

# A Balanced Analysis: Risks Vs Benefits of Estrogen Replacement Therapy

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## Abstract

As women age, there is a large increase in the incidence of stroke which has been observed in a number of cases. There is an increased interest in risks and benefits of HRT in females who are at-risk to CVD and stroke and for this estrogen has been studied in particular. But only limited data of trends is available and hence still the question of ERT to be used for prevention of CHD & stroke remains unanswered.

## Introduction

Ischemic stroke occurs due to clotting of blood leading to a blockage in the blood vessels of brain & hence estrogen helps in widening blood vessels as per research. Other factors such as age, genetics, environmental & lifestyle are also responsible for estrogen levels.

### Benefits of HRT

CVD - There has been found an inverse relationship or association between ERT and CVD in post menopausal women in a no. of studies [1-19] mostly showing a fall of 50% approximately in IHD, a few show no association [7, 8] and a few have shown harm [9, 19].

- In Framingham study results from one source show increased risk of CVD in postmenopausal women using estrogen [19].
- In other results from different areas of same study, women of 50 to 59 yrs, there was significant reduction in risk of women using ERT since past 10 years. There was only the increased risk of stroke associated with estrogen in this study mainly in older women.

There were certain drawbacks of studies i.e. lower reported cases of mortality, also only conjugated equine estrogen (Premarin) was used without progestin and that too in very high doses.

Hence the beneficial or protective effects of ERT cannot be given clearly.

**Osteoporosis:** Use of ERT decreases the postmenopausal bone loss rate and therefore the risk of fractures later. Immediate benefit can only be seen by single/dual photon absorptiometry in these

women. It has been seen that estimated relative risk of fracture associated with estrogen is approximately 50% when used for 4 or more years.

Researches have also shown to increase the risk of cardiac and stroke death after stopping estrogen in the 1st year of intake thereby suggesting the crucial protective role it plays in cardiac health of patients [20].

A study in Neurology journal also published lower risk of stroke (both ischemic stroke and intracerebral haemorrhage) with longer exposure to estrogen [20].

A study was done in China which revealed that a number of reproductive factors like increased reproductive life span and use of HRT or contraceptives led to increase in estrogen levels linking it to decreased risk of intracerebral haemorrhage and stroke thereby opening a new arena for consideration of ideas for stroke prevention eg: considering people for screening who had short lifetime exposure to estrogen [20].

It was quoted somewhere in an article “ The longer reproductive lifespan reduces the risk of stroke in women likely due to cardio-protective benefits of endogenous estrogen hormone wherein endogenous as we donot want people to start estrogen supplementation without further research” [20].

It is important to note that artificial form of estrogen i.e. in OCP's has been associated with increased stroke risk.

### ***Estrogen And Stroke***

It has been repeatedly observed and found by many great experts and professors in this field that longer reproductive life span has lower stroke risk may be due to estrogen exposure for a longer period and hence estrogen provides protective effect against stroke. It could be because of the following reasons [20]:

- a. Neuroprotective and antioxidant effects of estrogen causing decreased neuronal damage
- b. Estrogen causes widening of vessels (vasodilation) thereby increasing Nitric oxide and prostacyclin synthesis in endothelial cells and also acts as an activator of specific Ca<sup>++</sup> channels thereby relaxing the smooth muscles of blood vessels
- c. Estrogen has shown protective effect to brain from stroke in experimental animal studies of all strains including Hypertension and Diabetes by improving the physiological, behavioral and histological outcomes [21-24].

There is a narrow therapeutic range of estrogen therefore careful dosing with monitoring of plasma levels is required. HRT as combination of estrogen + progesterone has not been studied well for its effects [25].

The risk of Cardiovascular disease is decreased by 30-50% in postmenopausal women using estrogen replacement therapy [26-30].

### ***Risks of ERT***

***Endometrial Cancer:*** The majorly known risk associated with ERT is endometrial cancer, which depends on duration and dose of estrogen and also the presence of risk factors like obesity. It has generally been observed that 5-year usage of unopposed estrogen increases the risk of endometrial cancer. Some studies show decreased death rate in women using estrogen and had endometrial cancer than those who neither used estrogen nor had cancer [31].

### ***Breast Cancer & ERT***

***Breast Cancer:*** Most studies show no association between the use of estrogen and an increased risk of breast cancer. Two large studies, however, suggested an increased risk of breast cancer seen after 15-20 years of ERT, wherein it was seen either no risk in a few years of usage or double /triple risk in use for more than 20 years [32, 33].

### Factors affecting estrogen levels

A number of factors which can influence estrogen levels [20]:

- a. **Genetics:** Genetics can play a role in determining estrogen levels.
- b. **Age:** Estrogen levels naturally reduce with age as women approach menopause.
- c. **Body weight:** Obesity affect estrogen levels, as body fat produce and store estrogen.
- d. **Pregnancy:** Estrogen levels increase during pregnancy
- e. **Hormonal birth control:** The use of hormonal birth control (pill/IUD) can alter a woman's estrogen levels.
- f. **Lifestyle factors:** Alcohol consumption and smoking can affect estrogen levels
- g. **Environmental factors:** Exposure to endocrine-disrupting chemicals, such as phthalates, can impact estrogen levels.

### Conclusion

Currently No data/study supports the usage of HRT for any kind of prevention of vascular disease. It is mainly known for prevention or delay of osteoporosis. But it is an interesting topic concerning the increased public health importance. Many of beneficial properties of estrogen can actually be put to use when its undesirable effects can be removed, hence, proving it to be an important therapy for women at risk of stroke or CVD leading to decreased morbidity & mortality.

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