Post-Menopausal Bleeding Primary Care Pathway Quick Pathway primer Expanded details (2) Patient resources links: 1. History 🕥 Risk factors for endometrial cancer: Patient profile: Age > 40 years Obesity (BMI > 30 kg/m2) ■ > 40 years old Gather recent history, including: One year of no • Nulliparity • Diabetes • Current Tamoxifen use bleeding followed Evaluate bleed (pattern & quantity) • Polycystic ovarian syndrome w/irregular cycles by new onset of · Pregnancy risk / sexual history · Hereditary non-polyposis colorectal cancer vaginal bleeding · Assess risk factors for endometrial cancer · Unopposed estrogen exposure Red flags: 2. Physical exam 🕥 Red flags Patient looks unwell · Tachycardia/hypotension Call RAAPID for Vitals / general appearance Vulva / vagina: Atrophic change • Flooding through >1 pad every hour gynecology or or trauma · Large uterine or cervical mass which is 911 if urgent Bimanual exam obstructing voiding · Concerning cervical mass Speculum exam / inspect cervix 3. Investigations () If due If abnormal Pap test Manage, as per guidelines If positive Treat, as per guidelines STI screen If relevant, consider If positive Pregnancy test Manage pregnancy For all If low CBC/Ferritin Iron therapy patients, order Transvaginal pelvic ultrasound More details 4. Treat / manage 🕥 Endometrial polyp or Endometrial Endometrial More details submucosal fibroid thickness < 5mm thickness > 5mm More details More details Referrals: Stop hormone therapies Essential information Reassure patient, to include: no need to refer Obtain endometrial biopsy ■ History exam, inc. Available in community? Yes pap results No Treat atrophy ■ Lab & if necessary DI results Hyperplasia If recurrent, Proliferative Inadequate Attempted ongoing endometrium with atypia or sample treatments bleeding or hyperplasia malignancy & outcome Refer to without atypia gynecology If persistent or recurring symptoms Progesterone Refer to









(Prometrium, Mirena IUD)





gyne-ONCOLOGY

PATHWAY PRIMER

- Post-menopausal bleeding is defined as new onset bleeding that occurs in a woman older than 40 years of age
 after one year of no bleeding (amenorrhea). Post-menopausal bleeding occurs in between 4% 11% of women,
 and is usually attributable to an intrauterine source.¹ However, bleeding can occur from the cervix, vagina, vulva,
 fallopian tubes, the bladder, or bowel, so a thorough physical assessment is recommended.
- The American College of Obstetricians and Gynecologists suggests that the assessment of any postmenopausal bleeding should be completed promptly, as abnormal uterine bleeding is the presenting sign of endometrial cancer in 90% of women.² Endometrial cancer is a very common gynaecologic malignancy, with an incidence in Canada of 19 cases per 100,000 women.³
- This pathway was created to facilitate the prompt management of post-menopausal bleeding in the patient's medical home and to provide primary care clinicians with guidance on evidence-based diagnosis, investigations, medical management, and guidelines for when to make a referral to Gynecology or to RAAPID. This pathway does not apply to women of reproductive age who have abnormal uterine bleeding please refer to the Enhanced Primary Care Pathway for Abnormal Uterine Bleeding for that guidance.

EXPANDED DETAILS

1. History

The patient history obtained from a woman who presents with vaginal bleeding after menopause should focus on a review of risk factors for endometrial cancer and on eliminating other possible causes for bleeding as listed in the differential diagnosis. The average age for women with endometrial cancer is 61 years, but 5% - 30% of cases can occur in pre-menopausal women.⁴ Women younger than 50 years of age can share many of the same risk factors for endometrial cancer as older women.

- . Evaluate the bleeding pattern, including quantity and timing
- Assess pregnancy risk and sexual history
 - Assess if there is potential for pregnancy. See <u>Important Treatment Considerations Confirmed Pregnancy</u> for more information on managing pregnancy with abnormal bleeding.
 - Assess if there is risk of a Sexually Transmitted Infection (STI), see <u>Investigations</u> for more information on treatment
- Review the risk factors for endometrial cancer 5
 - o Age > 40 years
 - Obesity (BMI > 30 kg/m2)
 - o Nulliparity
 - o PCOS (polycystic ovarian syndrome) with irregular cycles
 - o Diabetes
 - o HNPCC (hereditary non-polyposis colorectal cancer)
 - Current Tamoxifen use
 - o Unopposed estrogen exposure

If the patient is taking hormonal therapies, consider stopping these therapies.

