

Appendix Table 7. The Effects of Hormone Therapy on Female Urinary Incontinence: Results from Randomized Controlled Clinical Trials*

Author Sample Followup	Active Treatment	Control Treatment	Outcome	(Events/ (Active Treatment)) [Events/Control Treatment]	Relative Risk (95% CI)	Risk Difference (95%CI)	Quality Issues
Akhila, 2006(126) N= 116, post-menopausal symptoms 12 month followup	Estradiol gel percutaneous 1.25 g/day	Transdermal patch with 50 mg/day estradiol	Self Reported Continence	(26/29) [40/40]	0.89 (0.78; 1.02)	-0.10 (-0.22; 0.02)	No intention to treat. Open label. Allocation concealment unclear. Baseline data confirmed the adequacy of randomization. Sample size not justified.
Chompoota weep 1998, (164) N = 20, urogenital symptoms related to estrogen deficiency 2 month followup	Combined contraceptive Intravaginal 1 pill/ week at bedtime with 250 mg levonorgestrel +30 micrograms ethinyl estradiol	Intravaginal conjugated estrogen cream (1 g = 0.625mg conjugated equine estrogens) at bedtime	Self Reported Continence	(9/10) [9/10]		0.00 (-0.32; 0.32)	Intention to treat not stated. Open label. Randomization procedure not reported. Allocation concealment unclear. Baseline data confirmed the adequacy of randomization. Sample size not justified.
Akhila, 2006(126) N = 116 post-menopausal symptoms 12 month followup	Conjugated equine estrogen 0.625 orally/day	Transdermal patch with 50 mg/day estradiol	Self Reported Continence	(19/47) [40/40]	0.41 (0.29; 0.58)	-0.60 (-0.74; -0.45)	No intention to treat. Open label. Allocation concealment unclear. Baseline data confirmed the adequacy of randomization. Sample size not justified.

Waetjen, 2004(165) N = 963 36 month followup	Raloxifene 60mg /day or Raloxifene 120mg/day	Placebo	Self Reported Continence	(243/638) [125/325]	0.99 (0.84; 1.17)	0.00 (-0.07; 0.06)	No intention to treat Open label. Randomization and allocation concealment not reported. Baseline data confirmed adequacy of randomization. Sample size justified.
Rufford, 2003(124) N = 40, urgency 6 month followup	25mg 17 beta-estradiol implant subcutaneous tissue	Placebo implant	Self Reported Continence	(7/20) [6/20]	1.17 (0.48; 2.86)	0.05 (-0.24; 0.34)	No intention to treat. Double blind. Allocation concealment adequate. Baseline data confirmed the adequacy of randomization. Sample size justified.
Mikkelsen, 1995(127) N = 47 36 month followup	Vagifem (25 micrograms oestradiol) administered as vaginal pessaries daily 3 weeks prior to surgery	Placebo administered as vaginal pessaries daily 3 weeks prior to surgery	Self Reported Continence	(5/21) [6/19]	0.75 (0.27; 2.07)	-0.08 (-0.35; 0.20)	No intention to treat. Double blind. Allocation concealment unclear. Baseline data not presented. Sample size not justified.
Kok, 1999(141) N = 102 6 month followup	2mg 17 b-oestradiol in combination with either 2.5, 5, 10, or 15 mg dydrogesterone, orally once a day	Changes from baseline. No placebo group	Self Reported Continence	(23/102) [0/102]	47.00 (2.89; 763.52)	0.23 (0.14; 0.31)	Intention to treat not stated. Double-blind. Randomization with permuted blocks Allocation concealment unclear. Nonparametric tests for randomization bias. Baseline data confirmed the adequacy of randomization. No justification for sample size.
Holtedahl, 1998(116) N = 90, positive pad test 6 month followup	Local estrogen in vagitories or jelly plus physiotherapy and electro stimulation	No treatment	Self Reported Continence	(8/36) [0/44]	20.68 (1.23; 346.46)	0.22 (0.08; 0.36)	No intention to treat. Randomization by phone from the university department. Allocation concealment unclear. Open label. Baseline data confirmed adequacy of randomization. Sample size justified.
Rufford, 2003(124) N = 40, urgency 6 month followup	25mg 17 beta-estradiol implant subcutaneous tissue	Placebo implant	Self Reported Continence	(4/20) [3/20]	1.33 (0.34; 5.21)	0.05 (-0.18; 0.28)	No intention to treat. Double blind. Allocation concealment adequate. Baseline data confirmed the adequacy of randomization. Sample size justified.
			Stress Incontinence % Cured	(4/20) [3/20]	1.3 (0.3; 5.2)	0.05 (-0.18; 0.28)	

			Urgency, % Of Cured	(3/20 [2/20]	1.5 (0.3; 8.0)	0.05 (-0.15; 0.25)	
Grady, 2001(166) N = 1,525 48 month followup	0.625mg of conjugated estrogens plus 2.5mg of medroxyprogesterone acetate in one tablet daily	Placebo	Self Reported Continence	(109/768) [134/757]	0.80 (0.64; 1.01)	-0.04 (-0.07; 0.00)	No Intention to treat. Double blind. Randomization using randomly permuted blocks of size 4 stratified by site. Allocation concealment adequate (reported previously). Sample size justified
Jackson, 1999(167) N = 67, urodynamic stress UI 6 month followup	Change from baseline after oestradiol valerate 2mg daily	Change from baseline after placebo	Self Reported Continence	(5/33) [5/34]	1.03 (0.33; 3.23)	0.00 (-0.17; 0.18)	No Intention to treat. Double-blind Randomization (computer generated simple random sampling) by hospital pharmacy. Allocation concealment unclear Sample size justified for the primary outcome-% of total collagen. No baseline comparison reported
Dessole, 2004 (168) N = 88, positive stress test 6 month followup	Intravaginal estriol ovules: 1 ovule (1mg) once daily for 2 weeks and then 2 ovules once weekly	Placebo vaginal suppositories	Continence, improved continence	(30/44) [7/44]	4.29 (2.11; 8.71)	0.52 (0.35; 0.70)	Intention to treat. Double-blind. Randomization was obtained using sets of sequenced, sealed, opaque envelopes, each containing the bottle number to be given to each participant. Allocation concealment adequate. Baseline data confirmed adequacy of randomization. Sample size justified.
Kok, 1999(141) N = 102 6 month followup	2mg 17 b-oestradiol in combination with either 2.5, 5, 10, or 15 mg dydrogesterone, orally once a day	Changes from baseline. No placebo group	Disappearance of nocturia	(67/102) [0/102]	135.00 (8.47; 2,151.44)	0.66 (0.56; 0.75)	Intention to treat not stated. Double-blind. Randomization with permuted blocks Allocation concealment unclear. Nonparametric tests for randomization bias. Baseline data confirmed the adequacy of randomization. No justification for sample size.
Ahlstrom, 1990(169) N = 29, stress UI 1.5 month followup	Estriol 4mg once daily and phenylpropanolamine 50 mg twice daily	Estriol 4mg once daily	Improved continence	(13/29) [11/29]	1.18 (0.64; 2.19)	0.07 (-0.18; 0.32)	No intention to treat. Double blind. Allocation concealment unclear. Baseline data not provided but reported as balanced. Sample size not justified.

