EE395

Economic Evaluations, Cost and Healthcare Resource Utilization in early Triple-Negative and Low Hormone Receptor-Positive Breast Cancer: A Comprehensive Systematic Review

Amin Haiderali[1]; Jagadeswara Rao Earla[1]; Asheer Dovari[2]; Jyothsna Nathani[3]; Sugandh Sharma[4];

[1]Merck & Co., Inc., Rahway, NJ, USA; [2]Parexel International, Mumbai, India; [3]Parexel International, Bengaluru, India; [4]Parexel International, Chandigarh, India.

Background and objectives

- Triple-negative breast cancer (TNBC) which lacks expression of Hormone Receptor (HR) and Human Epidermal growth factor Receptor 2 (HER2), and breast cancer (BC) with HR- low positive (HR ≤ 5% by immunohistochemistry) HER2- are aggressive subtypes with significant economic implications.
- This review synthesized evidence on economic evaluations, healthcare resource utilization (HCRU), and costs associated with adjuvant therapy in these populations.

Methodology

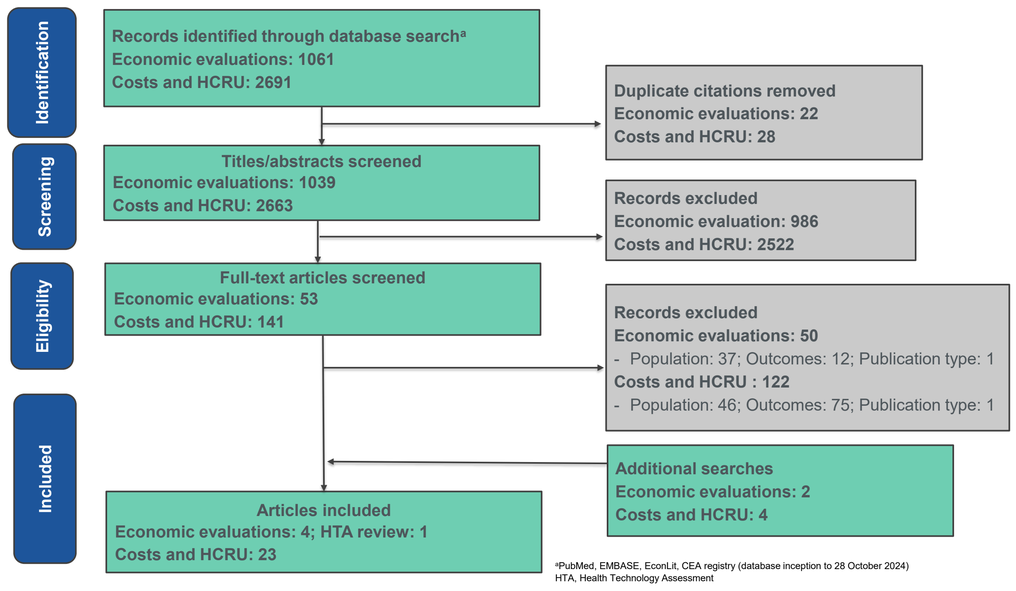
- The systematic literature review followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines with the eligibility criteria as provided in **Table 1**.
- Multiple databases (Embase, MEDLINE, Tufts CEA Registry, Econlit) were searched for English language studies from inception to October 2024. This was supplemented by conference proceedings (2021-2024) and bibliographic searching of relevant reviews.
- Two independent reviewers conducted screening, data extraction, and quality assessment, with a third reviewer resolving any discrepancies to ensure methodological rigor.

Table 1: Eligibility criteria (PICOS)

Parameters	Economic evaluations	Costs and HCRU
Population	Stage I-III TNBC or low HR-positive and/or HER2 borderline BC receiving adjuvant therapy; metastatic TNBC was excluded	Stage I-III TNBC or low HR-positive and/or HER2 borderline BC; metastatic TNBC was excluded
Intervention	Pembrolizumab, Paclitaxel, Gemcitabine, Docetaxel, Vinorelbine tartrate, Epirubicin, Eribulin, Olaparib, Ixabepilone, Methotrexate, Fluorouracil, Cyclophosphamide, Carboplatin, Talazoparib, Cisplatin, Doxorubicin, Capecitabine	No restriction
Outcomes	Cost-effectiveness outcomes such as ICER, cost per QALY etc.	HCRU outcomes; Direct, indirect costs
Study design	No restriction	
Language	Full texts published in the English language	
Geography and timeframe	Global; Database inception to 28 October 2024	

BC, Breast Cancer; HCRU, Healthcare Resource Utilization; HER2, Human Epidermal growth factor Receptor 2; HR, Hormone Receptor; ICER, Incremental Cost-Effectiveness Ratio; QALY, Quality-Adjusted Life Year; TNBC, Triple-Negative Breast Cancer

Figure 1: PRISMA flow



[a]PubMed, EMBASE, EconLit, CEA registry (database inception to 28 October 2024)
HTA, Health Technology Assessment

Economic evaluations in TNBC

- Four economic evaluations and one health technology assessment (HTA) were identified.
- Adjuvant olaparib versus watch and wait was found to be cost-effective for germline BRCA mutation (gBRCA)1/2-mutated early BC in three studies.
- The study from the UK showed that adding bevacizumab to adjuvant chemotherapy could be cost-effective with an ICER ≤£43,804 per QALY.

