National Women & Infants Health Programme

National Clinical Practice Guideline

Assessment and Management of Postmenopausal Bleeding (PMB)

INSTITUTE OF OBSTETRICIANS & GYNAECOLOGISTS

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

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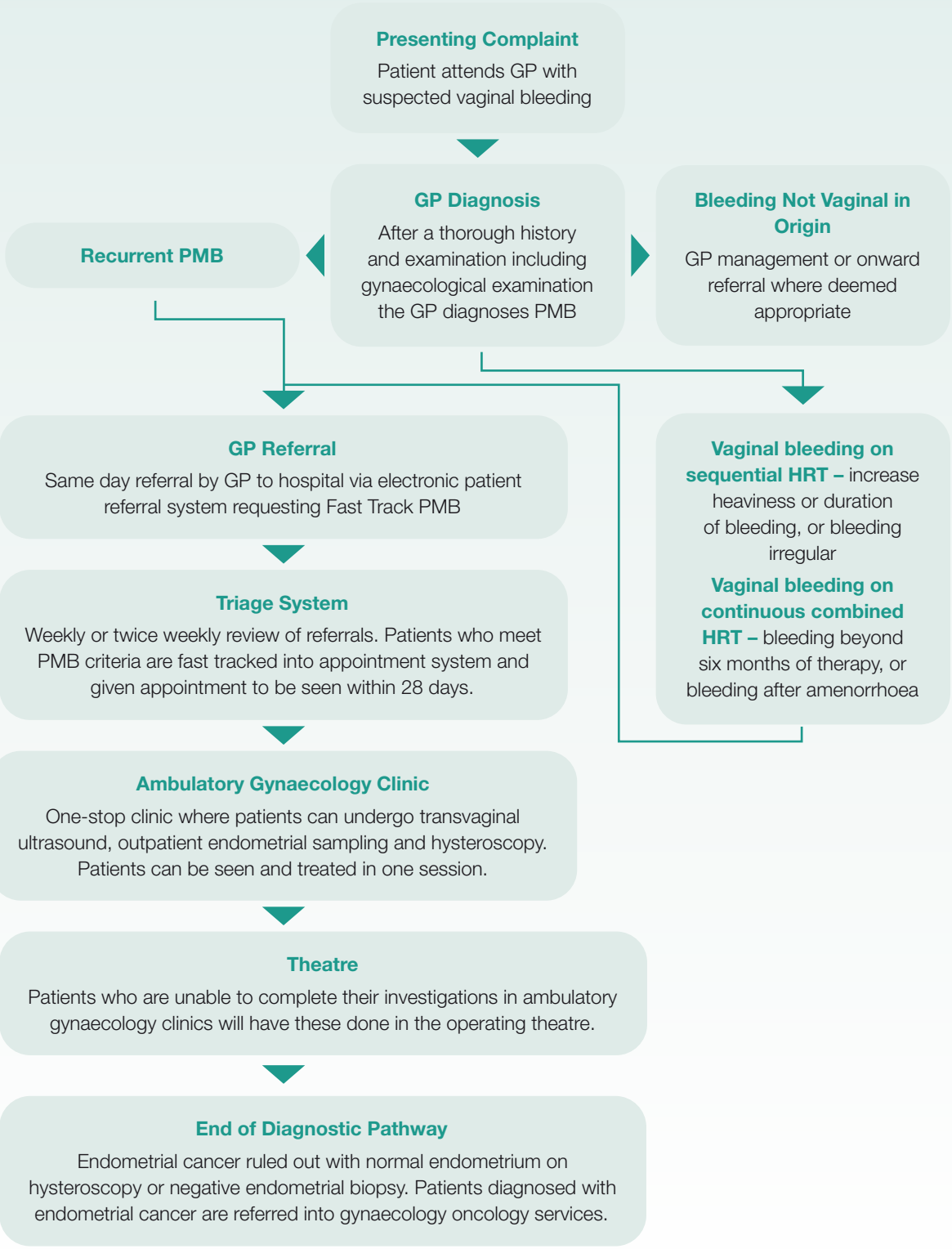
Algorithm


Presenting Complaint
Patient attends GP with suspected vaginal bleeding
GP Diagnosis
After a thorough history and examination including gynaecological examination the GP diagnoses PMB
Recurrent PMB
Bleeding Not Vaginal in Origin
GP management or onward referral where deemed appropriate
GP Referral
Same day referral by GP to hospital via electronic patient referral system requesting Fast Track PMB
Vaginal bleeding on sequential HRT – increase heaviness or duration of bleeding, or bleeding irregular
Vaginal bleeding on continuous combined HRT – bleeding beyond six months of therapy, or bleeding after amenorrhoea
Triage System
Weekly or twice weekly review of referrals. Patients who meet PMB criteria are fast tracked into appointment system and given appointment to be seen within 28 days.
Ambulatory Gynaecology Clinic
One-stop clinic where patients can undergo transvaginal ultrasound, outpatient endometrial sampling and hysteroscopy. Patients can be seen and treated in one session.
Theatre
Patients who are unable to complete their investigations in ambulatory gynaecology clinics will have these done in the operating theatre.
End of Diagnostic Pathway
Endometrial cancer ruled out with normal endometrium on hysteroscopy or negative endometrial biopsy. Patients diagnosed with endometrial cancer are referred into gynaecology oncology services.

Key Recommendations

1. We recommend that menopause should be defined as the final menstrual period followed by 12 months of amenorrhoea. *Grade 1A*
2. We recommend that postmenopausal bleeding in women not taking hormone replacement therapy is defined as an episode of vaginal bleeding occurring 12 months or more after the final menstrual period. *Grade 1A*
3. We suggest that assessments should aim to identify and monitor the multiple identifiable risk factors associated with endometrial cancer. *Best practice*
4. We recommend that vaginal, vulval and cervical cancers are also considered in the differential diagnosis for women presenting with postmenopausal bleeding. *Grade 1B*
5. We recommend that urological and gastrointestinal cancers are also considered in the differential diagnosis for women presenting with bleeding that is thought to be coming from the genital tract. *Grade 1C*
6. We recommend that all women presenting with postmenopausal bleeding in the general practice setting should undergo a focused history and examination, including a vaginal and speculum examination, prior to referral to gynaecological services. *Best practice*
7. We recommend that all women with postmenopausal bleeding who are not on HRT require referral for investigation. *Best practice*
8. We recommend that all women with abnormal bleeding on HRT require referral for investigation. *Best practice*
9. We recommend that all women with abnormal bleeding on Tamoxifen require referral for investigation. *Best practice*
10. We recommend that women referred for investigations of postmenopausal bleeding should be seen within gynaecology units within 28 days. *Best practice*
11. We suggest that where possible, women referred for investigation of postmenopausal bleeding or abnormal uterine bleeding on HRT should be seen in an ambulatory gynaecology (AG) clinic. *Best practice*
12. We recommend that all gynaecology services should be able to assess and investigate women with postmenopausal bleeding. Where comprehensive ambulatory services are not yet available, in the interim, there should be a managed fast-track pathway for women with postmenopausal bleeding. *Best practice*
13. We recommend that all women referred for investigation of postmenopausal bleeding or abnormal uterine bleeding on HRT should undergo a transvaginal pelvic ultrasound to assess the thickness and features of the endometrium. *Best practice*
14. We recommend that women with postmenopausal bleeding with an endometrial thickness of ≥4mm should undergo endometrial sampling. *Grade 1C*

15. We recommend that a diagnostic hysteroscopy should be carried out where transvaginal ultrasound has detected focal endometrial pathology, or the endometrial thickness is greater than 4mm. *Grade 1A*
16. We recommend that women on Tamoxifen with abnormal uterine bleeding are offered diagnostic hysteroscopy with endometrial sampling as well as transvaginal ultrasonography for assessment of the endometrium in these women is a not a useful tool for triage. *Grade 1B*
17. We suggest that transabdominal ultrasound should be used to compliment transvaginal ultrasound where there is an enlarged uterus or pelvic mass. *Grade 1A*
18. We recommend that isolated dilation and curettage should not be used as the first line method for obtaining endometrial samples in the investigation of postmenopausal bleeding. *Best Practice*
19. We recommend that endometrial sampling in the form of office-based biopsy is used in conjunction with transvaginal ultrasound with or without hysteroscopy for the investigation of women with postmenopausal bleeding. Blind endometrial sampling in isolation is not sufficient for investigation. *Best practice*
20. We recommend that the vaginoscopic approach should be the standard technique in outpatient hysteroscopy as it is better tolerated by the woman when compared to conventional hysteroscopy techniques. *Grade 1B*
21. We suggest that women with no contraindications can be advised to consider taking a non-steroidal anti-inflammatory drug (NSAID) 1-2 hours prior to their hysteroscopy to reduce post-procedure pain. This should be communicated to them in their appointment letter. *Grade 1C*
22. We recommend that hysteroscopy and repeat endometrial biopsy should be considered in women who experience unexplained, persistent, or recurrent postmenopausal bleeding in the setting of prior reassuring investigations. A low threshold for reinvestigation of these women should be maintained. Care of this patient group should be guided by a consultant gynaecologist. *Grade 1C*
23. We suggest that in postmenopausal women without bleeding, transvaginal ultrasound findings of increased endometrial thickness ≥ 11mm requires further investigation. *Grade 2A*
24. We recommend that women taking HRT should be referred for investigation if their bleeding is persistent. *Grade 1B*
25. We recommend that women taking sequential HRT should be referred for investigation if they experience irregular bleeding despite adjustment, more than 3 months of commencing treatment, or if their bleeding increases in heaviness or duration. *Grade 1A*
26. We recommend that women taking continuous combined HRT should be referred for investigation if they experience bleeding beyond six months of commencing therapy, or if bleeding occurs after a significant spell of amenorrhoea. Where additional risk factors exist clinical discretion may warrant earlier referral. *Grade 1A*

Chapter 1: **Initiation**

The National Clinical Effectiveness Committee (NCEC) and Health Information and Quality Authority (HIQA) define clinical guidelines as systematically developed statements, based on a thorough evaluation of the evidence, to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances, across the entire clinical spectrum.[1]

1.1 Purpose

This document outlines considerations for the assessment and care of women with postmenopausal bleeding (PMB). It provides advice for healthcare professionals around the provision of safe, evidence-based care to women presenting with PMB. These guidelines are designed to guide clinical judgement but not replace it.

1.2 Scope

Target Users

The Guideline is a resource for all clinicians working in General Practice and Gynaecology.

Target Population

The Guideline is a resource for all women in the perimenopausal and postmenopausal period.

1.3 Objective

To provide evidence-based recommendations for the care of women with postmenopausal bleeding as well as promoting a standardised approach nationally across all General Practice and Gynaecology units.

1.4 Guideline development process

The Guideline Developers agreed to undertake this work under the direction of the Guideline Programme Team (GPT). An Expert Advisory Group (EAG) was commissioned by the GPT. Their role was to critically review the Guideline prior to submission to the National Women and Infants Health Programme (NWIHP) for final approval.

See Appendix 1 for EAG group membership and Appendix 2 for Guideline Programme Process.

The Clinical Practice Guideline writing group members were Dr Ailbhe Duffy, Dr Meabh Ní Bhuinneain, Dr Naomi Burke and Dr Cliona Murphy.

1 National Clinical Effectiveness Committee (NCEC) and Health Information and Quality Authority (HIQA) (2015) National quality assurance criteria for clinical guidelines. Version 2. Dublin: NCEC and HIQA. https://www.hiqa.ie/sites/default/files/2017-01/National-Quality-Assurance-Criteria.pdf

1.5 Stakeholder involvement

Stakeholders are people who have a common interest in improving health services. This includes persons that are responsible for delivering and those who receive services related to the clinical Guideline.

