Evaluation of Rejected Reimbursement Decisions in NICE and CADTH Submissions for Non-Small Cell Lung Cancer

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Background

- Lung cancer is the most prevalent cancer in Canada and the third most common in the United Kingdom (UK),^{1,2} with >80% of cases being non-small cell lung cancer (NSCLC).^{3,4}
- Health technology assessment (HTA) agencies such as the National Institute for Health and Care Excellence (NICE) in the UK and Canada's Drug Agency (CDA; previously Canadian Agency for Drugs and Technologies in Health [CADTH]) play critical roles in evaluating new interventions for NSCLC.
- HTA submissions are subject to rigorous review and must demonstrate sufficient evidence of cost-effectiveness to be approved. Each agency applies distinct criteria and thresholds to assess new technologies.
- Despite the considerable burden of NSCLC, many submissions fail to meet HTA criteria, resulting in rejection by NICE and/or CDA.

Objectives



This review examines the reasons for HTA rejection of NSCLC submissions by NICE in the UK, with comparison of HTA decisions between NICE and CDA.

Methods

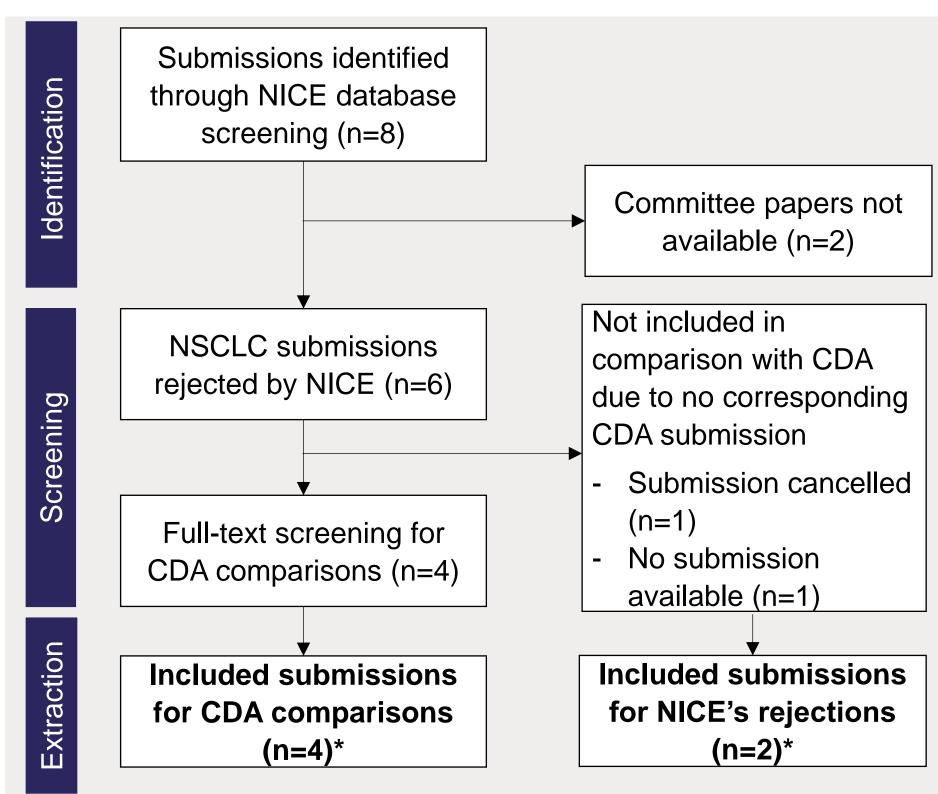
Targeted review

- A targeted review was conducted to identify NSCLC submissions rejected by NICE and the corresponding accepted submissions by CDA between January 2014 and May 2024 (Figure 1).
- Submissions that lacked fully documented committee papers or had been replaced by later resubmissions were excluded from this review.

