



Cost-Effectiveness of Targeted Newborn Screening for Congenital Cytomegalovirus Infection in Japan

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INTRODUCTION

Congenital Cytomegalovirus Infection

- Congenital cytomegalovirus (cCMV) infection is a leading cause of childhood hearing loss and developmental disabilities.
- 10-15% of infected infants are symptomatic at birth [1].
- Sensorineural hearing loss affects 25-40% of symptomatic infants [1].

Discussion of Expanding Newborn Screening Program in Japan

- In Japan, the infection rate is approximately 0.31% among newborns [1].
- The inclusion of cCMV in newborn screening (NBS) programs warrants consideration due to:
 - Recent Japanese Developments:
 - Insurance coverage for cCMV testing (since 2018)
 - Valganciclovir approval for treatment of symptomatic cCMV infection (2023)
 - Economic Considerations:
 - Cost-effectiveness is crucial for NBS program inclusion [2]
 - Economic evaluation alongside clinical benefits guides policy decisions

OBJECTIVE

To evaluate the cost-effectiveness of targeted cCMV screening (for infants failing hearing screening tests) compared to no screening within the Japanese healthcare system.

METHOD

Model Design

- This cost-effectiveness analysis employs a decision tree combined with a Markov model using TreeAge Pro Healthcare to compare targeted newborn screening with the current practice of no screening.
- The model simulates lifetime clinical progression through health states including normal hearing, varying degrees of hearing loss (HL), cochlear implant status, and death.

Screening Program Structure

- The targeted screening pathway begins with universal newborn hearing screening, followed by auditory brainstem response (ABR) testing for those who fail initial screening.
- Infants requiring further evaluation undergo urine PCR testing for CMV within 21 days of birth.
- Those with confirmed cCMV infection receive medical evaluation, baseline investigations, and regular audiologic monitoring according to standardized protocols.
- Treatment with valganciclovir is initiated within 2 months of age and the treatment duration is set at 6 months.

Cost Assessment

- Costs are analyzed from the Japanese healthcare payer's perspective, incorporating direct medical costs such as screening tests, medical evaluations, valganciclovir treatment, follow-up care, and hearing devices.
- The calculation of direct medical costs is based on the JMDC Claims Database.

Outcome Measures and Analysis Parameters

- The primary health outcome measure is Quality-adjusted life years (QALYs), with particular focus on hearing-related outcomes including prevention of HL and improvements from early intervention.
- The analysis uses a lifetime horizon of 84 years with an annual discount rate of 2% for both costs and outcomes.
- Cost-effectiveness is evaluated against Japan's willingness-to-pay threshold of JPY 5 million per QALY gained.
- Sensitivity analyses are conducted to test the robustness of results under varying assumptions.

RESULTS

Parameters and Model

- The constructed model is shown in Fig 1 and 2.
- Some input parameters are showed in Table 1.

Base Case Analysis

- The targeted NBS program is both less costly and more effective than no screening (Table 2).

➤ The targeted NBS is dominant strategy

One-Way Sensitivity Analysis

- Tornado diagram is showed top 5 with large fluctuation ranges in several independent variables (Fig 3).