Holtedahl, 1998(116) N = 90, positive pad test 6 month followup	Local estrogen in vagitories or jelly plus physiotherapy and electro stimulation	No treatment	Reduction in frequency amount, or wet episodes	(14/36) [4/44]	4.28 (1.54; 11.87)	0.30 (0.12; 0.48)	No intention to treat. Randomization by phone from the university department. Allocation concealment unclear. Open label. Baseline data confirmed adequacy of randomization. Sample size justified.
Waetjen, 2004(165) N = 963 36 month followup	Raloxifene 60mg/day or Raloxifene 120mg/day	Placebo	Incontinent episodes/day at 3 years Improved urinary incontinence at 3 years	(57/638) [22/325]	1.3 (0.8; 2.1)	-0.11 (-0.20; - 0.02)	No intention to treat Open label. Randomization and allocation concealment not reported. Baseline data confirmed adequacy of randomization. Sample size justified.
Waetjen, 2005(125) N = 417 36 month followup	14mg/day of transdermal E2 for 4 months	Placebo for 4 months	Improved incontinence: the number of incontinence episodes per week decreased by 2 or more	(52/208) [74/209]	0.7 (0.5; 1.0)	-0.10 (-0.19; - 0.02)	Intention to treat. Double-blind. Computer-generated randomization stratified by clinical center in blocks of 4. Treatment numbers were printed on labels adhered to identical-looking study medications. Allocation concealment adequate. Baseline data confirmed the adequacy of randomization. Sample size justified.
Vardy, 2003(139) N = 58 5 month followup	Conjugated equine estrogen 0.625mg	Placebo	Pelvic organ prolapse quantization, % of subjects with improved scores	(4/15) [0/13]	7.9 (0.5; 133.8)	0.27 (0.03; 0.51)	Intention to treat not stated. Double-blind. Allocation concealment unclear. Subjects had Incontinence at baseline (32.7%) with unknown distribution in the groups. No justification for sample size.
Long, 2006(170) N = 73 3 month followup	Oral 0.625mg of conjugated equine estrogen per tablet	Topical 0.63mg conjugated equine estrogen per 1 g vaginal cream	Improved scores in Bristol Female Lower Urinary Tract Symptoms Questionnaires	(8/37) [9/36]		-0.03 (-0.23; 0.16)	No Intention to treat. Two investigators were blind to each other's results. Allocation concealment unclear. No justification for the sample size. No comparison provided between groups, before/after treatments only.

Vardy, 2003(139) N = 58 5 month followup	Conjugated equine estrogen 0.625mg	Placebo	Improvement of urinary symptoms; Average change in angle of deflection	(3/15) [0/13]	6.1 (0.3; 108.6)	0.20 (-0.02; 0.42)	Intention to treat not stated. Double-blind. Allocation concealment unclear. Subjects had Incontinence at baseline (32.7%) with unknown distribution in the groups. No justification for sample size.
Waetjen, 2005(125) N = 417 4 month followup 24 month followup	14mg of transdermal E2 per day	Placebo 4 months	Decrease by >2 incontinence episodes per week	(30/208) [57/209]	0.53 (0.36; 0.79)	-0.13 (-0.21; 0.05)	Intention to treat. Double-blind. Computer-generated randomization stratified by clinical center in blocks of 4. Treatment numbers were printed on labels adhered to identical-looking study medications. Allocation concealment adequate. Baseline data confirmed the adequacy of randomization. Sample size justified.
	14mg of transdermal E2 per day for 2 years	Placebo 2 years	Decrease by >2 incontinence episodes per week	(27/208) [35/209]	0.78 (0.49; 1.23)	-0.04 (-0.11; 0.03)	
			Improved stress incontinence: the number of incontinence episodes per week decreased by 2 or more	(37/208) [61/209]	0.6 (0.4; 0.9)	0.00 (-0.07; 0.06)	
Vardy, 2003(139) N = 58 5 month followup	Raloxifene 60mg	Placebo	Improvement of urinary symptoms and angle of deflection	(1/15) [0/13]	2.63 (0.12; 59.40)	0.07 (-0.11; 0.24)	Intention to treat not stated. Double-blind. Allocation concealment unclear. Subjects had Incontinence at baseline (32.7%) with unknown distribution in the groups. No justification for sample size.
Grady, 2001(166) N = 1,525 100% female 4 month followup 12 month followup 24 month followup 36 month followup	0.63mg of conjugated estrogens plus 2.5mg of medroxyprogesterone acetate in one tablet daily	Placebo	Decrease by at least 2 episodes per week	(215/768) [241/757]	0.88 (0.75; 1.03)	-0.04 (-0.08; 0.01)	No Intention to treat. Double blind. Randomization using randomly permuted blocks of size 4 stratified by site. Allocation concealment adequate (reported previously). Sample size justified
				(214/768) [248/757]	0.85 (0.73; 0.99)	-0.05 (-0.10; 0.00)	
				(191/768) [236/757]	0.80 (0.68; 0.94)	-0.06 (-0.11; 0.02)	
				(181/768) [222/757]	0.80 (0.68; 0.95)	-0.06 (-0.10; 0.01)	