The Guideline Development Group consisted of Gynaecologists with a special interest in PMB. The Expert Advisory Group also has representatives from Gynaecology as well as Gynaecology-Oncology. Membership of the EAG also included professionals from the area of General Practice, Midwifery, Pathology, Histopathology and patient representation from advocacy groups.

1.6 Disclosure of interests

Guideline developers and reviewers bring a range of experiences and perspectives to the work of the national Guideline Programme. It is likely that both Guideline developers and stakeholders/reviewers will have a variety of interests, arising from different contexts and activities done in a professional or personal capacity. These can include employment and other sources of income, speaking engagements, publications and research, and membership of professional or voluntary organisations. The involvement of individuals with relevant content expertise is essential for enhancing the value of Guideline recommendations, but these individuals may also have interests that can lead to conflicts of interest, as may peer reviewers, patient representatives and researchers.

All interests should be declared if, in the view of a reasonable person, they are relevant, or could be perceived to be relevant, to the work of the Clinical Practice Guideline in question[2]. Declaring an interest does not mean there is a conflict of interest.

It is important that interests are openly declared so they can be appropriately managed. Conflicts of interest can bias recommendations and ultimately be harmful to patients and the health system. Disclosures of interests and appropriate management of conflicts of interest, when identified, are therefore essential to producing high-quality, credible health guidelines.[3]

The Guidelines International Network (GIN), a global network of Guideline developers that aims to promote best practices in the development of high-quality guidelines, developed a set of 9 principles to provide guidance on how financial and non-financial conflicts of interest should be both disclosed and managed. It is recommended that Guideline developers follow the GIN principles.[4]

For this National Clinical Practice Guidelines, all Guideline developers are asked to complete a conflict of interest declaration form. The response to declared interests will be managed by the Guideline programme team, in accordance with GIN principles. Conflicts of interest may be reported in the published Guideline and declarations of interest can be made available.

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2 NICE (2019) Policy on declaring and managing interests for NICE advisory committees. https://www.nice.org.uk/Media/Default/About/Who-we-are/Policies-and-procedures/declaration-of-interests-policy.pdf

3 Traversy G, Barnieh L, Akl EA, Allan GM, Brouwers M, Ganache I, Grundy Q, Guyatt GH, Kelsall D, Leng G, Moore A, Persaud N,Schünemann HJ, Straus S, Thombs BD, Rodin R, Tonelli M. CMAJ. 2021, 193(2):E49-E54. DOI: 10.1503/cmaj.200651 https://www.cmaj.ca/content/193/2/E49

4 Holger J. Schünemann, Lubna A. Al-Ansary, Frode Forland, *et al.*; for the Board of Trustees of the Guidelines International Network. Guidelines International Network: Principles for disclosure of interests and management of conflicts in guidelines. Ann Intern Med. 2015;163:548-553. doi:10.7326/M14-1885 https://www.acpjournals.org/doi/10.7326/m14-1885

1.7 Disclaimer

These guidelines have been prepared to promote and facilitate standardisation and consistency of good clinical practice, using a multidisciplinary approach. Information in this Guideline is current at the time of publication.

The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the Clinician in light of clinical data presented by the patient and the diagnostic and treatment options available.

Clinical material offered in this Guideline does not replace or remove clinical judgment or the professional care and duty necessary for each specific perimenopausal or postmenopausal woman.

Clinical care carried out in accordance with this Guideline should be provided within the context of locally available resources and expertise.

This Guideline does not address all elements of standard practice and assumes that individual clinicians are responsible for:

- Discussing care with women in an environment that is appropriate and which enables respectful confidential discussion. This includes the use of interpreter services where necessary
- Advising women of their choices and ensure informed consent is obtained
- Provide care with professional scope of practice, meeting all legislative requirements and maintaining standards of professional conduct
- Applying standard precautions and additional precautions, as necessary, when delivering care
- Documenting all care in accordance with local and mandatory requirements

1.8 Use of language

Within this guidance we use the terms ‘woman’ and ‘women’s health’. However, it is important to acknowledge that people who do not identify as cis-gender women are excluded from this descriptor, including people who identify as transgender, gender diverse and gender non-binary[5]. We also appreciate that there are risks to desexing language when describing female reproduction[6 7]. Services and delivery of care must be appropriate, inclusive and sensitive to the needs of people whose gender identity does not align with the sex they were assigned at birth. This includes training and education regarding diverse pathways to pregnancy and the use of practices which affirm the sexual and gender identities of all people using Obstetrics and Gynaecology services.

5 Moseson H, Zazanis N, Goldberg E, et al. The Imperative for Transgender and Gender Nonbinary Inclusion. Obstet Gynecol. 2020;135(5):1059-1068. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7170432/

6 Brotto LA, Galea LAM. Gender inclusivity in women’s health research. BJOG: An International Journal of Obstetrics & Gynaecology. https://obgyn.onlinelibrary.wiley.com/doi/full/10.1111/1471-0528.17231

7 Gribble KD, Bewley S, Bartick MC, et al. Effective Communication About Pregnancy, Birth, Lactation, Breastfeeding and Newborn Care: The Importance of Sexed Language. *Frontiers in Global Women’s Health*. 2022;3. Accessed June 9, 2022. https://www.frontiersin.org/article/10.3389/fgwh.2022.818856

Language use is key to effectively communicate options, recommendations, and respectfully accept a woman's fully informed decision [8]. With this in mind, the use of birth is preferable to the term delivery in all circumstances and is used consistently where possible throughout the guidelines. It is acknowledged that in some circumstances (e.g., in the case of a medically indicated intervention or surgery) and in some contexts, substituting with the term delivery is considered appropriate and this term may be used instead.

8 https://blogs.bmj.com/bmj/2018/02/08/humanising-birth-does-the-language-we-use-matter/

Chapter 2: **Clinical Practice Guideline**

Background

Vaginal bleeding after the menopause is not normal and any bleeding that occurs more than a year after the last menstrual period should be reported to a doctor. Though there may be a simple explanation, up to 9%of these women will have an underlying endometrial cancer [1]. Endometrial cancer is one of the most common cancers of the female genital tract, ranking second to cervical cancer in terms of incidence [2].

In 2020, 417,367 women were diagnosed with endometrial cancer worldwide, which accounts for 4.5% of all malignancies in women [2]. Irish data on endometrial cancer rates amongst women with PMB is sparse. Unpublished data from an AG clinic in Ireland identified a 4.1% rate of endometrial cancer in a sample of 68 women with PMB [3]. Another unpublished Irish study found no endometrial cancer in a sample of 43 women with PMB and an endometrial thickness between 3mm and 3.9mm[4].

Endometrial cancer is associated with multiple risk factors including obesity [5], unopposed oestrogen hormone replacement therapy [6], tamoxifen use for breast cancer treatment [7], nulliparity [8] and some familial cancers [9]. Early recognition of postmenopausal bleeding and urgent referral for investigation and management is paramount.

Other national guidelines with relevant recommendations include:

National Clinical Practice Guideline on the Management of Menopause in Specialist Services (due 2023)

Introduction

For the majority of women, the postmenopausal period represents a significant portion of their lifetime, particularly as life expectancy increases. Defining menopause is critical for the future management of conditions in the postmenopausal period.

Clinical Question 2.1: **What is the definition of menopause?**

Evidence Statement

The International Menopause Society and World Health Organisation define menopause as the final menstrual period, a retrospective diagnosis that can only be made when followed by 12 months of amenorrhoea [10,11]. Amongst women in Europe, the median age of onset of menopause ranges from approximately 50 to 53 years [12]. Women are said to be postmenopausal when menstruation has ceased for 12 months [13], but accurately pinpointing the “final menstrual period” can be challenging due to multi-month amenorrhoea in the perimenopause

Clinical Practice

The following definition of menopause is recommended for use in the clinical setting, the final menstrual period followed by 12 months of amenorrhoea.

Recommendations

1. **We recommend that menopause should be defined as the final menstrual period followed by 12 months of amenorrhoea.**

Introduction

There is a lack of consensus in the literature regarding the interval of amenorrhoea preceding an episode of bleeding that would allow for the definition of PMB. Clearly defining PMB is important to enable the identification of those women that require referral to specialist gynaecological services for prompt and accurate investigation.

Clinical Question 2.2: **What is the definition of postmenopausal bleeding?**

Evidence Statement

For the purpose of this clinical Guideline, an episode of bleeding 12 months or more after the final menstrual period will be accepted as postmenopausal bleeding [10,11]. In postmenopausal women not taking hormone replacement therapy (HRT), any vaginal bleeding requires investigation [14]. Clinical question 2.8 addresses unscheduled bleeding in women taking HRT.

Clinical Practice

We recommend that the definition of PMB used in this Guideline is applied to the clinical setting to aid clinicians in diagnosing PMB and identifying those women who need referral for investigation.

Recommendations

2. **We recommend that postmenopausal bleeding in women not taking hormone replacement therapy is defined as an episode of bleeding occurring 12 months or more after the final menstrual period.**

Introduction

Postmenopausal bleeding is most frequently due to benign gynaecological conditions, such as vaginal or endometrial atrophy secondary to oestrogen deficiency, endometrial or cervical polyps, uterine prolapse and endometritis [15,16]. Disease of the urinary or gastrointestinal tract may also give rise to bleeding that may appear to be gynaecological in origin, therefore careful history and examination is crucial in making a diagnosis of PMB.

Clinical Question 2.3: **What are the causes of postmenopausal bleeding?**

Evidence Statement

Endometrial hyperplasia and endometrial cancer

A recent large scale meta-analysis and systematic review of over 40,000 women found that almost 90% of women with endometrial cancer experienced PMB while only 9% of those with PMB were diagnosed with endometrial cancer [1]. Rates of endometrial cancer in the context of PMB vary widely between studies and populations. Endometrial hyperplasia is more commonly identified, with up to 12.4% of those presenting with PMB receiving this diagnosis [17]. The risk of progression of endometrial hyperplasia with atypia to cancer has been quoted as 9% according to a systematic review and meta-analysis examining different classification systems for endometrial hyperplasia [18].

Endometrial hyperplasia and endometrial cancer are commonly associated with multiple risk factors and the aim of assessment should be to identify, monitor and modify these factors. Unopposed oestrogen hormone replacement therapy was associated with an increased risk of endometrial hyperplasia, and therefore is not recommended in women with a uterus [6]. Other known risk factors for endometrial hyperplasia and endometrial cancer include Tamoxifen [7,19], obesity, advancing age [5,20] and Hereditary Non-Polyposis Colorectal Cancer [9].

Cervical, vulval and vaginal cancer

Non-endometrial gynaecological cancers must also be considered in the differential diagnosis for women presenting with PMB. Cancers of the vaginal and vulva are rare, effecting approximately 10 women in Ireland per year and 60 women in Ireland per year respectively with most of these women being post-menopausal [21,22]. PMB is a frequently occurring symptom of vaginal and vulval cancers [21,22]. Cervical cancer is the fourth most common cancer effecting women globally [23] with approximately 300 women in Ireland per year diagnosed [24]. It generally effects a younger cohort when compared to vaginal or vulval cancers, but postmenopausal women can also develop cervical cancer [25] and PMB may be the presenting symptom of this disease.