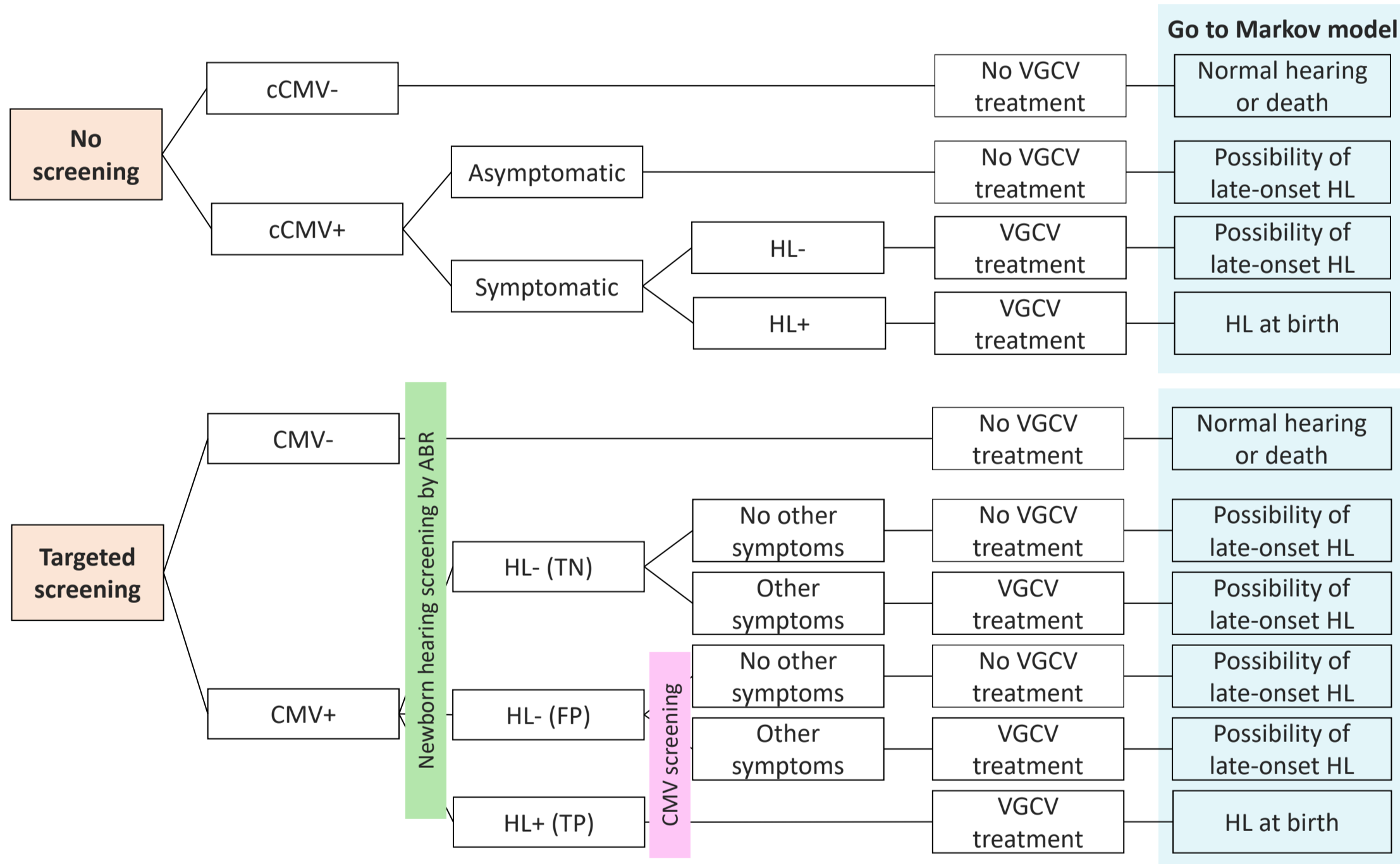


Fig 1. Decision tree model

Table 2. Result of Base Case Analysis

Strategy	Cost, USD	Incremental Costs, USD	Effectiveness, QALYs	Incremental Effectiveness, QALYs	ICER, USD per QALY gained
No Screening	21.67		39.5582		
Targeted Screening	5.05	-16.62	39.5626	0.004407	-3,771.49 (JPY -565,724)