• Review Differential Diagnoses

Other potential causes for post-menopausal bleeding include:

- o Non-gynecologic sources of bleeding: bladder/kidney, urethral caruncle, and bowel as a source
- o Endometrial or cervical polyp
- o Proliferative endometrium, or endometrial hyperplasia (with atypia and without atypia)
- o Endometrial carcinoma
- o Cervical dysplasia or cervical cancer
- o Vulvar, vaginal or endometrial atrophy
- Submucosal fibroid
- o Sexually transmitted infection
- o Foreign body in the vagina (e.g. a retained pessary)

2. Physical Exam

The physical examination should identify evidence of any systemic conditions that can cause bleeding, as well as evaluate any anatomical causes, such as fibroids or cervical polyps. In stable patients, conduct a physical examination for structural abnormality: vulva, vagina, speculum (cervix) and bimanual examinations. Examine the external genitalia for ulcers or atrophic tissue, which could be the source of the bleeding.

- If ulcers are present, initiate an urgent referral to Gynecology for biopsy and medical management. A biopsy can be taken by the GP if skilled in this area.
- If vaginal or vulvar atrophy is the cause for bleeding, perform a Transvaginal Pelvic Ultrasound to assess endometrial thickness.

Alarm Features/Red flags

- · Patient looks unwell
- · Hypotension or Tachycardia
- · Hemorrhage or heavy bleeding defined as soaking through a pad or tampon every hour
- · Large uterine or cervical mass which is obstructing voiding
- Concerning cervical mass (irregular, possibly associated with inflammatory discharge (pus). Cervical cancer must be ruled out with an urgent tissue sample.

If alarm features/red flags are present or the patient is medically unstable, call RAAPID for an urgent referral to Gynecology for immediate hospital evaluation.

3. Investigations

Laboratory tests

- Pap test: If the patient is due, perform a Pap test (<u>TOP Cervical Cancer Screening Guideline</u>). If there is post-coital bleeding or vaginal discharge, test for STI and possible other causes for alteration of vaginal flora:
 - o Chlamydia
 - o Gonorrhea
 - o Trichomonas
 - o Bacterial Vaginosis
 - Yeast

STI testing can be performed with swab or a urine test.

- o If STI testing is positive, treat as per provincial guidelines (Alberta STI Guidelines).
- If STI testing is negative, but the cervix appears friable, initiate a trial treatment for mucopurulent cervicitis
 (<u>Alberta STI Guidelines</u>). Persistent symptoms that do not respond to treatment should be referred to
 Gynecology.

Confirmed pregnancy

- Perform a pregnancy test if there is any possibility of pregnancy. If confirmed, identify the patient's RH status.
 - If they are RH negative and negative for Anti-D antibodies on type and screen, give the Anti-D antibody (e.g. WinRho®/RhoGam® in 300mcg IM injection)
 - If the patient has a positive pregnancy test and is bleeding, ensure the pregnancy is viable and intrauterine with a pelvic ultrasound.
 - o Link to Early Pregnancy Loss clinic if the pregnancy is NOT viable and intrauterine and the patient is stable.
 - If this is a possible ectopic pregnancy or the patient is bleeding heavily or is medically unstable, call RAAPID for referral to Gynecology.

CBC/Ferritin

For stable patients, consider ordering a CBC/Ferritin if there are concerns of possible anemia or iron deficiency.
 Treat as appropriate with iron therapy, especially if there is continued menstrual bleeding. There is no utility to requesting FSH / LH / estradiol or progesterone levels.⁶

Thyroid testing

Thyroid functioning testing is not indicated unless there are clinical findings suggestive of an index of suspicions
of thyroid disease.⁷

Coagulation Disorders

• Testing for coagulation disorders should only be considered in women with heavy bleeding since menarche or who have a family history/personal history of abnormal bleeding.

