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Research



**Tuomikoski P *et al.*,  
Coronary Heart Disease Mortality and  
Hormone Therapy Before and After  
the Women's Health Initiative**

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# Background

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## Hormone therapy and coronary heart disease

HT\* have been recommended for prevention of coronary heart disease (CHD). Women's health Initiative study (WHI)\*\* showed that HT failed in the primary prevention of CHD. Guidelines for the optimal use of HT were modernized after WHI, resulting in e.g. lower doses of HT in Finland.

## Aim of this study

- To assess whether CHD mortality in Finnish HT users differed before and after 2002 when the WHI was published.

## Study design

- Register-based linkage study

## Methods

- The risks of CHD death in HT users in relation to the year- and age-matched background population were studied using a standardized mortality ratio with 95% confidence intervals.

\* Hormone therapy with conjugated estrogens alone, or in combination with medroxyprogesterone acetate.

\*\* The Journal of the American Medical Association, 2002

# Data sources

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## National reimbursement register

- In Finland postmenopausal HT is available only by a doctor's prescription, and part of the price is reimbursed by national health insurance. All Finnish HT prescriptions that have been picked up have been entered into the national reimbursement register since 1994. All women who had started systemic HT use at 40 years age or older were identified from this register.

## Causes of Death Register

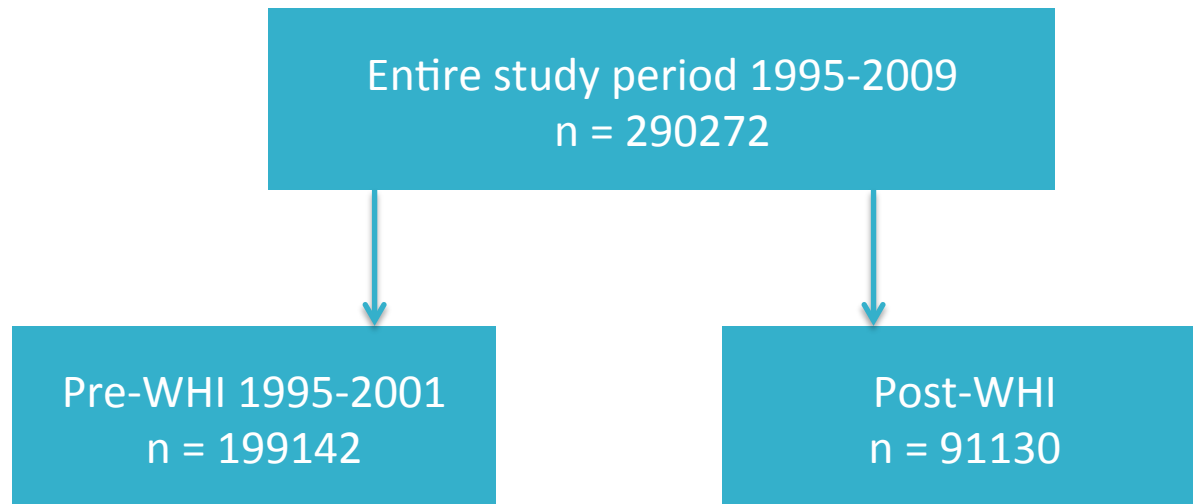
- In Finland all deaths are recorded in the Causes of Death Register. All deaths resulting from CHD\* were identified in women aged 40 years or older during 1995-2009.

\*ICD-9: 410-414 (year 1995), ICD 10: I20-I25 (since 1996)

# Description of study population

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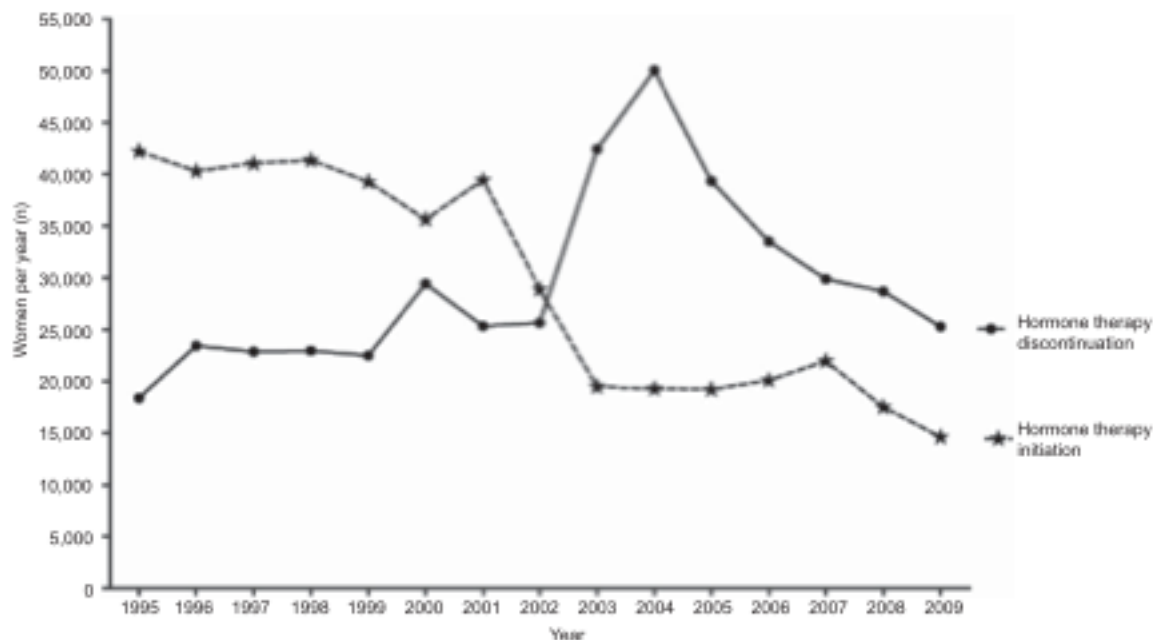
The broad study population included all women, who had started systemic HT use at 40 years of age or older years 1994-2009. After exclusion of women younger than 40 years at start (n=63189), who had only progestin regimens (n=47492), who had solely vaginal estrogens (n=195756), and started in years 1994, the final study population was 290272 women.



