Assessment and management of Abnormal Uterine Bleeding (AUB) in non-pregnant women of reproductive age group

New Zealand AUB working group.

Ko te tapu a te wāhine, kei te wāhine te whare tangata, a wā tātou tātai heke, wā tātou whakapapa.

Ko ia tēnā o te tapu a te wāhine

Ko te tapu a te Tane, hei karawhiu i te tewhatewha

Ko ia te kaitiaki o ngā wāhine katoa, kei rotu i tana whānau, tana hapū, tuku iho aka i tona Iwi

The sacredness of women is that is women who hold the house of the genealogy

The sacredness of our men is that is our responsibility of our men to be the provider and the protector of every woman in his family, in his hapū, in his whānau his Iwi.

Gifted by Dame Rangimarie Naida Glavish DNZM. JP

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THE ROYAL NEW ZEALAND COLLEGE OF GENERAL PRACTITIONERS ENDORSED GUIDANCE CUM SCIENTIA CARITAS VALID UNTIL 31 DECEMBER 2027 TE WHARE TOHU RATA O AOTEAROA

Sexual Wellbeing Aotearoa

Summary of assessment and management of AUB

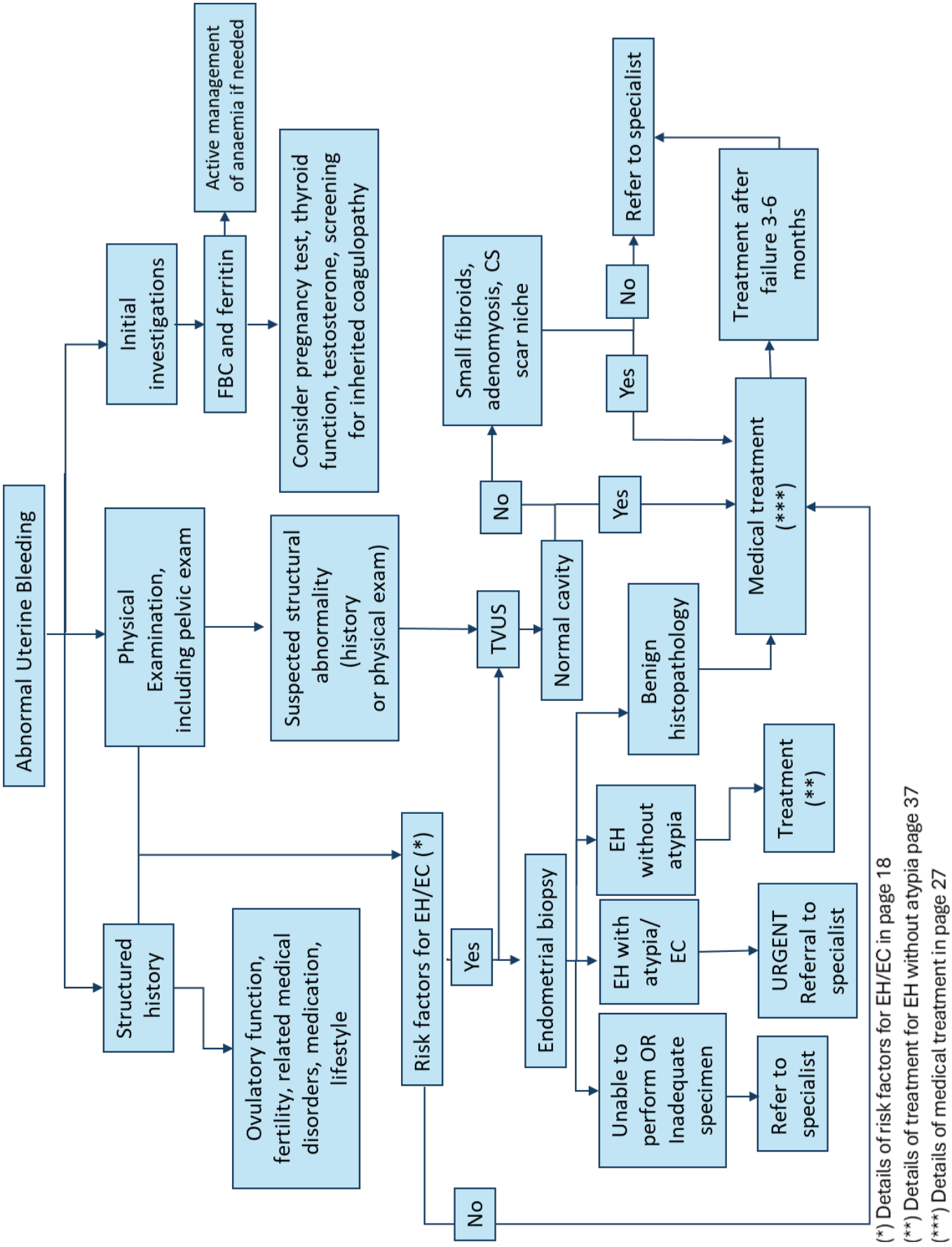

Table 1 Summary assessment of abnormal uterine bleeding (AUB)

History

- Duration, regularity, frequency, volume of menstrual cycles and duration of symptoms
- Sexual and reproductive health: possibility of pregnancy, desire for fertility, need for contraception
- Associated symptoms (eg pain) and symptoms associated with systemic or other causes (such as hirsutism, acne, or coagulation disorders)
- Medical, Surgical and Medication history
- Goals of treatment (regular cycles, amenorrhoea etc)

Examination

- General (vital signs, BMI, signs of androgen excess or other systemic illness)
- Abdominal and Gynaecological Exam
    - Inspection, Palpation
    - Speculum exam, liquid-based cytology and HrHPV test if indicated (if not performed in the last 6 months), swab for STIs if appropriate
    - Bimanual examination

Laboratory tests

- CBC, Ferritin
- Pregnancy test
- Others as indicated (eg, testosterone level if suspected PCOS, TSH if signs or symptoms of thyroid disease, coagulation screen if suspected coagulopathy)

Imaging

Transabdominal and Transvaginal ultrasound scan

Indications for ultrasound scan:

1. History and or examination suggests structural cause for bleeding
2. Conservative management has failed
3. There is a risk of malignancy
    - Recommended for all women > 45
    - Women <45 with risk factor(s) (See *Table 5*).

MRI/ CT- usually not indicated as part of the initial investigations

Endometrial sampling methods

Aspiration endometrial sample (such as a Pipelle biopsy)

Indications for endometrial sampling

- **Women aged 19 and under**

Endometrial sampling is not routinely recommended for women who present with AUB in this age group. An individualised approach should be taken for assessment and if endometrial sampling is considered, a referral to secondary care is indicated.

- **Women between the ages of 20 and 30**

The decision to perform endometrial sampling should be individualised in women under the age of 30 based on imaging and risk factors.

Endometrial sampling should be considered at, or soon after, the initial presentation in those who have had long-standing unopposed oestrogen stimulation and or those who have multiple risk factors for EH or EC.

- **Women between the ages of 30 and 45**

Endometrial sampling is recommended for women who present with AUB and have risk factor(s), for EH or EC.

- **Women over the age of 45**

Endometrial sampling is recommended in all women who present with AUB over the age of 45, particularly in the presence of risk factors.

Māori and Pacific Peoples are disproportionately affected by EC or EH. Investigations including TVUSS and or aspiration endometrial sampling should be considered at or soon after initial presentation for all Māori and Pacific Peoples presenting with AUB.

Hysteroscopy directed endometrial sample

Hysteroscopy with directed endometrial sampling is recommended for those with structural endometrial pathology on ultrasound scans. These include:

- Endometrial polyps or endometrial thickness ≥ 16 mms
- Hypervascularised/ heterogenous endometrium
- Endometrium with cystic spaces
- Symptomatic submucosal fibroid(s) not responsive to medical treatment

Endometrial sample (Pipelle) is recommended if delay in hysteroscopy is expected

Table 2 Summary Management – No structural causes and no risk factors for endometrial pathology

<table>
<tr><th colspan="2">No structural causes and no risk factors for endometrial pathology</th></tr>
<tr><td colspan="2">Heavy menstrual bleeding

Pharmacological (usually first line)

Non-Hormonal

• NSAIDS eg, mefenamic acid or naproxen
• Antifibrinolytics, eg, tranexamic acid

Hormonal

• LNG-IUD (Mirena ®)
• Combined hormonal contraceptives
• Oral progestogens (21 days per cycle or continuous)
• Injected progestogens (off-label)

Surgical (usually second line)

• Endometrial ablation
• Hysterectomy</td></tr>
<tr><td colspan="2">Intermenstrual Bleeding may suggest cervical causes or the presence of an endometrial polyp.</td></tr>
<tr><td colspan="2">Infrequent bleeding (previously known as oligomenorrhoea) should prompt assessment for anovulatory causes and be managed accordingly.</td></tr>
<tr><td colspan="2">Referral to secondary care should be considered in all women who do not respond to medical therapy after 3 to 6 months of treatment.</td></tr>
<tr><th colspan="2">Women with risk factors for endometrial cancer or hyperplasia (with or without structural abnormalities)</th></tr>
<tr><td colspan="2">Women with risk factors for developing EH or EC should be counselled regarding the risk and its associated implications in a culturally appropriate manner.

The risk of developing EH or EC may be reduced by management of risk factors as well as hormonal treatment to reduce unopposed oestrogen exposure to the endometrium.

Management should include education about lifestyle and nutritional factors which may contribute to risk factors, ongoing menstrual abnormalities, and other associated diseases.</td></tr>
</table>

Summary Management – Structural abnormalities

Structural abnormalities
Polyps
Polypectomy with direct visualisation (hysteroscopy) and histopathological analysis of the specimen is recommended for women who present with AUB in whom an endometrial polyp has been detected. Hormonal treatment for endometrial protection is recommended for women who have AUB with ongoing risk factors for EH or EC following polypectomy.
Fibroids
AUB related to small fibroids may be treated with pharmacological methods, including an LNG-IUD (Mirena ®). If symptoms do not resolve with medical treatment within 3 to 6 months, referral to secondary care is indicated for ongoing management. The effectiveness of pharmacological treatments for symptom control may be limited in women with large (variably defined in the literature) fibroids. Referral to secondary care simultaneously as commencing initial treatment is appropriate in women with large fibroids. Management options in secondary care may include GnRH agonists, uterine artery embolisation, myomectomy, and hysterectomy (by the least invasive surgical route)
Adenomyosis
The most common symptoms are heavy menstrual bleeding and dysmenorrhea. Pharmacological treatment is usually the first choice of treatment. If symptoms do not resolve with pharmacological treatment, referral to secondary care is recommended for ongoing management.
AVM
A rare, usually acquired cause of AUB in women. The bleeding may be life-threatening with hemodynamic instability. Prompt referral to secondary care for ongoing management is recommended.
Cs niche
An uncommon cause of AUB. It is reasonable to consider pharmacological treatment for the initial management of symptoms in women who do not wish to get pregnant. Surgical resection via operative hysteroscopy, vaginal surgery, laparotomy/laparoscopy, or a combined approach has been described[1-3]. There is a lack of evidence with regard to the role of surgical treatment with view to improving fertility or reducing obstetric risks in women.

