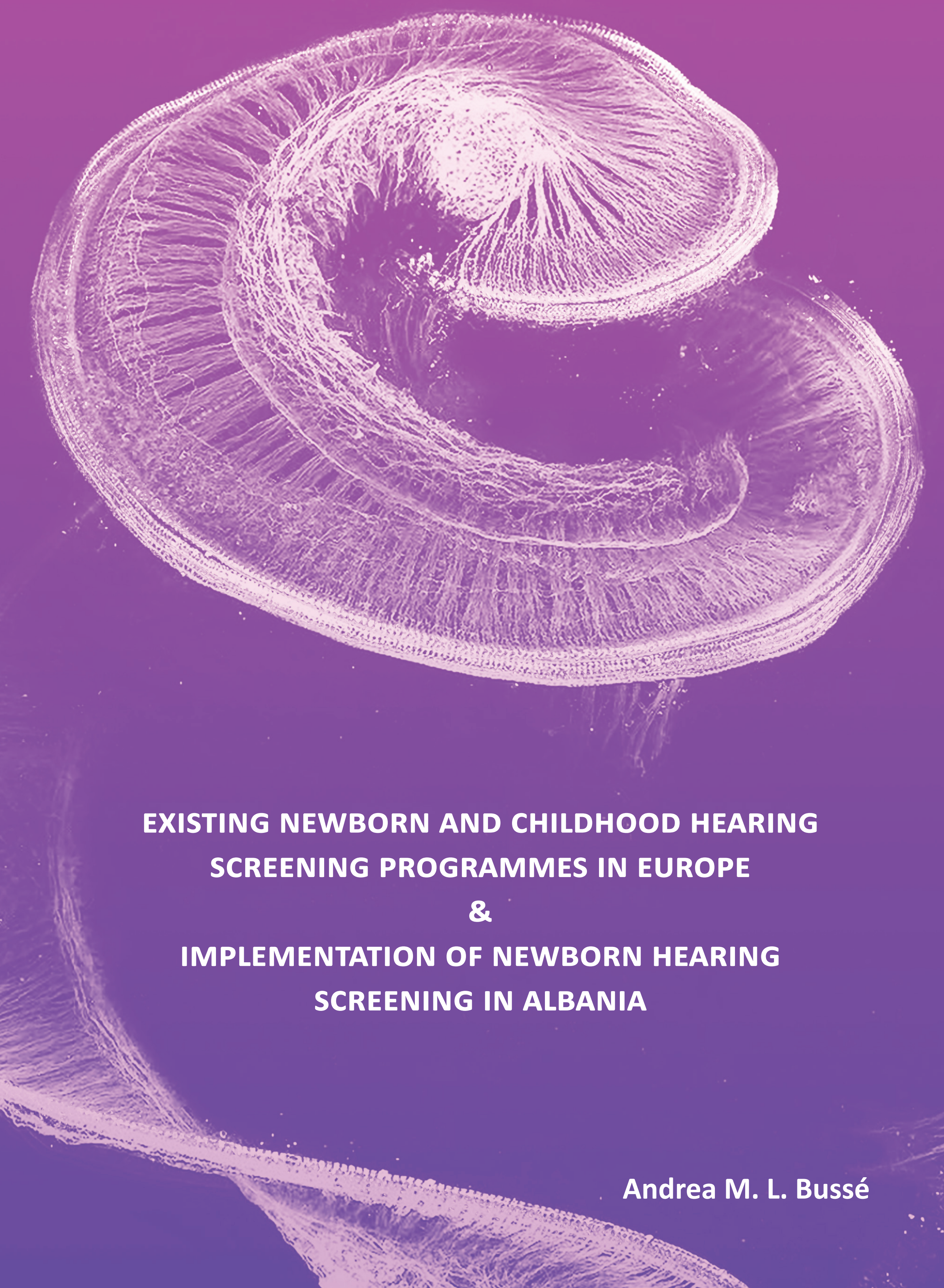


EXISTING NEWBORN AND CHILDHOOD HEARING SCREENING PROGRAMMES IN EUROPE
&
IMPLEMENTATION OF NEWBORN HEARING SCREENING IN ALBANIA

Andrea M. L. Bussé

Existing Newborn and Childhood Hearing Screening Programmes in Europe
&
Implementation of Newborn Hearing Screening in Albania

Andrea Marianne Louisa Bussé

The work presented in this thesis was conducted within the EUSCREEN project, and was financially supported by the European Union's Horizon 2020 research and innovation programme [grant agreement No 733352]. This study sponsor had no role in the study design, or the collection, analysis and interpretation of the data or in the writing of the report or in the decision to submit the article for publication.

ISBN: 978-94-6361-559-4
Author: Andrea M.L. Bussé
Cover: AML Bussé & E Geboers
Photo cover: Dr. Michael Perny; University of Bern Institute for Infectious Diseases; Bern, Switzerland
Lay-out and printing: Optima Grafische Communicatie

Copyright © Andrea M.L. Bussé, 2021, Rotterdam, the Netherlands. All rights reserved. No part of this thesis may be reproduced, stored in a retrieval system or transmitted in any form or by any means, without permission of the author or, when appropriate, of the publishers of the publication.

Existing Newborn and Childhood Hearing Screening Programmes in Europe
&
Implementation of Newborn Hearing Screening in Albania

Bestaande neonatale gehoorscreening en gehoorscreening op kinderleeftijd in Europa
&
Implementatie van neonatale gehoorscreening in Albanië

Proefschrift

ter verkrijging van de graad van doctor aan de
Erasmus Universiteit Rotterdam
op gezag van de rector magnificus

Prof.dr. F.A. van der Duijn Schouten

en volgens besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op
woensdag 30 juni 2021 om 15.30 uur

door

Andrea Marianne Louisa Bussé
geboren te Leuven, België.

Erasmus University Rotterdam

PROMOTIECOMMISSIE:

Promotoren	Prof.dr. H.J. de Koning
	Prof.dr. H.J. Simonsz
Overige leden	Prof.dr. I.K.M. Reiss
	Prof.dr. M. Broeders
	Prof. A. Davis
Copromotor	Dr.ir. A. Goedegebure

Paranimfen	Sarah Vandendael
	Mandy Nordmann

Never say never, because limits, like fears, are often just an illusion.

- Michael Jordan

TABLE OF CONTENTS

Chapter 1

GENERAL INTRODUCTION

Hearing impairment (HI) is a common sensory deficit in early childhood. Worldwide it is estimated that around 466 million people (6.1% of the total population) have a disabling HI of which 34 million are children below the age of 18 [1]. These children may have a HI that was already present at birth (congenital) or the HI may have developed after birth (delayed-onset or acquired). A HI can affect one or both ears (unilateral or bilateral), and is classified according to degree (mild, moderate, severe, profound [2]) and type (permanent/transient, sensorineural/conductive). An untreated HI during childhood, especially a sensorineural HI, may have a major impact on speech, language and general development [3-5]. These delays affect communication, family relations, social and emotional development [6]. Delays in development may lead to academic underachievement and reduced job opportunities which may eventually result in an economic burden to society [7].

Congenital HI, delayed-onset or acquired permanent HI have a number of different causes. The presence of these causes varies across regions of the world and influences the prevalence of HI in these regions [8, 9]. In the newborn period, HI can be caused by pre- or postnatal infections (most commonly cytomegalovirus), genetic disorders that are often autosomal recessive, premature birth and interventions associated with admission to the neonatal intensive care unit. In childhood, sensorineural HI may be delayed-onset HI caused by pre- or perinatal infections or hereditary factors. It may also be acquired HI caused by ototoxic medications, trauma, or postnatal infection [10].

Conductive HI can be caused by conditions of the middle ear such as otitis media (OM; inflammation of the middle ear) [11]. The incidence of OM varies between regions of the world [12]. Otitis media with effusion (OME) is very common during childhood and is accompanied by fluid in the middle ear causing a transient conductive HI [11]. OME is diagnosed in 1-30% of all children between 1 and 8 years old, its highest prevalence is found around 3-4 years [13, 14]. About half of the children that are diagnosed with OME have a HI related to the disease [15, 16]. This HI is present during the time in which speech and language are still developing, yet the effects of OME and its accompanying HI on a child's development are not unanimously confirmed [17-19]. If OM evolves into a permanent HI, it can cause lasting effects on speech and language development if not adequately intervened [20, 21]. Chronic suppurative otitis media (CSOM) is characterised by purulent discharge from the middle ear through a perforation in the tympanic membrane, and a conductive HI. The estimated prevalence of CSOM is 2% among children between 1 and 4 years old and 2.5% among children between 5 and 10 years old [12].

Information on the prevalence of HI at different ages is essential to understand the pathophysiology of HI and to organise healthcare provisions such as detection, intervention and prevention. Congenital permanent HI is estimated to affect between 1-2 infants per 1,000 [22, 23]. However, the prevalence of HI in low-income countries was reported to be higher [24]. After the newborn period the prevalence of permanent HI was reported to double by the time children are 9 years of age [22, 25]. This increase in prevalence is mainly caused by a delayed, progressive or acquired HI [26], although some of these HI may have been missed at birth.

Negative outcomes as a result of an untreated HI may be avoided by early detection of HI and subsequent intervention through the implementation of a newborn hearing screening (NHS) programme [4-6] (not to be confused with the National Health Service in the UK). Before NHS programmes were instated hearing in infants was either not assessed, monitored through an inventory of risk factors, or screened using the distraction test. Unfortunately, when only children with known risk factors for HI are screened at least half of the children with a HI may be missed [27-29]. Furthermore, the distraction test has low sensitivity and specificity, could not be performed before 7 months of age, and identification and intervention were often delayed [28, 30]. New objective technologies were introduced in the 1990s, which allowed hearing screening to be performed accurately in the newborn population. Electrophysiological hearing testing such as otoacoustic emission (OAE) and automated auditory brain stem