48 month followup				(162/768) [203/757]	0.79 (0.66; 0.94)	-0.06 (-0.10; - 0.01)	
			Improved or markedly improved continence	(158/768) [194/757]	0.80 (0.67; 0.97)	-0.05 (-0.09; - 0.01)	
Jackson, 1999(167) N = 67, urodynamic stress UI 6 month followup	Post oestradiol valerate 2mg daily	Placebo	Urge UI	(33/33) [33/34]	1.03 (0.95; 1.12)	0.03 (-0.05; 0.11)	No Intention to treat. Double-blind Randomization (computer generated simple random sampling) by hospital pharmacy. Allocation concealment unclear Sample size justified for the primary outcome-% of total collagen. No baseline comparison reported
			Stress UI	(33/33) [34/34]		0.00 (-0.06; 0.06)	
			Frequency of incontinence episodes (more than never)	(33/33) [34/34]		0.00 (-0.06; 0.06)	
			Quantity of lost urine (more than none)	(33/33) [34/34]		0.00 (-0.06; 0.06)	
			Urinary urgency	(31/33) [33/34]	0.97 (0.87; 1.07)	-0.03 (-0.13; 0.07)	
			Unexplained UI	(24/33) [16/34]	1.55 (1.02; 2.34)	0.26 (0.03; 0.48)	
			Wearing protection	(24/33) [24/34]	1.03 (0.76; 1.39)	0.02 (-0.19; 0.24)	
Steinauer, 2005(122) N = 184, any UI 50.4 month followup	Oral daily conjugated estrogen (0.63mg) and medroxy progesterone acetate (2.5mg)	Placebo	Incident UI	(382/597) [302/611]	1.29 (1.17; 1.43)	0.15 (0.09; 0.20)	Intention to treat. Double-blind. Randomization in each of 20 clinical centers using randomly permuted blocks of 4. Groups of continent women were comparable at baseline. No justification for sample size Incontinence - secondary outcome.

Jackson, 1999(167) N = 67, urodynamic stress UI 6 month followup	Oestradiol valerate 2mg daily	Placebo	Inability to stop midstream	(20/33) [24/34]	0.86 (0.60; 1.22)	-0.10 (-0.33; 0.13)	No Intention to treat. Double-blind Randomization (computer generated simple random sampling) by hospital pharmacy. Allocation concealment unclear Sample size justified for the primary outcome-% of total collagen. No baseline comparison reported
Steinauer, 2005(122) N = 184 50.4 month followup	Oral daily conjugated estrogen (0.63mg) and medroxy progesterone acetate (2.5mg)	Placebo	Incident UI in women younger than 60 years Incident of weekly stress UI	(57/96) [42/88] (322/597) [232/611]	1.24 (0.95; 1.64) 1.42 (1.25; 1.61)	0.12 (-0.03; 0.26) 0.16 (0.10; 0.22)	Intention to treat. Double-blind. Randomization in each of 20 clinical centers using randomly permuted blocks of 4. Groups of continent women were comparable at baseline. No justification for sample size Incontinence - secondary outcome.
Jackson, 1999(167) N = 67, urodynamic stress UI 6 month followup	Oestradiol valerate 2mg daily	Placebo	Changing outer clothing Intermittent stream	(17/33) [17/34] (17/33) [20/34]	1.03 (0.64; 1.65) 0.85 (0.55; 1.32)	0.02 (-0.22; 0.25) -0.09 (-0.32; 0.15)	No Intention to treat. Double-blind Randomization (computer generated simple random sampling) by hospital pharmacy. Allocation concealment unclear Sample size justified for the primary outcome-% of total collagen. No baseline comparison reported
Steinauer, 2005(122) N = 1,208 50.4 month followup	Oral daily conjugated estrogen (0.63mg) and medroxy progesterone acetate (2.5mg)	Placebo	Incident of weekly urge UI	(287/597) [220/611]	1.34 (1.17; 1.53)	0.12 (0.07; 0.18)	Intention to treat. Double-blind. Randomization in each of 20 clinical centers using randomly permuted blocks of 4. Groups of continent women were comparable at baseline. No justification for sample size Incontinence - secondary outcome.

Waetjen, 2005(125) N = 417 24 month followup	14mg of transdermal E2 per day for 2 years	Placebo 2 years	Incident UI	(81/208) [77/209]	1.06 (0.83; 1.35)	0.02 (-0.07; 0.11)	Intention to treat. Double-blind. Computer-generated randomization stratified by clinical center in blocks of 4. Treatment numbers were printed on labels adhered to identical-looking study medications. Allocation concealment adequate. Baseline data confirmed the adequacy of randomization. Sample size justified.
Lose, 2000(171) N = 251 6 month followup	Oestradiol-releasing ring, 7.5mg oestradiol	Oestriol pessaries 0.5 mg every second day	Stress UI Urge UI	(46/134) [48/117] (44/134) [0/117]	0.84 (0.61; 1.15) 77.79 (4.84; 1,249.40)	-0.07 (-0.19; 0.05) 0.33 (0.25; 0.41)	Intention to treat. Open label. Central randomization. Allocation concealment unclear. Baseline data confirmed the adequacy of randomization. Sample size justified.
Dessole, 2004(168) N = 88, positive stress test 6 month followup	Intravaginal estriol ovules: 1 ovule (1mg) once daily for 2 weeks and then 2 ovules once weekly for 6 months.	Placebo vaginal suppositories	Stress UI	(14/44) [37/44]	0.38 (0.24; 0.59)	-0.52 (-0.70; -0.35)	Intention to treat. Double-blind. Randomization was obtained using sets of sequenced, sealed, opaque envelopes, each containing the bottle number to be given to each participant. Allocation concealment adequate. Baseline data confirmed adequacy of randomization. Sample size justified.
Lose, 2000(171) N = 251 6 month followup	Oestradiol-releasing ring, 7.5mg oestradiol	Oestriol pessaries 0.5 mg every second day	Nocturia	(42/134) [41/117]	0.89 (0.63; 1.27)	-0.04 (-0.15; 0.08)	Intention to treat. Open label. Central randomization. Allocation concealment unclear. Baseline data confirmed the adequacy of randomization. Sample size justified.
Jackson, 1999(167) N = 67, urodynamic stress UI 6 month followup	Oestradiol valerate 2mg/day	Placebo	Abnormal stream	(10/33) [7/34]	1.47 (0.64; 3.41)	0.10 (-0.11; 0.30)	No Intention to treat. Double-blind Randomization (computer generated simple random sampling) by hospital pharmacy. Allocation concealment unclear Sample size justified for the primary outcome-% of total collagen. No baseline comparison reported