# Results:

## Number of women starting or discontinuing HT

The number of annual new HT starters decreased and those who discontinued HT use increased during follow-up time 1995-2009. After 2002 the yearly number of women discontinuing was greater than the yearly number of initiators.



# Results: CHD mortality

- The use of HT was associated with significant reductions in CHD mortality compared with background population during both study eras.
- The reduction of the CHD risk was not related to the type of HT (any HT, only estradiol or estradiol-progestin HT).
- No differences was observed between the study eras.

Type of hormone therapy	Exposure	Pre-WHI SMR (95% CI)	Post-WHI SMR (95% CI)
Any HT	≤ 1 year	<b>0.71 (0.63-0.80)</b>	0.82 (0.76-1.00)
	1-8 years	<b>0.57 (0.48-0.66)</b>	<b>0.46 (0.32-0.64)</b>
Estradiol only	≤ 1 year	<b>0.70 (0.60-0.81)</b>	0.78 (0.59-1.02)
	1-8 years	<b>0.48 (0.37-0.61)</b>	<b>0.46 (0.26-0.75)</b>
Estradiol-progestin therapy	≤ 1 year	<b>0.70 (0.59-0.82)</b>	0.83 (0.63-1.06)
	1-8 years	<b>0.62 (0.50-0.7)</b>	<b>0.43 (0.27-0.67)</b>

# Results:

## CHD mortality and age at initiation

- Data was analyzed also stratified by age at initiation of HT: younger than 60 years and 60 years or older.
- During post-WHI era a significant protective effect against CHD death was detected only in women who initiated at age younger than 60 years and had 1-8 years of exposure.

HT exposure	Age at initiation	Pre-WHI SMR (95% CI)	Post-WHI SMR (95% CI)
≤ 1 year	≤ 60 years	<b>0.56 (0.40-0.77)</b>	0.80 (0.54-1.15)
	> 60 years	<b>0.74 (0.65-0.84)</b>	0.83 (0.66-1.03)
> 1-8 years	≤ 60 years	<b>0.54 (0.41-0.71)</b>	<b>0.30 (0.17-0.49)</b>
	> 60 years	<b>0.58 (0.47-0.70)</b>	0.70 (0.45-1.06)

# Results:

## CHD mortality when discontinuing HT

- Discontinuation of HT was associated with increase in CHD death risk within the first year of discontinuation.
- The elevated risk vanished with longer time since discontinuation.
- No difference was observed between the study eras.

Time since last HT	Pre-WHI SMR (95% CI)	Post-WHI SMR (95% CI)
≤ 1 year	<b>1.42 (1.17-1.71)</b>	1.31 (0.92-1.82)
1-8 years	0.94 (0.81-1.08)	0.83 (0.66-1.02)



# Discussion

- The study shows how the WHI modified the Finnish HT-prescribing policy.
- Instead of finding higher CHD death risk in HT users during pre-WHI era, we found in this study that the use of HT was associated with significant reductions in risk of death resulting from CHD.
- Healthy woman bias is one possible explanation for the significant reduction of the risk of CHD death.
- Reduction for risk of CHD death for only under 60 years at initiation indicates that estrogen is beneficial in healthy coronary arteries, but not perhaps in those affected by atherosclerotic plaques, likely to be present in arteries of elderly women.
- Increased risk of CHD deaths within first year of HT discontinuation, may be due to collection of deaths after myocardial infarction experienced during HT exposure. Roughly half of the patients die within the first postinfarction year. Also an acute withdrawal of estradiol may have resulted in coronary occlusion and perhaps in myocardial infarction.

# Acknowledgements

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