Humanistic and Economic Burden of Primary Biliary Cholangitis: A Systematic Review of Health-Related Quality of Life, Healthcare Resource Utilization, and Associated Cost

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Dilip Makhija[1], Marvin Rock[1], Chong H Kim[1], Caroline Burk[1], Mirko von Hein[2], Ryan Thaliffdeen[1], Oskar Eklund[3], Sumeet Attri[4], Gagandeep Kaur[4], Barinder Singh[4]

[1]Gilead Sciences, Inc., Foster City, CA, USA, [2]Gilead Sciences, London, United Kingdom, [3]Gilead Sciences AB, Solna, Sweden, [4]Pharmacoevidence, Mohali, India

CONCLUSIONS

- PBC significantly impairs HRQoL and imposes a substantial economic burden due to high HCRU and treatment costs
- This review underscores the critical need for timely and effective therapies for disease modification, symptom management, and overall patient well-being
- The findings indicate that PBC imposes a persistent burden on both patients and healthcare systems, underscoring the considerable unmet needs associated with the disease

PLAIN LANGUAGE SUMMARY

- Patients with primary biliary cholangitis (PBC) were associated with significant humanistic burden, increased healthcare resource utilization, and substantial cost burden
- Symptoms such as severe pruritus and fatigue significantly impacted the quality of life (QoL) of PBC patients. Similarly, the emotional well-being, physical health, and daily activities were largely impacted in PBC patients
- Costs related to liver transplantation, hospitalization, drugs, and hospital visits were reported as the major contributing factors to the higher total cost incurred by PBC patients

INTRODUCTION

- Primary biliary cholangitis (PBC) is a chronic cholestatic autoimmune liver disorder, marked by a destructive, small duct, and lymphocytic cholangitis, that can lead to biliary cirrhosis and liver failure if left untreated[1]
- The pooled global prevalence and incidence of PBC were 18.1 cases per 100,000 people and 1.8 per 100,000 person-years, respectively[2]
- Given the chronic and progressive course of PBC, the development of cirrhosis has been linked to further negative clinical outcomes, which could substantially translate to higher humanistic and economic burden[3]