Long, 2006(170) N = 73 3 months followup	Oral 0.63mg of conjugated equine estrogen per tablet	Topical 0.63mg conjugated equine estrogen per 1 g vaginal cream	Nocturia	(10/37) [3/36]	3.24 (0.97; 10.83)	0.19 (0.02; 0.36)	No Intention to treat. Two investigators were blind to each other's results. Allocation concealment unclear. No justification for the sample size. No comparison provided between groups, before/after treatments only.
Lose, 2000(171) N = 251 6 month followup	Oestradiol-releasing ring, 7.5mg oestradiol	Oestriol pessaries 0.5mg every second day	Self reported urgency	(36/134) [39/117]	0.81 (0.55; 1.18)	-0.06 (-0.18; 0.05)	Intention to treat. Open label. Central randomization. Allocation concealment unclear. Baseline data confirmed the adequacy of randomization. Sample size justified.
Waetjen, 2004(165) N = 963 36 month followup	Raloxifene 60mg /day or raloxifene 120mg/day	Placebo	Urge UI	(164/638) [89/325]	0.94 (0.75; 1.17)	-0.02 (-0.08; 0.04)	No intention to treat Open label. Randomization and allocation concealment not reported. Baseline data confirmed adequacy of randomization. Sample size justified.
Vardy, 2003(139) N = 58 5 month followup	Conjugated equine estrogen 0.63mg;	Placebo	Any indicator of prolapse.	(3/15) [2/13]	1.30 (0.26; 6.62)	0.05 (-0.24; 0.33)	Intention to treat not stated. Double-blind. Allocation concealment unclear. Subjects had Incontinence at baseline (32.7%) with unknown distribution in the groups. No justification for sample size.
Vestergaard, 2003(140) N = 1,006 60 month followup	Sequential oral oestrogen and progestogen	No HRT	UI with mild discomfort	(100/502) [101/504]	0.99 (0.78; 1.27)	0.00 (-0.05; 0.05)	Intention to treat. Open label. Group 1 and 2 were block-randomized in groups of ten by the envelope method. Baseline data providing difference between treatment regimens not analyzed. No justification for sample size. Outcomes reported in two groups: HRT vs. No HRT.
Waetjen, 2004(165) N = 963 36 month followup	Raloxifene 60mg/day or raloxifene 120mg/day	Placebo	Mixed UI	(111/638) [47/325]	1.20 (0.88; 1.65)	0.03 (-0.02; 0.08)	No intention to treat Open label. Randomization and allocation concealment not reported. Baseline data confirmed adequacy of randomization. Sample size justified.

Hendrix, 2005(121) N = 3,073 12 month followup	Estrogen alone: 0.625mg conjugated equine estrogen	Placebo	Incident Stress Urinary Incontinence	(266/1526) [131/1547]	2.1 (1.7; 2.5)	0.09 (0.07; 0.11)	Intention to treat Double-blind. Central randomization at a 1:1 ratio. The study pill bottles had unique bar codes and computer-based selection to enable double-blinded dispensing. Incontinence - secondary outcome. Baseline data confirmed adequacy of randomization.
Goldstein, 2002(172) N = 2,924 36 month followup	Levomeloxifene 0.5mg/day	Placebo	Self reported Urinary incontinence on both active groups	(338/978) [37/970]	9.1 (6.5; 12.6)	0.31 (0.28; 0.34)	Intention to treat not stated. Double-blind. No justification for the sample size. Allocation concealment unclear. Only a subset of the data was ever validated; no summary statistics were calculated for demographic data. No justification for sample size.
Long, 2006(170) N = 73 3 month followup	Oral 0.63mg of conjugated equine estrogen per tablet	Topical 0.63mg conjugated equine estrogen per 1 g vaginal cream	Stress UI	(6/37) [13/36]	0.45 (0.19; 1.05)	-0.20 (-0.40; 0.00)	No Intention to treat. Two investigators were blind to each other's results. Allocation concealment unclear. No justification for the sample size. No comparison provided between groups, before/after treatments only.
Hendrix, 2005(121) N = 5,182 12 month followup	0.63mg of CEE plus 2.5mg of medroxyprogesterone acetate	Placebo	Incident Stress UI	(429/2675) [218/2507]	1.84 (1.58; 2.15)	0.07 (0.06; 0.09)	Intention to treat Double-blind. Central randomization at a 1:1 ratio. The study pill bottles had unique bar codes and computer-based selection to enable double-blinded dispensing. Incontinence - secondary outcome. Baseline data confirmed adequacy of randomization.
Waetjen, 2004(165) N = 963 36 month followup	Raloxifene 60mg/day or raloxifene 120mg/day	Placebo	Stress UI	(99/638) [55/325]	0.92 (0.68; 1.24)	-0.01 (-0.06; 0.04)	No intention to treat Open label. Randomization and allocation concealment not reported. Baseline data confirmed adequacy of randomization. Sample size justified.
Vestergaard, 2003(140) N = 1,006 60 month followup	Sequential oral oestrogen and progestogen	No HRT	Frequent voiding: mild discomfort	(70/502) [81/504]	0.87 (0.65; 1.17)	-0.02 (-0.07; 0.02)	Intention to treat. Open label. Group 1 and 2 were block-randomized in groups of ten by the envelope method. Baseline data providing difference between treatment regimens not analyzed. No justification for sample size. Outcomes reported in two groups: HRT vs. No HRT.

