Consolidating Methods of Cost-utility Analysis for Newborn Screening of Spinal Muscular Atrophy: A Systematic Review

Yewon Jang[1], Ahyoung Kim[1], Hankil Lee[1*]

[1] College of Pharmacy, Ajou University, South Korea

(Presenting Author: jyw1130@ajou.ac.kr), *(Corresponding Author: hankil@ajou.ac.kr)

BAPEL since 2021

KEYWORDS: Spinal Muscular Atrophy, Rare Disease, Newborn Screening, Cost-utility Analysis, Systematic Review

BACKGROUND

What is Spinal Muscular Atrophy(SMA)?

Spinal muscular atrophy (SMA) is a **rare and fatal genetic disorder** affecting 1 of 6,000-10,000 birth. Symptoms of SMA include progressive muscle degeneration which leads to respiratory failure and death. SMA is diagnosed by genetic testing of the SMN1/2 genes.

Why is Newborn Screening essential?

Early detection of SMA through newborn screening (NBS) is essential for pre-symptomatic treatmen. **Earlier treatment leads to more effective treatment which ultimately leads to saving costs** involved with the disease.

Importance of Conducting a Cost-Utility Analysis

The gene therapies available for SMA – Nusinersen, Onasemnogene abeparvovec, Risdiplam – are effective but expensive. NBS can save healthcare costs by enabling early diagnosis and treatment. A cost-utility analysis (CUA) of NBS for SMA assesses the economic benefits of gene therapies, supporting better policy decisions.

OBJECTIVES

We aimed to *summarize the methods and data resources of CUA of NBS for SMA* by systematically reviewing the related studies.

METHODS

LITERATURE SEARCH

- Database: PubMed, Embase, Cochrane Library databases
- Date: March 20th 2024.
- Inclusion/ Exclusion criteria**(TABLE 1)**: Relevant studies were selected based on pre-defined criteria. The screening process adhered to the PRISMA[1)] guidelines.

TABLE 1. Inclusion / Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
- Study intervention on newborn screening	- Study intervention not on newborn screening
- Study intervention on spinal muscular atrophy	- Study intervention not on spinal muscular atrophy
- Cost-effectiveness study	- Not a cost-effectiveness study

DATA EXTRACTION

- Author, published year, country, treatment, comparator, modeling approach, health states, perspective, efficacy data, utility and cost.

RISK OF BIAS

- Assessment tool: 2022 CHEERS[2)] checklist.

1) Preferred Reporting Items for Systematic reviews and Meta-Analyses
2) Consolidated Health Economic Evaluation Reporting Standards

