

# Understanding the humanistic and economic burden associated with early-stage HR+/HER2- breast cancer: A systematic literature review

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## Objectives

- Hormone receptor positive and human epidermal growth factor receptor 2 negative (HR+/HER2-) breast cancer (BC) accounts for ~70% of early-stage cases<sup>1,2</sup>
- Given the high unmet need and emerging new therapies for early-stage HR+/HER2- BC, it is important to understand the humanistic and economic burden in this setting<sup>3</sup>
- This systemic literature review summarized published evidence on economic and humanistic burden

## Methods

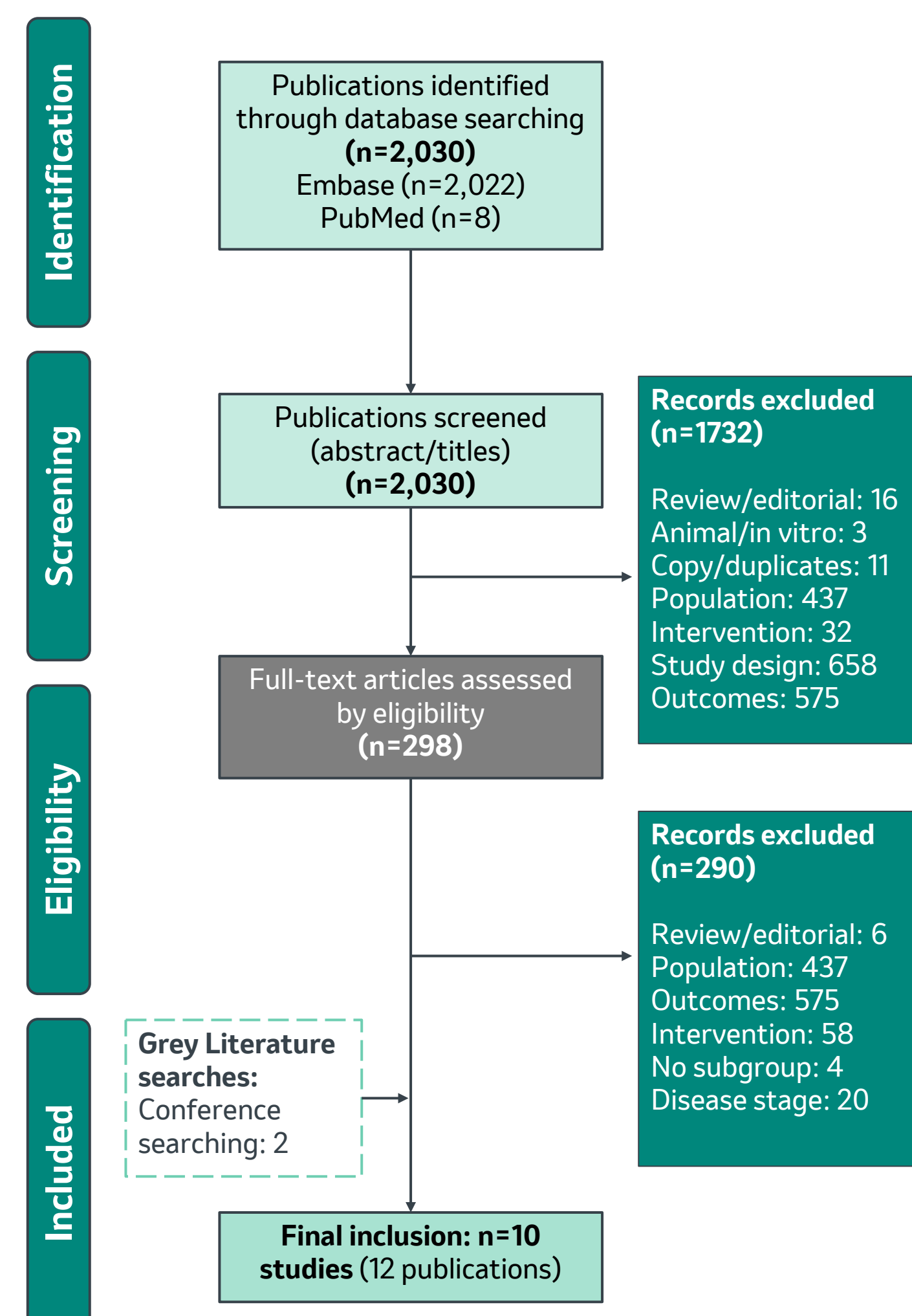
- Embase<sup>®</sup>, MEDLINE<sup>®</sup>, Tufts cost-effectiveness analysis (CEA), EconLit, and Center for Reviews and Dissemination (CRD) York databases were searched (from database inception to May 10, 2023) for English language publications reporting relevant economic and HRQoL outcomes in patients with early-stage HR+/HER2- BC (**Table 1**)
- Relevant conference proceedings were also searched (from 2020-2023). Study selection was in accordance with the National Center for Health and Care Excellence (NICE) recommendations.

