

## **Factors affecting uptake and adherence to breast cancer chemoprevention: A systematic review and meta-analysis**

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Chemoprevention is a risk reduction option for women who have increased risk of breast cancer. Selective Estrogen Receptor Modulators (SERMs) have been extensively tested, and alternative agents are being evaluated. Long-term adherence to chemoprevention is critical to obtaining the drug's full benefit. We systematically reviewed articles reporting uptake rates and adherence among healthy adult women, who were prescribed medication to prevent primary breast cancer. We also extracted data on the clinical, socio-demographic and psychological predictors of uptake and adherence.

Searches were performed in PubMed, CINAHL, EMBASE, and PsychInfo, yielding 3851 unique articles. Title, abstract and full text screening left 53 articles that met inclusion criteria, and a further 4 studies were identified from reference lists, giving a total of 57. The mean quality score using the Mixed Methods Appraisal Tool was 3 out of 4.

Thirty-one articles reported uptake, of which 14 tested predictors, and 23 reported adherence of which 11 tested predictors. Seven studies reported qualitative data. Most studies (50) involved SERMs, but 5 tested Aromatase Inhibitors, 1 tested Aspirin, 1 tested a statin. Twenty studies included data from a clinical setting, 35 reported trial data, and 2 reported both.

Twenty-four studies reporting 26 instances of uptake in 21,423 women were included in a meta-analysis. The pooled uptake estimate was 16.3% (95% CI, 13.6-19.0), with high heterogeneity ( $I^2=98.9\%$ ,  $p<0.0001$ ). Uptake was unaffected by study location or agent, but was significantly higher in trials (25.2% [95% CI, 18.3-32.2]) than in clinical settings (8.7% [95% CI, 6.8-10.9]). Factors associated with higher uptake in two or more studies included having an abnormal biopsy, a physician recommendation, higher objective risk, fewer side-effect or trial-related concerns, and older age. Heterogeneity in data collection prevented a meta-analysis of adherence. Data suggested adequate day-to-day adherence among women who initiated treatment, with 5/6 studies reporting  $\geq 80\%$  of medications being taken appropriately. Persistence over 3-12 months was also high, with 5/7 studies reporting that  $\geq 80\%$  women were still taking chemoprevention. Long-term persistence was lower, with only 1/10 studies reporting a persistence of  $\geq 80\%$  by 5-years. Factors associated with lower adherence or persistence included allocation to Tamoxifen (vs. placebo or Raloxifene), depression, smoking, and older age. Objective and subjective risk was a theme in all qualitative studies, although other topics involved in decision-making included concerns about medications (6/7), low knowledge (3/7), lack of information (2/7), and trial-related issues (2/7).

Chemoprevention uptake for the prevention of breast cancer is low, and long-term adherence is often insufficient for the full preventive effect. Uptake rates were higher in trials than in clinical settings, suggesting further work should focus on implementing chemoprevention within routine patient care. Further research is warranted to identify factors amenable to modification and to improve informed decision-making surrounding chemoprevention.