Foreword

Abnormal uterine bleeding (AUB) is the most common gynaecological disorder presenting to primary and secondary care clinicians. In addition to significant physical and psychological sequelae, it may be a sign of serious underlying pathology. Despite this, consistent clinical guidance on how it can best be managed is lacking.

This guideline aims to delineate current evidence-based best practice. Where there is no evidence, good practice points are based on consensus.

The working group recognises the status of Māori as tangata whenua in Aotearoa, New Zealand, and is committed to meeting its obligations as Te Tiriti o Waitangi partners.

The development of these guidelines was supported by Health New Zealand | Te Whatu Ora - Northern Region, Northern Regional Integrated Cancer Services Programme Board, Te Aho o Te Kahu and Health Care Pathways Programme, Health New Zealand | Te Whatu Ora - Systems Improvement.

We are grateful to have had contributions from He Kamaka Waiora Health New Zealand | Te Whatu Ora (Māori Health Services, Health New Zealand) and to have been able to collaborate with the consumers and our radiology and pathology colleagues.

This guideline is intended to be used by clinicians for shared decision-making with women[1] with AUB and their whānau. Each district and region will need to review their current practice and align local guidance with this national guideline to facilitate consistent clinical practice.

[1] The working group use the term 'woman' in this document to include all individuals with a uterus needing gynaecological care, regardless of their gender identity.

Māori commentary

Kauria ai e kui te ara o
tō uha

Ka puta ai Tāne

Ki te ao marama

Ikura,

i ahuahua ai koe e Hine,

Ia te rere o te awa tapu

Maui tikitiki te natinga ōu
ki te awa atua

itanga ira tangata

Surging out on the
primordial waters

Tāne did discover

The realm of light

From the menstrual
earth

You were formed of
Hine-ahu-one and the
fertile waters flowed

Maui tikitiki vanquished

Begat the divine river

Confirming the lineage
of humanity

(Enoka, Murphy 2011)

Central to matauranga Māori is the significance of whakapapa, a genealogical link that ties the past, present and the future. Menarche was honoured with rites of knowledge, piercings, and moko kauae, and menstruation thereafter was a period of rest. Its importance is recited through purakau where Maui, a well-known demigod is crushed by Hine-nui-o-te-Po between her thighs, hence commencing his rebirth signalled through the first menarche known in te ao Māori and connecting menstruation to the moon and natural cycles of the world.

Colonisation has separated wahine Māori from matauranga Māori in waiwhero (also known as ikura, mate marama, mate wāhine, te awa tapu, māui), haputanga and breastfeeding practices. Deficit theory has maintained the notion that the menstrual cycle was unclean and removed the deeper spiritual aspects of menstruation. The restoration of maramataka has allowed some wahine Māori to connect regular menstruation to a moon cycle.

In Aotearoa, Māori and Pacific peoples suffer much higher rates of abnormal uterine bleeding and endometrial cancer, with yearly increases in incidence compared to European/Other. Māori are more likely to be diagnosed with endometrial cancer at a higher grade and have poorer survival. In 2019, the incidence rate for Māori (27.8 per 100,000 females) was 2.3 times higher than in European/other (13.1 per 100,000 females) ethnic groups, and approximately one-third of endometrial cancer cases diagnosed were Māori, with a total of 71 cases in the year of 2019[2].

[2] National Collections and Reporting, Health New Zealand | Te Whatu Ora

The inequities are, at least in part, the result of institutionalised racism which pervades all of our social structures including health. The Ministry of Health (2019)[3] defines equity as: "In New Zealand, people have differences in health that are avoidable, unfair, and unjust. Equity recognises that people with different levels of advantage require different approaches and resources to achieve equitable health outcomes". Honouring Te Tiriti o Waitangi is paramount when forming any national guideline.

Applying Te Tiriti o Waitangi to this AUB guideline in practice means:

- **Tino rangatiratanga** making wahine Māori central to system design and application which addresses their needs in the most culturally safe way
- **Equity** in governance and leadership, service design, interaction, communication, investigation and the management of abnormal uterine bleeding and endometrial cancer.
- **Active protection** of Māori health concepts and matauranga Māori
- **Providing options** and funding which incorporate and enhance kaupapa Māori services and
- **Partnership** in governance, administration, design, delivery and data collection.

A National Guideline for Abnormal Uterine Bleeding recognises that these statistics are inequitable and attempts to address this by providing an equitable nation-wide approach to implementing a system which is enabling for wahine Māori. The Aotearoa New Zealand Cancer Action Plan 2019–2029 advocates responding to Māori models that are holistic and whānau-centric, addressing racism and discrimination and achieving equity by design (MOH, 2019) [3] and therefore wahine Māori are identified as a priority group which needs to span primary, secondary, tertiary and radiological approaches to meeting these priorities. The guideline group recognises that updates need to continue to address racism, bias and inequities in order to best service our population now and in the future. A continuing connection between stakeholders and wahine Māori is vital to permit this.

[3] Ministry of Health. 2019. Achieving Equity in Health Outcomes: Summary of a discovery process. Wellington: Ministry of Health.

Pacific commentary

Pacific Commentary on the New Zealand National Guidelines on Abnormal Uterine Bleeding

'Pacific peoples' is a collective term used in Aotearoa New Zealand to recognise a diverse group of people from the South Pacific region living in New Zealand, who have migrated from Pacific island nations or identify with them because of ancestry or heritage[4].

There are more than 40 Pacific ethnic groups in New Zealand. The Pacific population is growing and becoming increasingly diverse. Twenty percent of Pacific people identify with more than one ethnic group[5]. 66% are New Zealand-born. Many Pacific peoples identify with values and cultural practices from both their ancestral Pacific Island homelands and contemporary New Zealand.

Despite the diversity of the Pacific population in Aotearoa New Zealand, Pacific peoples share many core cultural values. These include the central place of family, collectivism and communitarianism, the importance of spirituality, reciprocity and respect[5]. The vast majority of Pacific women identify their language, culture and identity as playing a significant role in their lives and wellbeing[4].

Understanding the diversity among Pacific peoples and weaving the core Pacific values into the delivery of health services is fundamental to the ability to have respectful and effective relationships with Pacific Peoples and to enable the delivery of quality health care for Pacific peoples.

Among Pacific women in New Zealand and the broader Pacific region, the burden of AUB is substantial yet remains inadequately documented due to a lack of specific data. This document highlights the need for local, ethnic-specific data on AUB and related diagnoses. This knowledge gap is compounded by a general lack of awareness among both women and health professionals regarding the symptoms of AUB, which can serve as an early indicator of serious conditions such as uterine cancer. The consequences of this knowledge gap are starkly reflected in the disproportionately poor outcomes for Pacific women diagnosed with endometrial cancer.

The disparities in outcomes for Pacific women with endometrial cancer highlight the urgent need for increased awareness and education about AUB for both women and health care providers in order to facilitate earlier symptom recognition, diagnosis and intervention.

Working with our Pacific peoples to enhance education and provide culturally appropriate care models are essential steps toward achieving equity in this area of Women's Health and ensuring that Pacific women receive the timely and effective treatment they deserve.

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[4] A Wellbeing Report Voices from Pacific Women and Girls in Aotearoa, New Zealand (2023). Health and Disability System Review. 2020. Health and Disability System Review – Final Report – Pūrongo Whakamutunga. Wellington: HDSR.

[5] Ministry of Health. 2020. Ola Manuia: Pacific Health and Wellbeing Ac□on Plan 2020-2025. Wellington: Ministry of Health.

Scope

This guideline aims to provide evidence-based assessment and management guidance for the evaluation and treatment of reproductive-aged women with abnormal uterine bleeding.

Detailed guidance for assessment and management of AUB in adolescents [6] is beyond the scope of this guideline.

This document does not address pregnancy-related bleeding or post-menopausal bleeding.

[6] Adolescence is defined by WHO as the period between 10 and 19 years of age (WHO).

Contents

Abbreviations

AEH	Atypical Endometrial Hyperplasia
AUB	Abnormal Uterine Bleeding
COCP	Combined oral contraceptive pill
EC	Endometrioid adenocarcinoma of the endometrium
EH	Endometrial Hyperplasia
EIN	Endometrioid Intraepithelial Neoplasia
FIGO	International Federation of Gynaecology and Obstetrics
HMB	Heavy Menstrual Bleeding
HNPCC	Hereditary non-polyposis colorectal cancer
HrHPV	High risk Human Papilloma Virus
LNG-IUD	Levonorgestrel-Releasing Intrauterine Device
NZ	New Zealand
POP	Progestogen-only pill
PCOS	Polycystic Ovarian Syndrome
WHO	World Health Organisation

Introduction

Abnormal Uterine Bleeding (AUB) presents a substantial global impact, affecting approximately one in three women of reproductive age at some stage. The prevalence of Heavy Menstrual Bleeding (HMB) varies considerably in studies, ranging from 3% to 37% [4]. There are no prevalence studies in Aotearoa, New Zealand, and therefore, we do not know the impact of AUB by age, region, or ethnicity.

Despite its potential to significantly affect the quality of life and lead to severe health outcomes such as iron deficient anaemia or endometrial cancer; there is inequitable access to investigations and management for AUB across Aotearoa, New Zealand. Up to half of affected women do not seek medical care; and for those that do, poor experiences along the continuum from primary healthcare to specialised secondary or tertiary centres are reported [4]. One New Zealand study [5] reported barriers to seeking care such as poor healthcare provider experience, communication and stigmatisation, low gynaecological health literacy and access to information (particularly what a ‘normal’ period is), low prioritisation of one’s health and taboo around menstruation. Women in New Zealand do not experience a linear trajectory to a specialist gynaecological appointment. Rather, they face compounded systemic and personal barriers while navigating the complex nature of AUB.