Hendrix, 2005(121) N = 5,182 12 month followup	Estrogen alone: 0.63mg of conjugated equine estrogen	Placebo	Incident urge UI	(210/1526) [184/1547]	1.16 (0.96; 1.39)	0.02 (-0.01; 0.02)	Intention to treat Double-blind. Central randomization at a 1:1 ratio. The study pill bottles had unique bar codes and computer-based selection to enable double-blinded dispensing. Incontinence - secondary outcome. Baseline data confirmed adequacy of randomization.
Goldstein, 2002(172) N = 2,924 36 month followup	Levorneloxifene 0.5mg/day	Placebo	Self reported micturition frequency in both active groups	(184/978) [39/970]	4.7 (3.4; 6.5)	0.15 (0.12; 0.18)	Intention to treat not stated. Double-blind. No justification for the sample size. Allocation concealment unclear. Only a subset of the data was ever validated; no summary statistics were calculated for demographic data. No justification for sample size.
Long, 2006(170) N = 73 3 months followup	Oral 0.63mg of conjugated equine estrogen per tablet	Topical 0.63mg conjugated equine estrogen per 1g vaginal cream	Urinary frequency	(3/37) [12/36]	0.24 (0.07; 0.79)	-0.25 (-0.43; -0.07)	No Intention to treat. Two investigators were blind to each other's results. Allocation concealment unclear. No justification for the sample size. No comparison provided between groups, before/after treatments only.
Jackson, 1999(167) N = 67, urodynamic stress UI 6 month followup	Oestradiol valerate 2mg/day	Placebo	UI with intercourse	(2/33) [1/34]	2.06 (0.20; 21.65)	0.03 (-0.07; 0.13)	No Intention to treat. Double-blind Randomization (computer generated simple random sampling) by hospital pharmacy. Allocation concealment unclear Sample size justified for the primary outcome-% of total collagen. No baseline comparison reported
Long, 2006(170) N = 73 3 month followup	Oral 0.63mg of conjugated equine estrogen per tablet	Topical 0.63mg conjugated equine estrogen per 1g vaginal cream	Urge UI	(2/37) [3/36]	0.65 (0.12; 3.66)	-0.03 (-0.15; 0.09)	No Intention to treat. Two investigators were blind to each other's results. Allocation concealment unclear. No justification for the sample size. No comparison provided between groups, before/after treatments only.

Goldstein, 2005(123) N = 619 36 month followup	Conjugated equine estrogen 0.63 mg/d	Placebo	Incident UI	(8/158) [1/152]	7.70 (0.97; 60.80)	0.04 (0.01; 0.08)	Intention to treat. Double-blind. Randomized block design (block size = 4); baseline data confirmed adequate randomization. No justification of sample size. Incontinence - secondary outcome.
Hendrix, 2005(121) N = 5,182 12 month followup	Estrogen alone: 0.63mg of conjugated equine estrogen plus 2.5mg of medroxyprogesterone acetate	Placebo	Incident mixed UI	(76/1526) [50/1547]	1.54 (1.09; 2.19)	0.02 (0.00; 0.03)	Intention to treat Double-blind. Central randomization at a 1:1 ratio. The study pill bottles had unique bar codes and computer-based selection to enable double-blinded dispensing. Incontinence - secondary outcome. Baseline data confirmed adequacy of randomization.
		Placebo	Incident mixed UI	(99/2675) [69/2507]	1.34 (0.99; 1.82)	0.01 (0.00; 0.02)	
Warming, 2003(173) N = 301 12 month followup	Levomeloxifene 1.25, 5,10, or 20 mg per day	Placebo	UI (including worsening of a previously existing condition)	(5) [0]		0.02 (-0.01; 0.06)	Intention to treat not stated. Double-blind. Allocation Concealment unclear. No justification for sample size. Outcomes reported independent of the dose of levormeloxifene.
Goldstein, 2005(123) N = 619 36 month followup	Raloxifene, 60mg/day	Placebo	Incident UI	(1/152) [1/152]	1.00 (0.06; 15.84)	0.00 (-0.02; 0.02)	Intention to treat. Double-blind. Randomized block design (block size = 4); baseline data confirmed adequate randomization. No justification of sample size. Incontinence - secondary outcome.
	Raloxifene, 150mg/day	Placebo	Incident UI	(1/157) [1/152]	0.97 (0.06; 15.34)	0.00 (-0.02; 0.02)	
Waetjen, 2004(165) N = 963 36 month followup	Raloxifene 60mg/day or Raloxifene 120mg/day	Placebo	Restricts daily activities: sometimes at 3 years	(389/638) [198/325]	1.0 (0.9; 1.1)	0.00 (-0.06; 0.07)	No intention to treat Open label. Randomization and allocation concealment not reported. Baseline data confirmed adequacy of randomization. Sample size justified.
			Effect on feelings: Somewhat at 3 years	(373/638) [191/325]	1.0 (0.9; 1.1)	0.00 (-0.07; 0.06)	