Urological and gastrointestinal cancers

Primary care assessment should aim to differentiate gynaecological bleeding from urological or gastrointestinal tract bleeding, however it may not always be possible to determine this in primary care. Albeit rare, there have been reports of metastatic urological and colorectal cancers presenting with vaginal bleeding [26,27]. Primary care teams and gynaecology units should be familiar with the fast-track pathways in their network for urological and colorectal referrals.

Bleeding

It is not appropriate to refer a woman with postmenopausal bleeding to an Emergency Department as onward referral to scheduled gynaecology services will still be required. Postmenopausal bleeding from the genital tract requires a fast-track pathway for urgent scheduled out-patient gynaecology care as outlined in this Guideline.

Clinical Practice

Step 1: A woman recognises PMB and self refers to a GP/community practitioner.

Step 2: An urgent history, abdominal, speculum and bimanual examination is carried out by the GP/community practitioner.

Step 3: If postmenopausal vaginal bleeding is suspected, refer urgently to the local specialist PMB clinic, or if unavailable, to the local gynaecology clinic. If bleeding is suspected to be urological or rectal, refer to the appropriate pathway within the hospital services. In the event of a lesion suspicious for cancer on the cervix, vulva, or vagina, a direct referral to gynaecology oncology services is recommended.

Step 4: The referral is received by the hospital services, triaged and an appointment is given, ideally within 28 days. The GP is informed of the proposed appointment.

In gynaecology units where a "one stop" ambulatory clinic whereby women can be seen, investigated and treated in one session is not yet available, consideration should be given to arranging a scan prior to the appointment if feasible, whilst ensuring this does not delay an outpatient assessment.

Recommendations

3. **We suggest that assessments should aim to identify and monitor the multiple identifiable risk factors associated with endometrial cancer.**
4. **We recommend that vaginal, vulval and cervical cancers are also considered in the differential diagnosis for women presenting with postmenopausal bleeding.**
5. **We recommend that urological and gastrointestinal cancers are also considered in the differential diagnosis for women presenting with bleeding that is thought to be coming from the genital tract.**

Introduction

Postmenopausal bleeding is a common symptom of endometrial cancer and has traditionally represented an absolute indication for referral to gynaecological services. Indeed, PMB is not specific for endometrial cancer and is often associated with benign conditions but this is not always possible to determine by clinical examination alone [1].

Clinical Question 2.4: **When should women with postmenopausal bleeding be referred for investigation?**

Evidence Statement

As part of the initial assessment in the general practice setting, all women with PMB should undergo a focused history and clinical examination, including a vaginal and speculum examination, prior to referral to gynaecological services. Examination in primary care should aim to triage women with gynaecological issues to the most appropriate gynaecological service.

The National Institute for Health and Care Excellence (NICE) suspected cancer recognition and referral guidance recommends that women with PMB be seen within two weeks of being referred [28]. NICE also recommends that primary care physicians request an ultrasound for women aged over 55 with unexplained vaginal discharge who are presenting for the first time [28].

There is no evidence that review within two weeks or four weeks will ultimately affect the long-term outcomes in women with endometrial cancer. However, services should aim to see women with postmenopausal bleeding as soon as possible to alleviate or prevent anxiety. As a minimum, women should receive confirmation of a clinic appointment within two weeks from referral and be seen in clinic within four weeks from referral.

Clinical Practice

- GP/Primary Care Provider
- Urgent history and in-person examination, including speculum, to rule out abdominal, cervical, vulval, vaginal, urological or gastro-intestinal cause of PMB.
- Same-day PMB referral to local gynaecology unit requesting “Fast-Track PMB”.
- Include the following details:
    - Past medical history – including prior history of endometrial hyperplasia
    - Past surgical history
    - Full list of medications – NB anticoagulant use
    - Post-menopausal bleeding following:
        - >12 months amenorrhoea, *or*
        - Mobility adequate for ambulant care or capacity for self-transfer to examination table
        - Capacity to consent to assessment
        - If undergoing palliative/end of life care, woman expresses explicit desire to undergo one-stop assessment
    - Interpreter required

Recommendations

6. **We recommend that all women presenting with postmenopausal bleeding in the general practice setting should undergo a focused history and examination, including a vaginal and speculum examination, prior to referral to gynaecological services.**
7. **We recommend that all women with postmenopausal bleeding who are not on HRT require referral for investigation.**
8. **We recommend that all women with abnormal bleeding on HRT require referral for investigation.**
9. **We recommend that all women with abnormal bleeding on Tamoxifen require referral for investigation.**
10. **We recommend that women referred for investigations of postmenopausal bleeding should be seen in gynaecology units within 28 days.**

Clinical Question 2.5: **How should postmenopausal bleeding be investigated?**

Evidence Statement

The clinical approach to PMB requires a detailed history, physical examination, and timely evaluation of the lower genital tract and endometrium, with ultrasound and hysteroscopy. Traditionally, this has been carried out via outpatient clinic consultations and subsequent inpatient day-surgeries.

More recently, this has moved to the ambulatory gynaecology (AG) setting as these services are "one-stop", "see-and-treat" clinics that shorten the care pathway, improve the patient experience and save resources [29,30]. There are many AG clinics fully operational throughout the country currently with a plan to have a total of 19 up and running in the coming years.

The National Women and Infants Health Programme (NWIHP) report 2020 has estimated that 70% of general gynaecology referrals are suitable for management in an ambulatory setting [31]. In order to provide an ambulatory gynaecology service, the NWIHP recommend the availability of the following resources; haematological investigations, pelvic ultrasound, diagnostic and out-patient operative hysteroscopy, endometrial biopsy, cervical polypectomy, endometrial polypectomy, and intrauterine device management [31].

Transvaginal Ultrasound (TVUS)

Transvaginal ultrasound is accepted as the first investigation in PMB internationally/worldwide [14,32,33]. It should be available in all gynaecology service settings. Provision and delivery of this service can include sonographers, radiographers, gynaecologists and radiologists.

An endometrial thickness measurement is obtained in the midsagittal view of the uterus by measuring the maximum anterior-posterior thickness of the endometrial echo, perpendicular to the midline and without including the endomyometrial junction [34]. In the presence of intracavitary fluid, the thickness of both single layers should be added to give the endometrial thickness, and in the presence of intracavitary pathology, the endometrial thickness should include the lesion unless it is a well-defined lesion that can be measured separately [34].

There is a lack of consensus for the different endometrial thickness cut-offs that may be used to recommend further investigations. These range from 3-5mm and are influenced by patient factors and characteristics [32,35,36]. A recent committee opinion by the American College of Obstetricians and Gynaecologists recommended a cut-off of 4mm as it has a 99% negative predictive value for endometrial cancer, however for women with persistent PMB and a normal endometrial thickness, it is recommended that they undergo further evaluation of the endometrial cavity [36].

The Australian Menopause Society uses the cut-off of 4mm for women with postmenopausal bleeding who have never taken HRT, have not taken HRT for the past 12 months, or who are taking continuous combined HRT and they quote a >20-22% probability of cancer in this patient group [14]. For those women with PMB who are currently on or have recently commenced cyclical HRT, they recommend a cut-off of 5mm and quote a 2-5% probability of cancer amongst these patient groups [14].

A recent study compared the typical ultrasound features of common endometrial pathologies with the histological outcomes in almost 3000 women presenting with abnormal uterine bleeding [37]. Women with a histological diagnosis of an atrophic endometrium typically had an endometrial thickness of 3-7mm, while those with endometrial polyps had an endometrial thickness of 8-14mm, a regular endometrial-myometrial junction and single blood vessels with or without branching.

In the case of endometrial hyperplasia without atypia the endometrial thickness ranged from 9-17mm, the endometrial-myometrial junction was regular and multiple vessels of multifocal origin or scattered were present. Endometrial hyperplasia with atypia had similar ultrasonographic features except for a broader endometrial thickness range of 8-18mm. Finally, endometrial cancer in postmenopausal patients was associated with an endometrial thickness of 11-26mm in 96%, an interrupted endometrial-myometrial junction in 96%, and multiple vessels of focal or multifocal origin in 87% of patients [37].

In the case of women taking Tamoxifen for the treatment of breast cancer, ultrasound is neither sensitive nor specific for endometrial cancer and is not a useful tool for assessment of the endometrium, it is therefore recommended that hysteroscopy with endometrial sampling should be offered to this patient group [9].

Transabdominal ultrasound (TAS) may be used to compliment transvaginal ultrasound in cases where the uterus is enlarged and a wider view is needed, and where transvaginal ultrasound is technically impossible or unacceptable to the patient, transabdominal ultrasound may be use as an adjunct to hysteroscopy [32]. TAS alone is not an adequate investigation for endometrial assessment.

Endometrial sampling

Definitive diagnosis of endometrial cancer or hyperplasia requires histological evaluation of endometrial tissue. Transvaginal ultrasound is recommended prior to the decision for endometrial biopsy. In the case of patients on Tamoxifen, endometrial thickness measurements are not useful for triage.

Historically, the first line of investigation for PMB was dilatation and curettage of the uterine cavity performed under general anaesthesia. Studies looking at pre-hysterectomy dilation and curettage procedures have shown that endometrial hyperplasia or cancer are commonly missed in the samples obtained by this method [38,39].One study found that less than half of the uterus had been curetted in 60% of patients [38].

Outpatient endometrial sampling has become common practice with studies revealing outpatient endometrial biopsy to be similarly efficacious when compared to inpatient dilation and curettage for the investigation of abnormal uterine bleeding [40]. Many endometrial sampling devices exist but a consensus on which device works best has not been achieved. The Medgyn Endosampler™ has been shown to yield greater tissue volumes when compared to the Pipelle® [41]. When compared to the Endocurette, the Endosampler required less device insertions and was the operators preferred device in an outpatient hysteroscopy setting in Ireland [42]. Regarding the diagnosis of endometrial hyperplasia and cancer, a meta-analysis found the Pipelle to be superior to other outpatient endometrial sampling techniques[43].

Hysteroscopy

Hysteroscopy facilitates the direct visualisation and examination of the uterine cavity and is considered the gold standard test in identifying endometrial disease. Furthermore, it allows for endometrial sampling and treatment of certain endometrial pathology. Hysteroscopy has been shown to be superior to blind endometrial sampling in the diagnosis of endometrial polyps, submucosal leiomyomas, intrauterine adhesions and other focal pathology [44=47]. A systematic review including over 26,000 women with abnormal uterine bleeding found hysteroscopy to be a highly accurate tool in diagnosing endometrial cancer and moderately accurate for endometrial hyperplasia [48].

Traditionally, hysteroscopy has been carried out in a formal theatre setting under general or regional anaesthesia. Advances in technology have significantly reduced the size of hysteroscopes without compromising the optical performance, thus enabling the practice of outpatient hysteroscopy [49]. Clinically, it is a simple, safe and well tolerated means of investigating abnormal uterine bleeding [48] and financially it is a cost-effective alternative to inpatient hysteroscopy [50]. Operative outpatient hysteroscopy has also become feasible in recent years with procedures such as endometrial polypectomy, treatment of submucosal fibroids, and endometrial ablation being performed. [51=53].

The conventional hysteroscopy technique involves inserting a speculum to expose the cervix, grasping the anterior lip of the cervix with forceps, and then introducing the hysteroscope. The vaginoscopic technique involves inserting the hysteroscope directly into the lower vagina, hydrodistending the vaginal canal with the distension medium and manipulating the hysteroscope to identify the external os to allow for the passage of the hysteroscope into the cervical canal and uterine cavity by gentle movements [54] Vaginoscopic hysteroscopy is better tolerated by the patient when compared to conventional hysteroscopy techniques [55] and may be associated with a reduced operating time [56]. The UK Green-top guidelines recommend vaginoscopy as the standard outpatient hysteroscopy technique[57].

