



Australian Government

**National Health and
Medical Research Council**

Making decisions:

Should I use hormone replacement therapy? (HRT)



Acknowledgement

This decision aid was developed using the decision support format of the Ottawa Health Decision Centre at the University of Ottawa and Ottawa Health Research Institute, Ontario, Canada.

We would like to acknowledge all the women and clinicians who reviewed and commented on earlier drafts of the decision aid.

We are extremely grateful for your help. Thank you.

Developed by the Sydney Health Decision Group, School of Public Health, The University of Sydney on behalf of the National Health and Medical Research Council (NHMRC).



The University of Sydney



© Commonwealth of Australia 2005

Paper-based publications

This work is copyright. Apart from any use as permitted under the *Copyright Act 1968*, no part may be reproduced by any process without prior written permission from the Commonwealth available from the Department of Communications, Information Technology and the Arts. Requests and inquiries concerning reproduction and rights should be addressed to the Commonwealth Copyright Administration, Intellectual Property Branch, Department of Communications, Information Technology and the Arts, GPO Box 2154, Canberra ACT 2601 or posted at <http://www.dcita.gov.au/cca>.

© Commonwealth of Australia 2005

Electronic documents

This work is copyright. You may download, display, print and reproduce this material in unaltered form only (retaining this notice) for your personal, non-commercial use or use within your organisation. Apart from any use as permitted under the *Copyright Act 1968*, all other rights are reserved. Requests for further authorisation should be directed to the Commonwealth Copyright Administration, Intellectual Property Branch, Department of Communications, Information Technology and the Arts, GPO Box 2154, Canberra, ACT 2601 or posted at <http://www.dcita.gov.au/cca>.

ISBN Print: 1864962429 Online: 1864962488

Endorsed March 2005

Cover photo courtesy of Les Irwig

Contents

Making decisions about HRT	1
Introduction	2
What is menopause?	3
How does menopause affect most women?	3
What is HRT?	5
Recommended advice	5
What types of hormones are available for menopausal symptoms?	6
Quality of research information	6
What are the benefits of HRT?.....	7
Tables	8 – 11
What are the risks of HRT?	13
Tables	14 – 17
Other possible health effects of HRT	18
What can I expect when stopping HRT?	19
Summary table of key points	20
HRT – Making the decision	22
Step 1: How troublesome are my menopausal symptoms?	23
Step 2: What risk factors do I have that might be worsened by HRT? ..	24
Step 3: How important to me are the benefits and risks?	25
Do I need more information to help me make my decision?	26
Where can I find out more?	27
Appendix A: Other options for the relief of menopausal symptoms	29
Appendix B: Scientific references	31
Appendix C: How did we determine the number of affected women for this decision aid?	36



Making decisions about HRT

This decision aid is specially designed for women:

- who are approximately 50 years old and
- who are considering hormone replacement therapy (tablets or patches containing oestrogen and progesterone) and
- who have troublesome hot flushes.

This decision aid is designed to be used with a health worker who is aware of your health and personal situation — it should not replace professional health advice. It is part of a package of information provided by the National Health and Medical Research Council (NHMRC), which includes a summary of the research on HRT and a booklet with information about the menopause and treatment options. Other documents in the package include *Hormone Replacement Therapy: Exploring the Options for Women* and *Hormone Replacement Therapy: A Summary of the Evidence for General Practitioners and other Health Professionals* and are available on the NHMRC website www.nhmrc.gov.au/

This decision aid is less useful for you if:

- your hot flushes are mild
- you have had a hysterectomy (oestrogen-only HRT is usually prescribed and is not covered in detail here)
- you have had breast cancer (you should seek special advice from your doctor)
- you have had your menopause at a very young age.

Introduction

It used to be thought that long-term use of hormone replacement therapy (HRT) gave women some major health benefits, but new research now shows this is not the case. The research has changed the way HRT is offered to women in Australia. If you are thinking about starting HRT, this booklet will tell you about the new research results to help you make your decision.

In this decision aid, you will learn about:

- menopause and how it affects most women
- types of hormones available for menopausal symptoms
- the benefits (pros) of HRT
- the risks and side effects (cons) of HRT
- steps to help you make your decision about HRT.

We suggest that you:

- 1 Read through the information about HRT (pages 7-21).
- 2 Fill in the worksheet (pages 23-26), to help you weigh up the pros and cons of HRT for you personally.
- 3 Use the personal worksheet to discuss your options with a health professional before you make a final decision.

What is menopause?

Menopause is the time in a woman's life when she stops having periods (also known as the climacteric, or peri-menopause). Women may notice changes in their body during this time; these are called symptoms of menopause.

Around the time of menopause, a woman's ovaries slowly stop making the hormones that prepare the body for pregnancy (oestrogen and progesterone). Periods may get heavier or lighter, and may become more or less frequent, until they stop altogether. Often this happens slowly, but some women's periods stop quite quickly, without warning.¹

How does menopause affect most women?

The symptoms of menopause can vary greatly between women. Some women will have unpleasant and troublesome symptoms while for others, the menopause will have little effect. The number of symptoms and how long they last varies a lot too. Some common problems around this time are shown below.²

- Hot flushes
- Heavy periods
- Headaches and migraines
- Back pain
- Mood swings
- Anxiety
- Leaking urine
- Vaginal dryness
- Night sweats
- Irregular periods
- Severe tiredness
- Stiff or painful joints
- Difficulty sleeping
- Depression
- Concentration problems
- Painful intercourse

^{1, 2} Represents referencing techniques which are listed on page 31.

Research in Australian women shows that menopause symptoms last 4 years on average.¹ However, it is important to point out that many women who are *not* menopausal also experience some of these symptoms from time to time. So it is not always clear how much is due to menopause alone.

HRT can help relieve some of the unpleasant symptoms of menopause. However, new research shows there are also important health risks linked to taking HRT. This booklet describes the risks and benefits of HRT.



What is HRT?

Hormone replacement therapy – HRT (also known as ‘hormone therapy’) replaces the hormones that the ovaries stop making at menopause. HRT is most often taken in the form of *tablets*. *Skin patches*, *gels* and *slow-release pellets* (implanted under the skin) are also widely used, and a *nasal spray* is also available. For some women, *vaginal tablets* or *creams* may also be an option. HRT must be prescribed by a doctor. It is not available over the counter.



