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### Maximising returns

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# **Maximising returns: combining newborn screening with gene therapy for spinal muscular atrophy**

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*Summary sentence: Newborn screening has clinical and economic benefits when combined with gene therapies treating SMA.*

Few would argue that the recent series of breakthroughs successfully delivering effective SMN protein-restoring gene therapy to patients with Spinal Muscular Atrophy (SMA) represents a milestone achievement in the field of neuromuscular diseases. The approval of nusinersen (Spinraza), onasemnogene abeparvovec (Zolgensma) and risdiplam (Evrysdi) by regulatory agencies has, for the first time, provided genuine disease-modifying therapeutic options<sup>1,2</sup>. Whilst these therapies fall short of a cure, the benefits delivered far exceed what was realistically predicted and hoped for, both in terms of patient survival and achievement of major motor milestones<sup>2-4</sup>.

Understandably, significant efforts have been made by SMA patient organisations and charities to ensure rapid access to SMN-restoring therapies for as many patients as possible. However, access to these therapies has become a highly-charged societal and political debate, largely due to high list prices: onasemnogene abeparvovec has a list price of \$2.1 million per single dose, and nusinersen costs \$750,000 for the first year of treatment alone<sup>2</sup>. Whilst there have been notable successes with negotiating discounted prices by many health care providers, it is clear that cost remains a considerable issue with regards to providing access. Therefore, strategies that can either reduce costs, and/or maximise therapeutic benefits, are urgently being sought.

Extensive pre-clinical work, alongside emerging data from clinical trials, indicate that early treatment delivery has a significant impact on the efficacy of SMN-restoring therapies<sup>2,4</sup>. Thus, implementation of newborn screening (NBS), facilitating pre-symptomatic treatment, could have a major impact on the effectiveness and economic viability of SMA therapies. In this

issue, Shih et al.<sup>5</sup> report important new real-world data suggesting that NBS coupled with gene therapy improves the quality and length of life for SMA patients, whilst also delivering significant cost savings.

Shih and colleagues<sup>5</sup> took advantage of an Australian state-wide NBS programme for SMA, allowing them to estimate financial costs and also quality-adjusted life-years (QALYs). By accessing this unique and important dataset, Shih and colleagues demonstrated that the cost of combined NBS and early gene therapy would be less than \$50,000 per QALY. This represents a cost per QALY that falls well within the willingness-to-pay thresholds (of between \$50,000 per QALY to \$500,000 per QALY) suggested by the Institute for Clinical and Economic Review<sup>1</sup>, providing strong evidence to support clinical- and cost-effectiveness for NBS.

However, it should be noted that these findings<sup>5</sup> are geographically-restricted, and may not reflect the situation outside of Australia. Given the widespread introduction of NBS programmes for SMA in the USA over the last few years, comparable data from a different geographical and healthcare setting will likely soon be forthcoming. Moreover, the clinical landscape for SMA is already shifting towards a second generation of therapies, where SMN+ approaches are being developed<sup>2,4</sup>. Resulting competition in the SMA ‘marketplace’ will hopefully serve to reduce list prices and increase access for the wider patient population. The findings of Shih and colleagues<sup>5</sup> suggest that NBS, and therefore early pre-symptomatic treatment of SMA patients, has a key role to play in this future landscape, from both clinical and financial perspectives.

## **CONFLICT OF INTEREST STATEMENT**

The author has served on SMA advisory boards for Roche.

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