4. Treat/Manage

A Transvaginal Pelvic Ultrasound should be the first line for imaging abnormal uterine bleeding.⁸ For all stable patients, perform a Transvaginal Pelvic Ultrasound to rule out uterine structural causes for abnormal bleeding (e.g. polyp). A transvaginal ultrasound allows for assessment of anatomical abnormalities of the uterus and endometrium. A post-menopausal endometrial thickness assessment is best evaluated with a transvaginal ultrasound, so please encourage the patient to be prepared for this assessment.

Ultrasound findings:

• Fibroids / Polyps:

- If a polyp or submucosal fibroid is present, these findings many cause post-menopausal bleeding and a referral to Gynecology is indicated.
- o Intramural fibroids and serosal fibroids do not usually cause post-menopausal bleeding, but if your patient is experiencing pressure symptoms or pain, a referral to Gynecology is indicated.

• Endometrial Thickness Assessment:

 Endometrial thickness < 5mm: If endometrial thickness < 5mm with vaginal bleeding due to atrophy, attempt medical therapy.

- Trial of topical moisturizer (e.g. Replens®)
- Trial of topical estrogen (insertion)
 - For 14 days, applied at night daily, then two to three times/week for maintenance if symptoms improve
- If the patient is taking Tamoxifen®, initiate a referral to Gynecology for any vaginal bleeding. Do not prescribe vaginal estrogens for atrophy, but you may trial Replens® or a non-hormonal vaginal moisturizer while awaiting referral.
- Endometrial thickness > 5mm: If endometrial thickness > 5mm with vaginal bleeding, refer to Gynecology or skilled community GP for endometrial sampling. Counsel patient to stop any hormone therapies if taking estrogen.
 - **Hyperplasia with atypia or endometrial carcinoma:** If sampling suggests hyperplasia with atypia or endometrial carcinoma, make an urgent referral to GyneONCOLOGY. Contact Specialist LINK for advice (specialistlink.ca) if you are unsure where to refer the patient or if progesterone would be indicated.
 - **Hyperplasia without atypia:** If sampling suggests hyperplasia without atypia, begin progesterone treatment (Mirena® IUD or progesterone 200mg PO QHS). Bleeding should stop within three to six months. If bleeding persists, refer to Gynecology. Repeat endometrial sampling is indicated in three to six months to ensure resolution of endometrial hyperplasia even if bleeding has ceased.
 - **No hyperplasia or malignancy:** If sampling finds proliferative endometrium, no hyperplasia or malignancy, start medical treatment with Progesterone-only methods (e.g. Prometrium® 100-200mg or Mirena® IUD).

Follow-up

- If there is successful cessation of bleeding on progesterone therapy, discontinue the therapy after one year.
- If there is successful cessation of bleeding with Mirena® IUD, remove after duration of device (~five years).
- If the patient has any further bleeding, she will need to be re-assessed again with transvaginal ultrasound, endometrial sampling, and should have a referral to Gynecology for consideration of hysteroscopic sampling.

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BACKGROUND

About this pathway

 The pathway is intended to provide evidence-based guidance to support primary care providers in caring for patients with common gynecological conditions within the medical home.

Authors and conflict of interest declaration

 This pathway was reviewed and revised under the auspices of the Calgary Zone Department of Gynecology in 2020 by a multidisciplinary team led by family physicians and gynecologists. Names of participating reviewers and their conflict of interest declarations are available on request.

Pathway review process, timelines

 Primary care pathways undergo scheduled review every year if there is a clinically significant change in knowledge or practice.

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DISCLAIMER

This pathway represents evidence-based best practice but does not override the individual responsibility of health care professionals to make decisions appropriate to their patients using their own clinical judgment given their patients' specific clinical conditions, in consultation with patients/alternate decision makers. The pathway is not a substitute for clinical judgment or advice of a qualified health care professional. It is expected that all users will seek advice of other appropriately qualified and regulated health care providers with any issues transcending their specific knowledge, scope of regulated practice or professional competence.

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PROVIDER RESOURCES

Advice options, referral guidelines

When to refer to specialty or call RAAPID, Specialist Link/eReferral Advice Request

- Severe bleeding or medical instability (i.e. soaking through a pad an hour or abnormal vital signs). This patient needs to be directed to hospital through RAPPID or the ER. Call RAPPID for on-call Gynecologist or 911.
- Ultrasound findings of endometrial hyperplasia with atypia or endometrial carcinoma should result in an urgent referral to **GyneONCOLOGY**.
- For any Gynecology referral please include: a complete patient history, results from Pap test, laboratory and diagnostic imaging investigations, and any attempted treatments with outcomes. This information allows for the appropriate triage of your patient.