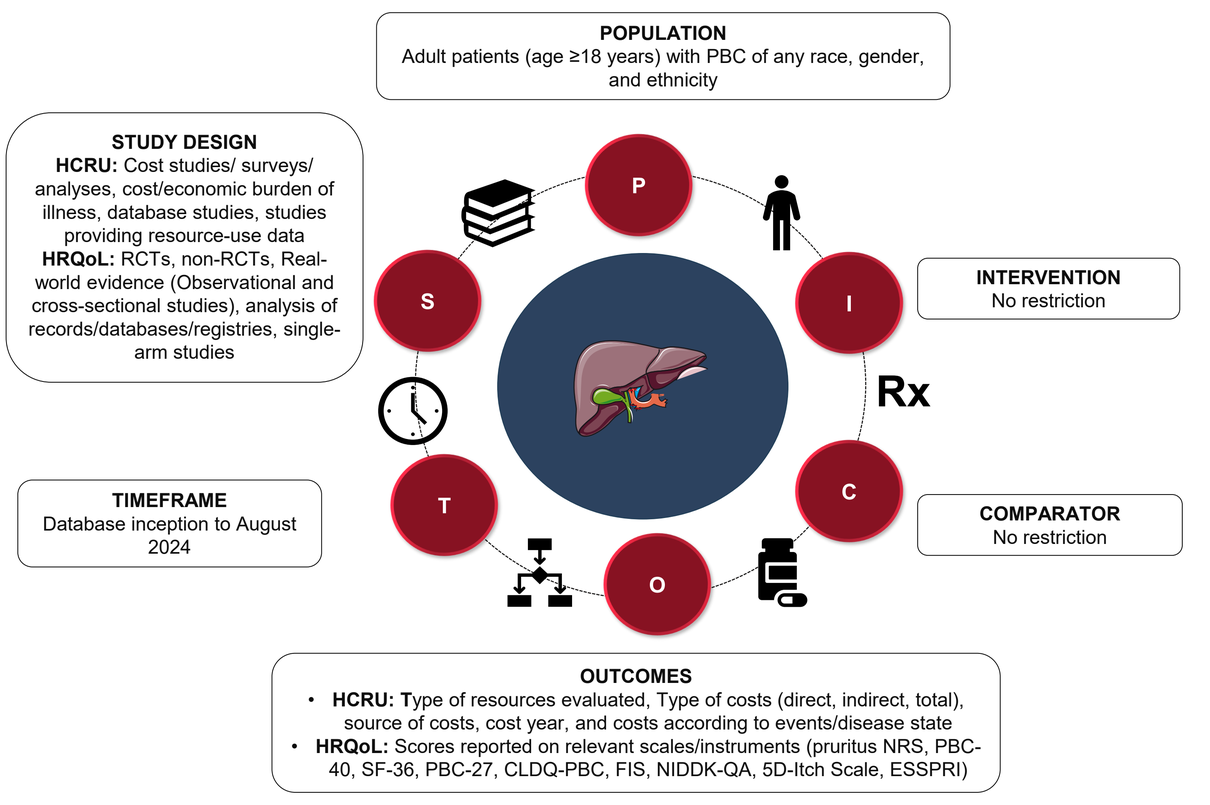
OBJECTIVE

- This systematic literature review (SLR) aimed to summarize published evidence regarding health-related quality of life (HRQoL), healthcare resource utilization (HCRU), and associated costs in adult patients with PBC

METHODS

- This study adhered to National Institute for Health and Care Excellence (NICE) and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[4] guidelines for SLRs, following standard methodology with a transparent, reproducible, and unbiased approach
- Key biomedical databases, including EMBASE®, MEDLINE®, and CENTRAL, were searched for English-language articles from database inception to August 2024 using relevant keywords
- The prespecified eligibility criteria is presented in **Figure 1**
- Evidence was screened using both a manual approach and a Gen-AI tool, with quality check by a subject matter expert (human) as per NICE UK[5], and Canada Drug Agency (CDA)[6] position papers