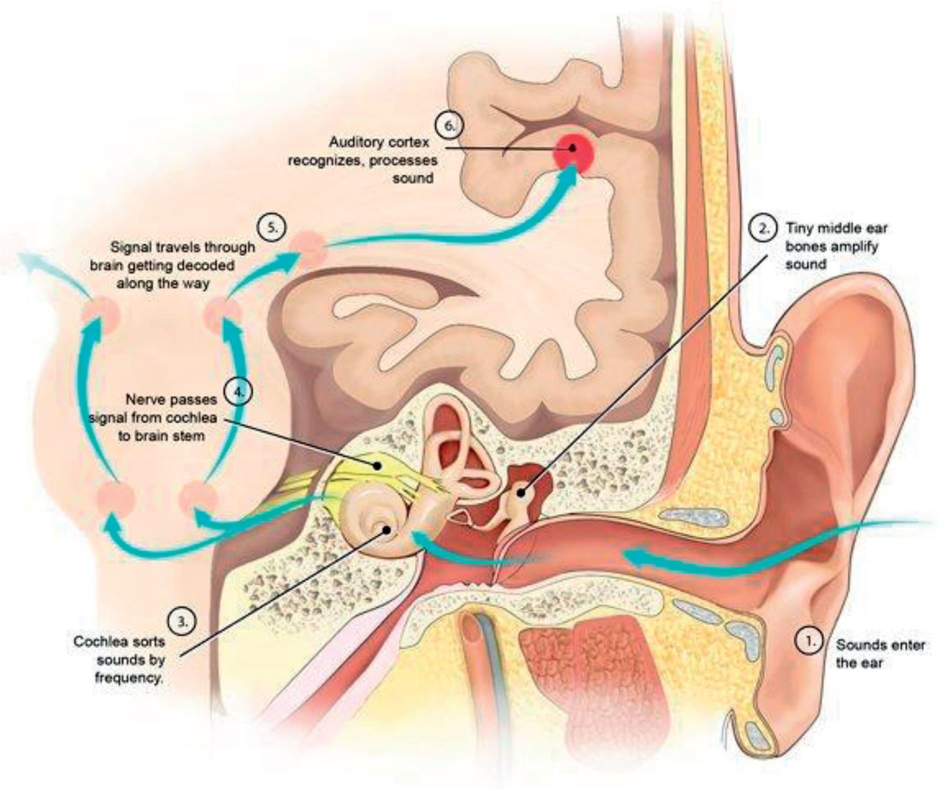


Figure 1. *Auditory pathway (source: https://www.entsaustin.com/audiologic-services/types-hearing-loss/) an OAE screen measures the reaction of the outer hair cells in the cochlea (3) to sound, an aABR screen measures changes in the auditory brain stem (4) as a reaction to sound.*

response (aABR) not only reduced the age of screening, but also the costs of screening [31, 32]. The availability of these technologies enabled hearing screening to take place within a few days after birth, and diagnostic assessment as well as intervention to take place in the first months of life. Hearing aids, when necessary, could now be fitted within the first months after birth and parent-child interaction could be improved significantly at earlier age. Fitting cochlear implants was made possible within the first year. Amplification through hearing aids or cochlear implants in combination with family intervention allowed a child with a HI to develop speech and language in a similar way as their normal-hearing peers, minimising possible negative outcomes associated with a HI [33, 34].

When an OAE or aABR screen is performed, a probe is placed in the infant's ear canal and a tone or click is presented separately for each ear. For an OAE screen, the microphone in the probe measures the reactive sound that is emitted by the outer hair cells in the cochlea as a reaction to the tone or click. An aABR screen requires placing three electrodes on the infant's head. These electrodes detect changes in brain wave activity in the auditory brain stem as a reaction to the tone or click. Both screening tests have high sensitivity and specificity (between 90% and 100%) [35-37], are performed automatically and can be administered by a range of professionals, provided that these professionals are appropriately trained and have gained sufficient experience with the device. An NHS screening protocol includes either OAE, aABR or both types of screening in one or multiple steps. Screening using multiple steps increases the specificity of the protocol [38], which reduces the number of infants who are unnecessarily referred to diagnostic assessment.

Figure 2. *Newborn hearing screening in two infants using OAE (left) and aABR (right). (Permission from the parents was obtained to use these pictures.)*

Screening without an appropriate intervention pathway would of course not be beneficial. Many countries in the world have implemented NHS as part of early hearing detection and intervention programmes. They aim to identify infants with a HI in the early weeks or months of their lives so the infants and their families can receive early support and intervention. These interventions allow the infant to develop optimally and improve outcomes. Early research found the biggest advantage of early detection and intervention in children with a HI who were identified and received intervention within the first 6 months of life [4-6, 33, 34]. International position statements were developed to provide guidance for best practice, benchmarks and quality measure [39-42]. The recommendations made in these position statements include age at screening, diagnostics and intervention, and benchmarks for quality measures used in NHS such as coverage rate (benchmark of 95- 97%), referral rate (benchmark of 4% for referral to diagnostic assessment) and follow-up rate (benchmark of 90-97%) [39, 43-45]. Most position statements recommend to perform screening within 1 month, perform diagnostics within 3 months and start intervention within 6 months after birth [39]. More recently, even earlier deadlines for diagnostics and intervention have been proposed for programmes that meet the so-called '1-3-6' guidelines [42].

Children with a HI who are born in countries without an established NHS programme or children whose HI is not present yet when NHS is performed may remain undetected for many years. Even with an NHS programme in place up to 50% of school-aged children with a permanent HI have been reported to not being detected at birth [22, 46]. Detection of infants with a HI at birth may not be effective, for example screening is not offered to all infants, screening has a high number of false negatives, infants are lost to follow-up or parents refuse screening. [26, 47] Even when an effective screening programme is in place, its target condition does not necessarily include all types of HI and a mild or unilateral HI may easily be missed. When detected late, these children may not receive appropriate intervention during the time speech and language develop or during their school-aged years. HI in these children may be detected by their caregivers [46, 47] or during post-NHS follow-up [22, 48].

Routine follow-up after NHS includes targeted surveillance of children with risk factors for HI, hearing screening before school-entry or during school-going years. Targeted surveillance programmes may miss children that have no known risk factors for HI [49] and not all of these programmes are able to achieve high attendance [50, 51]. When the majority of children attends kindergarten or school, high attendance may be achieved during school screening. Alternatively, high attendance may be achieved during paediatric health examination. Unlike NHS, the effectiveness of childhood hearing screening (CHS) after the newborn period is not universally agreed upon. A study in England was unable to find a significant difference between a region with CHS and a region without CHS in the number of children with a HI detected. CHS also did not significantly reduce the age of identification [49].

A number of factors influence the effectiveness of CHS. These include the number of children with a HI that have already been detected, the tests selected, the protocol design, programme features and the local circumstances in a country or region. A variety of tests may be used, e.g., parent/teacher questionnaires, pure-tone audiometry, speech (in noise) tests or OAE. The test choice depends on the age and development of the target population. However, the accuracy of these tests was found to vary across studies [49]. Fortnum et al. (2016) concluded that for the two regions included in the study, CHS was not cost-effective [49]. Fortnum et al. (2016) noted that the effectiveness of CHS also depended on the effectiveness of the alternative scenarios. On the other hand, a review by Yong et al. (2020) found that when local circumstances are taken into account, CHS may be cost-effective [50], especially in rural areas [51] and areas where NHS is not (yet) available [52]. Unfortunately, high quality information to evaluate the cost-effectiveness of CHS is scarce [53].

The EUSCREEN study

The EUSCREEN study [54], in which this thesis is embedded, is a multi-centre study that was set up to compare the cost-effectiveness of vision and hearing screening programmes in countries in Europe and beyond. The EUSCREEN study consists of three components: the collection of data on vision and hearing screening to compare screening programmes across countries, the development of a cost-effectiveness model assisted by the data collected on screening programmes, and the implementation of a vision and hearing screening programme in two countries where vision and hearing screening are not yet performed.

Data on hearing and vision screening programmes were collected through an extensive questionnaire. This questionnaire contained 191 questions on hearing screening, 126 questions on vision screening and 82 questions on general screening that were categorised into nine domains: demography and epidemiology, administration and general background, existing screening programmes, coverage and attendance, tests and devices, follow up and diagnostic assessment, treatment options, costs and benefits and adverse effects. Hearing, vision and general screening experts from participating countries provided information on their local screening programmes. For hearing, the provision and effectiveness of childhood screening programmes (both NHS and CHS) was inventoried across participating countries. The similarities and diversity across screening programmes in the organisation of screening, screening outcome and possible features that are important to estimate the efficiency of screening were explored and screening quality measures were investigated in relation to protocol features used. The information gathered on existing hearing screening programmes in the participating countries was used for the development of the model.

The MIcrosimulation SCreening ANalysis (MISCAN) model [55] was originally developed to simulate the natural history of diseases and to evaluate screening programmes such as cancer screening. It was adapted to calculate the optimal, most cost-effective vision and hearing screening programme taking the local circumstances of a country into account. Local circumstances include the professionals that are available to screen and the existing screening pathways. The model can be used to assist policymakers with the introduction, modification or disinvestment of a screening programme. For the development of this model, detailed information was used on vision and hearing screening protocols, organisation of general preventive healthcare and local societal background. This information was aggregated through the EUSCREEN questionnaire. The cost-effectiveness model assisted with the implementation of vision screening in Romania and NHS in Albania by making a preliminary prediction of the most cost-effective screening programme for each country. Results of these implementation studies were used to validate and calibrate the model to improve its predictions for other countries.

For the implementation of NHS in Albania, the model compared several possible NHS programmes, taking into account local circumstances in Albania such as demography and geography, natural history of HI in Albania and costs. The implementation of NHS was evaluated in four maternity hospitals that are located in three provinces in Albania: Tirana, Pogradec and Kukës. A little over 11,000 infants are born in these four maternity hospitals each year. The two largest maternity hospitals are located in Tirana and account for approximately 6000 and 4000 births annually. The maternity hospitals in Pogradec and Kukës each account for approximately 500 births annually. These locations were chosen because they accurately represent both urban and rural populations and they include a range of socio-economic circumstances. Most births take place in maternity hospitals in Albania so it was decided that NHS would be performed in the maternity hospital before discharge.

Research aims and outline of this study

The main objective of this thesis is to determine factors that need to be considered when organising a hearing screening programme. Within this thesis screening organisation is inventoried, screening outcome evaluated and the cost-effectiveness of existing hearing screening programmes across Europe is compared. Is the natural history of hearing impairment the same in every country? How are hearing screening programmes organised? What variation can be found between programmes and what causes these variations? What circumstances play a role in the design, choices made and functioning of hearing screening programmes? What determines the performance of a screening programme? What data needs to be collected to perform quality control and to compare the effectiveness and cost-effectiveness of a hearing screening programme? What screening quality measures need to be collected and are the benchmarks as suggested by international position statements acceptable? What factors are important when implementing or modifying a hearing screening programme? Are there any competing healthcare interests?

To answer these questions, we reviewed literature on the prevalence of HI in the first year of life, inventoried existing hearing screening programmes in a number of European countries, developed a model to calculate and compare the cost-effectiveness of screening programmes given the local circumstances and studied the implementation of a hearing screening programme in Albania. Results were used to explore the variety of choices that can be made when organising hearing screening programmes, how these choices influence the performance of screening and to determine screening outcome and quality measures that can be used to evaluate the performance of screening.

A general outline of the chapters in this thesis is provided below.

The main body of this thesis comprises of three parts. First, we describe the prevalence of HI in the newborn period across the world. Prevalence rates are essential knowledge for programmes that aim to detect HI early and provide subsequent intervention, especially with cost-effectiveness in mind.

Chapter two describes a systematic review and Bayesian meta-analysis on the prevalence of permanent newborn HI.