Recommended advice

The Australian Drug Evaluation Committee, a group that provides independent, scientific advice on drugs to the Australian Government, reviewed all recent scientific information on HRT use.³ They now advise women to consider using HRT only to relieve serious hot flushes and for no longer than is necessary to achieve this. HRT should not be used for the prevention of osteoporosis and is no longer thought to be protective against heart disease. In fact, there may be an increased risk of heart disease, particularly in the first year of HRT use. You should review your HRT use each year with your doctor, weighing up the benefits of symptom relief against the risks. **For long-term use and for women without severe symptoms, the risks of HRT appear to outweigh the benefits.**

What types of hormones are available for menopausal symptoms?

This booklet focuses on daily oestrogen and progestogen and cyclical oestrogen and progestogen. These are the most commonly used types of HRT for women who have not had a hysterectomy.⁴ HRT is available in many forms:

- *Daily oestrogen and progestogen* (continuous combined HRT) – this is usually prescribed for women who have had no period for at least 12 months. It may be taken via patches or tablets.
- *Cyclical oestrogen and progestogen* (the synthetic form of *progesterone*) – this involves taking oestrogen daily and adding progestogen for 10–14 days each month (patches or tablets).
- *Tibolone* – this is an artificial tablet form of oestrogen and progestogen.

For more information about other ways to relieve menopausal symptoms see Appendix A (page 29) in this book and the other booklet in this series called *'Hormone Replacement Therapy: Exploring the Options for Women'*.

Quality of research information

Research studies vary in quality and this affects how confident we can be in their results. The quality of a study depends on the design of the study and how it was carried out.

Throughout this booklet we have used Stars to show how confident we are about each piece of research information presented.

- ★★ Two gold stars indicates information that has been **confirmed** by results from well-designed and conducted research.
- ★ One silver star indicates information that is **suggested but not confirmed** because we are **less** confident in the quality of the research.

What are the benefits of HRT?

HRT can reduce the severity of some menopause symptoms. It may also reduce the risk of some serious illnesses. It is unclear how long this effect lasts after stopping HRT.

Benefits of HRT:

Taking HRT means you have a reduced chance of:

Menopause symptoms

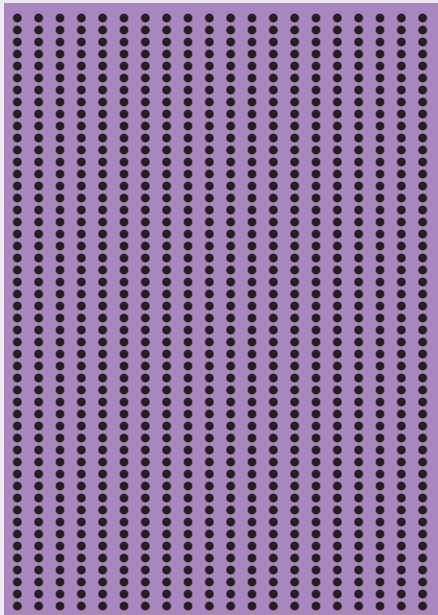
- Hot flushes^{5,6} ★★
- Night sweats^{5,7} ★★
- Sleep disturbance⁷⁻¹⁰ ★★

Bowel cancer¹¹ ★★

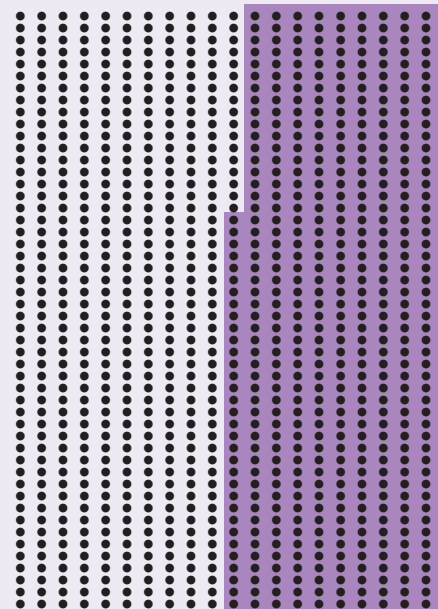
Bone fractures¹¹ ★★

The diagrams on the following pages show how many women are likely to experience the main benefits of HRT compared to women who are not.

Of 1000 women in their 50s who **DO NOT** take HRT:

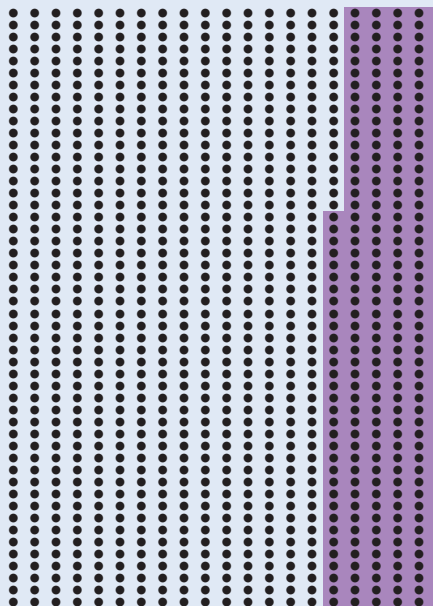


Imagine **1000** women who are experiencing troublesome **hot flushes**.^{1,2} Remember that this booklet is designed for women who have troublesome hot flushes and are thinking about taking HRT to relieve these.



If these 1000 women took a placebo tablet (a 'fake' pill with no active ingredients) only **483** would still have **hot flushes** after one year. In other words, hot flushes will resolve in many women within one year without any form of treatment.

Of 1000 women in their 50s who **DO** take HRT¹¹:

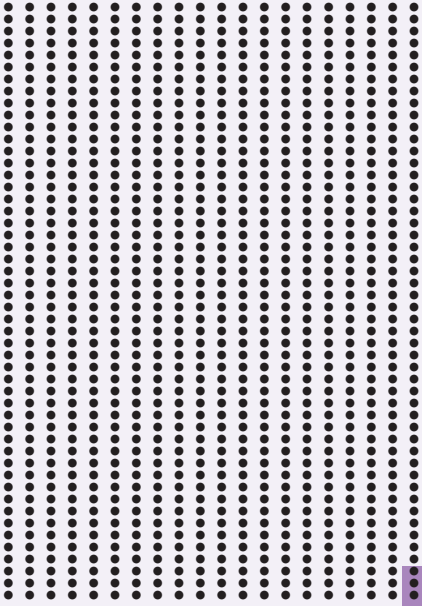


If the 1000 women took HRT only about **233** women will still have **hot flashes** after 12 months. Most get immediate relief from their symptoms.

