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Cost-effectiveness of *HLA-B*15:02* screening in Malaysia

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This issue of BJD includes an interesting article considering the cost-effectiveness of *HLA-B*15:02* screening in Malaysia [1]. Adverse drug reactions (ADRs) are a major cause of iatrogenic morbidity, mortality and treatment costs [2,3,4]. Strategies to avoid ADRs, including pharmacogenetic prediction, have clear therapeutic potential. There is strong evidence associating *HLA-B*15:02* with increased susceptibility to severe cutaneous ADRs, including Stevens-Johnson syndrome (SJS) and toxic-epidermal necrolysis (TEN), in patients prescribed carbamazepine. Consequently, the US Food and Drug Administration requires (and the Health Canada Santé Canada recommends) screening prior to initiation of carbamazepine for patients with ancestry from genetically at-risk populations [5].

Economic evaluations of *HLA-B*15:02* screening indicate that routine testing may be cost-effective in Thai and Singaporean populations, however results are sensitive to allele prevalence and choice of comparator [6,7,8]. In this issue, Chong and colleagues present a decision-analytic model to assess the cost-effectiveness of screening for *HLA-B*15:02* in an ethnically diverse population of Malaysian epilepsy patients. The analysis compares realistic strategies of universal carbamazepine initiation without screening (current practice); universal screening for *HLA-B*15:02* with carbamazepine or sodium valproate prescribed depending on test result; and universal prescription of sodium valproate. In cases of treatment failure with sodium valproate, topiramate is assumed as a third line option. The analysis is conducted from a Malaysian societal perspective, and is therefore inclusive of patient and carer out-of-pocket expenses and productivity loss. Results are reported over a lifetime horizon capturing the full effects of SJS/TEN sequelae and the impact of alternative treatments.

The results of the base-case analysis indicate that current practice is both less costly and more effective than either alternative strategy, hence, screening is unlikely to be cost-effective in Malaysia.

This contrasts with previous studies, principally by accounting for the long-term differential impacts of the evaluated antiepileptic drugs on seizure control. This is consistent with other economic evaluations of pharmacogenetics in epilepsy [9] and follows good modelling practice in taking full consideration of downstream costs and effects [10]. Consequently, as sodium valproate is less effective than carbamazepine in achieving seizure remission, unnecessary changes in prescription (e.g. because of false positive test results) will lead to less effective control of epilepsy, and offset the benefits of testing.

The economic model predicts that screening 222 patients will avoid 1 case of SJS/TEN, but at the expense of 3 additional patients having uncontrolled epilepsy. The utility experienced in these 3 patients (0.69) compared to those in remission (0.96) goes some way to counter the gains made through the avoidance of one SJS/TEN event associated with a utility of 0.29.

The authors use a (published) local study to inform the parameter value for mortality (4.2%); significantly lower than is typically quoted for SJS/TEN (15%-50%) [3,4]. It would perhaps have been interesting to see the impact of this parameter on cost-effectiveness, but also highlights that with improved recognition and diagnosis, that survival outcomes can be improved, which should be acknowledged in future economic evaluations.

The findings of this evaluation highlight the importance of carrying out robust, population-specific economic analyses to best inform local evidence-based policy.

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