EE648

Systematic review of the cost effectiveness of newborn screening for spinal muscular atrophy

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Background

Spinal muscular atrophy (SMA) is a rare condition which causes irreversible damage to motor nerves, leading to muscle wasting/weakness. Recently, drugs have been developed which may modify the clinical course of SMA, with evidence that earlier treatment may improve patient outcomes. These include: nusinersen (Spinraza®), onasemnogene abeparvovec ((OA) Zolgensma®) and risdiplam (Evrysdi®). OA is a gene therapy which acts to replace the missing or non-functional survival motor neuron 1 (*SMN1*) gene. It is administered as a one-off treatment. Both nusinersen and risdiplam act to enhance the production of SMN protein from the *SMN2* gene, and are believed to require lifelong maintenance treatment.

This systematic review aimed to identify and appraise the literature on the cost effectiveness of newborn screening for SMA, compared to diagnosis through clinical symptoms or family history.

Methods

A systematic literature search was undertaken from inception to 31 January 2023, using Medline, Embase, the Cochrane library and grey literature sources to identify economic evaluations of population-based screening versus no organised screening. Citations were independently reviewed by two reviewers according to pre-defined criteria (**Table 1**). Data extraction and quality appraisal were completed in duplicate.

To facilitate comparison, costs were converted to 2021 Irish Euro. The CHEC-list and ISPOR questionnaire were used to assess methodological quality and transferability of the economic evaluations, respectively. The reporting adhered to Preferred Reporting Items for Systematic Reviews and Meta-Analyses criteria.

Table 1 Inclusion criteria

Population	Newborns
Intervention	Population-based newborn bloodspot screening for SMA
Comparator	No population-based newborn bloodspot screening for SMA (Identification based on standard care)
Outcome	ICER (for example, per life-year gained or quality-adjusted life-year) or NMB
Study design	Full economic evaluations: • Cost-utility analysis • Cost-effectiveness analysis • Cost-benefit analysis.

Key: ICER – incremental cost-effectiveness ratio; NMB - net monetary benefit.

Results

Five studies met the inclusion criteria: four cost-utility analyses (CUA) and one cost-effectiveness analysis.

Considering willingness-to-pay thresholds of €20,000 to €45,000 per quality-adjusted life year (QALY) gained, results from two CUAs suggested that screening would be cost saving, results from one CUA suggested incremental cost-effectiveness ratios (ICERs) in excess of €213,000 per QALY gained, and the final CUA presented two scenarios in which results ranged from screening being cost saving to an ICER of €307,746 per QALY gained (**Figure 1**).

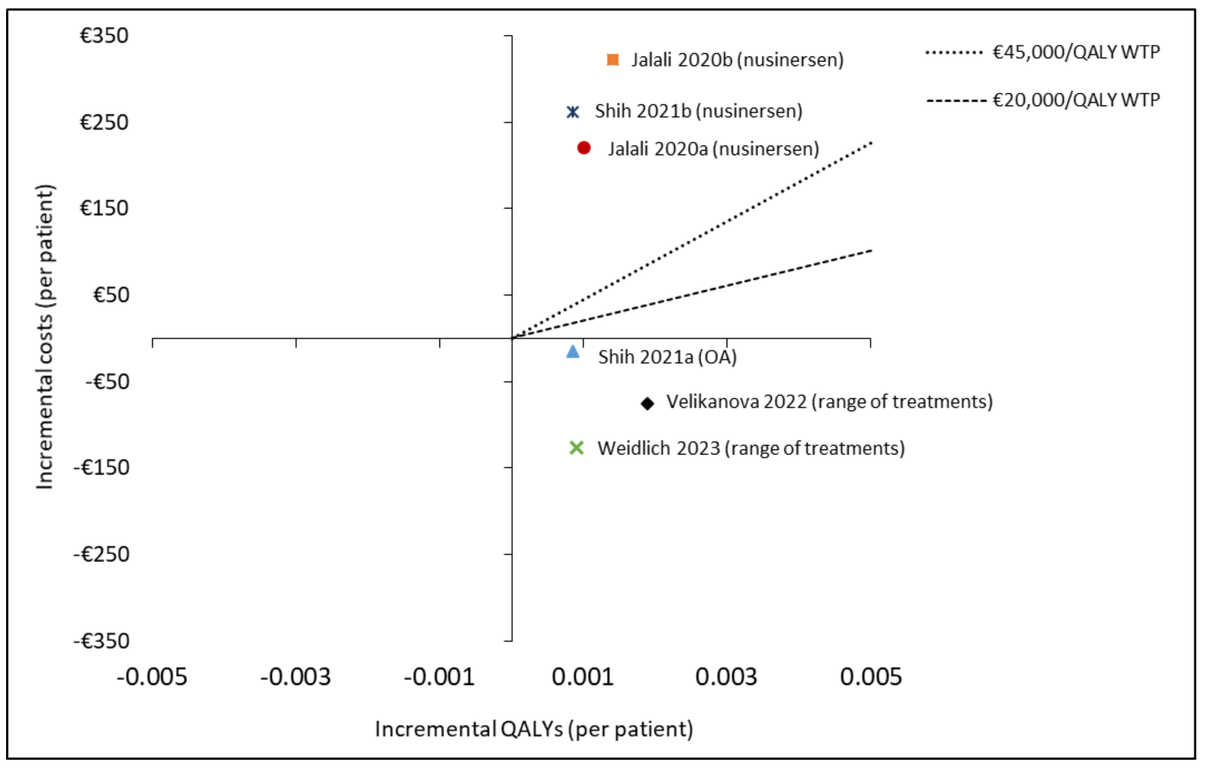
Results were highly sensitive to assumptions regarding the cost of the treatment strategy, and sensitive to a lesser extent to resource use, utility values and incidence of SMA.