Consideration should be given to the need for analgesia before, during and after outpatient hysteroscopy. Studies on the use of non-steroidal anti-inflammatory drugs (NSAIDs) prior to outpatient hysteroscopy have generated mixed results. One randomised, double-blind, placebo-controlled study looked at the effect of 50mg of oral diclofenac administered 1-2 hours before outpatient hysteroscopy versus a placebo pill and found no difference between groups in reported pain scores during and after hysteroscopy [58]. Another NSAID study compared mefenamic acid 500mg given 1 hour before outpatient hysteroscopy with placebo [59]. The mefenamic acid group reported significantly less pain post procedure than the placebo group, but there was no difference between groups for pain reported during the procedure [59]. The efficacy of mefenamic acid compared to paracervical block for outpatient hysteroscopy has also been investigated and no statistical difference was found between the two groups, although mefenamic acid was associated with fewer side effects [60].

A systematic review and meta-analysis looking at local anaesthesia for pain control during outpatient hysteroscopy found that paracervical local anaesthetic injection was the best method for pain management in this patient group[61]. The authors do however acknowledge that the injection in itself is a painful procedure and that the reported pain scores from the studies reviewed may not have taken this into account. A further recommendation from this study is for the use of topical local anaesthetic when applying a tenaculum to the cervix, although this is not associated with reduced pain from the hysteroscopy itself [61]. The use of conscious sedation for outpatient hysteroscopy has also been studied, and a systematic review and meta-analysis of seven and five studies respectively showed that conscious sedation was associated with multiple side effects in the absence of a clear reduction in pain for the patients undergoing this procedure [62].

Challenges in ambulatory gynaecology clinics

Not all women will desire or be able to complete the necessary investigations for PMB in the AG clinic setting. Challenges encountered may include pain management, vasovagal response, anxiety, weight excess, cervical stenosis, pelvic organ prolapse, endometrial pathology, care of the elderly and inexperience of the provider [63]. As a result, a small proportion of women will be referred from AG clinic for inpatient hysteroscopy and endometrial sampling. The AG clinic should provide a trauma-informed approach to care – whereby the clinician/nurse/care assistant is aware of the potential for any patient attending the clinic to have a history of sexual or gender based violence [64]. Communication should be de-stigmatising to encourage engagement with the service and examination should emphasise that the woman is in full control and may discontinue at any point if they wish to do so [64].

Occasionally, a woman may have a strong preference for traditional inpatient management under general or regional anaesthesia and this must be considered when referring the patient. In addition, there may be cases whereby formal inpatient sampling is required for further histological analysis.

Clinical Practice

PMB Fast-Track Pathway:

Day 0-2: GP/Primary Care Provider – urgent history, examination and "fast-track PMB" referral. (See 'clinical practice' section 2.4 for details).

Day 0-7: Ambulatory Gynaecology designated clinician* and administrator triage the PMB referrals and issue "Fast-Track PMB" appointment with patient information leaflet.

*Consultant Gynaecologist or advanced nurse practitioner, scheduled weekly/twice weekly including unit-designated cover for triage provision during leave.

Day 14: Webtext reminder of appointment is issued with unit contact details for any questions or cancellation to minimise appointment default.

Day 14-28: Ambulatory Gynaecology care:

1. Administrative registration including explanation of electronic medical record (where applicable), image capture, audit activity and communication of results.
2. Nursing/Team check-in – may include history-taking that is trauma-informed in approach, allergy & medication check, cervical screening history with opportunistic screening offered if not up to date, possible need for urine pregnancy test if under 55 years and without 12 months amenorrhoea, explanation of procedures and verbal consent documented, pain management options/expectations and documentation if self-medicated analgesics or unit dispensed, after-care and results handling.
3. Gynaecologist/Advanced Nurse practitioner with health-care worker chaperone and patient family member if desired. (Steps 2 and 3 may be combined). Review of history, allergy and medication, expectation, informed choice and consent (both verbal and written are acceptable). Intimate examination room and toileting environment.

   If it is expected from the history that transabdominal ultrasound may be required, the woman is asked not to void until just before the transvaginal exam and the TAS is performed first. Then the woman voids as completely as possible.

On an automated gynaecology couch, the TVS is performed with the gowned woman in a Lloyd Davis or lithotomy position or seated throne according to medical condition and the endometrial anatomy, thickness, junctions and any focal lesions are documented. On occasion, the need for TAS only becomes apparent post TVS and an interval may be required to allow for bladder filling.

In general, the ovaries are screened, although ovarian cancer rarely presents as PMB; if not visible, the adnexal areas are fully inspected and documented. If any ovarian abnormality is found, tumour markers are reserved and RCOG guidelines no. 34 and no. 62 [65,66] are followed in the general gynaecology out-patients or onwards in Gynae-Oncology.

If there is global endometrial thickness of >4mm without any focal change and a clear endo-myometrial interface, then a sized speculum is passed, the lower genital tract is examined and an endometrial sample by suction is obtained. On occasion, a cervical block, single-tooth tenaculum or fine sound or saline distension is required to instrument the endocervical canal and access the endometrial cavity. If the endometrium is thin, a sized speculum is passed, the lower genital tract is examined, findings documented and the examination is complete.

If there is a focal lesion identified on TVUS or if the TVUS did not provide adequate views of the entire endometrium, the operator switches directly to office hysteroscopy. No preparation of the lower vaginal tract is indicated. A vaginoscopy approach is used with angulation appropriate to scope angle if not zero degrees.

In general, instrumentation of the endocervix is straight-forward in direct hysteroscopy. If not, the troubleshooting for biopsy as above with speculum is used. If a focal lesion is confirmed, hysteroscopy-directed biopsies are taken. If polypoid endometrial change is identified, a suction sample may be preferred. The examination is complete. The woman may stand and retire to the en-suite toilet to dress if feels well enough or may be assisted if required.

The specimens – histological, haematological and biochemical, and images are labelled and the specimen tracking register is completed.

Any findings are explained, treated if indicated, reassurance offered and discharged if appropriate (90-95% of referrals) or prepared for next steps, including turn-around-time on specimens, multidisciplinary meetings (MDM), and staging diagnostic imaging if required.

If a tumour is suspected clinically at this visit, complete the following

- full physical examination for blood pressure (BP), body mass index (BMI), nodes, mass effect
- Venous thromboembolism (VTE) risk assessment and completion of relevant screening forms for pre-operative anaesthetic assessment
- preparation for computerised tomography (CT)/ magnetic resonance imaging (MRI)(renal function and implanted metal)
- Gynae-Oncology multi-disciplinary team review is performed at an appropriate time.

If it is not possible to complete the investigations for technical, situational or preference reasons and further endometrial assessment is indicated, an urgent day-surgery/in-patient procedure is scheduled, ideally within 7-10 days.

The woman receives contact details, follow up plan for results and future appointments. In addition, the woman is informed of the very small risk of procedural related infection, the red-flag symptoms and access routes for care.

It is required that the unit has staff, facilities and equipment available to manage emergency situations e.g. collapse, vaso-vagal reaction. This should include a resuscitation trolley that holds algorithms and medications for symptomatic bradycardia.

Each provider has scheduled time (approx. 0.25 of the sessional time) in AG to review the results and added-on investigations of the previous one-to-two weeks, to carry out virtual follow-up appointments, to engage in gynae-oncology referral work, to train, to check fail-safes with the administrative team and to measure key performance areas.

A generalist trained provider, new to AG, providing a one-stop strictly PMB service in a single-room would schedule four x 45-minute appointments per session. If a mixed list of abnormal uterine bleeding cases and PMB, the schedule would be 6 x 30-minute appointments. If a second room is available to a trainee, these numbers could increase by 1.5. If scheduling a case where it is known that morcellation will be required, a 60-minute appointment is appropriate.

Day 14-35*: Electronic note issued to GP same day as AG clinic visit for women who have no investigations or histology pending.

Scheduled urgent day-surgery/in-patient care if required.

Histology results received by clinician and authorised.

Electronic note issued to GP.

Supplementary imaging if indicated.

Gynae-oncology referral, MDMs, first visit and treatment decision *ideally <28 days

Day 42-56: Cancer treatment commences if indicated.

Recommendations

11. We suggest that where possible women referred for investigation of postmenopausal bleeding or abnormal uterine bleeding on HRT should be seen in an ambulatory gynaecology (AG) clinic.
12. We recommend that all gynaecology services should be able to assess and investigate women with postmenopausal bleeding. Where ambulatory services are not yet available, in the interim, there should be a managed fast-track pathway for women with postmenopausal bleeding.

13. We recommend that all women referred for investigation of postmenopausal bleeding or abnormal uterine bleeding on HRT should undergo a transvaginal pelvic ultrasound to assess the thickness and features of the endometrium.
14. We recommend that women with postmenopausal bleeding with an endometrial thickness of ≥4mm should undergo endometrial sampling.
15. We recommend that a diagnostic hysteroscopy should be carried out where transvaginal ultrasound has detected focal endometrial pathology, or the endometrial thickness is greater than 4mm.
16. We recommend that women on Tamoxifen with abnormal uterine bleeding are offered diagnostic hysteroscopy with endometrial sampling as transvaginal ultrasonography for assessment of the endometrium in these women is not a useful tool for triage.
17. We suggest that transabdominal ultrasound should be used to compliment transvaginal ultrasound where there is an enlarged uterus or pelvic mass.
18. We recommend that isolated dilation and curettage should not be used as the first line method for obtaining endometrial samples in the investigation of postmenopausal bleeding.
19. We recommend that endometrial sampling in the form of office-based biopsy is used in conjunction with transvaginal ultrasound with or without hysteroscopy for the investigation of women with postmenopausal bleeding. Blind endometrial sampling in isolation is not sufficient for investigation.
20. We recommend that the vaginoscopic approach should be the standard technique in outpatient hysteroscopy as it is better tolerated by the woman when compared to conventional hysteroscopy techniques.
21. We suggest that women with no contraindications can be advised to consider taking a non-steroidal anti-inflammatory drug (NSAID) 1-2 hours prior to their hysteroscopy to reduce post-procedure pain. This should be communicated to them in their appointment letter.

Introduction

There is a paucity of evidence in the literature regarding the degree of concern that should be exercised in the case of isolated bleeds versus recurrent bleeds, and light bleeds versus heavy bleeds. There is no consensus on how much time needs to have elapsed before these women warrant reinvestigation, but it is clear that management of women experiencing recurrent PMB must be individualised. Women must be made aware of the need to represent with new or persistent PMB and local patient information leaflets should highlight this.

Clinical Question 2.6: **How should women with recurrent postmenopausal bleeding be managed?**

Evidence Statement

For the purposes of this Guideline, recurrent PMB is the representation of a woman with PMB after initial negative investigations for prior episode(s) of PMB. Repeated episodes of PMB prior to any investigations are not considered 'recurrent' PMB in this document. A study conducted in the UK investigated almost 2000 women with postmenopausal bleeding, 106 (5%) of whom had recurrent episodes [15]. It was found that those with recurrent postmenopausal bleeding were less likely to have premalignant or malignant endometrial disease, instead they were more likely to have benign endometrial polyps when compared to women who presented with a first episode of postmenopausal bleeding. The authors concluded that first line investigations with a high degree of accuracy for focal endometrial disease, such as outpatient hysteroscopy should be used in women presenting with recurrent postmenopausal bleeding [15]. Similarly, another research study recommends evaluation of the endometrium by hysteroscopy when persistent postmenopausal bleeding is associated with a previous benign endometrial sample [67].

