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POSITION STATEMENT

South African Menopause Society revised consensus position statement on menopausal hormone therapy, 2014

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The South African Menopause Society (SAMS) consensus position statement on menopausal hormone therapy (HT) 2014 is a revision of the SAMS Council consensus statement on menopausal HT published in the *SAMJ* in May 2007. Information presented in the previous statement has been re-evaluated and new evidence has been incorporated. While the recommendations pertaining to HT remain similar to those in the previous statement, the 2014 revision includes a wider range of clinical benefits for HT, the inclusion of non-hormonal alternatives such as selective serotonin reuptake inhibitors and serotonin noradrenaline reuptake inhibitors for the management of vasomotor symptoms, and an appraisal of bioidentical hormones and complementary medicines used for treatment of menopausal symptoms. New preparations that are likely to be more commonly used in the future are also mentioned. The revised statement emphasises that commencing HT during the 'therapeutic window of opportunity' maximises the benefit-to-risk profile of therapy in symptomatic menopausal women.

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1. Introduction

Clinicians are expected to practise in accordance with the findings of evidence-based medicine. This implies that the clinician is familiar with the strongest evidence available. It may be difficult for the following reasons:

- The results of a given clinical trial can often only be applied to the specific population group and circumstances applicable to that specific trial. This is especially important in hormone therapy (HT), where initiation of therapy during the 'therapeutic window of opportunity' (between 50 and 60 years of age or within 10 years of onset of menopause) results in a much better benefit-to-risk profile than initiation in older patients.
- A small group of individuals may react to medication in a unique way, so studies must be adequately powered.
- Statistical significance does not always equate to clinical significance.
- Different methods of defining statistical significance may yield different answers when applied to the same data.
- Publications often only quote relative risks and ignore the clinically more relevant absolute risks.
- The patient's perception is always important. For example, the weak association between postmenopausal HT and breast cancer may be of greater concern to women and the lay press than the stronger association between HT and thromboembolic disease.
- The side-effects of preventive medicine in healthy individuals have different implications to those resulting from the treatment of individuals with disease.
- For many years, the options for use of HT were based mainly on data from observational trials. Although these have generally been superseded by data from large randomised controlled clinical trials (RCTs), when considering HT the large body of observational data derived from women with a similar profile to that seen in everyday practice cannot be completely disregarded in favour of RCT data derived from older asymptomatic women.
- Because there are still major gaps in our knowledge, clinical guidelines are unable to cater for all situations.
- The final decision regarding therapy must be a joint decision between the healthcare provider and an informed patient, based on her current clinical status and ongoing new scientific evidence.

- The general public is always looking for alternative medical treatment strategies to manage menopausal symptoms. The vast majority are ineffectual and some may be dangerous.

2. Abbreviations used in this statement

ET = oestrogen therapy alone; EPT = oestrogen and progestogen therapy in combination; HT = hormone therapy, which refers to either ET or EPT.

3. Position statement regarding menopausal HT

3.1 HT and quality of life

HT significantly improves menopause-specific quality of life (QoL), mainly through relief of symptoms, and especially vasomotor symptoms (VMSs). It may also result in a global improvement in sense of wellbeing. Health-related benefits depend on the severity of associated menopausal symptoms. Health-related and menopause-related QoL improves more obviously in women who had significant menopausal symptoms before receiving HT, with considerably less improvement occurring in women without significant symptoms.[1]

3.2 HT and weight gain

Although weight gain associated with HT is a major concern for most women initiating HT, there is very little evidence to support this fear. There is invariably a redistribution of fat mass at the time of menopause, which may become apparent during the menopausal transition with an increase in waist-to-hip ratio. Evidence shows that neither ET nor EPT is responsible for an increase in weight. The route of hormone administration does not appear to have an impact on weight gain.[2]

3.3 HT and VMSs

HT remains the only treatment that consistently has a greater effect than placebo on alleviation of menopause-related VMSs. VMSs generally last 2 - 5 years, but in some individuals may last much longer. Patients reporting VMS for the rest of their lives are not rare. ET is effective in relieving VMS even in low dosages, and this therapeutic effect is enhanced by the addition of a progestogen. Lifestyle-related strategies may also be of benefit.

