Health economic evaluations of prevention and management strategies for cholangiocarcinoma: a systematic review

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INTRODUCTION

- Cholangiocarcinoma (CCA) is a rare but highly aggressive cancer of the biliary epithelium, with a rising global incidence, especially in regions where liver fluke infection is endemic.
- Surgical resection remains the only potentially curative treatment. However, the clinical and economic burden of CCA is substantial due to delayed detection, limited treatment options, and complex management.
- **Objective:** To summarise the health economic evidence on the prevention and management strategies for CCA.

METHODS

Eligible Criteria

P
- Individuals at risk of developing primary CCA
- Patients who were diagnosed with primary CCA

I
- Prevention and management strategies for CCA

C
- Any relevant comparator

O
- Any economic evaluation outcome

S
- Economic evaluation: cost-benefit, cost-consequence, cost-effectiveness, cost-minimisation, and cost-utility analyses

- **Databases**: EMBASE, MEDLINE, EconLit, iHTA databases and the Tuft CEA registry
- **Search Period**: Inceptus - August 2025
- **Data Extraction**: Summarising key elements of extraction
- **Quality Assessment Tool**: CHEERS 2022 checklist.
- **Data Synthesis Method**: Narrative synthesis summarising findings on the included studies

RESULTS

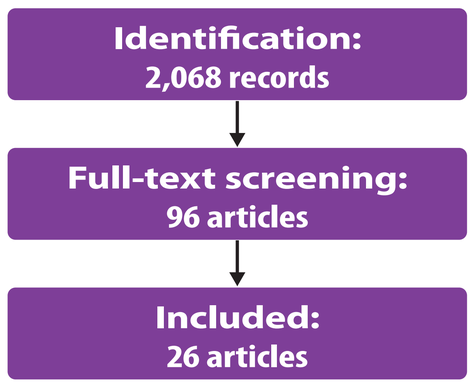


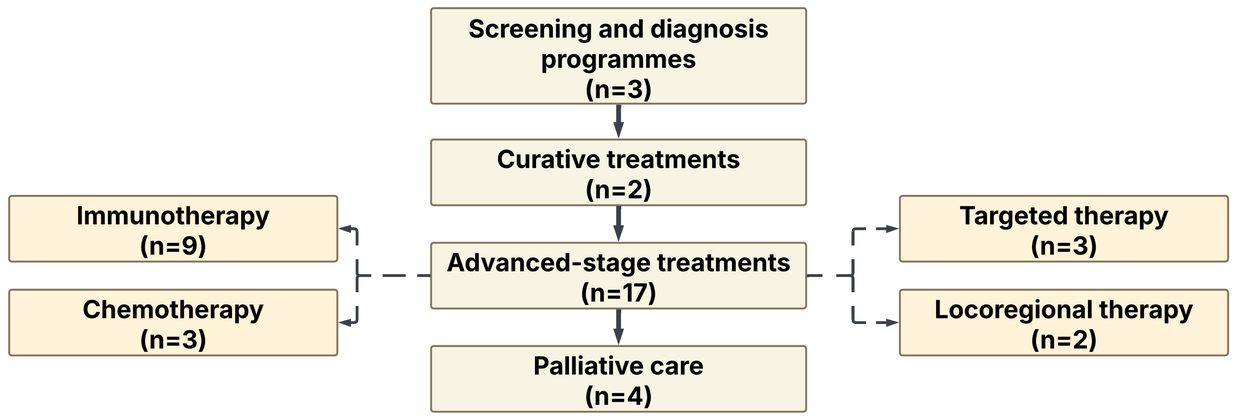
Figure 2. Study Selection Diagram

- Figure 2 outlines the study selection process.
- **Total studies**: 26 economic evaluation studies
- **Publication year:** 2002–2025
  - 16 studies (62%) published in the past three years
- **Countries of study**:
  - **Asia (n=19)**
    - China (n=10)
    - Taiwan (n=4)
    - Thailand (n=3)
    - Japan (n=2)
  - **North America (n=6)**
    - United States (n=6)
  - **Europe (n=1)**
    - United Kingdom (n=1)
  - Five studies conducted parallel evaluations in both China and the United States, allowing comparison of cost-utility results between these two healthcare settings