**Table 1. Study selection criteria and outcomes used**

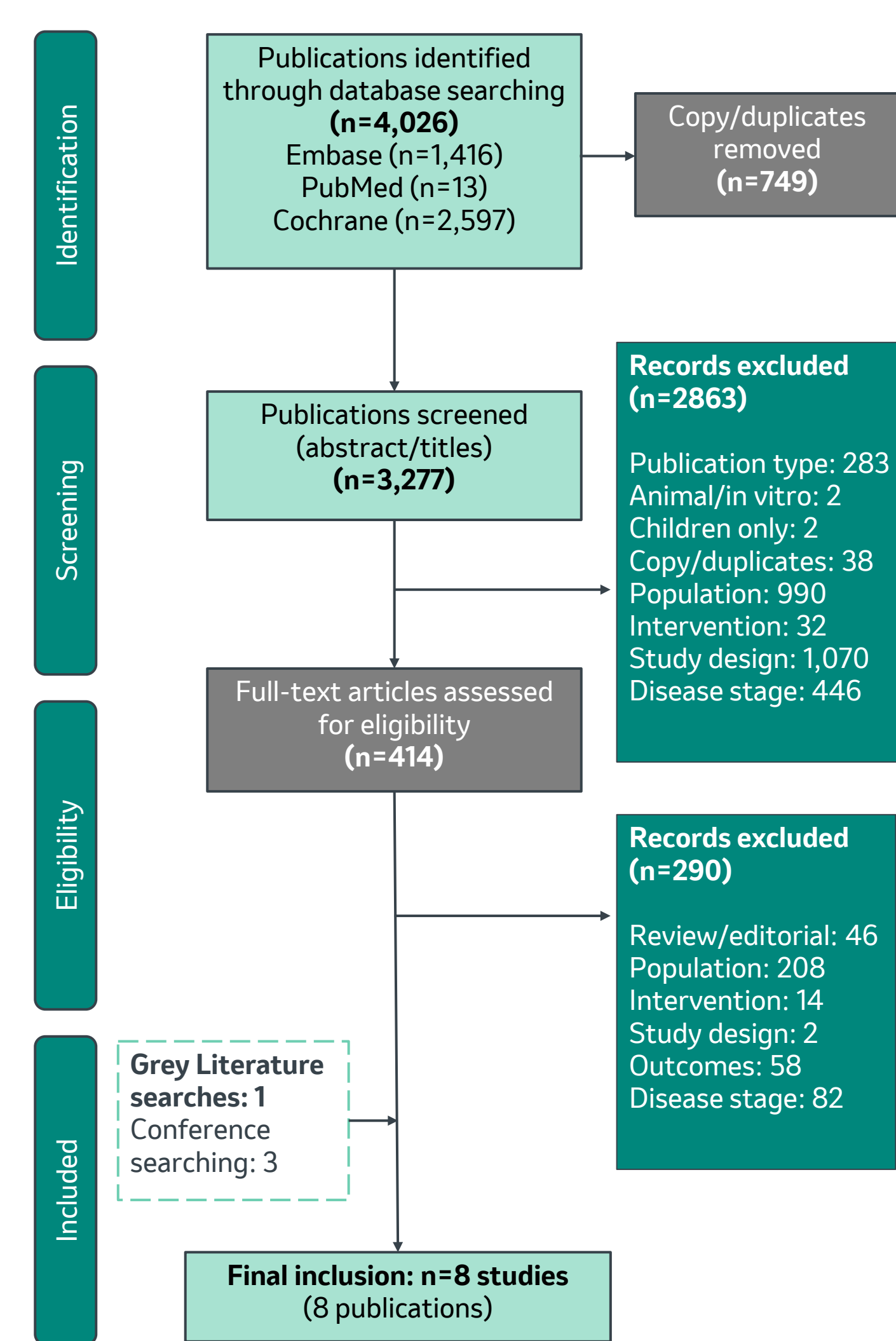
Parameters	Selection criteria
<b>Population(s)</b>	<ul style="list-style-type: none"> <li>Adult patients with early-stage (stage I-III) HR+/HER2- BC with a localized invasive breast ductal adenocarcinoma, which includes either T1c-T2 (tumor size ≥2 cm), cN stage cN1-cN2, or T3-T4, cN0-cN2, confirmed HR+/HER2-, Grade 3 (or high-grade tumors) BC</li> </ul>
<b>Interventions</b>	<ul style="list-style-type: none"> <li>Economic and humanistic burden review without restriction</li> <li>All adjuvant therapies including endocrine therapies were included, while neoadjuvant endocrine therapies were excluded</li> </ul>
<b>Comparators</b>	<ul style="list-style-type: none"> <li>No restrictions</li> </ul>
<b>Outcomes</b>	<p><b>Economic burden:</b></p> <ul style="list-style-type: none"> <li>Health care resource utilization (HCRU) parameters: inpatient visits/hospitalizations and admissions, length of hospital stays, ER visits, outpatient visits</li> </ul> <p><b>Humanistic burden:</b></p> <ul style="list-style-type: none"> <li>HRQoL burden of disease</li> <li>Correlates of the HRQoL</li> </ul>
<b>Study design</b>	<ul style="list-style-type: none"> <li>Clinical trials, observational studies</li> </ul>
<b>Time frame</b>	<ul style="list-style-type: none"> <li>Database inception to 10th May 2023</li> </ul>
<b>Language</b>	<ul style="list-style-type: none"> <li>Studies with full texts published in the English language</li> </ul>
<b>Regions</b>	<ul style="list-style-type: none"> <li>Global (no restriction)</li> </ul>