Clinical Practice

Strong consideration should be given to repeat imaging with hysteroscopy and endometrial biopsy and review of previous investigations in women with recurrent episodes of postmenopausal bleeding and prior negative results. With persistent negative results, individualised care, according to the woman's risk profile and preferences, should be guided by a consultant Gynaecologist.

Recommendations

22. **We recommend that hysteroscopy and repeat endometrial biopsy should be considered in women who experience unexplained, persistent, or recurrent postmenopausal bleeding in the setting of prior reassuring investigations. A low threshold for reinvestigation of these women should be maintained. Care of this patient group should be guided by a consultant gynaecologist.**

Clinical Question 2.7: **How should an incidental finding of increased endometrial thickness (greater than 4mm) in postmenopausal women be managed?**

Many postmenopausal women will undergo imaging of the pelvis for reasons such as a back or abdominal pain where endometrial images and measurements will be taken. Incidental findings of increased endometrial thickness must be anticipated, correctly interpreted, and managed appropriately.

Evidence Statement

Endometrial thickness assessment is not an effective tool in endometrial cancer screening amongst asymptomatic postmenopausal women [68]. If an incidental finding of increased endometrial thickness is found on a scan that was not a non-transvaginal pelvic ultrasound or pelvic MRI, then evaluation in the form of transvaginal ultrasound should take place to assess the endometrium immediately.

In postmenopausal women without bleeding and an endometrial thickness of ≥ 11mm, the risk of endometrial cancer is 6.7% and it is recommended that these women undergo endometrial sampling [69]. This risk is similar to the risk of endometrial cancer in postmenopausal women with bleeding and a transvaginal ultrasound endometrial thickness ≥ 5mm [69]. If the 11mm cut-off is used, only 0.25% of women would undergo endometrial biopsy and yet 87% of cases of occult endometrial cancer would still be detected [69]. If the biopsy threshold is lowered to ≥ 8mm, the rate of biopsies being carried out on postmenopausal women with incidentally found endometrial thickening would increase to nearly 1% [69]. It is argued that performing such large volumes of biopsies for the evaluation of a disease that typically presents with symptoms and at a curable stage, would be inappropriate at population level [69]. However, the woman's preference for investigation should prevail.

Furthermore, there is evidence that asymptomatic women undergoing hysteroscopic evaluation of endometrial lesions or increased endometrial thickness have higher rates of uterine perforation and serious surgical complications [70].

Other research recommends sampling the endometrium in postmenopausal women without bleeding where ultrasound features such as increased endometrial vascularity, inhomogeneity of the endometrium and particulate fluid are present [71]. Decisions about further investigations should be individualised and risk factors for endometrial cancer such as obesity, age, Tamoxifen usage and family history should be considered.

Clinical Practice

When an increased endometrial thickness is observed in an asymptomatic postmenopausal woman, a transvaginal ultrasound should be carried out to assess the endometrium appropriately. Where the endometrium is ≥11mm it is recommended that the woman undergo hysteroscopy and endometrial biopsy. Where the endometrium is 4mm-11mm, the woman's risk factors for endometrial cancer should be considered and further management individualised based on the perceived risk.

Recommendations

23. **We suggest that in postmenopausal women without bleeding, transvaginal ultrasound findings of increased endometrial thickness ≥ 11mm require further investigation.**

Clinical Question 2.8: **When should women taking HRT be referred for investigation of abnormal bleeding?**

Evidence Statement

The Women's Health Initiative [72] and the Million Women Study [73] found that the risks of prescribing HRT outweighed the benefits and since their publication, the number of prescriptions for HRT have reduced by almost half [74]. The 2021 publication of the NICE Guideline on Menopause set out to provide a balanced view of the risks and benefits of HRT to enable clinicians and women to make informed decisions on HRT prescribing [74]. As the population of Ireland ages [75] it is reasonable to anticipate an increase in menopause related referrals to gynaecology services, including unscheduled or abnormal bleeding on HRT.

In women taking HRT, bleeding is common making the identification of those who need investigation challenging. Abnormal bleeding in women on HRT can be defined as follows [9]:

- For women taking sequential HRT – bleeding at an unscheduled time, or bleeding at a scheduled time (post progestin withdrawal) that is unusually heavy or prolonged
- For women on continuous combined HRT – bleeding six months or more post HRT initiation, or bleeding after amenorrhoea has been established.

The British Menopause Society (BMS) recommends referral to secondary care under the following circumstances – when women taking sequential HRT experience an increase in heaviness or duration of bleeding, or if their bleeding is irregular; and when women taking continuous combined HRT experience bleeding beyond six months of therapy, or if bleeding occurs after a spell of amenorrhoea [76]. The NHS Scotland recommends referral to a PMB clinic within 2 weeks under the following circumstances – when women on HRT experience persistent bleeding; when women on sequential HRT experience unscheduled bleeding after 3 months of starting; and when women on continuous combined HRT experience unscheduled bleeding after 6 months of starting [77]. Bleeding within the first 6 months of starting continuous combined HRT can be normal and is very common [77,78].

Clinical Practice

- The details of the recommended clinical practice for GP/primary carer have been previously outlined in clinical practice section 2.4.
- Additional details to include in the GP referral to the gynaecology services include, type of HRT, duration of use, detail of bleeding pattern of concern, menopausal status prior to commencement of HRT, and age of menopause.

Recommendations

24. **We recommend that women taking HRT should be referred for investigation if their bleeding is persistent.**
25. **We recommend that women taking sequential HRT should be referred for investigation if they experience irregular bleeding despite adjustment, more than 3 months of commencing treatment, or if their bleeding increases in heaviness or duration.**
26. **We recommend that women taking continuous combined HRT should be referred for investigation if they experience bleeding beyond six months of commencing therapy, or if bleeding occurs after a significant spell of amenorrhoea. Where additional risk factors exist clinical discretion may warrant earlier referral.**

Chapter 3: Development of Clinical Practice Guideline

3.1 Literature search strategy

A comprehensive search of the electronic databases PUBMED (1970 – December 2021) and the Cochrane Library were undertaken. These databases were searched using relevant medical subject headings and keywords. The main keywords used were 'postmenopausal bleeding' in combination with 'endometrial hyperplasia', 'endometrial cancer', 'referral', 'transvaginal ultrasound', and 'hysteroscopy'. There were no restrictions placed on the searches. The results yielded from these searches were reviewed. A detailed literature review was subsequently carried out, this also included international Clinical Practice Guidelines on relevant subject areas.

3.2 Appraisal of evidence

Following a comprehensive literature review the quality, validity and relevance of the evidence gathered were critically appraised by the Guideline developers under the following headings:

- Study design
- Relevance of primary and secondary outcomes
- Consistency of results across studies
- Magnitude of benefit versus magnitude of harm
- Applicability to practice context

A number of evidence-based recommendations for management of PMB were agreed upon. They have been adapted to reflect care in the Irish healthcare setting.

3.3 AGREE II process

While being developed, the Guideline was assessed using the AGREE II checklist (Appendix 3) as recommended by the Department of Health in the How to develop a National Clinical Guideline: A manual for Guideline developers.[9]

The purpose of AGREE II is to provide a framework to:

1. Assess the quality of guidelines;
2. Provide a methodological strategy for the development of guidelines; and
3. Inform what information and how information ought to be reported in guidelines

9 Department of Health (2019). How to develop a National Clinical Guideline: A manual for guideline developers. Available at: https://www.gov.ie/en/collection/cd41ac-clinical-effectiveness-resources-and-learning/

3.4 Literature review

Details of supportive evidence-based literature for this Guideline are reported in chapter two.

- The review of the literature was conducted by Dr Ailbhe Duffy between 08/2021 and 04/2022.
- The final documents selected were reviewed by Dr Ailbhe Duffy and Dr Meabh Ní Bhuinneain
- There is substantial evidence available to answer the clinical questions proposed
- The quality of evidence available is, for the most part, strong evidence
- The evidence reviewed comes from both national and international studies and has been adapted to fit the Irish context
- Literature was used when the evidence was relevant, strong and applicable to the Irish setting and omitted when this was not the case.

3.5 Grades of recommendation

GRADE offers a transparent and structured process for developing and presenting evidence summaries and for carrying out the steps involved in developing recommendations [79]. [10] While we acknowledge that for this particular work an extensive GRADE approach is not possible, we have used the suggested language set out in the GRADE table when making recommendations.[11] (Appendix 4)

3.6 Future research

An important outcome of the Guideline development process is in highlighting gaps in the evidence base.

The questions of relevance to this Guideline include;

1. Optimal timing and type of oral analgesia in outpatient hysteroscopy
2. Optimal management of women with recurrent postmenopausal bleeding
3. Optimal management of women with incidental findings of increased endometrial thickness without postmenopausal bleeding
4. Investigation of women on HRT attending AG clinics for reported PMB – to focus on the type of HRT, duration of HRT, investigation findings and outcomes
5. Examination of how best to approach the care and treatment of Women with a history of physical or psychological trauma
6. Investigation of social and cultural barriers to progressing with treatment
7. Further research looking at the health economics of AG clinics versus standard gynaecology clinics.

10 Guyatt, Gordon, et al. "GRADE Guidelines: 1. Introduction – GRADE Evidence Profiles and Summary of Findings Tables." *Journal of Clinical Epidemiology*, vol. 64, no. 4, 2011, pp. 383=94, https://doi.org/10.1016/j.jclinepi.2010.04.026.

11 SMFM adopts GRADE (Grading of Recommendations Assessment, Development, and Evaluation) for clinical guidelines. Society for Maternal-Fetal Medicine (SMFM), Chauhan SP, Blackwell SC. Am J Obstet Gynecol. 2013 Sep;209(3):163-5. doi: 10.1016/j.ajog.2013.07.012. PMID: 23978245 https://pubmed.ncbi.nlm.nih.gov/23978245/

Chapter 4: Governance and Approval

4.1 Formal governance arrangements

This Guideline was written by the Guideline Developers under the direction of the Guideline Programme Team. An Expert Advisory Group was formed to review the Guideline prior to submission for final approval with the National Women and Infants Health Programme. The roles and responsibilities of the members of each group and their process were clearly outlined and agreed.

4.2 Guideline development standards

This Guideline was developed by the Guideline Developer Group (GDG) within the overall template of the HSE National Framework[12] for developing Policies, Procedures, Protocols and Guidelines (2016) (Appendix 5) and under supervision of the Guideline Programme Team (GPT).

A review was conducted by a group of experts, specialists and advocates (the EAG) prior to approval by the Clinical Advisory Group (CAG) of the National Women and Infants Health Programme (NWIHP) with final sign off for publication by CAG Co-Chairs, the Clinical Director of NWIHP and the Chair of the IOG. See Appendix 6 for list of CAG members.

12 Health Service Executive (2016). National Framework for developing Policies, Procedures, Protocols and Guidelines (PPPGs). Available from: https://www.hse.ie/eng/about/who/qid/nationalframeworkdevelopingpolicies/

Chapter 5: Communication and Dissemination

A communication and dissemination plan for this Guideline has been developed by the GPT and endorsed by NWIHP.

Effective ongoing clear communication is essential in explaining why the Guideline is necessary and securing continued buy-in. It provides an opportunity to instil motivation within staff, helps overcome resistance to change and gives an opportunity for feedback.[13]

The Clinical Guideline will be circulated and disseminated through the Guideline Programme Team as well as through the professional networks who participated in developing and reviewing the document.

Senior management within the Gynaecology units and hospital networks are responsible for the appropriate dissemination of new and updated guidelines. Local hospital groups including guideline committees are also instrumental in the implementation of new and updated guidelines and promoting their use in the relevant clinical settings.

