Indirect Comparisons of Clinical Effectiveness in NICE HTA Submissions: Software Use Trends, 2000-2022

HTA240

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Introduction

- Indirect comparisons methods such as network meta-analysis (NMA) are frequently used by health technology assessment (HTA) agencies, including the National Institute for Health and Care Excellence (NICE), to indirectly compare technologies' clinical effectiveness and safety.[1-2]
- NICE Decision Support Unit (DSU) Technical Support Documents (TSD) encourage the use of WinBUGS to conduct an NMA[3] and R for population-adjusted indirect comparisons (PAIC).[4]
- WinBUGS has high computational demands and can be challenging due to prescriptive code and limited data manipulation and graphical illustration capabilities.[5-6] Although NICE supports the use of WinBUGS, the frequency of use and the acceptability of specific software packages used in technology appraisal (TA) submissions is unclear.

Aim: To explore software-use trends for indirect comparison analyses within NICE TA submissions between 2000 and 2022.

Methods

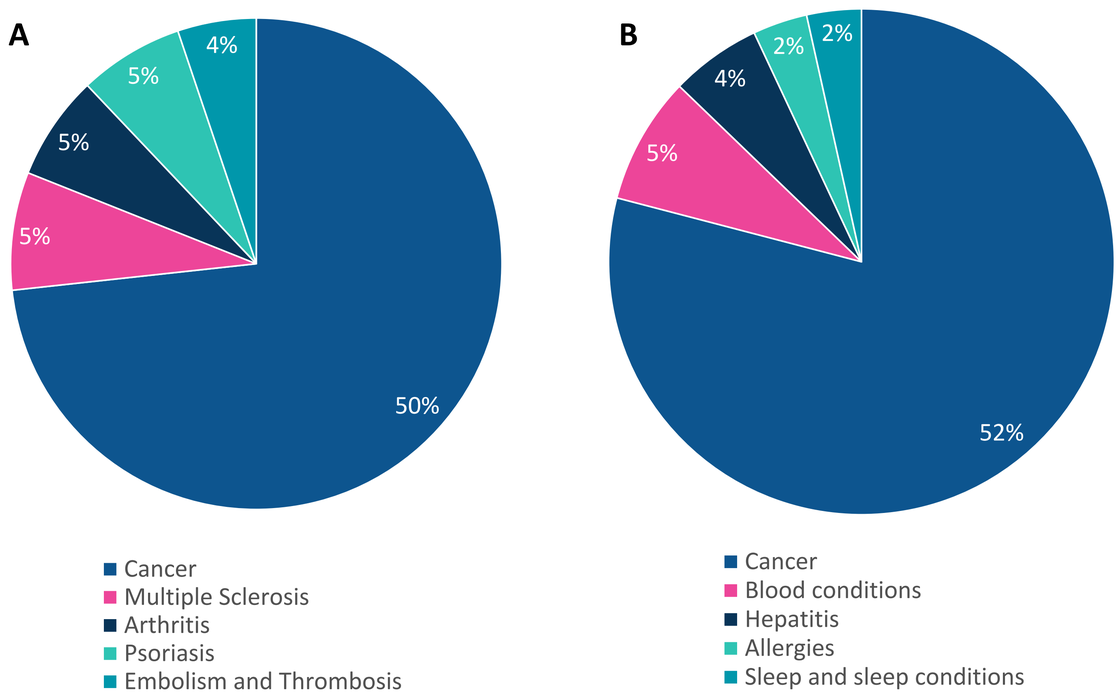
- NICE TA submissions (March 2000-May 2022) that had not been terminated were eligible.[7]
- For each publication year, 50% of TAs were randomly selected for inclusion.
- For each eligible appraisal, one reviewer extracted data from the company submission and EAG critique, and a second reviewer quality checked 25% of the data, considering:
  i. Disease area and NICE recommendation for reimbursement
  ii. Whether an indirect comparison was conducted; if so, type of indirect comparison and software used
  iii. Comments from either the company or the EAG regarding convergence errors
  iv. If a company reported using BUGS software, whether NICE DSU TSD code was used
- If more than one type of indirect comparison was reported within a given TA, all types of indirect comparisons were counted.

Results

Overview

- Of 603 TAs published (N=77 terminated), 299 were assessed. Cancer, including metastases, was the most common disease area reported by approximately 50% of all TAs regardless of an indirect comparison being conducted.
- For TAs that included at least one indirect comparison (**Figure 1A**), approximately 5% reported on multiple sclerosis, arthritis, and psoriasis.
- For TAs that did not include an indirect comparison (**Figure 1B**), 5% reported on blood conditions and 4% on hepatitis.