Figure 1: PICOS criteria for inclusion in the SLR

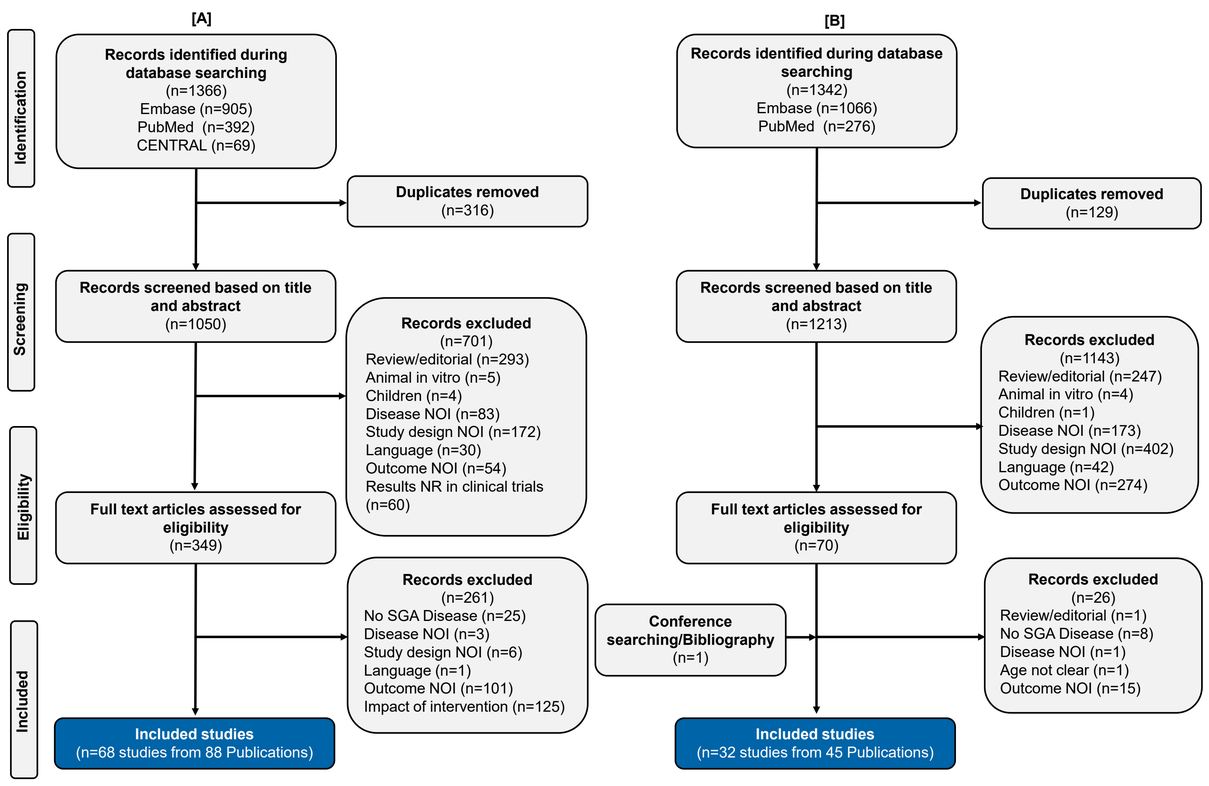


CLDQ, Chronic Liver Disease Questionnaire; ESSPRI, EULAR Sjogren's Syndrome Patient Reported Index; FIS, Fatigue Impact Scale; HCRU, Healthcare Resource Utilization; HRQoL, Health-Related Quality of Life; NIDDK, National Institute of Diabetes and Digestive and Kidney Diseases; NRS, Numeric Rating Scale; PBC, Primary Biliary Cholangitis; RCT, Randomized Controlled Trial; SF-36, Short Form 36; SLR, Systematic Literature Review

RESULTS

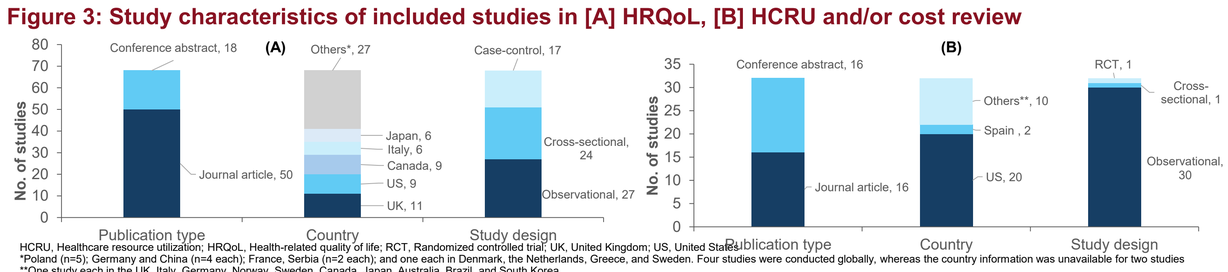
- Out of 2,714 publications, 100 studies were included (HRQoL=68, HCRU and/or cost=32 studies)
- **Figure 2** summarizes the review process adopted to retrieve the studies, and the characteristics of the included studies are depicted in **Figure 3**

Figure 2: Flow of studies in the SLR [A] HRQoL [B] HCRU and/or Cost



HCRU, Healthcare resource utilization; HRQoL, Health-related quality of life; NOI, Not of Interest; SGA, Subgroup analysis; SLR, Systematic Literature Review

Figure 3: Study characteristics of included studies in [A] HRQoL, [B] HCRU and/or cost review