The second part gives an overview of existing hearing screening programmes across countries and regions that provided information through the EUSCREEN questionnaire. An inventory was made of the variations across programmes and these variations were related to socio-economic factors. **Chapter three, four and five** analyse the results of the data-collection by means of an extensive questionnaire. More specifically, **chapter three** reports on the provision of NHS, **chapter four** reports on the outcome measures of NHS and **chapter five** reports the provision and outcome measures of CHS.

The third part describes the implementation of an NHS programme in four maternity hospitals in Albania. **Chapter six** describes the model that was used to calculate the most cost-effective screening programme in Albania given the local circumstances and **chapter seven** describes the observations made during the implementation.

Chapter eight takes together the results of the studies described in the previous chapters and discusses the main findings of this thesis.

LIST OF ABBREVIATIONS:

HI	Hearing impairment
OM	Otitis media
OME	Otitis media with effusion
CSOM	Chronic suppurative otitis media
NHS	Newborn hearing screening
OAE	Otoacoustic emission
aABR	Automated auditory brain stem response
CHS	Childhood hearing screening
MISCAN	MIcrosimulation SCreening ANalysis

REFERENCES

1. World Health Organization Fact sheet. Deafness and hearing loss. 2019 20 March 2019 [cited 2019 August 15, 2019]; Available from: https://www.who.int/en/news-room/fact-sheets/detail/deafness-and-hearing-loss.
2. World Health Organization. Grades of hearing impairment. 2019 [cited 2019 November 15]; Available from: https://www.who.int/pbd/deafness/hearing_impairment_grades/en/.
3. Moeller, M.P., Early intervention and language development in children who are deaf and hard of hearing. Pediatrics, 2000. 106(3): p. E43.
4. Yoshinaga-Itano, C. and M.L. Apuzzo, The development of deaf and hard of hearing children identified early through the high-risk registry. Am Ann Deaf, 1998. 143(5): p. 416-24.
5. Yoshinaga-Itano, C., et al., Language of early- and later-identified children with hearing loss. Pediatrics, 1998. 102(5): p. 1161-71.
6. Yoshinaga-Itano, C. and M.L. Apuzzo, Identification of hearing loss after age 18 months is not early enough. Am Ann Deaf, 1998. 143(5): p. 380-7.
7. Schroeder, L., et al., The economic costs of congenital bilateral permanent childhood hearing impairment. Pediatrics, 2006. 117(4): p. 1101-12.
8. Mathers, C.D., A. Smith, and M. Concha, Global burden of hearing loss in the year 2000, in World Health Organization, Geneva. 2003. p. pp 1–30.
9. Stevens, G., et al., Global and regional hearing impairment prevalence: an analysis of 42 studies in 29 countries. Eur J Public Health, 2013. 23(1): p. 146-52.
10. Smith, R.J., J.F. Bale, Jr., and K.R. White, Sensorineural hearing loss in children. Lancet, 2005. 365(9462): p. 879-90.
11. Schilder, A.G., et al., Otitis media. Nat Rev Dis Primers, 2016. 2: p. 16063.
12. Monasta, L., et al., Burden of disease caused by otitis media: systematic review and global estimates. PLoS One, 2012. 7(4): p. e36226.
13. Casselbrant, M.L. and E.M. Mandel, Chapter 10 Epidemiology, in Evidence-Based Otitis Media, R.M. Rosenfeld and C.D. Bluestone, Editors. 2003, BC Decker Inc Hamilton: London. p. 147-162.
14. Mandel, E.M., et al., The incidence, prevalence and burden of OM in unselected children aged 1-8 years followed by weekly otoscopy through the "common cold" season. Int J Pediatr Otorhinolaryngol, 2008. 72(4): p. 491-9.
15. Gravel, J.S., Hearing and Auditory function, in Evidence-Based Otitis Media, R.M. Rosenfeld and C.D. Bluestone, Editors. 2003, BC Decker Inc Hamilton: London. p. 342-359.
16. World Health Organization, Chronic suppurative otitis media: Burden of Illness and Management Options. 2004, World Health Organization: Geneva, Switzerland.
17. Roberts, J.E., R.M. Rosenfeld, and S.A. Zeisel, Otitis media and speech and language: a meta-analysis of prospective studies. Pediatrics, 2004. 113(3): p. e238-e248.
18. Schilder, A.G., et al., The effect of otitis media with effusion at preschool age on some aspects of auditory perception at school age. Ear Hear, 1994. 15(3): p. 224-31.
19. Bennett, K.E., et al., Behaviour and developmental effects of otitis media with effusion into the teens. Arch Dis Child, 2001. 85(2): p. 91-5.
20. Klein, J.O., The burden of otitis media. Vaccine, 2000. 19 Suppl 1: p. S2-S8.
21. Verhoeff, M., et al., Chronic suppurative otitis media: a review. International journal of pediatric otorhinolaryngology, 2006. 70(1): p. 1-12.
22. Fortnum, H.M., et al., Prevalence of permanent childhood hearing impairment in the United Kingdom and implications for universal neonatal hearing screening: question-

naire based ascertainment study. Bmj, 2001. 323(7312): p. 536-40.

23. Van Naarden, K., P. Decoufle, and K. Caldwell, Prevalence and characteristics of children with serious hearing impairment in metropolitan Atlanta, 1991-1993. Pediatrics, 1999. 103(3): p. 570-5.
24. Olusanya, B.O., et al., Costs and performance of early hearing detection programmes in Lagos, Nigeria. Trans R Soc Trop Med Hyg, 2009. 103(2): p. 179-86.
25. le Clercq, C.M.P., et al., Prevalence of Hearing Loss Among Children 9 to 11 Years Old: The Generation R Study. JAMA Otolaryngol Head Neck Surg, 2017. 143(9): p. 928-934.
26. Fortnum, H., Epidemiology of permanent childhood hearing impairment: Implications for neonatal hearing screening. Audiological Medicine, 2003. 1(3): p. 155-164.
27. Davis, A. and S. Wood, The epidemiology of childhood hearing impairment: Factors relevant to planning of services. British Journal of Audiology, 1992. 26(2): p. 77-90.
28. Davis, A., et al., A critical review of the role of neonatal hearing screening in the detection of congenital hearing impairment. Health Technol Assess, 1997. 1(10): p. i-iv, 1-176.
29. Mehl, A.L. and V. Thomson, Newborn hearing screening: the great omission. Pediatrics, 1998. 101(1): p. E4.
30. Davis, A., J. Bamford, and J. Stevens, Performance of neonatal and infant hearing screens: sensitivity and specificity. Br J Audiol, 2001. 35(1): p. 3-15.
31. Stevens, J., et al., The costs of early hearing screening in England and Wales. Archives of disease in childhood, 1998. 78(1): p. 14-19.
32. Uus, K., J. Bamford, and R. Taylor, An analysis of the costs of implementing the National Newborn Hearing Screening Programme in England. Journal of medical screening, 2006. 13(1): p. 14-19.
33. Yoshinaga-Itano, C., et al., Early Hearing Detection and Vocabulary of Children With Hearing Loss. Pediatrics, 2017. 140(2).
34. Ching, T.Y.C., et al., Learning from the Longitudinal Outcomes of Children with Hearing Impairment (LOCHI) study: summary of 5-year findings and implications. International Journal of Audiology, 2018. 57(sup2): p. S105-S111.
35. Bantock, H.M. and S. Croxson, Universal hearing screening using transient otoacoustic emissions in a community health clinic. Arch Dis Child, 1998. 78(3): p. 249-52.
36. Herrmann, B.S., A.R. Thornton, and J.M. Joseph, Automated Infant Hearing Screening Using the ABR. American Journal of Audiology, 1995. 4(2): p. 6-14.
37. Institute for Quality and Efficiency in Health Care: Executive Summaries. Neonatal screening for early detection of hearing impairment Executive summary of final report S05-01, Version 1.0. 2005 [cited 2018; Available from: https://www.ncbi.nlm.nih.gov/books/NBK84151/.
38. Clemens, C.J. and S.A. Davis, Minimizing false-positives in universal newborn hearing screening: a simple solution. Pediatrics, 2001. 107(3): p. E29.
39. Joint Committee on Infant Hearing, Year 2007 position statement: Principles and guidelines for early hearing detection and intervention programs. Pediatrics, 2007. 120(4): p. 898-921.
40. World Health Organization. Newborn and infant hearing screening. 2009 [cited 2019 13-03-2019]; Available from: https://www.who.int/blindness/publications/Newborn_and_Infant_Hearing_Screening_Report.pdf?ua=1.
41. European Consensus Statement on Neonatal Hearing Screening., European Consensus Statement on Neonatal Hearing Screening. Finalized at the European Consensus Development Conference on Neonatal Hearing Screening. Acta Paediatr, 1999. 88(1): p. 107-8.
42. Joint Committee on Infant Hearing, Year 2019 Position Statement: Principles and Guidelines for Early Hearing Detection and Intervention Programs. The Journal of Early

Hearing Detection and Intervention, 2019. 4(2): p. 1-44.

43. Neumann, K., et al., Newborn and Infant Hearing Screening Facing Globally Growing Numbers of People Suffering from Disabling Hearing Loss. International Journal of Neonatal Screening, 2019. 5(1): p. 7.
44. Patel, H. and M. Feldman, Universal newborn hearing screening. Paediatr Child Health, 2011. 16(5): p. 301-10.
45. Januario, G.C., et al., Quality indicators in a newborn hearing screening service. Braz J Otorhinolaryngol, 2015. 81(3): p. 255-63.
46. Watkin, P.M. and M. Baldwin, Identifying deafness in early childhood: Requirements after the newborn hearing screen. Arch Dis Child, 2011. 96(1): p. 62-66.
47. Prieve, B.A., et al., An Evidence-Based Systematic Review on the Diagnostic Accuracy of Hearing Screening Instruments for Preschool- and School-Age Children. Am J Audiol, 2015. 24(2): p. 250-67.
48. Weichbold,V., D. Nekahm-Heis, and K. Welzl-Mueller, Universal newborn hearing screening and postnatal hearing loss. Pediatrics, 2006. 117(4): p. e631-6.
49. Fortnum, H., et al., A programme of studies including assessment of diagnostic accuracy of school hearing screening tests and a cost-effectiveness model of school entry hearing screening programmes. Health Technology Assessment, 2016. 20(36).
50. Yong, M., et al., Cost-effectiveness of School Hearing Screening Programs: A Scoping Review. Otolaryngol Head Neck Surg, 2020: p. 194599820913507.
51. Nguyen, K.-H., et al., Cost-effectiveness analysis of a mobile ear screening and surveillance service versus an outreach screening, surveillance and surgical service for indigenous children in Australia. 2015. 10(9).
52. Baltussen, R. and A. Smith, Cost effectiveness of strategies to combat vision and hearing loss in sub-Saharan Africa and South East Asia: mathematical modelling study. Bmj, 2012. 344: p. e615.
53. Bamford, J., et al., Current practice, accuracy, effectiveness and cost-effectiveness of the school entry hearing screen. Health Technol Assess, 2007. 11(32): p. 1-168, iii-iv.
54. CORDIS Europa. Implementation of cost-optimized childhood vision and hearing screening programmes in middle-income countries in Europe. 2018 [cited 2018; Available from: https://cordis.europa.eu/project/rcn/207448/factsheet/en.
55. Habbema, J.D., et al., The MISCAN simulation program for the evaluation of screening for disease. Comput Methods Programs Biomed, 1985. 20(1): p. 79-93.

