

Cost-Effectiveness of Adjuvant Radiation Therapy vs. Tamoxifen Alone in Older Adult Women With Early-Stage Breast Cancer

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Background

Radiation therapy (RT) is commonly used as an adjuvant treatment option in early-stage breast cancer patients undergoing breast conserving surgery (BCS).^{1,2}

Recent studies, however, suggest that elderly female breast cancer patients aged 65+ receiving adjuvant endocrine therapy (tamoxifen) do not benefit from added RT.^{2,3}

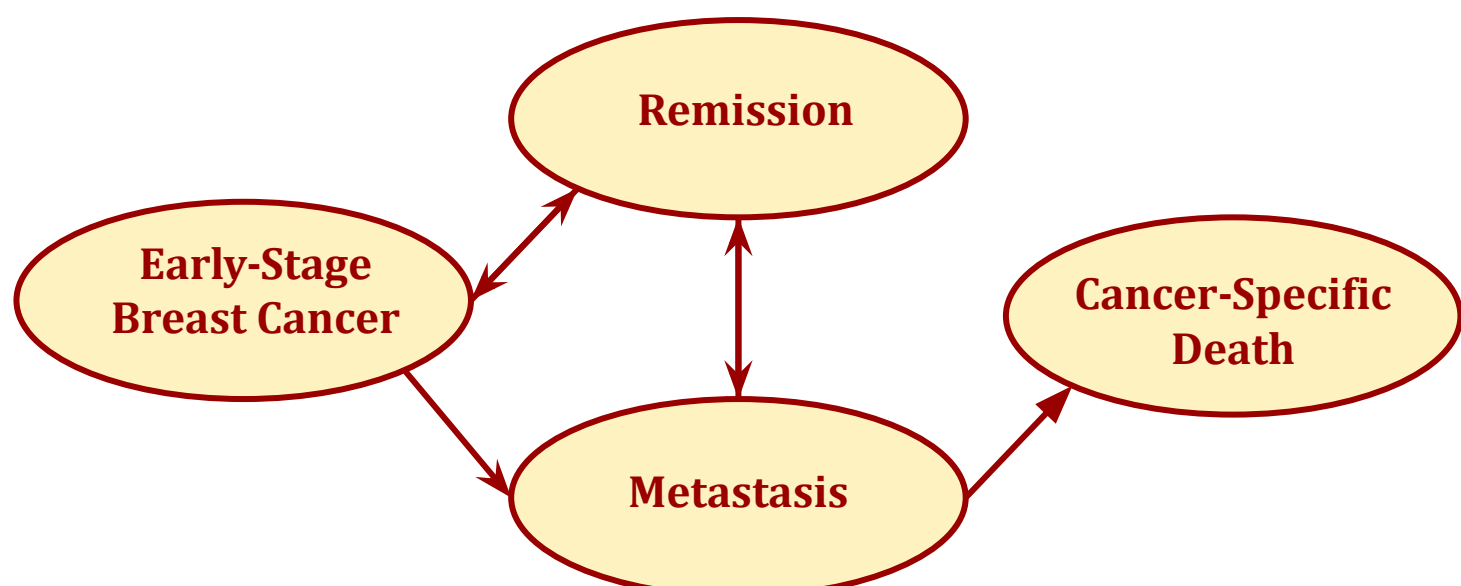
Objective

To evaluate the cost-effectiveness of **adjuvant tamoxifen + RT (tam+RT)** versus **adjuvant tamoxifen alone** in women aged 65+ undergoing BCS for early-stage estrogen receptor-positive (ER+) breast cancer.

Methods

Model type: Decision analytic/Markov model (5 year time horizon)

- **Intervention** - Adjuvant tam+RT
- **Comparator** - Adjuvant tamoxifen alone
- **Target population** - Early-stage ER+ female breast cancer patients aged 65+ treated with BCS
- **Structure** - 4 mutually exclusive health states:



Clinical efficacy & modeling: Model transition parameters were derived from CALGB 9343, a randomized clinical trial comparing outcomes on tam+RT versus tamoxifen alone in (n=636) women aged 70 and older with ER+ clinical stage I breast cancer, and a separate cohort of (n=888) women aged 65 and older with ER+ T1 breast cancer treated with BCS at Memorial Sloan Kettering Cancer Center from 2010-2015.⁴⁻⁹

Costs: Costs were informed by the Centers for Medicare & Medicaid Services (CMS) Medicare Part D Drug Spending Dashboard and various economic studies on average Medicare spending for RT, curative surgical procedures, and cumulative costs for treating locoregional (LR) and distant recurrence (metastasis), and were assessed in 2021 US dollars.⁴⁻⁹

Outcomes: Effectiveness was measured in quality-adjusted life years (QALYs) derived using five-year survival rates from the American Cancer Society and 15D HRQoL scores from patient reported outcomes assessments of breast cancer patients and survivors.¹⁰⁻¹⁴

Sensitivity analysis: We conducted both probabilistic and deterministic sensitivity analysis to test model assumptions and robustness.