Figure 1. Five most frequently reported disease areas for TAs (A) included indirect comparisons (N=167), and (B) did not include indirect comparisons (N=132)



Indirect comparisons: analysis summary

- Over half of the TAs assessed reported at least one indirect comparison (167/299; 56%).
- The most common indirect comparisons were NMA and mixed treatment comparisons (NMA/MTC; 115/167; 69%), PAIC (33/167; 20%) and Bucher indirect treatment comparisons (Bucher ITC; 29/167; 17%).
- Of the TAs conducting an NMA/ITC and reporting use of BUGS (WinBUGS or OpenBUGS), one third developed their own code for its use rather than an off-the-shelf code (20/67; 30%).[3]

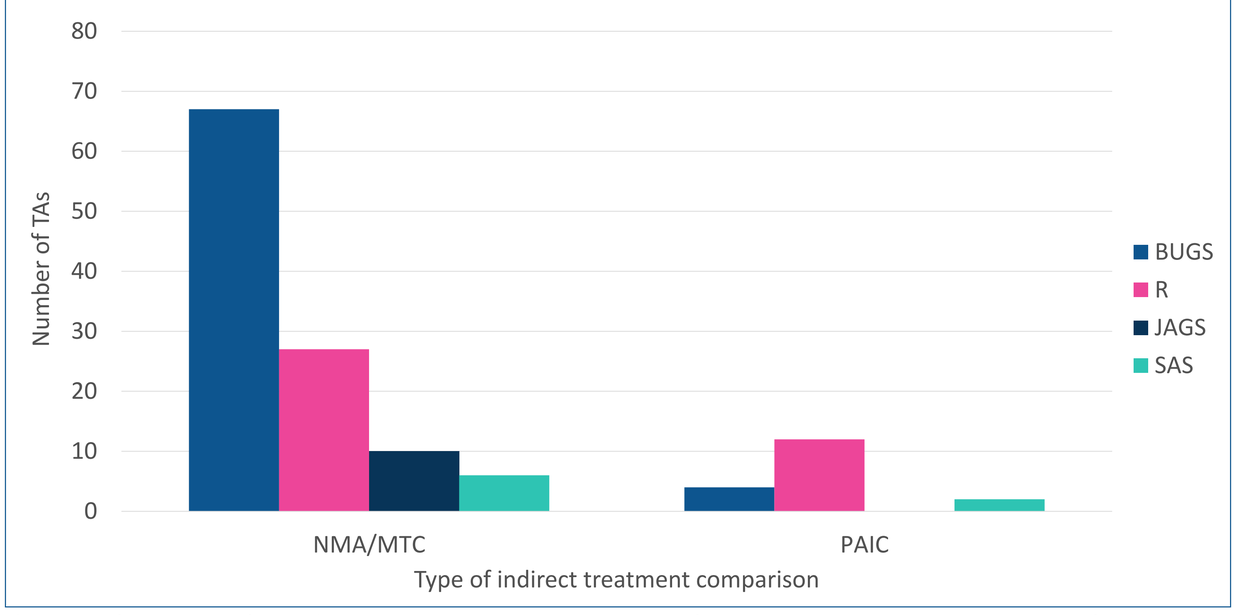
Indirect comparisons: software trends

- Of the TAs that reported at least one indirect comparison, two-thirds reported the software used to conduct the indirect comparisons (110/167; 66%). This included 92 NMA/MTC, 17 PAIC and 11 Bucher ITC.
- For NMA/MTC, most TAs used BUGS software for the analyses (67/92; 73%).
- R was used by almost one third of TAs reporting an NMA/MTC, either as standalone or as an interface for another software (27/92; 29%), whereas JAGS and SAS were used by 11% (10/92) and 7% of TAs (6/92), respectively (**Figure 2**).
- TA718 reported developing two in-house software tools for performing Bayesian NMAs (BATMAN) and frequentist NMAs (CHEETAH).
- Within submissions that included a PAIC, R was the most frequently used software (12/17; 71%), followed by BUGS (4/17; 24%) (**Figure 2**).
- There were temporal trends showing increased use of R and JAGS within TAs since 2015 and 2016, respectively. The use of BUGS has decreased as other software packages have become more frequently used (**Figure 3**).
- When only one software package was used, convergence errors were mentioned in almost one fifth of TAs using BUGS (10/53; 19%) and half of TAs using R (11/22; 52%). For TAs reporting BUGS use only, trap errors were seldom reported (2/53; 4%).

