Comparing the ICERs in Medicine Reimbursement Submissions to NICE and PBAC—Does the Presence of an Explicit Threshold Affect the ICER Proposed?

Shuhong Wang, PhD*, Debra Gum, PhD, Tracy Merlin, PhD

Adelaide Health Technology Assessment, School of Public Health, University of Adelaide, Australia

**ABSTRACT**

**Objectives:** The English National Institute for Health and Care Excellence (NICE) and the Australian Pharmaceutical Benefits Advisory Committee (PBAC) require evidence that a new medicine represents value for money before being publicly funded. NICE has an explicit threshold for cost effectiveness, whereas PBAC does not. We compared the initial incremental cost-effectiveness ratios (ICERs) proposed by manufacturers in matched submissions to each decision-making body, with the aim of exploring the impact of an explicit threshold on these ICERs. **Methods:** Data were extracted from matched submissions from 2005 to 2015. The ICERs in these submissions were compared within each pair and with respect to a cost-effectiveness threshold. **Results:** Fifty-eight pairs of matched submissions were identified. The median difference between the ICERs ($2635/quality-adjusted life year [QALY]) was significantly greater than zero (Wilcoxon signed-rank test, \( P = 0.0299 \)), indicating that the proposed ICERs in the submissions to NICE were higher than those in the matched submissions to PBAC. On 93% of occasions, NICE ICERs were within ~$17,772 to ~$48,422 of the corresponding PBAC ones (Bland-Altman analysis), demonstrating poor agreement. When an implicit threshold of AUD$50,000/QALY was assumed for PBAC decision making, only eight pairs of submissions had discordant ICERs falling above or below the respective threshold. **Conclusions:** The significantly higher ICERs in the submissions to NICE than those to PBAC may be a consequence of NICE’s explicit willingness-to-pay threshold, and/or other health system factors. Industry may be assuming an implicit threshold for PBAC when constructing their ICERs despite the lack of acknowledgement of such a threshold. **Keywords:** incremental cost-effectiveness ratio (ICER), NICE, PBAC, reimbursement, threshold.
threshold has been acknowledged [6,7], although research has indicated that there is a relationship between the incremental cost per QALY gained and the probability of rejection of a medicine [8]. The pharmaceutical industry claims that experience suggests an acceptable threshold is in the range of AUD$45,000 to AUD$60,000 per additional QALY gained [9]. Lowe and Dyson also stated that “PBAC decisions in the past have shown that the ICER is of the order of $50,000” [10].

The lack of standardization in conducting an economic evaluation gives wide scope to parties performing cost-effectiveness analyses [11]. If the producers of the economic models are aware of the existence of a threshold of willingness to pay, they may be able to exploit this information. Thresholds set by public agencies like NICE could incentivize manufacturers to target their economic models to a certain ICER. One of the few existing studies covering this area of research found that ICERs submitted to NICE by manufacturers differ significantly from those submitted by independent academic assessment groups [12]. Walley and Breckenridge claimed that a whole new industry emerged in the United Kingdom, with consulting companies undertaking NICE appraisals on behalf of pharmaceutical companies, guaranteeing to produce a submission with an ICER below NICE’s threshold [13]. This means that the desired favorable result of a submission would be known ex ante and that ICERs would be expected to cluster around the known threshold or predominantly fall below it.

There is growing evidence suggesting that the involvement of industry in cost-effectiveness analyses is more likely to bring about favorable results [12,14,15]. However, so far, there is no published study comparing the ICERS from economic evaluations submitted to funding organizations with and without explicit willingness-to-pay thresholds by the same manufacturers for exactly the same purpose. We aimed to conduct this analysis by comparing paired submissions to NICE and PBAC, to examine whether there is any difference between the paired ICERs in the submissions to these two funding organizations.

**Methods**

In this study, we compared the ICERs in submissions to NICE with those in the matched submissions to PBAC from the same manufacturers, for the same medicines, same clinical indications, same populations, and with the same comparators to examine whether the initial ICERs presented by manufacturers to each of these two funding organizations differed. The context of decision making in these two countries was also explored in an attempt to explain any observed differences in these paired ICERs.

