Health Economic Impact of Non-Persistence with Tamoxifen Adjuvant Endocrine Therapy in Pre-Menopausal Women with Early-Stage Breast Cancer: A Simulation Study

Soroush Fariman[1], Jennifer Elston Lafata[1, 2]

1. Division of Pharmaceutical Outcomes and Policy, Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, NC, USA.
2. Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, NC, USA

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Background

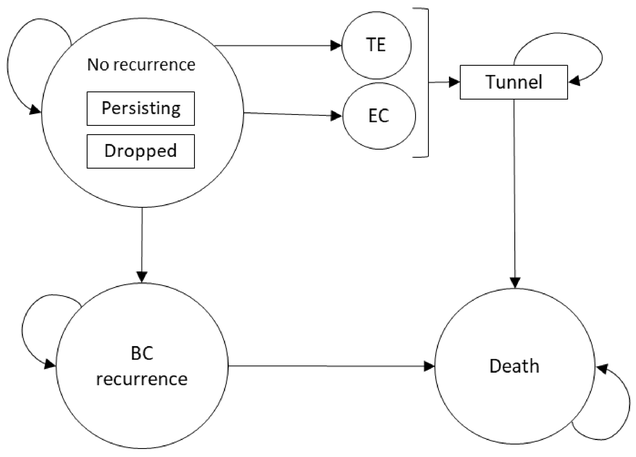
- Low persistence rates and racial disparities with tamoxifen adjuvant endocrine therapy (AET) among women with early breast cancer indicate a care gap and potential for improving patient outcomes.
- Improving persistence rates could contribute to bridging the racial gap in AET outcomes.
- **We aimed to quantify the burden of suboptimal persistence with tamoxifen in premenopausal women with early breast cancer in terms of healthcare costs and quality-adjusted life years (QALYs).**

Methods

A Markov model to simulate cohort of 10,000 premenopausal (age<45), ER+, HER2- early breast cancer patients prescribed 5 years of tamoxifen, from the US societal perspective, over a 10-year time horizon.

- Model states included No Recurrence, Recurrence, Thromboembolism and Endometrial Cancer (as tamoxifen-related major adverse events), and Death.
- Two contrasting scenarios regarding tamoxifen persistence were simulated:

- Direct and indirect costs in 2023 USD were included.
- A 3% annual discount rate was applied to both costs and QALYs.
- Survival and recurrence probabilities were estimated from the results of Early Breast Cancer Trialists' Collaborative Group[5].



Schematic Model Structure
BC: Breast cancer, EC: Endometrial cancer, TE: Thromboembolism

Model assumptions:

- All patients in the recurrence free state are assumed to start treatment with tamoxifen and some may discontinue tamoxifen after some time.
- Patients could experience one major ET-related adverse event, either TE or EC, and remain in that state or be cured and enter a tunnel state in which we assumed they would not be taking tamoxifen. Those who develop a major adverse event were assumed to discontinue ET.
- The effect of tamoxifen on recurrence and survival is largely similar regardless of age, the use of chemotherapy, PR status, and nodal status[5].
- We assumed types of recurrence to be contralateral (7%), loco-regional (18%) and distant (75%) recurrence[6].

Model inputs were derived from the literature and varied by their lower and upper bounds for univariate deterministic sensitivity analysis (DSA) and probabilistic sensitivity analysis (PSA) **(Available in the handout by scanning the QR code).**

Our findings demonstrate **substantial lost opportunity due to non-persistence with tamoxifen AET** in pre-menopausal patients with early-stage breast cancer, in terms of both **duration and quality of life.**

By quantifying the opportunity cost, we estimated the **health-related and economic value of improving tamoxifen persistence** in premenopausal women with early breast cancer.

Implementing strategies to improve tamoxifen persistence can yield significant return on investment.

Contact:
Soroush Fariman
Fariman@unc.edu

To access the handout, including model inputs scan the QR code.

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Results

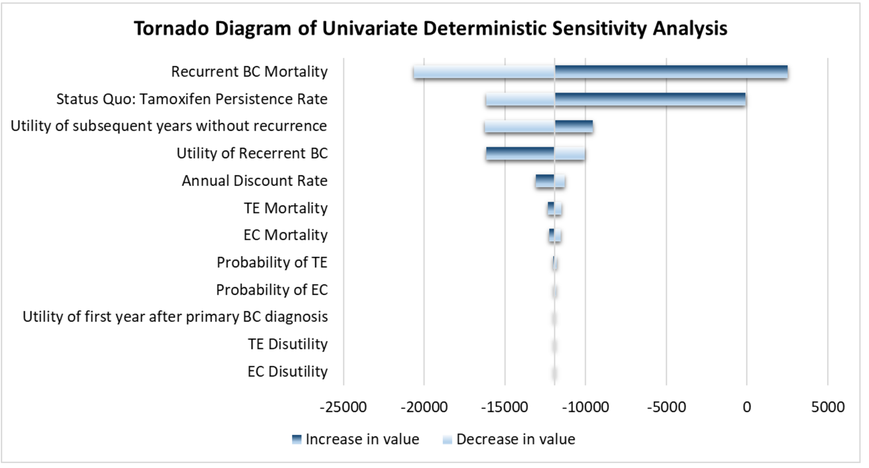
Base Case

Base-case	Number of BC Death	Total LY	Total QALY	Total Costs ($)
Status Quo	2,225	79,842	65,708	2,974,769,261
Full Persistence	1,884	81,354	67,432	2,954,251,694
Incremental	**-341**	**6,047**	**6,894**	**-20,517,567**

- **The incremental cost-effectiveness ratio (ICER) of full-persistence compared to status quo was estimated at-$11,904/QALY.**
- **Considering $100,000/QALY willingness-to-pay, the net monetary benefit (NMB) for changing a non-persistent patient to persistent was $19,287.**

Sensitivity Analyses

- Key model parameters according to univariate DSA are (i) **the probability of breast cancer death after recurrence,** and (ii) **status quo persistence rates**.



- According to the PSA, the full-persistence scenario **was dominant in 66.0% and cost-effective in 99.4% of iterations** (at WTP threshold of $100,000/QALY).

Limitations

- Model limitations include not accounting for AET with aromatase inhibitors, other forms of non-adherence, and longer time horizons.