

Economic Burden in Patients with Chronic Myeloid Leukemia in Early Lines of Therapy: A Literature Review

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KEY FINDINGS & CONCLUSIONS

- CML-CP patients experience a significant economic burden in early lines of therapy, majorly attributed to direct treatment costs and hospitalizations.
- Additionally, lower treatment adherence and indirect economic burdens resulting from work-absence and productivity loss due to disease progression/AEs, further contributed to the overall economic burden of CML-CP. Evidence also suggested that patients treated with imatinib first-line experienced a greater loss in work productivity compared to those who switched to nilotinib for second-line treatment.
- Thus, this study emphasized on the existing economic burden in early lines of CML-CP and thereby the importance of developing effective treatments with better safety profiles to address the disease burden.

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INTRODUCTION

- Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm with an incidence of 1–2 cases per 100,000 adults.¹
- Despite various treatment options for early-line chronic myeloid leukemia in chronic phase (CML-CP), disease burden remains high due to chronic treatment requirements, multiple adverse events (AEs), resistance/intolerance to tyrosine kinase inhibitor (TKI), and treatment switching.
- To better understand the burden of illness of CML and the unmet medical need, we conducted a targeted literature review on the economic burden in patients with CML-CP receiving early lines of therapy (including first and/or second-line).

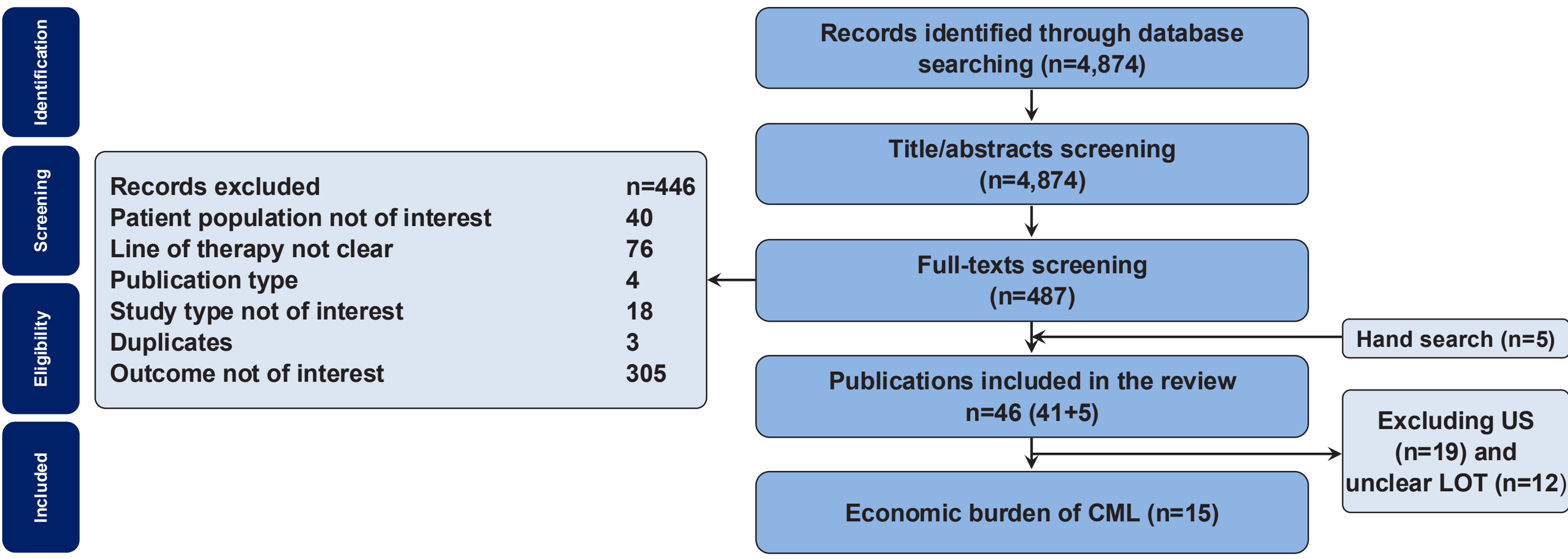
METHODS

- Robust searches were conducted in scientific databases such as Embase® and MEDLINE® and relevant conference-proceedings, for English-language publications, from database inception until June 16, 2023.
- Ex-US studies evaluating cost and/or healthcare-resource-utilization (HCRU) data for adults CML patients (aged ≥18 years) were included.
- A single reviewer screened initially the publications based on titles and abstracts followed by full-texts for eligibility based on pre-defined eligibility criteria of review.
- Publications which met the review inclusion criteria were listed and those corresponding to a single study were linked together. The retrieved studies were then extracted into a pre-defined data extraction grid.

