

Clinical trials of hormonal replacement therapy for cardiovascular prevention in secondary prevention

TrialResults-center www.trialresultscenter.org

1 hormonal replacement therapy

Trial	Treatments	Patients	Trials design and methods
combined estrogen and progestogen vs placebo			
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...

Trial	Treatments	Patients	Trials design and methods
WAVE , 2002 [NCT00000555] n=210/213 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) versus 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 double blind United States, Canada
WELL-HART (estrogen-progestin) , 2003 [NCT00000559] n=74/76 follow-up: 3.3 y	17 beta-estradiol plus sequentially administered medroxyprogesterone acetate versus placebo	Postmenopausal women with angiographically-documented coronary disease	double blind USA
WHISP , 2006 n=49/51 follow-up: 1 y	oral oestradiol-17beta 1 mg plus norethisterone acetate 0.5 mg daily versus placebo	post-menopausal women >55 years were enrolled between 2 and 28 days after an acute coronary syndrome	Parallel groups double-blind UK
estrogen vs placebo			
ERA (estrogen alone) , 2000 [NCT00000549] n=100/105 follow-up: 3.6y	estrogen alone (0.625 mg of conjugated estrogen per day) versus placebo	Postmenopausal women with established coronary atherosclerosis	Parallel groups double-blind USA
ESPRIT , 2002 n=513/504 follow-up: 24 months	oestradiol valerate 2 mg daily versus placebo	postmenopausal women, age 50-69 years who had survived a first myocardial infarction	Parallel groups double-blind England and Wales
Schulman (NHLBI) (estrogen alone) , 2002 [NCT00000601] n=100/99 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 versus placebo	Postmenopausal women with unstable angina	Parallel groups double blind USA, Brazil
WELL-HART (estrogen alone) , 2003 [NCT00000559] n=76/76 follow-up: 3.3 y	micronized 17beta-estradiol alone versus placebo	Postmenopausal women with angiographically-documented coronary disease	Parallel groups double blind USA

References

Schulman (NHLBI) (estrogen-progestogen), 2002:

Schulman SP, Thiemann DR, Ouyang P, Chandra NC, Schulman DS, Reis SE, Terrin M, Forman S, de Albuquerque CP, Bahr RD, Townsend SN, Cosgriff R, Gerstenblith G Effects of acute hormone therapy on recurrent ischemia in postmenopausal women with unstable angina. *J Am Coll Cardiol* 2002;39:231-7 [[11788212](#)]

EAGAR, 2006:

Ouyang P, Tardif JC, Herrington DM, Stewart KJ, Thompson PD, Walsh MN, Bennett SK, Heldman AW, Tayback MA, Wang NY Randomized trial of hormone therapy in women after coronary bypass surgery. Evidence of differential effect of hormone therapy on angiographic progression of disease in saphenous vein grafts and native coronary arteries. *Atherosclerosis* 2006;189:375-86 [[16442114](#)] [10.1016/j.atherosclerosis.2005.12.015](#)

ERA (estrogen plus medroxyprogesterone), 2000:

Herrington DM, Reboussin DM, Brosnihan KB, Sharp PC, Shumaker SA, Snyder TE, Furberg CD, Kowalchuk GJ, Stuckey TD, Rogers WJ, Givens DH, Waters D Effects of estrogen replacement on the progression of coronary-artery atherosclerosis. *N Engl J Med* 2000;343:522-9 [[10954759](#)] [10.1056/NEJM200008243430801](#)

EVTET, 2000:

Hibraaten E, Qvigstad E, Arnesen H, Larsen S, Wickstrøm E, Sandset PM Increased risk of recurrent venous thromboembolism during hormone replacement therapy—results of the randomized, double-blind, placebo-controlled estrogen in venous thromboembolism trial (EVTET). *Thromb Haemost* 2000;84:961-7 [[11154141](#)]

Hall, 1998:

Hall G, Pripp U, Schenck-Gustafsson K, Landgren BM Long-term effects of hormone replacement therapy on symptoms of angina pectoris, quality of life and compliance in women with coronary artery disease. *Maturitas* 1998;28:235-42 [[9571599](#)]

HERS, 1998:

Hulley S, Grady D, Bush T, Furberg C, Herrington D, Riggs B, Vittinghoff E Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. Heart and Estrogen/progestin Replacement Study (HERS) Research Group. *JAMA* 1998;280:605-13 [[9718051](#)]

Grady D, Applegate W, Bush T, Furberg C, Riggs B, Hulley SB Heart and Estrogen/progestin Replacement Study (HERS): design, methods, and baseline characteristics. *Control Clin Trials* 1998;19:314-35 [[9683309](#)]

Simon JA, Hsia J, Cauley JA, Richards C, Harris F, Fong J, Barrett-Connor E, Hulley SB Postmenopausal hormone therapy and risk of stroke: The Heart and Estrogen-progestin Replacement Study (HERS). *Circulation* 2001;103:638-42 [[11156873](#)]

WAVE, 2002:

Waters DD, Alderman EL, Hsia J, Howard BV, Cobb FR, Rogers WJ, Ouyang P, Thompson P, Tardif JC, Higginson L, Bittner V, Steffes M, Gordon DJ, Proschan M, Younes N, Verter JI Effects of hormone replacement therapy and antioxidant vitamin supplements on coronary atherosclerosis in postmenopausal women: a randomized controlled trial. *JAMA* 2002;288:2432-40 [[12435256](#)]

WELL-HART (estrogen-progestin), 2003:

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 [[12904518](#)] [10.1056/NEJMoa030830](#)

WHISP, 2006:

Collins P, Flather M, Lees B, Mister R, Proudler AJ, Stevenson JC Randomized trial of effects of continuous combined HRT on markers of lipids and coagulation in women with acute coronary syndromes: WHISP Pilot Study. *Eur Heart J* 2006;27:2046-53 [[16899475](#)] [10.1093/eurheartj/ehl183](#)

ERA (estrogen alone), 2000:

Herrington DM, Reboussin DM, Brosnihan KB, Sharp PC, Shumaker SA, Snyder TE, Furberg CD, Kowalchuk GJ, Stuckey TD, Rogers WJ, Givens DH, Waters D Effects of estrogen replacement on the progression of coronary-artery atherosclerosis. *N Engl J Med* 2000;343:522-9 [[10954759](#)] [10.1056/NEJM200008243430801](#)

Herrington DM, Reboussin DM, Klein KP, Sharp PC, Shumaker SA, Snyder TE, Geisinger KR The estrogen replacement and atherosclerosis (ERA) study: study design and baseline characteristics of the cohort. *Control Clin Trials* 2000;21:257-85 [[10822123](#)]

ESPRIT, 2002:

Cherry N, Gilmour K, Hannaford P, Heagerty A, Khan MA, Kitchener H, McNamee R, Elstein M, Kay C, Seif M, Buckley H Oestrogen therapy for prevention of reinfarction in postmenopausal women: a randomised placebo controlled trial. *Lancet* 2002;360:2001-8 [[12504395](#)]

Schulman (NHLBI) (estrogen alone), 2002:

Schulman SP, Thiemann DR, Ouyang P, Chandra NC, Schulman DS, Reis SE, Terrin M, Forman S, de Albuquerque CP, Bahr RD, Townsend SN, Cosgriff R, Gerstenblith G Effects of acute hormone therapy on recurrent ischemia in postmenopausal women with unstable angina. *J Am Coll Cardiol* 2002;39:231-7 [[11788212](#)]

WELL-HART (estrogen alone), 2003:

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 [[12904518](#)] [10.1056/NEJMoa030830](#)

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.

TrialResults-center is continually updated on a weekly basis. We continually search all new results (whatever their publication channel) and these news results are immediately added to the database with a maximum of 1 week.

TrialResults-center is non-profit and self-funded.