Data extraction

- Information from included submissions, e.g., summary of the economic evaluations, committee's critiques, and reasons for rejection, were extracted into a pre-defined extraction sheet.
- Reasons for rejection by NICE were categorised and compared with critiques in the CDA submissions.

Figure 1. PRISMA diagram



* The 2 excluded submissions without corresponding CAD submissions were discussed for NICE's rejection reasons only.

Abbreviations: CDA, Canada's Drug Agency; NICE, National Institute for Health and Care Excellence; NSCLC, non-small cell lung cancer; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

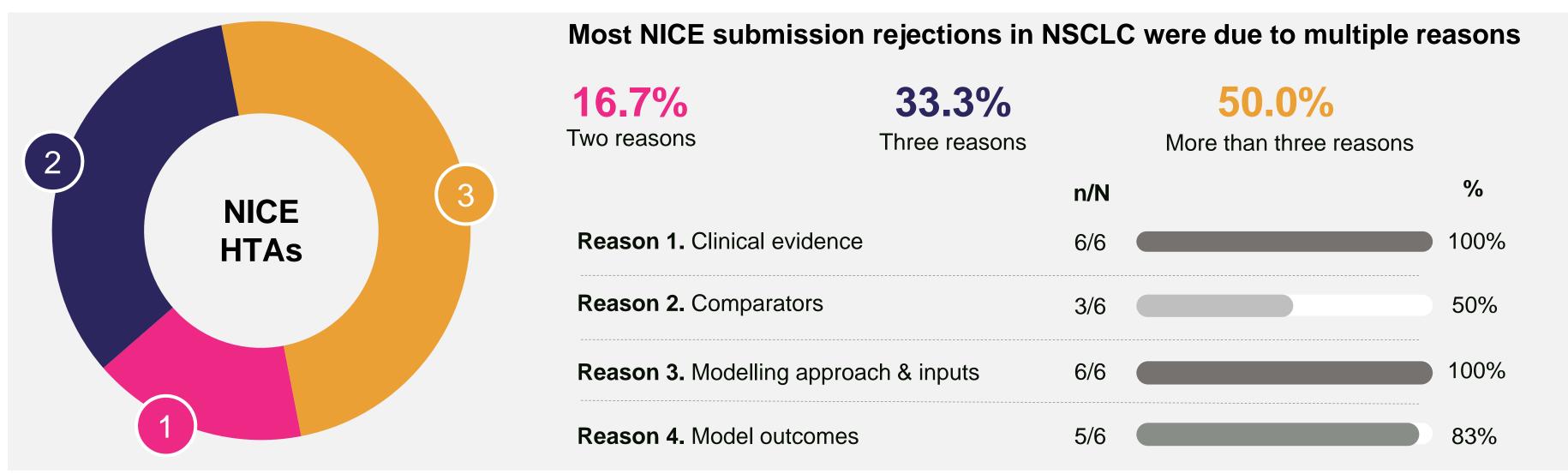
Results

Rejections from NICE

- Six appraisals were identified through the NICE database (TA812,⁵ TA403,⁶ TA411,⁷ TA909,⁸ TA724,⁹ and TA850¹⁰). Two were excluded due to unavailable committee paper (**Figure 1**).
- Reasons for rejection by NICE were: [1] clinical evidence (trial design, population, and immature data), [2] comparators, [3] modelling approach (ITC, survival data and extrapolation, treatment effect, and model structure) and inputs, and [4] model outcomes (**Figure 2**).
- All rejections were due to issues with clinical evidence (4 with trial design issues; 3 of which were single arm).
- Three submissions were criticised for comparators.
- All rejections were due to modelling approach and inputs (3 with substantial uncertainty, and 2 with systematic literature review methodological problems).
- Five rejections were due to model outcomes, primarily due to an incremental cost-effectiveness ratio (ICER) above the acceptable threshold.

Results (continued)

Figure 2. Summary of rejections from NICE



Abbreviations: HTA, health technology assessment; NICE, National Institute for Health and Care Excellence; NSCLC, non-small cell lung cancer.

