Menopausal Hormone Therapy Advice

This statement has been developed and reviewed by the Women’s Health Committee and approved by the RANZCOG Board and Council.

A list of Women’s Health Committee Members can be found in Appendix A.

Disclosure statements have been received from all members of this committee.

Disclaimer: This information is intended to provide general advice to practitioners. This information should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any patient. This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The document has been prepared having regard to general circumstances.

First endorsed by RANZCOG: July 2012
Current: July 2015
Review due: July 2018

Objectives: This statement will enable the reader to understand the indications for the use of Menopausal Hormone Therapy (MHT) and to identify the potential harmful side effects associated with its use.

Outcomes: The reader will be informed of appropriate doses and regimens available for treatment together with best practice initiation, monitoring and, where appropriate, cessation of treatment.

Target audience: All health professionals providing gynaecological care, and patients.

Values: The evidence was reviewed by the Women’s Health Committee (RANZCOG), and applied to local factors relating to Australia and New Zealand.

Background: This statement was first developed by Women’s Health Committee in July 2012 and reviewed in July 2015.

Funding: The development and review of this statement was funded by RANZCOG.
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1. Patient Summary

The main use of menopausal hormone therapy (MHT) is the relief of menopausal symptoms, such as hot flushes. However, there may be other benefits including reducing the risk of fractures of the hip, wrist, and spine. Because there may be some potential risks associated with use of MHT, it is important the women using, or planning to use, MHT should be carefully assessed and have treatment individualised to their needs and general health status. As women’s health may change over time, regular reassessment by a doctor experienced in use of MHT is important.

2. Summary of recommendations

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Grade</th>
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<tbody>
<tr>
<td>1. The primary indication for the use of MHT is the alleviation of distressing menopausal vasomotor symptoms.</td>
<td>Consensus-based recommendation</td>
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<tr>
<td>2. In women with primary ovarian insufficiency MHT should be continued until the normal age of the menopause.</td>
<td>Consensus-based recommendation</td>
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<td>3. MHT is also effective and appropriate for the prevention of osteoporosis related fracture in at risk women within 10 years of the menopause.</td>
<td>Consensus-based recommendation</td>
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<tr>
<td>4. The risk of VTE and stroke increases with oral MHT but the absolute risk is rare before age 60.</td>
<td>Consensus-based recommendation</td>
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<tr>
<td>5. In women within 10 years of the menopause MHT does not increase the risk of coronary heart disease.</td>
<td>Consensus-based recommendation</td>
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<tr>
<td>6. Combined MHT use for more than 5 years may be associated with an increased risk of breast cancer. This risk appears to be related to the use of a Progestogen and duration of therapy.</td>
<td>Consensus-based recommendation</td>
<td></td>
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<tr>
<td>7. Estrogen only MHT does not increase risk of breast cancer.</td>
<td>Consensus-based recommendation</td>
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<tr>
<td>8. Current safety data do not support the use of MHT in breast cancer survivors.</td>
<td>Consensus-based recommendation</td>
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<tr>
<td>9. For women who have had a hysterectomy estrogen-only therapy is appropriate and the estrogen may be delivered orally or trans-dermally.</td>
<td>Consensus-based recommendation</td>
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<tr>
<td>10. Estrogen plus Progestogen should be used in women with an intact uterus.</td>
<td>Consensus-based recommendation</td>
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<td>11. The dose and duration of therapy should be consistent with treatment goals.</td>
<td>Consensus-based recommendation</td>
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3. Introduction

The Menopause is a normal physiological event marked by permanent amenorrhoea and bought about by cessation of ovarian follicular activity. The average age of the menopause in Western women is 51 but it occurs earlier in Asian women. Menopause before age 45 is regarded as early and before age 40 as premature ovarian failure.

Symptoms of the menopause are common with Vasomotor Symptoms (VMS) of hot flushes and night sweats affecting approximately 80% of women of whom 20% are severely affected.

Menopausal Hormone Therapy (MHT, previously known as Hormone Replacement Therapy or HRT) is the most effective treatment for these symptoms and the primary indication for the use of MHT is troublesome menopausal symptoms.

MHT with systematic estrogen alone is associated with an increased risk of endometrial cancer. For women who have had a hysterectomy estrogen-only therapy is appropriate and the estrogen may be delivered orally or trans-dermally. For women with an intact uterus, the estrogen should be combined with a progestogen (progesterone or a synthetic progestin) either continuously or for 14 days per month to provide endometrial protection.