RESULTS

- Of the 4,874 records obtained from the database searches, 15 unique studies (journal articles, n=6 and conference abstracts, n=9) were included in this review (**Figure 1**).
- A majority of these studies were conducted in European countries (n=9), followed by Brazil (n=3), and China (n=1). Two multi-country studies were also included.
- The sample size varied largely from 20 to 3633 patients.
- The median age of patients ranged from 32 years to 65 years, with 60% of the studies showing a male predominance.
- Out of 15 studies, eight reported direct costs, six reported HCRU, and three reported indirect economic burden.

Figure 1. Study selection flowchart

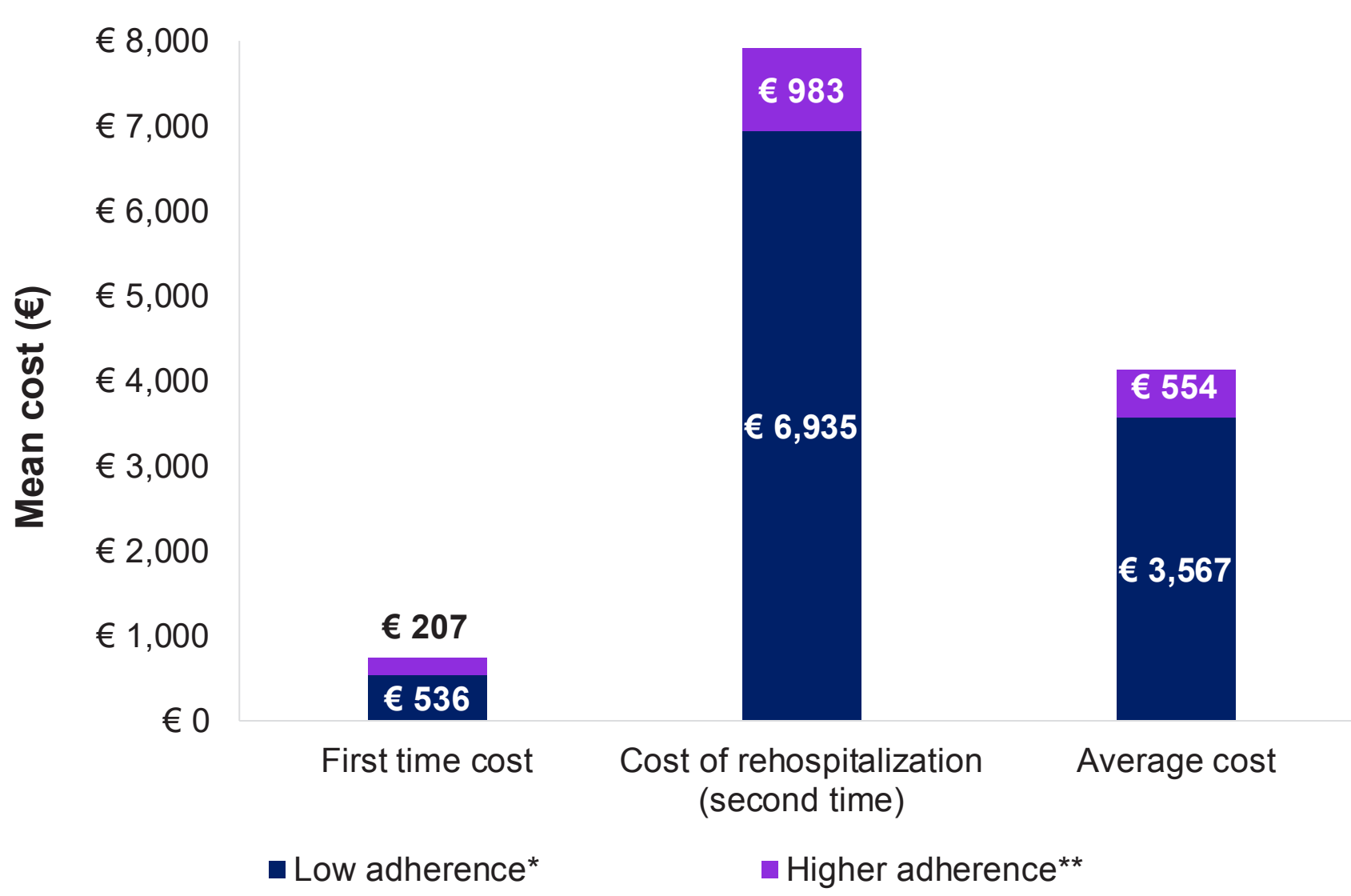


Abbreviations: CML: Chronic Myeloid Leukemia; LOT: Line of therapy; US: the United States