VMSs may recur to a varying degree with cessation of HT.[3]

In clinical practice, the individual patient is the best judge of the effect of HT on her QoL, particularly if she is symptomatic. Routine monitoring of hormone levels is not advocated unless oestradiol implants are being used.[4-6]

In women for whom HT is contraindicated, those who decline treatment, or those who cannot tolerate HT, alternatives include selective serotonin reuptake inhibitors (SSRIs) and serotonin noradrenaline reuptake inhibitors (SNRIs). Although it is not commonly used, gabapentin has also been shown to decrease the occurrence of hot flushes.[7]

3.4 HT and sleep

Sleep disorders are common in the menopause and may be associated with VMSs, depression, anxiety, insomnia, obstructive sleep apnoea, fibromyalgia, restless leg syndrome, comorbid disorders or medications, or may simply be related to age. HT appears to improve sleep quality and quantity in menopausal women, although this has not been conclusively confirmed in available studies, especially where polysomnography has been used as an assessment tool. HT appears to decrease episodes of awakenings and increase rapid eye movement (REM) sleep by decreasing night sweats and improving mood. Further studies are needed to substantiate this and to determine whether type, dose and mode of administration impact on the quality of sleep.[8]

3.5 HT and vulvovaginal atrophy (VVA)

Systemic HT is very effective in reversing VVA. In women who have symptoms related to VVA alone, topical local ET only is appropriate. In about 15% of women using systemic HT, additional topical vaginal therapy is needed to achieve reversal of the atrophic symptoms. Vaginal creams, vaginal rings or vaginal tablets are effective options.

Local oestrogen preparations, when used correctly as sole therapy, do not result in sufficient systemic absorption to warrant the use of progestogen for endometrial protection. At present there is not enough evidence to mandate progestogen use in women who persist with any local intravaginal oestrogen preparation beyond 6 months.

Vaginal lubricants or moisturisers, with or without local oestrogen preparations, are also effective options.

When HT is indicated for urological symptoms, local therapy is preferred to systemic therapy.

Local ET improves symptoms of detrusor instability, including urgency, urge incontinence, frequency and nocturia, and reduces the incidence of recurrent urinary tract infections. Sexual function is also improved through the reversal of vaginal skin atrophy with increased vaginal lubrication.[9]

3.6 HT and menopause-associated bone loss

The increased rate of bone resorption following the onset of menopause clearly indicates a hormonal influence on bone density in women. Both transdermal and oral HT are effective in preventing bone loss. Supplementing with calcium and vitamin D is advisable if these are deficient.

HT is effective in decreasing the incidence of all osteoporosis-related fractures. This is true for both patients at low risk of fracture and patients at high risk of fracture before the age of 60 years or within 10 years of the onset of menopause. HT decreases vertebral and non-vertebral fractures by approximately 50%.[3]

In some patients, a degree of fracture prevention persists after cessation of HT. Patients remaining at risk of fracture should receive ongoing therapy with proven bone-sparing medication once HT has been stopped. As some women lose bone rapidly after cessation of HT, close follow-up is needed for women not receiving ongoing treatment.[10]

3.7 HT and coronary heart disease (CHD)

Cardiovascular disease is the major cause of death in older women. Observational data have indicated that HT may reduce CHD by approximately 50%. This prompted several RCTs.

The following conclusions are based on an assessment of the total body of evidence:

3.7.1 HT does not offer secondary protection against CHD. This recommendation is based mainly on the data from the Heart and Estrogen/progestin Replacement Study (HERS), but also from data from the older women subset in the Women's Health Initiative (WHI) study.

3.7.2 Standard-dose ET may offer primary protection against CHD and lower all-cause mortality in women where therapy was initiated during the 'therapeutic window of opportunity'. This recommendation is based on data from RCTs, observational studies and meta-analyses.

The evidence that EPT in standard dosages offers primary protection against CHD when initiated in the window of opportunity is not

as consistent as the data for ET, although the effect on lowering mortality is the same.[3]

3.7.3 In the WHI study, an increase in non-fatal CHD was found in the first year of HT, but final analyses proved this to be statistically non-significant. It was not evident in the younger patients. It is therefore concluded that in women initiating therapy outside the 'therapeutic window of opportunity' who are likely to have established coronary artery atherosclerosis, HT is unlikely to offer significant protection and may cause a transient initial increase in adverse events.[11-16]

3.8 HT, insulin resistance and diabetes

Data suggest that combined HT reduces the incidence of diabetes in postmenopausal women, possibly mediated by a decrease in insulin resistance unrelated to body size. HT appears to reduce fasting glucose and fasting insulin levels, but should not be given with the primary intention of preventing diabetes in postmenopausal women.[17]

3.9 HT and stroke

The HERS and Women's Estrogen for Stroke (WEST) trials, which were both secondary prevention studies, demonstrated a null effect on the combined outcome of non-fatal stroke, fatal stroke or all-cause mortality relative to placebo in postmenopausal women with established cardiovascular disease. In the WHI study, a non-significant increase in the risk of ischaemic stroke was seen in all age groups. The magnitude of this risk was small, however, particularly in patients younger than 55 years of age, where the absolute increase in risk was 1.5 extra ischaemic strokes per 10 000 HT users per year. This complication is therefore extremely rare.

