Evaluating the Economic Burden of Polycythemia Vera Across the Disease Continuum: A Systematic Literature Review

EE441

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BACKGROUND AND OBJECTIVES

- Polycythemia vera (PV) is a rare and chronic myeloproliferative neoplasm (MPN), characterized by hematopoietic stem cell-derived clonal myeloproliferation, which results in erythrocytosis and often thrombocytosis, leukocytosis, and splenomegaly.[1]
- PV imposes a significant economic burden on patients and healthcare systems due to high inpatient/outpatient costs, further exacerbated due to occurrence of complications and disease progression to myelofibrosis (MF) or acute myeloid leukemia (AML).[2]
- There is currently no systematic literature review (SLR) that consolidates the economic impact of PV symptoms, complications, or disease progression. Thus, this SLR aims to fill this gap by identifying relevant evidence on PV costs, and healthcare resource utilization (HCRU) data, providing insights that can guide decision making.

METHODS

- This systematic review was conducted in accordance with the PRISMA guidelines, searched records from 2010 to 2025 in Medline, Embase and Cochrane Library, supplemented by grey literature and bibliographic review.
- Data were extracted using standardized extraction grid and synthesized narratively due to heterogeneity. The quality of the studies and publications was evaluated using standard appraisal tools.
- To improve comparability, the costs were adjusted to 2024 euros using the inflation rate as of December 2024. Thus, they may not reflect the reported values in the publications.

RESULTS

- Thirty studies reported in 55 of 2,534 identified records were included (**Figure 1**).
- Most studies were conducted in North America (n=10), followed by Europe (n=7), Asia (n=7), and one study each in Australia and Canada. Four studies were conducted across multiple countries. Studies reported direct and indirect costs, HCRU, and absenteeism. Baseline characteristics indicated a mean (range) patient age of nearly 60 years (42–71).
- Major cost drivers in PV were presence of complications, need for hospitalizations, high drug cost, and disease progression to MF/AML (**Figure 2**).

Direct costs

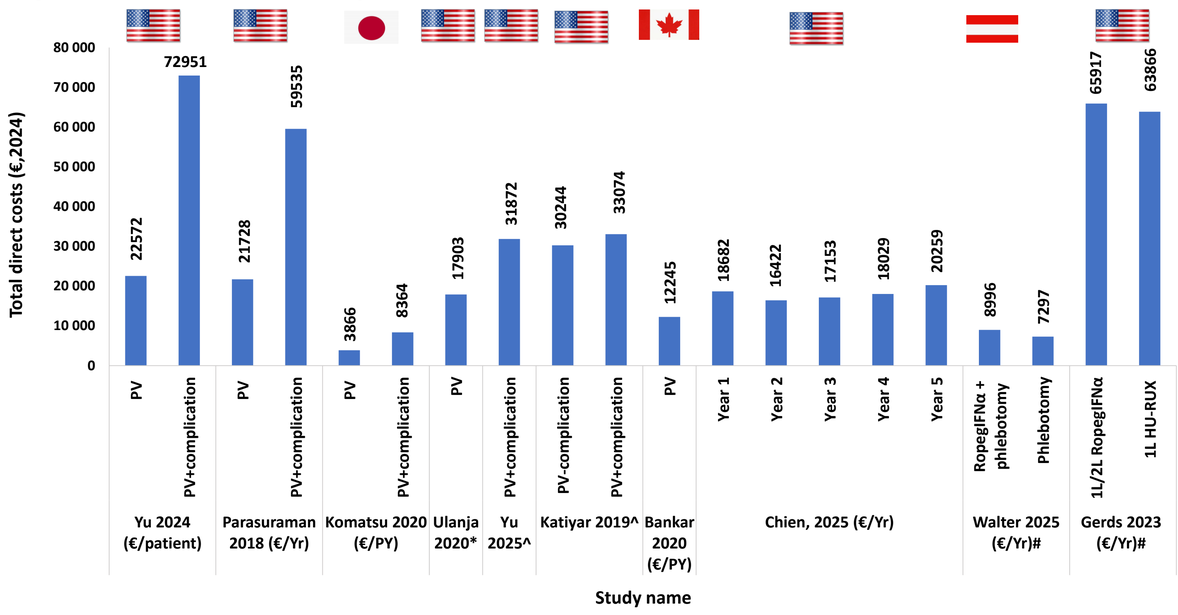
- Overall, the studies reporting total direct costs were heterogenous in terms of population assessed, cost year used, and geographical distribution (**Table 1)**.
- Patients with thromboembolic events incurred 2-3-fold higher total direct costs compared to those without thromboembolic events, whereby inpatient costs was the major contributor of this difference (**Figure 3**). This was supported by high resource use in patients with complications due to need for hospitalization.[3,4,5]
- Hydroxyurea (HU)-intolerant patients incurred higher costs compared with HU-stable patients; the total cost ratio was 2.65, with hospitalization costs being the major component, suggesting worse outcomes requiring increased monitoring in HU-intolerant patients.[6]
- A longitudinal cost analysis reported that, over five years, the mean annual costs for treating PV patients without pre-existing MF and AML, increased from €18,682 to €20,259, indicating that the economic burden of managing PV increased over time. The analyses also indicated that high-risk patients incurred 59.9% higher total annual costs than low-risk patients (**Figure 4**).[7]
- Two economic evaluations identified ropegIFNα as a cost-effective treatment in low-risk PV[8], and in both low- and high-risk PV[9]. The post-PV MF and AML total annual costs in low-risk PV patients were €1,787 and €304 in ropegIFNα group, and €2,553 and €362 for phlebotomy group, respectively.[8]