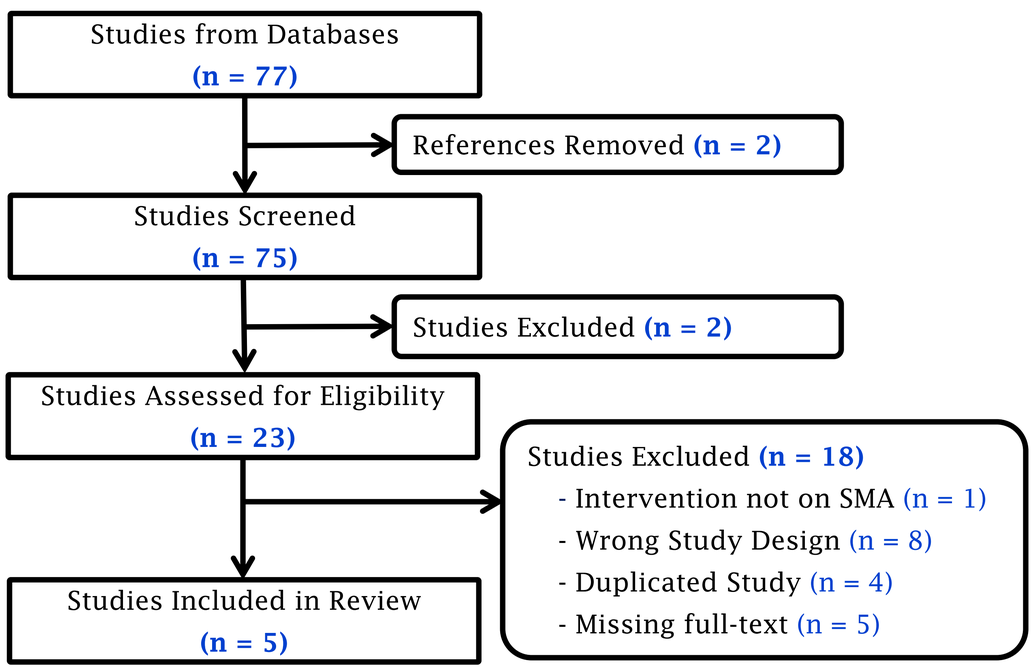

FIGURE 1. Flow chart of study inclusion

RESULTS

LITERATURE SEARCH **(FIGURE 1)**

- Among the 75 studies screened, **five CUA** studies were ultimately included.

DATA EXTRACTION **(TABLE 2, 3)**

Study Characteristics

- Each study was conducted in a **different country** and published after 2020.

Treatment

- All studies included treatments for SMA after diagnosis. Treatments included in the study depended on the timing of their approvals.

Modeling Approach

- Three studies employed **decision tree plus Markov model**, while two studies utilized **Markov model**. Decision tree was designed to capture the initial NBS outcomes, Markov model was designed to project health outcomes and cost.
- The key common health states were permanent ventilation, not sitting, sitting, walking and death.

Data Resources

- Efficacy data of treatments derived **mostly from clinical trials** of each treatment and only one study had used real-world data from observational study in Belgium between 2018-2022.
- Costs were sourced from list price, local studies, literature or direct calculation from questionnaires or pilot NBS program.

RISK OF BIAS

- The reporting quality of studies is **valid from 82% to 93%** (median 86%).

TABLE 2. Study Characteristics

Study No.	Author (Year)	Country	Treatment	Comparator
1	Jalali (2020)	United States	Nusinersen	No treatment/No NBS Vs NBS/No treatment Vs Treatment/No NBS Vs Treatment/NBS
2	Shih (2021)	Austrailia	Nusinersen, Onasemnogene abeparvovec	
3	Velikanova (2022)	Netherlands	Nusinersen, Onasemnogene abeparvovec	NBS vs No NBS
4	Weidlich (2023)	England	Nusinersen, Onasemnogene abeparvovec, Risdiplam	
5	Dangouloff (2024)	Belgium	Nusinersen, Onasemnogene abeparvovec, Risdiplam	

TABLE 3. Model & Data input resources

Study No.	Modeling Approach	Perspective	Time Horizon	Efficacy	Utility	Cost
1	Markov	Societal	30 months	RCT	Literature	Literature, CPT codes
2	Decision Tree + Markov	Societal	5 and 60 years	RCT	Literature	Pilot NBS program, Local study
3	Decision Tree + Markov	Payer	Lifetime (100 years)	RCT	Literature	Local study, Literature
4	Decision Tree + Markov	Payer	Lifetime (100 years)	RCT (short-term), Literature (long-term)	Literature	Local study, List price
5	Markov	Payer	Lifetime	Real-World Data	Measured with 'Health Utilities Index 2'	Questionnaire (patients or caregivers)

DISCUSSION

- For 4 out of 5 studies derived treatment efficacy from RCTs, while the most recent study utilized real-world data suggesting that **data on SMA patients undergoing gene-therapy has accumulated.**
- Five CUAs were conducted across different countries, with significant difference in cost input resources between studies. This emphasizes the **importance of developing country-specific CUAs.**

CONCLUSIONS

- This review aids in structuring cost-utility analysis to fit specific national contexts and the findings from this study can provide reliable data inputs for future cost-utility analysis studies evaluating newborn screening for SMA

CONFLICT OF INTEREST

All authors declare that they have no conflicts of interest.

ACKNOWLEDGEMENT

This work was supported by the National Research Foundation of Korea(NRF) grant funded by the Korea government(No.RS-2023-00276504).