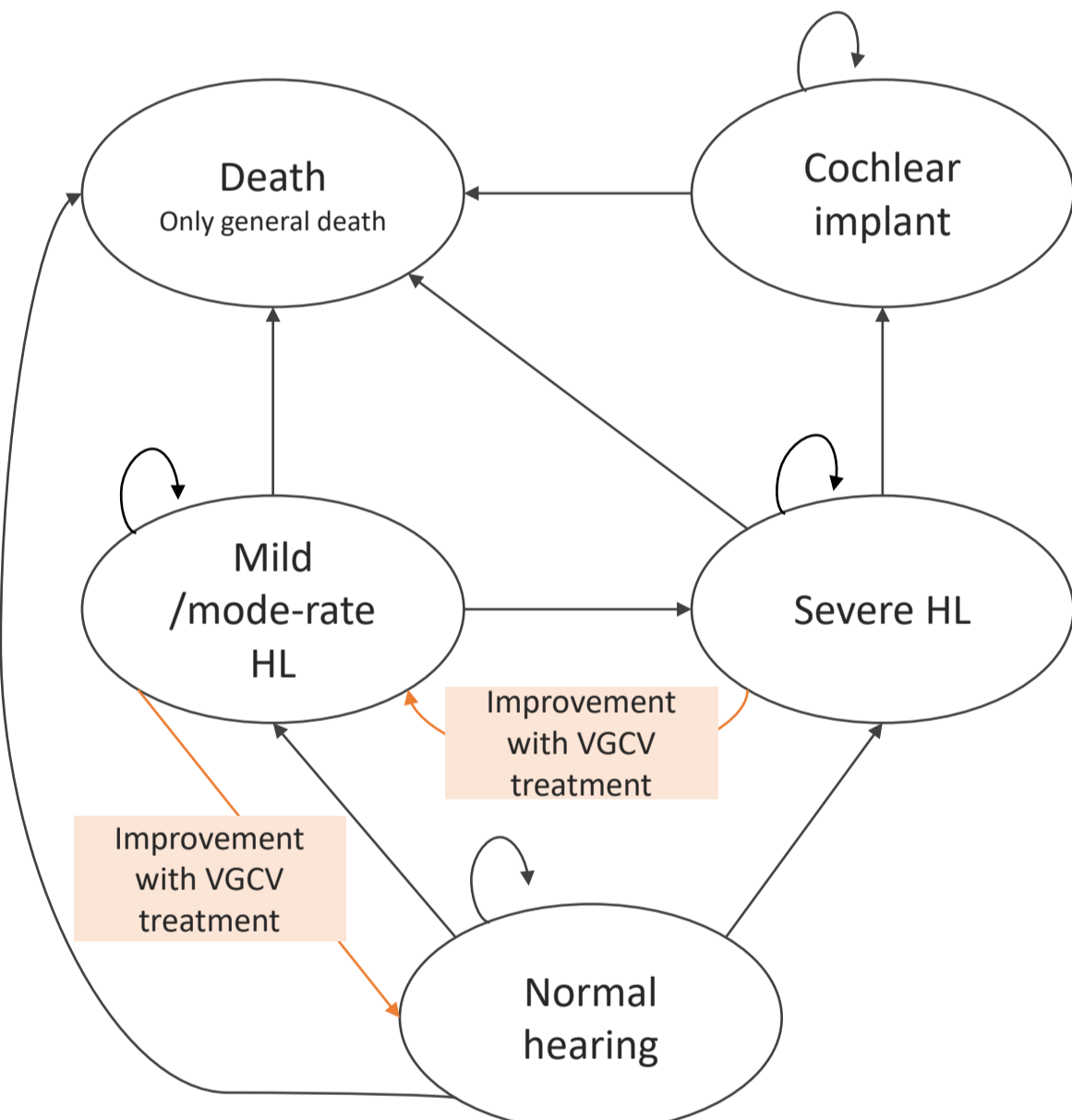


Fig 2. Markov model

Table 1. Input parameters

Parameters	Value	Ref.
Prevalence of cCMV infection (%)	0.31	1
Probability of symptomatic cCMV (%)	23.9	1
CMV PCR-Sensitivity (%)	100	3
CMV PCR-Specificity (%)	100	3
ABR -Sensitivity (%)	100	4
ABR-Specificity (%)	99	4
Cost (USD)		
Treatment of CMV	1,560.18	5
HL Follow-up	458.22	5
Treatment of HL	388.29	5
Cochlear implant	2971.59	5
ABR	56.67	6
QOL		
Mild/Moderate HL	0.677	7
Severe HL	0.616	7
Cochlear implant	0.575	7

