

## Assumptions and calculations

This information is only for those who want to know how the numbers were chosen and from where the numbers were taken for the risk estimates (the data sources, assumptions and calculations). You do not need to read it to use the calculator.

The following are the data sources, assumptions and calculations used by the School of Public Health in developing the HRT risks and benefits calculator. These are best estimates based on data available at the time this web page was published.

### Step 1

The following Australian information was collected:

- **Age-specific disease incidence**
- **Age-specific proportion of HRT users**

### Step 2

**Estimating risk of disease in HRT users and non-users**

### Step 3

**Comparison of risks of HRT use with risks associated with being overweight or obese**

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### Step 1

#### **Age-specific disease incidence**

The following age-specific incidence data for women aged 35–79 years were used:

1. Cancer:

Breast and colorectal cancer incidence rates (expressed as number of cases per 100,000 women) for 2001 were obtained from the Australian Institute of Health and Welfare (AIHW)<sup>i</sup> cancer database.

2. Cerebrovascular accident (stroke), venous thromboembolism/ thromboses (blood clots), fractured neck of femur (hip fracture) and coronary heart disease:

Numbers of hospitalisations (separations) due to each disease for 2001-2002 were obtained from the AIHW National Hospital Morbidity database<sup>ii</sup>, using the following international classification of disease (ICD) codes.

*Stroke:* I61, I62, I63 and I64 [Cerebrovascular accident: Intracerebral haemorrhage, Other non-traumatic intracranial haemorrhage, Cerebral Infarction, Stroke not specified]

*Venous thromboses (blood clotting):* I26 and I80.2 [Pulmonary Embolism and Deep Vein Thrombosis (DVT)]

*Hip Fracture:* 72.0 [fractured neck of femur]

*Coronary heart disease:* I21, I22 [Acute myocardial infarction, subsequent myocardial infarction]

Hospital admission rates were calculated using population estimates from the Australian Bureau of Statistics<sup>iii</sup>. Coronary heart disease estimates were compared to the MONICA Australian<sup>iv</sup> results to ensure hospital separations data provided reasonable estimates.

## Age-specific proportion of HRT users

Data on the prevalence of hormone replacement therapy (HRT) use in Australian women aged 35–79 were obtained from the 2001 National Health Survey<sup>v</sup>. We included those respondents who did not state their HRT use as non-users of HRT. Data from a survey of South Australian women<sup>vi</sup> was used to verify these figures.

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## Step 2

### Estimating risk of disease in HRT users and non-users

Since incidence rates reflect a mixture of users and non-users of HRT, disease estimates were adjusted to estimate the rates of disease in women who do not currently use HRT. The Hazard Ratio (HR) for each year was obtained from the Women's Health Initiative (WHI) Trial<sup>vii</sup> and applied to the relevant years of use for each disease. The following equations were used:

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

y = incidence in HRT users

x = incidence in HRT non-users

p = proportion of people using HRT

I = adjusted incidence (cumulative risk) from STEP TWO above

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

$$\text{Thus } y = x * \text{hazard ratio}$$

The Hazard Ratios used in these calculations are reproduced in the table below:

Hazard Ratios	1 <sup>st</sup> year of use	2 <sup>nd</sup> year of use	3 <sup>rd</sup> year of use	4 <sup>th</sup> year of use	5 <sup>th</sup> year of use
Breast cancer*	*1.00	*1.00	1.16	1.73	2.64
Colorectal Cancer	0.64	1.17	0.72	0.43	0.47
Coronary Heart Disease	1.78	1.15	1.06	0.99	2.38
Venous thromboembolism	3.60	2.26	1.67	1.84	2.49
Stroke <sup>†</sup>	*1.00	1.72	1.79	1.70	1.87
Hip Fracture	0.64	0.59	0.87	0.69	0.58

\*NB: for simplicity these hazard ratios have been rounded to one.

The WHI trial examined the effect of HRT in women aged 50–79 years. We estimated extra cases in women aged 40–44 and 45–49 years by assuming that Hazard Ratios for women 50–79 years of age also apply to women in these younger age groups.

The cumulative rate of disease over 5 years was estimated by calculating the sum of age specific incidence for each disease multiplied by the number of years per age interval<sup>viii</sup>. Cumulative risk of disease for one and five years was estimated using the hypothetical cohort method described by Taylor, Heard and Boyages<sup>ix</sup>, where we estimated the disease experience for a hypothetical cohort of women as they passed through the age-specific rates obtained from Australian data sources [and where cumulative risk =  $1 - e^{-\text{cumulative rate}}$ ]. We assumed that women who had taken HRT for 5 years, and women who are deciding whether to take HRT for 5 years would be using the risk calculator therefore we estimated the average of the risks for these two scenarios.

The following tables present the age and disease specific risk estimates per thousand women (users and non users of HRT). Risks are presented for one year of HRT use and for five years of HRT use.