Tibolone is an oral synthetic steroid preparation with estrogenic, androgenic and progestogenic properties, which may also be used as MHT. Topical low dose estrogen is preferred for those women whose symptoms are limited to vaginal dryness and dyspareunia.

4. Discussion and recommendations

4.1 Clinical indications for MHT
The principal indication for the use of MHT is to alleviate troublesome menopausal symptoms, the commonest of which are vasomotor symptoms (VMS) followed by muscle and joint aches and pains.

Although once thought to be of short duration, recent studies in Australia and The USA have found that VMS persist in 42% of women aged 60-65. Consistent with that finding the International Menopause Society Global Consensus Statement on MHT recommends that the dose and duration of therapy of MHT should be consistent with treatment goals and not subject to an arbitrary limit. Each woman should be assessed for individual risks and benefits before commencement and an annual follow up is recommended. Starting MHT over the age of 60 is generally not recommended although, in the presence of persistent troublesome symptoms, continuation of existing therapy is not contra-indicated at that age.

For women with premature ovarian failure (age 40) or early menopause (< age 45) current guidelines recommend continuing MHT until the normal menopausal age (ie approximately 51 years of age). (RANZCOG College Statement C-Gyn 16).

While randomised clinical trials have shown MHT to reduce fracture risk in low risk post-menopausal women, bone protection is not an approved primary indication for MHT.

Similarly, treatment of low mood and libido is not a primary indication for MHT.
4.2 How well does MHT work?
MHT is the most effective treatment for VMS. A systematic review\(^2\) showed a significant reduction in both the frequency and severity of hot flushes by 87% compared with placebo whilst a review by the National Institutes of Health\(^7\) found MHT alleviated menopausal symptoms in 96% of women.

Large randomised trials have also confirmed that MHT reduces fracture risk\(^8\) vaginal dryness and sexual function and may also improve sleep, muscle aches and pains and quality of life in symptomatic women.\(^4\) The relative efficacy of Tibolone compared to MHT is not well established. In randomised trials, Tibolone has been shown to alleviate VMS, improve bone density and reduce fracture risk, to have a modest effect on some domains of female sexual function and to stimulate breasts less than combined MHT. Tibolone is also associated with less bleeding in the first 3 months of treatment. Tibolone is not approved for treatment of breast cancer survivors.\(^9\)

4.3 How safe is MHT?
For most women MHT is safe and effective when used within the first 10 years of menopause. However it is contraindicated in some circumstances and may also occasionally lead to adverse outcomes. Whilst there are no large randomised trials addressing the benefits and risks of MHT in recently menopausal women a number of large, well-controlled and long duration observational studies have been performed.\(^10\) The background risk of most adverse effects of MHT increase with age. The Women’s health Initiative Randomized Trial,\(^8\) using either conjugated estrogens or conjugated estrogens plus medroxyprogesterone acetate, primarily examined the role of MHT in the prevention of chronic disease in an older population (mean age 63 at recruitment) but did not address the issue of symptom relief or quality of life. The extrapolation of health outcomes from this older population to recently menopausal women has resulted in a misinterpretation of the risks and benefits of MHT in the latter population.

The principal risks of MHT are considered to be venous thromboembolic disease and cardiovascular disease, gall bladder disease and hormone dependent cancers.

4.4 MHT and thromboembolic disease
Combined oral estrogen plus progestin has been shown to increase the relative risk of VTE twofold\(^11\) whereas the risk with oral estrogen only therapy is less and often of borderline significance.\(^3\) Risk increases with age and is subject to other risk factors including the dose of hormone, obesity, smoking, immobility and previous VTE. Observational studies have found no increased risk of VTE for transdermal estrogen or estrogen plus progestin therapy and accordingly women at increased risk of VTE should use transdermal therapy. In the absence of a personal or family history, screening for thrombophilias is not indicated before starting MHT.
4.5 MHT and stroke

An increased risk of stroke has been reported amongst women over the age of 60 or > 10 years from the menopause using either oral estrogen or combined therapy. The increased risk is confined to ischaemic stroke and is probably related to thromboembolic risk. A large observational study found that whilst oral estrogen and high doses of transdermal therapy increased stroke risk, no increase was seen when transdermal doses of 50ug or less were used.\(^\text{12}\)