Table 1. Characteristics of studies reporting direct costs

Study name (Country)	Population	Currency, Cost year	Population characteristics	Resource use
Chien, 2025[7] (US)	PV	US$, 2024	PV patients without pre-existing MF and AML	NR
Walter, 2025[8] (Austria)	Low-risk PV	€, 2024	Low-risk PV patients (those younger than 60 years without prior thrombosis); ropegIFNα to phlebotomy compared to phlebotomy alone	NR
Yu, 2025[15] (US)	PV with TE	US$, 2021	Patients with predefined TEs with a mean (SD) CCI score of 3.2 (2.3).	LOS: 7 (9) days
Cabibbo, 2024[16] (Italy)	PV	€, NR	Patients treated with erythrocytapheresis or phlebotomy over a four-year period. 55% patients had splenomegaly	Total number of procedures: Erythrocytapheresis: 28; Phlebotomy: 320
Ellis, 2024[6] (Israel)	PV - HU stable/ intolerant	NR*	PV patients who were HU-intolerant (cytopenia; alternative treatment (busulfan, IFN-α or ruxolitinib) or HU-stable (remained on continuous HU treatment)	*HU-Stable/ intolerant:* Hospitalizations: 3.8 (3.5)/6.5 (5.4) LOS: 17.6 (24.6)/ 35.1 (33.3) days Phlebotomies: 6.9 (8.0)/9.8 (9.5)
Ngo, 2024[14] (Australia)	PV	AU$, NR	Cost-funding analysis; patients who received at least 2 sessions of erythrocytapheresis or venesection	No. of sessions in 1st year of treatment#: Erythrocytapheresis: 3.8 (3.3-4.4) Venesection: 5.3 (4.6-6.0)
Yu, 2024[5] (US)	PV *Subgroup:* PV with TE	US$, 2019	Patients with at least 1 medical claim for a doctor visit. Subgroup of patients with a TE during the 12-month follow-up period	PV: STD: 4.5 (24.6) days; LTD: 1.2 (16.1) days PV with TE: STD: 13 (37.7) days; LTD: 4.8 (30.8) days
Gerds, 2023[9] (US)	PV	US$, 2022	PV patients including 22.7% low-risk and 77.3% high-risk patients; ropegIFNα used as first- or second-line treatment	NR
Darbà, 2022[17] (Spain)	PV	€, NR	Hospitalized patients presenting age-related conditions such as hypertension, diabetes or anemia	LOS, Median (95% CI): 7 (6-7) days
Bankar, 2020[13] (Canada)	PV	CDN$, 2018	PV patients with some developing thrombosis (arterial or venous) at any time within 2 years before the index event date	ER; hospitalization visits: 1.2; 5.2/PY Specialist; GP visits: 7.5; 6.6/PY Long-term; Home care: 10.7; 12.5/PY
Komatsu, 2020[4] (Japan)	PV with/without TE	¥, NR	PV patients managed in a hospital-based care setting with TE and CVC as the major risk factor	PV with/without TE: LOS: 31.5 (51.8)/9.4 (27.3) days Admission rate (95% CI)/PY: 0.43 (0.35, 0.51)/ 0.21 (0.19, 0.24)
Ulanja, 2020[11] (US)	PV with/without TE	US$, 2016	Survey of patients from the National Inpatient Sample (NIS) database who were hospitalized in 2016	NR
Katiyar, 2019[12] (US)	PV with/without VTE	US$, NR	Patients with a record of hospitalization majorly non-VTE related (95.8%)	LOS; Median (with/without TE): 5/4 days
Parasuraman, 2018[3] (US)	PV *Subgroup:* PV with TE	US$, 2013	PV patients newly treated with HU. Subgroup of patients with a TE within 12 months of HU initiation.	PV (with/without TE) Inpatient admissions: 1.7 (1.2)/1.3 (0.7); LOS/admission: 5.9 (4.1)/ 6.1 (6.1) ER visits: 1.9 (1.4)/ 1.7 (1.4) Physician office visits: 18.9 (9.1)/14.1 (7.7) OP pharmacy claims: 45.8 (27.3)/36.2 (25.9)
Byun, 2017[18] (Korea)	PV	US$, 2004-2013	Nationwide population-based descriptive epidemiology study	Total number of hospital visits (2004-2013): 1,68,726
Mehta, 2014[19] (US)	PV	US$, 2010	PV patients with mean (SD) CCI of 1.24 (1.84)	Admissions/LOS: 0.27 (1.0)/ 1.67 (7.9) days OP claims: 61.9 (63.7); Physician/ ER visits: 30.6 (31.9)/0.8 (2.6)