Risk of disease in non-users of HRT per 1000 women for one year						
Age	Breast Cancer	Colorectal Cancer	Coronary Heart Disease	Venous thromboses	Stroke	Hip Fracture
40-44	1.45	0.22	0.41	0.67	0.28	0.03
45-49	2.10	0.38	0.76	0.86	0.42	0.08
50-54	2.75	0.63	1.16	0.91	0.71	0.19
55-59	3.26	1.07	1.81	1.20	1.21	0.37
60-64	3.44	1.80	2.39	1.06	2.10	0.76
65-69	3.36	2.48	3.52	1.35	3.78	1.67
70-74	3.20	3.21	5.56	1.86	6.87	3.75
75-79	3.07	3.69	6.94	2.09	9.09	5.37

  

Risk of disease in users of HRT per 1000 women for one year of HRT use						
Age	Breast Cancer	Colorectal Cancer	Coronary Heart Disease	Venous thromboses	Stroke	Hip Fracture
40-44	1.45	0.14	0.73	2.42	0.28	0.02
45-49	2.10	0.24	1.36	3.09	0.42	0.05
50-54	2.75	0.40	2.06	3.29	0.71	0.12
55-59	3.26	0.69	3.21	4.31	1.21	0.24
60-64	3.44	1.15	4.26	3.80	2.10	0.49
65-69	3.36	1.59	6.27	4.86	3.78	1.07
70-74	3.20	2.05	9.89	6.68	6.87	2.40
75-79	3.07	2.36	12.36	7.52	9.09	3.44

Risk of disease in non-users of HRT per 1000 women for five years						
Age	Breast Cancer	Colorectal Cancer	Coronary Heart Disease	Venous thromboses	Stroke	Hip Fracture
40-44	7.22	1.10	2.06	3.39	1.38	0.16
45-49	10.45	1.89	3.84	4.34	2.09	0.42
50-54	13.23	3.15	5.94	5.01	3.38	0.94
55-59	15.67	5.35	9.27	6.56	5.76	1.84
60-64	15.28	8.92	13.16	6.79	8.92	3.77
65-69	14.93	12.29	19.37	8.68	16.08	8.25
70-74	14.46	15.92	30.09	11.56	29.95	18.62
75-79	13.86	18.32	37.58	13.01	39.59	26.63

  

Risk of disease in users of HRT per 1000 women for five years of HRT use						
Age	Breast Cancer	Colorectal Cancer	Coronary Heart Disease	Venous thromboses	Stroke	Hip Fracture
40-44	10.84	0.75	3.02	8.04	2.23	0.11
45-49	15.69	1.29	5.64	10.27	3.37	0.28
50-54	19.52	2.14	8.61	11.71	5.43	0.63
55-59	23.11	3.64	13.44	15.35	9.26	1.24
60-64	21.64	5.92	18.47	15.50	14.17	2.53
65-69	21.15	8.16	27.19	19.81	25.54	5.53
70-74	20.66	10.64	42.52	26.53	47.71	12.89
75-79	19.79	12.24	53.12	29.84	63.06	17.87

### **Step 3**

#### **Comparison of risks of HRT use with risks associated with being overweight or obese**

We compared the risks of HRT use on breast cancer and cardiovascular disease with risk of being overweight or obese. Hazard ratios for the effects of overweight and obese on risk of breast cancer were obtained from an extensive review of studies in Europe<sup>x</sup>. Hazard ratios for the effects of overweight and obese on risk of cardiovascular disease were obtained from a large study of women in the United States<sup>xi</sup>.

These hazard ratios were applied to the age specific estimates of numbers of "non-users" of HRT to obtain comparable estimates of risk for overweight and obese women.

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- <sup>i</sup> <http://www.aihw.gov.au/cancer/datacubes/index.cfm> Australian Institute of Health and Welfare. Cancer age specific data cubes.
- <sup>ii</sup> <http://www.aihw.gov.au> Australian Institute of Health and Welfare. Hospital Morbidity database.
- <sup>iii</sup> Australian Bureau of Statistics. Cat. No. 3105.0.65.001 Australian Historical Population Statistics.
- <sup>iv</sup> <http://www.aihw.gov.au/publications/cvd/wmsa84-93/> MONICA Australian results [Appendix One – Rate of fatal and non-fatal events].
- <sup>v</sup> ABS Catalogue number 4364.0 *National Health Survey. Summary of Results: 2001*.
- <sup>vi</sup> MacLennan A, Wilson D and Taylor A. HRT in women at risk of cardiovascular disease and osteoporosis in South Australia in 1997. *MJA* 1999 Jun, 170: 524-527.
- <sup>vii</sup> Writing group for the Women's Health Initiative (2002). Risks and Benefits of Estrogen plus Progestin in Healthy Postmenopausal Women: Principle results from the WHO RCT. *JAMA* 288(3): 321-333.
- <sup>viii</sup> Taylor R, Standardisation. In Kerr C, Taylor R, Heard G. *Handbook of public health methods*. McGraw-Hill 1998. p282
- <sup>ix</sup> Taylor R, Heard G and Boyages J. Estimating a woman's risk of breast cancer: the effects of age and family history. *NSW Public Health Bulletin* 2001, 12(2):36-40
- <sup>x</sup> Bergstrom A, Pisani P, Tenet V, Wolk A and Adami H-O. Overweight as an avoidable cause of cancer in Europe. *International Journal of Cancer*, 2001. 91:421-430.
- <sup>xi</sup> Wilson P, D'Agostino R, Sullivan L, Parise H and Kannel W. Overweight and obesity as determinants of cardiovascular risk: The Framingham experience. *Archives of Internal Medicine*, 2002. 162:1867-1872