## Results

**Figure 1. PRISMA flow diagram for economic burden review**



**Figure 2. PRISMA flow diagram for humanistic burden review**



## Economic burden

Ten studies were identified for economic burden spanning North America (6), Europe (2), Oceania (1), and globally (1) (**Figure 1**). Four studies provided HRCU data on inpatient and outpatient costs:

### Total health care services costs

- Total health care costs per patient were reported for Canada (CAN\$22,662; n=21,360), US (US\$24,955; n=177), and New Zealand (NZ\$24,341-28,662; n=22,948)<sup>4,5,8</sup> (**Table 2**)
- Mean difference in treatment costs between node negative (\$12,618) vs node positive (\$17,564) patients was mainly driven by G-CSF cost (\$7,677 and \$10,895, respectively)<sup>5</sup>
- In Portugal, the median overall cost per patient with HR+/HER2- BC (of whom 99.8% had received endocrine therapy) was €10,540 (€7,480-13,611) over the first 3 years from diagnosis<sup>7</sup>

### Inpatient utilization and length of stay (LOS)

- Three studies reported proportion of patients using inpatient services: 44.8% (n=21,360, 2012-2017), 38.9% (n=537, 2012), 18.9% (n=222, 2010-2014)<sup>4,5,7</sup>
- During a 4-year period, a higher percentage of US patients on chemotherapy (54%, n=50) were hospitalized compared to patients on hormonal therapy (9%, n=177). Most hospitalizations in the hormonal therapy group (23 times) were unrelated to treatment, whereas the majority in the chemotherapy group (31 times) could be attributed to treatment<sup>5</sup>
- Mean LOS was 2.0 days (SD: 11.4) per person per year. Mean LOS for inpatient rehabilitation, mental health, and long-term care was 0.2 days (SD: 1.9), 0.2 days (SD: 5.2), and 4.7 days (SD: 37.0), respectively<sup>4</sup>

### Outpatient utilization

- In Canada, 98.58% (n=21,356) of patients required outpatient visits (mean=5.4 visits/year, SD: 4.9) between 2012 and 2017, compared to 24.6% (n=537) in Portugal<sup>4,7</sup>
- The 6-month outpatient mean costs in the US for chemotherapy were higher (\$24,955, n=50) compared to hormonal therapy (\$2,654, n=177)<sup>5</sup>
- Between 2010 and 2016, US patients over 65 years (n=2,121) had 69 median outpatient days (range: 49-87)<sup>9</sup>