Jackson, 1999(167) N = 67, urodynamic stress UI 6 month followup	Post oestradiol valerate 2mg/day	Post placebo	More than 7 episodes of nocturnal incontinence	(31/33) [28/34]	1.1 (1.0; 1.4)	0.12 (-0.04; 0.27)	No Intention to treat. Double-blind Randomization (computer generated simple random sampling) by hospital pharmacy. Allocation concealment unclear Sample size justified for the primary outcome-% of total collagen. No baseline comparison reported
Waetjen, 2005(125) N = 417 36 month followup	14mg/day transdermal E2 for 4 months	Placebo 4 months	Unchanged urge incontinence: the number of incontinence episodes/week increased or decreased no more than 1	(178/208) [162/209]	1.1 (1.0; 1.2)	0.08 (0.01; 0.15)	Intention to treat. Double-blind. Computer-generated randomization stratified by clinical center in blocks of 4. Treatment numbers were printed on labels adhered to identical-looking study medications. Allocation concealment adequate. Baseline data confirmed the adequacy of randomization. Sample size justified.
Goldstein, 2005(123) N = 619 36 month followup	Conjugated equine estrogen 0.625mg/day	Placebo	Severity of incontinence: moderate or severe	(9/158) [1/152]	8.66(1.1;67.52)	0.05 (0.01;0.09)	Intention to treat. Double-blind. Randomized block design (block size = 4); baseline data confirmed adequate randomization. No justification of sample size. Incontinence - secondary outcome.
Jackson, 1999(167) N = 67, urodynamic stress UI 6 month followup	Post oestradiol valerate 2mg/day	Post placebo	More than 7 episodes of daytime incontinence	(25/33) [23/34]	1.1 (0.8; 1.5)	0.08 (-0.13; 0.30)	No Intention to treat. Double-blind Randomization (computer generated simple random sampling) by hospital pharmacy. Allocation concealment unclear Sample size justified for the primary outcome-% of total collagen. No baseline comparison reported
Vardy, 2003(139) N = 58 5 month	Raloxifene 60mg	Placebo	Consideration of any indicator of prolapse.	(11/15) [2/13]	4.8 (1.3; 17.7)	0.58 (0.28; 0.88)	Intention to treat not stated. Double-blind. Allocation concealment unclear. Subjects had Incontinence at baseline (32.7%) with unknown distribution in the groups. No justification for sample size.

Waetjen, 2005(125) N = 417 24 month followup	14mg/day transdermal E2 for 2 years	Placebo 2 years	Unchanged stress incontinence: the number of incontinence episodes/week increased or decreased no more than 1	(151/208) [129/209]	1.2 (1.0; 1.3)	0.11 (0.02; 0.20)	Intention to treat. Double-blind. Computer-generated randomization stratified by clinical center in blocks of 4. Treatment numbers were printed on labels adhered to identical-looking study medications. Allocation concealment adequate. Baseline data confirmed the adequacy of randomization. Sample size justified.
Vardy, 2003(139) N = 58 5 month followup	Raloxifene 60mg	Placebo	Pelvic organ prolapse quantitation, % of subjects with worsened scores	(10/15) [2/13]	4.3 (1.2; 16.3)	0.51 (0.20; 0.82)	Intention to treat not stated. Double-blind. Allocation concealment unclear. Subjects had Incontinence at baseline (32.7%) with unknown distribution in the groups. No justification for sample size.
	Tamoxifen 20mg;	Placebo	Consideration of any indicator of prolapse.	(9/15) [2/13]	3.9 (1.0; 14.9)	0.45 (0.13; 0.76)	
Waetjen, 2004(165) N = 963 36 month followup	Raloxifene 60mg/day or Raloxifene 120mg/day	Placebo	No change in urinary incontinence at 3 years	(218/638) [119/325]	0.9 (0.8; 1.1)	-0.02 (-0.09; 0.04)	No intention to treat Open label. Randomization and allocation concealment not reported. Baseline data confirmed adequacy of randomization. Sample size justified.
Waetjen, 2005(125) N = 417 4 months followup	14mg/day transdermal E2 for 4 months	Placebo for 4 months	Unchanged incontinence: ≤1 increase/decrease incontinence episodes/week	(106/208) [95/209]	1.1 (0.9; 1.4)	0.06 (-0.04; 0.15)	Intention to treat. Double-blind. Computer-generated randomization stratified by clinical center in blocks of 4. Treatment numbers were printed on labels adhered to identical-looking study medications. Allocation concealment adequate. Baseline data confirmed the adequacy of randomization. Sample size justified.
			Wears protection for incontinence at 3 years	(161/208) [67/209]	1.2 (1.0; 1.6)	0.05 (-0.01; 0.10)	
Grady, 2001(166) N = 1,525 36-48 months followup	0.625mg of conjugated estrogens plus 2.5mg of medroxyprogesterone acetate in one tablet daily	Placebo	Worsened or markedly worsened 48 months	(293/768) [202/757]	1.43 (1.23; 1.66)	0.11 (0.07; 0.16)	No Intention to treat. Double blind. Randomization using randomly permuted blocks of size 4 stratified by site. Allocation concealment adequate (reported previously). Sample size justified
			Worsened-increase ≥2/week episodes 48 months	(290/768) [212/757]	1.35 (1.17; 1.56)	0.10 (0.05; 0.14)	