Table 2: Summary of economic evaluations in TNBC

Study, Country (cost year)	Interventions	Incremental Cost	Incremental QALYs	ICER (per QALY)	Conclusion
Polyzoi 2024[1], Sweden (2022)	Adjuvant olaparib vs WaW	465,928 SEK	1.25	371,522 SEK	Cost-effective at list price
Cedillo 2024[2], Spain (2023)	Adjuvant olaparib vs WaW	€ 50,164	1.28	€ 39,084	Could be cost-effective
Sousa 2024[3], Portugal (NR)	Adjuvant olaparib vs WaW	€ 42,801	1.1	€ 38,917	Generally acceptable incremental cost
Ray 2009[4], UK (NR)	Adjuvant bevacizumab + chemo vs chemo alone	-	0.82	≤£43,804	Could be cost-effective
NICE TA886 2023[5], UK(2019-2020)	Adjuvant olaparib vs WaW	-	-	£29,732 (TNBC)	Cost-effective with Patient Access Scheme pricing

* ICER, incremental cost-effectiveness ratio; NR, not reported; QALY, quality-adjusted life years; WaW, wait and watch

HCRU in TNBC

- Ten studies reported HCRU data including hospitalization rates, outpatient visits and length of hospital stays (LoS) with five studies from the USA.
- Mean number of emergency room (ER) visits ranged from 0.6-1.4 per person per year (PPPY)[8] and 0.2-1.3 visits per person per month (PPPM) (USA, Canada and Brazil)[8,9,10]
- Outpatient services were heavily utilized, with professional/office visits ranging from 47.1% to 100%[6,11] of patients and OP visits ranging from 4.6-44.3 PPPY[7,8], with office visits reaching 82.2 PPPY in the USA[8]
- Supportive care procedures increased (20.05 to 53.37 PPPM, Brazil) from early to progressive disease states[10]
- Resource use peaked during active treatment phases, then significantly decreased during follow-up periods[11]
- Average LoS ranged from 4.2-10.9 days PPPY (USA, Canada, Thailand) [6,7,8] while cancer-related stays were 4.2 days[8] (USA).
- Hospitalization rates across four studies ranged from 1.1[6] to 2.3[7] PPPY.
- Cancer-related hospitalizations were reported in one study showing a higher rate (1.6 PPPY) than all-cause hospitalizations (1.2 PPPY)[8]

Figure 2: HCRU in TNBC (PPPY)

