

Economic Burden of Wilson's Disease: A Systematic Review

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INTRODUCTION

- Wilson's disease (WD), or hepatolenticular degeneration, is a rare autosomal recessive disorder of defective copper metabolism in the liver.¹ This disease is attributed to a mutation in the *ATP7B* gene present on chromosome 13, which controls the protein transporter responsible for excreting excess copper into bile and out of the body
- WD affects 1 in 30,000 individuals with indications such as weakness, abdominal pain, jaundice, personality change and seizures
- Treatment consists of heavy metal toxicity medications like copper chelation therapy with penicillamine or trientine, and liver transplant as a surgical approach^{2,3}

OBJECTIVES

- This systematic literature review (SLR) aimed to comprehensively explore the economic burden of WD in terms of healthcare resource utilization and costs

METHODOLOGY

- PubMed® and Embase® were systematically searched, in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines⁴, by pairing relevant keywords to identify English language studies reporting on the economic burden of WD
- The electronic database search was limited to studies published from 2013 to 2023, without any search limit on study country (Table 1)
- Two independent reviewers performed initial screening of title and abstract for each record identified by the electronic databases search. Two reviewers assessed each potentially relevant full-text record. Any uncertainty regarding the inclusion of a record was reconciled by a third reviewer

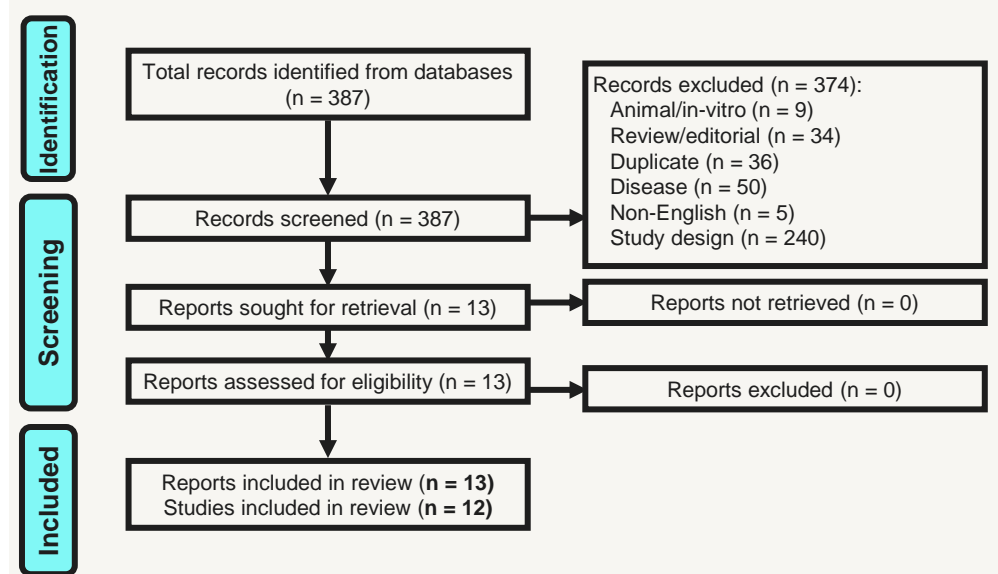
Table 1: Methodology for conducting the economic burden SLR in WD

Population	<ul style="list-style-type: none"> Patients with Wilson disease
Outcomes	<ul style="list-style-type: none"> Direct and indirect cost components Total cost Healthcare resource cost Resource use data Cost and management of treatment-related adverse events Societal costs, cost of carer and productivity losses
Study designs	<ul style="list-style-type: none"> Cost studies Resource use studies Economic evaluations reporting costs or resource use Cost/economic burden studies Budget impact analysis Cost-benefit analysis Cost-consequence analysis Cost-minimization analysis Cost-utility analysis SLR and meta-analysis (for cross referring only)
Intervention and comparator	<ul style="list-style-type: none"> No limits were applied
Database searched	<ul style="list-style-type: none"> MEDLINE® In-Process (using PubMed) Embase® and MEDLINE (Using Embase.com)
Study selection	<ul style="list-style-type: none"> Preliminary selection by two independent reviewers Any discrepancies resolved by a third reviewer
Data collection	<ul style="list-style-type: none"> Data extracted by one reviewer and any discrepancies resolved by second, senior reviewer
Other limits	<ul style="list-style-type: none"> No geographical limits on country were applied Language was limited to English only Publication timeframe was from 2013 to 2023

RESULTS

- Out of the 12 included studies (Figure 1), nine were conducted in the US, while one study each was conducted in France, Germany and South Korea

Figure 1: PRISMA flow diagram



- All the included studies were retrospective in nature and focused on analysing cost or resource use related data