A meta-analysis of observational studies has shown a non-significant increase in the risk of overall stroke and thrombotic stroke (by approximately 10% and 20%, respectively). The increased risk of stroke associated with HT persists throughout treatment, but decreases after discontinuation.

Observational data suggest that lower doses of oral therapy than that used in the WHI will result in even less risk, and that normal and low-dose transdermal therapy (≤50 μg) are uncommonly associated with an increase in the risk of ischaemic stroke.

There is no role for HT in the primary or secondary prevention of stroke.[18-23]

3.10 Route of administration

Transdermal administration of HT is associated with a lower risk of adverse events, and particularly cardiovascular adverse events, than oral administration. Transdermal HT does not appear to increase the risk of thromboembolic disease significantly. It is therefore prudent to consider the transdermal route in women at high risk for cardiovascular events, namely obese women, smokers and hypertensive women, and especially if there is any history of thrombosis.(3)

3.11 HT and venous thromboembolism (VTE)

The relative risk of VTE increases with the use of HT. In the WHI study the absolute risk of VTE was increased by 18 additional cases per 10 000 women per year with EPT, and 7 cases per 10 000 women per year with ET.[24] The effect is maximal in the first year of treatment and decreases over time. Risk factors include obesity, previous VTE, underlying thrombophilia and initiation of HT after age 60 years. The risk of VTE in the age group 50 - 60 years is very small, but increases four-fold in the 60 - 69-year-old and seven-fold in the 70 - 79-year-old age groups.[25] The route of delivery will impact on risk, with the highest risk being associated with oral EPT, followed by oral ET, and the lowest risk being associated with transdermal HT.[26,27]

3.12 HT and breast cancer

The risk of breast cancer associated with HT in menopausal women is a complex issue.

Data suggest that HT may not be causal, but rather a promoter of pre-existing breast cancer. The absolute risk of breast cancer attributable to HT is low and falls into the same risk category as several preventable risk factors that are associated with a similar low relative risk for developing breast cancer. Examples of these are obesity, nulliparity and never having breastfed, having a first pregnancy after the age of 37 years and excessive alcohol intake. The increased risk of breast cancer is primarily associated with the addition of a progestogen to oestrogen therapy. In the WHI study, standard-dose ET was consistently associated with a lower risk of breast cancer than placebo, and at 12 years of follow-up this difference was statistically significant. Standard-dose EPT was associated with an increased risk of breast cancer compared with placebo. It is, however, important to note that on final adjudication and appropriate adjustment, this increase was not statistically significant. Furthermore, the increased risk was confined to women with prior exposure to EPT.

The increased risk of breast cancer seems to be related to the duration of hormone use. Observational studies show no increased risk for 15 - 20 years of ET use. Combined conjugated equine estrogen and medroxyprogesterone acetate (CEE/MPA) in the WHI study did not increase breast cancer risk over 7 years in new users. However, observational studies point to a small increased risk in long-term users of CEE/MPA. This effect was not seen when natural progesterone was used.[28-29]

The HT-related increase in breast cancer risk decreases after HT is stopped and disappears by about 5 years.

Breast cancer risk on HT is increased in lean women.[30-33]

3.13 HT and breast density

Higher degrees of mammographic breast density in women not taking HT reflect higher levels of endogenous oestrogen secretion in breast tissue and correlate with increased breast cancer risk.[33]

Breast density may be increased by use of ET, but this is more likely to occur with the use of EPT. This increased breast density may impede the diagnostic interpretation of mammograms. In such cases, cessation of EPT for 2 - 4 weeks and repeat breast image screening may be helpful.[34]

If available, it would be prudent for women to undergo digital mammography and ultrasound. Thermal screening should be avoided as a diagnostic tool.

Before initiating any HT, it is recommended that the breasts are examined carefully and that mammographic imaging is undertaken and followed conventionally thereafter.

