeding is caused by wide variety of organic or non-organic causes. Histopathological examination of endometrial sample remains the gold standard for diagnosis of endometrial pathology. Aim: To study the clinicopathological spectrum of endometrium in abnormal uterine bleeding in peri-menopausal and post-menopausal age groups. Material and methods: The study included prospective analysis of 119 cases of endometrial samples in patients of abnormal uterine bleeding above 40 years of age. The specimens were routinely processed and H&E stained slides were studied. Patients were categorized into peri-menopausal (40-49 years) and post-menopausal (> 50 years) age group. Results: A total of 119 specimens of endometrium were analyzed. Maximum number (73.94%) of cases were from peri-menopausal age group. The most common presenting complaint was menorrhagia (48.86%) followed by post-menopausal bleeding (26.05%). In peri-menopausal age group proliferative endometrium (35.22%) was the predominant histopathological pattern followed by endometrial hyperplasia (23.86%). Atrophic endometrium (25.80%) was the most frequent finding followed by endometrial hyperplasia (19.35%) in post-menopausal age group. Three cases of endometrial carcinoma were reported in post-menopausal age group only. Conclusion: A thorough histopathological work up and clinical correlation is mandatory in cases of abnormal uterine bleeding above the age of 40 years to find out organic lesions. Careful screening can detect early cancer of endometrium which has excellent prognosis and it will help in further management.

[Complex hyperplasia with and without atypia: clinical outcomes and implications of progestin therapy](#)

Authors: Reed, Susan D.;Newton, Katherine M.;Garcia, Rochelle L.;Allison, Kimberly H.;Voigt, Lynda F.;Jordan, C. Diana;Epplein, Meira;Swisher, Elizabeth;Upson, Kristen;Ehrlich, Kelly J. and Weiss, Noel S.

Publication Date: -08th ,2010

Journal: Obstetrics and Gynecology 116(2 Pt 1), pp. 365–373

Abstract: Objective: Limited data exist to inform clinicians and patients as to the likelihood of long-term endometrial hyperplasia response to progestin therapy, especially for atypical hyperplasia. We evaluated women with complex and atypical endometrial hyperplasia, comparing those prescribed progestin with those not prescribed progestin. Methods: This retrospective cohort study was conducted in 1985-2005 among women aged 18-88 years at an integrated health plan in Washington State. Women were ineligible if they achieved an outcome (endometrial carcinoma, hysterectomy, or both) within 8 weeks of hyperplasia diagnosis. Exposure was progestin use for at least 14 days by duration and recency. Outcomes included rate of 1) endometrial carcinoma, 2) hysterectomy, or 3) both. Analyses performed included Kaplan-Meier, incident rate ratios, and Cox proportional hazard ratios. Results: One thousand four hundred forty-three eligible women were identified. One thousand two hundred one had complex (n=164 no progestin) and 242 had atypical (n=62 no progestin)





hyperplasia. During follow-up, a median of 5.3 years (range 8 weeks to 20.8 years), 71 women were diagnosed with endometrial carcinoma (35 complex, 36 atypia) and 323 underwent hysterectomy (216 complex, 107 atypia). Among women with complex and atypical hyperplasia, rates of endometrial carcinoma among progestin users were 3.6 and 20.5 per 1,000 woman-years, respectively (compared with women who did not use progestin, 10.8 and 101.4). Among women with complex and atypical hyperplasia, rates of hysterectomy among progestin users were 23.3 and 61.4 per 1,000 woman-years, respectively (compared with women who did not use progestin, 55.1 and 297.3). Conclusion: Endometrial carcinoma risk is diminished approximately threefold to fivefold in women diagnosed with complex or atypical endometrial hyperplasia and dispensed progestin; hysterectomy risk is also decreased. Level of evidence: II.

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ARTICLES

Proliferative Endometrium in Menopause: To Treat or Not to Treat?

Authors: Abraham, Cynthia

Publication Date: Feb 1 ,2023

Journal: Obstetrics and Gynecology 141(2), pp. 265–267

Abstract: CLINICAL VIGNETTE: A 62-year-old postmenopausal woman presents with vaginal bleeding. Medical history is significant for morbid obesity. Endometrial biopsy is performed. Pathology shows proliferative endometrium. She asks about next steps.

The best course of management for proliferative endometrium in menopause remains to be elucidated.

