A Systematic Literature Review (SLR) of Economic Burden of Patients With Hormone Receptor-Positive/Human Epidermal Growth Factor Receptor 2-Negative (HR+/HER2-) Metastatic Breast Cancer (mBC) With at Least One Prior Therapy

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CONCLUSIONS



In addition to their clinical and humanistic burden, CTs had a substantial economic burden in terms of medical and indirect costs, which highlights the need for newer more efficacious treatments for these patients



The main drivers of CT costs and resource utilization were IP care, AE management, and lower productivity



There is a need for more research to inform cost-effective approaches to treatment, particularly in Europe and in later-line studies



Few studies examined indirect costs in HR+/HER2- mBC, and there is a lack of data on the impact of new treatments



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BACKGROUND

- Breast cancer (BC) accounted for 12% (2.3 million) of new cancer cases worldwide in 2020.1 Approximately 68% of BC cases are classified as HR+/HER2-2
- The outlook remains poor in HR+/HER2- mBC, with a 5-year survival of ~30% for distant disease²
- Endocrine therapy (ET) is the primary treatment for HR+/HER2

 mBC,³ but many patients develop resistance, and may require chemotherapy (CT)
- While the clinical and health-related quality of life outcomes in patients with pretreated HR+/HER2- mBC has been characterized,4-11 the economic burden has not been reviewed systematically

OBJECTIVE

 To summarize the economic burden among patients with HR+/HER2- mBC who received ≥ 1 line of therapy in the metastatic setting

METHODS

- An SLR was performed in accordance with PRISMA and Cochrane guidance^{12,13}
- Embase®, MEDLINE®, the Cochrane library, and health technology assessment databases were searched for records using OvidSp; relevant congresses were manually searched
- The inclusion criteria are summarized in **Table 1**
- Records were screened and data extracted by 2 independent reviewers
- Quality assessment was conducted using the National Institute for Health and Care Excellence (NICE) checklist for economic evaluations¹⁴

Table 1. Inclusion Criteria

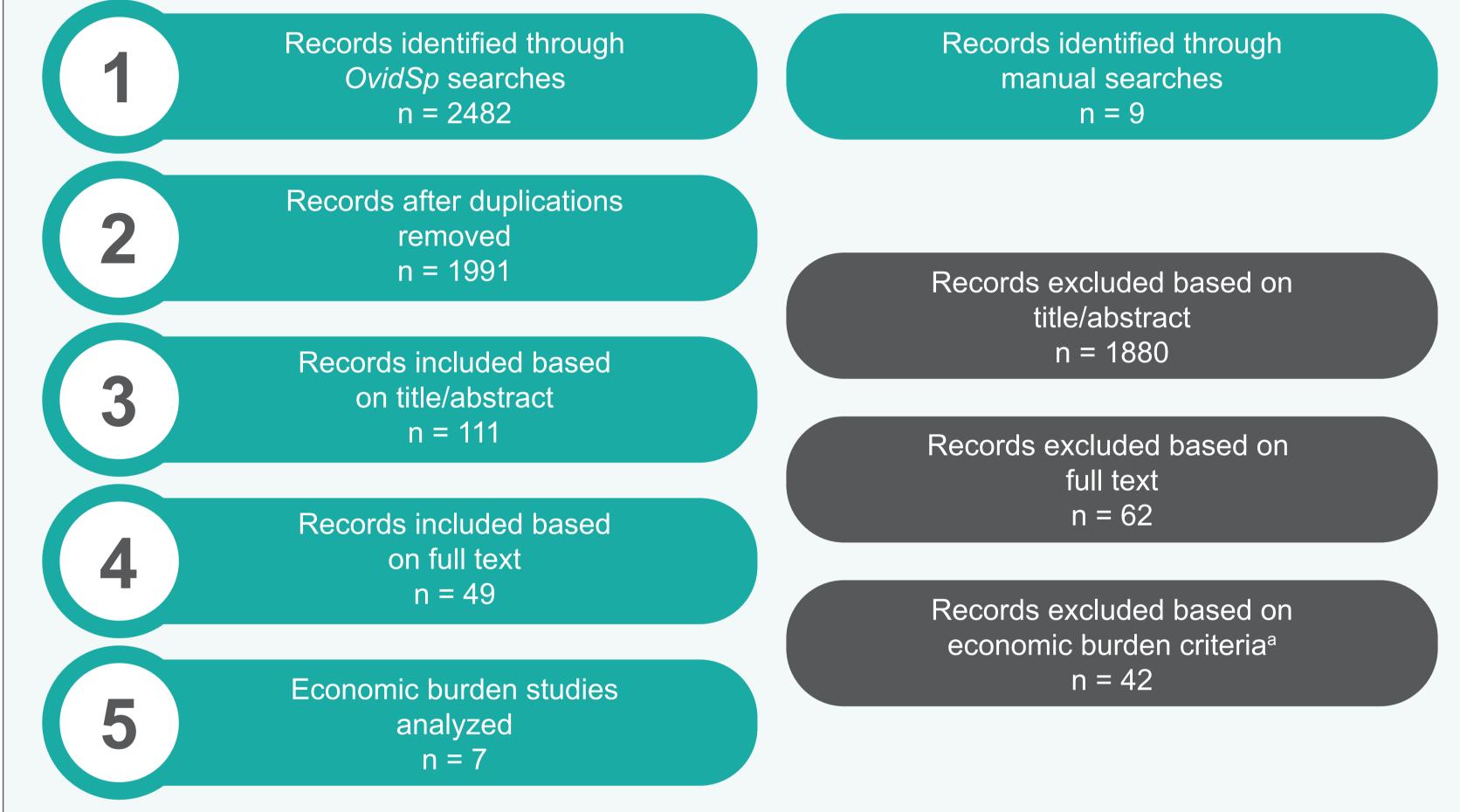
Population	Adults (≥ 18 years) with HR+/HER2– mBC who received ≥ 1 prior line of therapy in the metastatic setting				
Interventions	Any				
Comparators	Any				
Outcomes	Direct or indirect treatment costs or resource use				
Studies	Real-world or observational studies				
Other	English, any geography Search dates: January 01, 2012 to February 25, 2022 and April 01, 2022 (congresses only)				