Definitions and nomenclature

The International Federation of Gynaecology and Obstetrics (FIGO) system of definition of AUB, related terms and classification system for causes of AUB are utilised in this guideline [4, 6].

The use of terms such as menorrhagia, metrorrhagia, oligomenorrhoea, dysfunctional uterine bleeding to describe AUB are no longer recommended.

AUB is defined as bleeding from the uterine corpus that is abnormal in regularity, volume, frequency or duration and occurs in the absence of pregnancy.[6]. The condition may be acute or chronic.

Chronic AUB is AUB that is present for most of the previous six months [6]

Acute AUB refers to an episode of heavy bleeding that, in the opinion of the clinician, is of sufficient quantity to require immediate intervention to prevent further blood loss [6]. Acute AUB may occur in isolation or in the context of chronic AUB. See Appendices

Appendix 1. Management of Acute AUBfor the management of acute AUB.

A menstrual cycle that is considered normal[7] is usually between 24 to 38 days [4]

Abnormality in Frequency

- **Secondary amenorrhoea** is the absence of menstrual bleeding for 180 days or more, in an individual who has had at least one spontaneous menstruation [7].
- **Infrequent menstrual cycles** - bleeding that occurs less frequently than every 38 days.
- **Frequent menstrual cycles** - bleeding that occurs more often than every 24 days.

Abnormality in Regularity

- **Irregular menstrual cycles** are considered menstrual cycles with ≥10 days variation between the longest and the shortest cycles. Menstrual cycles with ≤9 days between the shortest and the longest menstrual cycle are considered regular.

  It is acknowledged that a higher degree of variation in menstrual bleeding patterns can be encountered at each end of the reproductive spectrum (ie in adolescence or the peri- menopause). Depending upon age, the following variation between the longest and shortest cycles are considered normal (18–25 years ≤9 days; 26–41 years ≤7 days; 42–45 years ≤9 days) [4] .

Abnormality in Volume

- **Heavy Menstrual Bleeding (HMB).** The definition of HMB has evolved from a quantitative approach that required a direct measure of blood loss (over 80 ml per cycle) to a qualitative definition. The current definition of HMB is excessive menstrual blood loss which interferes with a woman's physical, social, emotional and or material quality of life [4, 6, 8].

[7] Normal – as defined by the 5th-95th centile from large scale epidemiological studies.

- Light Menstrual bleeding is a patient-determined symptom. It is a rare presenting symptom. In some instances, it may be a symptom of cervical stenosis or intrauterine adhesions.

Others

- **Prolonged menstrual bleeding** is bleeding > 8 days (‘Normal’ ≤ 8 days)
- **Intermenstrual bleeding (IMB**) is spontaneous bleeding occurring between regular menstrual periods. This may be cyclical (predictable) or random.
- **Unscheduled bleeding** is unexpected bleeding while on hormonal medication (progestogen-only or combined oestrogen and progestogen).
- **Post-coital bleeding** refers to spotting or bleeding that occurs after intercourse and is not related to menstruation.
- **Post-menopausal bleeding (PMB)** is defined as bleeding occurring >1 year after the acknowledged menopause. ‘‘The menopause’’ is the last natural menstrual period that a woman will experience and is determined in retrospect following 12 months of amenorrhoea. PMB is abnormal and warrants investigation. The evaluation and management of PMB is beyond the scope of this guideline. PMB is generally grounds for further investigation.

Note some individuals have their abnormal bleeding ‘normalised’ by family, friends and/or health care providers and therefore can consider their abnormal bleeding ‘normal.’ It is therefore important to clarify bleeding symptoms with specific questions regarding regularity, volume, frequency and duration of bleeding.

Direct measurement of blood loss is not routinely possible. Indirect assessments of menstrual volume, such as pictorial blood loss assessment charts, assessment of the number of sanitary protection changes required per day of menstruation, the number of school days or work missed as a result of menstruation, or menstrual symptoms, can also help assess the severity of bleeding and related symptoms.

Women's voice: Screen for AUB

Check menstrual health opportunistically when able. For eg when presenting with unrelated non-specific illness; or with anaemia.

Women support development of primary care clinicians with an interest in Women's Health.

Women support development of a health workforce which understands the health needs of people with different world views.

1. Causes of AUB

FIGO proposed a classification system in 2011 for consistent and standardised categorisation of causes of AUB [6]. There are nine main categories, which are arranged in accordance with the acronym PALM-COEIN: polyp; adenomyosis; leiomyoma; malignancy and hyperplasia; coagulopathy; ovulatory dysfunction; endometrial; iatrogenic; and not yet classified.

The components of the *PALM* group are structural entities that can be identified with imaging modalities and/or histopathology, whereas the *COEIN* group is related to non-structural entities (and not defined by imaging or histopathology) [6] (see Figure 1). An individual may have more than one entity that is contributing to their AUB, or potentially a structural entity that is asymptomatic (eg adenomyosis) and therefore investigation for non-structural entities may also be necessary.

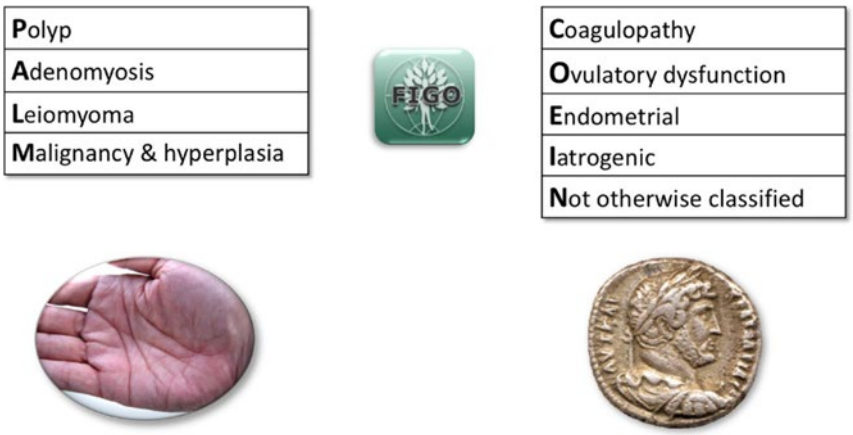

Figure 1: The FIGO Classification system (PALM- COEIN) for cause of abnormal bleeding in non-pregnant women of reproductive age group [6].

In assessing people with AUB, it is crucial that non-uterine causes of vaginal bleeding are excluded. Some of the common causes of non-uterine, lower genital tract bleeding are listed in *Table **3***.

Table 3 Common non-uterine causes of lower genital tract bleeding

- Vulvovaginal atrophy/ atrophic vaginitis
- Vulval dermatoses
- Sexually transmitted infections - eg chlamydia
- Malignancy - cervix, vagina, vulva
- Cervical ectropion
- Urethral causes eg urethral caruncle

1.1 Endometrial polyp.

Endometrial polyps are focal overgrowths of endometrial glands, stroma and vessels that typically protrude into the uterine cavity.

1.2 Adenomyosis.

Adenomyosis is a benign uterine disorder in which endometrial glands and stroma are pathologically demonstrated in the myometrium.

1.3 Leiomyoma.

Leiomyomas, also called myomas or fibroids, are the most common benign gynaecological tumour in premenopausal women. Leiomyomas are comprised of monoclonal cells arising from the myometrium.

1.4 Malignancy and hyperplasia

Endometrial Hyperplasia (EH) is diagnosed histologically in the presence of a proliferation of the endometrial glands resulting in an increase in gland-to-stroma ratio.

The utilisation of 2020 World Health Organization (WHO) Classification System is most widely used for categorising EH. EH is classified into two groups:

- EH without atypia
- EH with atypia (also referred to as atypical endometrial hyperplasia (AEH) and endometrioid intraepithelial neoplasia [EIN]).

EH is a clinically significant diagnosis and is associated with an increased risk of progression to the endometrioid subtype of endometrial carcinoma (EC). There is a risk of concurrent malignancy in those diagnosed with EH with atypia.

All endometrial carcinomas are classified according to the 5th edition of the WHO Classification of Tumours, Female Genital Tumours. Histological tumour type is an important prognostic predictor in endometrial carcinoma. Low-grade endometrioid adenocarcinoma is the most common type of endometrial malignancy.

1.5 Coagulopathy

Coagulopathy is often broadly defined as any derangement of haemostasis resulting in either excessive bleeding or clotting. Coagulation should be assessed in cases of heavy,

prolonged menses from an early reproductive age; history of frequent bruising, epistaxis, gum/dental bleeding, postpartum haemorrhage, and severe surgical bleeding; and a family history of coagulation disorders. Von Willebrand disease is the most common coagulopathy, and 60-100% of women affected will present with AUB [9].

1.6 Ovulatory dysfunction

Ovulatory dysfunction includes not ovulating on a regular basis or infrequently, resulting in irregular bleeding and, less commonly, amenorrhoea. The causes of ovulatory dysfunction may be physiological or pathological and are summarised in *Table 4*.

Table 4 The causes of ovulatory dysfunction. Modified from Management of Abnormal Uterine Bleeding Associated with Ovulatory Dysfunction. ACOG Practice Bulletin 136 Mar 2000.

Physiological	Pathological
• Adolescence • Perimenopause • Lactation • Pregnancy • BMI>30	• Hyperandrogenic anovulation (eg, polycystic ovarian syndrome (PCOS), congenital adrenal hyperplasia or androgen-producing tumours) • Hypothalamic dysfunction • Hyperprolactinaemia • Thyroid disease • Primary pituitary disease • Premature ovarian failure • Iatrogenic (eg radiation or chemotherapy) • Medications

1.7 Endometrial

Endometrial disorders are due to primary dysfunction of local endometrial haemostasis. This includes women with ovulatory cycles where other identifiable causes for bleeding are excluded. Chronic endometritis has also been linked to AUB [10].

1.8 Iatrogenic

The most common iatrogenic causes of AUB are due to hormonal contraceptives. Systemic agents (eg antidepressants) that contribute to disorders of ovulation, such as those that interfere with dopamine metabolism or cause hyperprolactinemia, may also lead to AUB. Anticoagulants (such as warfarin and rivaroxaban) may cause HMB, prolonged menses, and postmenopausal bleeding [11].