Exploratory analyses: use of software and likelihood of recommendation

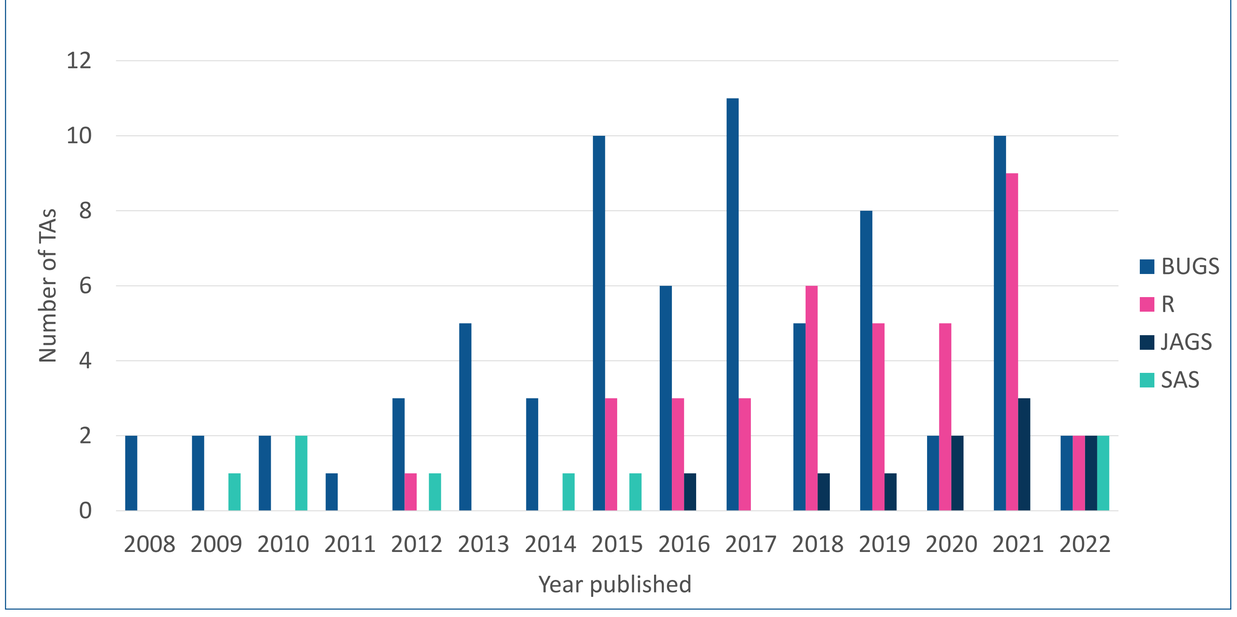
- Exploratory analyses of software choice and likelihood of being recommended for reimbursement were conducted for TAs that reported the choice of either BUGS or R. Eleven TAs used both BUGS and R and were excluded from the analyses (2/11; 18%, not recommended for reimbursement).
- Of 84 TAs, 58 used BUGS and 26 used R. The likelihood of being recommended for reimbursement was similar for TAs using BUGS (53/58; 91%) and R (23/26; 88%).

Figure 2. Software reported within indirect comparisons (NMA/MTC and PAIC)*



* Includes software reported for NMA/MTC and PAIC. Excludes Bucher ITC and types of indirect analyses assessed as unclear. Excludes software included in fewer than three TAs. If more than one analysis but only one software package was reported, the software was counted twice.

Figure 3. Indirect comparison software in NICE HTA submissions (2008 – May 2022)



Opportunities for Further Work

- Incomplete or inconsistent reporting was a common issue. Details on software use, analysis code, and any errors encountered were not always reported within publicly available documents. Additionally, the structure and content of older TAs varied considerably.
- If more than one software package was used to conduct the indirect comparison or more than one indirect comparison was reported, it was not always clear how each software was used.
- Due to time and resource constraints, a subset of eligible submissions was included, and quality checked. Analysis of all published TAs may provide more comprehensive conclusions.

Conclusions

- Over half of NICE TA submissions reviewed included indirect comparisons. The reporting of indirect comparison software use within NICE submissions is inconsistent, with only approximately two thirds including this information within publicly available documents.
- BUGS is the most commonly reported software within submissions, potentially due to its endorsement by NICE DSU and the provision of code that can be directly used in the analyses.
- The likelihood of a TA being accepted was not related to the software used. However, these analyses were limited to BUGS and R due to the small number of TAs including other software.

Key messages: Despite the dominance of BUGS software use, there was an increase in the use of other software such as R, JAGS and SAS in recent years. This demonstrates the diversified use and acceptance of statistical software beyond that recommended by NICE DSU.

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