Beyond the health sector: Estimating the societal and fiscal impact of primary biliary cholangitis in the United States

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Conclusions

- People living with primary biliary cholangitis not reaching alkaline phosphatase and total bilirubin normalization (not effectively managed) on first-line ursodeoxycholic acid monotherapy are at higher risk of adverse clinical outcomes and death compared to effectively managed individuals
- This enduring clinical burden leads to elevated healthcare costs and high productivity losses for patients and caregivers, affecting health systems, employers, and public finances
- An effective second-line therapy, leading to timely disease control, could potentially mitigate the burden to individuals and avoid broader economic spillovers.

Plain Language Summary

- This study measured health outcomes, employment, lost work time, and related costs to the US society and government in people living with primary biliary cholangitis and not responding to ursodeoxycholic acid treatment.
- A model followed an individual with primary biliary cholangitis and his caregivers from the age of 45 to 65 years old. Health and economic outcomes were compared to people without the disease.
- The study found that, over 20 years, each person with primary biliary cholangitis (and their caregiver) could cause total economic losses of about $1.06 million to society and $0.67 million to public finances compared to people without the disease.
- Besides high healthcare costs, uncontrolled primary biliary cholangitis causes high economic losses from low work productivity.
- The economic burden is higher for younger patients and grows over time because they lose more work years. Better treatments and earlier disease control may address unmet need and reduce costs for patients, healthcare systems, and society.

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Introduction

- Primary biliary cholangitis (PBC) is a chronic liver disease causing immune-mediated destruction of the small intrahepatic bile ducts, cholestasis, and fibrosis, consequently progressing to cirrhosis, hepatocellular carcinoma, which can progress to liver failure and death.[1]
- PBC prevalence is 18.1 per 100,000 people, being highest in North America and Europe, and predominantly affecting 40- to 60-year-old women.[2]
- Ursodeoxycholic acid (UDCA) remains the first-line therapy, however 30% to 60% of patients on UDCA do not achieve normal alkaline phosphatase (ALP)[3-5], with up to 70% not reaching deep response.[6] Raised ALP and total bilirubin levels are PBC markers that allow determination of the risk for adverse clinical outcomes, including liver transplant and death.[4,5]
- Persistent symptoms, particularly fatigue and pruritus, significantly impair quality of life, social functioning, and disrupt lifetime productivity, leading to important losses to family finances and the broader economy.[7]
- However, the broader economic repercussions for governments and society, including tax revenues and informal care, remain poorly quantified.
- To evaluate the impact of PBC's morbidity and mortality on lifetime patient and caregiver productivity, a simulation model was developed linking PBC health states to work activity.

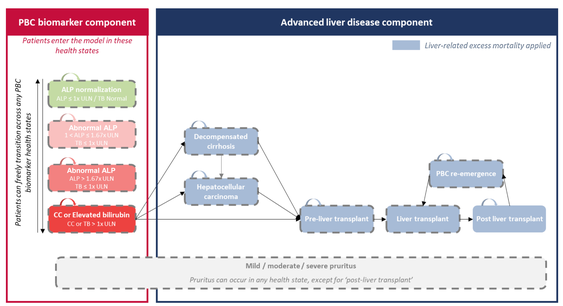
Objective

- To estimate the US societal and fiscal economic consequences associated with PBC's morbidity and mortality in patients with an inadequate response to ursodeoxycholic acid monotherapy, the current first-line treatment, and their informal caregivers, compared to an average individual and informal caregiver unaffected by the disease.

Methods

- **Modeling structure** - The natural history of PBC was modeled from age 45 over a 20-year time horizon using a cohort-level state transition model composed of 10 health states and a death absorbing state (**Figure 1**). The model used a 3-month cycle and 3% discount rate.
- **Clinical inputs** – The baseline distribution and transitions between biomarker health states were based on the RESPONSE trial intention-to-treat population on UDCA monotherapy.[8,9]
- Transitions between advanced liver disease states were informed by the Global/UK PBC cohorts and NICE TA443 data.[10]
- In the PBC biomarker states, death rates were those for the general US population.[11] In the advanced liver disease states, excess mortality was informed by NICE TA443.[10]
- **Healthcare costs** – The analysis considered the costs of UDCA acquisition, pruritus management, background healthcare utilization, and adverse event management, which were sourced from peer-reviewed publications.
- **Effect on productivity** – Published evidence of PBC's impact on labor participation, including employment, disability, absenteeism, presenteeism, and early retirement, was applied to individuals according to health state membership. Pruritus-related productivity losses were captured using the Work Productivity and Activity Impairment questionnaire.
- **Model results** – The impact of PBC was translated into estimates of Societal and Fiscal economic consequences using an established framework.[12-15] Societal productivity burden was valued using lifetime employment earnings and productivity losses (valued in gross domestic product terms) for both patients and informal caregivers. Fiscal outcomes reflected foregone tax revenues due to employment withdrawal and reduced productivity (absenteeism and presenteeism), with additional consideration of productivity losses specific to the public sector labor force. Results were reported in US dollars 2025.

Figure 1. Schematic diagram of the health states transition model structure



ALP, alkaline phosphatase, CC, compensated cirrhosis, PBC, primary biliary cholangitis, TB, total bilirubin, ULN, upper limit of normal.

Results

- People living with PBC and informal caregivers were associated with lower labor participation and productivity, and higher healthcare costs compared to an identical individual and caregiver dyad, unaffected by PBC.
- Over a 20-year period, a person living with PBC managed with UDCA and his or her informal caregiver were associated with 9.9 productive life-years lost, and an excess of 2.6 disability life-years, compared to the general US population. The condition was also associated with157 absenteeism and 1,891 additional presenteeism days (**Table 1**).