			Worsened-increase ≥ 2 /week episodes 36 months	(256/768) [187/757]	1.35 (1.15 ; 1.58)	0.09 (0.04; 0.13)	
Vardy, 2003(139) N = 58 5 month followup	Tamoxifen 20mg	Placebo	Increase or worsening in symptoms of incontinence	(5/15) [2/13]	2.2 (0.5; 9.3)	0.18 (-0.13; 0.49)	Intention to treat not stated. Double-blind. Allocation concealment unclear. Subjects had Incontinence at baseline (32.7%) with unknown distribution in the groups. No justification for sample size.
Grady, 2001(166) N = 1,525 24 months followup	0.625mg of conjugated estrogens plus 2.5mg of medroxyprogesterone acetate in one tablet daily	Placebo	Worsened-increase of at least 2/ week episodes 24 months	(246/768) [178/757]	1.36 (1.16 ; 1.61)	0.09 (0.04; 0.13)	No Intention to treat. Double blind. Randomization using randomly permuted blocks of size 4 stratified by site. Allocation concealment adequate (reported previously). Sample size justified
Vardy, 2003(139) N = 58 5 month followup	Tamoxifen 20mg	Placebo	Pelvic organ prolapse quantitation, % of subjects with worsened scores	(5/15) [2/13]	2.2 (0.5; 9.3)	0.18 (-0.13; 0.49)	Intention to treat not stated. Double-blind. Allocation concealment unclear. Subjects had Incontinence at baseline (32.7%) with unknown distribution in the groups. No justification for sample size.
Grady, 2001(166) N = 1,525 12 month followup	0.625mg of conjugated estrogens plus 2.5mg of medroxyprogesterone acetate in one tablet daily	Placebo	Worsened-increase of at least 2/ week episodes 12 months	(224/768) [180/757]	1.23 (1.04 ; 1.45)	0.05 (0.01; 0.10)	No Intention to treat. Double blind. Randomization using randomly permuted blocks of size 4 stratified by site. Allocation concealment adequate (reported previously). Sample size justified
Holtedahl, 1998(116) N = 90, positive pad test 6 month followup	Local estrogen in vagitories or jelly plus physiotherapy and electro stimulation	No treatment	Unchanged incontinence: no changes in frequency, amount, or wet episodes	(10/36) [27/44]	0.5 (0.3 ; 0.8)	-0.34 (-0.54; 0.13)	No intention to treat. Randomization by phone from the university department. Allocation concealment unclear. Open label. Baseline data confirmed adequacy of randomization. Sample size justified.

Grady, 2001(166) N = 1,525 4 month followup	0.625mg of conjugated estrogens plus 2.5mg of medroxyprogesterone acetate in one tablet daily	Placebo	Worsened-increase of at least 2/ week episodes 4 months	(202/768) [166/757]	1.20 (1.00; 1.43)	0.04 (0.00; 0.09)	No Intention to treat. Double blind. Randomization using randomly permuted blocks of size 4 stratified by site. Allocation concealment adequate (reported previously). Sample size justified
Vardy, 2003(139) N = 58 5 month followup	Conjugated equine estrogen 0.625mg	Placebo	Pelvic organ prolapse quantitation, % of subjects with worsened scores	(4/15) [2/13]	1.7 (0.4; 8.0)	0.11 (-0.18; 0.41)	Intention to treat not stated. Double-blind. Allocation concealment unclear. Subjects had Incontinence at baseline (32.7%) with unknown distribution in the groups. No justification for sample size.
Waetjen, 2005(125) N = 417 36 month followup	14mg/day transdermal E2 for 4 months	Placebo 4 months	Worsened incontinence: the number of incontinence episodes/week increased by 2 or more	(50/208) [40/209]	1.3 (0.9; 1.8)	0.05 (-0.03; 0.13)	Intention to treat. Double-blind. Computer-generated randomization stratified by clinical center in blocks of 4. Treatment numbers were printed on labels adhered to identical-looking study medications. Allocation concealment adequate. Baseline data confirmed the adequacy of randomization. Sample size justified.
Waetjen, 2004(165) N = 963 36 month followup	Raloxifene 60mg/day or Raloxifene 120mg/day	Placebo	Incontinent episodes <1/month at 3 years	(146/638) [67/325]	1.1 (0.9; 1.4)	0.02 (-0.03; 0.08)	No intention to treat Open label. Randomization and allocation concealment not reported. Baseline data confirmed adequacy of randomization. Sample size justified.
Waetjen, 2005(125) N = 417 36 month followup	14mg/day transdermal E2 for 4 months	Placebo 4 months	Worsened stress incontinence: the number of incontinence episodes/week increased by 2 or more.	(42/208) [28/209]	1.5 (1.0; 2.3)	0.07 (0.00; 0.14)	Intention to treat. Double-blind. Computer-generated randomization stratified by clinical center in blocks of 4. Treatment numbers were printed on labels adhered to identical-looking study medications. Allocation concealment adequate. Baseline data confirmed the adequacy of randomization. Sample size justified.

Vestergaard, 2003(140) N = 1,006 60 month followup	Sequential oral oestrogen and progestogen	No HRT	Frequent voiding: Moderate to severe discomfort (2-4)	(100/502) [96/504]	1.0 (0.8; 1.3)	0.01 (-0.04; 0.06)	Intention to treat. Open label. Group 1 and 2 were block-randomized in groups of ten by the envelope method. Baseline data providing difference between treatment regimens not analyzed. No justification for sample size. Outcomes reported in two groups: HRT vs. No HRT.
Vardy, 2003(139) N = 58 5 month followup	Raloxifene 60mg	Placebo	Increase or worsening in symptoms of incontinence	(2/15) [2/13]	0.9 (0.1; 5.3)	-0.02 (-0.28; 0.24)	Intention to treat not stated. Double-blind. Allocation concealment unclear. Subjects had Incontinence at baseline (32.7%) with unknown distribution in the groups. No justification for sample size.
Waetjen, 2005(125) N = 417 24 month followup	14mg/day transdermal E2 for 2 years	Placebo 2 years	Worsened incontinence: the number of incontinence episodes/week increased by 2 or more.	(35/208) [35/209]	1.0 (0.7; 1.5)	0.00 (-0.07; 0.07)	Intention to treat. Double-blind. Computer-generated randomization stratified by clinical center in blocks of 4. Treatment numbers were printed on labels adhered to identical-looking study medications. Allocation concealment adequate. Baseline data confirmed the adequacy of randomization. Sample size justified.
Vardy, 2003(139) N = 58 5 month followup	Raloxifene 60mg	Placebo	Increase or worsening in symptoms of incontinence	(2/15) [2/13]	0.9 (0.1; 5.3)	-0.02 (-0.28; 0.24)	Intention to treat not stated. Double-blind. Allocation concealment unclear. Subjects had Incontinence at baseline (32.7%) with unknown distribution in the groups. No justification for sample size.
Waetjen, 2004(165) N = 963 36 month followup	Raloxifene 60mg/day or Raloxifene 120mg/day	Placebo	Worsened urinary incontinence at 3 years	(53/638) [21/325]	1.3 (0.8; 2.1)	0.02 (-0.02; 0.05)	No intention to treat Open label. Randomization and allocation concealment not reported. Baseline data confirmed adequacy of randomization. Sample size justified.
Waetjen, 2005(125) N = 417 36 month followup	14mg/day transdermal E2 for 2 years	Placebo 2 years	Worsened urge incontinence: the number of incontinence episodes/week increased by 2 or more.	(27/208) [38/209]	0.7 (0.5; 1.1)	-0.05 (-0.12; 0.02)	Intention to treat. Double-blind. Computer-generated randomization stratified by clinical center in blocks of 4. Treatment numbers were printed on labels adhered to identical-looking study medications. Allocation concealment adequate. Baseline data confirmed the adequacy of randomization. Sample size justified.

