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Menopausal hormone therapy and breast cancer.

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Abstract

Observational and randomized controlled trial data have extensively examined the relationship between menopausal hormone therapy (MHT) and risk of developing breast cancer. **A highly influential study from the Women's Health Initiative (WHI) in 2002 reported that a MHT regimen of conjugated equine estrogens and medroxyprogesterone acetate increased the risk of breast cancer by 26%.** Later reports from the WHI indicated that a **MHT regimen with conjugated equine estrogens alone decreased the risk of breast cancer by 23%.** Critical re-examination of the WHI study noted that the average participant age was 63, that few women had symptoms, and that the WHI results might not apply to younger, symptomatic women shortly after menopause. Since the original publications, several post hoc analyses and observational studies have stimulated reconsideration of the WHI findings. Emphasis has been directed toward risks in younger women just entering the menopause, the subgroup who are most likely to be considering MHT use. The goal of this treatise is to integrate available mechanistic and clinical information related to the use of estrogen alone or estrogen plus a progestogen for five years or less. **These data suggest that estrogen alone neither decreases nor increases risk in younger women initiating therapy close to the time of menopause but decreases risk in older women. Both younger and older women experience an excess risk with estrogen plus a progestogen.** The attributable risk in younger women is less in those with a low underlying Gail Model risk score. Effects of MHT on risk largely reflect actions on pre-existing, occult, undiagnosed breast cancers. Tumor kinetic models suggest that the pro-proliferative effects of estrogen plus a progestogen on occult tumors provide a mechanistic explanation for the increased risk with this therapy. **Pro-apoptotic effects of estrogen alone may explain the reduction of breast cancer in women starting this therapy at an average age of 63 as reported in the WHI study.** This article is part of a Special Issue entitled 'Menopause'.