Chapter 2

Prevalence of permanent neonatal hearing impairment: Systematic review and Bayesian meta-analysis

Andrea ML Bussé
Hans LJ Hoeve
Kazem Nasserinejad
Allison R Mackey
Huibert J Simonsz
André Goedegebure

ABSTRACT

Objective

To investigate the variance in reported prevalence rates of permanent neonatal hearing impairment (HI) worldwide.

Design

A systematic review and meta-analysis was performed on reported prevalence rates of sensorineural and permanent conductive or mixed HI worse than 40 dB in neonates, detected as a result of a screening programme or audiometric study.

Study sample

For meta-analysis, 35 articles were selected, 25 from high-income countries and 10 from middle-income countries according to the world bank classification system.

Results

The prevalence rate of permanent uni- and bilateral HI worse than 40 dB in neonates varied from 1 to 6 per 1000, the overall prevalence was 2.21 per 1000 [1.71, 2.8]. In NICU populations the prevalence rate was higher with a larger fraction of bilateral cases. Although not significant, prevalence rates were slightly higher in Asia compared to Europe and the number of infants lost to follow-up appeared higher in countries with lower gross national income.

Conclusion

Substantial variations exist in prevalence rates of neonatal permanent HI across countries and regions. There is a strong need for more data from low-income countries to identify demographic factors that account for this variability in reported prevalence rates. Reporting these data in a uniform way is advocated.

INTRODUCTION

Hearing impairment (HI) is a rather common sensory deficit in children in their first years of life, but it is not easily noticed. Deficiency in auditory input at a young age may cause a delay in speech, language and general development and poor academic performance (Yoshinaga-Itano and Apuzzo 1998a, 1998b). Early detection of congenital HI and appropriate intervention is crucial to minimise its impact (Joint Committee on Infant Hearing, American Academy of Pediatrics 2007; Downs and Yoshinaga- Itano 1999).

Prevalence rates of HI at various ages and from all over the world are indispensable to better understand the pathophysiology of HI and to organise health care provisions such as detection, intervention and prevention.

Permanent hearing impairment (PHI) in childhood is caused by both genetic factors and environmental factors. These factors are likely to vary across the world (Grundfast 2002; Smith and Taggart 2004). Neonatal PHI of genetic origin is in many cases autosomal recessive (Grundfast 2002; Smith and Taggart 2004; Denoyelle et al. 1997; Zelante et al. 1997). PHI can also be acquired in utero or during early childhood as a complication of infectious disease, a consequence of ototoxic medication, or in connection with premature birth. This explains the higher prevalence of PHI in infants treated at the neonatal intensive care unit (NICU) (Grundfast 2002). Variations exist in the worldwide availability and quality of health care provisions such as birth clinics, NICU's, medication and vaccination programmes. The aforementioned factors all influence the prevalence of neonatal PHI to some extent and may cause variations across the world.

The World Health Organization (WHO) (2018) reported that prevalence rates of HI are higher in low-income countries (Mathers, Smith, and Concha 2003; Stevens et al. 2013). However, these concerns both conductive and sensorineural HI in children at school age, when otitis media plays an important role (Mathers, Smith, and Concha 2003; Stevens et al. 2013; Smith 2008). The Global Research on Developmental Disabilities Collaborators (2018) estimated the number of children with HI to be the highest in South Asia and the lowest in North America. The highest number of children with or at risk for developmental disabilities were found in low- and middle-income countries such as India, China and Nigeria.

During the past 20 years universal neonatal hearing screening (NHS) programmes, targeted at detecting PHI, have been introduced in many high- and middle-income countries (Joint Committee on Infant Hearing, American Academy of Pediatrics 2007). In some countries, NHS has been implemented at a local level or for a limited period of time. As a result, prevalence rates of PHI in neonates from a variety of countries are increasingly becoming available. This new knowledge may help to find explanations for variations in prevalence rates.

Most NHS programmes aim to detect PHI >40 dB HL, and use a two- or three-step screening protocol (Sloot et al. 2015; Vos et al. 2016; Kanji, Khoza-Shangase, and Moroe 2018). Two types of objective screening tests are most commonly used: otoacoustic emission tests (OAE) and automated auditory brainstem response tests (aABR). An OAE measures the reaction (emissions) of the outer hair cells in the cochlea to an auditory stimulus, presented in the infant's ear canal. An aABR measures the electrical response of the auditory brainstem to an auditory stimulus set at 35 or 40 dB nHL. Both tests detect HI worse than 40 dB HL, and have high sensitivity and specificity (Wolff et al. 2010). In contrast to OAE, aABR screening is able to also detect cases of auditory neuropathy. An infant who fails the first step of the screening programme is invited to return for the next step of screening. The specificity of a screening programme increases with the number of steps used.

Infants are referred for full diagnostic assessment when they have failed the final step of the screening programme. Auditory brainstem response (ABR) and auditory steady-state responses (ASSR), which measure the electrical response in the central auditory pathway, are used to objectively estimate the hearing threshold. Quite often more extensive examinations are needed to obtain a final diagnostic result that includes type of HI and the threshold.

The aim of this study is to investigate the prevalence of PHI in neonates by means of a systematic literature review and analyse the results using a Bayesian meta-analysis. In more detail, we aim to:

- Summarise the literature that reports on the prevalence of neonatal PHI of 40 dB or worse;
- Combine the findings in a meta-analysis to obtain an accurate estimation of the overall prevalence rate of neonatal PHI;
- Analyse the degree of variation in reported prevalence rates of neonatal PHI and identify explanatory factors.

MATERIALS AND METHODS

Literature search

Current scientific literature was systematically searched to identify original peer-reviewed studies that explore the prevalence of permanent sensorineural or conductive HI in children. This review was carried out based on the guidelines of Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA P) 2015 statement. This includes the use of the PRISMA P checklist and following the methodological approaches recommended for systematic reviews based on the PRISMA statement (Moher et al. 2015; Shamseer et al. 2015).

The systematic literature search was carried out in November 2017, and updated in November 2018, within the following electronic databases: Embase, PubMed/Medline Ovid, Web of Science, Cochrane Central and Google Scholar. Search terms included: "prevalence", "incidence", "epidemiology", "hearing disorder", "hearing impairment", "pediatric", "preschool", "newborn", "infant", "child", which were used to develop a search string. These terms were combined in different ways using Boolean operators such as "AND" and "OR". The complete search strings used have been attached in Appendix 1 (see Supplementary material). Although the search included infants up to 12 years of age, in this study we only consider articles that describe the prevalence of infants up to one year of age.

The articles obtained from the electronic databases were compiled using EndNote and duplicates were eliminated. All titles and abstracts were screened independently by three reviewers (A.B., H.H., A.M.). Studies were included in the literature review if they contained original data on prevalence rates of PHI among the general infant population or subgroups: infants admitted to the NICU and/or well babies (WB). Studies were excluded if they reported only on subgroups of infants (e.g., infants with syndromes), if the study population or threshold were poorly defined, if the diagnostic process was not described, if errors were made when calculating the prevalence rate, or if the full text was not available in English. Definitions of the terms used in this article are provided in Table 1.

Table 1. Definitions.

PHI	Permanent hearing impairment includes sensorineural, permanent conductive (e.g., malformation), and excludes transient hearing impairment (e.g., otitis media), in one or both ears.
Bilateral PHI	Permanent hearing impairment of both ears. The degree of PHI is determined by the better hearing ear.
Unilateral PHI	Permanent hearing impairment in one ear. The degree of PHI is determined by the worse hearing ear.
Population	The number of neonates that entered the screening program or study.
NICU / WB	Within the neonatal population two subgroups are defined: NICU indicates infants treated in a neonatal intensive care unit (NICU), and well babies (WB) are all other infants.
General population	The neonatal population that includes all subgroups.
Prevalence	The number of neonates with PHI in the population.
Prevalence rate	The number of neonates with PHI per 1000 of the population.

The remaining articles underwent a full-text review by two authors (A.B. and H.H.), and further selection was made based on a number of inclusion and exclusion criteria. Studies were included if they reported on sensorineural and permanent conductive or mixed HI, considered both bilateral and unilateral PHI or bilateral PHI only, and used hearing thresholds from 20 to 40 dB HL. PHI had to be diagnosed as a result of a screening programme or audiometric study and confirmed by means of ABR or ASSR. During the diagnostic process following a NHS programme, a number of tests may be needed to determine the definitive hearing thresholds. When studies reported on the variability of these results, the most definitive result obtained during the first year of life was used to calculate the prevalence rate. When more than one study reported on the same population, prevalence rates were used from the most recent study that adequately met all inclusion criteria.

Studies were excluded if they reported on transient HI only or when transient HI figures were not eliminated from the final reported prevalence rates. This selection also excluded all articles that reported prevalence on older children, the selection focussed only on the prevalence of PHI in infants. Disagreements about the interpretation of data were resolved by discussion, and when disagreements could not be resolved, A.G. acted as a referee.

Prevalence rates for a hearing threshold of 35 or 40 dB HL were used when this information was available. Some studies reported only on prevalence rates for thresholds of 20, 25 or 30 dB HL. All reported prevalence rates resulted from a study using OAE, aABR or ABR.

Selected studies

A data extraction sheet was developed to record specific information from the article (title, author, year), year(s) when the data were collected, information about the population (geographic, ethnic, socio-economic), general neonatal population or NICU/WB subgroups, population size, definition of PHI, screening and diagnostic tests, degree of PHI, unilateral or bilateral PHI, age at time of diagnosis, percentage lost to follow-up (LTFU), and prevalence rate of PHI.

The Newcastle Ottawa Scale (Wells et al. 2018) is a quality assessment tool for cohort studies used to score the quality of studies included in reviews. Since not all subscales of the Newcastle Ottawa Scale were applicable to our set of data, we adapted the criteria to fit our study. This resulted in a list of seven items (Table 2). Criteria were scored on a two-point or three-point scale. For study group composition, a representative group was one in which no more than 10% of infants were admitted to the NICU (Harrison and Goodman 2015; Gijsen and Harbers 2015). The criterion "percentage of infants LTFU" was based on the recommendations of the JCIH to achieve a return to follow-up of 70% of infants or more (Joint Committee on Infant Hearing, American Academy of Pediatrics 2007; Joint Committee on Infant Hearing 2000; Prieve and Stevens 2000). Inadequate accuracy concerned ambiguity such as calculation uncertainties. The final quality score was calculated to a maximum of eight points and converted to a percentage. The cut-off value was set at 75% to distinguish between studies of low and high quality.