Holtedahl, 1998(116) N = 90, positive pad test 6 month followup	Local estrogen in vagitories or jelly plus physiotherapy and electro stimulation	No treatment	Worse incontinence: self reported worsening of severity or impact	(4/36) [13/44]	0.4 (0.1; 1.1)	-0.18 (-0.35; -0.01)	No intention to treat. Randomization by phone from the university department. Allocation concealment unclear. Open label. Baseline data confirmed adequacy of randomization. Sample size justified.
Waetjen, 2005(125) N = 417 24 month followup	14mg/day transdermal E2 for 2 years	Placebo 2 years	Worsened stress incontinence: the number of incontinence episodes/week increased by 2 or more.	(20/208) [19/209]	1.1 (0.6; 1.9)	0.01 (-0.05; 0.06)	Intention to treat. Double-blind. Computer-generated randomization stratified by clinical center in blocks of 4. Treatment numbers were printed on labels adhered to identical-looking study medications. Allocation concealment adequate. Baseline data confirmed the adequacy of randomization. Sample size justified.
Waetjen, 2004(165) N = 963 36 month followup	Raloxifene 60mg/day or Raloxifene 120mg/day	Placebo	Incontinent episodes/day at 3 years	(57/638) [22/325]	1.3 (0.8; 2.1)	0.02 (-0.01; 0.06)	No intention to treat Open label. Randomization and allocation concealment not reported. Baseline data confirmed adequacy of randomization. Sample size justified.
Vestergaard, 2003(140) N = 1,006 60 month followup	Sequential oral oestrogen and progestogen oral continuous oestradiol	No HRT	Incontinence with moderate to severe discomfort (2-4)	(40/502) [45/504]	0.9 (0.6; 1.3)	-0.01 (-0.04; 0.02)	Intention to treat. Open label. Group 1 and 2 were block-randomized in groups of ten by the envelope method. Baseline data providing difference between treatment regimens not analyzed. No justification for sample size. Outcomes reported in two groups: HRT vs. No HRT.
Goldstein, 2005(123) N = 619 36 month followup	Conjugated equine estrogen 0.625mg/day	Placebo	New or worsening urinary incontinence during the study	(11/158) [2/152]	5.3 (1.2; 23.5)	0.06 (0.01; 0.10)	Intention to treat. Double-blind. Randomized block design (block size = 4); baseline data confirmed adequate randomization. No justification of sample size. Incontinence - secondary outcome.
Waetjen, 2004(165) N = 963 36 month followup	Raloxifene 60mg/day or Raloxifene 120mg/day	Placebo	Severe and very severe at 3 years	(29/638) [14/325]	1.1 (0.6; 2.0)	0.00 (-0.02; .03)	No intention to treat Open label. Randomization and allocation concealment not reported. Baseline data confirmed adequacy of randomization. Sample size justified.

Warming, 2003(173) N = 301 12 month followup	Levormeloxifene 1.25, 5, 10, or 20mg/day	Placebo	Urogenital prolapse	(6/201) [0/50]	3.3 (0.2; 57.3)	0.03 (-0.01; 0.07)	Intention to treat not stated. Double-blind. Allocation Concealment unclear. No justification for sample size. Outcomes reported independent of the dose of levormeloxifene.
Waetjen, 2005(125) N = 417 4 months followup	14mg/day transdermal E2 for 4 months	Placebo 4 months	Worsened urge incontinence: the number of incontinence episodes/week increased by 2 or more.	(5/208) [21/209]	0.2 (0.1; 0.6)	-0.08 (-0.12; -0.03)	Intention to treat. Double-blind. Computer-generated randomization stratified by clinical center in blocks of 4. Treatment numbers were printed on labels adhered to identical-looking study medications. Allocation concealment adequate. Baseline data confirmed the adequacy of randomization. Sample size justified.
Warming, 2003(173) N = 301 12months after active drug	12 months after discontinuation of levormeloxifene 1.25, 5, 10, or 20mg/day,	Placebo	Urogenital prolapse	(2/201) [0/50]	1.3 (0.1; 25.9)	0.01 (-0.02; 0.04)	Intention to treat not stated. Double-blind. Allocation Concealment unclear. No justification for sample size. Outcomes reported independent of the dose of levormeloxifene.
Waetjen, 2004(165) N = 963 36 month followup	Raloxifene 60mg/day or Raloxifene 120mg/day	Placebo	Restricts daily activities: Most of the time at 3 years	(3/638) [2/325]	0.8 (0.1; 4.6)	0.00 (-0.01; 0.01)	No intention to treat Open label. Randomization and allocation concealment not reported. Baseline data confirmed adequacy of randomization. Sample size justified.
Goldstein, 2005(123) N = 619 36 month followup	Raloxifene, 150mg/day	Placebo	New or worsening UI during the study	(1/157) [2/152]	0.48 (0.04; 5.3)	-0.01 (-0.03; 0.02)	Intention to treat. Double-blind. Randomized block design (block size = 4); baseline data confirmed adequate randomization. No justification of sample size. Incontinence - secondary outcome.

*Bold - significant relative risk at 95% confidence level. HRT = hormone replacement therapy; UI = urinary incontinence.