1.9 Not otherwise classified

This group of AUB causes is poorly defined, inadequately examined, and in general rare. It includes entities such as arteriovenous malformation, myometrial hypertrophy, and caesarean scar niche [11].

2. Assessment

2.1 History

The history should be tailored to the individual and culturally responsive with consideration given to Meihana [12] and or Fonofale [13] models of history taking where appropriate. Establishing trust with the patient is important, as well as recognising the sensitive nature of presenting symptoms. The history should take into account the possible causes of abnormal uterine bleeding outlined above and other causes of lower genital tract bleeding.

The history and examination will often indicate the cause of AUB and direct the need for further investigations and treatment.

Women's voice: People skills

People matter. A good experience can come down to people skills eg introduce yourself and your role.

It is important to be empathetic, cognisant of women's feelings (eg, anxiety or stress), and aware of their priorities (eg, childbearing).

Avoid making assumptions based on an individual's cultural identity

The following should be considered when obtaining a history:

a) The duration of symptoms, regularity and frequency of menstrual cycles and volume and duration of bleeding
b) Sexual and reproductive health, possibility of pregnancy, desire for fertility and/ or contraception and cervical screening history
c) Impact of symptoms on activities of daily living and quality of life
d) Associated symptoms such as pelvic pain, and infertility
e) Symptoms associated with systemic causes such as PCOS (hirsutism, acne), other endocrine conditions (such as hypothyroidism and hyperprolactinaemia) or coagulation disorders
f) Risk factors for endometrial cancer (see *Table 5*).

Māori and Pacific peoples are disproportionately affected by endometrial cancer.

According to a recently published New Zealand study, Pacific people have a relative risk of EC of 5.11 and Māori 2.47 compared to other ethnicities [11]. The incidence of endometrial cancer is highest in Pacific people and the rates are rising particularly in women under the age of 50. Ethnicity should, therefore, be taken into account when considering investigations in women who present with AUB.

Table 5 Risk factors for endometrial hyperplasia (EH) and endometrioid adenocarcinoma (EC)

Risk factor	Risk
• **Obesity** (BMI > 30) The risk is directly proportional to the BMI Data from NZ indicates this is the main risk factor in premenopausal women for developing EH and EC [14]	Odds Ratio (OR) 4 for EH or Cancer [14, 15] • BMI 30–39.9, RR 2.18 (1.29–3.67) [16] • BMI 40–49.9, RR 3.81 (2.18–6.68) [16] • BMI ≥50, RR 7.82 (4.34–14.08) [16]
• **Diabetes Mellitus**	RR 1.97 (95%CI 1.71-2.27) [17, 18]
• **Polycystic ovulation (PCOS) and/or Chronic anovulation** (usually presenting with infrequent bleeding, less than 4 episodes of menstrual bleeding in 12 months)	Lifetime three-fold risk of EH and 9% lifetime risk of cancer [19]
• **Anaemia**	OR 2.38 (95%CI 1.25-4.56) for EH or Cancer [14]
• **Nulliparity** More relevant for women over 35 years	3.08 for EH or Cancer [14]
• Increasing age (peak incidence 45-50 years old in pre-menopausal women) [17] • Unopposed oestrogen therapy • Tamoxifen therapy (see special circumstances on page 34) • Early Menarche (variably defined in literature as <10-12 years old)[20] • Late menopause (after age 55) • Oestrogen-secreting tumour • Hereditary non-polyposis colorectal cancer (HNPCC), also known as Lynch Syndrome • Cowden Syndrome hereditary condition characterised by PTEN mutation. Clinically presenting with mucocutaneous lesions with a strong personal or family history of thyroid, breast, endometrial, and colorectal cancer) • Family history of endometrial, ovarian, breast or bowel cancer	

The most relevant risk factors for premenopausal women aged under 35 are high BMI, PCOS and diabetes.

All women with AUB and a known genetic predisposition to endometrial cancer (HNPCC or Cowden syndrome) should be referred to secondary care for assessment and management.

Recommendation

Investigations to exclude EH or EC should be considered at, or soon after, the initial presentation for all Māori and Pacific peoples	GPP

Women's voice: Access

Offer community clinics at varying times (eg After school or work) where possible, with easy access to parking.

Some women prefer being assessed and treated by a female clinician for gynaecological conditions.

2.2 Examination

The examination needs to be done in a culturally responsive manner, acknowledging the sensitive nature of the gynaecological examination. Care must be taken to understand patients' context, establish trust, obtain appropriate informed consent and offer a chaperone.

General

Check for pallor, pulse, BP, BMI, signs of androgen excess (eg, hirsutism, acne), metabolic syndrome and other endocrine diseases such as thyroid disease.

Abdominal and Gynaecological exam

- Palpate the abdomen for masses
- Exclude other causes for bleeding by inspection (vulva, vaginal, cervix and urethra).
- Perform speculum examination*, visualise the cervix, collect liquid-based cytology and high-risk HPV screen (if not performed in the last 6 months) and take swabs for STIs if appropriate.
- Perform bimanual examination *.

*These examinations might be conducted at the initial or subsequent visit; in some cases (such as women who have never been sexually active or with pelvic floor muscle hyperactivity), a secondary care referral may be required for an examination under anaesthesia.

Note: Those with severe acute bleeding, severe anaemia or evidence of hemodynamic instability should be referred to secondary care for acute assessment. See Appendices

Appendix 1. Management of Acute AUBfor assessment and management of acute AUB.

2.3 Investigations

Managing acute AUB and anaemia should not be delayed while investigations are pending.

The following investigations should be considered in women who present with AUB.

2.3.1 Urine and blood tests

- CBC, Ferritin
- Urine bHCG if appropriate
- Other investigations as clinically indicated such as:
    - Testosterone if signs or symptoms of hyperandrogenism or anovulation
    - HbA1c if risk factors present for diabetes
    - TSH if signs or symptoms of thyroid disease
    - Coagulation screen if suspected coagulopathy

2.3.2 Imaging

- **Ultrasound scan (USS)**

Abdominal and transvaginal (TV) USS is a useful investigation to characterise structural causes of AUB. The optimal time for an ultrasound scan to evaluate the endometrium is within the first 10 days of the menstrual cycle, when endometrial thickness (ET) should be at its thinnest. In practice, this may not be achievable due to a history of AUB and the practicality of being able to schedule ultrasound scans based on menstrual cycles.

In pre-menopausal women, the ET is dynamic, varying at different stages of the menstrual cycle as summarised on Table 6 [21-23]. In premenopausal women with or without AUB, an optimal cut-off for 'normal' ET has not yet been established. **Therefore, the routine use of ET alone is not recommended to confirm suspicions of endometrial malignancy or hyperplasia** [24].

USS findings of heterogeneous, hypervascularised and or cystic endometrium are suggestive of possible endometrial pathology.

Table 6 ET at different stages of the menstrual cycle [21-23]

- During menstruation: 2-4 mm
- Early proliferative phase (day 6-14): 5-7 mm
- Late proliferative/preovulatory phase: up to 11 mm
- Secretory phase: 7-16 mm

These measurements are a guide only, as endometrial thickness may be variable from individual to individual.

Indications for imaging with TVUSS

1. History or examination suggests structural cause for bleeding
2. Conservative management has failed
3. There is a risk of malignancy
    a. Recommended in all women > 45
    b. Women <45 with risk factor(s) (See *Table 5*).

Recommendations

Imaging by a TVUSS should be considered for all women who present with AUB aged over 45, or under 45 with risk factors for EH or EC (see *Table 5*) as part of the initial investigation	GPP
Imaging by TV-USS is recommended for women with AUB with no risk factors who have not responded to first-line treatment within 3-6 months	GPP
USS is recommended when a structural abnormality (such as fibroid or polyp) is suspected on history or examination.	GPP

Other imaging modalities

CT abdomen and pelvis and/or MRI abdomen and pelvis are usually not indicated as part of the initial investigations for AUB.

Management of asymptomatic women with incidental findings of structural abnormalities is summarised in Appendix 2. Incidental finding of endometrial pathology on imaging on people who are not symptomatic

2.4 Aspiration Endometrial Sampling:

Women's voice: Invasive procedures

Women may need time to consider the information provided and prepare for invasive procedures such as a pelvic exam or endometrial sampling.

Offer for a support person to be present (or chaperone).

If available, consider exploring women's preferences for the gender of the practitioner for the procedures and or pelvic examination

Consider providing a longer appointment or a follow-up appointment for investigations or procedures (such as endometrial sampling).

Aspiration endometrial sampling (such as a Pipelle) is an office-based procedure that samples the endometrium to allow for direct histological evaluation [25].

Ideally, endometrial sampling is obtained prior to the commencement of hormonal treatment as part of the initial investigation in primary care, as treatment effects on the endometrium can impact histological assessment and diagnosis. This is not always possible.

Aspiration endometrial sampling has high sensitivity for detecting premalignant and malignant intrauterine pathologies [26]. According to a recently published systematic review including 12 studies and over 1600 participants, the sensitivity of endometrial sampling compared to final histopathology is 0.774 (95% CI 0.56 to 0.90), and the specificity is 0.98 (95% CI 0.93 to 0.997)[27].

2.4.1 Indications for endometrial sampling.

Women aged 19 and under

The commonest cause for AUB in young women are anovulatory cycles. The incidence of EC in adolescence is extremely rare and has only been reported in case studies.

Women under the age of 30

EC is uncommon in women under the age of 30.

The majority of women under the age of 30 are *un*likely to require sampling of the endometrium at the initial consultation for AUB. The decision to perform endometrial sampling should be individualised based on imaging and risk factors. Endometrial sampling (ie Pipelle) at first presentation should be considered for those who have had long-standing unopposed oestrogen stimulation and or those who have multiple risk factors for EH or EC.

Women between the ages of 30 and 45

Endometrial sampling is recommended for women who present with AUB with risk factor(s) in this age group.

Women over the age of 45 until menopause

The majority of AUB in this age group is physiological, relating to menopausal transition. It cannot however be assumed and therefore., endometrial sampling is recommended in all women who present with AUB over the age of 45, particularly in the presence of risk factors.