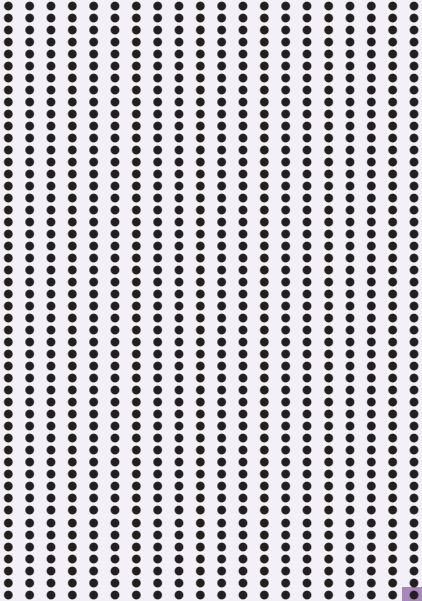
In other words, HRT helps most women's hot flashes

¹¹ This information comes from a ★★ two gold star study in which women took HRT for an average of 4 years and outcomes were measured over 5 years

Of 1000 women in their 50s who **DO NOT** take HRT, over five years:



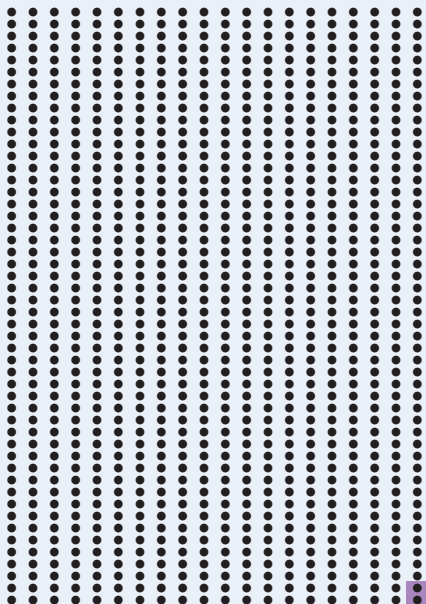
3 women may get
bowel cancer



1 woman may have
a **hip fracture**

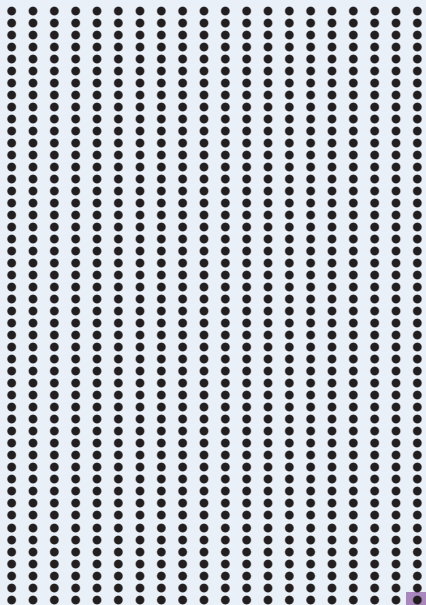


Of 1000 women in their 50s who **DO** take HRT, over five years¹¹:



2 women may get **bowel cancer**

In other words, 1 less case of bowel cancer in the HRT group



Less than one woman (0.67) may have a **hip fracture**

In other words, less than one fewer hip fracture in HRT users

¹¹ This information comes from a ★★ two gold star study in which women took HRT for an average of 4 years and outcomes were measured over 5 years





What are the risks of HRT?

Research shows the use of HRT may also have harmful effects for some women. These include some nuisance symptoms and also increased risk of some serious illnesses. It is unclear how long these risks last after stopping HRT.

Risks:

If you take HRT you have an increased chance of:

Breast cancer ¹¹ ★★

Abnormal mammogram during screening ¹² ★★

Stroke ¹¹ ★★

Serious blood clots (thromboembolic disease) ¹¹ ★★

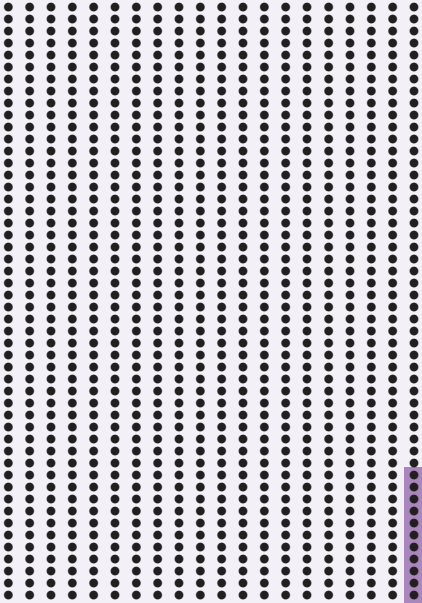
Breast tenderness ⁸ ★★

Spotting or the return of periods ¹³ ★★

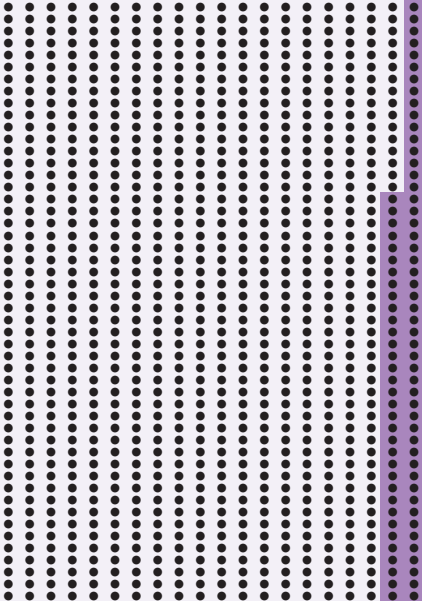
NB. It is important to note 2 yearly mammographic screening for breast cancer is recommended for all women aged 50-69 years. Most women who have an abnormal mammogram do not have cancer on further testing. In other words, only a small number of those who need follow-up after an abnormal mammogram actually have cancer.

The diagrams over the page show how many women are likely to experience the main risks of HRT compared to women who do not.