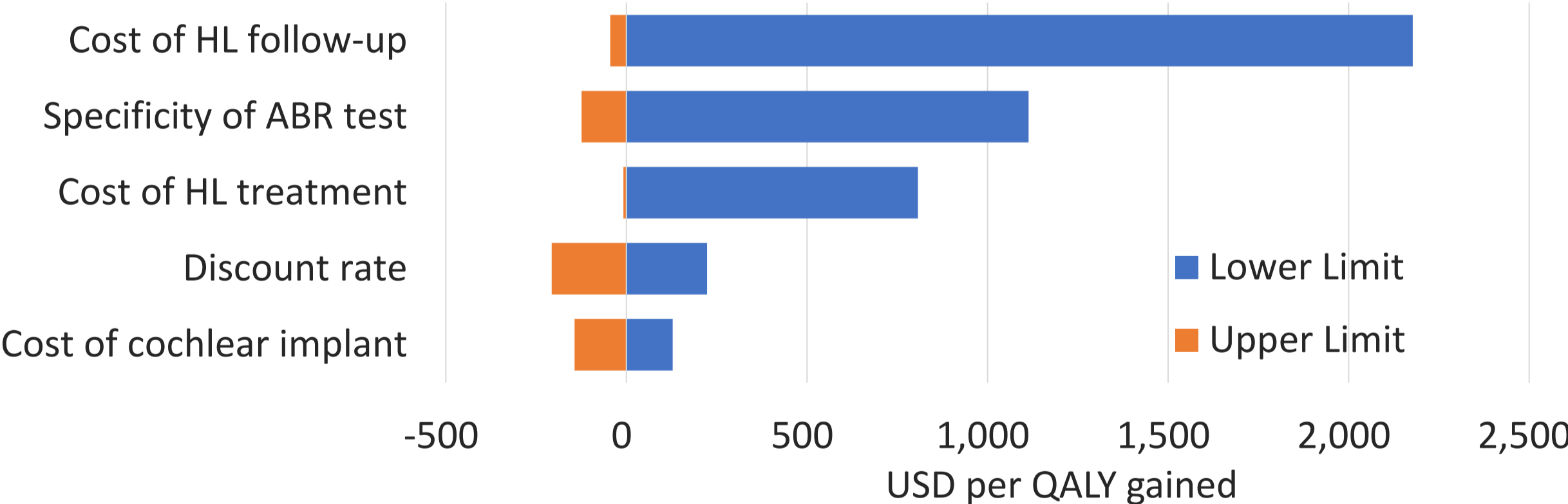


Fig 3. Tornado diagram

CONCLUSIONS

Key Findings: The base case analysis demonstrates that implementing a targeted newborn screening program for cCMV in Japan appears cost-effective, improving health outcomes while potentially reducing overall healthcare costs. When compared to no screening, targeted screening shows favorable incremental cost-effectiveness ratios within acceptable Japanese willingness-to-pay thresholds.

Limitations: Despite its cost-effectiveness, targeted screening has significant limitations in case detection. This approach fails to identify asymptomatic cCMV cases and those without hearing loss at birth, capturing only approximately 40% of CMV-related hearing loss cases. Additionally, it cannot detect infants at risk of developing late-onset symptoms.

Future Research Directions: Further research is needed in two key areas. First, additional sensitivity analyses should refine model variables to better assess program feasibility within the Japanese healthcare context. Second, comprehensive evaluation of universal screening's cost-effectiveness is warranted, considering international evidence and broader outcome measures beyond hearing loss. This expanded analysis would help determine the most appropriate screening strategy for Japan's healthcare system.

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