Budget Impact Modelling: A Systematic Literature Review for Non-Small-Cell Lung Cancer (NSCLC) and Adherence to Best Practice Guidelines

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I3LUNG

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AIM

Identify and characterize NSCLC budget impact models (BIMs), assess adherence to best practices, and inform conceptualization of a BIM suitable for evaluating I[3]Lung AI tool.

INTRODUCTION

- Budget impact analysis—i.e., forecasting the expected budgetary implications associated with adopting a new technology—is routinely used by stakeholders to inform coverage decisions and to inform possible budget reallocations.[1,2]
- BIMs must accurately predict future financial impacts and should preferably follow existing best practice recommendations (e.g., provided by the International Society for Pharmacoeconomics and Outcomes Research [ISPOR][3] and leading HTAs[4]).
- Despite being common, BIMs are historically rarely published in peer-reviewed journals, complicating critical assessment of quality and adherence to best practices.
- Recently, economists have found novel ways to assess unpublished evaluations, finding that predictions can differ considerably from reality:
  - A US study found that six 5-year ICER predictions were 36 times higher vs reality.[5]
  - A study of 12 Irish HTA decisions found estimates from -1017% to +72% vs reality.[6]
- I[3]LUNG, a Horizon Europe project, is developing an AI tool that will improve matching of effective and costly immunotherapy-based treatments in NSCLC patients, making it possible to reduce waste and improve patient outcomes.[7]
- I[3]LUNG is conceptualizing a BIM suitable for evaluating this AI tool, which included a literature search for previously published BIMs for NSCLC.

METHODS

- Systematic literature review of BIM studies published for lung cancer since 2010.
  - We did not limit to NSCLC as studies of non-specific lung cancer and SCLC were thought to be useful for informing the general model structure.
- A study plan was created and study results were reported according to 2020 PRISMA Statement.[8]

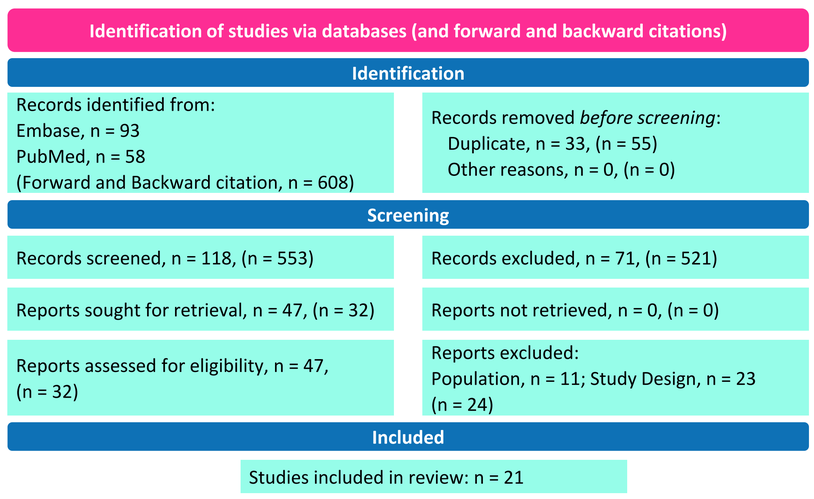
The Search

- Searches conducted in PubMed and EMBASE adopting intentionally inclusive search terms:
  - ***(economic model [Title/Abstract] OR budget impact [Title/Abstract]) AND (NSCLC [Title/Abstract] OR lung cancer [Title/Abstract]) AND (model [Title/Abstract])***
- Forward and backward citation searches were performed on qualifying studies ("snowballing"[9]).
- Review articles were excluded, but reference lists were searched for qualifying studies.
- Study inclusion and exclusion criteria were defined using Patient, Intervention, Comparison, Outcomes, and Study Design (PICOS) framework.[10] Studies were scanned for relevance by two trained health economists (MW and AN).
- Study characteristics, modelling methods, costs supported, data sources, and assumptions about market uptake were extracted.

Analysis

- Each unique BIM was reviewed and summarized
- Quality assessment was performed by assessing adherence to a best practice guidelines checklist from ISPOR Principles of Good Practice.[3]

RESULTS



Search Results

- PubMed and EMBASE searches yielded 151 hits. Thirty-three duplicates were identified and removed, leaving 118 unique publications.
- Eighteen publications were excluded based on title review, 53 publications excluded based on abstract review, and 34 publications excluded based on full-length review.
- Forward and backward reference searches on the 13 qualifying studies yielded 8 additional qualifying studies, yielding a total size of 21 studies.
- All studies described a unique model.