Recommendations

Women aged 19 and under Endometrial sampling is not routinely recommended for women who present with AUB in this age group. An individualised approach should be taken for assessment and if endometrial sampling is considered, a referral to secondary care is indicated. **Women between the ages of 20 and 30** The decision to perform endometrial sampling should be individualised in women under the age of 30 based on imaging and risk factors. Endometrial sampling should be considered at, or soon after, the initial presentation in those who have had long-standing unopposed oestrogen stimulation and or those who have multiple risk factors for EH or EC. **Women between the ages of 30 and 45** Endometrial sampling is recommended for women who present with AUB and have risk factor(s) for EH or EC. **Women over the age of 45 until menopause** Endometrial sampling is recommended in all women who present with AUB over the age of 45 particularly in the presence of risk factors.	GPP
If an endometrial sample is unable to be performed or the sample is considered inadequate for histopathological assessment referral to secondary care is indicated.	GPP

Aspiration endometrial sampling (Pipelle) where indicated should ideally be performed in primary care as it will reduce delays in investigation and treatment.	GPP

2.5 Hysteroscopy

Hysteroscopy with targeted biopsy has the highest diagnostic accuracy. Office hysteroscopy is considered the international gold standard for investigations of endometrial causes for AUB and is performed in a secondary care setting [26].

In settings without the capacity to perform office hysteroscopy, aspiration endometrial sampling (Pipelle) may be used for endometrial assessment [26].

Recommendations

Hysteroscopy with directed endometrial sampling is recommended for those with structural endometrial pathology on ultrasound scans. These include: • Endometrial polyps or thickness ≥ 16 mm • Hypervascularised/heterogenous endometrium • Endometrium with cystic spaces • Symptomatic submucosal fibroid(s) not responsive to medical treatment Endometrial sample (Pipelle) is recommended if a delay in hysteroscopy is expected.	GPP

Women's voice: Information on what to expect and avoiding multiple appointments

Provide verbal and written information on anticipated procedures or investigations at initial appointment (example- warn about possibility of pelvic exam at specialist appointment, aspiration endometrial sampling, transvaginal ultrasound scan)

Provide verbal information during the procedure (example- explanation around equipment such as transvaginal probe)

Avoid the need for multiple appointments if able (eg rapid access clinics where multiple investigations or appointments may be completed in one visit)

3. Management

Detailed management of each individual cause of AUB is beyond the scope of this guideline.

This section is intended to provide guidance on the management of AUB in primary care and a brief overview of potential management in secondary care settings.

Conditions causing abnormal bleeding and structural abnormalities can commonly co-exist.

The goals of management of AUB are to:

- Improve quality of life
- Provide timely care in the community and timely escalation to secondary care where indicated
- Correct underlying primary cause if present and feasible
- Prevent acute uterine bleeding
- Prevent and or treat anaemia related to AUB
- Establish a regular bleeding pattern or amenorrhoea, considering patient preference
- Prevent and early detection of EH/EC

Treatment for AUB is individualised. When determining the best treatment option for an individual patient, consider the cause, associated symptoms and other gynaecological issues (eg, pain, infertility), presence of risk factors for endometrial hyperplasia and carcinoma, contraceptive needs, medical comorbidities, and patient preference.

Management should include education about lifestyle and nutritional factors which may contribute to menstrual abnormalities and other associated diseases (eg PCOS, diabetes, BMI >30).

Women's voice: Appointments and what to expect

Provided information on what may be expected at a specialist appointment - this may be provided via a link when the appointment is scheduled, verbally via a phone call or written (pamphlet, check the patient is able to read the language in which the pamphlet is written).

Patient appointment letters should acknowledge all upcoming appointments in order, including the newly made appointment, with clarity about what each appointment is for. This may prevent unintentional non-attendance for patients; and they are able to come better prepared and informed about the purpose of their appointment.

3.1 No structural causes for symptoms and no risk factors for endometrial pathology

The treatment should be decided considering the severity of the symptoms, past medical history (including previous treatment failure), age, the desire for pregnancy (current or future) and menstrual cycle preference (monthly, longer interval or amenorrhoea).

Heavy Menstrual Bleeding

Table 7 Summary of treatments for HMB

Pharmacological (1st line)	Surgical (Usually 2nd line)
Non-hormonal 1. Non-Steroidal Anti-inflammatory Drugs (NSAIDs) such as naproxen and mefenamic acid. 2. Antifibrinolytics (such as tranexamic acid) **Hormonal** 1. Levonorgestrel-releasing intrauterine device (LNG-IUD (Mirena®)) 2. Combined hormonal contraceptives 3. Oral progestogens (21 days per cycle or continuous) 4. Injected progestogens (off-label)	**Endometrial ablation** A minimally invasive procedure in which the endometrium is removed or destroyed. It could be done as an outpatient or under general anaesthesia. **Hysterectomy** Abdominal, vaginal or laparoscopically-robotic assisted (by the least invasive method possible).

See Appendix 3.

First line treatment for HMBfor details of treatments for HMB (women without structural causes for symptoms and no risk factors for endometrial pathology), including efficacy, patient satisfaction and associated benefits such as provision of contraception.

Intermenstrual bleeding may suggest cervical causes or the presence of an endometrial polyp. Gynaecological examination and TVUSS should be considered and managed based on findings of clinical assessment and imaging. If there is no structural cause, consider hormonal management according to Table 7.

Infrequent bleeding (previously known as oligomenorrhoea) should prompt assessment for anovulatory causes and managed accordingly.

Recommendation

Referral to secondary care should be considered in all women who do not respond to medical therapy after 3 to 6 months of treatment.	GPP

3.2 Women with risk factors for endometrial cancer or hyperplasia (with or without structural abnormalities)

Uterine cancer[8] is the most common gynaecological cancer in Aotearoa. In 2019, 686 uterine cancers were registered in Aotearoa, with an incidence of 18.4 per 100,000 women [28]. The peak incidence is in women aged between 45-64 [28]. In 2019, 9.5% of women who had endometrial cancer were under the age of 45 [28].

The rate of EC is increasing globally, and these trends are reflected in Aotearoa. Data from Counties Manukau between 2000 to 2014 indicate that the increase was most marked in women below the age of 50 (annual percental change [APC] of 12.2; 95% CI 5.2–19.7). Pacific women had the highest rate of rise in EC incidence [29]. This trend is noticeable in clinical practice, where an increasing number of EH and EC diagnoses are being made in women of reproductive age group.

There is no published national data reporting the incidence of EH. A large retrospective cohort study at Te Toka Tumai, Health New Zealand | Te Whatu Ora (previously Auckland District Health Board) reported a 4.9% incidence of EH (complex, with or without atypia) or EC in premenopausal women with AUB who underwent endometrial biopsy [14].

All women with risk factors for developing EH or EC should be counselled regarding the risk. The risk of developing EH or EC may be prevented by management of risk factors as well as hormonal treatment to reduce unopposed oestrogen exposure to the endometrium (See Table 7).

Management should include education about lifestyle and nutritional factors that may contribute to ongoing menstrual abnormalities and other associated diseases.

Recommendations

Women with risk factors for developing EH or EC should be counselled regarding the risk and its associated implications in a culturally appropriate manner.	GPP
The risk of developing EH or EC may be reduced by management of risk factors as well as hormonal treatment to reduce unopposed oestrogen exposure to the endometrium.	GPP
Management should include education about lifestyle and nutritional factors which may contribute to risk factors, ongoing menstrual abnormalities and other associated diseases.	GPP

[8] Uterine cancer is the term used for all cancers arising from the uterus in the NZ cancer registry. The commonest form of uterine cancer is low-grade endometrioid adenocarcinoma.

3.3 Women with structural abnormalities

3.3.1 Polyps

Polyps may be asymptomatic, cause abnormal uterine bleeding and may be associated with infertility [30].

The prevalence of polyps in the general population without AUB is estimated to be 10-15% [31]. In women with AUB, the prevalence of endometrial polyps is considered to be between 20 and 30% [31]. Up to 25% of women with cervical polyps have a coexisting endometrial polyp [32]; thus, endometrial assessment by TV-USS should be considered in women where a polyp appears to be arising from the endometrium or endocervical canal on examination.

The estimated prevalence of premalignant and malignant lesions in patients with endometrial polyps is estimated about 1% in premenopausal women [33]. The risk is higher in the presence of abnormal uterine bleeding [33]. The risk of malignancy may be higher in those with additional risk factors for EH or EC (as per *Table 5*). Hysteroscopy and polypectomy with histopathological analysis of the specimen is the recommended investigation and treatment for women who present with AUB in whom an endometrial polyp has been detected. Hormonal treatment for endometrial protection is recommended for women who have AUB with ongoing risk factors for EH or EC following polypectomy. [31, 33]

Recommendations

Polypectomy with direct visualisation (hysteroscopy) and histopathological analysis of the specimen is recommended for women who present with AUB in whom an endometrial polyp has been detected.	Strong [34]
Hormonal treatment for endometrial protection is recommended for women who have AUB with ongoing risk factors for endometrial pathology following polypectomy.	GPP

3.3.2 Fibroids

Fibroids are also known as myomas or leiomyomas. They are common, affecting ≥ 70% of women [6, 35, 36]. There is no local data on incidence in Aotearoa. An estimated 30% of patients with fibroids may experience symptoms [35] which can include AUB, pelvic pain, and bulk symptoms related to the bladder or rectum (ie pelvic pressure, obstructive symptoms, increased urinary frequency) and fertility issues.

Symptoms caused by fibroids vary depending on the size, location and number of fibroids. The effectiveness of pharmacological treatments for symptom control may be limited in women with very large fibroids (not clearly defined in the literature). Referral to secondary care simultaneously as commencing initial treatment is appropriate in women with very large fibroids.

Treatment of women with fibroids must be individualised, taking into account symptoms, size, location of fibroids, age, and desire for fertility.

Conservative treatments

Small fibroids that are not causing significant distortion of the uterine cavity may be treated with pharmacological methods, including an LNG-IUD (Mirena ®), as summarised in Table 7.

If symptoms do not resolve with medical treatment, referral to secondary care is indicated for ongoing management.

Recommendations

AUB related to small fibroids may be treated with pharmacological methods, including an LNG-IUD (Mirena ®) as summarised in section 5	GPP
If symptoms do not resolve with medical treatment within 3 to 6 months, referral to secondary care is indicated for ongoing management.	GPP
The effectiveness of pharmacological treatments for symptom control may be limited in women with large fibroids. Referral to secondary care simultaneously as commencing initial treatment is appropriate in women with large fibroids.	GPP

- **Uterine artery embolisation (UAE)**

UAE is an effective treatment for the management of symptomatic fibroids in appropriately selected candidates. The treatment is performed by an interventional radiologist in women who wish to preserve their uterus and or fertility. The procedure involves delivery of an embolic agent through catheterisation of both uterine arteries, usually through a single incision, to cause fibroid devascularisation and involution [35, 37].