The HSE will make this Guideline available to all employees and primary care colleagues through standards networks as well as storing it in the online PPPG repository. Electronic versions available on the NWIHP (https://www.hse.ie/eng/about/who/acute-hospitals-division/woman-infants/clinical-guidelines/) and RCPI websites (https://www.rcpi.ie/faculties/obstetricians-and-gynaecologists/national-clinical-guidelines-in-obstetrics-and-gynaecology/) and other communication means can be used to maximise distribution. The NWIHP website will also provide a training webinar introducing each Guideline and where relevant a downloadable version of the recommended algorithm will be available.

This Guideline should also be distributed to other providers of women's healthcare in the community and private care settings in order to improve the cross-referral interface.

13 Department of Health (2018). NCEC Implementation Guide and Toolkit. Available at: https://health.gov.ie/national-patient-safety-office/ncec/

Chapter 6: **Implementation**

6.1 Implementation plan

Implementation was considered at the beginning, and throughout the Guideline development process. The local multidisciplinary clinical team, senior executive and clinical management in each maternity and gynaecology unit are ultimately responsible for the appropriate structured adoption and implementation of the Guidelines within their area of responsibility. They must ensure that all relevant personnel under their supervision have read and understood the Guideline and monitor both its effectiveness and adoption.

Within each site, local multidisciplinary teams are responsible for the clinical implementation of Guideline recommendations and ensuring that their local clinical practices and processes reflect and are aligned with the Guideline recommendations.

The following have been put in place to help facilitate the implementation of this Guideline.

- Quick Summary Document (QSD) for clinical staff (includes key recommendations, auditable standards, algorithms and recommended reading)
- Clinical Guideline mobile application
- Plain language summary

6.2 Education plans required to implement the Guideline

It is acknowledged that this Guideline should be complemented by ongoing education, training and assessment where required.

6.3 Barriers and facilitators

To ensure successful implementation of guidelines, it is first necessary to look at potential barriers and facilitators. Taking these into account when developing the implementation plan should improve levels of support from relevant users. (DOH 2018, 2019)

Barriers may be categorised as internal (specific to the Guideline itself) or external (specific to the clinical environment).

The Guideline Development Group has aimed to address any internal barriers during the development of this Guideline.

Potential external barriers include:

- Structural factors (e.g. budget or service redesign)
    - Scalability of the service
- Organisational factors (e.g. lack of facilities or equipment)
    - Multifunctional rooms suitable for intimate gynaecological examination

  - En suite toileting
  - Prioritisation in terms of sharing resources
- Individual factors (e.g. knowledge, skills, training)
- Patient acceptability and experience

In the case of this Guideline, it will be necessary to examine possible barriers and consider implementation strategies to address them. By example, this may include discussion with relevant management groups with regards budgetary impact or providing training to the relevant staff.

Internal barriers

- Staff knowledge and behaviour
- Evolving evidence required – we acknowledge that we cannot answer all the clinical pathways that intersect with the PMB pathway due to the scope of the Guideline.

6.4 Resources necessary to implement recommendations

The implementation of this Guideline should be undertaken as part of the quality improvement of each hospital. Hospitals should review existing service provision against this Guideline, identifying necessary resources required to implement the recommendations in this Guideline.

Chapter 7: Audit and Evaluation

7.1 Introduction to audit

It is important that both implementation of the Guideline and its influence on outcomes are audited to ensure that this Guideline positively impacts on patient care. Institutions and health professionals are encouraged to develop and undertake regular audits of Guideline implementation. Personnel tasked with the job of conducting the audit should be identified on receipt of the most recent version of the guideline.

7.2 Auditable standards

Audit using the key recommendations as indicators should be undertaken to identify where improvements are required and to enable changes as necessary. Audit should also be undertaken to provide evidence of continuous quality improvement initiatives.

Auditable standards for this Guideline include:

1. Time from first GP/community practitioner presentation to referral being made by GP/community practitioner to gynaecology services
2. Time from referral being made by GP/community practitioner to appointment date being given hospital services
3. Number of cases completed in one Ambulatory Gynaecology clinic visit
4. Number of cases that could not be completed in Ambulatory Gynaecology and subsequently required inpatient investigations and management.
5. The time from incomplete outpatient investigations to complete inpatient investigations and management
6. Number of women who took pre-procedure analgesia and their reported pain scores during and after hysteroscopy
7. Percentage of adequate endometrial samples
8. False negative investigation outcome
9. Timeline from referral to cancer diagnosis and to cancer treatment
10. Unscheduled hospital admissions following Ambulatory Gynaecology appointment for a related clinical event
11. Patient experience
12. The number of women who withdraw from the diagnostic track

7.3 Evaluation

Evaluation is defined as a formal process to determine the extent to which the planned or desired outcomes of an intervention are achieved (HIQA. 2012).[14]

Implementation of this Guideline will be audited periodically at national level, with standards for this set by the NWIHP. Evaluation of the auditable standards should also be undertaken locally by senior clinical management to support implementation.

14 Health Information Quality Authority (2012). National Standards for Safer Better Healthcare [Internet]. Available from: https://www.hiqa.ie/reports-and-publications/standard/national-standards-safer-better-healthcare

Chapter 8: Revision Plan

8.1 Procedure for the update of the Guideline

It may be a requirement to amend, update or revise this Guideline as new evidence emerges. This Guideline will be reviewed at national level every three years, or earlier if circumstances require it, and updated accordingly.[15]

The Guideline Development Group will be asked to review the literature and recent evidence to determine if changes are to be made to the existing Guideline. If the Guideline Development Group are unavailable, the GPT along with the NWIHP senior management team will select a suitable expert to replace them.

If there are no amendments required to the Guideline following the revision date, the detail on the revision tracking box must still be updated which will be a new version number and date.

The recommendations set out in this Guideline remain valid until a review has been completed.

8.2 Method for amending the Guideline

As new evidence become available it is inevitable that guideline recommendations will fall behind current evidence-based clinical practice. It is essential that clinical guidelines are reviewed and updated with new evidence as it becomes available.

In order to request a review of this Guideline one of the following criteria must be met:

a) 3 years since the Guideline was published

b) 3 years since last review was conducted

c) Update required as a result of new evidence

Correspondence requesting a review of the Guideline should be submitted to the National Women and Infants Health Programme. Any such requests should be dealt with in a timely manner.

15 Health Service Executive (2016). National Framework for developing Policies, Procedures, Protocols and Guidelines (PPPGs). Available from: https://www.hse.ie/eng/about/who/qid/nationalframeworkdevelopingpolicies/

Chapter 9: **References**

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Supporting evidence

GRADE: http://www.gradeworkinggroup.org/

AGREE: http://www.agreetrust.org/agree-ii/

HSE: https://www.hse.ie/eng/about/who/qid/nationalframeworkdevelopingpolicies/

Glossary
(for the Purpose of this Guideline)

ACOG American College of Obstetricians and Gynaecologists

AG Ambulatory Gynaecology

AGREE Appraisal of Guidelines for Research and Evaluation

BMI Body Mass Index

BMS British Menopause Society

BP Blood Pressure

CAG Clinical Advisory Group

CT Computerised Tomography

EAG Expert Advisory Group

FIGO International Federation of Gynaecology and Obstetrics

GP General Practitioner

GPT Guideline Programme Team

HIQA Health Information and Quality Authority

HRT Hormone Replacement Therapy

HSE Health Service Executive

IOG Institute of Obstetricians and Gynaecologists

MRI Magnetic Resonance Imaging

MDM Multi-Disciplinary Meeting

NCEC National Clinical Effectiveness Committee

NHS National Health Service

NICE The National Institute for Health and Care Excellence

NSAIDs Non-Steroidal Anti-Inflammatory Drugs

NWIHP National Women and Infants Health Programme

PMB Postmenopausal Bleeding

PPPG Policy, Procedures, Protocols and Guidelines

RCOG Royal College of Obstetricians and Gynaecologists

RCPI Royal College of Physicians of Ireland

TAS Transabdominal Ultrasound Scan

TVS Transvaginal Ultrasound Scan

VTE Venous thromboembolism

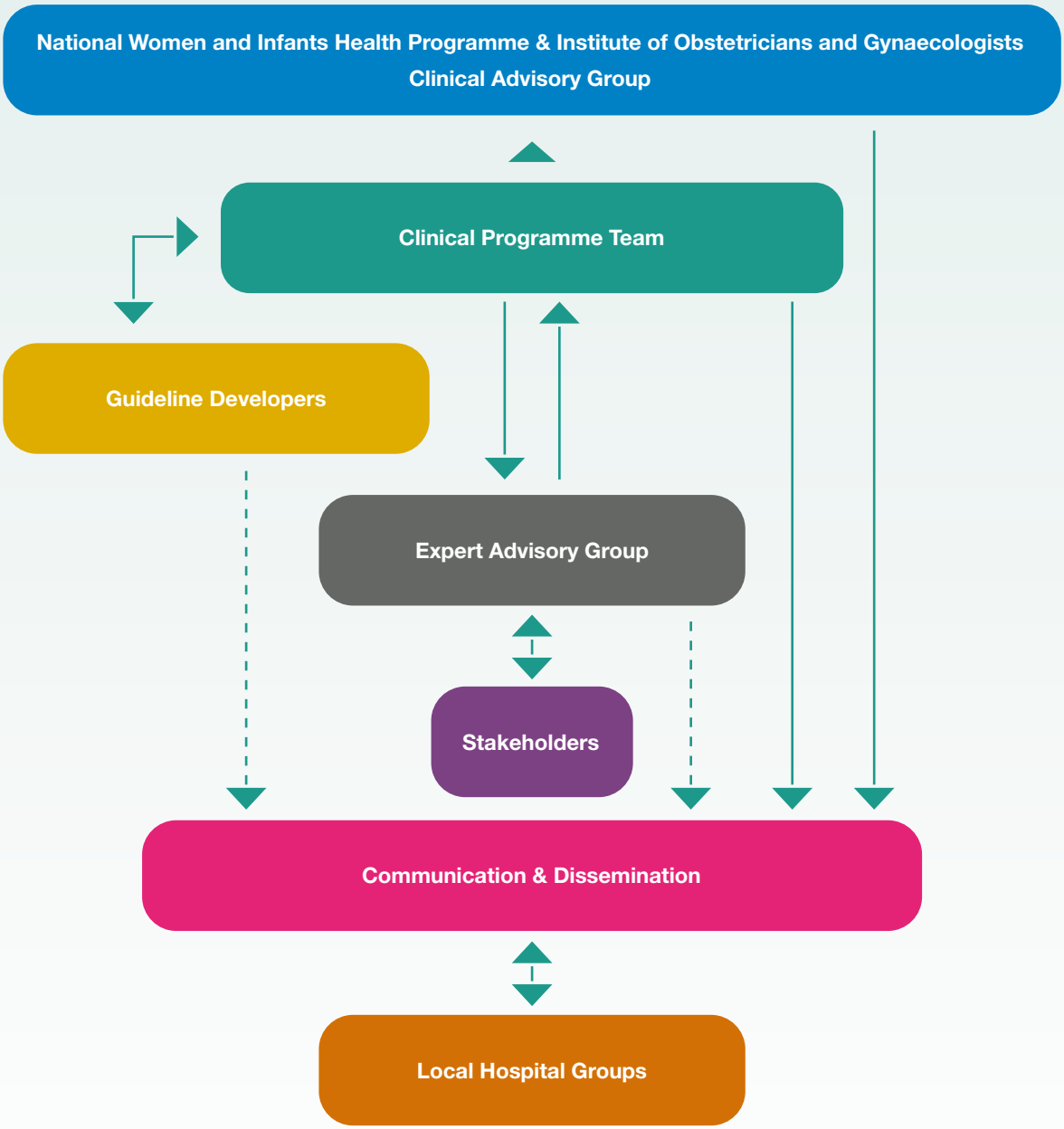
Appendix 1:
Expert Advisory Group Members 2021-