<table>
<thead>
<tr>
<th>Recommendation 4</th>
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<tr>
<td>The risk of VTE and stroke increases with oral MHT but the absolute risk is rare before age 60.</td>
<td>Consensus-based recommendation</td>
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4.6 MHT and cardiovascular disease

The relationship between MHT and cardiovascular disease is complicated by age and time since the menopause. In the follow up of The Women’s Health Initiative RCT\(^\text{11}\) Coronary Heart Disease was not increased during the intervention or post intervention phase for either estrogen only or combined therapy. When stratified for women aged 50-59 there was no increase in risk during the intervention phase for either regimen but in cumulative follow up the risk was significantly reduced for users of estrogen only therapy (HR 0.65, 95%CI 0.44-0.96) and not increased for users of combined MHT. A recent Cochrane analysis\(^\text{13}\) concluded that, overall, MHT conferred no protective effect on all-cause mortality, cardiovascular death, non-fatal infarction, angina or revascularisation but did increase risk of stroke and VTE. However, in women who started MHT less than 10 years after the menopause there was lower mortality (RR0.70, 95%CI 0.52-0.95), and also a lower incidence of coronary heart disease. There was no evidence of increased risk of stroke in this group. These findings are supportive of the ‘window of opportunity’ hypothesis that initiation of MHT in women within 10 years of their last period is associated with maximum benefit and minimal risk.

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<thead>
<tr>
<th>Recommendation 4</th>
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<tr>
<td>In women within 10 years of the menopause MHT does not increase the risk of coronary heart disease.</td>
<td>Consensus-based recommendation</td>
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4.7 MHT and breast cancer

The increased risk of breast cancer in women over 50 associated with MHT is a complex issue and is primarily associated with the duration of use and the addition of a progestogen to estrogen therapy. The attributable risk is small and decreases when treatment is stopped. Cumulative long term follow up of the Women’s Health Initiative RCT\(^\text{11}\) found no increase in risk for women receiving estrogen only therapy but an increased risk for those receiving combined therapy amounting to approximately 0.1%. A large observational study\(^\text{14}\) found an unequal risk of breast cancer depending on which progestogen was used in combined therapy with risk not increased for estrogen plus progesterone or dydrogesterone combinations.

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<th>Recommendation 6</th>
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<td>Combined MHT use for more than 5 years may be associated with an increased risk of breast cancer. This risk appears to be related to the use of progestogen and duration of therapy.</td>
<td>Consensus-based recommendation</td>
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<td>Estrogen only MHT does not increase risk of breast cancer.</td>
<td>Consensus-based recommendation</td>
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<th>Recommendation 8</th>
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<tr>
<td>Current safety data do not support the use of MHT in breast cancer survivors.</td>
<td>Consensus-based recommendation</td>
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4.8 MHT and endometrial cancer  
In women who have an intact uterus, unopposed estrogen may lead to endometrial hyperplasia and an increased risk of endometrial cancer. For this reason women who retain their uterus and use estrogen should also take progestogen. Combined continuous HRT does not increase the risk of endometrial cancer and in long term RCTs was associated with a reduced risk compared to the untreated population. Sequential therapy will also provide endometrial protection provided the dose and duration of progestogen is appropriate. Tibolone does not increase the risk of endometrial hyperplasia or cancer.

4.9 MHT and ovarian cancer  
A large Meta-analysis has reported an increased risk of ovarian cancer for users of MHT. The increased risk was confined to serous and endometrioid subtypes whilst there was a reduction in risk of clear cell and mucinous subtypes. The absolute increase in risk was reported as 2.4 per 10,000 women per year although others have argued the increase was less. The risk was confined to prospective studies and no increase was seen in retrospective studies. Despite the authors' best efforts, data was incomplete bringing into question the validity of this very small change in risk derived from a Meta-analysis. The only large randomised trial examining MHT and ovarian cancer risk found no increase after 5 years of therapy. Overall, the association between MHT and ovarian cancer remains uncertain and a change in clinical practice is not warranted.

4.10 MHT and gallbladder disease  
Large RCT’s have shown an increased risk of cholecystitis with oral MHT use amounting to 12 extra cases per 1000 women per 5 years. Observational data suggests transdermal therapy will reduce that risk.