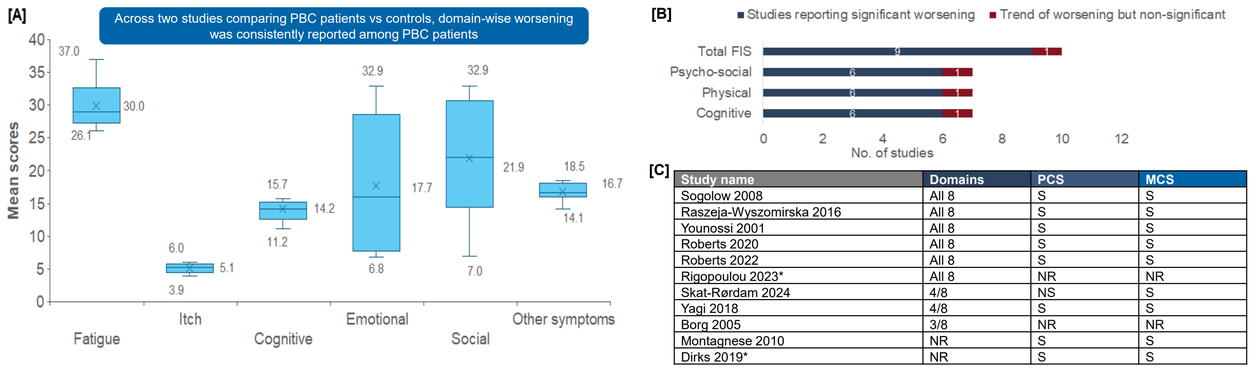


HCRU, Healthcare resource utilization; HRQoL, Health-related quality of life; RCT, Randomized controlled trial; UK, United Kingdom; US, United States
*Poland (n=5); Germany and China (n=4 each); France, Serbia (n=2 each); and one each in Denmark, the Netherlands, Greece, and Sweden. Four studies were conducted globally, whereas the country information was unavailable for two studies
**One study each in the UK, Italy, Germany, Norway, Sweden, Canada, Japan, Australia, Brazil, and South Korea

HRQoL

- Across the included evidence, frequently used HRQoL instruments (≥5 studies) included PBC-40 (n=32), Short Form 36 (SF-36; n=20), Fatigue Impact Scale (FIS; n=16), Numerical Rating Scale (NRS; n=8), PBC-27 (n=5), and Chronic Liver Disease Questionnaire (n=5)
- HRQoL was significantly impaired in adult PBC patients compared to healthy controls on the scales of SF-36 (n=11/12 studies), FIS (n=10/11), and PBC-40 (n=2/2) **(Figure 4)**. PBC patients showed significantly lower mean SF-36 scores than controls, particularly in physical component summary (PCS) (38.6-49 vs 45-79; n=3), mental component summary (MCS) (44.4-55 vs 51-77; n=3), and vitality domains (41.4-47 vs 50.2-67.5; n=3)
- Clinically significant itch/pruritus (n=4/4), high fatigue (n=3/3), and female gender (n=3/5) were associated with significantly worse HRQoL scores on the PBC-40, SF-36, and FIS scale
- Among the most utilized scales, fatigue was the most affected PBC-40 domain, with higher mean scores ranging from 26.1 to 37.0 (Possible range: 11-55, higher score worse HRQoL) **(Figure 4)**. Further, the mean SF-36 PCS and MCS scores ranged from 38.7-46.9 and 44.4-56.0, respectively (possible range: 0-100, higher score better HRQoL)

Figure 4: HRQoL scores and comparison between PBC patients and healthy controls across domains of [A] PBC-40 (n=2), [B] FIS (n=10), and [C] SF-36 (n=11)



[C]

Study name	Domains	PCS	MCS
Sogolow 2008	All 8	S	S
Raszeja-Wyszomirska 2016	All 8	S	S
Younossi 2001	All 8	S	S
Roberts 2020	All 8	S	S
Roberts 2022	All 8	S	S
Rigopoulou 2023*	All 8	NR	NR
Skat-Rørdam 2024	4/8	NS	S
Yagi 2018	4/8	S	S
Borg 2005	3/8	NR	NR
Montagnese 2010	NR	S	S
Dirks 2019*	NR	S	S

All 8 domains of SF-36 included: Bodily pain, General health, Mental health, Physical Functioning, Role emotional, Role physical, Social functioning, Vitality
FIS, Fatigue impact scale; HRQoL, Health-related quality of life; MCS, Mental component summary; NR, Not reported; NS, Non-significant worsening; PBC, Primary biliary cholangitis; PCS, Physical component summary; S, Significant worsening; SF-36, Short form 36; *Median data reported

HCRU and HCRU-related costs

- Of the 32 studies included, most reported both HCRU and related cost (n=17), whereas 14 focused on HCRU-related cost, and six studies on HCRU alone
- PBC patients demonstrated increased HCRU, with longer hospital stays, more outpatient (OP) visits, and higher pharmacy use. Patients with alkaline phosphatase ≥1.5 × ULN and cirrhosis were associated with significantly higher HCRU[7] **(Table 1; Table 2)**

Table 1: Mean all-cause and PBC-related HCRU per year in PBC patients according to ALP levels (Younossi et al)[7]

Type of resources	All-cause			PBC-related		
	ALP≥1.5×ULN (N=6083)	ALP<1.5×ULN (N=9792)	p-value	ALP≥1.5×ULN (N=6083)	ALP <1.5×ULN (N=9792)	p-value
Days receiving UDCA in the entire history	528.4	41.6	<0.0001	--	--	--
Office visits	7.12	6.18	<0.0001	1.87	1.41	<0.0001
OP services	1.83	1.64	0.0134	0.28	0.23	0.13
IP stays	1.71	1.81	<0.0001	0.19	0.23	<0.0001
ER visits	0.92	0.90	0.15	0.05	0.04	0.27
Urgent care visits	0.04	0.04	0.08	0.00	0.00	0.63