Of 1000 women in their 50s who **DO NOT** take HRT, over five years:



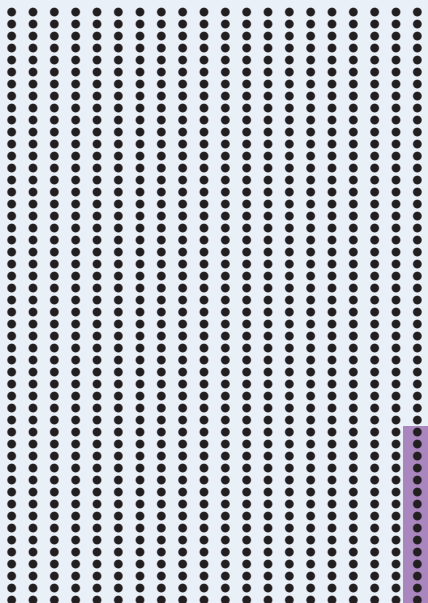
11 women may get **breast cancer**



84 women may have an **abnormal mammogram** if screened twice during this period (ie every 2 years)

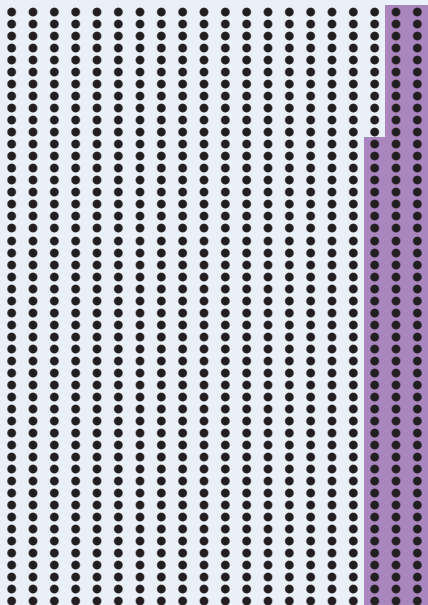


Of 1000 women in their 50s who **DO** take HRT, over five years¹¹:



15 women may get **breast cancer**

In other words, 4 extra cases of breast cancer in HRT users

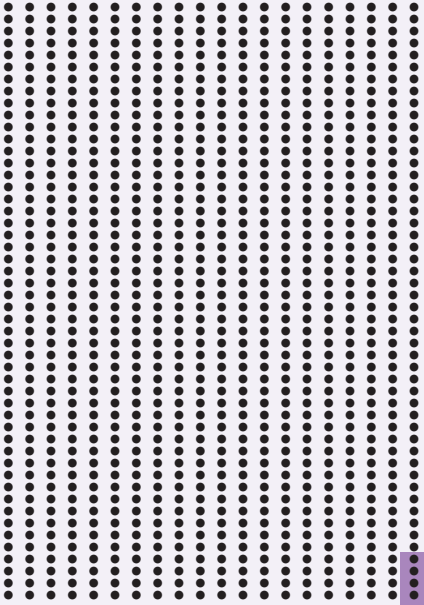


139 women may have an **abnormal mammogram** if screened twice during this period (ie every 2 years)

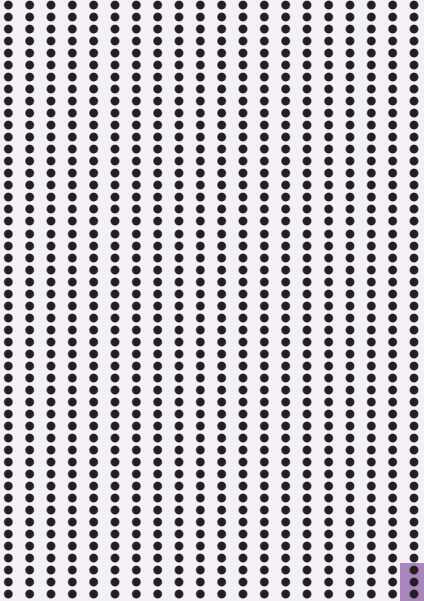
In other words, 55 extra abnormal mammograms in HRT users

¹¹ This information comes from a ★★ two gold star study in which women took HRT for an average of 4 years and outcomes were measured over 5 years

Of 1000 women in their 50s who **DO NOT** take HRT, over five years:



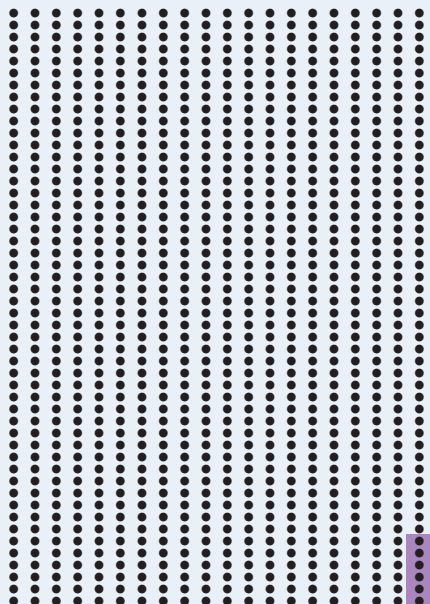
4 women may have a **stroke**



3 women may develop **serious blood clots**

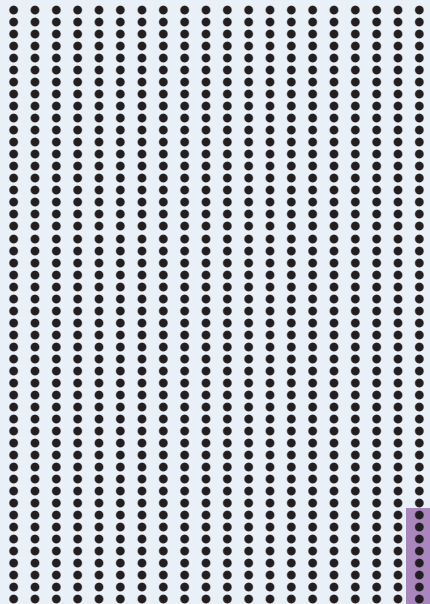


Of 1000 women in their 50s who **DO** take HRT, over five years¹¹:



6 women may have a **stroke**

**In other words,
2 extra cases of stroke
in HRT users**



8 women may develop **serious blood clots**

**In other words, 5 extra
cases of serious blood clots
in HRT users**

¹¹ This information comes from a ★★ two gold star study in which women took HRT for an average of 4 years and outcomes were measured over 5 years

Other possible health effects of HRT

Other health effects have been linked to HRT. Here, we describe what the latest research shows us and how confident we can be in the results. (Remember this book talks about cyclical oestrogen and progesterone, and daily oestrogen and progesterone only).