- **Gonadotropin-Releasing Hormone (GnRH) analogues**

GnRH analogues include both agonists and antagonists.

GnRH agonists (GNRHa) have been demonstrated to decrease menstrual bleeding, correct anaemia, and reduce fibroid volume [36]. The most commonly used GnRHa in Aotearoa is Goserelin (Zoladex®). These medications are used for fibroid management in secondary care setting.

Adjuvant therapy with GnRHa before surgical treatment is associated with significant improvement in both preoperative and postoperative haemoglobin; and intraoperative blood loss [36].

GnRHa are associated with significant side effects. Most of these effects are related to low oestrogen and include vasomotor symptoms, insomnia, urogenital atrophy, decreased libido, depression, arthralgia, fatigue, decreased skin elasticity, and breakthrough bleeding. There is also a risk of bone mineral density loss [36]. Due to the side effects and risks associated with prolonged therapy, treatment duration is generally (not always) limited to 6 months

- **Other** [35, 37]

Magnetic Resonance Guided Focused Ultrasound Surgery (MRgFUS) or High Intensity Focused Ultrasound (HIFU) is a newer non-invasive technique that uses focused high-energy ultrasound to ablate fibroid tissue. Other ablative techniques for the treatment of symptomatic uterine fibroids have been described and include cryomyolysis, percutaneous microwave ablation, radiofrequency ablation and laser ablation. These techniques are not

currently available in Aotearoa. Limited evidence exists on the safety and effectiveness of these techniques currently.

Surgical treatment

- **Myomectomy**

Surgical removal of fibroids is an option for women who wish to preserve their uterus and/or fertility. There is a risk of bleeding, risk of recurrence of fibroids, possible risk of hysterectomy at the time of myomectomy and a risk of hysterectomy in the future.

Hysteroscopic myomectomy is recommended for the management of all symptomatic submucosal fibroids [38]. There is a risk of incomplete resection with increasing size of the submucosal fibroids. The International Society for Gynaecologic Endoscopy has recently published a detailed guideline on hysteroscopic myomectomy [38].

Myomectomy by the least invasive surgical approach possible is recommended.

- **Hysterectomy**

Hysterectomy is the most effective and definitive treatment for symptomatic fibroids. Hysterectomy by the least invasive surgical approach possible is recommended.

Correction of pre-operative anaemia and treatment with pharmacological agents (such as GnRHa) to assist with a reduction in fibroid volume may be considered prior to surgical treatment (hysterectomy or myomectomy) [39, 40]

3.3.3 Adenomyosis

The epidemiology of adenomyosis is uncertain because data regarding adenomyosis have often relied on the assessment of the uterus following hysterectomy; estimates of the prevalence of adenomyosis vary from 5 to 70% [6].There is no local data on incidence in Aotearoa. This condition can co-exist with endometriosis.

The most common symptoms are heavy menstrual bleeding and dysmenorrhea. Pharmacological treatment (as summarised in Table 7) is usually the first choice of treatment. If symptoms do not resolve with pharmacological treatment, referral to secondary care is recommended for ongoing management.

3.3.4 AVM

Uterine Arteriovenous Malformations (AVMs) are a rare cause of AUB. They are usually an acquired condition, after uterine surgery or pregnancy, but may be congenital.

The exact incidence of uterine AVM is unknown, but has been reported to be up to 0.63% after birth or evacuation of products of conception [41].

Women with uterine AVMs commonly present with heavy or irregular vaginal bleeding- the bleeding can be life-threatening with hemodynamic instability. Initial management consists of hemodynamic stabilisation with intrauterine tamponade (eg, with a balloon or packing material) followed by uterine artery embolisation and or emergency hysterectomy. Uterine artery embolisation (UAE) is often considered a first-line uterine-sparing treatment for symptomatic uterine AVMs. A recently published systematic review has reported reasonable (88%) success rates with medical management of symptomatic uterine AVM in carefully

selected hemodynamically stable patients [42]. Several treatment regimens were described - progestogens and GnRH-a have been studied in the greatest number of patients.

3.3.5 Caesarean Scar Niche

Caesarean scar Niche (also known as CS scar defect, an isthmocele, or diverticulum) is a pouch-like defect in the anterior uterine isthmus. It occurs as a complication of a previous caesarean section. The exact prevalence of this condition is unclear [43].

This is a more recently recognised entity that has been associated with abnormal uterine bleeding. This condition has also been associated with pain, secondary infertility, caesarean scar ectopic and abnormal placental implantation [1].

Caesarean scar niche is not a common cause of AUB, and not all women with this finding will be symptomatic. In asymptomatic women who are not planning a pregnancy, intervention is not required.

It is reasonable to consider pharmacological treatment for the initial management of symptoms in women who do not wish to get pregnant. Surgical resection via operative hysteroscopy, vaginal surgery, laparotomy/laparoscopy, or a combined approach has been described [1-3].There is a lack of evidence with regard to the role of surgical treatment with view to improving fertility or reducing obstetric risks in women [3].

3.4. Special circumstances: Women on tamoxifen

Tamoxifen is a selective oestrogen receptor modulator. It is widely used as an adjunctive therapy for women with breast cancer. The mechanism of action is complex and includes anti-estrogenic activity in the breast and estrogenic effects in other tissues, including the endometrium.

Tamoxifen use is associated with increased risk of endometrial polyps, endometrial hyperplasia, endometrial cancer and uterine sarcomas [44, 45]. The risks of developing uterine pathology and malignancy are thought to be greater in postmenopausal women compared to pre-menopausal women.

Recommendation

Women who present with AUB in the context of Tamoxifen use should be investigated for uterine and endometrial pathology; including transvaginal USS and endometrial sampling with referral for hysteroscopy where focal endometrial lesions have been identified on imaging.	GPP

Non-hormonal treatment is recommended as first-line management for women with AUB in the context of tamoxifen use for breast cancer. LNG-IUD (Mirena ®) is considered the most appropriate second-line method, which can be used in consultation with the oncologist (or physician in charge of breast care). The LNG-IUD (Mirena ®) is likely to be more effective in symptom control compared with oral non-hormonal methods.

There is a theoretical risk of breast cancer recurrence with hormonal contraceptive use in women with a history of breast cancer; the association between hormonal contraceptive use and breast cancer recurrence in breast cancer survivors has not been well studied. There is no clear evidence from available evidence that the LNG-IUD (Mirena ®) affects the risk of breast cancer recurrence or breast cancer-related deaths [46].

3.5 Special circumstances: Women with abnormal bleeding and a history of previous endometrial ablation

Recurrence of uterine bleeding after endometrial ablation is not uncommon.

Studies suggest that the majority of bleeding recurrences after ablation occur within three years of the primary procedure [47]. Recurrence of normal bleeding in the low-risk, pre-menopausal patient, which is clearly cyclical, does not require additional assessment.

Destruction of the basal layer of the endometrium due to the ablative treatment can impair ultrasound assessment of endometrial thickness. However, studies have reported measurable endometrium in 70% of cases of abnormal bleeding after endometrial ablation [48].

Endometrial sampling and hysteroscopy may also be more challenging due to the presence of intrauterine adhesions; however, a recent systematic review reports 89% success in endometrial sampling despite prior ablation [49]. The risk of failed sampling, creation of false passage during dilatation and uterine perforation must be considered higher than in patients without prior ablation, and pre-operative counselling should include a full discussion of these risks. Consider cervical priming with sublingual misoprostol prior to procedure to reduce cervical resistance and reduce the need for mechanical cervical dilatation [50].

3.6 Women with abnormal histology following endometrial sampling for AUB

Women's voice: Follow up care and ongoing care

Provide continuity of care where possible

Provide follow up even when results are normal

Abnormal results are better relayed via face to face consultation. Offer longer appointments and a family friendly space for discussion of abnormal results.

Provide a safe environment for information sharing, questions and support when discussing treatment. Offer a family –oriented and family friendly space.

Check understanding and clarify uncertainty regarding treatment options. Joint decision making in the treatment process is important.

Offer follow up

Consumers find it useful to choose how they get follow up (eg in writing, by phone or in-person)

Suggest how consumer may be able to re-present to secondary care without repeated GP visits if required

Acknowledge alternative medicines such Rongoā Māori, acupuncture, spiritual healing.

3.6.1 Chronic endometritis

Chronic endometritis is characterised by plasma cell infiltration into the endometrial stromal area [10]. Histopathological reporting may indicate chronic endometritis in those undergoing endometrial sampling for AUB.

This is a non-specific finding and may be present in the absence of AUB. There is limited high-quality evidence on the management of this condition. Empiric antibiotic treatment may improve symptoms in some patients who present with AUB. Treatment with Doxycycline 100mg bd for 10-14 days has been suggested as first-line treatment [10, 51].

3.6.2 Disordered proliferative endometrium

Disordered proliferative endometrium is the presence of irregularly shaped dilated glands with relatively normal gland to stroma ratio.

This is not a precancerous condition but is present in the continuum of changes seen with persistent unopposed oestrogen stimulation, which can lead to EH without atypia. This may be a physiological finding in women who are perimenopausal (experiencing anovulatory cycles in the perimenopause) or suggestive of chronic anovulation in women who are not in the perimenopause (for eg in young women with PCOS and resultant anovulatory cycles).

In young women explore possibility of anovulation and manage any risk factors or causes of anovulation. Perimenopausal women with this histopathological report can generally be reassured.

3.6.3 EH without atypia

EH without atypia is a diffuse proliferation of endometrial glands of irregular size and shape with increased gland to stroma ratio, but without significant cytological atypia. [52].

Women with a diagnosis of EH without atypia have a low risk (<5%) of concurrent or subsequent endometrioid adenocarcinoma ([53, 54].

Management of this condition should be guided by the individual's desire for fertility, contraceptive needs and individual risk assessment for endometrial malignancy.

Risk factors for EC should be considered and addressed with active management of modifiable risk factors.

Treatment of EH without atypia

See *Figure 2* for a summary of management.

Progestogen therapy

Progestogen therapy is effective in treatment of EH without atypia. The choice of medical treatment should consider compliance, side effects, and patient preference.

Treatment is recommended for a minimum of 12 months with:

1. LNG-IUD (Mirena ®) 52 mg; or
2. Continuous oral progestogen

Low dose oral progestogen: MPA (Provera®) 30mg daily, as a single or divided dose (initial management)

High dose oral progestogen is **not** first line treatment in this setting. There is limited evidence of use of high dose oral progestogen in women diagnosed EH without atypia.