Comparing decisions from NICE and CDA

- Among the six included NICE submissions, four had corresponding CDA submissions (PC0218-000,¹¹ PC0283-000,¹² PC0289-000,¹³ and PC0249-000¹⁴); one CDA submission was cancelled (PC0078-000,¹⁵ linked to TA403). TA411 had no corresponding CDA submissions.
- All four corresponding CDA submissions were reimbursed with conditions (all with a condition of price reduction).
- NICE tended to be more critical than CDA, especially regarding trial design, modelling approaches, and input assumptions, while CDA often focused more on budget impact.

Figure 3. NICE vs CDA: critiques and comments on the submissions

NICE CDA Clinical evidence Single-arm trial (acceptable) [1] Single-arm trial [3] Immature data [2] Immature data (acceptable) [1] Population not representative of UK practice [1] Uncertainty in long-term benefits [1] Uncertainty around baseline CNS metastases Absence of direct comparison with affecting treatment effects [1] newer-generation TKIs [1] Lack of direct comparison [1] Lack of direct comparative evidence [1] Overestimation of survival [1] Dosing and stopping rules differed from clinical Comparators Trial comparators and subsequent treatments not practice, leading to overestimated costs [1] representative of UK practice [1] No direct comparison with standard NHS drugs [1] ITC included treatments not commonly used as ITC insufficiently robust [1] first-line therapy [1] **Uncertainties: Uncertainties:** Methodological and clinical heterogeneity of the Extrapolations [2] included trials in ITC [1] Modelling PPS and CNS progression [1] Comparative clinical evidence [1] • Utility data [1] Prognostic impact of RET fusion status and ITC (wide Cls) [1] effect on treatment outcomes [1] Appropriateness of using the same survival Uncertainty in OS from lack of comparative curves for all patients [1] evidence [1] Inconsistent approach (RDI calculations) [1] & inputs Bias and limitations in adjusted treatment Lack of appropriate data to inform the link between comparisons with RWD [1] non-CNS and CNS PD health states [1] Implausible choice of PFS extrapolation, Impact of evidence selection issues due to approach overestimating time to progression, and absence of systematic RWE source [1] implementation of subsequent treatment [1] ITC residual confounding and selection bias risk [1] No full incremental analysis [1] High ICER [2] Assumptions: Cost-effective with a price reduction • Treatment effect assumption of 3–5 years (no Reimburse only if cost-effective evidence for longer duration) [1] Inconclusive outcomes (HRQoL, symptoms Platinum-doublet chemotherapy distributions severity) [1] separately applied to subgroup [1] Subsequent treatment rates based on the CheckMate-227, not CheckMate-9LA [1] Utility based on disease progression, not time to death [1] Constant treatment benefit over time is questionable [1] ICERs above acceptable threshold [3] End-of-life criteria not met [1] Cost-effectiveness estimates uncertain [1]

Numbers in square brackets represent number of submissions that were criticized or received comments for the stated reason. Abbreviations: CDA, Canada's Drug Agency; CI, confidence interval; CNS, central nervous system; HRQoL, health-related quality of life; ICER, incremental cost-effectiveness ratio; ITC, indirect treatment comparison; NHS, National Health Service (UK); NICE, National Institute for Health and Care Excellence; OS, overall survival; PD, progressed disease; PFS, progression-free survival; PPS, post-progression survival; RDI, relative dose intensity; RET, rearrangement during transfection; RWD, real-world data; RWE, real-world evidence; TKIs, tyrosine kinase inhibitor; UK, United Kingdom.

Conclusions



- While CDA acknowledged similar issues as NICE regarding clinical evidence and modelling approaches, CDA's consideration of unmet needs and patient values underscored a more flexible approach compared with NICE's stringent requirements.
- A reverse comparison would be helpful to determine if the agencies are consistent in their criteria for rejecting or approving submissions.

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Disclosures

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