HRT has been found to have no effect on:

Uterine cancer¹⁴ ★★

Ovarian cancer¹⁴ ★★

Mental health⁷ ★★

General health⁷ ★★

Weight gain^{8, 15} ★★

Satisfaction with sex⁷ ★★

NB: vaginal oestrogens may improve vaginal dryness. See Appendix A

It is unclear whether HRT affects:**

Heart attacks^{† 11} ★★

Urinary symptoms¹⁶ ★★

Memory loss and dementia^{†† 17, 18} ★★

Improvements to skin and hair

Headache and migraine⁸ ★★

Nausea (feeling sick) and vomiting⁸ ★★

Fluid retention (bloating stomach)⁸ ★★

** Studies are conflicting, of poor quality or lacking, and we can't really be sure of the effect.

Extra comments about HRT and heart attacks

† Recent research shows that there is no protective effect against heart attacks when using HRT. There may be an increase in risk of heart attack with HRT, particularly in the first year.¹⁹

Extra comments about HRT and dementia

†† Recent research also showed that HRT did not prevent memory loss. In fact dementia was increased in 65-79 year old women taking HRT. It is possible that an extra 2 cases of dementia might occur in 1000 women taking HRT in this older age group. HRT is now only recommended for a short time in younger women with menopausal symptoms. It seems unlikely that memory loss would be prevented by HRT use and we can't be sure whether an increase in dementia might occur in younger women too.¹⁸

What can I expect when stopping HRT?

Most women will have some natural improvement in their hot flashes after 12 months,⁷ and troublesome symptoms usually resolve after several years.¹ A few women will have symptoms for longer. It seems that if your body has naturally gone through menopause, then stopping HRT will probably not cause your hot flashes to return.²⁰

There is also some evidence that breast cancer risk is related to current HRT use and how long you take it. Breast cancer risk is likely to return to near normal within several years of stopping HRT.²¹ Similarly, the risk of having a positive mammogram returns to near normal after several years.²² It also takes less than five years for the protective effect against fractures to be lost.^{23, 24}

You should talk to your doctor about how best to stop HRT.



Summary table of key points

BENEFITS
Reduced chance of:
Menopause symptoms:
■ Hot flushes
<i>767 women out of 1000 will get relief from hot flushes</i>
■ Night sweats
■ Sleep disturbance
Bowel cancer
<i>1 fewer case in 1000 women over 5 years</i>
Hip fractures
<i>Less than 1 fewer hip fractures in 1000 women over 5 years</i>

RISKS
Increased chance of:
Breast cancer
<i>4 extra cases in 1000 women over 5 years</i>
Abnormal mammogram
<i>55 extra abnormal mammograms women in 1000 women if screened twice during 5 years (ie every 2 years)</i>
Stroke
<i>2 extra cases in 1000 women over 5 years</i>
Serious blood clots
<i>5 extra cases in 1000 women over 5 years</i>
Breast tenderness
Spotting or the return of periods

Summary table of key points (continued)

NO EFFECT ON:

Uterine cancer

Ovarian cancer

Mental health

General health

Weight gain

Satisfaction with sex

UNCLEAR RESEARCH FINDINGS ABOUT:

Heart attacks

Memory loss and dementia

Improvements to skin and hair

Headache and migraine

Urinary symptoms

Nausea and vomiting

Fluid retention

HRT – Making the decision

What do I do now?

To help you decide whether to start HRT, we suggest you follow the steps listed below:

- Step 1 Think about how troublesome your menopausal symptoms are.

- Step 2 Think about your reasons for not taking HRT.
 Consider your own personal risk factors that may be worsened by HRT.

- Step 3 Weigh up the importance of the benefits and risks of HRT for you.



Step 1: How troublesome are my menopausal symptoms?

HRT is only recommended for the relief of troublesome menopausal symptoms such as hot flushes, night sweats and sleep disturbances. HRT is no longer recommended for preventing heart attacks or osteoporosis. The following are menopausal symptoms that can be relieved by HRT. Tick the box next to the ones that trouble you and are important for you to get relief from. The more boxes you tick the more you are troubled by the symptoms.

Note: If you don't tick any boxes then your symptoms are probably not serious enough to need HRT.

Benefits of taking HRT

Troublesome menopause symptoms*

- Hot flushes
- Night sweats
- Sleep disturbance

* See Appendix A on page 29 for alternatives to HRT.

Step 2: What risk factors do I have that might be worsened by HRT?

When thinking about reasons for not taking HRT you should think about your own personal risk factors. The list below includes factors that increase your risk of breast cancer, stroke and blood clots. Please tick the boxes that are relevant for you. The more boxes you tick, the greater your risk. Taking HRT increases your chance of these occurring.

RISKS OF TAKING HRT

Risk of breast cancer

- Personal history of breast cancer
- Family history of breast cancer
- Previous biopsies showing abnormal breast cells
- Never had children
- First child after 30
- First period at early age

Risk of stroke

- Family history of stroke
- Previous Transient Ischemic Attack (TIA) or stroke
- Atrial fibrillation
- High blood pressure
- Smoker
- Diabetes
- Heart disease

Risk of blood clots

- A previous blood clot
- Family history of blood clots
- Cancer
- Heart disease
- Being inactive for long periods
- Blood disorders that interfere with clotting
- Recent surgery

Step 3: How important to me are the benefits and risks?

Now that you've thought about your personal risk factors for and against HRT, consider which of these is most **important** to you. People often value risks differently so there are no right or wrong answers to this section. Please show how important the benefits and risks of HRT are to you by shading the circles beside the reasons. More shading shows more importance, for example:

Extremely important to you: Not at all important ●●●●○ Extremely important
 Not important to you: Not at all important ●○○○○○ Extremely important

BENEFITS OF TAKING HRT	RISKS OF TAKING HRT
<p>Relief from menopause symptoms (hot flushes, night sweats, sleep disturbance, irregular periods)</p> <p>Not at all important ○○○○○○ Extremely important</p>	<p>Increasing my risk of breast cancer and/or an abnormal mammogram</p> <p>Not at all important ○○○○○○ Extremely important</p>
<p>Other reasons for taking HRT important to you _____</p> <p>Not at all important ○○○○○○ Extremely important</p>	<p>Increasing my risk of stroke</p> <p>Not at all important ○○○○○○ Extremely important</p>
	<p>Increasing my risk of blood clots</p> <p>Not at all important ○○○○○○ Extremely important</p>
	<p>Increasing my risk of nuisance symptoms (breast tenderness, spotting/periods returning)</p> <p>Not at all important ○○○○○○ Extremely important</p>
	<p>Other reasons for NOT taking HRT important to you _____</p> <p>Not at all important ○○○○○○ Extremely important</p>

Which way are you leaning in your decision?