The countries of the study populations were classified into five geographical areas: Europe, Asia, the Americas, Africa and Australia. Websites of The World Bank Group (2018) and National Statistics Republic of China (Taiwan) for Taiwan (2018) were consulted to classify each country as high, upper-middle, lower-middle or low-income country, and to record its Gross National Income (GNI) per capita in 2017.

Table 2. List of criteria to indicate quality of the studies included for the meta-analysis.

Criterion	0	1	2
Study group composition	not representative / not mentioned	representative	
Study group origin	hospital(s)	region/country	
Study group size	< 5000	5000-10000	>10000
HI type(s)	not well defined	well defined	
HI threshold	<35 dB	35 or 40 dB	
% lost to follow up	≥ 30% / not mentioned	< 30%	
Accuracy	inadequate	adequate	

Statistical analysis

A Bayesian random-effects meta-analysis was used to estimate the prevalence rate of both unilateral and bilateral HI in different populations. Prevalence rates were estimated for the general neonatal population and separately for WB and infants admitted to NICU for the studies in which these numbers were reported on.

The central idea of the Bayesian approach is to combine the likelihood (data) with our prior knowledge to result in a revised probability (posterior probability). Posterior distributions are typically summarised by the median and the 95% credible intervals, which are the counterparts to 95% confidence intervals used in classical statistics.

The Bayesian approach is becoming more popular because it is intuitive and flexible due to recent advances in computational methods. In a meta-analysis framework, a Bayesian approach offers an advantage compared to the classical approach, especially when taking into account the limitations in misestimating the heterogeneity in a random-effects model (Sutton et al. 2000; Sutton and Abrams 2001). Statistical expertise has strongly recommended carrying out Bayesian meta-analyses (Higgins and Green 2011). In our model, random-effects were employed to take into account the heterogeneity between the studies. The SD of the random effects (tau) will be reported as the heterogeneity index.

In this study, we employed relatively non-informative priors for all parameters. We performed different relatively non-informative priors on random-effects' variance (i.e., an inverted gamma-distribution with low values and a uniform prior to the random-effects SD) as a sensitivity analysis to check the robustness of our meta-analysis results.

We performed two other sensitivity analyses. These aimed to assess the impact of variations of information that were implemented into the analytical model. One sensitivity analysis was performed using only high-quality studies (defined as ≥75% on the quality score), and the other one was performed using only studies where NHS programmes targeted a strict threshold of 35 dB HL or worse.

A Bayesian random-effects meta-regression was performed to assess the relationship between the overall prevalence rate of HI and the GNI per capita, infants LTFU, and geographical area. The calculated exceedance probability describes the posterior probability that the estimated parameter is greater or smaller than zero. The exceedance probability is a counterpart to the p value that is used in classical statistics. Extreme values for the exceedance probability (i.e., <0.05) indicate a significant difference.

Computations and graphics were performed in R programme language (Dalgaard 2010). All Bayesian computations were performed using the Markov Chain Monte Carlo sampler through Jags (Plummer 2016) interface in R programme language. Markov Chain Monte Carlo sampling was run for each analysis for 50k iterations after discarding the first 50k iterations (burning) to reach the convergence. The 95% credible intervals use 95% of the highest posterior probability in the posterior distribution.

The Egger test was used to check the publication bias via the metafor package (Viechtbauer 2010) in R programme language.

RESULTS

Our search strategy identified 7520 articles (Figure 1). After duplicates were eliminated, 4497 articles remained. Titles and abstracts were screened, and a further 4117 were eliminated because the inclusion criteria were not met or full text was not available in English. Of the remaining 380 articles on childhood PHI, 243 focussed on infants in their first year of life. A total of 209 of these 243 articles were excluded because they did not meet the inclusion criteria. Although some of these excluded studies reported on the prevalence of neonatal PHI, they were not used in our review for a variety of reasons: the composition of the study group was not suitable, the screening procedure, tests, or number of ears tested were not described, the description of results of post-screen diagnostics were insufficient or absent, PHI was poorly or not defined, PHI thresholds were not mentioned, the study design was unclear, or obvious calculation errors were found. The update of this search in November 2018 identified 278 additional articles. One was included in the final analysis of 35 articles (Table 3).

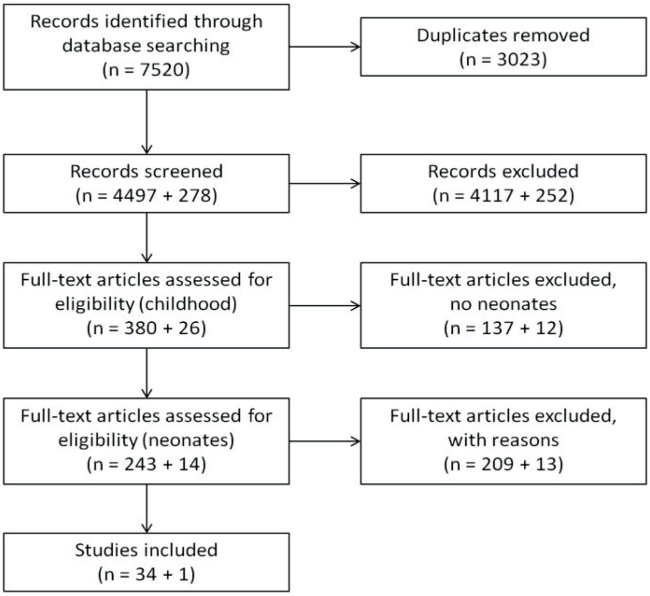


Figure 1. Flowchart showing the process followed to identify, screen, determine eligibility and select articles for inclusion in this review. The number of articles for each step is displayed as (the original search + the search update).

Table 3. Overview of the 35 studies in this review.

Author (ref)	Year data	Geography	Scale
General Population of Infants			
Adachi[49]	1999-2008	Japan (Saitama)	Region
Adelola[36]	2000-2007	Ireland (Galway)	Region
Antoni[50]	2005-2010	France (Île de France)	Region
Augustine[33]	2010	India (Vellore)	Hospital
Bailey[51]	2000-2001	Australia (Perth)	City, 5 hospitals
Berninger[52]	1999-2004	Sweden (Stockholm)	City, 2 hospitals
Bevilacqua[38]	2005-2007	Brazil (Bauru)	Hospital
Calcutt[53]	2009-2011	Australia (Queensland)	Region
Dalzell[54]	1995-1996	USA (New York state)	Region
De Capua[55]	1998-2006	Italy (Siena)	Region
Farhat[35]	2008-2010	Iran (Mashad)	City, 3 hospitals
Hsu[56]	2009-2010	Taiwan (Taipei)	Hospital
Kennedy[57]	1993-1996	UK (South-West England)	4 cities
Magnani[58]	2010-2013	Italy (Parma)	Hospital
Mason[59]	1992-1997	USA (Honolulu, Hawaii)	Hospital
Mehl[60]	1992-1999	USA (Colorado)	State
Neumann[61]	2005	Germany (Hessen)	Region
Ng[34]	1999	China (Hong Kong)	Hospital
Olusanya[32]	2005-2008	Nigeria (Lagos)	City, several clinics
Pastorino[62]	1997-2001	Italy (Milan)	Hospital
Qi[63]	2007-2009	China (Beijing)	Hospital
Sun[39]	2002-2007	China (Shanghai)	Region
Swanepoel[37]	2001-2005	South Africa (Gauteng)	Hospital
Uus[64]	2003-2004	UK (England)	Country
Watkin[65]	1992-1997	UK (London)	Hospital
Wenjin [66]	2012-2014	China (Guangxi)	Hospital
Wroblevska[67]	2013	Poland (Poznan)	Hospital
WB only			
Iwasaki[68]	2000-2001	Japan (Hamamatsu)	City, 2 hospitals
Van der Ploeg[69]	2002-2009	Netherlands	Country
Van Kerschaver[70]	2003-2004	Belgium (Flanders)	Country
NICU only			
Galambos[71]	1977-1991	USA (San Diego, CA)	City, 3 hospitals
Tajik[72]	2011-2015	Iran (Babol)	City, 2 hospitals
Van Dommelen[73]	2002-2005	Netherlands	Country
Van Straaten[74]	1998-2000	Netherlands	Country
Watson[75]	1982-1987	N-Ireland (Belfast)	Hospital

Most of the 35 studies included in the analysis were conducted in Europe, Asia, North America and Australia in the past 20 years. Only a few were conducted in Africa and South America. Twenty-five studies originate from high-income countries, eight from upper-middle-income countries and two from lower-middle-income countries. Thirteen studies had a quality score >75%. In particular, lower scores were achieved on the criteria composition of study group, local or national study group, and numbers LTFU (Figure 2).

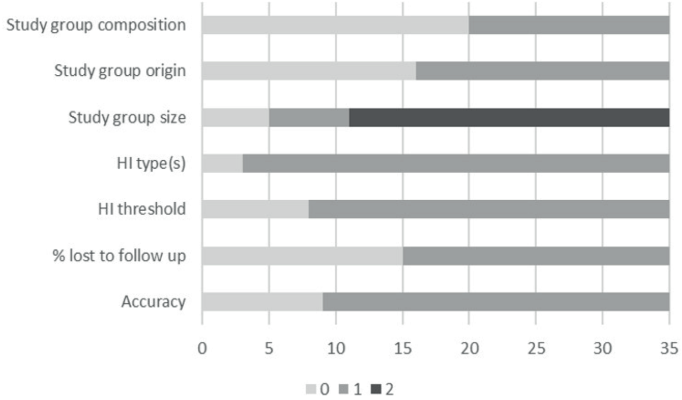


Figure 2. The number of studies per score for each quality criterion.

Prevalence rates were often readily presented in the article or were calculated from the supplied data. Only a few studies provided multiple thresholds obtained throughout the diagnostic process. Most studies reported prevalence rates with thresholds of 35 or 40 dB HL. However, for some studies only thresholds of 20, 25 or 30 dB HL were available. Notwithstanding this inconsistency, all studies screened for a target condition of 35 or 40 dB HL using OAE or aABR in a two-, three- or four-step screening programme. These techniques identify HI of 35–40 dB HL or worse, with a high specificity. How many cases of mild HI (20–40 dB HL) would actually be included in the prevalence rate estimations with a threshold of 20 dB HL depends on the specificity of the applied screening programme. Therefore, the impact of varying thresholds was evaluated in a sensitivity analysis.

Table 4 displays the prevalence rates of PHI (bilateral and unilateral) and PHI bilateral only for the general population of infants, the WB subgroup and the NICU infant subgroup as they are reported in each article.