Contact information

- For RAAPID South, call 1-800-661-1700 or 403-944-4486. Visit https://www.albertahealthservices.ca/info/Page13345.aspx for more details.
- Family physicians can request non-urgent advice online at specialistlink.ca or by calling 403-910-2551. The service is available from 8 a.m. to 5 p.m. (with some exceptions), Monday to Friday (excluding statutory holidays). Calls are returned within one hour.
- Obstetrics and Gynecology advice is available via Alberta Netcare eReferral Advice Request (responses are
 received within five calendar days). Visit https://www.albertanetcare.ca/eReferral.htm for more information.

Resources	Link
TOP Guideline – Cervical Cancer Screening	https://actt.albertadoctors.org/CPGs/Lists/CPGDocumentList/Cervi
	cal-Cancer-Screening-Summary.pdf
Alberta STI Treatment Guidelines	https://open.alberta.ca/publications/6880386
Post-menopausal uterine bleeding -	https://www.uptodate.com/contents/postmenopausal-uterine-
UpToDate®	bleeding?search=post%20menopausal%20bleeding&source=searc
	h result&selectedTitle=1~81&usage type=default&display rank=1

PATIENT RESOURCES

Resources	Link
MyHealth.Alberta.ca - Menopause	https://myhealth.alberta.ca/health/pages/conditions.aspx?Hwid=hw228763#h
and Perimenopause: Information	<u>w228868</u>
on causes, symptoms, treatments	
and resources for women	
UpToDate® Patient Education:	https://www.uptodate.com/contents/abnormal-uterine-bleeding-beyond-the-
Abnormal uterine bleeding	basics?search=post%20menopausal%20bleeding&source=search_result&sel
(Beyond the Basics)	ectedTitle=1~2&usage_type=default&display_rank=1

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¹ Goodman, A. Post-menopausal uterine bleeding. UpToDate®. Accessed on June 29 2020. <a href="https://www.uptodate.com/contents/postmenopausal-uterine-bleeding?search=post%20menopausal%20bleeding&source=search_result&selectedTitle=1~81&usage_type=default&display_rank

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²ACOG Committee Opinion No. 734 Summary: The Role of Transvaginal Ultrasonography in Evaluating the Endometrium of Women With Postmenopausal Bleeding, Obstetrics & Gynecology: May 2018 - Volume 131 - Issue 5 - p 945-946 doi: 10.1097/AOG.000000000002626

³ Wolfman, W. SOCG Clinical Practice Guideline No. 249 – Asymptomatic Endometrial Thickening. *J Obstet Gynaecol Can.* 2018;40(5):e367-377. https://doi.org/10.1016/j.jogc.2018.03.005

⁴ Sing, S, Best, C, Dunn, S et al. SOGC Clinical Practice Guideline No. 292 – Abnormal Uterine Bleeding in Pre-Menopausal Women. *J Obstet Gynaecol Can*. 2018;40(5):e391-e415

⁵ Sing, S, Best, C, Dunn, S et al. SOGC Clinical Practice Guideline No. 292 – Abnormal Uterine Bleeding in Pre-Menopausal Women. *J Obstet Gynaecol Can.* 2018;40(5):e391-e415

⁶ Choosing Wisely. Society of Obstetricians and Gynecologists of Canada: Nine Things Physicians and Patients Should Question. Choosing Wisely Canada; 2019. https://choosingwiselycanada.org/obstetrics-and-gynaecology/

⁷ Wolfman, W. SOCG Clinical Practice Guideline No. 249 – Asymptomatic Endometrial Thickening. J Obstet Gynaecol *Can.* 2018;40(5): e367-377. https://doi.org/10.1016/j.jogc.2018.03.005

⁸ Sing, S, Best, C, Dunn, S et al. SOGC Clinical Practice Guideline No. 292 – Abnormal Uterine Bleeding in Pre-Menopausal Women. *J Obstet Gynaecol Can*. 2018;40(5):e391-e415