Economic Burden in Metastatic Triple-Negative Breast Cancer: A Systematic Literature Review

Poster # EE356

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Conclusions

- This systematic literature review (SLR) highlights the substantial economic burden of metastatic triple-negative breast cancer (mTNBC)
- While direct costs were extensively studied, data on indirect costs were limited, and there were no studies on economic burden by programmed death ligand 1 (PD-L1) status, highlighting an unmet need for studies that provide data on these topics
- The potential role of novel therapies in reducing economic burden by delaying disease progression also warrants further investigation

Plain Language Summary

This review shows that there is a substantial cost to treat a hard-to-treat type of breast cancer called metastatic triple-negative breast cancer (mTNBC). Most studies looked at direct costs like hospital care, but there was not much information about other costs like lost work time. No studies looked at costs based on PD-L1 status, which indicates whether the protein PD-L1 is expressed on the cancer cells. Some cancer treatments are targeted to cells that express PD-L1, and PD-L1 expression may be linked to how people respond to cancer treatment and how long they can live after being diagnosed with cancer. More research is needed to develop new treatments that can slow the cancer, leading to lower costs.

Introduction

- Triple-negative breast cancer (TNBC) is the most aggressive subtype of breast cancer, characterized by a lack of estrogen/progesterone receptor expression and low or absent levels of human epidermal growth factor receptor 2 (HER2)[1]
- mTNBC has a poor prognosis; the 5-year relative survival is ~15%, and treatment options are limited[2]
- About 40% of patients with TNBC have PD-L1+ tumors; blocking this checkpoint boosts antitumor immunity[1,3]
- Limited treatment options for mTNBC contribute to a significant economic burden, including high healthcare costs and resource use
- The primary objective of this study is to evaluate the economic burden of mTNBC by PD-L1 status in published data

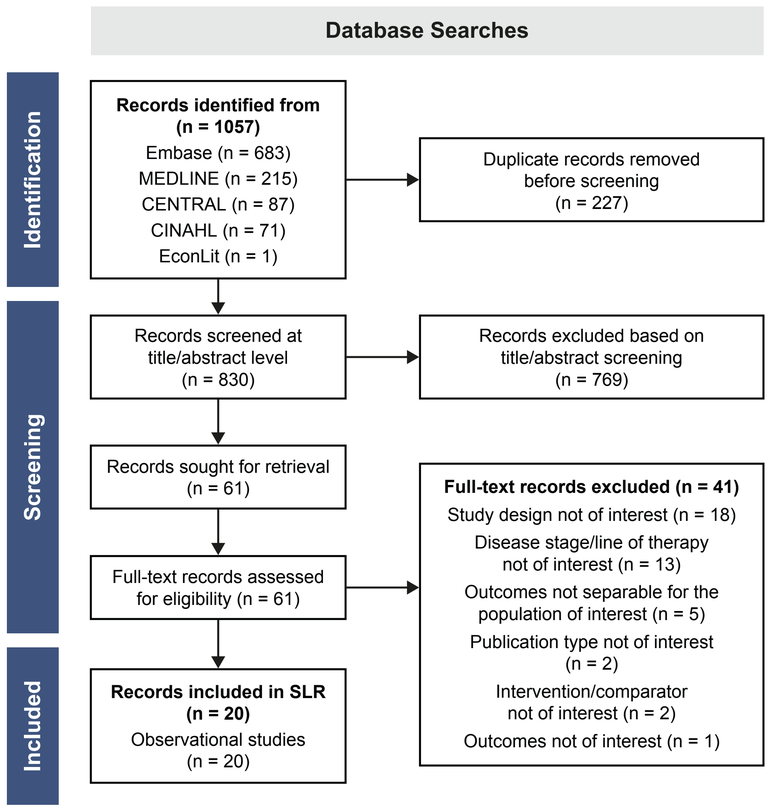
Methods

- An SLR following Cochrane methodologies was conducted to evaluate direct and indirect costs and healthcare resource use
- English language studies including patients with TNBC from MEDLINE, Embase, Cochrane Library, Cumulative Index to Nursing and Allied Health Literature, and EconLit up to June 2024 were included[4,5]
- Analysis included any observational study reporting primary data on costs and/or healthcare resource utilization in adult patients with locally advanced, metastatic, or general (non-stage specific) patients treated with first-line treatment (approved or being investigated)
- Two reviewers independently performed title/abstract and full-text screening, and a third reviewer resolved any disagreements

Results

- 1057 records were identified via database searches. Following screening, 20 publications from 19 primary observational studies (18 retrospective and 1 prospective) in TNBC with economic outcomes were evaluated (**Figure 1**)
- Studies were derived from North America (United States [US], n = 11; Canada, n = 1), Europe (n = 4), and Asia/Oceania (n = 3)
- Economic data were reported in 10 studies that enrolled patients with mTNBC, 5 studies that included patients with non-stage specific TNBC, 3 studies that included all TNBC with stage III/IV subgroup analysis, and 1 study that included TNBC with metastatic vs locoregional recurrence. Characteristics of these studies are summarized in **Table 1**
- No studies reported economic outcomes stratified by PD-L1 status

Figure 1. PRISMA Flow Diagram



CENTRAL, Cochrane Central Register of Controlled Trials; CINAHL, Cumulative Index to Nursing and Allied Health Literature; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; SLR, systematic literature review.