Name	Profession	Location (2021)
Dr Fergus McCarthy	Consultant Obstetrician, Gynaecologist, Senior Lecturer and Maternal-Fetal Medicine Sub-specialist	Cork University Maternity Hospital, University College Cork
Dr Mairead Butler	Consultant Obstetrician and Gynaecologist	University Hospital Waterford
Prof Declan Keane	Professor of Obstetrics and Gynaecology	National Maternity Hospital Dublin, Royal College of Surgeons in Ireland
Dr Katherine Astbury	Consultant Obstetrician and Gynaecologist Gynaecology Oncology Sub-specialist	University Hospital Galway
Dr Sarah Petch	Specialist Registrar, Obstetrics and Gynaecology	National Maternity Hospital Dublin
Dr Orla Donohoe	Specialist Registrar, Obstetrics and Gynaecology	Sligo University Hospital
Prof John Murphy	Consultant Neonatologist and Clinical Lead for the National Clinical Programme for Paediatrics and Neonatology	National Women and Infants Health Programme
Ms Siobhan Canny	Group Director of Midwifery	Saolta University Health Care Group
Ms Fiona Hanrahan	Director of Midwifery and Nursing	Rotunda Hospital Dublin
Ms Margaret Quigley	National Lead for Midwifery	Office of Nursing and Midwifery Services Director
Prof Valerie Smith	Professor of Midwifery	School of Nursing and Midwifery, Trinity College Dublin
Ms Triona Cowman	Director of the Centre for Midwifery Education	Centre for Midwifery Education, Coombe Women & Infants University Hospital
Ms Janet Murphy	Advanced Midwifery Practitioner	University Hospital Waterford

Attendee	Profession	Location (2021)
Dr Ciara McCarthy	General Practitioner and ICGP Womens Health Lead	Irish College of General Practitioners
Mr Fergal O' Shaughnessy *And* Dr Brian Cleary *(Shared nomination)*	Senior Pharmacist, Honorary Lecturer *And* Chief Pharmacist, Honorary Clinical Associate Professor and Medications Lead, Maternal & Newborn Clinical Management System	Rotunda Hospital Dublin Royal College of Surgeons in Ireland
Ms Marie Finn	Medical Social Work Counsellor	Saolta University Health Care Group
Ms Marie Culliton	Lab Manager/Chief Medical Scientist	National Maternity Hospital Dublin
Ms Marita Hennessy	Post-Doctoral Researcher	Pregnancy Loss Research Group, INFANT Centre, University College Cork
Ms Niamh Connolly-Coyne *And* Ms Mandy Daly *(Shared nomination)*	Board of Directors	Irish Neonatal Health Alliance
Ms Caroline Joyce	Principal Clinical Biochemist PhD Candidate	Cork University Hospital University College Cork
Dr Richard Duffy	Consultant Perinatal Psychiatrist	Rotunda Hospital Dublin
Ms Clare Farrell	Physiotherapy Manager	Coombe Women & Infants University Hospital
Ms Fiona Dunlevy *And* Ms Sinéad Curran *(Shared nomination)*	Dietician Manager	Coombe Women & Infants University Hospital National Maternity Hospital
Dr Nicholas Barrett	Lead for Obstetric Anaesthesiology services	Limerick University Hospital
Dr Brendan Fitzgerald	Consultant Perinatal Pathologist	Cork University Hospital
Dr Niamh Conlon	Consultant Histopathologist	Cork University Hospital

Appendix 2: **Guideline Programme Process**

Guideline Programme Process



Appendix 3: **Agree II Checklist**[16]

AGREE Reporting Checklist 2016

This checklist is intended to guide the reporting of clinical practice guidelines.

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
DOMAIN 1: SCOPE AND PURPOSE		
1. OBJECTIVES *Report the overall objective(s) of the guideline. The expected health benefits from the guideline are to be specific to the clinical problem or health topic.*	☐ Health intent(s) (i.e., prevention, screening, diagnosis, treatment, etc.) ☐ Expected benefit(s) or outcome(s) ☐ Target(s) (e.g., patient population, society)	
2. QUESTIONS *Report the health question(s) covered by the guideline, particularly for the key recommendations.*	☐ Target population ☐ Intervention(s) or exposure(s) ☐ Comparisons (if appropriate) ☐ Outcome(s) ☐ Health care setting or context	
3. POPULATION *Describe the population (i.e., patients, public, etc.) to whom the guideline is meant to apply.*	☐ Target population, sex and age ☐ Clinical condition (if relevant) ☐ Severity/stage of disease (if relevant) ☐ Comorbidities (if relevant) ☐ Excluded populations (if relevant)	
DOMAIN 2: STAKEHOLDER INVOLVEMENT		
4. GROUP MEMBERSHIP *Report all individuals who were involved in the development process. This may include members of the steering group, the research team involved in selecting and reviewing/ rating the evidence and individuals involved in formulating the final recommendations.*	☐ Name of participant ☐ Discipline/content expertise (e.g., neurosurgeon, methodologist) ☐ Institution (e.g., St. Peter's hospital) ☐ Geographical location (e.g., Seattle, WA) ☐ A description of the member's role in the guideline development group	

16 AGREE Reporting Checklist is available on the AGREE Enterprise website, a free and open access resource to support the practice guideline field (www. agreetrust.org)

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
5. TARGET POPULATION PREFERENCES AND VIEWS *Report how the views and preferences of the target population were sought/considered and what the resulting outcomes were.*	☐ Statement of type of strategy used to capture patients'/publics' views and preferences (e.g., participation in the guideline development group, literature review of values and preferences) ☐ Methods by which preferences and views were sought (e.g., evidence from literature, surveys, focus groups) ☐ Outcomes/information gathered on patient/public information ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	
6. TARGET USERS *Report the target (or intended) users of the guideline.*	☐ The intended guideline audience (e.g. specialists, family physicians, patients, clinical or institutional leaders/administrators) ☐ How the guideline may be used by its target audience (e.g., to inform clinical decisions, to inform policy, to inform standards of care)	
DOMAIN 3: RIGOUR OF DEVELOPMENT		
7. SEARCH METHODS *Report details of the strategy used to search for evidence.*	☐ Named electronic database(s) or evidence source(s) where the search was performed (e.g., MEDLINE, EMBASE, PsychINFO, CINAHL) ☐ Time periods searched (e.g., January 1, 2004 to March 31, 2008) ☐ Search terms used (e.g., text words, indexing terms, subheadings) ☐ Full search strategy included (e.g., possibly located in appendix)	
8. EVIDENCE SELECTION CRITERIA *Report the criteria used to select (i.e., include and exclude) the evidence. Provide rationale, where appropriate.*	☐ Target population (patient, public, etc.) characteristics ☐ Study design ☐ Comparisons (if relevant) ☐ Outcomes ☐ Language (if relevant) ☐ Context (if relevant)	

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
9. STRENGTHS & LIMITATIONS OF THE EVIDENCE *Describe the strengths and limitations of the evidence. Consider from the perspective of the individual studies and the body of evidence aggregated across all the studies. Tools exist that can facilitate the reporting of this concept.*	☐ Study design(s) included in body of evidence ☐ Study methodology limitations (sampling, blinding, allocation concealment, analytical methods) ☐ Appropriateness/relevance of primary and secondary outcomes considered ☐ Consistency of results across studies ☐ Direction of results across studies ☐ Magnitude of benefit versus magnitude of harm ☐ Applicability to practice context	
10. FORMULATION OF RECOMMENDATIONS *Describe the methods used to formulate the recommendations and how final decisions were reached. Specify any areas of disagreement and the methods used to resolve them.*	☐ Recommendation development process (e.g., steps used in modified Delphi technique, voting procedures that were considered) ☐ Outcomes of the recommendation development process (e.g., extent to which consensus was reached using modified Delphi technique, outcome of voting procedures) ☐ How the process influenced the recommendations (e.g., results of Delphi technique influence final recommendation, alignment with recommendations and the final vote)	
11. CONSIDERATION OF BENEFITS AND HARMS *Report the health benefits, side effects, and risks that were considered when formulating the recommendations.*	☐ Supporting data and report of benefits ☐ Supporting data and report of harms/side effects/risks ☐ Reporting of the balance/trade-off between benefits and harms/side effects/risks ☐ Recommendations reflect considerations of both benefits and harms/side effects/ risks	
12. LINK BETWEEN RECOMMENDATIONS AND EVIDENCE *Describe the explicit link between the recommendations and the evidence on which they are based.*	☐ How the guideline development group linked and used the evidence to inform recommendations ☐ Link between each recommendation and key evidence (text description and/or reference list) ☐ Link between recommendations and evidence summaries and/or evidence tables in the results section of the guideline	

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
13. EXTERNAL REVIEW *Report the methodology used to conduct the external review.*	☐ Purpose and intent of the external review (e.g., to improve quality, gather feedback on draft recommendations, assess applicability and feasibility, disseminate evidence) ☐ Methods taken to undertake the external review (e.g., rating scale, open-ended questions) ☐ Description of the external reviewers (e.g., number, type of reviewers, affiliations) ☐ Outcomes/information gathered from the external review (e.g., summary of key findings) ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations (e.g., guideline panel considered results of review in forming final recommendations)	
14. UPDATING PROCEDURE *Describe the procedure for updating the guideline.*	☐ A statement that the guideline will be updated ☐ Explicit time interval or explicit criteria to guide decisions about when an update will occur ☐ Methodology for the updating procedure	
DOMAIN 4: CLARITY OF PRESENTATION		
15. SPECIFIC AND UNAMBIGUOUS RECOMMENDATIONS *Describe which options are appropriate in which situations and in which population groups, as informed by the body of evidence.*	☐ A statement of the recommended action ☐ Intent or purpose of the recommended action (e.g., to improve quality of life, to decrease side effects) ☐ Relevant population (e.g., patients, public) ☐ Caveats or qualifying statements, if relevant (e.g., patients or conditions for whom the recommendations would not apply) ☐ If there is uncertainty about the best care option(s), the uncertainty should be stated in the guideline	
16. MANAGEMENT OPTIONS *Describe the different options for managing the condition or health issue.*	☐ Description of management options ☐ Population or clinical situation most appropriate to each option	

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
17. IDENTIFIABLE KEY RECOMMENDATIONS *Present the key recommendations so that they are easy to identify.*	☐ Recommendations in a summarized box, typed in bold, underlined, or presented as flow charts or algorithms ☐ Specific recommendations grouped together in one section	
DOMAIN 5: APPLICABILITY		
18. FACILITATORS AND BARRIERS TO APPLICATION *Describe the facilitators and barriers to the guideline's application.*	☐ Types of facilitators and barriers that were considered ☐ Methods by which information regarding the facilitators and barriers to implementing recommendations were sought (e.g., feedback from key stakeholders, pilot testing of guidelines before widespread implementation) ☐ Information/description of the types of facilitators and barriers that emerged from the inquiry (e.g., practitioners have the skills to deliver the recommended care, sufficient equipment is not available to ensure all eligible members of the population receive mammography) ☐ How the information influenced the guideline development process and/or formation of the recommendations	
19. IMPLEMENTATION ADVICE/TOOLS *Provide advice and/or tools on how the recommendations can be applied in practice.*	☐ Additional materials to support the implementation of the guideline in practice. For example: • Guideline summary documents • Links to check lists, algorithms • Links to how-to manuals • Solutions linked to barrier analysis (see Item 18) • Tools to capitalize on guideline facilitators (see Item 18) • Outcome of pilot test and lessons learned	