[Thickened Endometrium: When to Intervene? A Clinical Conundrum](#)

Authors: Giri, S. K.;Nayak, B. L. and Mohapatra, Janmejay

Publication Date: June 1 ,2021

Journal: Journal of Obstetrics and Gynaecology of India 71(3), pp. 216–225

Abstract: The endometrium is a dynamic target organ in a woman's reproductive life. It undergoes cyclical change regulated by the fine balance between oestrogen and progesterone. The endometrial thickness (ET) varies according to the phases of the menstrual cycle. Endometrium contains both oestrogen and progesterone receptors, which respond to above hormones, irrespective of whether the woman is in reproductive or menopausal phase. Abundance of oestrogen leads to endometrial hyperplasia, and paucity causes endometrial atrophy. The initial best modality of assessing ET or aberration is high resolution transvaginal ultrasonogram. Thickened endometrium is always a clinical conundrum. Dilemma does remain as to the thickness of endometrium which requires intervention, mostly in symptomatic pre and perimenopausal women. In post-menopausal women with bleeding, the cut-off of ET that warrants investigation is almost defined. However, the cut-off value of ET in asymptomatic postmenopausal women; beyond which intervention is required, is still debated. Dilemma also exists about the cut-off of ET in both symptomatic and asymptomatic women on HRT and Tamoxifen. This article will discuss the above issues and reach at some consensus about the cut-off of ET after critical analysis of evidence and experience and will help clinicians in arriving at a proper decision in dealing with such clinically confounding situations.

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CONFERENCE PAPERS



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[US Evaluation of Endometrial Thickness in Postmenopausal Patients as a Predictor of Endometrial Cancer: Systematic Review & Meta-Analysis](#)

Authors: Peixoto B.G., Garcia R.H., Sanches T.F., Fins R.J.P., Costa F.S., Reis F.J.C., Herren H., PoliNeto O.B. and RosaeSilva, J.C.

Publication Date: 2024

Publication Details: Journal of Minimally Invasive Gynecology. Conference: 53. Ernest N. Morial Convention Center, New Orleans United States. 31(11 Supplement) (pp S154); Elsevier B.V.,

Abstract: Study Objective: Systematic review of the literature in order to obtain the most appropriate endometrial thickness cut-off point for uterine invasive investigation.

[Evaluation of the Impact of Hrt on Endometrial Thickness and the Diagnosis of Endometrial Cancer \[please note, complete the form to request the article\]](#)

Authors: D'Souza N., Daas M., Halder K., Latimer J., Bolton H., Baldwin P., Pathiraja P. and Quaranta, M.

Publication Date: 2022

Publication Details: International Journal of Gynecological Cancer. Conference: European Congress on Gynaecological Oncology, ESGO 2022. Berlin Germany. 32(Supplement 2) (pp A167-A168); BMJ Publishing Group.

Abstract: Introduction/Background Following its introduction in the 1960s, the use of Hormonal Replacement Therapy (HRT) to treat postmenopausal symptoms has increased from 30% to 50%. However, this has resulted in an increased utilisation of services for the investigation of women with increased endometrial thickness (ET) subsequent to HRT. Methodology This was a retrospective case-control study carried out in a tertiary institute in the UK. Data of 452 women referred to the hysteroscopy clinic for postmenopausal bleeding was collected over a 2-year period. The women were divided into 2 cohorts - group 1 on HRT (N= 206) and group 2-not on HRT (N= 246). Results The mean age and BMI was 57 years and 27.54 kg/m² in group 1 and 61.54 years and 29.51 kg/m² in group 2. Analysis of group 1 revealed that the mean ET was 9.5 mm (95% CI 6.152-12.85 mm) in women who were diagnosed with an endometrial malignancy (N=8) and 6.89 mm (95% CI 6.404-7.381 mm) in women with benign endometrial histology (N=148). This difference was statistically significant (ttest; p=0.0201). However, further evaluation using a ROC curve, an ET of 9.5 mm leads to a sensitivity of only 50% to cancer (specificity = 85.8%) while the current cut off, 4 mm, detected nearly all cancers. This result was further corroborated by a ROC analysis of the non-HRT group which demonstrated similar results. Conclusion Increasing HRT utilisation will lead to a rise in the number of women with benign endometrial thickening. This may lead to a rise in unnecessary referrals. Our initial work has not demonstrated that increasing the ET cut off is useful in this group, however a downside of our work is the small number of patients with cancer in the HRT group. Thus larger robust studies would be useful to evaluate if this hypothesis has clinical merit.