Fill in one of the squares below to indicate which way you are leaning in your decision.

HRT			Not sure						No HRT

Do I need more information to help me make my decision?

Every woman's needs and health concerns are different. Before making a final decision, use this decision aid to help you discuss the options with your doctor or other health professional.

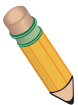
Your notes



Write in the space below any questions you would like to ask your doctor

My questions

Your doctor's notes



Your doctor or other health professional may wish to summarise some of the discussion you have about HRT

Notes from doctor or other health professional

Where can I find out more?

Good quality information about hormone replacement therapy and the menopause can be found at:

Suggested websites

Websites that you may find useful include the following:

- www.healthinsite.gov.au – the website of Health*Insite*, an Australian Government initiative that aims to improve the health of Australians by providing easy access to quality information about human health. There are over 40 articles and resources on menopause at www.healthinsite.gov.au/topics/Menopause
- www.menopause.org.au – the website of the Australasian Menopause Society, which provides both professional and community information
- www.imsociety.org – the website of the International Menopause Society
- www.nhmrc.gov.au/ – the NHMRC website, which includes the HRT Literature Review which informed this booklet, *Hormone Replacement Therapy: A Summary of the Evidence for General Practitioners and other Health Professionals*, and *Hormone Replacement Therapy: Exploring the Options for Women*
- www.menopause.org – the website of the North American Menopause Society. It also provides information for women and for professionals, although its strong North American perspective may not always be directly relevant to women in Australia
- www.pofsupport.org – a website for women with premature ovarian failure, which provides useful information and support for women with a specific range of menopausal issues
- www.jeanhailes.org.au – the website of the Jean Hailes Foundation, based in Melbourne, which provides information on women's health care, both for women and professionals, especially in the field of menopause. The Foundation's 'Early Menopause Australia Support Group' can be contacted by e-mail at: early_menopause_australia@hotmail.com
- www.womhealth.org.au – the website for Women's Health Queensland Wide, a not-for-profit, government-funded health, information and education centre. For menopause information, go to www.womhealth.org.au/healthinformation.html

- www.betterhealth.vic.gov.au – the website of the Better Health Channel, established by the Victorian Government. It includes a number of articles on menopause, produced in consultation with the Jean Hailes Foundation. Go to www.betterhealth.vic.gov.au/bhcv2/bhcarticles.nsf/pages/hc_reproductivesystem_menopause
- www.mhcs.health.nsw.gov.au – the website of the NSW Multicultural Health Communication Services, providing multilingual information on a wide range of topics as well as links to other sites and resources. For menopause information in 10 languages, go to www.mhcs.health.nsw.gov.au/health-public-affairs/mhcs/publications/800.html
- www.fpwa-health.org.au – the website of Family Planning Western Australia, and the only Australian family planning site that provides information on menopause, at www.fpwa-health.org.au/menopause.htm. It also provides information on various other sexual health issues
- www.osteoporosis.org.au – the website for Osteoporosis Australia
- www.whv.org.au – the website of Women’s Health Victoria, a women’s health promotion, advocacy and health information service. The website includes a menopause fact sheet and list of resources on menopause. Follow the links from www.whv.org.au/health_issues/menopause.htm
- www.tased.edu.au/tasonline/twhn/ – the website of the Tasmanian Women’s Health Network
- www.phimr.monash.edu.au – the website of the Prince Henry’s Institute, at Monash Medical Centre in Melbourne. The site includes fact sheets on HRT and menopause
- www.bci.org.au – the website of the NSW Breast Institute

Suggested reading

Hormone Replacement Therapy: Exploring the Options for Women

Hormone Replacement Therapy: A Summary of the Evidence for General Practitioners and other Health Professionals

Hormone Replacement Therapy: A Comprehensive Literature Review and all are available on the NHMRC website

www.nhmrc.gov.au/

Appendix A: Other options for the relief of menopausal symptoms

It is important to note that there may be health risks linked to using the products listed below. Many of these have been studied less than HRT, and the benefits and risks are unclear.

Hot flushes/Night sweats

Option	Number of women in 1000 whose hot flushes lessen
Hormone replacement therapy (HRT)	767 women
Lifestyle options (eg cooler rooms, layered clothing, paced abdominal breathing, exercise, avoiding caffeine, spicy food and hot drinks)	Some benefit for mild symptoms with no associated risks
Phytoestrogens from soy, red clover	Phytoestrogens available as soy foods, soy extracts and red clover extracts do not improve hot flushes ²⁵
Dong quai, evening primrose oil, ginseng, acupuncture, magnet therapy.	Single studies have found no benefit
Venlafaxine (An antidepressant that also helps hot flushes. Other antidepressants such as paroxetine and fluoxetine have also shown some benefit)	600 women
Clonidine (A blood pressure treatment that also helps hot flushes)	300 to 400 women
Placebo tablet ('fake' pill)	530 women
Bioidentical hormones ('troches') (Lozenges prepared by compounding pharmacist on doctor's prescription)	No studies on efficacy or safety
Black cohosh	Herb used for the relief of some menopausal symptoms.

Sleep disturbance

Other options are:

- Practise good sleep habits
www.stanford.edu/~dement/howto.html
- Short term use of medications such as mild sedatives or valerian. Some of these medications are habit forming and some have side effects. Discuss the pros and cons with your health practitioner.

Problems with memory and concentration

Other options are:

- Some studies suggest benefit from Ginkgo Biloba.²⁶

Mood swings

Other options are:

- Antidepressants
- St. John's Wort has been shown to be effective in improving symptoms of mild or moderate depression by 60 to 70%.²⁷ (ie out of 1000 women with depression, 600 will be improved by St John's Wort). It has the potential for drug interactions, but also has fewer side effects than many antidepressants. Do not use St. John's Wort without first consulting your health care practitioner.

Vaginal dryness/painful intercourse

Other options include:

- Vaginal moisturizers
- Lubricants for use during sex
- Vaginal oestrogen creams, pessaries and tablets.

Preventing broken bones from osteoporosis

Your decision should include considering other options such as:

- Calcium, Vitamin D, weight bearing exercise, stopping smoking
- Medications such as the bisphosphonates and Selective Estrogen Receptor Modulators (SERMS) (eg Raloxifene®).