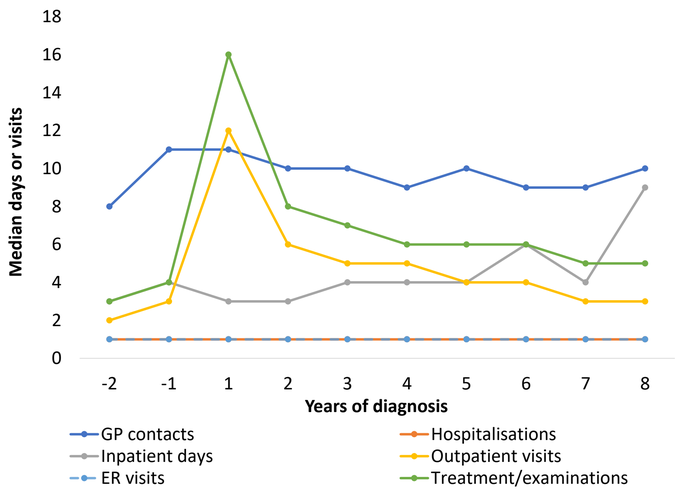
Abbreviations: AML, acute myeloid leukemia; CCI, charlson comorbidity index; CI, confidence intervals; CVC, cardiovascular complications; ER, emergency room; GP, general practioner; HU, hydroxyurea; IFN, interferon; LOS, length of stay; LTD, long-term disability; MF, myelofibrosis; NR, not reported; OP, outpatient; PV, polycythemia vera; PY, person year; STD, short-term disability; TE, thromboembolic event; VTE, venous thromboembolism
Note: Values are presented as mean (SD), unless specified otherwise.*Cost ratio; #Mean (95% CI)

Figure 4: Total direct costs adjusted to Euros, 2024



Abbreviations: HU, Hydroxyurea; PV, Polycythemia vera; PY, Person year; RUX, Ruxolitinib; Yr, year
Note:*Cost ratio; ^Hospitalization costs reported; #Lifetime costs were divided by lifetime horizon (30 years) to obtain cost per annum

Figure 5: Trend in HCRU pre-and post-diagnosis[20]

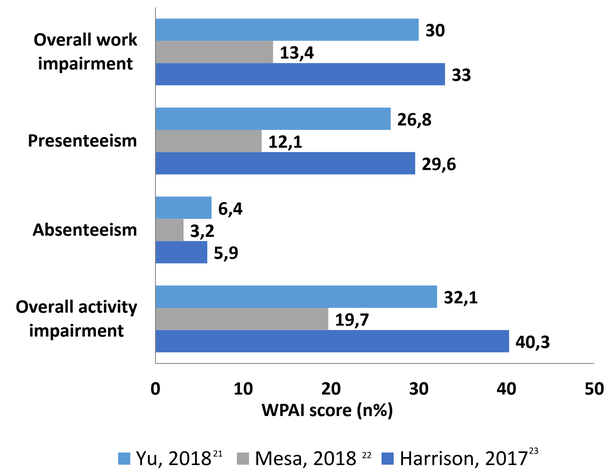


Abbreviations: ER, Emergency room; GP, General practitioner; HCRU, Healthcare resource utilization

Resource use

A Danish cohort study suggested that the frequency of outpatient visits and treatments/examinations was notably high in the first year (likely due to initial phlebotomy, diagnostic workups, and cytoreductive therapy) while inpatient days increased over time, peaking in the eighth year[20] (**Figure 5**).