3.14 HT and risk of other cancers

3.14.1 Colorectal cancer

There is continuing evidence that oral HT results in an approximately 40% reduction in the incidence of colorectal cancer, and that this benefit is more pronounced in the EPT group.

However, HT is not indicated for primary prevention of colorectal cancer.[35,36]

3.14.2 Endometrial cancer

Oestrogen-only therapy should not be prescribed for women with an intact uterus, who should always receive a progestogen

simultaneously. The primary indication for progestogen use in women on HT is endometrial protection. Combined EPT should not be prescribed for women who have had a hysterectomy, unless they have a history of extensive endometriosis.

Long-term use of continuous combined EPT offers superior protection of the endometrium compared with sequential regimens and hence reduces the risk of endometrial cancer significantly more than sequential HT. The maximum duration of sequential HT should not exceed 5 years, after which continuous combined EPT should be prescribed. Long-term cycle regimens with 3-monthly withdrawal bleeds are not recommended.[37,38]

The levonorgestrel intrauterine system plus ET is comparable to other progestogen regimens.

3.14.3 Ovarian cancer

There are as many studies showing an increased risk of epithelial cancer as there are studies showing a null effect or a negative effect in HT users compared with non-users. The risk is so small that it is unlikely to influence prescribing habits.[39,40]

3.14.4 Lung cancer

Although combined HT does not significantly increase the incidence of lung cancer, it does increase death from lung cancer, and the risk continues after cessation of therapy. This should be of concern to users of HT who are smokers or have other risk factors for lung cancer.[41]

3.15 HT in breast and gynaecological cancer survivors

3.15.1 Breast cancer survivors

At present, it is prudent not to offer HT routinely to breast cancer survivors for management of menopausal symptoms, even though the data are somewhat controversial. Three randomised trials have addressed this issue, two of which showed an increase in cancer recurrences, while the other did not. None of the three studies showed an increase in death from the disease.[42-44]

Data derived from observational studies, including two large meta-analyses, do not show an increase in recurrences or death rate in breast cancer survivors using HT.

HT should be prescribed only when patients are fully informed of the current available data and wish to use this therapeutic modality.

There is no evidence to suggest that transvaginal topical oestrogen increases recurrence, so it may be prescribed to patients with intractable symptoms associated with urogenital atrophy.[45]

3.15.2 Gynaecological cancer survivors

HT for the management of VMS is not contraindicated in survivors of vulval, vaginal or cervical cancer.

However, in survivors of endometrial or ovarian cancer, even though the data are controversial with many studies finding no detrimental effect of HT, it is prudent not to administer HT routinely.[46]

3.16 Alzheimer's disease (AD) and cognition

There is observational evidence that HT initiated during the 'therapeutic window of opportunity' may be protective against AD in later life. However, HT used after the age of 65 years carries an increased risk of all-cause dementia, which is more prevalent with EPT than with ET.

HT is not indicated for the prevention or treatment of AD.

Short-term memory dysfunction is common in the menopausal transition and is usually self-limiting. HT appears to benefit this dysfunction.[47,48]

3.17 Primary ovarian insufficiency (POI) (premature menopause)

POI refers to ovarian failure with at least 4 months of amenorrhoea and follicle-stimulating hormone levels in the menopausal range on two occasions within a 4 - 6-week interval, in women younger than 40 years of age. The principles of treatment that apply to women undergoing a natural menopause at ~51 years are not applicable to young women with POI.

Data from studies of women with POI show decreased survival, increased cardiovascular risk, increased risk of fracture, sexual dysfunction and possibly increased cognitive dementia and Parkinson's disease. HT will decrease these risks, alleviate symptoms and preserve bone density, especially after bilateral oophorectomy.[49-51]

It is recommended that HT or oral contraception be used at least until the natural age of menopause. For younger women, higher doses are often needed to control symptoms.[52]

3.18 Androgen therapy

Hypoactive sexual desire disorder (HSDD) is the commonest sexual dysfunction in the climacteric. Testosterone levels in women decline as a result of ageing, but not to the extent of the precipitous decline demonstrated by oestrogen in menopause. The reduced levels of testosterone in postmenopausal women are associated with loss of libido, decreased sexual activity, diminished feelings of wellbeing and fatigue. Testosterone is an effective treatment for HSDD in women receiving concomitant ET. Testosterone on its own is not advocated.