[Managing the histological finding of proliferative endometrium in postmenopausal women](#)

Authors: O'Connor E., Chakravorty S., Ragi S., Kochman A. and Gurram, S.

Publication Date: 2021

Publication Details: BJOG: An International Journal of Obstetrics and Gynaecology. Conference: Royal College of Obstetricians and Gynaecologists World Congress, RCOG 2021. Virtual. 128(SUPPL 2) (pp 17-18); Blackwell Publishing Ltd,

Abstract: Objective To investigate the current management of the histological diagnosis of proliferative endometrium in postmenopausal women, in the absence of agreed guidance. Design We performed a retrospective review of women presenting to NHS Lanarkshire with postmenopausal bleeding (PMB) and found to have a histological diagnosis of proliferative endometrium. We surveyed gynaecology trainees and consultants of the West of Scotland regarding their management of postmenopausal proliferative endometrium. Method The pathology department provided a list of all patients with a finding of proliferative endometrium from 5th January 2018 to 18th April 2019. We identified the patients who were post-menopausal with vaginal bleeding, and reviewed their case notes. We reviewed the demographics, risk factors, ultrasound findings, outcomes, follow up and further attendances within the gynaecology department. We conducted a survey via email covering a



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variety of clinical scenarios with the finding of proliferative endometrium to assess current management. Results We identified 77 reports of proliferative endometrium from post-menopausal women with vaginal bleeding. Median age was 54 years (interquartile range, IQR, 51- 57 years). Median BMI was 34.29 kg/m² (IQR 28.25- 39.75 kg/m²). 23 (30%) women were using HRT. 5 (6%) had a personal history of breast cancer. Progesterone was offered to 46% of eligible cases. 43 (56%) had no follow-up arranged, of these 7 (9%) were re-referred. 34 (44%) women were offered follow up. 4 (5%) women underwent hysterectomy-3 of these due to adnexal masses. 2 (3%) women had ovarian malignancy confirmed on hysterectomy specimen. 2 (3%) were subsequently diagnosed with simple endometrial hyperplasia. No patients were diagnosed with complex hyperplasia/endometrial malignancy. There were 13 complete responses to the survey from grades ST5 to consultant. This suggests there is widespread variability in the management of proliferative endometrium in postmenopausal women which includes recommending weight loss, hysteroscopic guided biopsy, repeat pipelle biopsy, progesterone, departmental ultrasound of ovaries or reassure and discharge depending upon the patient's risk factors. Conclusions Our study has shown there is no uniform approach to the management of these women. Though the majority have no underlying pathology, risk assessment is essential to rule out the possibility of significant underlying pathology. This also presents an opportunity to offer weight management. There are no official guidelines to manage this condition. We need a unified approach to avoid unnecessary follow up and over treatment.

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FOR OFFICE USE ONLY

DATABASES AND INFORMATION SOURCES USED					
	Pubmed		HMIC	x	BMJ Best Practice
x	Medline		Social Policy and Practice	x	Cochrane Library
	Emcare		CINAHL	x	TRIP
x	Embase		PsycINFO		Grey Literature
	AMED	x	UpToDate		Other

PURPOSE OF SEARCH			
	Patient info/health & well being	x	Clinical decision making (inc. patient care)
	Executive Team support	x	Research/Education/Professional development
	Quality Improvement		Primary Care & Neighbourhoods Directorate support
	KM/Management decision making		Other





USER CATEGORY OF REQUESTOR

	Medical students		Patients/public
x	Nursing/midwifery students		Physician Associates
	Doctor/Psychiatrist		Public Health (Somerset CC)
	Nurses/Midwives		Other
	Allied Health professionals		

HAS PERMISSION TO SHARE THE RESULTS BEEN OBTAINED FROM THE REQUESTOR?

x	YES - share		NO – do not share
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KEY WORDS/SEARCH STRATEGY INCLUDING MESH HEADINGS

LIMITS USED

Proliferative endometrium
Follicular phase endometrium
Endometrial proliferation
Endometrial thickening phase

Bleeding
H?emorrhage
Postmenopausal bleeding

Postmenopaus*
After menopause
Post-menopause
Menopause transition
Post-climacteric

Management
Guid*
Surveillance
Treatment
Test
SR (Systematic Reviews)

English