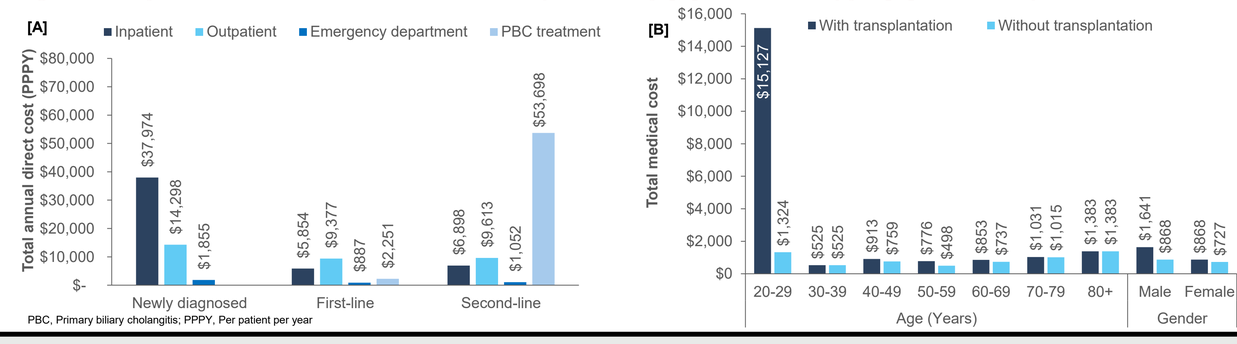
Table 2: Mean all-cause and PBC-related HCRU per year in PBC patients according to cirrhosis (Younossi et al)[7]

Type of resources	All-cause			PBC-related		
	PBC with cirrhosis (N=7367)	PBC without cirrhosis (N=8508)	p-value	PBC with cirrhosis (N=7367)	PBC without cirrhosis (N=8508)	p-value
Days receiving UDCA in the entire history	239.5	218.3	<0.0001	--	--	--
Office visits	7.85	5.40	<0.0001	1.71	1.47	0.59
OP services	2.48	1.04	<0.0001	0.32	0.19	<0.0001
IP stays	3.21	0.52	<0.0001	0.37	0.08	<0.0001
ER visits	1.52	0.38	<0.0001	0.07	0.02	<0.0001
Urgent care visits	0.05	0.04	0.20	0.00	0.00	0.20

Statistically significant; ALP, Alkaline phosphatase; ER, Emergency room; HCRU, Healthcare resource utilization; IP, Inpatient; OP, Outpatient; PBC, Primary biliary cholangitis; PPPY, Per patient per year; UDCA, Ursodeoxycholic acid; ULN, Upper limit of normal

- The average length of hospital stay ranged from 5.1 days[8] to 88.7 days[9]. An increasing trend in PBC-related hospitalizations was observed over time, with rates increasing from 1.70 to 2.50 per 100,000 persons (2007-2014)
- The mean number of OP claims/visits per patient per year (PPPY) was 2.1 (range 1.9 to 2.2)[10], 1.91 (all-cause)[7], and 0.25 (PBC-related)[7], whereas the mean all-cause emergency department (ED) visits PPPY was 0.91 (all-cause), 0.05 (PBC-related)[7], 0.78 (all patients), 3.33 (patients with ≥1 all-cause ED visits)[11]
- Key cost drivers included inpatient care (n=4 studies), outpatient visits (n=1), liver transplantation (LT; n=3), and medications (n=3). Second-line treatment with obeticholic acid (OCA)/fibrates ± ursodeoxycholic acid (UDCA) incurred the highest total direct cost, followed by untreated (newly diagnosed) and first-line (UDCA). Untreated patients incurred higher inpatient costs, largely due to LT, while in treated patients, medication expenses (OCA/fibrates, UDCA) were the main cost drivers[12] **(Figure 5)**

Figure 5: Key cost drivers of direct costs in PBC patients by [A] line of therapy[12] [B] liver transplantation[13]



PBC, Primary biliary cholangitis; PPPY, Per patient per year

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Disclosures

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