Model Inputs

Table 1. Model parameters: base-case values, lower bound values, upper bound values, and distributions for sensitivity analysis

Variable	Base-Case Value	Lower Value	Upper Value	Distrib.	Reference(s)
Cost of tamoxifen (five-year course)	\$825	\$360	\$23,654	Gamma	CMS, 2024 & Lexicomp, 2024 (4,5)
Cost of radiation	\$12,021	\$10,204	\$14,398	Gamma	Paravati et al., 2015 (6)
Cost of mastectomy	\$47,467	\$35,600	\$59,334	Uniform	Susman, 2015 (7)
Cost of breast conserving surgery	\$44,751	\$33,563	\$55,939	Uniform	Susman, 2015 (7)
Cost of axillary surgery	\$3,095	\$2,321	\$3,869	Uniform	Tom et al., 2021 (8)
Cost of treating metastasis	\$168,656	\$126,492	\$210,820	Uniform	Vitko et al., 2024 (9)
Cost of treating second LR recurrence	\$96,455	\$72,349	\$120,581	Uniform	Vitko et al., 2024 (9)
Probabilities of cancer recurrence (after first-line BCS)					
Locoregional recurrence (tam+RT)	0.0126	0.0095	0.0158	Uniform	Hughes et al., 2013 & Tringale et al., 2021 (2,3)
Locoregional recurrence (tam alone)	0.0598	0.0449	0.0748	Uniform	Hughes et al., 2013 & Tringale et al., 2021 (2,3)
Metastasis (tam+RT)	0.0336	0.0252	0.0420	Uniform	Hughes et al., 2013 & Tringale et al., 2021 (2,3)
Metastasis (tam alone)	0.0362	0.0272	0.0453	Uniform	Hughes et al., 2013 & Tringale et al., 2021 (2,3)
Probabilities of ipsilateral breast tumor recurrence (versus axillary) given locoregional recurrence					
Ipsilateral recurrence (tam+RT)	0.8000	0.6000	1.000	Uniform	Hughes et al., 2013 & Tringale et al., 2021 (2,3)
Ipsilateral recurrence (tam alone)	0.8182	0.6137	1.000	Uniform	Hughes et al., 2013 & Tringale et al., 2021 (2,3)
Probabilities of second-line mastectomy (versus BCS) given ipsilateral breast tumor recurrence					
Mastectomy (tam+RT)	0.6741	0.5056	0.8426	Uniform	Van den Bruele et al., 2021 (15)
Mastectomy (tam alone)	0.6388	0.4791	0.7985	Uniform	Van den Bruele et al., 2021 (15)
Probabilities of adjuvant radiation (in tamoxifen alone arm) following second-line mastectomy or BCS					
Radiation following mastectomy	0.1515	0.0000	0.3636	Uniform	McCready et al., 1992 (16)
Radiation following BCS	0.4130	0.3100	0.5163	Uniform	McCready et al., 1992 (16)

Table 2. Utility values for endpoints of interest; five-year survival rates and health-related quality of life scores used to derive utilities