4.11 Cautions associated with MHT  
- Long-term use of some forms of combined MHT may be associated with an increased risk of breast cancer. No increased risk has been reported with five or less years of treatment of combined MHT.
- At present there is insufficient evidence to recommend the use of MHT or Tibolone in breast cancer survivors.
- Women with a personal or family history of VTE may be at increased risk of that condition when using oral MHT. For these women, but not for unaffected women, screening and risk counselling is appropriate before commencing treatment. Transdermal therapy should be chosen for any woman considered at increased risk of VTE. Tibolone has not been found to increase VTE risk in a number of RCTs.
- Evidence from RCTs has suggested an increased risk of recurrence of cardiovascular disease in women initiating oral MHT with a prior history of that condition. Accordingly MHT should not be initiated in such women without careful evaluation of risks and benefits and after consulting her physician. Transdermal therapy should be preferred.
- MHT should not be commenced in women with undiagnosed vaginal bleeding. Combined MHT may be associated with unscheduled bleeding during the first six months of therapy. Persistent or new onset, bleeding beyond that time requires investigation.
- In women with abnormal liver function tests transdermal therapy should be preferred.
- Migraine is not a contraindication to MHT use however low dose transdermal therapy may be preferable.
- Women with a history of endometrial or ovarian cancer should have specialist review prior to commencing MHT.
4.12 Using MHT

Simple clinical guidance, designed to be used in conjunction with more detailed guidelines may be obtained from The Global Consensus Statement on MHT use.\(^3\)

The Practitioner’s tool kit,\(^1,\(^8\) endorsed by RANZCOG, provides simple algorithm based steps aimed to make the prescription of MHT safe and simple.

**Perimenopause**

Some perimenopausal women may benefit from MHT for the purpose of cycle control, contraception and symptom relief. The combined oral contraceptive pill provides contraception, cycle control, relief from VMS and other symptoms. It will also prevent bone loss and reduce acne often first noted at this time. Each woman’s risks must be assessed including smoking status, blood pressure, lipid profile and VTE risk. Eliminating placebo tablets or the addition of supplemental low dose estrogen may treat VMS developing in the pill free week.

The levonorgestrel releasing intrauterine system (LNG-IUS) provides contraception and is excellent for managing heavy menstrual bleeding. Estrogen may be added when VMS become troublesome.

Cyclical (sequential) MHT may be initiated during the peri menopause for alleviation of VMS however it is not contraceptive and will not regulate menstrual cycles.

*For Post menopausal women* treatment goals are alleviation of troublesome menopausal symptoms and improvement in quality of life. For women with an intact uterus MHT may be prescribed as estrogen plus a progestogen for 14 days per month (cyclical therapy) or every day (continuous combined therapy). Cyclical therapy results in scheduled progestogen withdrawal bleeds. Continuous combine therapy results in amenorrhoea in 90% of women after 12 months although spotting and breakthrough is common in the first 3-4 months of therapy.

For women who have undergone therapy estrogen only therapy is appropriate.

The dose and duration of therapy should be the lowest possible consistent with treatment goals.

For women in whom symptoms are confined to those of vulvo vaginal atrophy orgenito urinary symptoms of the menopause, topical estrogen preparations are preferred and, when used according to directions, do not require supplementary progestogens.

**Estrogen** may be used systemically as oral conjugated estrogens, micronized 17B oestradiol, oestradiol valerate or oestrone sulphate. Transdermal oestradiol patches, gel or implants may also be used.

**Progestogen** therapy is required for all women with an intact uterus and may be cyclical or continuous. Progestogens include micronized progesterone and synthetic progestins. There is evidence to suggest micronised progesterone is safer than synthetic progestins regarding breast cancer and cardiovascular risk.\(^1^9\) Micronised progesterone may be taken orally or the same capsule may be inserted vaginally. Synthetic progestins are usually taken orally in a fixed dose combination with estrogen or separately. Fixed dose combined transdermal patches are also available and the LNG-IUS may also be used for endometrial protection.

There is insufficient evidence to recommend the use of compounded progesterone creams.