Other conditions in which androgen levels are low and in which HSDD is likely to occur include POI, surgical menopause, adrenal insufficiency and hypopituitarism. These women are also candidates for testosterone therapy.[53-55]

There are currently no female testosterone therapies registered or available in South Africa (SA). Tibolone, which has weak androgenic, oestrogenic and progestogenic activity and does not increase sex hormone binding globulin, can be used as an alternative to testosterone.[56]

3.19 Targets beyond the obvious

Evidence is accumulating to support the beneficial effects of HT on the skin and, to a certain extent, on the oral cavity.[57,58]

3.20 New combinations and HT preparations

The new third-generation selective oestrogen receptor modulators and oestrogen combination preparations have a favourable impact on breast tissue and will be used more frequently to treat menopausal symptoms and osteoporosis.

- Bazedoxifene with conjugated oestrogens is such a preparation.
- Ospemifene, a new oral oestrogen receptor modulator, has been shown to be effective in reversing the symptoms associated with vulvovaginal atrophy, dyspareunia in particular.

3.21 Bioidentical HT (BHT) for menopausal symptoms

BHT is the use of hormones identical to those secreted in the ovary or adrenal gland, namely oestradiol, oestrone, oestriol, dehydroepiandrosterone (DHEA) and testosterone.[59] These are frequently compounded for specific patients in compounding pharmacies. The Federal Drug Administration reported a study of compounded pharmaceutical products that found significant aberrations with regard to quality and potency of these products.[60] In SA, conventional HT products require mandatory regulation and registration by the Medicines Control Council. This involves regular testing for purity, potency, efficacy and safety. Bioidentical hormone and compounding

products require no such regulation. There is no evidence to support claims of greater efficacy or safety for BHT compared with conventional HT. The addition of oestriol to oestradiol with or without oestrone does not significantly alter the oestrogenic content of the oestrogen compound and certainly does not reduce the risk of breast cancer as is claimed. The absorption of bioidentical progesterone cream is variable, unpredictable and unreliable, and its use for opposing the effects of oestrogen on the endometrium is therefore not recommended.[61,62]

There are no long-term safety studies for BHT, and no procedures exist for reporting adverse events. The use of BHT is not recommended.

3.22 Complementary and alternative medicines (CAMs) and menopausal symptoms

- CAMs are remedies not recognised in conventional medicine. They have become popular because of the mistaken belief that 'natural' medicines have no adverse effect. The term 'natural' gives a subliminal message of safety. There is no such thing as natural medicine. All medicinal products are manufactured in factories.
- Phyto-oestrogens are mainly sourced from soy and red clover, which express their pharmacological action through isoflavones. Most studies have shown a null effect or at most a minimal effect on VMSs in comparison with placebo.[63]
- Isoflavones appear to have no serious side-effects, although if high doses are used for long periods of time, they may stimulate the endometrium and breast.
- Black cohosh has no phyto-oestrogenic activity and is thought to have serotonin agonist properties. It appears to have poor efficacy for menopausal symptoms.[64]
- Black cohosh has been shown to be hepatotoxic.
- Both isoflavones and black cohosh should be avoided in women being treated for breast cancer.[65] Genistein (an isoflavone) may negate the inhibitory effect of tamoxifen on breast tumour growth.[66]

4. Clinical guidelines

- The menopausal transition should be utilised as a window of opportunity to assess and manage specific as well as general health-related matters. A medical history should be taken and general breast and gynaecological examinations, including cervical cytology, should be done.
- Special investigations should include a fasting lipogram, blood glucose measurement, mammography, thyroid function testing and, for patients considered to be at risk of osteoporosis, measurement of bone density by dual-energy X-ray absorptiometry. Investigations for hypercoagulable states before instituting HT are only required in patients at risk (personal or family history of VTE).
- Lifestyle modifications such as cessation of smoking, adjustment of diet, maintenance of an appropriate body mass index, exercise and stress control should be discussed.
- Treatment of dyslipidaemias, hypertension, diabetes and other medical conditions must be optimised.
- HT should only be initiated for specific proven indications, provided there are no contraindications, and should be individualised according to each patient's needs. Women need to be fully informed of all risks and benefits regarding HT.

4.1 Indications for HT

- Treatment of VMSs and associated sleep disorders
- Symptomatic urogenital atrophy
- Prevention of bone loss in women with premature menopause or secondary amenorrhoea, and in women with osteopenia who are at risk of fracture.
- Treatment of osteoporosis in women in the age group 50 - 60 years and at risk of fracture, with or without VMSs.