Table 1. Excess productivity losses due to PBC in a population managed with UDCA monotherapy compared with the general US population over 20 years

Productivity losses	Person living with PBC	Informal caregiver	Total
Productive life-years	6.1	3.7	9.9
Absenteeism days	90	68	157
Presenteeism days	1,874	18	1,891
Disability life-years	1.3	1.3	2.6
Retirement life-years	0.4	0.4	9.9

Informal caregivers were defined as the opposite sex spouse of the same age as the person affected by PBC.

PBC, primary biliary cholangitis; UDCA, ursodeoxycholic acid.

- Over 20 years, PBC was estimated to originate incremental losses of $1,057,986 (Societal) and $672,546 (Fiscal) per person living with PBC and caregiver, compared to the general population (**Figures 2 and 3**).
- Productivity losses of people living with PBC represented 49.1% of the estimated total burden to Society, and 22.9% of the overall Fiscal burden. Approximately 6.4% of the Societal and 3.9% of the Fiscal consequences related to caregiver productivity losses.
- Fiscally, patient and caregiver incremental tax losses over 20 years ($126,836 and $20,004, respectively) represented the largest share of non-healthcare costs.

Figure 2. Waterfall chart depicting the total fiscal losses per person affected by PBC and managed with UDCA

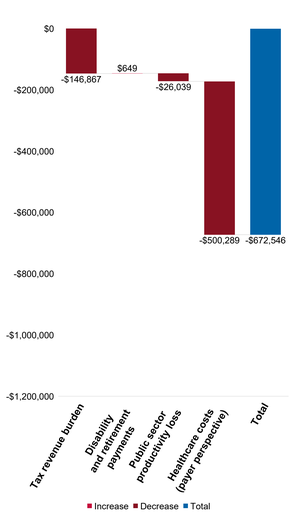
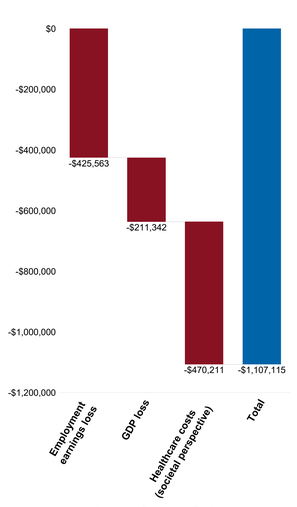


Figure 3. Waterfall chart depicting the total societal losses per person affected by PBC and managed with UDCA



Disability and retirement payments appear as positive values, indicating savings to the government linked to PBC. This reflects a perverse incentive: the state avoids pension payments because PBC-related deaths occur before individuals would otherwise receive these benefits. Negative numbers represent an economic loss to the US government (Fiscal) or US society.

GDP, gross domestic product; PBC, primary biliary cholangitis; UDCA, ursodeoxycholic acid.

- The average societal and fiscal burden per person occupying advanced PBC disease stages, and caregiver, were disaggregated (**Table 2**). We estimate that preventing 1 person from progressing to liver transplant could prevent a minimum of $90,426 in Societal losses and $50,443 from a Fiscal perspective, excluding healthcare costs.

Table 2. Incremental Fiscal and Societal burden of advanced PBC disease states compared to the general US population – Annual values excluding healthcare costs

Health state	Annual burden per person living with PBC	
	Fiscal	Societal
Decompensated cirrhosis	-$7,947	-$20,572
Hepatocellular carcinoma	-$6,633	-$24,073
Pre-liver transplant	-$7,036	-$18,614
Liver transplant	-$34,437	-$41,263
Post-liver transplant	-$8,970	-$30,549
Related to liver transplant	**-$50,443**	**-$90,426**

PBC, primary biliary cholangitis.

- The impact of varying the age at model start and analytical time horizon was examined and depicted in heatmaps (**Figure 4**). The economic burden was higher for younger individuals and for longer time horizons, reflecting the important contribution of productivity losses.

Figure 4. Heat maps of Fiscal and Societal PBC burden by age at model start and time horizon

Negative numbers represent an economic loss to the US government (Fiscal) or US society.

PBC, primary biliary cholangitis; USD, United States dollars.

Discussion

Strengths

- The analysis applies an established macroeconomic and fiscal framework to PBC, extending cost-of-illness beyond healthcare spending to capture tax revenues, transfers, and productivity losses in patients and caregivers.
- By linking biomarker-defined and advanced liver disease health states to labor force participation, absenteeism, presenteeism, and informal care, the model integrates clinical, economic, and occupational data that would be difficult to observe within a single primary study.
- Evaluating both fiscal and societal perspectives over a 20-year horizon highlights that a substantial share of the burden arises from foregone employment and on-the-job productivity losses, rather than healthcare costs alone.

Weaknesses

- In the absence of US-specific evidence for some health state specific productivity parameters, inputs were adapted from international sources, which may not fully reflect US labor market conditions or social protection systems. In addition, some measures of the impact of PBC health states on productivity were not available from PBC studies and were instead sourced from analogous liver disease publications.
- The results of the model are sensitive to the baseline distribution of PBC severity and cohort demographics so extrapolation to different PBC populations or to future treatment landscapes should therefore be made with caution.
- Because the cost estimates were based on a simulation using imperfect data and conservative assumptions, they likely underestimate the true burden of PBC. These findings should be validated against long-term PBC healthcare resource utilization data.