Cost of early-line therapy

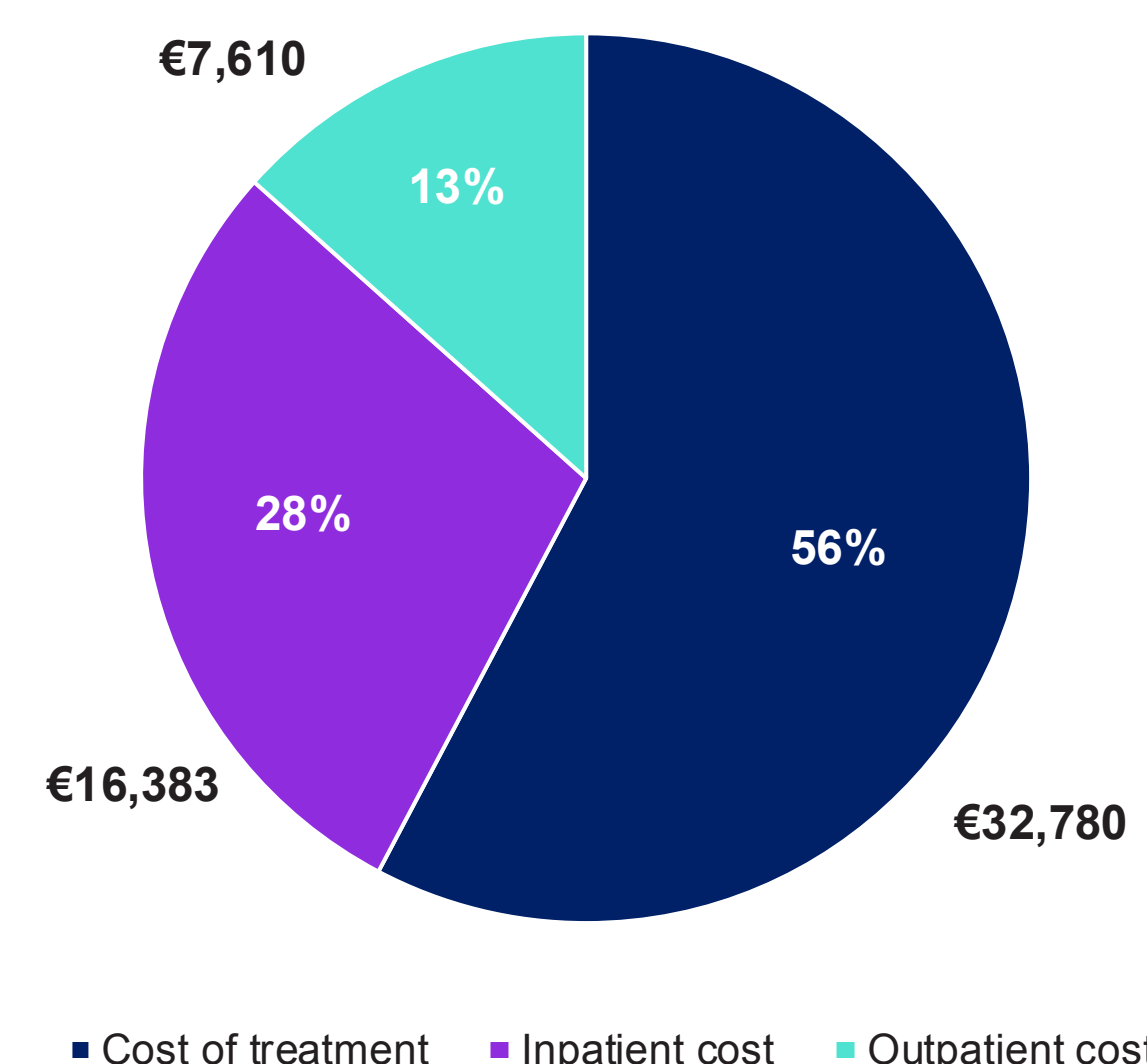
- A total of eight studies reported the direct cost of treating patients with CML-CP in early lines of therapy.
- The overall annual cost per patient for early-line therapy in CML patients during 2012-2019 ranged from €20,042 to €58,230.²⁻³
 - In Italy (n=3), the annual direct cost of CML patients on first-line therapy during 2018-2019 was €20,042, with anti-cancer pharmacological interventions being the major cost driver (€16,517).² Notably, hospitalization costs were higher for patients with lower adherence compared to those with higher adherence to treatment. Furthermore, cost of subsequent hospitalizations increased for patients with lower adherence compared to those with higher adherence to treatment (**Figure 2**).⁴
 - Among patients undergoing second-line therapy, the highest annual cost per patient (excluding TKI costs) between 2015-2018 was observed with those on ponatinib, primarily due to comorbidity-related hospitalizations and other hospitalizations. This was followed by patients on bosutinib, dasatinib, nilotinib, and imatinib, respectively (**Figure 3**).⁵
 - A study from Germany reported that majority of patients undergoing early-line therapies (first and second) incurred a mean annual cost was €58,230, primarily attributed to treatment (60-70% accounting on TKI), inpatient and outpatient services (**Figure 4**).³
 - A significant reduction in economic burden was reported in a study from Brazil conducted in 2015, where a treatment free remission attempt in imatinib treated CML patients with a deep molecular response for at least 24 months reduced the overall disease monitoring costs from \$1,550 to \$520 per patient over three years.⁶