Review of Budget Impact Models

Author (Year)	Country	Perspective	Disease Stage	Intervention	Comparator	Time horizon (years)	Open/Closed Cohort?	Market Uptake?
Carlson et al (2011)[11]	US	Commercial Payer	III-IV	Erlotinib	SoC	1	Closed	Time-varying
Bayle et al (2013)[12]	France	Single payer	NR	Fixed dose nivolumab and pembrolizumab	Flexible dose nivolumab and pembrolizumab	1	Closed	NR
Bajaj et al (2014)[13]	US	Commercial Payer	IIIB or IV	Erlotinib	Chemotherapy	1	Open	90%
Kalluri et al (2015)[14]	Canada	Hospital diagnostic unit perspective	NR	Rapid on-site evaluation	SoC	1	Closed	100%
Hess et al (2016)[15]	US	Commercial Payer, Medicare, Hospital	NR	Ramucirumab + docetaxel	SoC	1	NR	15%
Thongprasert et al (2017)[16]	Thailand	Single payer	NR	Crizotinib	SoC	3	Open	100%
Goldstein et al (2017)[17]	US	Societal perspective	III or IV	Pembrolizumab (Personalized dosing)	Pembrolizumab (Fixed dosing)	1	Closed	35%
Aguiar et al (2017)[18]	Brazil, Argentina, Peru	Single payer	NR	Pembrolizumab	SoC	5	NR	100%
Norum et al (2017)[19]	Norway	Single payer	III or IV	Pembrolizumab	Docetaxel and pemetrexed	NR	Closed	NR
Bly et al (2018)[20]	US	Commercial Payer, Medicare	NR	Necitumumab + gemcitabine + cisplatin	SoC	3	Open	Time-varying
Graham et al (2018)[21]	US	Commercial Payer	NR	Afatinib	gefitinib	5	Open	Time-varying
Signorovitch et al (2019)[22]	US	Commercial Payer	IIIb or IV	Comprehensive genomic profiling	SoC	1	NR	2-10%
Westerink et al (2020)[23]	The Netherlands	Single payer	IIIb or IV	Afatinib	Osimertinib	5	Open	100%
Monirul et al (2020)[24]	France	Single payer	NR	Nivolumab and pembrolizumab (Fixed dose)	Nivolumab and pembrolizumab (Flexible dose)	1	Open	100%
Cheng et al (2020)[25]	Greece	Single payer	IIIb or IV	(1) Plasma test; (2) Combined testing; (3) Reflex testing	Tissue biopsy only	1	NR	NR
Stargardter et al (2021)[26]	US	Commercial Payer	IV	Tepotinib	Capmatinib, crizotinib, and SoC	3	Open	Time-varying
Rachev et al (2021)[27]	Belgium, Slovenia, Austria, Italy	Single payer	Advanced	Anti-PD-1/PD-L1	SoC	5	Closed	11-12%
Patel et al (2021)[28]	Canada	Single payer	IIIb or IV	Comprehensive genomic profiling	SoC	3	Open	Time-varying
Cai et al (2021)[29]	US	Commercial Payer	NR	Capmatinib	SoC	3	Closed	Time-varying
Abraham et al (2022)[30]	US	Commercial Payer	I or II (SCLC)	Trilaciclib	SoC	5	Closed	Time-varying
Duff et al (2022)[31]	US	Commercial Payer	Advanced or metastatic	Pralsetinib	Selpercatinib, cabozantinib, pembrolizumab, and pemetrexed/ carboplatin	3	Open	Time-varying

NR not reported, SCLC small-cell lung cancer, SoC Standard of care, US United States

Overview

- 18 studies modeled NSCLC, 1 modelled SCLC, and 2 modelled lung cancer broadly.
- Most models adopted single payer or commercial payer perspectives.
- 13 different countries were covered with US as most common (52%).

Modelling methods

- 12 studies reported model structure including 5 cost calculator models, 4 decision-tree models, 1 cohort Markov model, and 1 partitioned survival model.
- Time horizons varied between 1 and 5 years (1 year 43%, 3 years 24%, 5 years 24%). One study did not report.
- Ten models adopted the closed cohort approach, 7 adopted the open cohort approach, and 4 did not report.
- There was considerable variability in types of costs that were supported in the models (e.g., limited to drug costs only, inclusion of diagnostic testing, and disease management).

Treatment uptake

- 18 studies evaluated pharmaceutical interventions (8 of which considered immunotherapy-based treatments).
- Five studies assumed complete (100%) market uptake in the first year.
- For eleven studies, market uptake was based on assumption (ranging from 2% to 100%), of which 7 studies presented a range for various alternatives and scenarios and 5 did not report.
- Data sources used for uptake were generally limited to unpublished sources and assumption.

Model Quality

- All studies satisfied (at least crudely) 60% of the ISPOR criteria, with an average adherence of 80% and a maximum of 90%.
- Sensitivity analysis was reported in 18 studies.
- Only one study provided a justification for the time horizon (1 year), stating "this choice seems justified regarding the constant evolution of therapeutic strategies in the treatment of lung cancer".[24]
- Only 1 study reported external validation.[23]

DISCUSSION AND CONCLUSION

- More BIMs than expected were identified; with an increase over time.
- Many BIMs relied on assumptions for key drivers (e.g., market penetration).
- Types of costs included in models varied considerably. All costs relevant from the analytic perspective should be considered.
- Few models considered time-varying market uptake for time horizon stretching longer than 1 year.
- The crude assessment of model quality suggests limited adherence to current guidelines and minor systematic improvement over time.
- We performed a protocol-driven and systematic search, which likely captured most BIMs published in English language. However, BIMs in other languages and unpublished BIMs were overlooked.
- The assessment of quality was based on informal analysis and proportion satisfying ISPOR best practice recommendations.
- The study reflects our interpretation with risk for misunderstanding.

We identified 21 BIMs, promisingly more than expected. Model structures and quality varied considerably. None had complete best practices adherence and none had all the features necessary to perform multi-setting budget impact analysis for the diagnostic I3Lung AI tool.

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