Notes on progestogen options for treatment of EH without atypia

LNG-IUD (Mirena®) is considered the first-line treatment for women in this setting. It may be associated with a higher treatment efficacy compared to oral progestogen therapy [55-57]. IUDs have the added benefit of offering long-acting contraception, reduced systemic side effects and ensures perfect compliance.

Oral progestogens are an acceptable alternative for the treatment of EH without atypia for those who decline treatment with an IUD, where IUD insertion is difficult or in the setting of repetitive IUD expulsions.

Standard doses and or types of oral progestogens have not been well studied in this patient group. Continuous oral progestogen treatment is preferred over a cyclical regimen.

For patients who require non-contraceptive oral progestogens

1. MPA (Provera®) 30mg daily, as a single or divided dose
2. Norethisterone is less well studied compared to MPA, but 5-15mg daily may be effective
3. Micronised progesterone is not well studied in this setting and is not a recommended treatment
4. High-dose oral MPA use has been described in this setting (usually not first-line treatment)

For patients who require contraception

1. Combined oral contraceptive pill (COCP) have not been studied for the treatment of EH, but in theory, can be used for treatment for those with no contraindications for COCP use
2. Progestogen-only pill (POP) Noriday, Cerazette and other POPs are not well studied in this setting

Other preparations

Progestogen injections and implants have not been well studied for the treatment of EH and are not typically used as first-line treatment for EH.

These may be considered in women who are not tolerant of oral treatment and do not find an LNG-IUD (Mirena®) 52mg a suitable method of treatment

Surgical therapy

Surgical therapy by means of hysterectomy is not considered first-line treatment in this setting.

Hysterectomy, bilateral salpingectomy with individualised consideration given to oophorectomy may be considered in certain circumstances with multidisciplinary input where required (examples: history of breast cancer, family complete, patient preference to avoid hormonal treatment and preference over observation and surveillance for surgical treatment; abnormal bleeding not controlled with medical treatment).

Surveillance

For patients with a diagnosis of EH without atypia who are being treated with progestogen, follow-up endometrial sampling is recommended at 6 and 12 months after diagnosis and/ treatment initiation.

Response is defined as adequate endometrial sample negative for hyperplasia with or without atypia or malignancy within 12 months of initiating treatment.

An adequate aspiration endometrial sample (Pipelle) is suitable for follow-up sampling. Hysteroscopy and directed sampling or dilation and curettage is recommended if:

- Aspiration sampling is not successful or considered insufficient for histopathological diagnosis
- Symptoms persist despite medical treatment

Response to treatment within 12 months

Once response to treatment has been confirmed (2 consecutive adequate endometrial samples, 6 months apart, negative for EH with or without atypia; with no evidence of malignancy), ongoing treatment is based on desire for fertility and ongoing risk factors for progression to malignancy.

If risk factors for EC are ongoing, then treatment with progestogen is recommended.

Annual sampling may be considered in those who have ongoing risk factors for endometrial pathology and choose not to be treated with progestogen.

Repeat endometrial sampling is recommended in women who have abnormal bleeding despite treatment with progestogen.

Those with no risk factors for EC may be discharged with advice for medical review if symptoms return.

Non-response to treatment

If persistent EH without atypia at six months despite treatment, consider an increase in the dose of oral progestogen or an additional form of progestogen therapy. There is limited evidence for using a high dose of oral MPA (Provera®) in this setting. An LNG-IUD (Mirena ®) is recommended if possible. Address modifiable risk factors and resample at 12 months.

If persistent EH without atypia following 12 months of treatment discuss definitive treatment with hysterectomy, bilateral salpingectomy with individualised consideration given to oophorectomy. If definitive treatment is not possible, or declined by the patient, ongoing high dose progestogen therapy may be considered. Patients should be counselled about the risks and benefits of continuing with non-definitive treatment; as well as the lack of evidence to guide management in this situation.

In women who are strongly motivated to preserve fertility and accepting the risk of progression to EH with atypia or malignancy, address modifiable risk factors (such as weight and diabetes control).

If EH with atypia is identified in follow up sampling- an urgent referral to secondary care services is indicated.

If endometrial malignancy is identified in follow up sampling- an urgent referral to secondary care is indicated and the patient should then be referred to the regional gynaecological-oncology multidisciplinary team.

Recommendations

Women with EH without atypia may be managed in primary care by primary care physician with a low threshold for referral to secondary care.	GPP

Where management in primary care is not possible, women with EH without atypia should be referred to secondary care. If managed in primary care and there is no clinical response to treatment at 3 months or no histological response at 12 months referral to secondary care is recommended.	
Pharmacological treatment is recommended for women with EH without atypia for a minimum of 12 months. [57, 58] with follow-up endometrial sampling at 6 and 12 months. First-line treatment are (1) LNG-IUD (Mirena®) 52 mg; OR (2) Continuous oral progestogen* *Low-dose oral progestogen: Medroxyprogesterone acetate (MPA) (Provera®) 30mg daily, as a single or divided dose.	Strong
Surgical treatment is not considered first-line treatment for EH without atypia in premenopausal women	GPP

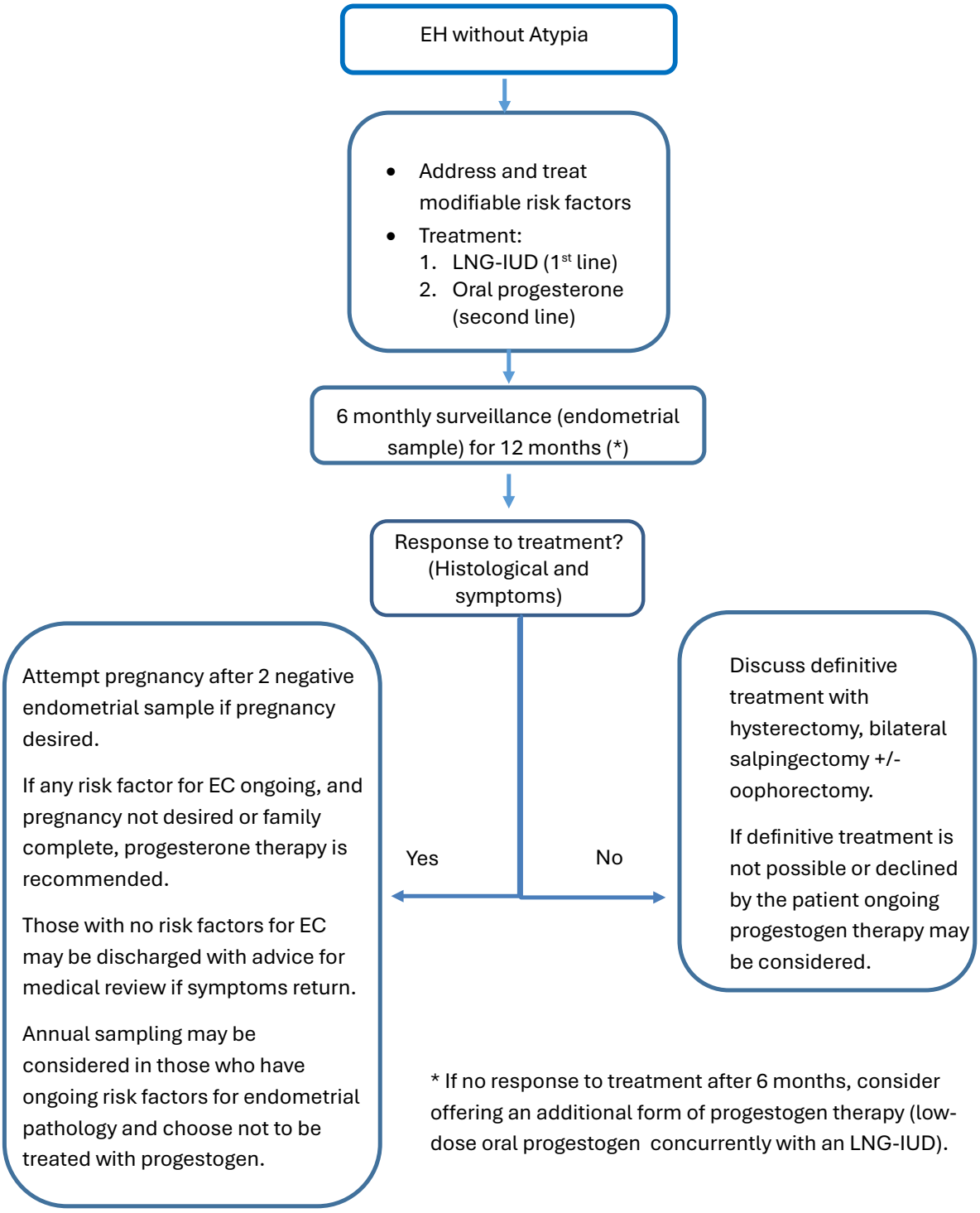

Figure 2 Management of EH without atypia.

3.7 EH with atypia/atypical endometrial hyperplasia/endometrioid intraepithelial neoplasia

EH with atypia/AEH/EIN is characterized by crowded glands lined by cytologically altered cells with reduced intervening stroma, and typically seen as a discrete expansile focus that is distinct from the surrounding endometrium.

Women with a diagnosis of EH with atypia have a high (≥ 20%) risk of concurrent or subsequent endometrioid adenocarcinoma [53, 54]. Those with a diagnosis of EH with atypia should be referred urgently to secondary gynaecology services.

There is a risk of co-existing endometrial cancer in those diagnosed with EH with atypia on endometrial sampling (32.6%; 95% CI: 24.1%, 42.4%) [54]. The rate of progression to endometrial cancer in those with EH with atypia is 82.3 per 1,000 person-years (95% CI 39.3, 172.6), equivalent to 8.2% per year [54]. Patients should be counselled about the risks of underlying malignancy, and subsequent progression to endometrial cancer.