Figure 2. Hospitalizations costs per patient for CML on first-line therapy in Italy



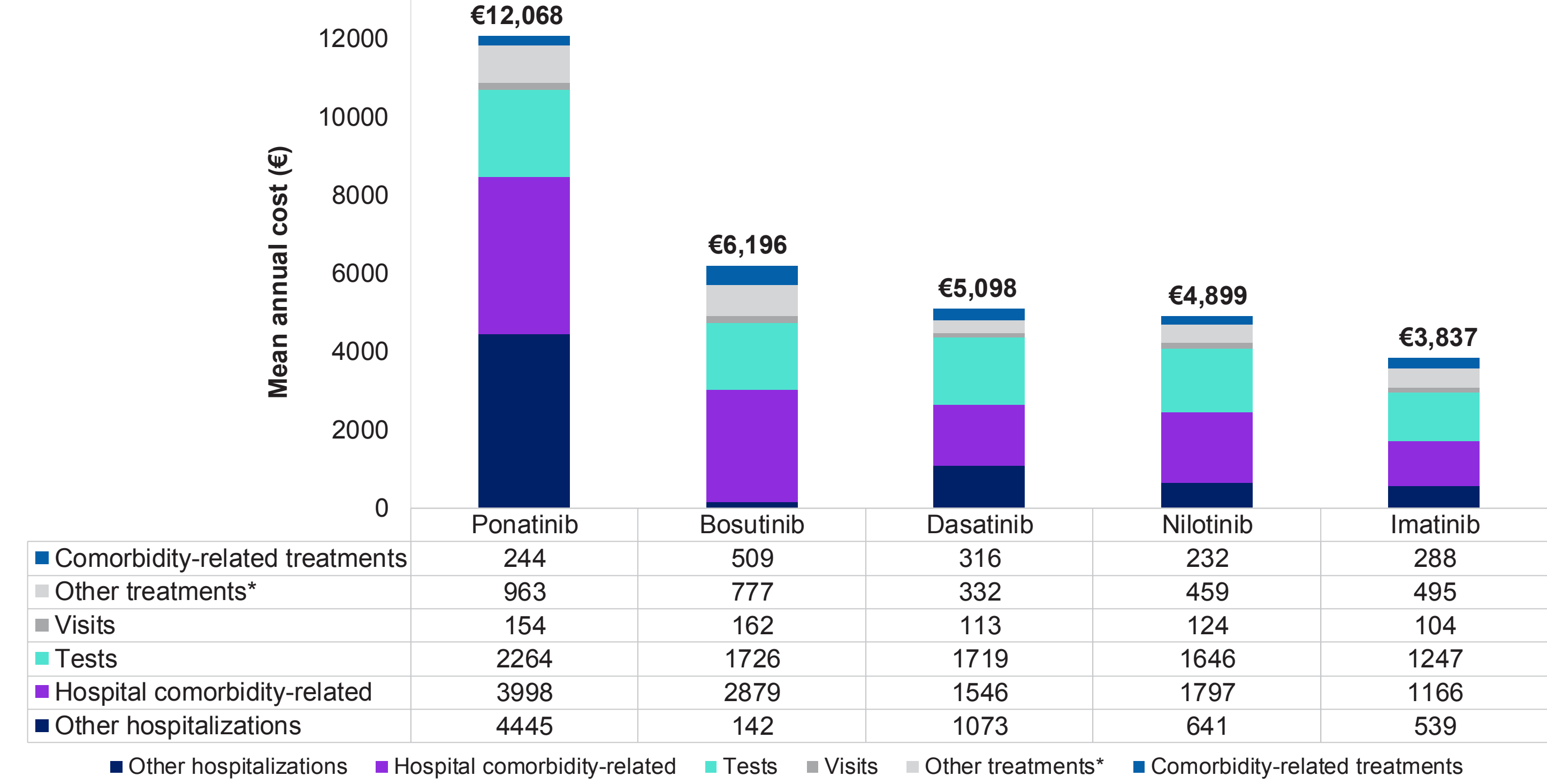
Source: Esposti 2014
*Proportion of days covered (PDC) 40%-79%; ** PDC ≥80%