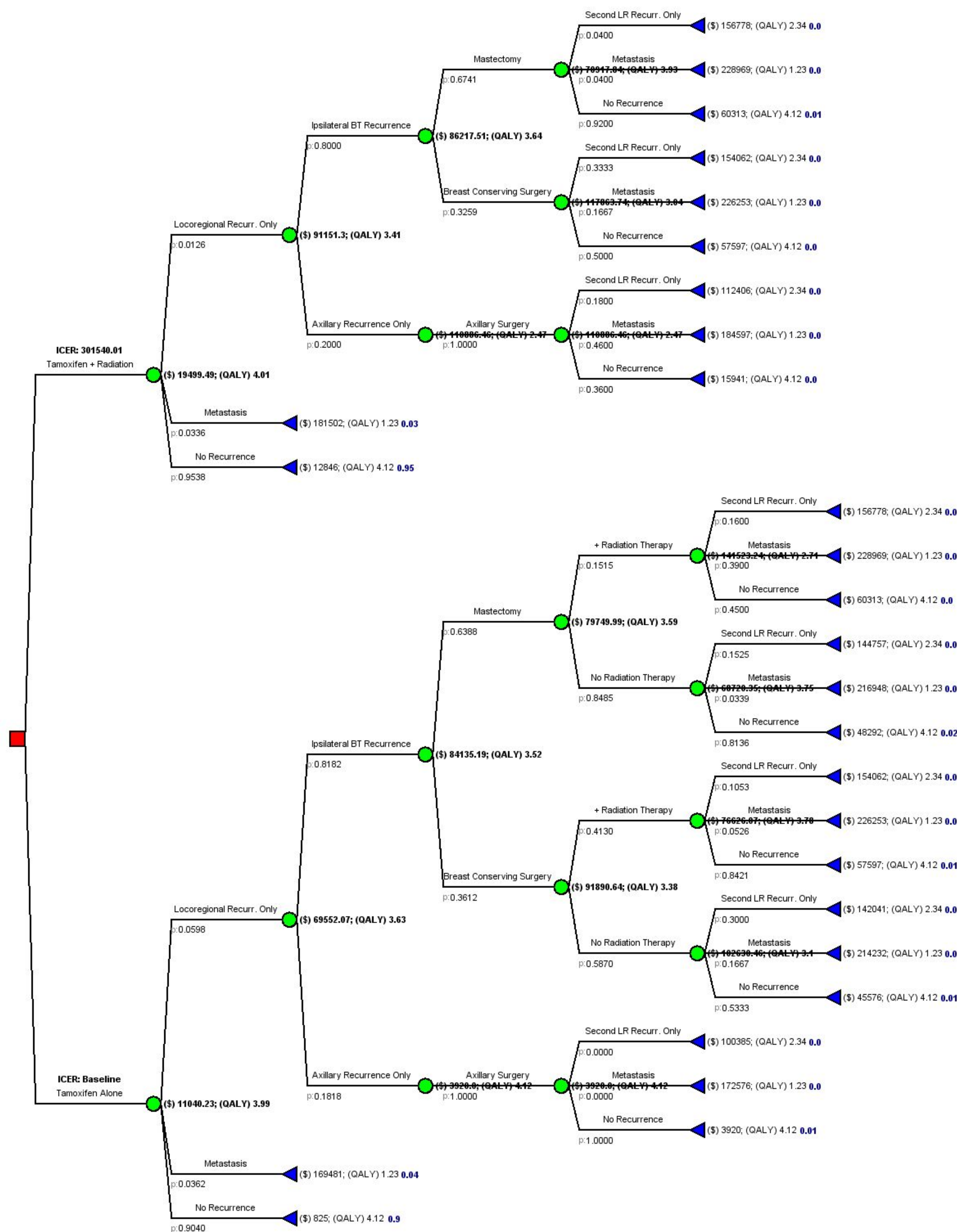
Endpoint	Utility Value (QALYs)	Five-Year Survival	HRQoL (15D Score)	References
No recurrence	4.12	91%	0.905	ACS, 2024 & Roine et al., 2021 (10,11)
Second locoregional recurrence	2.34	53%	0.883	Wapnir et al., 2017 & Luutonen et al., 2014 (12,13)
Metastasis	1.23	30%	0.820	ACS, 2024 & Rautalin et al., 2017 (10,14)

Base-Case Analysis

Table 3. Base-case cost-effectiveness analysis output

Strategy	Avg. Cost	Avg. QALYs	Δ Avg. Cost	Δ Avg. QALYs	ICER
Tamoxifen alone	\$11,040.23	3.99			
Tam+RT	\$19,499.49	4.01	+\$8,459.26	+0.02	\$301,540/QALY

Figure 1. Decision tree with rollback results



Sensitivity Analysis

Figure 2. ICE scatter plot (1000 Monte Carlo simulations)

