TABLE 413-1 BENEFITS AND RISKS OF POSTMENOPAUSAL HORMONE THERAPY IN THE OVERALL STUDY POPULATION OF WOMEN 50–79 YEARS OF AGE IN THE INTERVENTION PHASE OF THE WOMEN'S HEALTH INITIATIVE (WHI) ESTROGEN-PROGESTIN AND ESTROGEN-ALONE TRIALS[a]

		Estrogen-Progestin		Estrogen Alone	
Outcome	**Effect**	**Relative Benefit or Risk**	**Absolute Benefit or Risk[b]**	**Relative Benefit or Risk**	**Absolute Benefit or Risk[b]**
Definite Benefits					
Symptoms of menopause	Definite improvement	↓65–90% decreased risk[c]		↓65–90% decreased risk[c]	
Osteoporosis	Definite increase in bone mineral density and decrease in fracture risk	↓33% decreased risk for hip fracture	6 fewer cases (11 vs. 17) of hip fracture	↓33% decreased risk for hip fracture	6 fewer cases (13 vs. 19) of hip fracture
Definite Risks[h]					
Endometrial cancer	Definite increase in risk with estrogen alone (see below for estrogen-progestin)	See below	See below		4.6 excess cases (observational studies)
Pulmonary embolism	Definite increase in risk	↑98% increased risk	9 excess cases (18 vs. 9)	↑35% increased risk (n.s.)	4 excess cases (14 vs. 10)
Deep vein thrombosis	Definite increase in risk	↑87% increased risk	11.5 excess cases (25 vs. 14)	↑48% increased risk	7.5 excess cases (23 vs. 15)
Breast cancer	Definite increase in risk with long-term use (≥5 years) of estrogen-progestin	↑24% increased risk	8.5 excess cases (43 vs. 35)	↓21% decreased risk (n.s.)	7 fewer cases (28 vs. 35)
Gallbladder disease	Definite increase in risk	↑57% increased risk	47 excess cases (131 vs. 84)	↑55% increased risk	58 excess cases (164 vs. 106)
Probable or Uncertain Risks and Benefits[h]					
Coronary heart disease[d]	Probable increase in risk among older women and women many years past menopause; possible decrease in risk or no effect in younger or recently menopausal women[e]	↑18% increased risk (n.s.)	6 excess cases (41 vs. 35)	No increase in risk	No difference in risk
Myocardial infarction	Significant interaction by age group for estrogen alone, with reduced risk in younger—but not older—women (*p* for trend by age = .02)	↑24% increased risk (n.s.)	6 excess cases (35 vs. 29)	No increase in risk[e]	No difference in risk[e]
Stroke	Probable increase in risk	↑37% increased risk	9 excess cases (33 vs. 24)	↑35% increased risk	11 excess cases (45 vs. 34)
Ovarian cancer	Probable increase in risk with long-term use (≥5 years)	↑41% increased risk (n.s.)	1 excess cases (5 vs. 4)	Not available	Not available
Endometrial cancer	Probable decrease in risk with estrogen-progestin during long-term follow-up (see above for estrogen alone)	↓33% decreased risk[f]	3 fewer cases (7 vs. 10)	See above	See above
Urinary incontinence	Probable increase in risk	↑49% increased risk	549 excess cases (1661 vs. 1112)	↑61% increased risk	852 excess cases (2255 vs. 1403)
Colorectal cancer	Probable decrease in risk with estrogen-progestin; possible increase in risk in older women with estrogen alone (*p* for trend by age = .02 for estrogen alone)	↓38% decreased risk	6.5 fewer cases (10 vs. 17)	No increase or decrease in risk[e]	No difference in risk[e]
Type 2 diabetes	Probable decrease in risk	↓19% decreased risk	16 fewer cases (72 vs. 88)	↓14% decreased risk	21 fewer cases (134 vs. 155)
Dementia (age ≥65)	Increase in risk in older women (but inconsistent data from observational studies and randomized trials)	↑101% increased risk	23 excess cases (46 vs. 23)	↑47% increased risk (n.s.)	15 excess cases (44 vs. 29)
Total mortality	Possible increase in risk among older women and women many years past menopause; possible decrease in risk or no effect in younger or recently menopausal women (*p* for trend by age <.05 for both trials combined)	No increase in risk	No difference in risk	No increase in risk[e]	No difference in risk[e]
Global index[g]	Probable increase in risk or no effect among older women and women many years past menopause; possible decrease in risk or no effect in younger or recently menopausal women (p for trend by age = 0.02 for estrogen alone)	↑12% increased risk	20.5 excess cases (189 vs. 168)	No increase in risk[e]	No difference in risk[e]

[a]The estrogen-progestin arm of the WHI assessed 5.6 years of conjugated equine estrogen (0.625 mg/d) plus medroxyprogesterone acetate (2.5 mg/d) versus placebo. The estrogen-alone arm of the WHI assessed 7.1 years of conjugated equine estrogen (0.625 mg/d) versus placebo. [b]Number of cases per 10, 000 women per year. [c]The WHI was not designed to assess the effect of HT on menopausal symptoms. Data from other randomized trials suggest that HT reduces risk for menopausal symptoms by 65–90%. [d]*Coronary heart disease* is defined as nonfatal myocardial infarction or coronary death. [e]There was a significant interaction by age; that is, the association between HT and the specified outcome was different in younger women and older women. [f]This is the risk reduction that was observed during a cumulative 12-year follow-up period (5.6 years of treatment plus 6.8 years of postintervention observation). [g]The *global index* is a composite outcome representing the first event for each participant from among the following: coronary heart disease, stroke, pulmonary embolism, breast cancer, colorectal cancer, endometrial cancer (estrogen-progestin arm only), hip fracture, and death. Because participants can experience more than one type of event, the global index cannot be derived by a simple summing of the component events. [h]Includes some outcomes where results were divergent between the estrogen-progestin arm and the estrogen-alone arm.

Abbreviation: n.s., not statistically significant.

Source: Data from JE Manson et al: JAMA 310:1353, 2013.