Figure 4. Distribution of annual costs incurred by CML patients in Germany during early-line therapy



Source: Saussele 2019

Figure 3. Mean annual costs with different second line CML therapies in Italy (excluding TKI costs)



Source: Breccia 2021; * Treatments other than TKIs

Indirect economic burden

- Three studies reported the indirect economic burden, including those attributed to productivity loss and work-absence in CML patients who underwent early-line therapy, though the associated cost was not evaluated.
 - In France, 65.2% of patients on first-line CML treatment experienced work absence due to disease/treatment-related AEs.⁷ Another study conducted in France from 2011 to 2014 reported that over 25% of working-age CML patients reported absence from work within 2-years of TKI initiation, with the median duration of sick-leave being 115 days. A higher impact was observed in patients on second-generation TKIs (nilotinib, dasatinib).⁸
 - In Italy, the productivity was evaluated through a quantitative survey using a self-administered questionnaire. The results showed that patients undergoing first-line imatinib treatment experienced a greater loss in work productivity compared to those who switch to second-line nilotinib (64% vs 33% respectively).⁹

Healthcare-resource utilizations

- Six studies reported data on HCRU, including hospitalizations, length of hospital stay, and cardiovascular (CV)-related hospitalizations in CML patients receiving various early-line therapies (**Table 1**).
 - For patients receiving first-line therapy, hospitalizations (1%-22.5%)¹⁰⁻¹¹, and CV-related hospitalization (3.2%-7.5%)¹¹⁻¹² were frequently reported.
 - CV complications were more prevalent among patients receiving nilotinib, resulting in a hospitalization rate twice that of patients on dasatinib (27.4 vs.12.6 per 1000/year), and longer hospital stays (263 days vs. 68 days).¹²
 - Among patients receiving second-line therapy, HCRU was dominated by hospitalizations, all-cause visits, and drug prescriptions (excluding TKIs).¹³
 - In France, patients reporting absence from work utilized more healthcare resources, including hospital stays and outpatient consultations, compared to those not reporting a work-absence due to CML treatments.⁸

Table 1. Resource use in patients with CML

Authors, years	Populations	Resource use	n (%) /mean(SD)/Median
Hospitalizations			
Pajep 2021	CML-1L	Hospitalization at inclusion	60 (1)
		Hospitalization during follow-up	536 (15)
		At least one hospitalization in the 12 months preceding the index date	1251 (34.4)
		Long term disease, at least one hospitalization in the 12 months preceding the index date	1815 (65.5)
Paquette 2015	CML-1L	Hospitalization	329 (22.5)
		CV-related hospitalization	46 (3.2)
Mauro 2018	CML-1L, DAS	CV-related hospitalization	9 (5)
	CML-1L, NIL	CV-related hospitalization	12 (7.5)
	CML-1L, DAS	Numbers of CV-related hospitalizations	16 (8.5)
	CML-1L, NIL	Numbers of CV-related hospitalizations	36 (21.4)
Breccia 2022	CML-2L	All-cause hospitalizations	0.6 (1.1)*
Length of hospital stay			
Nicolau 2007	CML-1L, Inpatients	LOS due to transplantation including readmissions	28 (16 to 81) days**
	CML-1L, Outpatients	LOS due to transplantation including readmissions	17 (1 to 149) days**
	CML-1L, Outpatients	LOS after readmission	12 (1 to 75) days**
Mauro 2018	CML-1L, DAS	Durations of hospital stay related to CV disorders	68 days*
	CML-1L, NIL	Durations of hospital stay related to CV disorders	263 days*
Conte 2022	CML-1L,2L	Hospital stays	1 (0-2)**
Paquette 2015	CML-1L	Hospitalization duration	5.9 (7.2)*

Abbreviations: 1L: First-line; 2L: Second-line; CML: Chronic myeloid leukemia; DAS: Dasatinib; IM: Imatinib; IQR: Interquartile range; LOS: Length of stay; NIL: Nilotinib; CV: Cardiovascular; * Mean (SD); ** Median (IQR)

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Disclosures

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