## Humanistic burden

Among 8 studies reporting HRQoL data, 5 were cross-sectional studies and 3 RCTs (**Figure 2**)

### EuroQoL-Visual Analogue Scales (EQ-VAS) (**Figure 3**)

- There were no significant HRQoL differences between the active adjuvant treatment (n=867) and post-adjuvant surveillance groups (n=237) (EQ-VAS mean: 74.9 [SD: 17.2] and 74.4 [SD: 16.1], respectively)<sup>10</sup>
- In a multinational (FR, DE, IT, JP, ES, UK, and US) survey, mean EQ-VAS was similar between treatment arms and ranged from 74.9 (active treatment) to 74.5 (surveillance). It decreased by age from 78.9 (25-34) to 69.3 (75+) and by country from 78.9 (UK) to 68.0 (DE)<sup>11</sup>
- Patients with greatest work productivity impairment (n=28; WPAI ≥50; mean EQ-VAS: 66.2) had significantly lower scores (P<0.001) than those with the lowest productivity impairment (n=30; WPAI <20; mean EQ-VAS: 88.2)<sup>12</sup>

### European Organization for Research & Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ) (**Figure 4**)

- Both QLQ-C30 global and functional scores and QLQ-BR23 functional score were generally higher among women with early-stage BC (Stage I, n=189; mean: 68.98, SD: 22.12) compared to those of women with late-stage BC (Stage >III, n=37; mean: 67.34, SD: 24.48)<sup>13</sup>
- A modest decline in GHS scores from baseline was seen post-adjuvant treatment in the ribociclib+letrozole (R+L) group (n=106; mean: -5.2), whereas a notable decline was seen in the chemotherapy group (n=106; mean: -23.6), indicating a worsening in patients undergoing chemotherapy<sup>14</sup>
- No clinically significant differences were observed between palbociclib + endocrine therapy (mean QLQ-C30: 71.4) vs endocrine therapy alone (mean QLQ-C30: 74.0), with an overall mean QLQ-C30: 71.7 (n=3615, CI: 95%)<sup>15</sup>

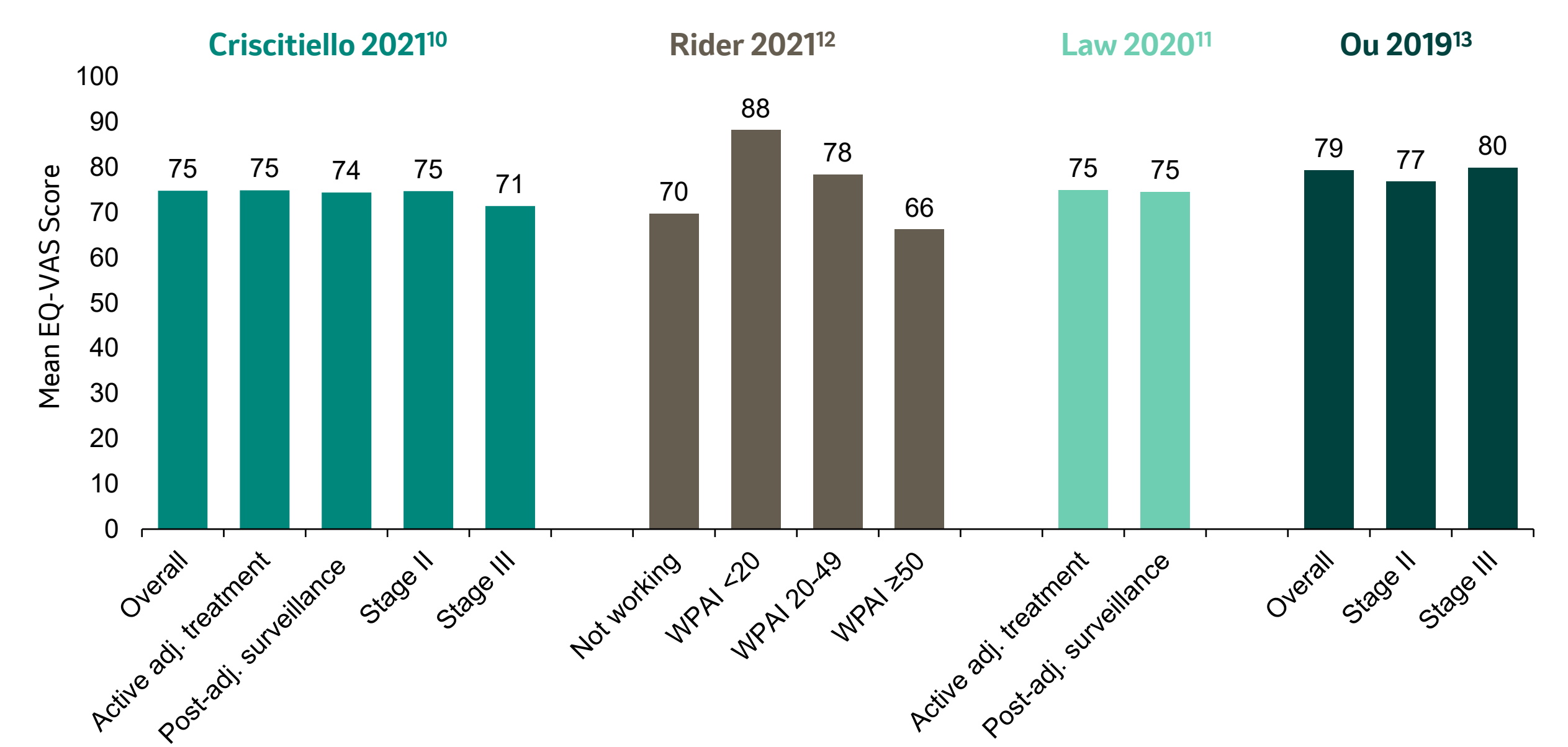
### Functional Assessment of Cancer Therapy (FACT):