Common side effects of MHT include nausea, headache and breast tenderness. Initiating therapy with low doses will minimise these side effects whilst transdermal therapy is also less likely to induce nausea.
All women using MHT should be reviewed after 6 months therapy. This should include a general health check, a breast check and a mammogram every two years, Bone densitometry should be performed where indicated and any unexpected vaginal bleeding after 6 months therapy requires appropriate investigation. The need for ongoing MHT should be reviewed regularly.

Base the decision on whether to advise continuation of HRT on symptoms and ongoing risks and benefits rather than a set minimum or maximum duration of therapy. Cessation of HRT leads to recurrent symptoms for up to 50% of women. Consider the potential impact of recurrent symptoms on quality of life. The risks of HRT may be related to duration of HRT use - for example, the risk of venous thromboembolism is greatest in the first year of use, but the risk of breast cancer increases with duration of use. Most guidelines recommend using HRT for up to four to five years. No clear consensus has emerged on how to discontinue HRT, and symptoms may recur regardless of whether HRT is stopped slowly or suddenly.

4.14 What are the alternatives to HRT for menopausal symptoms?
For women who cannot take hormone based therapies there remain a number of alternatives.

Several serotonin-norepinephrine reuptake inhibitors (venlafaxine and desvenlafaxine) and selective serotonin reuptake inhibitors (paroxetine, citalopram, and escitalopram) have been shown in short-term trials to alleviate VMS but to a lesser degree than MHT.

Selective serotonin reuptake inhibitors that induce CYP2D6 particularly paroxetine and fluoxetine, should be avoided in women who take tamoxifen as they may interfere with the metabolism of tamoxifen.

Gabapentin is the only non-hormonal product shown to be equally effective as low dose estrogen for vasomotor symptoms.

Clonidine, an alpha-adrenergic agonist is mildly effective.

Relaxation therapy, mindfulness based therapies, and cognitive behaviour therapy may improve vasomotor symptoms. A recent systematic review showed no effect for any other interventions (including acupuncture, homeopathy, vitamin E, or magnetic devices) for hot flushes after breast cancer.

Overall, data from large randomised controlled trials do not support the efficacy of black cohosh or other "natural remedies" for the treatment of hot flushes.

So-called "bio-identical" hormones have not been shown to be safe or effective.

Vaginal dryness can be effectively treated with topical estrogen. Vaginal estrogens can be used safely in the long term without additional progestogens.
Non-hormonal options for atrophic vaginitis include lubricants and vaginal moisturizers, although there is little evidence to suggest they offer the sustained benefit associated with vaginal estrogen.

5. References

11. Manson J. MHT and Health outcomes during intervention and post stopping phases of WHI, JAMA. 2013;310:1353-68.
6. **Other suggested reading**

Doctors may read a comprehensive review of the literature on the NHMRC web site: 


DW Sturdee and A Pines on behalf of the International Menopause Society Writing Group. Updated IMS recommendations on postmenopausal hormone therapy and preventive strategies for midlife health. CLIMACTERIC 2011; 14: 302-320.

7. **Links to other College statements**

Consent and provision of information to patients in Australia regarding proposed treatment (C-Gen 2a)

Consent and provision of information to patients in New Zealand regarding proposed treatment (C-Gen 2b)

Evidence-based Medicine, Obstetrics and Gynaecology (C-Gen 15)

8. **Patient information**

A range of RANZCOG Patient Information Pamphlets can be ordered via: 
https://www.ranzcog.edu.au/Womens-Health/Patient-Information-Guides/Patient-Information-Pamphlets/
Appendices