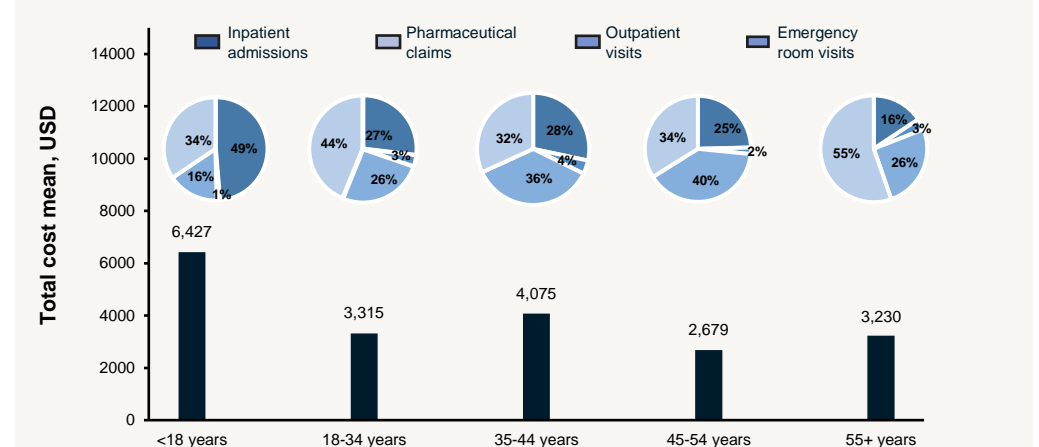
- In the cohorts identified from the Truven Health MarketScan Commercial Claims database (USA), average monthly total health care cost and resource utilization as total number of claims were considerably higher for patients with WD than those with chronic liver disease without WD – i.e. USD 3.89 versus USD 1.98 and 3.35 versus 2.65, respectively, in the year 2020 (Table 2)⁷

Table 2: Monthly average utilization of Wilson disease patients

Monthly average utilization (n = 424)	Mean (standard deviation)	Median (25 th , 75 th percentile)
Total number of claims	3.35 (3.54)	2.33 (1.17, 4.25)
Number of inpatient admissions	0.14 (0.57)	0 (0, 0)
Total length of stay, days	0.13 (0.58)	0 (0, 0)
Number of emergency department visit	0.05 (0.14)	0 (0, 0.08)
Number of outpatient admissions	1.82 (2.39)	1.17 (0.50, 2.25)
Number of pharmaceutical claims	1.34 (1.37)	1 (0.33, 1.92)

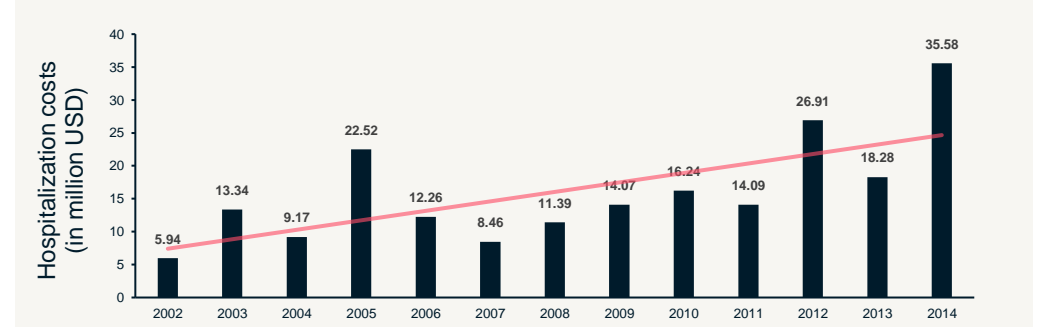
- During 2007–2017, monthly average healthcare cost was higher in patients <18 years of age compared with 18+ age groups, with inpatient admissions cost being major component of the total expense (Figure 2)⁷

Figure 2: Monthly average health care costs by age groups of patients with WD



- The annual cost of hospitalization identified from the National Inpatient Sample consistently increased over time from USD 5.94 million in 2002 to USD 35.58 million in 2014 (Figure 3)¹¹

Figure 3: Annual hospitalization costs for patients with WD (adjusted to 2020 USD)



- Across the included studies, the average length of stay in hospital for patients with WD ranged from 3.8 days due to metabolic reasons to 19.3 days due to liver transplant. Mean length of stay for patients with WD with cirrhosis was significantly higher than for those without cirrhosis (difference 1.7 days; $p < 0.01$)^{9,13}
- In South Korea, mean annual total direct medical cost per person with WD was USD 1,643¹⁷
- Liver transplantation was the major cost driver in Germany, accounting for 44.5% of total annual costs of WD-related hospitalization (EUR 1,336,901) in 2017⁹

LIMITATIONS

- None of the included studies reported indirect costs
- No published health economic models specific to WD were identified
- Most of the included evidence was identified from the US, limiting the generalizability of results

CONCLUSIONS

- Evidence identified in the SLR suggests a substantial economic burden associated with WD
- Liver transplantation and inpatient admissions were the key cost and resource use drivers. Furthermore, comorbid liver disease was associated with increased cost and resource use
- Additional data are required to understand the overall impact of costs associated with the management of WD, with or without comorbidity, from a societal perspective

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