The Bayesian random-effects meta-analysis of the prevalence rates of PHI in the general neonatal population resulted in an overall prevalence rate of 2.21 per 1000 with a credible interval of [1.71, 2.8] (Tau: 0.51 95% CI (0.34, 0.73)) (Table 5). The corresponding forest plot is depicted in Figure 3, in which studies are ranked according to GNI per capita in the country of origin. The highest prevalence rates were found in Nigeria (Olusanya and Somefun 2009), India (Augustine et al. 2014), China (Hong- Kong) (Ng et al. 2004) and Iran (Farhat et al.

Table 4. Geographical areas from selected articles, reported prevalence rates of PHI (bi- and unilateral) and PHI bi (bilateral only), for general neonatal, WB and NICU populations, including HI threshold, quality score and LTFU.

Country (region, city)	N Pop	Threshold	P per 1000	P bi per 1000	Quality >75%	LTFU <30%
General Population of Infants						
Ireland (Galway)[36]	25.742	40 dB	1.2	0.7	+	+
Sweden (Stockholm)[52]	31.092	40 dB		1.7	-	-
UK (South-West England)[57]	21.279	40 dB		1.3	+	-
UK (England)[64]	169.487	40 dB		1.0	-	-
UK (London)[65]	25.199	40 dB	1.7	1.4	+	+
Germany (Hessen)[61]	17.439	40 dB	2.1	1.7	+	+
France (Ile de France)[50]	26.780	35 dB		0.6	+	+
Italy (Siena)[55]	19.700	30 dB	1.8	1.2	+	+
Italy (Parma)[58]	11.592	40 dB	3.3	2.2	-	+
Italy (Milan)[62]	19.777	40 dB	3.2	1.7	+	+
Poland (Poznan)[67]	6.827	40 dB	3.1	2.5	-	+
Japan (Saitama)[49]	101.912	35 dB	3.1	1.6	+	-
China (Hong Kong)[34]	1.064	40 dB	5.6	2.8	-	-
China (Beijing)[63]	10.983	30 dB	3.2	1.1	-	-
China (Guangxi)[66]	19.098	30 dB	2.3		-	-
China (Shanghai)[39]	560.432	40 dB	1.0	1.2 (1)	+	-
Taiwan (Taipei)[56]	3.361	35 dB	1.5	0.6	-	+
Iran (Mashad)[35]	8.987	25 dB	3.5		-	+
India (Vellore)[33]	9.448	35 dB	4.1	3.2	-	-
USA (New York state)[54]	43.311	20 dB	2.0	1.1	-	-
USA (Colorado)[60]	55.324	40 dB	1.5	1.1 (2)	+	+
USA, Hawaii (Honolulu)[59]	10.372	35 dB		1.4	-	+
Brazil (Bauru)[38]	11.466	40 dB	1.0	0.8	-	+
Nigeria (Lagos)[32]	11.897	40 dB	6.0	4.8	-	-
South Africa (Gauteng)[37]	6.241	35 dB	1.0	0.6	-	-
Australia (Perth)[51]	12.708	35 dB		0.7	-	+
Australia (Queensland)[53]	175.911	40 dB		0.7 (3)	+	+
WB						
Netherlands[69]	547.061	40 dB	1.3	0.8	+	+
Belgium (Flanders)[70]	103.835	35 dB	1.5	0.9	+	+
Japan (Hamamatsu)[68]	4.085	40 dB	3.7	2.0	-	+
China (Guangxi)[66]	12.134	30 dB	1.98		-	-
Iran (Mashad)[35]	8.724	25 dB	3.0		-	+
USA, Hawaii (Honolulu)[59]	8.971	35 dB		0.9	-	-
NICU						
Netherlands[73]	10.830	35 dB	18	15	-	-
Netherlands[74]	2.484	35 dB	24	18	-	+

Table 4. Geographical areas from selected articles, reported prevalence rates of PHI (bi- and unilateral) and PHI bi (bilateral only), for general neonatal, WB and NICU populations, including HI threshold, quality score and LTFU. (continued)

Country (region, city)	N Pop	Threshold	P per 1000	P bi per 1000	Quality >75%	LTFU <30%
N-Ireland (Belfast)[75]	417	40 dB	21	17	-	+
China (Guangxi)[66]	6.964	30 dB	2.7	2.0	-	-
Iran (Mashad)[35]	263	25 dB	19		-	+
Iran (Babol)[72]	3.362	20 dB	11	10	-	-
USA, Hawaii (Honolulu)[59]	1.401	35 dB		5	-	+
USA (San Diego CA)[71]	5.901	35 dB	47	33	-	-

Pop: population; P: prevalence rate; (1) threshold of 25 dB, (2) 35 dB, (3) only sensorineural PHI; LTFU: lost to follow up.; +: meets criteria; -: does not meet criteria

2015). The lowest prevalence rates were found in Ireland (Adelola et al. 2010), South Africa (Swanepoel et al. 2007), Brazil (Bevilacqua et al. 2010) and China (Shanghai) (Sun et al. 2009). The prevalence rate for bilateral PHI only (unilateral PHI excluded) was 1.33 per 1000 [1.01, 1.63], which is about 2/3 of the overall prevalence rate. The prevalence rate for unilateral PHI only (bilateral PHI excluded) was 0.78 per 1000 [0.51, 1.07] (Table 5).

Additional meta-analyses were performed for the studies reporting on NICU and WB populations. Table 5 summarises the most relevant results. The prevalence rate in the WB population (1.93 [1.06, 2.98]) was lower than the prevalence rate for the general neonatal population (2.21 [1.71, 2.8]). As expected, a substantially higher prevalence rate was found for NICU infants (15.77 [4.65, 29.25]) when compared to both the general and WB population (Table 5).

The relationship between prevalence rates of unilateral PHI and all PHI (uni- and bilateral) was calculated for NICU infants and infants in the general neonatal population. Among the general infant population, 34% [25, 42%] of infants with PHI have a unilateral loss. Among NICU infants, 22% [12, 30%] of infants with PHI have a unilateral loss.

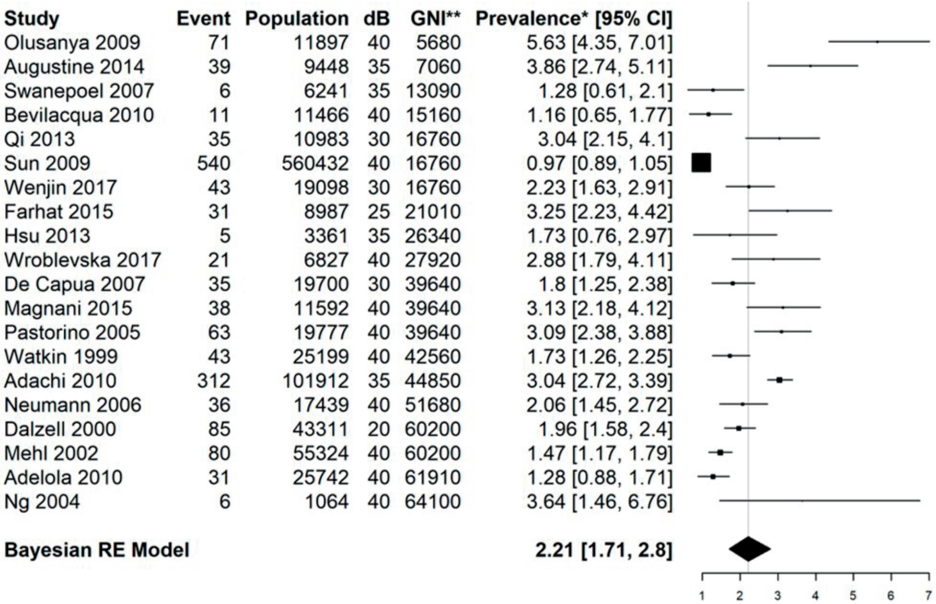
The first sensitivity analysis showed that, when only studies with a high-quality score (>75%) were included, the overall prevalence rate was 1.75 per 1000 [1.16, 2.37]. The second sensitivity analysis concerned the threshold of PHI. When a stricter criterion was applied for the threshold (35 dB HL), the overall prevalence rate was 2.14 per 1000 [1.47, 2.88]. Both sensitivity analyses found overall prevalence rates that did not differ significantly from the overall prevalence rate in the general population. We included all selected studies regardless of quality score and choice of threshold in the meta-analyses.

Analysis of variations in prevalence rates

For the analysis between geographical areas and prevalence rates of PHI, geographical areas were categorised into five continents. Despite the appearance of prevalence rates varying by geographical area, no statistically significant differences were found (Figure 4, See Supplemen-

Table 5. Overall prevalence rates in a Bayesian random-effects model.

	Overall prevalence rate (per 1000)	**Credible interval** (per 1000)	**Number of studies**
General population PHI	2.21	1.71, 2.8	20
General population bilateral PHI	1.33	1.01, 1.63	23
General population unilateral PHI	0.78	0.51, 1.07	16
Well babies	1.93	1.06, 2.98	5
NICU Infants	15.77	4.65, 29.52	7
General population PHI, high quality studies	1.75	1.16, 2.37	8
General population PHI, threshold ≥35 dB HL	2.14	1.47, 2.88	15
	Ratio	**Credible interval**	**Number of studies**
Ratio uni/uni+bi in general population	0.34	0.25, 0.42	16
Ratio uni/uni+bi in NICU infants	0.22	0.12, 0.3	6



Study	Event	Population	dB	GNI**	Prevalence* [95% CI]
Olusanya 2009	71	11897	40	5680	5.63 [4.35, 7.01]
Augustine 2014	39	9448	35	7060	3.86 [2.74, 5.11]
Swanepoel 2007	6	6241	35	13090	1.28 [0.61, 2.1]
Bevilacqua 2010	11	11466	40	15160	1.16 [0.65, 1.77]
Qi 2013	35	10983	30	16760	3.04 [2.15, 4.1]
Sun 2009	540	560432	40	16760	0.97 [0.89, 1.05]
Wenjin 2017	43	19098	30	16760	2.23 [1.63, 2.91]
Farhat 2015	31	8987	25	21010	3.25 [2.23, 4.42]
Hsu 2013	5	3361	35	26340	1.73 [0.76, 2.97]
Wroblevska 2017	21	6827	40	27920	2.88 [1.79, 4.11]
De Capua 2007	35	19700	30	39640	1.8 [1.25, 2.38]
Magnani 2015	38	11592	40	39640	3.13 [2.18, 4.12]
Pastorino 2005	63	19777	40	39640	3.09 [2.38, 3.88]
Watkin 1999	43	25199	40	42560	1.73 [1.26, 2.25]
Adachi 2010	312	101912	35	44850	3.04 [2.72, 3.39]
Neumann 2006	36	17439	40	51680	2.06 [1.45, 2.72]
Dalzell 2000	85	43311	20	60200	1.96 [1.58, 2.4]
Mehl 2002	80	55324	40	60200	1.47 [1.17, 1.79]
Adelola 2010	31	25742	40	61910	1.28 [0.88, 1.71]
Ng 2004	6	1064	40	64100	3.64 [1.46, 6.76]
Bayesian RE Model					**2.21 [1.71, 2.8]**

Figure 3. Bayesian Random-effects Model, PHI prevalence rates (per 1000) of the general neonatal population sorted by GNI per capita. (Tau: 0.51 95% CI (0.34, 0.73))
(Event: Number of infants with PHI; *Weighted prevalence for each study; ** GNI: Gross National Income)
Please note that the prevalence rates in this figure are based on the fitted random-effects model and thus differ from the prevalence rates in table 4. This discrepancy is due to the so-called shrinkage estimates that occur in random-effects models.

tary Appendix 2 material) Prevalence rates seemed to be higher in Asia compared to Europe, but the difference was not statistically significant (p=0.06). The relationship between PHI prevalence rate and GNI per capita was not statistically significant (p=0.29) according to the

Bayesian logistic regression analysis. No significant trend was observed between prevalence rate and the year in which the data had been collected (p=0.12). Additionally, no significant association was observed between prevalence rate and the percentage of infants LTFU during the screening and diagnostic process (p=0.16). Larger percentages LTFU were generally associated with lower GNI per capita, but this association did not reach statistical significance (p=0.07).