The standard treatment for EH with atypia is total hysterectomy, bilateral salpingectomy with washings and individualised consideration given to removal of ovaries. Refer to NZGCG guidelines for fertility-preserving management of atypical endometrial hyperplasia. (NZGCG-Fertility-Preserving-Management-of-Atypical-Endometrial-Hyperplasia.pdf (tewhatuora.govt.nz))

3.8 Endometrial malignancy

Those with a diagnosis of endometrial malignancy should be referred urgently to secondary gynaecology services, followed by a referral from secondary care to the regional gynaecological-oncology multidisciplinary team. Refer to NZGCG guidelines for fertility-preserving management of early stage, low risk endometrial cancer. (Link Endometrial hyperplasia and cancer guidelines (non-surgical and fertility preserving management) – Health New Zealand | Te Whatu Ora)

The following research and service provision gaps have been identified by the working group:

Research gaps

Data collection to monitor incidence of common gynaecological conditions including AUB, EH.

Development of EC risk prediction model specific for Aotearoa New Zealand.

Issues relating to access for women and training for health care providers

Lack of culturally responsive education-awareness campaign about normal menstruation patterns and the importance of seeking medical advice for abnormal bleeding.

Considering the inequitable access to funded ultrasound scan and endometrial sampling in the community.

Lack of formal and informal opportunities for upskilling primary care clinicians in endometrial sampling.

Limited access for primary care clinicians for training and maintaining skills regarding IUD insertions.

Inequitable access to primary care physicians with special interest and training in women's health.

Inequitable access to office hysteroscopies.

Updating the guidelines

These guidelines will be reviewed in 36 months from publication and updated as required.

Appendices

Appendix 1. Management of Acute AUB

Women may present with significant and or life-threatening blood loss. Timely diagnosis and treatment in an acute setting is key.

Recommended management in this setting:

1. Stabilise patient (and arrange prompt transfer to secondary care if initial assessment is in a primary care setting)
    a. Follow general principles of acute resuscitation
    b. Assess vital signs
    c. IN those with hypovolemic shock
        i. Commence immediate fluid resuscitation with crystalloid solution and blood products as necessary
2. History/Examination/Diagnosis/Investigations
    a. Obtain a targeted history
    b. Examination
        i. Include Inspection and palpation of abdomen, speculum and bimanual examination
    c. Exclude pregnancy
    d. CBC, Consider coagulation screen and blood group and cross match

Note management as outlined below is usually commenced prior to any additional imaging or investigations.

    e. Imaging
        i. Transabdominal and transvaginal ultrasound is the initial imaging of choice in this setting to assess for structural causes of bleeding
    f. Biopsy
        i. An endometrial biopsy may be arranged as soon as able after initial management (biopsy result does not change initial management in an acute setting and an adequate biopsy may not be possible in the setting of heavy bleeding)
3. Management of Acute Uterine Bleeding (Initial management is aimed at resuscitation and to arrest bleeding)
    a. Appropriate resuscitation with IV fluid and blood products
    b. Medical management
        i. Tranexamic acid 1g QID IV or oral
        ii. MPA 10mg po TDS (dose titrated up as needed)
        iii. Oral combined oral contraceptive pill (if no contraindications)
    c. Surgical treatment is rarely indicated in an acute setting
        i. Uterine artery embolization may be considered acutely for those diagnosed with an AVM
    d. Maintenance treatment
    e. A more detailed history including assessment for risk factors for EC or EH
    f. Further evaluation as required
        i. Endometrial sampling and or hysteroscopy and directed biopsy
    g. Maintenance treatment with pharmacological methods as summarised in *Table* **7** *Summary of treatments for HMB*and or surgical treatment if indicated

Appendix 2. Incidental finding of endometrial pathology on imaging on people who are not symptomatic

An individualised approach should be taken to assess and manage those who have had incidental findings of endometrial or uterine pathology on imaging.

Endometrial polyps (asymptomatic)

Asymptomatic endometrial polyps are detected in up to 12% of patients having a pelvic ultrasound scan. Whilst generally benign, they can contain malignant (0.8%) or pre-malignant (3.1%) changes on histology.

Evidence suggests that the risk of malignancy is increased for patients with risk factors for endometrial hyperplasia or malignancy [59, 60]. There is no association between increasing polyp size and increasing malignancy risk, and the use of hormone therapy [2].

Hysteroscopy and endometrial polypectomy is recommended for women with risk factors for endometrial hyperplasia and malignancy.

Expectant management is considered reasonable in asymptomatic patients without risk factors for EH or EC following discussion and careful counselling [60, 61]. A repeat pelvic ultrasound scan (3- 6 months) is recommended in this situation to confirm resolution of the endometrial polyp. If a polyp is persistent- referral to secondary care for hysteroscopy and endometrial polypectomy is recommended.

Fibroids and adenomyosis (asymptomatic)

Those with small fibroids or adenomyosis which are not symptomatic do not require further investigations or treatment.

Increased endometrial thickness, heterogeneous or hyper-vascular endometrium (asymptomatic)

In premenopausal women an optimal cut off for ‘normal’ ET has not yet been established [24], although an endometrial thickness of 16 mm or over in considered abnormal at any stage of the menstrual cycle.

If endometrial thickness is incidentally considered to be abnormal on sonographic appearances (thicker than expected for stage of menstrual cycle, endometrial appearance heterogeneous, cystic or hyper-vascularised) on an ultrasound scan organised to investigate symptoms other than AUB (for example, pelvic pain):

History should be revisited to ensure there are no risk factors for EH or EC;

Pregnancy and infection should be excluded.

In women with risk factors for endometrial pathology, aspiration endometrial sampling should be considered with patient consent and discussion of potential outcomes, including non-diagnostic samples.

Expectant management is considered reasonable in asymptomatic patients without risk factors for endometrial hyperplasia or malignancy following discussion and careful counselling [60, 61]. A repeat pelvic ultrasound scan (3-6months) may be considered to ensure resolution of the abnormal finding.

Appendix 3.

First line treatment for HMB

	Efficacy	Satisfaction	Discontinuation (or requirement of further treatment	Contraceptive	Duration	Reversible	Amenorrhoea	Contraindication	Recommendation	Level of evidence
LNG-IUD	(++++)	(+++)	10%	Yes	7 years	Yes	20%/1 year 50%/2 years	#1	A	1a
Antifibrinolytics	(+++)	(+++)		No	(-)	-	No (extremely unlikely)	#2	A	1a
COC	(+++)	(+++)	N/A	Yes	Daily pill	Yes	Depends on the regime (#3)	#4	A	1a
Combined vaginal ring	(+++)	(+++)	N/A	Yes	Monthly	Yes	Unlikely		A	1a
Long cycle progestogen	(++)	N/A		No	21 day/ cycle	-	Unlikely		A	1a
NSAIDS	(++)			No	(-)	-	Unlikely			1a
Luteal phase progestogen and ethamsilate	No ≠ placebo			No		-	No		A	1a
DMPA - Progesterone only pill and Implant: Off label use based on the amenorrhoea rate in contraceptive users				Yes					D	5

[62-68] Contraindications are based on eligibility criteria for contraceptive use.

#1 Contraindications to LNG-IUD (UKMEC 3-4)

- Postpartum 48 hours to 4 weeks
- PID/symptomatic chlamydia/ sepsis (insertion)
- Purulent cervicitis (insertion)
- Complicated organ transplant
- IHD (LNG continuation only)
- Known long QT (insertion only)
- Unexplained vaginal bleeding (insertion only)
- Gestational trophoblastic disease with decreasing (3) or persistently elevated (4) hCG
- Cervical cancer awaiting treatment (insertion)
- Radical trachelectomy
- Endometrial cancer (insertion, only for contraception)
- Breast cancer
- Distorted uterine cavity including fibroids
- HIV CD4 count<200
- Hepatocellular carcinoma/adenoma
- Severe cirrhosis
- Pelvic TBC (insertion)

#2 Contraindications to tranexamic acid

- History or risk of venous or arterial thrombosis
- Active thromboembolic disease such as deep vein thrombosis, pulmonary embolism and cerebral thrombosis.
- Acquired disturbances of colour vision
- Subarachnoid haemorrhage
- Fibrinolytic conditions following consumption coagulopathy
- Severe renal impairment (risk of accumulation)
- History of convulsions
- Hypersensitivity to tranexamic acid
-

#3 Combined oral contraceptives regime

Different regimens for COC use		
	Active pills	Placebo
Standard	21	7
Shortened hormone-free interval*	21	4 (not available in NZ, but can remove the last 3 sugar pills)
Extended	63-84**	4-7 (Achievable in NZ by using 3 or 4 packages of active pills and only one set of placebo)
Continuous	Continuous	None (taking only active pills)

#4 COC Contraindication (UKMEC 3-4)

- Postpartum <6 week
- Smoker> 15 cigarettes daily and >=35 years
- BMI>=35
- Complicated organ transplant
- Multiple risk factors for CVD
- Hypertension
- Vascular disease
- Ischaemic heart disease
- Stroke
- History or current VTE / FH VTE<45 years
- Major surgery with prolonged immobilisation
- Immobility
- Known thrombogenic mutations
- Complicated valvular and congenital heart disease
- Cardiomyopathy with impaired cardiac function

- Atrial fibrillation
- Migraine with aura (any age)
- Breast cancer (or suspected) or carrier of BRCA 1-2
- Diabetes with Nephropathy retinopathy or other vascular disease
- Past COC related Cholestasis or active gallbladder disease
- Active hepatitis (start COC)
- Severe cirrhosis (decompensated)
- Hepatocellular adenoma or carcinoma
- Positive antiphospholipid antibodies

Second-line treatment for HMB

LNG IUC is included in both groups as it may not have been tried as a first line treatment.

Treatment List	Efficacy	Satisfaction	Discontinuation (or requirement of further treatment)	Contraceptive	Duration	Reversible	Amenorrhoea	Contraindication	Grade of	Level of evidence
Hysterectomy	(++++)	(*)	0	yes		No	100% if total hysterectomy		A	1a
REA	(+++)		5-12% at 1 y Up to 16% at 2 y		5 years			# 5	A	1a
NREA	(+++)			No		No			A	1a
LNG-IUC	(++)	(**)	0.27	yes	5 to 7 years	Yes	Likely, no significant difference		A	1a

(*) Varies according to the type of hysterectomy

(**) Comparable satisfaction, QoL improvement and sexual function scores [50, 52]

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National AUB Guidelines Endorsements

Organisation	Date Endorsed	Endorsed Until
Fatu Fono Ola, Pacific Health Senate	October 2024	N/A
RANZCOG	May 2025	May 2028
Sexual Wellbeing Aotearoa	November 2024	N/A
The National Clinical Directors Network	September 2024	N/A
The Royal New Zealand College of General Practitioners	December 2024	December 2027