

# Clinical trials of hormonal replacement therapy for cardiovascular prevention in all type of patients

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## 1 hormonal replacement therapy

| Trial  | Treatments  | Patients   | Trials design and methods                |
|--|---|--|--|
| <b>combined estrogen and progestogen vs placebo</b>                                      |   |  |  |
| Schulman (NHLBI) (estrogen-progestogen) , 2002 [NCT00000601] n=94/99 follow-up: 6 months | intravenous estrogen followed by oral conjugated estrogen plus medroxyprogesterone for 21 days versus placebo   | Postmenopausal women with unstable angina  | Parallel groups double blind USA, Brazil |
| EAGAR , 2006 [NCT00000605] n=44/51 follow-up: 33 months                                  | estradiol +/-medroxyprogesterone versus placebo   | Postmenopausal women who had undergone coronary artery bypass graft                          | Parallel groups double blind USA, Canada |
| ERA (estrogen plus medroxyprogesterone) , 2000 [NCT00000549] n=104/105 follow-up: 3.6y   | estrogen plus medroxyprogesterone acetate ( 0.625 mg of conjugated estrogen plus 2.5 mg of medroxyprogesterone acetate per day) versus placebo  | Postmenopausal women with established coronary atherosclerosis                               | Parallel groups double-blind USA         |
| EVTET , 2000 n=71/69 follow-up: 24 months  | 2 mg estradiol plus 1 mg norethisterone acetate, 1 tablet daily versus placebo  | postmenopausal women younger than 70 years who had suffered previous DVT or PE               | Parallel groups double-blind Norway      |
| Hall , 1998 n=40/20 follow-up: 1 y   | transdermal 17 beta-estradiol at a dose of 50 micrograms per 24 h alone for 18 days followed by 10 days of combined treatment with medroxyprogesterone acetate (MPA) 5 mg orally versus placebo | postmenopausal women with coronary artery disease aged 44-75 years                           | Parallel groups double-blind Sweden      |
| HERS , 1998 [NCT00319566] n=1380/1383 follow-up: 4.1 y                                   | Premarin .625 mg daily plus medroxyprogesterone 2.5 mg daily versus placebo   | women with coronary disease, younger than 80 years, and postmenopausal with an intact uterus | Cross over double-blind US               |

continued...

| <b>Trial</b>   | <b>Treatments</b>   | <b>Patients</b>   | <b>Trials design and methods</b>                              |
|--|---|---|---|
| <b>WAVE , 2002</b><br>[NCT00000555]<br>n=210/213<br>follow-up: 2.8 y                         | 0.625 mg/d of conjugated equine estrogen (plus 2.5 mg/d of medroxyprogesterone acetate for women who had not had a hysterectomy)<br>versus<br>placebo | Postmenopausal women, up to age 86, with angiographically documented coronary artery disease of at least 15 percent, but no more than 75 percent occlusion                            | Factorial plan<br>double blind<br>United States, Canada       |
| <b>WELL-HART (estrogen-progestin) , 2003</b><br>[NCT00000559]<br>n=74/76<br>follow-up: 3.3 y | 17 beta-estradiol plus sequentially administered medroxyprogesterone acetate<br>versus<br>placebo   | Postmenopausal women with angiographically-documented coronary disease  | double blind<br>USA   |
| <b>WHI , 2002</b><br>n=8506/8102<br>follow-up: 5.2 y   | conjugated equine estrogens, 0.625 mg/d, plus medroxyprogesterone acetate, 2.5 mg/d, in 1 tablet<br>versus<br>placebo                                 | postmenopausal women aged 50-79 years with an intact uterus at baseline   | Factorial plan<br>double-blind<br>USA                         |
| <b>WHISP , 2006</b><br>n=49/51<br>follow-up: 1 y   | oral oestradiol-17beta 1 mg plus norethisterone acetate 0.5 mg daily<br>versus<br>placebo   | post-menopausal women >55 years were enrolled between 2 and 28 days after an acute coronary syndrome  | Parallel groups<br>double-blind<br>UK                         |
| <b>WISDOM , 2007</b><br>[ISRCTN63718836]<br>n=2196/2189<br>follow-up: 11.9 months            | combined estrogen and progestogen<br>versus<br>placebo  | postmenopausal women aged 50-69   | Parallel groups<br>double-blind<br>UK, Australia, New Zealand |
| <b>error vs placebo</b>  |   |   |   |
| <b>PHASE</b> <i>ongoing</i><br>n=NA  | -   | -   |   |
| <b>estrogen vs placebo</b>   |   |   |   |
| <b>EPAT , 2001</b><br>n=111/111<br>follow-up: 2 y  | micronized 17beta-estradiol (1 mg/d)<br>versus<br>placebo   | postmenopausal women 45 years of age or older without preexisting cardiovascular disease and with low-density lipoprotein cholesterol levels of 3.37 mmol/L or greater (>/=130 mg/dL) | Parallel groups<br>double-blind<br>USA                        |
| <b>ERA (estrogen alone) , 2000</b><br>[NCT00000549]<br>n=100/105<br>follow-up: 3.6y          | estrogen alone (0.625 mg of conjugated estrogen per day)<br>versus<br>placebo   | Postmenopausal women with established coronary atherosclerosis  | Parallel groups<br>double-blind<br>USA                        |
| <b>ESPRIT , 2002</b><br>n=513/504<br>follow-up: 24 months                                    | oestradiol valerate 2 mg daily<br>versus<br>placebo   | postmenopausal women, age 50-69 years who had survived a first myocardial infarction  | Parallel groups<br>double-blind<br>England and Wales          |