RESULTS

Study Selection

- Twelve economic burden studies were identified; of those, 7 with data on intervention and resource utilization were analyzed (Figure 1)
- Few studies described health care resource utilization of patients with HR+/HER2mBC who received ET and additional systemic therapies in the metastatic setting

Figure 1. PRISMA Flow Chart



^aNot economic burden studies (n = 37), economic burden studies excluded with no intervention or resource utilization (n = 5).

Direct Costs

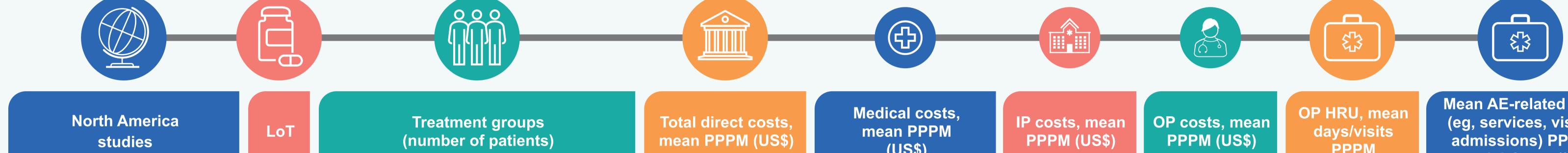
- Greater direct medical costs (eg, hospitalization, and outpatient [OP] services) were incurred by patients receiving CT versus other therapies (eg, ET or targeted treatments) across all lines of therapy in HR+/HER2- mBC (Table 2 and Table 3)
- Medical costs and inpatient (IP) costs were high across all studies, with a trend toward increasing IP costs across later lines of therapy

Health Care Resource Utilization

- The main drivers of resource use were OP care and adverse event (AE) management, which were higher with CT than other therapies (Table 2 and Table 3)
- CT was also associated with lower productivity, but there were few studies that examined indirect costs

Limitations

 The SLR was subject to selection biases and study heterogeneity. Study periods differed so costs may not be comparable. There was limited literature outside the US **Table 2**. Key Total Direct Costs and HRU Associated With HR+/HER2– mBC Treatment in North America Studies¹⁵⁻¹⁹