In general, studies were considered to be of low to moderate quality largely due to limitations in the evidence base and inadequate reporting (**Figure 2**).

Conflicts of interest arising from relationships with pharmaceutical companies were reported in three out of the five included studies.

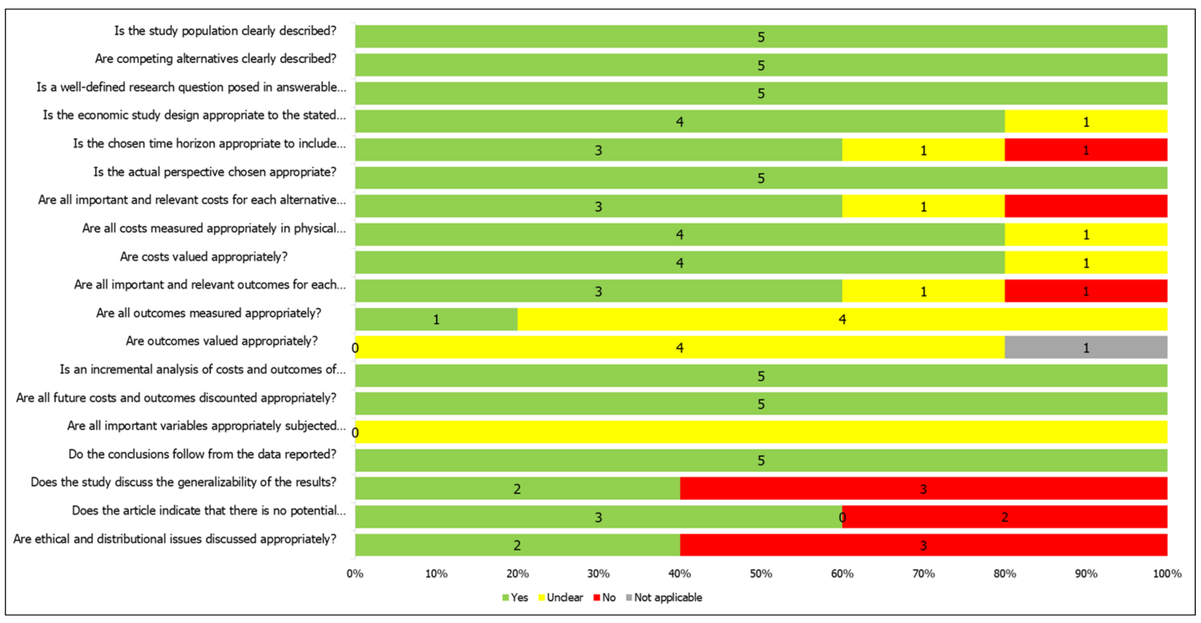
The transferability of the results of included analyses to other jurisdictions is highly dependent on factors such as local reimbursement prices and clinical care pathways.

Figure 1 ICERs presented on a cost-effectiveness plane



Key: ICERs - incremental cost-effectiveness ratios; OA - onasemnogene abeparvovec; QALY – quality-adjusted life year; WTP – willingness-to-pay.

Figure 2 Methodological quality assessment of economic evaluations using CHEC-list



Key findings

Published economic evaluations adopted diverse approaches to estimating the cost effectiveness of newborn screening for SMA, relative to clinical presentation, leading to heterogeneous results. The available evidence suggests that the cost effectiveness of newborn bloodspot screening for SMA is highly dependent on the choice of disease-modifying treatment following a positive screening test result.

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