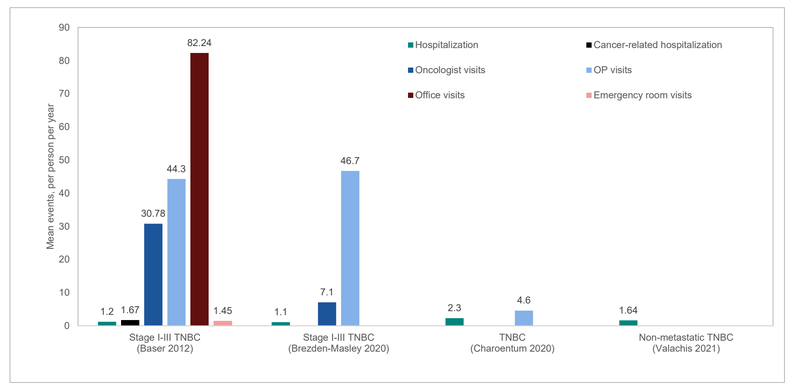


Table 3: Summary of HCRU in TNBC

Study , Country	Population	HCRU Component	Value
Sanno 2024[12], Japan	Early TNBC	Hospitalizations	100% of patients (N=3925)
Sullivan 2024[13], USA	Elderly patients (≥66 years) with early-stage TNBC receiving neoadjuvant chemotherapy and adjuvant capecitabine	ER visits/hospitalizations	Twenty-seven (28%) patients had ER/hospitalization during capecitabine treatment
Haiderali 2021[11], USA	Early TNBC	Hospitalizations: Initial neoadjuvant treatment	0.26 PPPM
		Hospitalizations: Post-surgery period	0.08 PPPM
Schwartz 2018[9], USA	Stage III TNBC (intervening treatment period)	Hospitalizations	1.50 PPPM
		ER visits	1.30 PPPM
		Outpatient visits	23.80 PPPM
Sieluk 2022[14], USA	TNBC without recurrence	Cancer-related hospitalizations	0.005 events/person-month
		Outpatient visits; ER visits	0.400; 0.004 events/person-month
	TNBC with metastatic recurrence	Cancer-related hospitalizations	0.112 events/person-month
		Outpatient visits; ER visits	1.949; 0.033 events/person-month
Carlos Souto 2023[10], Brazil	Early TNBC	Hospitalizations	0.23 PPPM
		ER visits	0.25 PPPM
	TNBC with progressive disease	Hospitalizations	0.48 PPPM
		ER visits	0.57 PPPM

PPPM, Per Patient Per Month; PPPY, Per Patient Per Year

Costs in TNBC

- Sixteen studies reported cost data including total costs, direct costs and indirect costs.
- Total costs ranged from €7,140 PPPY in Portugal (2019)[19] to $95,338 PPPY in the USA (2012)[8]
- Multiple US studies showed PPPM costs between $4,810 in 2013[9] to $14,466 in 2018[11]
- Costs increased with advancing stage - One New Zealand study reported median costs (2019-2020) of $25,581 for Stage I vs $34,628 for Stage III[15]
- Recurrence substantially increased costs: Non-recurrence ($1,944 PPPM) vs. metastatic recurrence ($13,013 PPPM)[14] in the USA (2019).
- Outpatient costs is often the largest cost component, ranging from $2,478 (Thailand)[7] in 2018 to $34,949 PPPY(USA)[8] in 2012.
- Treatment-specific costs varied across studies for different components:
  - Chemotherapy: €398 (Portugal, 2012) [16] to ₹170,000 per treatment (India, 2017-2020)[17]
  - Radiation: €2,649 (Portugal) - $6,111 (Belgium) per treatment in 2012[16, 18]
  - Surgery: $1,344 (Belgium) - €2,522 (Portugal) in 2012[16,18]
- Indirect costs also varied by disease severity
  - Productivity losses: Ranged from $451-$1,454 PPPM (USA, 2019), increasing with disease severity[14]
  - Total indirect burden: In Portugal, indirect costs represented 44% of total economic burden (€22.2M of €50M total annual cost)[19]

Table 4: Total costs in TNBC

Study (Year), Country	Population	Total Cost	Currency, (Time Frame)
Baser 2012[8], USA	All TNBC (n=403)	95,338	USD, PPPY (NR)
	Cancer-related	69,376	USD, PPPY (NR)
Brandão 2020[16], Portugal	All TNBC (n=54)	11,224	Euros, Median (2012)
Brezden-Masley 2020[6], Canada	Stage I-III (n=3081)	35,064	CAD, PPPY (2017)
Carlos Souto Maior Borba 2023[10], Brazil	Early/locally advanced (n=1034)	7,352	USD, PPPM (2023)
Haiderali 2021[11], USA	Early-stage NAT (n=236)	14,466	USD, PPPM (2018)
	Early-stage NAT+AT (n=72)	12,989	USD, PPPM (2018)
Lao 2022[15], New Zealand	All TNBC (n=996)	31,722	NZD, median (2019/2020)
Sieluk 2022[14], USA	Non-recurrence (n=1170)	1,944	USD, PPPM (2019)
	Locoregional (n=934)	5,116	USD, PPPM (2019)
Silva 2021[19], Portugal	All TNBC (n=7052)	50 million	Euro, per year (2019)
		7,140	Euro, PPPY (2019)

AT, Adjuvant Therapy; CAD, Canadian Dollar; NAT, Neoadjuvant Therapy; NZD, New Zealand Dollar; PPPM, Per Patient Per Month; PPPY, Per Patient Per Year; USD, US Dollar

Conclusions

- This review highlights the significant economic burden with stage I-III TNBC, while evidence specific to HR-low positive HER2- BC was scarce.
- Economic evaluations primarily focused on adjuvant Olaparib for BRCA-mutated patients, with limited evidence for unmutated TNBC patients.
- Despite some adjuvant therapies demonstrating cost-effectiveness, high recurrence and progression costs emphasize the need for effective interventions to optimize outcomes and resource allocation.