North America studies	LoT	Treatment groups (number of patients)	Total direct costs, mean PPPM (US\$)	Medical costs, mean PPPM (US\$)	IP costs, mean PPPM (US\$)	OP costs, mean PPPM (US\$)	OP HRU, mean days/visits PPPM	Mean AE-related HRU (eg, services, visits, admissions) PPPM or sick leave (%)
Gauthier, 2018	1L	ET (1101) vs CT (2036)	6521 vs 16,842	6304 vs 16,003 ^b	1101 vs 1199	4590 vs 3477	3.8 vs 6.0°	
Hao, 2016	1L	EVT (19) vs CT (195)		4483 vs 7259 ^b	2380 vs 2719	1622 vs 4168	3.875 vs 5.659	1.239 vs 1.683 (AEs)
Li, 2016	1L	EVT (66) vs CT (553)		5191 vs 8889 ^b	1814 vs 3700	3058 vs 4757	3.442 vs 5.500	0.760 vs 1.635 (AEs)
Lambert-Obry, 2018	1L	PF (67) vs PD (17)	983 vs 802ª		550 vs 431ª			31% vs 33% (sick leave)
Gauthier, 2018	2L	ET (660) vs CT (1467)	4440 vs 12,868	4261 vs 12,316 ^b	668 vs 1321	2870 vs 4205	3.3 vs 6.1°	
Hao, 2016	2L	EVT (59) vs CT (234)		4209 vs 6035 ^b	2038 vs 2824	2032 vs 2949	3.094 vs 4.733	0.826 vs 1.476 (AEs)
Li, 2016	2L	EVT (261) vs CT (823)		5023 vs 8885 ^b	1746 vs 4335	3066 vs 4200	3.389 vs 4.764	0.871 vs 1.487 (AEs)
Princic, 2018	2L	EVT (70) vs ET (186) vs CT (193)		5043 vs 6767 vs 11,505				
Lambert-Obry, 2018	2L+	PF (89) vs PD (29)	352 vs 531 ^a		64 vs 243ª			10% vs 40% (sick leave)
Gauthier, 2018	3L	ET (914) vs CT (260)	4555 vs 16,129	4400 vs 15,189 ^b	795 vs 3219	3238 vs 5453	3.4 vs 5.5°	
Hao, 2016	3L	EVT (82) vs CT (269)		3077 vs 10,268 ^b	1187 vs 7041	1764 vs 2844	3.295 vs 4.691	0.880 vs 1.728 (AEs)
Li, 2016	3L	EVT (331) vs CT (1004)		6158 vs 8493 ^b	2833 vs 4156	3010 vs 3977	3.298 vs 4.497	0.782 vs 1.449 (AEs)
Hao, 2016	4L	EVT (80) vs CT (241)		2954 vs 6731 ^b	1214 vs 3261	1558 vs 3085	3.199 vs 4.388	0.985 vs 1.658 (AEs)
Li, 2016	4L	EVT (282) vs CT (1030)		4790 vs 8770 ^b	1580 vs 3907	2828 vs 4375	3.207 vs 4.715	0.890 vs 1.556 (AEs)

Table 3. Key Total Direct Costs and HRU Associated With HR+/HER2– mBC Treatment in EU Studies^{20,21}

EU studies	LoT	Treatment groups (number of patients)	Total direct costs, mean PPPM (€)	Treatment costs, mean PPPM (€)	Other key HRU
Jerusalem, 2015 ^d	1L	ET±TT (218) vs CT±ET±TT (111)	447 vs 2983	231 vs 2424	19% vs 41% (sick leave) ^e
Jerusalem, 2015 ^d	2L	CT±ET±TT (218)	2338	1894	41% (sick leave) ^e
Giuliani, 2020	2L	F/P (347) vs F/R (484) vs F/A (446)		4570 vs 2070 vs 3346 ^f	4570 vs 2069 vs 3346 (cost [€] difference between P/R/A per month for PFS gained)

Footnotes for tables:

^aReported as Can\$ over a 3-month period for totals: 2949, 2405 (1L), 1057, 1592 (2L+), and hospitalizations: 1650, 1292 (1L), 192, 729 (2L+).

^bCosts for IP, OP, emergency room, and other medical service costs. Reported over a 6-month period: 22.9, 35.9 (1L), 19.5, 36.3 (2L), 20.1, 32.9 (3L).

Belgium, France, Germany, the Netherlands, Sweden. eBased on 1L ET (n = 109) or CT (n = 70) or 2L CT (n = 109).

fBased on annual costs for P/R/A of €54,840, €24,840, €40,152.

1L, first-line; 2L, second-line; 2L+, second-line or later; 3L, third-line; 4L, fourth-line; AE, adverse event; CT, chemotherapy, EVT, everolimus therapy; F/A, F/P, F/R, fulvestrant plus abemaciclib, palbociclib or ribociclib; HRU, health care resource utilization; IP, inpatient; LoT, line of therapy; OP, outpatient; PD, progressive disease; PF, progression-free; PFS, progression-free survival; PPPM, per patient per month; TT, targeted therapy.

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DISCLOSURES

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