- Between active adjuvant treatment (n=865, FACT-B: 99.4, SD:21.9) and post-adjuvant surveillance groups (n=237; FACT-B: 97.7, SD: 19.69), the mean FACT-B total (99.0, SD: 21.9), FACT-G total (72.5, SD: 17.8), EWB, FWB, and BCS scores were comparable, but there were significant differences for PWB and SWB, P=0.0441 and P=0.0009, respectively)<sup>10</sup>
- Patients with greatest work productivity impairment (n=28; WPAI ≥50) had lower mean FACT-B (92.1) and FACT-G (67.1) scores compared to patients not working (97.8 and 70.4, n=213) or patients with low (126 and 94.3, n=30 WPAI<20) or moderate impairment (105.6 and 78.1, n=56, WPAI 20-49)<sup>12</sup>

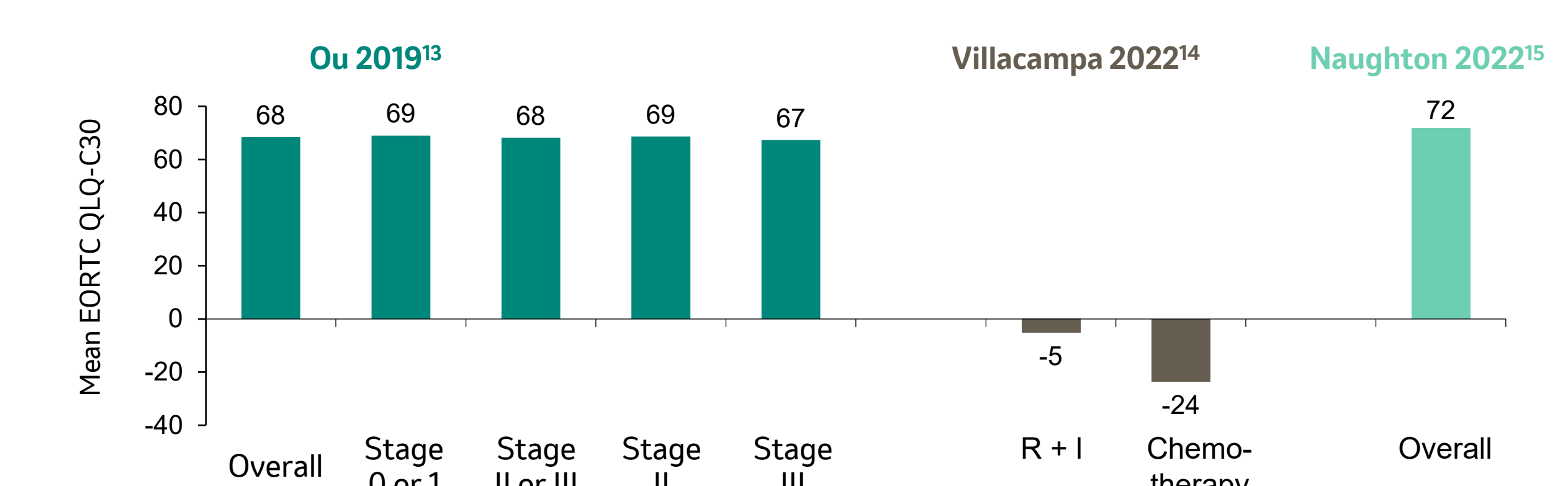
**Table 2. Overview and key results from studies describing total health care and services costs in stage I-III HR+/HER2- BC patients**