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
20. RESOURCE IMPLICATIONS *Describe any potential resource implications of applying the recommendations.*	☐ Types of cost information that were considered (e.g., economic evaluations, drug acquisition costs) ☐ Methods by which the cost information was sought (e.g., a health economist was part of the guideline development panel, use of health technology assessments for specific drugs, etc.) ☐ Information/description of the cost information that emerged from the inquiry (e.g., specific drug acquisition costs per treatment course) ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	
21. MONITORING/ AUDITING CRITERIA *Provide monitoring and/or auditing criteria to measure the application of guideline recommendations.*	☐ Criteria to assess guideline implementation or adherence to recommendations ☐ Criteria for assessing impact of implementing the recommendations ☐ Advice on the frequency and interval of measurement ☐ Operational definitions of how the criteria should be measured	
DOMAIN 6: EDITORIAL INDEPENDENCE		
22. FUNDING BODY *Report the funding body's influence on the content of the guideline.*	☐ The name of the funding body or source of funding (or explicit statement of no funding) ☐ A statement that the funding body did not influence the content of the guideline	
23. COMPETING INTERESTS *Provide an explicit statement that all group members have declared whether they have any competing interests.*	☐ Types of competing interests considered ☐ Methods by which potential competing interests were sought ☐ A description of the competing interests ☐ How the competing interests influenced the guideline process and development of recommendations	

From: Brouwers MC, Kerkvliet K, Spithoff K, on behalf of the AGREE Next Steps Consortium. The AGREE Reporting Checklist: a tool to improve reporting of clinical practice guidelines. BMJ 2016;352:i1152. doi: 10.1136/bmj.i1152.

For more information about the AGREE Reporting Checklist, please visit the AGREE Enterprise website at http://www.agreetrust.org.

Appendix 4: **Grades of Recommendation**[17]

Grade of recommendation	Clarity of risk/ benefit	Quality of supporting evidence	Implications	Suggested Language
1 A. Strong recommendation, high-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Consistent evidence from well-performed randomised, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk	Strong recommendations can apply to most patients in most circumstances without reservation. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present	We strongly recommend… We recommend that …should be performed/ administered… We recommend that … is indicated/ beneficial/ effective…
1 B. Strong recommendation, moderate-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Evidence from randomised, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate	Strong recommendation and applies to most patients. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present	We recommend… We recommend that … should be performed/ administered… We recommend that … is (usually) indicated/ beneficial/ effective…

17 SMFM adopts GRADE (Grading of Recommendations Assessment, Development, and Evaluation) for clinical guidelines. Society for Maternal-Fetal Medicine (SMFM), Chauhan SP, Blackwell SC. Am J Obstet Gynecol. 2013 Sep;209(3):163-5. doi: 10.1016/j.ajog.2013.07.012. PMID: 23978245 https://pubmed.ncbi.nlm.nih.gov/23978245/

Grade of recommendation	Clarity of risk/ benefit	Quality of supporting evidence	Implications	Suggested Language
1 C. Strong recommendation, low-quality evidence	Benefits appear to outweigh risk and burdens, or vice versa	Evidence from observational studies, unsystematic clinical experience, or from randomised, controlled trials with serious flaws. Any estimate of effect is uncertain	Strong recommendation that applies to most patients. Some of the evidence base supporting the recommendation is, however, of low quality	We recommend… We recommend that … should be performed/ administered… We recommend that … Is (maybe) indicated/ beneficial/ effective…
2A. Weak recommendation, high-quality evidence	Benefits closely balanced with risks and burdens	Consistent evidence from well-performed randomised, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk	Weak recommendation: best action may differ depending on circumstances or patients or societal values	We suggest… We suggest that … may/might be reasonable…
2B. Weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burdens, some uncertainty in the estimates of benefits, risks and burdens	Evidence from randomised, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate	Weak recommendation; alternative approaches likely to be better for some patients under some circumstances	We suggest… We suggest that … may/might be reasonable…

Grade of recommendation	Clarity of risk/ benefit	Quality of supporting evidence	Implications	Suggested Language
2C. Weak recommendation, low-quality evidence	Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens	Evidence from observational studies, unsystematic clinical experience, or from randomised, controlled trials with serious flaws. Any estimate of effect is uncertain	Very weak recommendation: other alternatives may be equally reasonable.	We suggest… is an option We suggest that … may/might be reasonable.
Best practice	A recommendation that is sufficiently obvious that the desirable effects outweigh undesirable effects, despite the absence of direct evidence, such that the grading of evidence is unnecessary			We recommend… We recommend that … should be performed/ administered… We recommend that … Is usually) indicated/ beneficial/effective

Appendix 5: **Policies, Procedures, Protocols and Guidelines Checklist**

The PPPG Checklists were developed to assist staff to meet standards when developing Clinical PPPGs.

Standards for developing clinical PPPG	
Stage 1 initiation	**Checklist**
The decision making approach relating to the type of PPPG guidance required (policy, procedure, protocol, guideline), coverage of the PPPG (national, regional, local) and applicable settings are described.	☐
Synergies/co-operations are maximised across departments/organisations (Hospitals/ Hospital Groups/Community Healthcare Organisations (CHO)/National Ambulance Service (NAS)), to avoid duplication and to optimise value for money and use of staff time and expertise.	☐
The scope of the PPPG is clearly described, specifying what is included and what lies outside the scope of the PPPG.	☐
The target users and the population/patient group to whom the PPPG is meant to apply are specifically described.	☐
The views and preferences of the target population have been sought and taken into consideration (as required).	☐
The overall objective(s) of the PPPGs are specifically described.	☐
The potential for improved health is described (e.g. clinical effectiveness, patient safety, quality improvement, health outcomes, quality of life, quality of care).	☐
Stakeholder identification and involvement: The PPPG Development Group includes individuals from all relevant stakeholders, staff and professional groups.	☐
Conflict of interest statements from all members of the PPPG Development Group are documented, with a description of mitigating actions if relevant.	☐
The PPPG is informed by the identified needs and priorities of service users and stakeholders.	☐
There is service user/lay representation on PPPG Development Group (as required).	☐
Information and support is available for staff on the development of evidence-based clinical practice guidance.	☐

Stage 2 development	**Checklist**
The clinical question(s) covered by the PPPG are specifically described.	☐
Systematic methods used to search for evidence are documented (for PPPGs which are adapted/ adopted from international guidance, their methodology is appraised and documented).	☐
Critical appraisal/analysis of evidence using validated tools is documented (the strengths, limitations and methodological quality of the body of evidence are clearly described).	☐
The health benefits, side effects and risks have been considered and documented in formulating the PPPG.	☐
There is an explicit link between the PPPG and the supporting evidence.	☐
PPPG guidance/recommendations are specific and unambiguous.	☐
The potential resource implications of developing and implementing the PPPG are Identified e.g. equipment, education/training, staff time and research.	☐
There is collaboration across all stakeholders in the planning and implementation phases to optimise patient flow and integrated care.	☐
Budget impact is documented (resources required).	☐
Education and training is provided for staff on the development and implementation of evidence- based clinical practice guidance (as appropriate).	☐
Three additional standards are applicable for a small number of more complex PPPGs:	☐
Cost effectiveness analysis is documented.	☐
A systematic literature review has been undertaken.	☐
Health Technology Assessment (HTA) has been undertaken.	☐
Stage 3 governance and approval	**Checklist**
Formal governance arrangements for PPPGs at local, regional and national level are established and documented.	☐
The PPPG has been reviewed by independent experts prior to publication (as required).	☐
Copyright and permissions are sought and documented.	☐
Stage 4 communication and dissemination	**Checklist**
A communication plan is developed to ensure effective communication and collaboration with all stakeholders throughout all stages.	☐
Plan and procedure for dissemination of the PPPG is described.	☐
The PPPG is easily accessible by all users e.g. PPPG repository.	☐

Stage 5 implementation	**Checklist**
Written implementation plan is provided with timelines, identification of responsible persons/ units and integration into service planning process.	☐
Barriers and facilitators for implementation are identified, and aligned with implementation levers.	☐
Education and training is provided for staff on the development and implementation of evidence- based PPPG (as required).	☐
There is collaboration across all stakeholders in the planning and implementation phases to optimise patient flow and integrated care.	☐
Stage 6 monitoring, audit, evaluation	**Checklist**
Process for monitoring and continuous improvement is documented.	☐
Audit criteria and audit process/plan are specified.	☐
Process for evaluation of implementation and (clinical) effectiveness is specified.	☐
Stage 7 revision/update	**Checklist**
Documented process for revisions/updating and review, including timeframe is provided.	☐
Documented process for version control is provided.	☐

To view in full refer to website: https://www.hse.ie/eng/about/who/qid/nationalframeworkdevelopingpolicies/

Appendix 6: **NWIHP/IOG CAG Membership 2022**

Dr Cliona Murphy (Chair). Consultant Obstetrician and Gynaecologist, Coombe Women and Infants University Hospital. Clinical Director, National Women and Infants Health Programme.

Dr Sam Coulter-Smith. Consultant Obstetrician and Gynaecologist, Rotunda Hospital. Chair, Institute of Obstetricians and Gynaecologists.

Angela Dunne. Director of Midwifery, National Women and Infants Health Programme.

Kilian McGrane. Director, National Women and Infants Health Programme.

Dr Peter McKenna. Clinical Lead, Obstetric Event Support Team, National Women and Infants Health Programme.

Prof John Murphy. Clinical Lead Neonatology, National Women and Infants Health Programme.

Prof Maeve Eogan. Consultant Obstetrician and Gynaecologist, Rotunda Hospital. Clinical Lead, Sexual Assault Treatment Units, National Women and Infants Health Programme.

Dr Aoife Mullaly. Consultant Obstetrician and Gynaecologist, Coombe Women and Infants University Hospital. Clinical Lead, Termination of Pregnancy Services, National Women and Infants Health Programme.

Prof Keelin O'Donoghue. Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital. Clinical Lead, National Guidelines, National Women and Infants Health Programme.

Prof Nóirín Russell. Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital. Clinical Director, Cervical Check.

Prof Richard Greene. Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital. Clinical Director, National Perinatal Epidemiology Centre, University College Cork.

Prof John Morrison. Consultant Obstetrician and Gynaecologist, University Hospital Galway. Clinical Director, Saolta Maternity Directorate.

Dr Suzanne O'Sullivan. Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital. Director of Education and Training, Obstetrics and Gynaecology, Institute of Obstetricians and Gynaecologists.

Prof Fergal Malone. Master, Consultant Obstetrician and Gynaecologist, Rotunda Hospital.

Prof John Higgins. Cork University Maternity Hospital, Consultant Obstetrician and Gynaecologist, Clinical Director, Ireland South Women and Infants Directorate.

Dr Mendinaro Imcha. Clinical Director, Consultant Obstetrician and Gynaecologist, University Maternity Hospital Limerick.

Prof Shane Higgins. Master, Consultant Obstetrician and Gynaecologist, National Maternity Hospital.

Prof Mike O'Connell. Master, Consultant Obstetrician and Gynaecologist, Coombe Women and Infants University Hospital.

Dr Brian Cleary. Chief Pharmacist, Rotunda Hospital. Medications Lead, Maternal and Newborn Clinical Management System Project.