continued...

| <b>Trial</b>  | <b>Treatments</b>   | <b>Patients</b>   | <b>Trials design and methods</b>               |
|---|---|---|--|
| <b>Schulman (NHLBI) (estrogen alone) , 2002</b><br>[NCT00000601]<br>n=100/99<br>follow-up: 6 months | intravenous followed by oral conjugated estrogen for 21 days, intravenous estrogen followed by oral conjugated estrogen plus medroxyprogesterone for 21 days<br>versus<br>placebo | Postmenopausal women with unstable angina   | Parallel groups<br>double blind<br>USA, Brazil |
| <b>WELL-HART (estrogen alone) , 2003</b><br>[NCT00000559]<br>n=76/76<br>follow-up: 3.3 y            | micronized 17beta-estradiol alone<br>versus<br>placebo  | Postmenopausal women with angiographically-documented coronary disease                    | Parallel groups<br>double blind<br>USA         |
| <b>WEST , 2001</b><br>n=337/327<br>follow-up: 2.8 y   | estrogen therapy (1 mg of estradiol-17beta per day)<br>versus<br>placebo  | postmenopausal women who had recently had an ischemic stroke or transient ischemic attack | Parallel groups<br>double-blind<br>USA         |
| <b>hormonal replacement therapy vs placebo</b>  |   |   |  |
| <b>PEPI , 1995</b><br>[NCT00000466]<br>n=875<br>follow-up: 3 years                                  | estrogen replacement therapy<br>versus<br>placebo   | Postmenopausal women, ages 45 to 64   | Parallel groups<br>double blind<br>USA         |

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Hodis HN, Mack WJ, Azen SP, Lobo RA, Shoupe D, Mahrer PR, Faxon DP, Cashin-Hemphill L, Sanmarco ME, French WJ, Shook TL, Gaarder TD, Mehra AO, Rabbani R, Sevanian A, Shil AB, Torres M, Vogelbach KH, Selzer RH Hormone therapy and the progression of coronary-artery atherosclerosis in postmenopausal women. *N Engl J Med* 2003;349:535-45

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## 2 About TrialResults-center.org

TrialResults-center is an innovative knowledge database that collects the results of RCTs and provides dynamic interactive systematic reviews and meta-analysis in the field of all major heart and vessels diseases.

The TrialResults-center database provides a unique view of the treatment efficacy based on all data provided directly from clinical trial results, offering a valuable alternative to personal bibliographic search, published meta-analysis, etc. Furthermore, it would allow comparing easily the various concurrent therapeutic for the same clinical condition.

Rigorous meta-analysis method is used to populate TrialResults-center: widespread search of published and non published trials, study selection using pre-specified criteria, data extraction using standard form.

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