Results (continued)

Table 1. Study Characteristics

Author, Year, Country	Data Source	Population/ Subpopulation Description	Sample Size	Metastatic, %	Mean[a] Age, Years (SD)	Outcomes Reported
Abbass, 2022,[6] US	IQVIA PharMetrics Plus	mTNBC	2700	100	Range: 51-55	Direct costs, HCRU
Aly, 2019,[7] US	SEER-Medicare database	mTNBC (≥ 66 years)	625	100	76.8 (7.3)	Direct costs, HCRU
Baser, 2012,[8] US	IIOM cancer registry	Stage I-IV TNBC	450	10	54.2 (11.5)	Direct costs, HCRU
Baser, 2012,[9] US	IIOM cancer registry	mTNBC	134	100	56.5 (12.62)	Direct costs, HCRU
Brezden-Masley, 2020,[10] Canada	Ontario Cancer Registry	Stage IV mTNBC	190	100	63.9 (15.7)	Direct costs, HCRU
Chehayeb, 2022,[11,12] US	Flatiron Health EHR database	mTNBC	1457	100	60.2 (12.90)	Direct costs, HCRU
Houts, 2019,[13] US	Vector Oncology Data Warehouse	mTNBC (*BRCA*-mutated) on 1L treatment	57	100	48.2 (12.72)	Direct costs, HCRU
Quek, 2019,[14] US	Flatiron Health EHR database	mTNBC (germline *BRCA* mutation)	64	100	51.7 (15.2)	HCRU
Schwartz, 2018,[15] US	SEER-Medicare database	Stage III TNBC (≥ 65 years)	828	100	NR	Direct costs, HCRU
		Stage IV TNBC (≥ 65 years)	416	100	NR	
Sieluk, 2021,[16] US	SEER-Medicare database	mTNBC (age ≥ 65 years) on systemic therapy	152	100	Median (range): 73 (65-90)	Direct costs
		mTNBC (age ≥ 65 years) not on systemic therapy	150	100	Median (range): 80 (65-99)	
Sieluk, 2022,[17] US	Optum Health Reporting and Insights database	TNBC with metastatic recurrence	236	24	53.7 (8.1)	Direct costs, indirect costs, HCRU
		TNBC with locoregional recurrence	934	< 1	53.6 (7.7)	
Skinner, 2021,[18] US	Vector Oncology Data Warehouse	1L mTNBC	505	100	56.6 (13.1)	Direct costs
		2L mTNBC	303	100	NR	
		3L overall	178	100	NR	
Mery, 2019,[19] France	Chart review of institute medical records	Stage I-IV TNBC (1L paclitaxel+bevacizumab)	45	29	62 (12.4)	Direct costs
Schilling, 2019,[20] Germany	OBTAIN trial	Stage I-IV TNBC	91	23	58 (12.5)	HCRU
Hsu, 2022,[21] Taiwan	Nation-level databases	mTNBC	535	100	NR	Direct costs
Kimura, 2024,[22] Japan	Japanese medical claims database	mTNBC	2236	100	Median (IQR): 66.0 (53.0-73.0)	Direct costs
Lao, 2023,[23] New Zealand	National Cancer Registries, databases, and death certificates	Stage IV TNBC	91	100	NR	Direct costs
Carreras, 2023,[24] Spain	Vall d'Hebron University Hospital	TNBC on antineoplastic agents	344	NR	NR	Direct costs
Schneider, 2021,[25] Netherlands	SONABRE Registry	TNBC	69	NR	NR	Direct costs, HCRU

[a]Unless mentioned otherwise.
1L, first line; 2L, second line; 3L, third line; *BRCA*, breast cancer susceptibility gene; EHR, electronic health record; HCRU, healthcare resource utilization; IIOM, Impact Intelligence Oncology Management; mTNBC, metastatic triple-negative breast cancer; MORT, Mortality Collection; NR, not reported; SEER, Surveillance, Epidemiology, and End Results Program; TNBC, triple-negative breast cancer; US, United States.

Direct and Indirect Costs

- Direct costs were reported by 17 studies, and studies indicated high costs for patients with stage IV TNBC (**Table 2**)
- One study reported indirect costs.[17] Higher workdays lost and disability costs (per person per month) with mTNBC (US$606) compared with locoregional disease (US$480) and no recurrence (US$259), respectively, were reported. Lost workdays were identified as key drivers of indirect costs