References

1. Polyzoi, M., et al. (2024). "Cost-Effectiveness Analysis of Adjuvant Olaparib Versus Watch and Wait in the Treatment of Germline BRCA 1/2-Mutated, High-Risk, HER2-Negative Early Breast Cancer in Sweden." PharmacoEconomics-Open 8(2): 277-289.S: 2. Cedillo, S., et al. (2024). "Cost-Utility Analysis of Adjuvant Olaparib for Germline BRCA1/2-Mutated, High-Risk HER2-Negative Early Breast Cancer in Spain." PharmacoEconomics-Open 8(6): 887-896.4: 3. Sousa R, et al. (2024). Cost-Effectiveness of Adjuvant Olaparib for Patients With Germline BRCA1/2-Mutated, High-Risk, Human Epidermal Growth Factor-2-Negative Breast Cancer in Portugal. 2024-11, ISPOR Europe 2024. Barcelona, Spain, Value in Health. 27.: 4. Ray, J., et al. (2009). "PCN51 PROJECTED LONG-TERM ECONOMIC OUTCOMES ASSOCIATED WITH BEVACIZUMAB TREATMENT IN PATIENTS WITH ADJUVANT TRIPLENEGATIVE BREAST CANCER TO INFORM EARLY DECISION MAKING." Value in Health 3(12): A45-A46.: 5. NICE TA886 (2023) Olaparib for adjuvant treatment of high-risk HER2-negative, BRCA-positive early breast cancer after chemotherapy 6. Brezden-Masley, C., et al. (2020). "A population-based comparison of treatment patterns, resource utilization, and costs by cancer stage for Ontario patients with triple-negative breast cancer." Cancer Medicine 9(20): 7548-7557.: 7. Charoentum, C., et al. (2020). "PCN101 Healthcare Resource Utilization, Costs, and Clinical Outcomes in Patients with Triple-Negative Breast Cancer in Northern Thailand: A Real-World Evidence Using Electronic Health Records." Value in Health Regional Issues 22: S24.: 8. Başer, O., et al. (2012 2). "Burden of early-stage triple-negative breast cancer in a US managed care plan." Health Outcomes Research in Medicine 3(2): e57-e65.: 9. Schwartz, K. L., et al. (2018). "Clinical and economic burden associated with stage III to IV triple-negative breast cancer: A SEER-Medicare historical cohort study in elderly women in the United States." Cancer 124(10): 2104-2114.: 10. Carlos Souto Maior Borba, M. A., et al. (2023). "Treatment patterns and healthcare resource utilization for triple negative breast cancer in the Brazilian private healthcare system: a database study." Scientific Reports 13(1): 15785.: 11. Haiderali, A., et al. (2021). "Healthcare resource utilization and cost among patients treated for early-stage triple-negative breast cancer." Future Oncology 17(29): 3833-3841.: 12. Sanno, H., et al. (2024). "Treatment patterns, healthcare resource utilization and outcomes for early stage triple-negative breast cancer in Japan." Future Oncology 20(13): 833-849.: 13. Sullivan, M., et al. (2024). "Abstract PO3-03-08: Use of adjuvant Capecitabine after neoadjuvant chemotherapy: A Cohort Study among Elderly Patients with Early-Stage Triple-Negative Breast Cancer." Cancer Research 84(9_Supplement): PO3-03-08-PO03-03-08.: 14. Sieluk, J., et al. (2021). "Early triple-negative breast cancer in women aged≥ 65: retrospective study of outcomes, resource use and costs, 2010–2016." Future Oncology 17(9): 1039-1054.: 15. Lao, C., et al. (2022). "Differences in breast cancer costs by cancer stage and biomarker subtype in New Zealand." PharmacoEconomics-Open 6(4): 539-548.: 16. Brandão, M., et al. (2020). "Healthcare use and costs in early breast cancer: a patient-level data analysis according to stage and breast cancer subtype." ESMO open 5(6): e000984.: 17. Sharma, P., et al. (2022). "Anemia requiring transfusion in breast cancer patients on dose-dense chemotherapy: Prevalence, risk factors, cost and effect on disease outcome." Supportive Care in Cancer 30(6): 5519-5526.: 18. Roman, E., et al. (2020). "Variability in hospital treatment costs: a time-driven activity-based costing approach for early-stage invasive breast cancer patients." BMJ open 10(7): e035389.: 19. Silva, J., et al. (2024). "Economic Burden of Triple-Negative Breast Cancer in Portugal.": 20. Valachis, A., et al. (2021). "Treatment patterns, risk for hospitalization and mortality in older patients with triple negative breast cancer." Journal of Geriatric Oncology 12(2): 212-218.

Acknowledgments
Not Applicable

Disclosures (if required)
Amin Haiderali and Jagadeswara Rao Earla are employees of Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA and hold stock in Merck & Co., Inc., Rahway, NJ, USA.

Contact information
Amin Haiderali
Email ID: amin.haiderali@merck.com

https://bit.ly/4pYG8gL

Presented at ISPOR EU, November 9 – 12, 2025