Cost-effectiveness of targeted and population based screening strategies for multiple endocrine neoplasia type 2B

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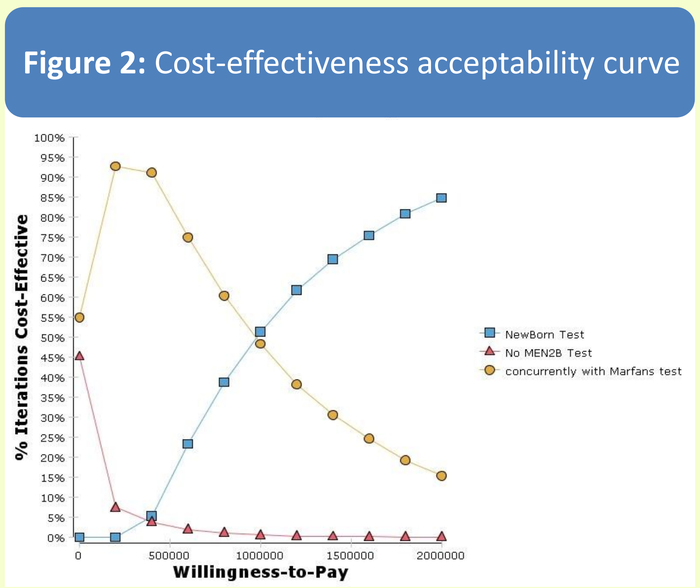
Introduction

Multiple endocrine neoplasia type 2 (MEN2) is an autosomal dominant, inherited disorder resulting in a high lifetime risk of developing medulallary thyroid carcinoma (MTC). The MEN2B subtype has a prevalence of ~1:600,000[1] and is associated with aggressive early onset MTC in children that metastasises early and responds poorly to conventional chemotherapy[2]. In 80% of carriers, MEN2B is associated with a specific phenotype that becomes more obvious with age and includes marfanoid body habitus and joint laxity[3].

Screening for MEN2B is appealing. Firstly, the condition is serious with a well understood natural history; secondly, prophylactic thyroidectomy, if done early enough, is a preventative treatment option for MTC; and finally, there is a reliable screening tests that can detect a causative mutation in 98% of individuals with a MEN2B phenotype.

Figure 2: Cost-effectiveness acceptability curve



Aim

The aim of this study was to evaluate the cost-effectiveness of the following scenarios:

- 1) Current practice – symptomatic diagnostic testing of MEN2B;
- 2) Targeted screening of MEN2B in presymptomatic patients expressing Marfanoid habitus; and
- 3) MEN2B screening as part of the national newborn screening program.

Methods

A decision analytical model was developed to capture the natural progression of MEN2B (Figure 1). The rationale of the model is that MEN2B screening will lead to fewer cases of MTC, which in turn leads to measurable impacts on both mortality and morbidity.

Model parameters were obtained from a literature review or based on expert opinion. The following inputs were used; prevalence of MEN2B (1:600,000); prevalence of Marfans syndrome (1:5000); probability of MEN2B carrier having Marfanoid habitus (75%) and the probability of having a metastatic MTC (95%). The sensitivity and specificity of the initial genetic test was 98% and 99%, respectively. Confirmatory tests were assumed to be 100% sensitive/specific.

Costs: The following costs were used: Newborn screening test ($10), genetic test based on marfanoid habitus ($20), confirmatory test ($400), thyroidectomy ($1,024) and cost of treating late-diagnosed MTC ($100,380). All costs are in Australian dollars (2012)

Utility values: Age-weighted utility values were used in the model. For patient with MTC, 0.54 was applied and patient with hypoparathyrodism, 0.778. (Kebebew et al (2000)).

To verify the robustness of the base case analysis, one-way sensitivity analyses were performed on each parameter within a range that represents plausible high and low values. Probabilistic sensitivity analysis was also conducted. Costs and benefits were discounted at 5%.