Methodological Approaches

- **Types of economic evaluation:**
  - Majority were cost-utility analysis (79%)
  - Two studies also included cost-effectiveness analysis, with results reported as cost per life-year gained
- **Study design:**
  - All studies, with the exception of two economic evaluation alongside clinical trials, were model-based evaluations.
- **Modelling approach:**
  - 50% used partitioned survival model.
- **Analytical perspective:**
  - Three studies adopted a societal perspective, while the remaining studies adopted healthcare payer perspective.
- **Time horizon:**
  - 73% adopted lifetime horizon.

Interventions Across Treatment Pathway



- Studies evaluated a wide range of strategies, including screening, surgery, chemotherapy, locoregional therapy, immunotherapy, targeted therapy, and palliative care.
- Most studies focused on advanced-stage CCA, reflecting its late clinical presentation and the emphasis on improving survival outcomes where treatment options remain limited

Screening and Diagnosis Programmes

Data Sources: - Clinical data from clinical trials, meta-analyses, and cohort studies
- Costs from market prices, hospital records, and literature
- Utilities from hepatocellular carcinoma studies

Findings: All interventions proved cost-effective, with evidence emerging mainly in recent years.

Curative Treatments

Data Sources: - Clinical data from randomised controlled trials (RCTs) and hospital databases
- Costs from hospital financial records
- Utilities from colorectal cancer studies

Findings: Preoperative biliary drainage demonstrated favourable cost-effectiveness, while adjuvant chemotherapy was cost-effective only in specific patient subgroups.

Advanced-Stage Treatments

Data Sources: - Clinical data from key RCTs (e.g., ClarIDHy, TOPAZ-1, KEYNOTE series).
- Costs from hospital and national cost databases.
- Utilities from colorectal, hepatocellular, and renal cell carcinoma studies

Findings: Locoregional therapies consistently demonstrated favourable cost-effectiveness across studies. In contrast, targeted therapies and immunotherapies were generally not cost-effective, although durvalumab appeared relatively more cost-effective than pembrolizumab. Evidence for chemotherapy remained inconclusive.

Palliative care

Data Sources: - Clinical data from cohort studies, RCTs, hospital records, and national databases
- Costs from hospital and national databases
- Utilities from CCA patients, and published literature

Findings: Endoscopic biliary drainage using plastic stents was identified as the most cost-effective palliative option, whereas other palliative strategies were not economically favourable.

Challenges in Economic Evaluation of CCA

Scarcity of robust clinical data
- The rarity of the disease has resulted in a limited number of clinical trials.
- Several studies relied on short-term data and small sample sizes.
- Data were often derived from subgroups or single RCTs, limiting their reliability.
- A lack of long-term or real-world evidence hindered the ability to capture lifetime outcomes.

Limited health utility measurements
- Utility values were frequently borrowed from other cancers (e.g., colorectal, hepatocellular, or renal cell carcinoma) rather than measured in the CCA population.

Absence of whole disease pathway modelling
- Existing studies often adopted isolated modelling approaches rather than representing the whole disease pathway.
- Integrated models are needed to estimate health system-wide costs and health benefits, supporting optimal health resource allocation.

Cost-effectiveness of new interventions
- Although immunotherapies and targeted therapies showed clinical promise, They were generally not cost-effective due to high costs and modest survival gains.
- Some studies applied higher willingness-to-pay thresholds (up to three times GDP per capita), but the interventions remained not cost-effective.

CONCLUSION

Only a minority of evaluated interventions were found to be cost-effective, with some showing economic benefits only in specific patient subgroups. However, treatments for advanced-stage CCA were generally not cost-effective, particularly targeted therapies and immunotherapies, due to high costs and limited survival gains. The lack of clinical and utility data remains a major challenge and most studies focused on isolated interventions rather than the entire disease pathway. Considering the whole disease pathway is crucial to capture the complexity of CCA management and better inform healthcare decisions. Improving the quality of primary studies on CCA is also essential to strengthen the evidence base and enhance data reliability.

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