Appendix B: Scientific references

If you would like to read some of the original research, go to your favourite search engine (eg www.google.com.au) and type in 'PubMed'. This will take you to the US National Library of Medicine, which hosts a free version of the medical database 'Medline'. Type in the surname of the first author AND a keyword from the title and you should be able to find the article of interest. (NB: Not all journal articles are available in their complete form free of charge).

- ★ 1 Guthrie J, Dennerstein L, Taffe J, Donnelly V. Health care-seeking for menopausal problems. *Climacteric* 2003;6(2):112-117.
- ★ 2 Mishra G, Lee C, Brown W, Dobson A. Menopausal transitions, symptoms and country of birth: the Australian Longitudinal Study on Women's Health. *Australian and New Zealand Journal of Public Health* 2002;26:563-70.
- 3 Australian Drug Evaluation Committee. Advice of Chair of Expert Advisory Group on HRT Hormone Replacement Therapy.
- 4 Australian Bureau of Statistics. National Health Survey. Summary of Results: 2001 ABS Catalogue number 4364.0, 2001.
- ★★ 5 MacLennan A, Lester S, Moore V. Oral oestrogen replacement therapy versus placebo for hot flushes (Cochrane Review). *The Cochrane Library* 2000;1.
- ★★ 6 Greendale G, Reboussin B, Hogan P, Barnabei V, Shumaker S, Johnson S, *et al.* Symptom relief and side effects of postmenopausal hormones: Results from the postmenopausal estrogen/progestin interventions trial. *Obstetrics and Gynaecology* 1998;92:982-8.

- ★★ 7 Hays J, Ockene J, Brunner R, Kotchen J, Manson J, Patterson R, *et al.* Effects of estrogen plus progestin on health-related quality of life. *New England Journal of Medicine* 2003;348(19):Hays1-Hays-16.
- ★★ 8 Barnabei V, Grady D, Stovall D, Cauley J, Lin F, Stuenkel C, *et al.* Menopausal symptoms in older women and the effects of treatment with hormone therapy. *Obstetrics and Gynecology* 2002;100(6):1209-1218.
- ★★ 9 Strickler R, Stovall DW, Merritt D, Shen W, Wong M, Silfen SL. Raloxifene and estrogen effects on quality of life in healthy postmenopausal women: A placebo-controlled randomized trial. *Obstetrics and Gynecology* 2000;96(2):359-365.
- ★★ 10 Wiklund I, Karlberg J, Mattsson LA. Quality of life of postmenopausal women on a regimen of transdermal estradiol therapy: A double-blind placebo-controlled study, vol. 168, no. 3 I, pp. 824-830. *American Journal of Obstetrics and Gynecology* 1993;168(31):824-830.
- ★★ 11 Women's Health Initiative. Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women. *JAMA* 2002;288:321-333.
- ★★ 12 Cheblowski R, Hendrix S, Langer R, Stefanick M, Gass M, Lane D, *et al.* Influence of Estrogen plus Progestin on Breast Cancer and Mammography in Healthy Postmenopausal Women. *JAMA* 2003;289(24):3243-3253.
- ★★ 13 Lethaby A FC, Sarkis A, Roberts H, Jepson R, Barlow D. Hormone replacement therapy in postmenopausal women: endometrial hyperplasia and irregular bleeding (Cochrane Review). *The Cochrane Library* 2004;Issue 2.
- ★★ 14 Anderson G, Judd H, Kaunitz A, Barad D, Beresford S, Pettinger M, *et al.* Effects of Estrogen plus progestin on gynaecologic cancers and associated diagnostic procedures. *JAMA* 2003;290:1739-1748.

- ★★ 15 Norman R, Flight I, Rees M. Oestrogen and progestogen hormone replacement therapy for peri-menopausal and post-menopausal women: weight and body fat distribution. *Cochrane database of systematic reviews* 2000.
- ★★ 16 Cardozo L, Bachmann G, McClish D, Fonda D, Birgerson L. Meta-analysis of estrogen therapy in the management of urogenital atrophy in postmenopausal women: Second report of the hormones and urogenital therapy committee. *Obstetrics and Gynecology* 1998;92(4):722-727.
- ★★ 17 Rapp S, Espeland M, Shumaker S, Henderson V, Brunner RL, Manson J, *et al.* Effect of estrogen plus progestin on global cognitive function in postmenopausal women. *JAMA* 2003;289(2663-2672).
- ★★ 18 Shumaker S, Legault C, Rapp S, Thal L, Wallace R, Ockene J, *et al.* Estrogen plus progestin and the incidence of dementia and mild cognitive impairment in postmenopausal women. *JAMA* 2003;289(201):2651-2662
- ★★ 19 Manson J, Hsia J, Johnson KC, Rossouw J, Assaf A, Lasser N, *et al.* Estrogen plus progestin and the risk of coronary heart disease. *New England Journal of Medicine* 2003;349(6):523-34.
- ★★ 20 Hammar M, Ekblad S, Lonnberg B, Berg G, Lindgren R, Wyon Y. Postmenopausal women without previous or current vasomotor symptoms do not flush after abruptly abandoning estrogen replacement therapy. *Maturitas* 1999;31(2):117-22.
- ★ 21 Million Women's Study Collaborators. Breast cancer and hormone-replacement therapy in the Million Women Study. *The Lancet* 2003;362:419-27.
- ★ 22 Banks E, Reeves G, Beral V, Bull D, Crossley B, Simmonds M, *et al.* Impact of use of hormone replacement therapy on false positive recall in the NHS breast screening programme: results from the million women study. *BMJ* 2004;328:1291-2.