Table 2. Summary of Direct Costs

Author, Year, Population, Country	Cost Type Reported	Statistically Significant /Trends Observed
Aly, 2019,[7] mTNBC in US	Total cost	• Mean costs decrease with each additional line of therapy ($P < .001$), but total costs PPPM increase due to longer survival
Baser, 2012,[8] TNBC in US	Overall annual costs	• Costs PPPY increase in patients with stage IV vs stage I-III disease
Brezden-Masley, 2020,[10] TNBC in Canada	Total costs	• Costs PPPY increase in patients with stage IV vs stage I-III disease
Kimura, 2024,[22] mTNBC 1L therapy in Japan	Total costs	• Costs per patient and per patient per day increase on 1L to 2L to 3L treatment
Lao, 2023,[23] TNBC in New Zealand	Public medical costs	• Costs PPPY decreased over time in stage I-III patients for the initial treatment phase (3 months preceding and 1 year after diagnosis) vs years 2-5 following diagnosis • Costs PPPY remained high in stage IV patients during the whole follow-up period
Skinner, 2021,[18] TNBC in US	Healthcare costs	• Costs increase with line of treatment, with the highest cost from 2L platinum + taxane

1L, first line; 2L, second line; 3L, third line; mTNBC, metastatic triple-negative breast cancer; PPPM, per patient per month; PPPY, per patient per year; TNBC, triple-negative breast cancer; US, United States.

Healthcare Resource Utilization

- Higher hospital, intensive care unit, and emergency department (ED) admissions for patients with mTNBC on no chemotherapy or third-line or higher chemotherapy vs pretreatment (medical costs during time from diagnosis to start of first-line treatment) and first-line or second-line chemotherapy were observed (**Table 3**)
- Higher hospitalization rates and hospitalization length of stay were observed for more advanced stages of TNBC (**Table 3**)
- Higher hospitalization rates and increased ED admissions were observed for metastatic vs locoregional recurrent TNBC (**Table 3**)

Table 3. Summary of Healthcare Resource Utilization

Author, Year, Population, Country	HCRU Type Reported	Statistically Significant /Trends Observed
Hospitalization Rate		
Aly, 2019,[7] mTNBC in US	Hospitalizations	• Per patient admissions increased on no chemotherapy and 3L+ regimens vs pretreatment, 1L and 2L
	ICU admissions	• Per patient admissions increased on no chemotherapy and 3L+ regimens vs pretreatment, 1L and 2L • Per patient admissions on pretreatment decreased vs first regimen
Baser, 2012,[8] TNBC in US	All-cause hospitalization days	• PPPY hospitalization days increased in TNBC vs non-TNBC ($P < .0001$) • PPPY hospitalization days increased in stage I-III TNBC vs non-TNBC ($P < .0001$) • PPPY hospitalization days increased in stage IV vs stage I-III TNBC
	Hospitalizations	• PPPY hospitalizations increased in TNBC vs non-TNBC ($P < .0001$) • PPPY hospitalizations increased in stage I-III TNBC vs non-TNBC ($P < .0001$) • PPPY hospitalizations increased in stage IV TNBC vs non-TNBC ($P = .039$)
	Cancer-related hospitalization days	• PPPY cancer-related hospitalization days increased in stage I-III TNBC vs non-TNBC ($P < .0001$)
	Cancer-related hospitalization	• PPPY cancer-related hospitalizations increased in stage I-III TNBC vs non-TNBC ($P < .0001$)
Brezden-Masley, 2020,[10] TNBC in Canada	Inpatient visits	• PPPY visits increased for stage IV vs stage I-III TNBC
Sieluk, 2022,[17] TNBC in US	Events of inpatient admissions	• PPPM admissions increased for metastatic recurrent TNBC vs locoregional recurrent TNBC • PPPM admissions increased for metastatic recurrent TNBC vs non-recurrent TNBC ($P < .001$) • PPPM admissions increased for locoregional recurrent TNBC vs non-recurrent TNBC ($P < .001$)
	Events of inpatient days	• PPPM days increased for metastatic recurrent TNBC vs locoregional recurrent TNBC • PPPM days increased for metastatic recurrent TNBC vs non-recurrent TNBC ($P < .001$) • PPPM days increased for locoregional recurrent TNBC vs non-recurrent TNBC ($P < .001$)
	Hospice care days	• PPPM days increased for metastatic recurrent TNBC vs locoregional recurrent TNBC • PPPM days increased for metastatic recurrent TNBC vs non-recurrent TNBC ($P < .001$)
Hospital LOS		
Brezden-Masley, 2020,[10] TNBC in Canada	Inpatient LOS (hospitalization)	• PPPY LOS increased for stage IV vs stage I-III TNBC
	Inpatient LOS (rehabilitation)	• PPPY LOS increased for stage IV vs stage I-III TNBC
ED Admissions		
Aly, 2019,[7] mTNBC in US	ER admissions	• Per patient admissions increased on no chemotherapy and 3L+ regimens vs pretreatment, 1L and 2L
Sieluk, 2022,[17] TNBC in US	Events of ED visits	• Per patient visits increased for metastatic recurrent TNBC vs locoregional recurrent TNBC ($P < .001$) • Per patient visits increased for locoregional recurrent TNBC vs non-recurrent TNBC ($P = .044$) • Per patient visits increased for metastatic recurrent vs locoregional TNBC ($P < .001$)

1L, first line; 2L, second line; 3L, third line; ED, emergency department; ER, emergency room; ICU, intensive care unit; LOS, length of stay; mTNBC, metastatic triple-negative breast cancer; PPPM, per patient per month; PPPY, per patient per year; TNBC, triple-negative breast cancer; US, United States.

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