Author, year, country	Analysis set (N)	Measure of cost	Average cost	Primary cost contributors
Brezden-Masley, 2021, Canada <sup>4</sup>	Stage I-III (21,360)	Average annual per-patient cost	Annual mean: CAN\$22,662	Ambulatory visits, hospital inpatient services, and OHIP professional fees
Waintraub, 2017, US <sup>5</sup>	Previously untreated stage I or II (177)	Mean total outpatient costs	6-month mean: Chemotherapy - \$24,955 Hormonal therapy - \$2,654	Chemotherapy: hematopoietic growth factors and supportive care medications
Berdunov, 2022, US <sup>6</sup>	Early stage (NR)	Mean differences in costs of treatment	Node negative vs node positive: \$12,618 and \$17,564 Distant recurrence 1L vs 2L: \$175,386 and \$91,646	1L and 2L: CDK4/6 inhibitors
Brandao, 2020, Portugal <sup>7</sup>	Stage I-III (537)	Median overall cost of care (3 years after diagnosis)	€10,540	Radiotherapy, surgery, and hospitalizations
Lao, 2022, New Zealand <sup>8</sup>	Stage I-III (22,948)	Median cost of treatment	Stage II: \$24,341 Stage III: \$28,662	NR

**Figure 3. Summary of studies reporting data for EQ-VAS (n=4 studies)**



**Figure 4. Summary of studies reporting data for EORTC-QLQ30 (n=3 studies)**



## Conclusions

- Among patients with early-stage HR+/HER2- BC, existing treatment regimens were associated with high overall direct costs and characterized by utilization of both inpatient and outpatient resources
- HRQoL was found to be negatively impacted among patients with early-stage HR+/HER2- BC, with deterioration in HRQoL particularly observed among those experiencing high work productivity impairment (vs lower work productivity impairment) and those receiving adjuvant chemotherapy (vs adjuvant targeted therapy)
- The current management of early-stage HR+/HER2- BC was associated with notable health care resource use, cost burden, and decremental impact on HRQoL, indicative of an unmet need for novel treatment approaches in this setting

**Abbreviations:** 1L, first-line; 2L, second-line; AE, adverse event; BC, breast cancer; BCS, breast cancer subscale; CDK, cyclin-dependent kinase; CEA, cost-effectiveness analysis; cN, clinical node; CRD, Center for Reviews and Dissemination; CT, chemotherapy; DE, Germany; DSP, disease-specific programs; EBC, early-stage breast cancer; ES, Spain; ET, endocrine therapy; EWB, emotional well-being; FR, France; FWB, functional well-being; G-CSF, granulocyte-colony stimulating factor; GHS, global health status; HCRU, health care resource utilization; HER, human epidermal growth factor receptor 2; HR, hormone receptor; HRQoL, health-related quality of life; IT, Italy; LOS, length of stay; NICE, National Institute for Health and Care Excellence; NR, not reported; OHIP, Ontario Health Insurance Plan; PRO, patient-reported outcomes; PWB, physical well-being; R+L, ribociclib plus letrozole; RCT, randomized controlled trial; SLR, systematic literature review; SWB, social well-being; UK, United Kingdom; US, United States; WPAI, Work Productivity and Activity Impairment.

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