4.2 Contraindications

HT should generally not be prescribed in the following circumstances:

- Current, past or suspected breast cancer
- Known or suspected oestrogen-dependent malignant tumours
- Undiagnosed genital bleeding
- Untreated endometrial hyperplasia
- Previous idiopathic or current VTE
- Known arterial CHD
- Active liver disease
- Porphyria cutanea tarda
- Thrombophilia.

4.3 General guidelines

- The duration of HT should be based on the indication for treatment.
- The indication for therapy should be reviewed on an annual basis. The decision whether to continue treatment for the relief of climacteric symptoms may be made by temporarily discontinuing treatment. If symptoms do not recur, HT does not have to be resumed. Topical therapy for relief of urogenital atrophy symptoms may need to be continued long-term.
- Only long-term therapy is effective for the prevention or treatment of osteoporosis. Long-term HT may be considered for bone effects, weighing benefit and risks against those of alternative therapies. At present there is no compelling evidence to restrict duration of treatment as long as treatment goals are maintained.
- HT should ideally be commenced during the 'therapeutic window of opportunity', especially if therapy is to maximise the beneficial impact on the cardiovascular system and the brain.
- Systemic HT should not be initiated in women older than 60 years of age.
- All oestrogens and progestogen formulations, including tibolone, should be considered similar in terms of clinical risks and benefits.
- These statements are applicable to all routes of administration, including transdermal application. The non-oral route avoids the first-pass effect in the liver and is preferable in women with hypertriglyceridaemia, liver disease, migraine, glucose intolerance and an increased risk of VTE, and in those who are smokers.
- Should EPT be required for longer than 5 years, it is recommended to convert from sequential HT to continuous combined HT.
- Low-dose therapy has been shown to be effective in symptom control and for prevention of bone loss; the principle of the lowest effective dose should therefore be adhered to.
- Low-dose and ultra-low-dose oestrogen preparations have fewer adverse effects than standard-dose therapy.
- Women with a history of stroke or transient ischaemic attack should be discouraged from initiating HT.
- Prior to commencing HT, all patients should be advised to undergo breast screening, including digital mammography (where available) and ultrasound examination. Ideally all menopausal women should have regular mammography.
- Abnormal bleeding is quite common in the first 6 months of using continuous combined HT, especially if the patient is less than 1 year post menopause. If abnormal bleeding or spotting persists for more than 6 months after initiating the HT, endometrial surveillance in the form of an endometrial sampler, determining endometrial thickness by saline hysterography, direct hysteroscopic assessment and biopsy, or a formal diagnostic dilatation and curettage should be considered.

- The use of bioidentical HT is not recommended. Studies on phyto-oestrogens and botanicals have shown inconsistent results. Most good studies show no clear benefit and some potential for harm. Further research is required in order to make firm recommendations.
- No published data exist on the use of traditional African medicines for menopausal symptoms.
- No therapy for menopausal symptoms should be initiated without proper clinical assessment, including breast and pelvic examination.
- If HT is contraindicated or not tolerated, effective alternatives for VMSs include SSRIs, SNRIs and gabapentin.
- Provided there are no contraindications, HT can be administered for more than 5 years. Once the decision has been taken to discontinue HT, the dose can be tapered over time before it is stopped totally.
- These statements are applicable to all routes of administration.

5. Conclusion

In order to assist the patient in making informed decisions about her menopausal management, every practitioner needs to be aware of the latest evidence regarding HT. It is anticipated that HT in conjunction with lifestyle modifications will remain the treatment of choice for acute menopausal symptoms for the immediate future. It is to be hoped that ongoing research will be able to identify a patient profile or method of application where longer use of HT is without risk. This will unlock the true potential of HT in the prevention and treatment of osteoporosis and allow new understanding of its role in the primary prevention of cardiovascular disease. Oestrogen receptors are ubiquitous in women. Consequently, even though HT impacts most positively on the management of acute menopausal symptoms, if used from the 'window of opportunity' its global benefits extend to a wide number of other organs, especially the cardiovascular system, skeletal system and brain. Provided the patient has no untoward complications and continues to be monitored appropriately, we believe that HT can be prescribed for long-term use, and need not be routinely stopped within 5 years or by age 65 years.

Concern about HT was accelerated by the WHI studies. Many of those data have since been reinterpreted and revisited. This is an ongoing process that may result in this position statement being reviewed and updated again in the future.

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