DISCUSSION

In this systematic review and meta-analysis, the prevalence of PHI in neonatal populations worldwide was investigated, as well as possible associations between prevalence and its determinants. The overall prevalence rate of PHI of 40 dB HL or worse in one or both ears, was 2.21 per 1000. As expected, the prevalence rate of PHI in NICU infants was much higher when compared to both WB and all infants, confirming earlier reports (Garinis et al. 2018; Wang et al. 2017).

Interestingly, a PHI is more likely to be bilateral in NICU infants compared to the general infant population. PHI in NICU infants is more likely to be acquired as the consequence of, among others, infections, hyperbilirubinemia, hypoxia or ototoxic medication. These risk factors for PHI would seem to have an effect on both ears, while other causes may affect one or both ears (Garinis et al. 2018; Wang et al. 2017; Hille et al. 2007).

The highest prevalence rates were reported by studies performed in Nigeria (Olusanya and Somefun 2009), India (Augustine et al. 2014), China (Hong-Kong) (Ng et al. 2004) and Iran (Farhat et al. 2015), but they concerned rather small populations. The lowest prevalence rates were found in Ireland (Adelola et al. 2010), South Africa (Swanepoel et al. 2007), Brazil (Bevilacqua et al. 2010) and China (Shanghai) (Sun et al. 2009).

Prevalence rates were higher in studies from Asia than Europe, however, this difference was not statistically significant. Countries with lower GNI per capita appeared to have higher but widely distributed, prevalence rates. A statistical association between prevalence and GNI was not found. Higher prevalence rates in developing countries and higher prevalence rates in Asia compared to Europe, were found by Stevens and Mathers in their WHO studies (Mathers, Smith, and Concha 2003; Stevens et al. 2013). These studies, however, concern older children, include conductive HI and apply various thresholds. The current study concerns neonates, PHI and strictly defined thresholds. The current study did not demonstrate a statistically significant association between the prevalence of PHI in the neonatal period and geographical region or low- and high-income countries, but such an association may still exist.

Unfortunately, both the current study and those by Stevens and Mathers contain a sparsity of data from low-income countries (Mathers, Smith, and Concha 2003; Stevens et al. 2013). Although this review includes studies from all over the world, the majority of the studies report on results of NHS programmes in high-income countries or large cities. Far less information is available from Africa and South America. The results of this review inevitably reflect a great extent the situation in high- income countries, which possibly causes an under- or overestimation of the overall prevalence rate. It is obvious that there is a strong need for more prevalence studies from low-income countries and regions.

The prevalence rate of PHI, as reported in a study, should be considered with caution. The reported prevalence rate in an approximation of the "real" prevalence rate and is not only determined by medical factors, but also by study factors. Medical factors determine the "real" prevalence, which is the factual (but unknown) number of infants affected in a population. A study uses methods (study factors) to reveal the "real" prevalence. Unfortunately, these methods may influence the outcome to an unknown extent.

Direct medical factors include genetic disorders, antenatal or postnatal infections, hyperbilirubinemia, hypoxia, medication (aminoglycosides, diuretics). Indirect medical factors include the availability and quality of health care provisions such as birth clinics, NICU and vaccination programmes, but also consanguinity and mortality rates. These factors are highly dependent on social, economic and cultural circumstances, and therefore, likely to vary considerably across countries. Congenital CMV is one of the most important non-genetic causes of PHI in neonates (Grosse, Ross, and Dollard 2008). It was found to be more prevalent in Nigeria, China, India and the Middle East (Zuhair et al. 2019). The incidence of infectious diseases and presence of vaccination programmes are likely to be associated with the economic situation of a country (Stevens et al. 2013), in contrast to global distribution of genes causing HI, and the prevalence of consanguineous marriages (Mathers, Smith, and Concha 2003; Stevens et al. 2013; Freeland, Jones, and Mohammed 2010). Consanguinity is especially common in North-Africa, the Middle East, South-West Asia and India (Black 2018). Neonatal PHI is assumed to be hereditary in more than 50% of cases, the majority being autosomal recessive (Grundfast 2002; Smith and Taggart 2004; Denoyelle et al. 1997; Zelante et al. 1997). As aetiological data on neonatal PHI mainly originate from developed countries, we cannot be certain whether this percentage also applies to the rest of the world. Study of the distribution of the numerous genes associated with HI across the world is complex, but more information is gradually becoming available (Chan and Chang 2014).

This systematic review targets "real" prevalence rates and how they depend on medical, economic and cultural circumstances. Nevertheless, the differences in study design and screening procedures between articles must be considered, as these factors influence the reported prevalence rates.

Study factors are the choice of the population studied, its size and composition, the definition of PHI, including the threshold, characteristics and quality of the audiometric testing and numbers of infants LTFU. The selected population determines to a large extent the reliability and relevance of a reported prevalence rate. The definition of PHI, the type and threshold used, has an effect on the reported prevalence rate. A poorly performed test will lead to more false "refers", and thus more re-testing, which is likely to increase the number of infants LTFU. A high percentage LTFU will result in an underestimated prevalence rate because the denominator (the population) is usually defined as the number of neonates entering the screening programme or study group. The high percentage of infants LTFU may contribute to the reported low prevalence rate in the study by Sun in Shanghai (Sun et al. 2009). The number of infants LTFU may be especially high in developing countries, as the socio-economic circumstances too often impede the functioning and use of medical facilities. This implies that the "real" PHI prevalence rates in developing countries could be even higher than the reported ones. Although the assumption that LTFU may be associated with GNI, was not confirmed by the statistical analysis (p=0.07), inclusion of more data from high-quality studies could possibly make a difference. The prevalence rate calculated for studies with a high-quality score was 1.75 per 1000, and the prevalence rate for all included studies was 2.21 per 1000. However, this result could have been biased by regional factors, as most high-quality studies were performed in Western Europe.

Proposal reporting prevalence

Several studies reported on prevalence rates but did not describe their results in a way that was useful for this study. There is clearly no uniform methodology for defining, calculating or reporting data on prevalence rates of HI. Therefore, it is proposed that future studies reporting on prevalence rates define the studied type(s) of HI in terms of sensorineural, permanent conductive, transient conductive and mixed HI, with a defined cut-off value (preferably 40 dB HL in neonates) for prevalence rate calculation; indicate if HI is bilateral, unilateral or both bi- and unilateral; use the most recent WHO (2018) classification to report on the degree of HI; state the age at which the diagnosis is definitive, the audiometric tests used for screening and diagnostics, the study group size, composition, proportion NICU/ WB, and number of infants LTFU.

CONCLUSION

Worldwide prevalence rates of HI in children of various age groups are becoming increasingly available, partially due to the ongoing implementation of universal NHS programmes. Much of the existing information concerns older children, and reported prevalence rates in neonates originate mainly from high-income countries. Our systematic review shows that approximately 2 per 1000 neonates worldwide are identified with neonatal PHI, of which approximately two-thirds are bilateral. Although no statistical significant correlations were found with demographic or study factors, prevalence rates in neonates tend to be higher in countries with lower incomes, and higher in Asia than in Europe. A marked lack of uniformity exists in studies, especially with regard to the definition of HI.

Acknowledgments

We thank Wichor Bramer from the Medical Library of the Erasmus Medical Center for his help in designing and conducting the search strategy. This study sponsor had no role in the study design, or the collection, analysis and interpretation of the data or in the writing of the report or in the decision to submit the article for publication.

REFERENCES

Adachi, N., K. Ito, H. Sakata, and T. Yamasoba. 2010. "Etiology and OneYear Follow-up Results of Hearing Loss Identified by Screening of Newborn Hearing in Japan." Otolaryngology – Head and Neck Surgery 143 (1): 97–100. doi:10.1016/j.otohns.2010.02.008.

Adelola, O. A., V. Papanikolaou, P. Gormley, J. Lang, and I. J. Keogh. 2010. "Newborn Hearing Screening: A Regional Example for National Care." Irish Medical Journal 103 (5): 146–149.

Antoni, M., I. Rouillon, F. Denoyelle, E. N. Garabedian, and N. Loundon. 2016. "Newborn Hearing Screening: Prevalence and Medical and Paramedical Treatment of Bilateral Hearing Loss in a Neonatal Series in the ÎIle-de-France Region of France." European Annals of Otorhinolaryngology, Head and Neck Diseases 133 (2): 95–99. doi:10.1016/j.anorl.2015.10.001.

Augustine, A. M., A. K. Jana, K. A. Kuruvilla, S. Danda, A. Lepcha, J. Ebenezer, R. R. Paul, et al. 2014. "Neonatal Hearing Screening – Experience from a Tertiary Care Hospital in Southern India." Indian Pediatrics 51 (3): 179–183. doi:10.1007/s13312-014-0380-5.

Bailey, H. D., C. Bower, J. Krishnaswamy, and H. L. Coates. 2002. "Newborn Hearing Screening in Western Australia." Medical Journal of Australia 177 (4): 180–185. doi:10.5694/j.1326-5377.2002.tb04728.x.

Berninger, E., and B. Westling. 2011. "Outcome of a Universal Newborn Hearing-Screening Programme Based on Multiple Transient-Evoked Otoacoustic Emissions and Clinical Brainstem Response Audiometry." Acta Oto-Laryngologica 131 (7): 728–739. doi:10.3109/00016489.2011. 554440.

Bevilacqua, M. C., K. D. F. Alvarenga, O. A. Costa, and A. L. M. Moret. 2010. "The Universal Newborn Hearing Screening in Brazil: From Identification to Intervention." International Journal of Pediatric Otorhinolaryngology 74 (5): 510–515. doi:10.1016/j.ijporl.2010.02.009.