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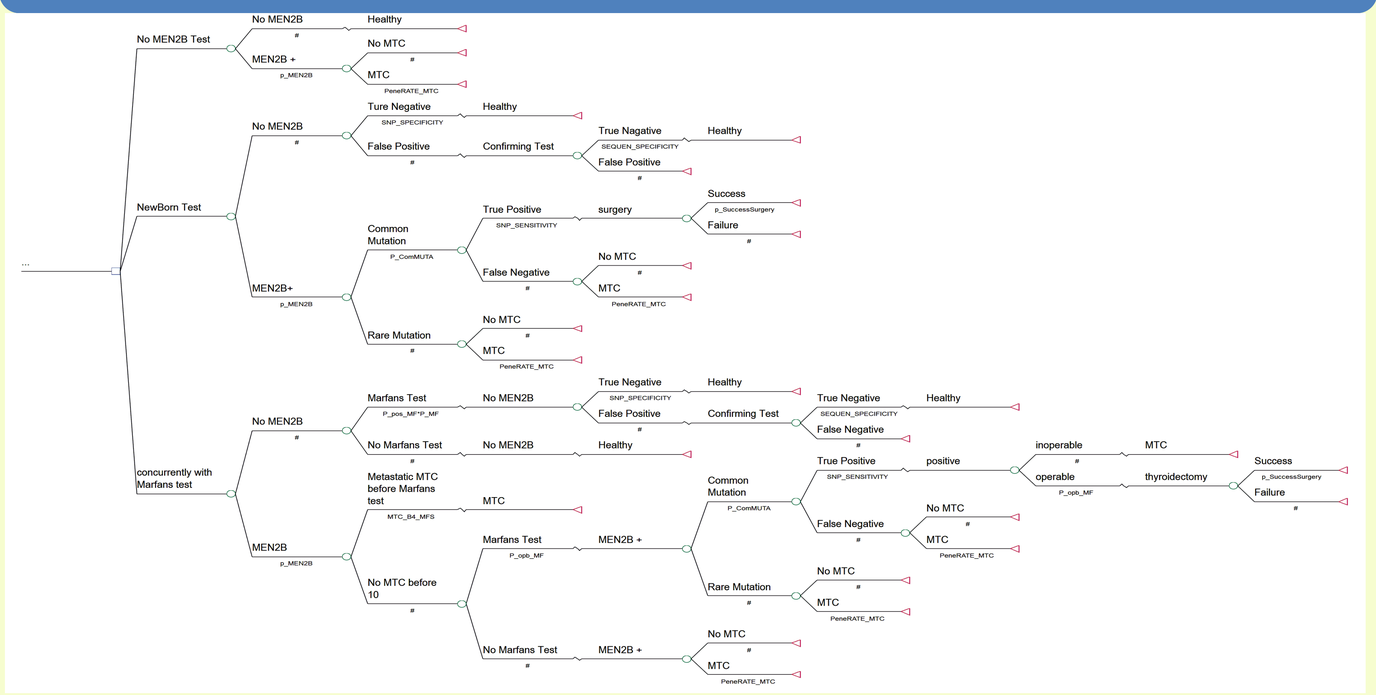
Figure 1: Decision analytical model of the following MEN2B screening strategies; 1) genetic testing all newborn babies, and 2) targeted genetic testing based on marfanoid habitus



Results

The results demonstrate the current practice (no testing) is dominated by targeted screening. This is due to the significant costs associated with treating late-diagnosed MTC. Targeted screening is cheaper than newborn screening, but less effective. The ICER for newborn screening is $1,216,551 per QALY, which is above acceptability in Australia.

The results are most sensitive to the cost of the genetic test (particularly for the newborn screening strategy). The model is also sensitive to the success rate of preventative surgery, the cost of treating late-diagnosed MTC and the prevalence of MEN2B

The cost-effectiveness acceptability curve (figure 2) demonstrates that current practice is always dominated by targeted screening, whilst newborn screening becomes cost-effective beyond a threshold of $1,000,000.

Table 1: Incremental cost-effectiveness

	Mean cost $	Mean QALY	ICER
MFS testing	$0.07	20.608659	0
Newborn testing	$14.01	20.608671	$1,216,551
Current practice	$0.08	20.608658	Dominated

Implications

This study provides the first comprehensive cost-effectiveness analysis for MEN2B testing. Interesting targeted MEN2B testing, based on physical characteristics, yields better outcomes at lower costs than current clinical management.

The Newborn Screening Policy in Australia[4] recommends that a condition should be included, provided that: there is benefit for the individual from early diagnosis; this benefit is reasonably balanced against financial and other costs; there is a reliable screening test available; and there is a suitable system in place to deal with diagnostic testing, counselling, treatment and follow-up of patients identified by the test. MEN2B Newborn testing fulfils many of these criteria, however at present this option is not cost-effectiveness.

References

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