**Functioning of NICE and PBAC Decision Process**

In both England and Australia, manufacturers are required to apply for their medicines to be publicly subsidized. In England, NICE provides guidance to the National Health Service within its program of technology appraisals. When NICE was initially set up in 1999, the evidence and analyses were supplied by both the manufacturer and an academic assessment group. Since introducing a Single Technology Appraisal (STA) process in late 2005 (a process which imitated—to a large extent—the process used by PBAC), the evidence and analyses have been principally provided by the manufacturer [16], and evaluated by an independent evidence review group. In Australia, applications for listing of medicines on the Pharmaceutical Benefits Scheme are independently assessed by PBAC, which then provides advice to the Federal Minister for Health. In both countries, the manufacturer is required to carry out an economic evaluation as part of a submission presented in support of the application. More details of the submission processes are described elsewhere [4,17–20].

**Selection of Submissions/Data Extraction for the Study**

English data were sourced from publicly available NICE technology appraisals from the inception of STA until May 2015. The treatment, clinical indication, population, comparator, manufacturer, submission date, and ICER were extracted from all submissions to NICE over the period of interest. Corresponding Australian data were obtained from confidential commentaries on submissions to PBAC, the advice of PBAC’s Economics Sub-Committee and PBAC meeting minutes. We identified all submissions from the same sponsor for the same medicine, that were evaluated by both NICE and PBAC for the same clinical indication within the same population, and in which the cost effectiveness of the proposed medicine was compared with that of the same existing treatment. We only included submissions in which an ICER was expressed in terms of cost per QALY gained. As we were interested in the behavior of manufacturers in submitting their initial economic evaluation, only submissions in which the manufacturer sought listing of the medicine for the specific indication and population for the first time were included. If the ICER was revised during the evaluation process, the original estimate was used. The extracted data were double-checked by a second researcher and discussed with team members, when necessary.

To ensure comparability of ICERs, the scenario that was most comparable between English and Australian submissions was chosen (i.e., same intervention and comparator, with the same dosage regimen). To ensure that only the original ICERs proposed by the manufacturers were analyzed, resubmissions were only included if the original submission did not present the result in terms of the incremental cost per QALY gained, or if the requested listing in the resubmission was revised and was more consistent with that in the counterpart submission.

**Statistical Analysis**

We compared the ICERs in the submissions to NICE with those in the corresponding submissions to PBAC by analyzing the matched pair data. To enable the comparison, ICERs were converted into international dollars per QALY gained (Int$/QALY) using purchasing power parity (Total) conversion factors reported for the year of submission [21]. We also compared the ICERs in both submissions to NICE and PBAC with NICE’s threshold. The upper and lower limits of NICE’s threshold (£20,000/QALY and £20,000/QALY) were also converted from pound sterling to international dollars using purchasing power parity reported for the respective year of NICE and PBAC submissions. First, we examined the distributions of the ICERs and of the differences between the initial ICER and NICE threshold. Second, we conducted a Wilcoxon signed-rank test for the matched pair data to determine if the proposed ICERs submitted to NICE differed significantly from those in the matched submissions to PBAC. Third, we presented Bland-Altman analyses for the paired submissions to determine the level of agreement between the submitted ICERs. Finally, we tested whether an implicit threshold was affecting submissions to PBAC. We assumed an explicit threshold of £30,000/QALY for NICE (upper limit of the range) and an implicit threshold of AUD$50,000/QALY for PBAC and compared the proportion of the matched English and Australian ICERs above or below the respective threshold (McNemar’s chi-squared test). As NICE’s threshold of £20,000 to £30,000 per QALY gained has remained the same in NICE’s method guidance since 2004 [22], and as it is also debatable whether the threshold should change over time [23], a constant threshold value in pound sterling or in Australian dollars has been used in this study.
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