These new key messages are based on recent research findings on the risks associated with the use of Combined Hormone Replacement Therapy and Estrogen Replacement Therapy. They replace the advice published by the NZGG in May 2001.

**REVISED KEY MESSAGES**

**COMBINED HRT (estrogen with progestogen):**
- Combined HRT is not recommended for long-term use except in limited circumstances because the risks of breast cancer, venous thromboembolism (VTE), stroke and coronary heart disease (CHD) outweigh the benefits of fracture reduction and reduced risk of colorectal cancer.
- Combined HRT should not be used for the prevention or treatment of coronary heart disease or stroke.
- For women at high risk of osteoporosis, combined HRT may be considered only where other treatment is not tolerated and the woman is at low cardiovascular disease (CVD) risk and is fully informed of the risks of HRT.
- Combined HRT is effective for the control of troublesome menopausal symptoms of hot flushes and night sweats. However, even short-term use is associated with an increased risk of venous thromboembolism, stroke and coronary heart disease. HRT should only be used where menopausal symptoms are troublesome and women are fully informed of the risks.

**UNOPPOSED ESTROGEN THERAPY**
- Unopposed estrogen replacement therapy should only be used by women who have had a hysterectomy.
- Unopposed estrogen replacement therapy is effective for the control of menopausal symptoms of hot flushes, night sweats and vaginal dryness.
- Use of unopposed estrogen replacement therapy is associated with an increased risk of venous thromboembolism.
- Use of unopposed estrogen therapy may be associated with an increased risk of ovarian cancer.
- Use of unopposed estrogen therapy (for more than 5 years) is associated with an increased risk of breast cancer.
- It is not clear whether unopposed estrogen therapy increases the risk of CHD and stroke. Further definitive information is expected by 2005. In the meantime, women should be informed of the lack of evidence for CHD and stroke benefit or harm.

**PREMATURE MENOPAUSE**
- The new studies have not provided any data on the risk or benefits for women with premature or surgical menopause.

**TOPICAL ESTROGEN THERAPY**
- Topical vaginal estrogen (cream or ring) is effective for the control of vaginal dryness and is safe to use long-term in doses that do not cause systemic absorption.
NEW INFORMATION ABOUT COMBINED HORMONE REPLACEMENT THERAPY

The New Zealand Guidelines Group HRT Guideline Development Team reconvened in August 2002 to discuss the implications of the publication of three articles in JAMA on the 3rd and 17th of July on the New Zealand guideline entitled “The Appropriate Prescribing of HRT” which was published in May 2001.

The first article published the results of the Women’s Health Initiative (WHI) trial that had looked at the effects of combined HRT in healthy postmenopausal women aged 50 to 79. The trial, initially due to report in 2005, was stopped prematurely because of an excess risk of breast cancer in the HRT group and an increase in the global index that was designed to weigh up the risks and benefits of HRT.

The second study reported was the 6.8 year follow-up to the original Heart and Estrogen Replacement Study (HERS) study of HRT in women with known cardiac disease. The third study was a large cohort study of unopposed estrogen therapy use and the risk of ovarian cancer.

The HRT guideline recommendations and key messages have been adjusted to incorporate this new evidence and will be accessible on the NZGG website at a later date. The site is www.nzgg.org.nz

There is now more certainty about the risks and benefits of combined HRT. It is clear that combined HRT should not be used for the treatment or prevention of cardiac disease. The increased risk from heart disease, stroke and breast cancer means that combined HRT is no longer recommended as first line treatment for the prevention of osteoporosis and fractures. It was considered important that all women contemplating combined HRT for the treatment of menopausal symptoms be better informed of the risks of HRT and of alternatives for managing their symptoms. The other part of the WHI trial, assessing the effects of unopposed estrogen therapy in women who have had a hysterectomy, is continuing and results are expected by 2005. It is expected that the HRT Guideline will be fully updated in 2005. This will involve new literature searches and assessment of all the evidence that has emerged since publication in 2001.

For further information on these studies www.nhlbi.nih.gov/whi/htupg/index.htm and www.nlm.nih.gov/medlineplus/hormonereplacementtherapy.html

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GUIDANCE FOR PRACTITIONERS AND WOMEN

In view of the increased risks of combined HRT reported in the WHI study, women should only consider short-term use of HRT if they have problematic hot flushes and night sweats. This new information has implications for women presently using HRT as well as for future consultations with women who are considering HRT use.

The continued use of HRT should be reviewed by women and their doctors at the time of the next prescription or within 3 months whichever is sooner. In order for women to make fully informed decisions, review should include discussion of:

- indications for HRT use
- duration of treatment
- risks/benefits of treatment
- other prevention, treatment and management options.

Withdrawal from HRT

When the woman decides to stop taking HRT, practitioners should be proactive in assisting and advising women in their withdrawal from HRT.

Women who have been using HRT for flushes should be advised that slow withdrawal is important to avoid rebound flushes. The dose of estrogen should be gradually reduced over a period of 6 - 12 weeks continuing with the dose of progestogen until the estrogen is stopped. Some women may require a longer period of time to reduce the dose. Mild flushes that appear during the withdrawal of HRT may be self-limiting and of short duration.

It is not known how long it takes for the CVD and VTE risk to return to baseline after stopping combined HRT therapy. The increased risk of breast cancer disappears 5 years after unopposed estrogen therapy is discontinued. It is not known how long it takes for breast cancer risk to return to baseline after stopping combined HRT therapy.

Strategies for reducing HRT doses gradually

Using a lower dose HRT

A lower dose of the existing HRT can be used or change to a lower strength brand. This lower dose can be used for 2 - 3 weeks, then you should alternate the pills with one day on and one day off, then one pill followed by two pill-free days and so on until the reduction is complete.

Cutting HRT pills in half

Some HRT brands (eg, Trisequens) can be cut in half and the regimen above for lowering the dose followed.

Using a patch with reducing doses

The use of the matrix estrogen patch can be an effective way of reducing HRT. Small increments can be cut off the patch each week so lesser amounts of HRT are applied. This may be easier for some women than reducing oral HRT doses.

Women with premature menopause

There are limited data on the risks or benefits for women with premature or surgical menopause. These women should be reviewed for management of their symptoms and advised about bone protection. There is some consensus that women with premature menopause may be treated with HRT up until the age of 50. However, more data are required.