Figure 6: WPAI scores in PV patients

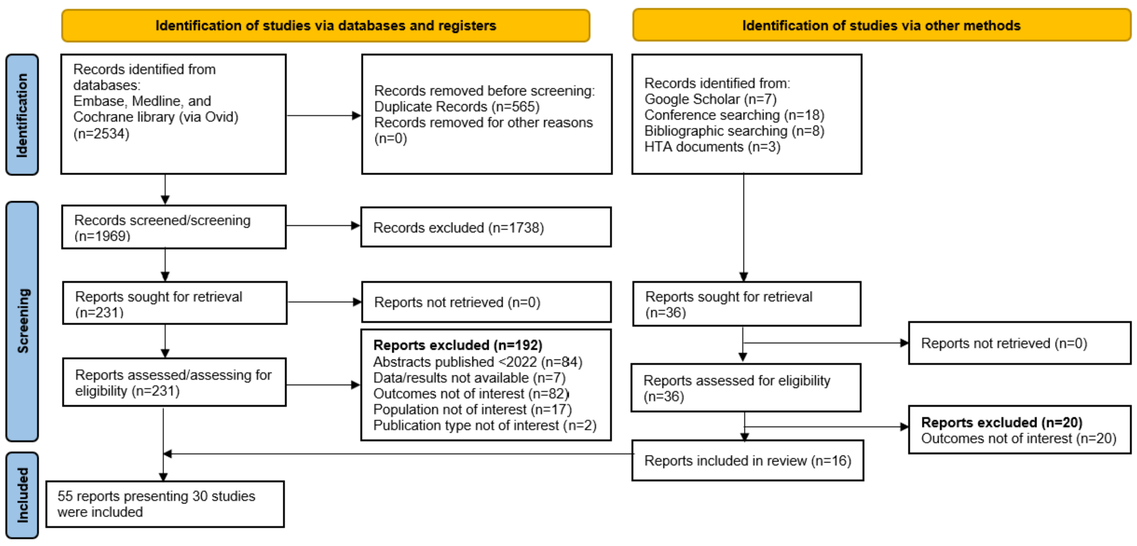


Abbreviations: PV, Polycythemia vera; WPAI, Work Productivity and Activity Impairment
The values represent the % work hours lost/impaired

Indirect costs

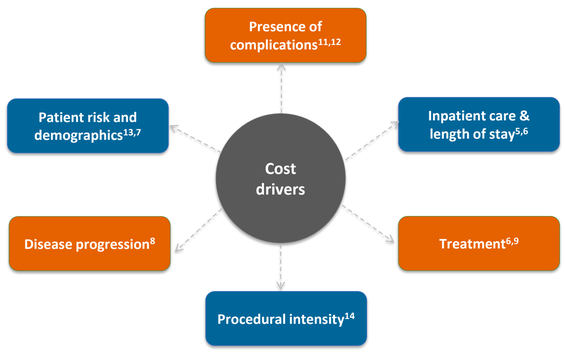
- Across three studies, patients reported 19.7% to 40.3% of their activity was impaired, while there was 13.4% to 33.0% of work time missed or impaired, assessed using WPAI questionnaire (**Figure 6**).[21-23]
- A US based retrospective analysis reported markedly higher indirect costs due to absenteeism in patients with complications vs. overall cohort; short- term (€1,853 vs. 638) and long-term disability leaves(€692 vs. 171).[5]

Figure 1: PRISMA flow diagram



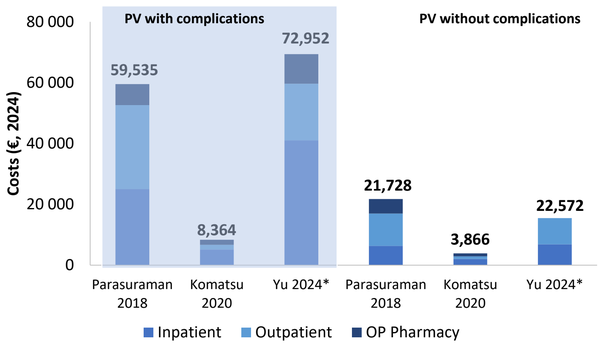
Abbreviations: PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses. **Source**: Page MJ et. al., 2021[10]
Note: *In addition to the 25 studies identified through database; 3 HTA documents, 1 poster, and 1 trial were also identified through bibliographic searching

Figure 2: Major cost drivers in PV



Abbreviation: PV, Polycythemia vera

Figure 3: Total direct costs (with vs. w/o complications)



Abbreviations: OP, Outpatient ; PV, Polycythemia vera; w/o, without
Note: The mean total direct cost is mentioned above each bar. *Some of the cost components not reported

CONCLUSIONS

PV imposes a substantial economic burden. Despite study variability, costs are largely driven by disease progression, complications, and treatment resistance incurring high inpatient costs. Earlier diagnosis and therapies with proven, disease-modifying effect may reduce long-term healthcare costs. More studies are warranted to assess the indirect costs associated with PV to understand the full societal burden of PV.

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