Appendix A Women’s Health Committee Membership

<table>
<thead>
<tr>
<th>Name</th>
<th>Position on Committee</th>
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<tbody>
<tr>
<td>Associate Professor Stephen Robson</td>
<td>Chair and Board Member</td>
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<tr>
<td>Dr James Harvey</td>
<td>Deputy Chair and Councillor</td>
</tr>
<tr>
<td>Associate Professor Anusch Yazdani</td>
<td>Member and Councillor</td>
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<tr>
<td>Associate Professor Ian Pettigrew</td>
<td>Member and Councillor</td>
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<tr>
<td>Dr Ian Page</td>
<td>Member and Councillor</td>
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<tr>
<td>Professor Yee Leung</td>
<td>Member of EAC Committee</td>
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<tr>
<td>Professor Sue Walker</td>
<td>General Member</td>
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<tr>
<td>Dr Lisa Hui</td>
<td>General Member</td>
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<tr>
<td>Dr Joseph Sgroi</td>
<td>General Member</td>
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<tr>
<td>Dr Marilyn Clarke</td>
<td>General Member</td>
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<tr>
<td>Dr Donald Clark</td>
<td>General Member</td>
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<tr>
<td>Associate Professor Janet Vaughan</td>
<td>General Member</td>
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<tr>
<td>Dr Benjamin Bopp</td>
<td>General Member</td>
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<tr>
<td>Associate Professor Kirsten Black</td>
<td>General Member</td>
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<tr>
<td>Dr Jacqueline Boyle</td>
<td>Chair of the ATSIWHC</td>
</tr>
<tr>
<td>Dr Martin Byrne</td>
<td>GPOAC representative</td>
</tr>
<tr>
<td>Ms Catherine Whitby</td>
<td>Community representative</td>
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<tr>
<td>Ms Sherryn Elworthy</td>
<td>Midwifery representative</td>
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<tr>
<td>Dr Nicola Quirk</td>
<td>Trainee representative</td>
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Appendix B Overview of the development and review process for this statement

i. Steps in developing and updating this statement

This statement was originally developed in July 2012 and was most recently reviewed in July 2015. The Women’s Health Committee carried out the following steps in reviewing this statement:

- Declarations of interest were sought from all members prior to reviewing this statement.
- Structured clinical questions were developed and agreed upon.
- An updated literature search to answer the clinical questions was undertaken.
- At the July 2015 face-to-face committee meeting, the existing consensus-based recommendations were reviewed and updated (where appropriate) based on the available body of evidence and clinical expertise. Recommendations were graded as set out below in Appendix B part iii)

ii. Declaration of interest process and management

Declaring interests is essential in order to prevent any potential conflict between the private interests of members, and their duties as part of the Women’s Health Committee.

A declaration of interest form specific to guidelines and statements was developed by RANZCOG and approved by the RANZCOG Board in September 2012. The Women’s Health Committee members
were required to declare their relevant interests in writing on this form prior to participating in the review of this statement.

Members were required to update their information as soon as they become aware of any changes to their interests and there was also a standing agenda item at each meeting where declarations of interest were called for and recorded as part of the meeting minutes.

There were no significant real or perceived conflicts of interest that required management during the process of updating this statement.

### iii. Grading of recommendations

Each recommendation in this College statement is given an overall grade as per the table below, based on the National Health and Medical Research Council (NHMRC) Levels of Evidence and Grades of Recommendations for Developers of Guidelines. Where no robust evidence was available but there was sufficient consensus within the Women’s Health Committee, consensus-based recommendations were developed or existing ones updated and are identifiable as such. Consensus-based recommendations were agreed to by the entire committee. Good Practice Notes are highlighted throughout and provide practical guidance to facilitate implementation. These were also developed through consensus of the entire committee.

<table>
<thead>
<tr>
<th>Recommendation category</th>
<th>Description</th>
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<tbody>
<tr>
<td>Evidence-based</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>Body of evidence can be trusted to guide practice</td>
</tr>
<tr>
<td>B</td>
<td>Body of evidence can be trusted to guide practice in most situations</td>
</tr>
<tr>
<td>C</td>
<td>Body of evidence provides some support for recommendation(s) but care should be taken in its application</td>
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<tr>
<td>D</td>
<td>The body of evidence is weak and the recommendation must be applied with caution</td>
</tr>
<tr>
<td>Consensus-based</td>
<td>Recommendation based on clinical opinion and expertise as insufficient evidence available</td>
</tr>
<tr>
<td>Good Practice Note</td>
<td>Practical advice and information based on clinical opinion and expertise</td>
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Appendix C Full Disclaimer
This information is intended to provide general advice to practitioners, and should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any patient.

This information has been prepared having regard to general circumstances. It is the responsibility of each practitioner to have regard to the particular circumstances of each case. Clinical management should be responsive to the needs of the individual patient and the particular circumstances of each case.

This information has been prepared having regard to the information available at the time of its preparation, and each practitioner should have regard to relevant information, research or material which may have been published or become available subsequently.

Whilst the College endeavours to ensure that information is accurate and current at the time of preparation, it takes no responsibility for matters arising from changed circumstances or information or material that may have become subsequently available.