- ★ 23 Yates J, Barrett-Connor E, Barlas S, Chen YT, Miller P, Siris E. Rapid loss of hip fracture protection after estrogen cessation: evidence from the National Osteoporosis Risk Assessment. *Obstetrics & Gynaecology* 2004;103(3):440-6.
- ★ 24 Banks E, Beral V, Reeves G, Balkwill A, Barnes I. Fracture incidence in relation to the pattern of use of hormone therapy in postmenopausal women. *JAMA* 2004;291: 2212-2220.
- ★★ 25 Krebs E, Ensrud K, MacDonald R, Wilt T. Phytoestrogens for Treatment of Menopausal Symptoms: A systematic review. *Obstetrics and Gynaecology* 2004;104(4):824-36.
- ★★ 26 Birks J, Grimley EV, Van Dongen M. Ginkgo Biloba for cognitive impairment and dementia (Cochrane Review). *The Cochrane Library*, Issue 2 2004.
- ★★ 27 Linde K, Barner M, Egger M, Mulrow C. St John's wort for depression (Cochrane Review). *The Cochrane Library* Issue 2 2004.
- 28 Australian Institute of Health & Welfare. National Cancer Clearing House: Interactive Data Cubes, 2000.
- 29 Australian Institute of Health & Welfare. National Hospital Morbidity Database: Interactive Data Cubes. 2000.
- 30 Barratt A, Howard K, Irwig L, Salkeld G, Houssami N. Outcomes of screening mammography: information to support informed choices. (*in press*) 2004.
- 31 Australian Bureau of Statistics. National Health Survey. Summary of Results Catalogue number 4364.0, 2001.
- 32 Glazsiou P. Meta-analysis adjusting for compliance: The example of screening for breast cancer. *Journal of Clinical Epidemiology* 1992;45(11):1251-1256.
- 33 Glasziou P, Irwig L. An evidence-based approach to individualising treatment. *British Medical Journal* 1995;311:1356-1359.

- 34 Guyatt G, Rennie D. *Users' Guides to the Medical Literature: Essentials of Evidence-Based Clinical Practice.*: AMA Press, 2002.
- 35 Schmid C, Lau J, McIntosh M, Capelleru J. An empirical study of the effect of the control rate as a predictor of treatment efficacy in meta-analysis of clinical trials. *Statistics in Medicine* 1998;17:1923-1942.

Appendix C: How did we determine the number of affected women for this decision aid?

How did we determine the effect of HRT on menopausal symptoms?

This decision aid is designed for women who have troublesome hot flushes. The Women's Health Initiative (WHI) study showed that taking HRT would reduce the severity of hot flushes in 76.7% of 50-54 year olds after 12 months.⁷ The same study found that 51.7% women taking a placebo had fewer hot flushes after 12 months. The WHI reported no association between menopausal symptoms and heart disease, stroke and thrombosis. This model assumes no association between menopausal symptoms and breast cancer, bowel cancer and osteoporosis.

How did we determine the risk of developing key outcomes without HRT?

The main outcomes of interest in this decision aid (apart from symptom relief) are bowel cancer, hip fracture risk, breast cancer, abnormal mammograms, stroke and thromboembolic disease. Note: heart disease was not included as the 95% confidence intervals (except for first year of use) included the null value.

We estimated the 'natural' risk of developing these outcomes in average Australian women aged 50 years, by obtaining figures from a number of government registers and databases. For breast and bowel cancer risks, these were obtained from the National Cancer Statistics Clearing House,²⁸ for fracture, stroke and thromboembolic disease these were obtained from the National Hospital Morbidity Database²⁹ and for mammographic screening outcomes we used a model that we developed using data from BreastScreen Australia.³⁰ For consistency, we used cancer data for 2000 and hospital morbidity data for 1 July 2000 to 30 June 2001. Menopausal symptom studies were published in 1999 and 2002.

Definitions of the above outcomes were matched as closely as possible to the WHI study, using International Classification of Diseases (ICD-10) codes. Bowel cancer included cancer of the colon, rectum and rectosigmoid junction; stroke included haemorrhagic and ischaemic causes; and thromboembolic disease included pulmonary embolus, phlebitis and thrombophlebitis of deep structures of lower extremities.

We know from a survey on 40,000 women (the National Health Survey 2001³¹) that approximately 30 per cent of Australian women reported that they took HRT in 2001. Since our estimates in Table 1 are calculated from a population in 2000, who were a mixture of users and non-users of HRT, we needed to 'adjust' our figures to reflect the rates only in women who were *not* HRT users.

We did this using the following formula:

$$x = I / [p*HR + (1-p)]$$

Where:

$$I = py + (1-p)x$$

$$y = \text{incidence in HRT users} = x*HR$$

$$x = \text{incidence in HRT non-users}$$

$$HR = \text{hazard ratio} = y/x$$

$$p = \text{proportion of people using HRT}$$

Having calculated the chance of developing each outcome in non-HRT users aged 50-54 years over one year, we then estimated the cumulative chance of developing these over five years, using the formula below. A summary of the estimates is shown in Table 1.

$$\text{Cumulative risk} = 1 - e^{-\text{cumulative rate}}$$

Table 1: Risk of developing main outcomes in 1000 Australian women aged 50 yrs without HRT over the next five years

Outcome	No. of cases over the next five years in 1000 non-users of HRT aged 50 years
Hot flushes	483*
Breast cancer	11
Colorectal cancer	3
Abnormal mammograms	84
Stroke	4
Serious blood clots	3
Hip fractures	<1

* Note: we assume that all 1000 women considering HRT have troublesome hot flushes and that this will reduce to 483 in 1000 after one year even if they all take a placebo tablet.⁷ After five years, most women have no further hot flushes, regardless of HRT.

How did we calculate the risk of developing key outcomes with HRT?

The WHI trial was stopped after 5.2 years, with approximately 30% of participants stopping HRT at some time during the trial. We communicated personally with the WHI investigators and found that the average duration of HRT use in the trial was 4.4 years. We used a formula to adjust for the fact that not all women in the trial took HRT as prescribed.³² We therefore based our figures on the assumption that women take HRT regularly.

These ‘compliance-adjusted ratios’ were derived from the original WHI hazard ratios published in 2002¹¹ to give us estimates of the effects of HRT if taken as prescribed. These were directly applied to the ‘natural’ 5-year risk without HRT and the results are summarised in Table 2. Although the mean age of the WHI was 62 years, there was no interaction with age for the main outcomes. We have therefore applied the relative increase or decrease in risk to the appropriate baseline risk for Australian women aged 50 years.³³⁻³⁵

Table 2: Risk of developing main outcomes in 1000 Australian women aged 50 years with HRT over the next five years

Outcome	No. of cases over the next five years in 1000 users of HRT aged 50 years
Hot flushes	233**
Breast cancer	15
Colorectal cancer	2
Abnormal mammograms	139
Stroke	6
Serious blood clots	8
Hip fractures	0.67

** The WHI conducted a subanalysis on 50-59 year old participants and showed a 76.7% reduction in vasomotor symptoms at 12 months in HRT users compared with a 51.7% in placebo users.⁷

