



# Endocrine Therapy and Risk of Dementia in Patients with Breast Cancer: A Scoping Review

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## BACKGROUND

- Breast cancer is the most common cancer in women worldwide.
- Adjuvant therapy is used after initial, effective treatment to prevent recurrence of breast cancer.
- Current adjuvant agents of choice include selective estrogen receptor modulators (SERM) and aromatase inhibitors (AI), also classified as endocrine therapy (ET).
- ET works by reducing the body's production of and ability to use estrogen in breast tissue.
- Estrogen also has neuroprotective effects, and it is hypothesized that ET may have beneficial effects on cognitive function.
- Previous studies on ET and cognitive function were inconclusive

## OBJECTIVE

The purpose of this review is to evaluate current literature for the effect of adjuvant ET on the risk of incident dementia diagnosis in adult women with breast cancer.

## METHODS

- Databases:** PubMed/MEDLINE (1966-2021), EMBASE (1947-2021), and Cochrane/CENTRAL (1908-2021)
- Keywords/MeSH Terms:** Alzheimer's, dementia, breast cancer, endocrine therapy/antagonist, AI, SERM, tamoxifen, anastrozole, raloxifene, exemestane, letrozole
- Screening:** independently reviewed by BC and AT, using RAYYAN software
- Inclusion Criteria:** (1) Adult women with breast cancer; (2) ET use; (3) Dementia diagnosis as outcome; (4) Results as statistical comparisons; (5) Full text in English.
- Exclusion Criteria:** (1) Pre-existing dementia, brain cancer, Alzheimer's, Parkinson's, stroke, or alcohol or drug abuse; (2) non-pharmacologic interventions; (3) non-human studies.

## RESULTS

Figure 1. Attrition Chart

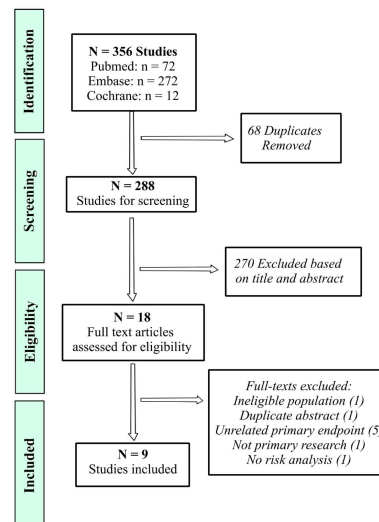
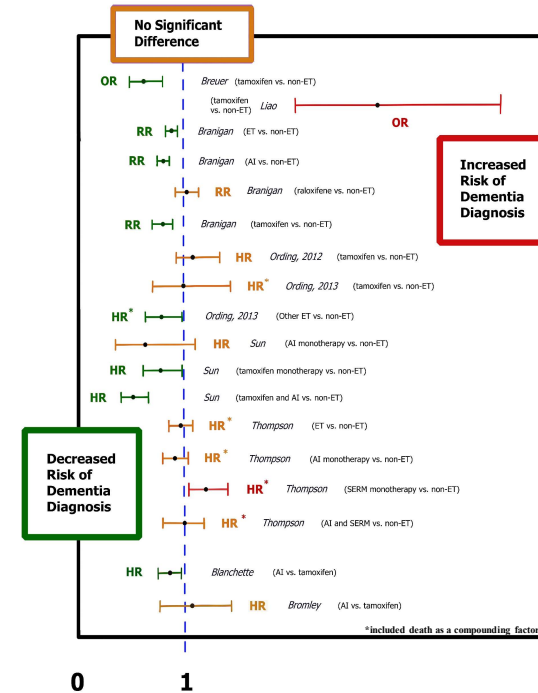


Table 1. Data Sources

Author	Study Design	Participants
Breuer et al., 2000, USA	Cross-Sectional	New York MDS (n=93,031)
Liao et al., 2017, Taiwan	Retrospective Case Control	Taiwan National Health Insurance Program (n=173)
Branigan et al., 2020, USA	Retrospective Cohort	Humana data set (n=57,843)
Ording et al., 2012, Denmark	Retrospective Cohort	Danish Nationwide Medical Registries (n=16,805)
Ording et al., 2013, Denmark	Retrospective Cohort	Danish Breast Cancer Cooperative Group Registry (n=16,419)
Sun et al., 2016, Taiwan	Retrospective Cohort	Taiwanese National Health Insurance Database (n=24,197)
Thompson et al., 2021, USA	Retrospective Cohort	SEER – Medicare (n=25,777)
Blanchette et al., 2020, Canada	Retrospective Cohort	Institute of Clinical Evaluative Sciences healthcare administrative databases (n=12,077)
Bromley et al., 2019, UK	Retrospective Cohort	UK primary care EHR (n=14,214)

Figure 2. Findings



## KEY FINDINGS AND DISCUSSION

### Discussion:

- Results from this scoping review found mixed evidence for the risk of dementia diagnosis.
- ET vs. non-ET group:**
  - 7 measures in 4 studies found a decreased risk of dementia with ET use
  - 7 measures in 5 studies found no association

- 2 measures in 2 studies found an increased risk of dementia
- AI vs. tamoxifen group:**
  - 1 study claimed decreased risk with AI use
  - 1 study claimed no difference
- Study by Liao et al. had a small size and utilized a case-control study design, limiting its generalizability.
- Studies varied by experimental design, study population, and comparators, making definitive comparisons difficult.
- Only two studies included protopathic bias as a potential compounding factor. Both studies found no overall association.

## STRENGTHS AND WEAKNESSES

**Strengths:** large sample size, national registries, definable outcomes (diagnosis specific), primarily cohort design

**Weaknesses:** multiple statistical measures, varied exposure/follow-up periods, types of dementia, and age at treatment, and different compounding factors acknowledged

## CONCLUSIONS

- The study found mixed evidence for the risk of dementia diagnosis with adjuvant ET use in adult women with breast cancer.
- More research with strong study design and methods is needed to address the possible neuroprotective effects of ET on dementia diagnosis and cognitive decline.

## REFERENCES

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