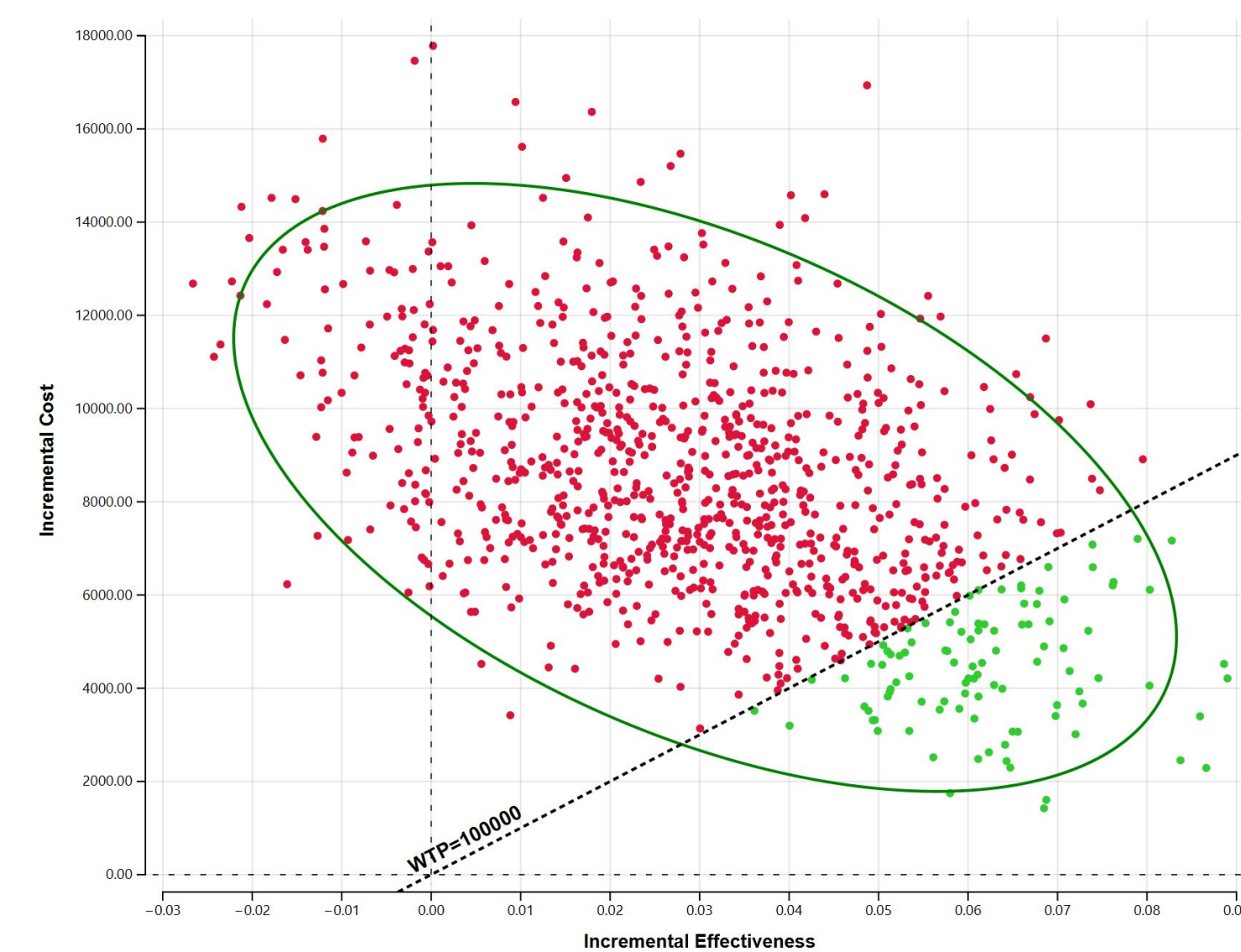


Table 4. Text report for above scatter plot

Quadrant (tam+RT vs. tamoxifen alone)	Within \$100,000 WTP threshold?	Proportion
I (more costly, more effective)	Yes	10.1%
I (more costly, more effective)	No	80.7%
II (more costly, less effective)	No	9.2%

Results

Base-case analysis: In our base-case analysis, total costs for adjuvant tam+RT were **\$19,499.49**, compared to **\$11,040.23** for adjuvant tamoxifen alone. Total QALYs for tam+RT were **4.01**, compared to **3.99** for tamoxifen alone, yielding a base-case ICER of **\$301,540/QALY**.

Probabilistic sensitivity analysis: Sensitivity analysis indicated that adjuvant tam+RT had a **10.1%** probability of being cost-effective at a willingness-to-pay (WTP) threshold of **\$100,000/QALY**, and a **24.2%** probability of being cost-effective at a WTP threshold of **\$150,000/QALY**.

Deterministic sensitivity analysis: Sensitivity analysis indicated that our rollback decision was primarily driven by the costs of of radiation therapy, tamoxifen, and treating metastasis, as well as the probabilities of metastasis following first-line treatment in either arm.

Conclusion

Despite common utilization of tam+RT as an adjuvant therapy following BCS, our model highlights serious concerns regarding its cost-effectiveness vs. tamoxifen alone in older adult women with ER+ T1 breast cancer.

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