# Impact of Adjuvant Endocrine Therapy in Estrogen Receptor-Low Breast Cancer: A Systematic Review and Meta-Analysis

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## INTRODUCTION

- **Defining hormone-receptor (HR) positive** breast cancer (BC) remains **one of the most debated issues** in breast oncology.
- **Current ASCO-CAP guidelines**: a **cut-off of ≥1%** expression of estrogen receptor (ER).
- **ER-low tumors (ER 1-9%)** share similar biology, clinical outcomes and sensitivity to CT/ICI as TNBC

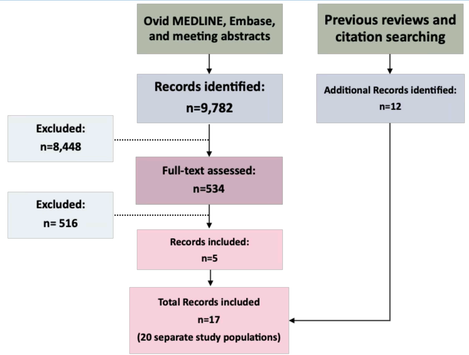
## OBJECTIVES

1) Is **adjuvant endocrine treatment** (ET) **effective** in patients with **ER-low tumors**?
2) Do patients with **ER-low tumors** have worse **clinical outcomes** than patients with **ER-rich (≥10%)**?

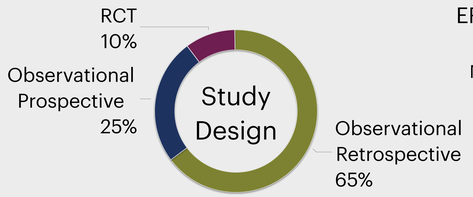
## METHODS: SYSTEMATIC REVIEW and META-ANALYSIS

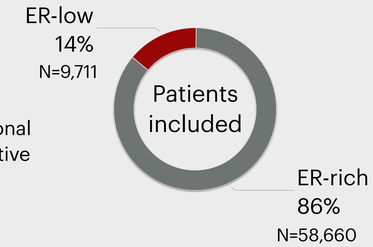
| PICO Element | Definition |
|---|---|
| **Population** | Adults (≥18 y) with early-stage (I–III) ER-positive (≥1%)/HER2-negative breast cancer |
| **Intervention** | Endocrine therapy (tamoxifen, aromatase inhibitors) |
| **Comparator** | ER-low (1-9%) vs ER-rich (≥10%) defined by immunohistochemistry |
| **Outcomes** | Overall survival (OS), Disease-free survival (DFS), Relapse-free survival (RFS) |
| **Study types** | Phase II–IV RCTs; retrospective/prospective observational studies |

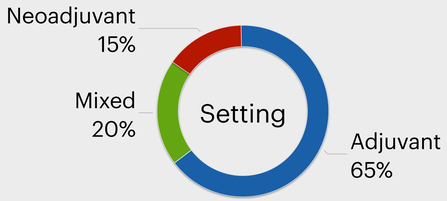
## STUDY SELECTION




## RESULTS

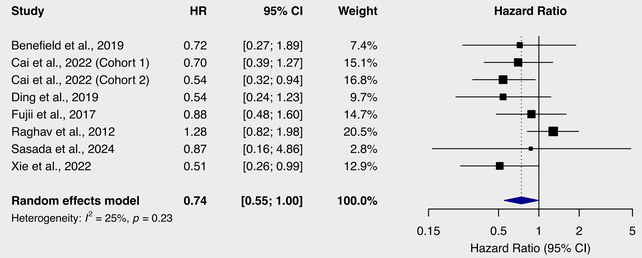


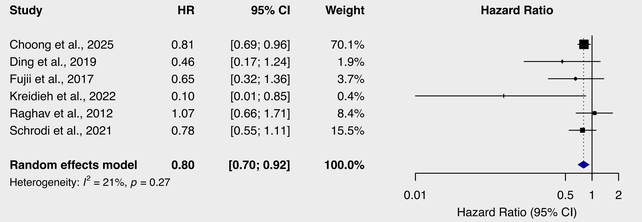




### ENDOCRINE TREATMENT: EFFICACY in ER-LOW

#### Relapse-free survival

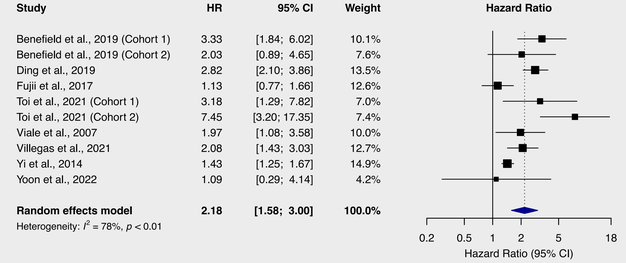



#### Overall Survival

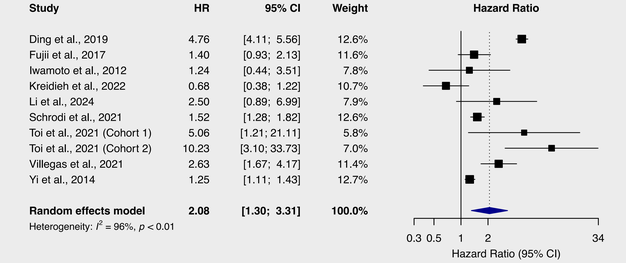



### PROGNOSIS of ER-LOW vs ER-RICH

#### Relapse-free survival




#### Overall Survival




## CONCLUSIONS

- **Adjuvant endocrine treatment improves outcome in ER-low tumors >** ET administration is associated with a **26% reduction in the risk of relapse or death** (HR 0.74, 95%CI 0.55-1.00) **and 20% reduction in the risk of death** (HR 0.80, 95%CI 0.70-0.92)
- Patients with **ER-low breast** cancer experience a significantly **worse prognosis** compared to those with **ER-rich tumors,** with a **>2x higher risk of relapse or death** (HR 2.18, 95CI% 1.58-3.00 for RFS; HR 2.08, 95%CI 1.30-3.31 for OS):
- In addition to therapeutic strategies appropriate for such **high-risk profile – such as chemotherapy** – the potential benefit of **adjuvant endocrine therapy should not be overlooked** and ought to be **part of the clinical discussion for patients with early-stage ER-low tumors**.

### KEY CLINICAL SIGNALS

Adjuvant ET in ER-low:
⬇26% risk of relapse or death
⬇20% risk of death

ER-low vs ER-rich: ⬆2x risk of relapse/death

Ref: Allison KH ASCO-CAP 2020; Massa D. JNCI 2024; Dieci MV NPJ 2021; Cardoso F. Nat Med 2025

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