Black, M. 2018. "Global prevalence of consanguinity." Accessed 28 August 2017. http://consang.net/index.php/Global_prevalence.

Calcutt, T. L., D. Dornan, R. Beswick, and D. I. Tudehope. 2016. "Newborn Hearing Screening in Queensland 2009–2011: Comparison of Hearing Screening and Diagnostic Audiological Assessment between Term and Preterm Infants." Journal of Paediatrics and Child Health 52 (11): 995–1003. doi:10.1111/jpc.13281.

Chan, D. K., and K. W. Chang. 2014. "GJB2-Associated Hearing Loss: Systematic Review of Worldwide Prevalence, Genotype, and Auditory Phenotype." The Laryngoscope 124 (2): E34–E53. doi:10.1002/lary.24332.

Dalgaard, P. 2010. R: A Language and Environment for Statistical Computing. Vienna: R Development Core Team, R Foundation for Statistical Computing.

Dalzell, L., M. Orlando, M. MacDonald, A. Berg, M. Bradley, A. Cacace, D. Campbell, et al. 2000. "The New York State Universal Newborn Hearing Screening Demonstration Project: Ages of Hearing Loss Identification, Hearing Aid Fitting, and Enrollment in Early Intervention." Ear and Hearing 21 (2): 118–130. doi:10.1097/00003446-200004000-00006.

De Capua, B., D. Costantini, C. Martufi, G. Latini, M. Gentile, and C. De Felice. 2007. "Universal Neonatal Hearing Screening: The Siena (Italy) Experience on 19,700 Newborns." Early Human Development 83 (9): 601–606. doi:10.1016/j.earlhumdev.2007.01.001.

Denoyelle, F., D. Weil, M. A. Maw, S. A. Wilcox, N. J. Lench, D. R. AllenPowell, A. H. Osborn, et al. 1997. "Prelingual Deafness: High Prevalence of a 30delG Mutation in the Connexin 26 Gene." Human Molecular Genetics 6 (12): 2173–2177. doi:10.1093/hmg/6.12.2173.

Downs, M. P., and C. Yoshinaga-Itano. 1999. "The Efficacy of Early Identification and Intervention for Children with Hearing Impairment." Pediatric Clinics of North America 46 (1): 79–87. doi:10.1016/S00313955(05)70082-1.

Farhat, A., M. M. Ghasemi, J. Akhondian, A. Mohammadzadeh, H. Esmaeili, R. Amiri, A. A. Raoof Saeb, et al. 2015. "Comparative Study of Hearing Impairment among Healthy and Intensive Care Unit Neonates in Mashhad." Iranian Journal of Otorhinolaryngology 27 (81): 273–277. PMCID: PMC4710879.

Freeland, A., J. Jones, and N. K. Mohammed. 2010. "Sensorineural Deafness in Tanzanian Children – Is Ototoxicity a Significant Cause? A Pilot Study." International Journal of Pediatric Otorhinolaryngology 74 (5): 516–519. doi:10.1016/j.ijporl.2010.02.010. Galambos, R., M. J. Wilson, and P. D. Silva. 1994. "Identifying Hearing Loss in the Intensive Care Nursery: A 20-Year Summary." Journal of the American Academy of Audiology 5 (3): 151–162. PMID: 8075411.

Garinis, A. C., A. Kemph, A. M. Tharpe, J. H. Weitkamp, C. McEvoy, and P. S. Steyger. 2018. "Monitoring Neonates for Ototoxicity." International Journal of Audiology 57 (sup4): S41–S48. doi:10.1080/14992027.2017. 1339130.

Gijsen, R., and M. Harbers. 2015. "Opnamen neonatale intensive care unit." Accessed 20 November 2018. https://www.volksgezondheidenzorg.info/ onderwerp/zorg-rond-de-geboorte/cijfers-context/gebruik#!node-opnamen-neonatale-intensive-care-unit.

Global Research on Developmental Disabilities Collaborators. 2018. "Developmental Disabilities among Children Younger than 5 Years in 195 Countries and Territories, 1990–2016: A Systematic Analysis for the Global Burden of Disease Study 2016." The Lancet. Global Health 6 (10): e1100–e1121. doi:10.1016/S2214-109X(18)30309-7.

Grosse, S. D., D. S. Ross, and S. C. Dollard. 2008. "Congenital Cytomegalovirus (CMV) Infection as a Cause of Permanent Bilateral Hearing Loss: A Quantitative Assessment." Journal of Clinical Virology 41 (2): 57–62. doi:10.1016/j.jcv.2007.09.004.

Grundfast, K. M. 2002. "Chapter 16. Hearing Loss." In Pediatric Otolaryngology, edited by C. D. Bluestone and S. E. Stool. Philadelphia, PA: W.B. Saunders.

Harrison, W., and D. Goodman. 2015. "Epidemiologic Trends in Neonatal Intensive Care, 2007–2012." JAMA Pediatrics 169 (9): 855–862. doi:10. 1001/jamapediatrics.2015.1305.

Higgins, J. P. T., and S. Green, eds. 2011. "Cochrane handbook for systematic reviews of interventions." Accessed 14 November 2011. www.cochranehandbook.org.

Hille, E. T., H. I. van Straaten, P. H. Verkerk, and Dutch NICU Neonatal Hearing Screening Working Group. 2007. "Prevalence and Independent Risk Factors for Hearing Loss in NICU Infants." Acta Paediatrica 96 (8): 1155–1158. doi:10.1111/j.1651-2227.2007.00398.x.

Hsu, H. C., F. P. Lee, and H. M. Huang. 2013. "Results of a 1-Year Government-Funded Newborn Hearing Screening Program in Taiwan." Laryngoscope 123 (5): 1275–1278. doi:10.1002/lary.23713.

Iwasaki, S., Y. Hayashi, A. Seki, M. Nagura, Y. Hashimoto, G. Oshima, T. Hoshino, et al. 2003. "A Model of Two-Stage Newborn Hearing Screening with Automated Auditory Brainstem Response." International Journal of Pediatric Otorhinolaryngology 67 (10): 1099–1104. doi:10.1016/S01655876(03)00199-X.

Joint Committee on Infant Hearing. 2000. "Year 2000 Position Statement: Principles and Guidelines for Early Hearing Detection and Intervention Programs." American Journal of Audiology 9 (1): 9–29. doi:10.1044/10590889(2000/005).

Joint Committee on Infant Hearing, American Academy of Pediatrics. 2007. "Year 2007 Position Statement: Principles and Guidelines for Early Hearing Detection and Intervention Programs." Pediatrics 120 (4): 898–921. doi:10.1542/peds.2007-2333.

Kanji, A., K. Khoza-Shangase, and N. Moroe. 2018. "Newborn Hearing Screening Protocols and Their Outcomes: A Systematic Review." International Journal of Pediatric Otorhinolaryngology 115: 104–109. doi: 10.1016/j.ijporl.2018.09.026.

Kennedy, C. R., L. Kimm, D. Cafarelli Dees, M. J. Campbell, A. R. D. Thornton, J. Bamber, V. Innes, et al. 1998. "Controlled Trial of Universal Neonatal Screening for Early Identification of Permanent Childhood Hearing Impairment." The Lancet 352 (9145): 1957–1964. doi:10.1016/ S0140-6736(98)06359-4.

Magnani, C., G. Bacchi, A. M. Borghini, D. Delmonte, G. Fava, A. M. Occasio, A. Sarti, et al. 2015. "Universal Newborn Hearing Screening: The Experience of the University Hospital of Parma." Acta BioMedica 86 (3): 273–277. PMID: 26694155.

Mason, J. A., and K. R. Herrmann. 1998. "Universal Infant Hearing Screening by Automated Auditory Brainstem Response Measurement." Pediatrics 101 (2): 221–228. doi:10.1542/ peds.101.2.221.

Mathers, C. D., A. Smith, and M. Concha. 2003. Global Burden of Hearing Loss in the Year 2000. Geneva: World Health Organization.

Mehl, A. L., and V. Thomson. 2002. "The Colorado Newborn Hearing Screening Project, 1992–1999: On the Threshold of Effective PopulationBased Universal Newborn Hearing Screening." Pediatrics 109 (1): E7. doi: 10.1542/peds.109.1.e7.

Moher, D., L. Shamseer, M. Clarke, D. Ghersi, A. Liberati, M. Petticrew, P. Shekelle, et al. 2015. "Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 Statement." Systematic Reviews 4 (1): 1–9. doi:10.1186/2046-4053-4-1.

National Statistics Republic of China (Taiwan). 2018. "Latest Indicators, per Capita GNI (US Dollars)." https://eng.stat.gov.tw/point.asp?index=1.

Neumann, K., M. Gross, P. Böttcher, H. A. Euler, M. Spormann-Lagodzinski, and M. Polzer. 2006. "Effectiveness and Efficiency of a Universal Newborn Hearing Screening in Germany." Folia Phoniatrica et Logopaedica 58 (6): 440–455. doi:10.1159/000095004.

Ng, P. K., Y. Hui, B. C. C. Lam, W. H. S. Goh, and C. Y. Yeung. 2004. "Feasibility of Implementing a Universal Neonatal Hearing Screening Programme Using Distortion Product Otoacoustic Emission Detection at a University Hospital in Hong Kong." Hong Kong Medical Journal = Xianggang yi Xue za Zhi 10 (1): 6–13. PMID: 14967849.

Olusanya, B. O., and A. O. Somefun. 2009. "Place of Birth and Characteristics of Infants with Congenital and Early-Onset Hearing Loss in a Developing Country." International Journal of Pediatric Otorhinolaryngology 73 (9): 1263–1269. doi:10.1016/j.ijporl.2009.05.018.

Pastorino, G., P. Sergi, M. Mastrangelo, P. Ravazzani, G. Tognola, M. Parazzini, F. Mosca, et al. 2007. "The Milan Project: A Newborn Hearing Screening Programme." Acta Paediatrica 94 (4): 458–463. doi:10.1111/j. 1651-2227.2005. tb01918.x.

Plummer, M. 2016. "rjags: Bayesian Graphical Models Using MCMC. R package version 4-6." https://CRAN.R-project.org/package=rjags.

Prieve, B. A., and F. Stevens. 2000. "The New York State Universal Newborn Hearing Screening Demonstration Project: Introduction and Overview." Ear and Hearing 21 (2): 85–91. doi:10.1097/00003446-200004000-00003.

Qi, B., X. Cheng, H. En, B. Liu, S. Peng, Y. Zhen, Z. Cai, et al. 2013. "Assessment of the Feasibility and Coverage of a Modified Universal Hearing Screening Protocol for Use with Newborn Babies of Migrant Workers in Beijing." BMC Pediatrics 13 (1): 116. doi:10.1186/1471-243113-116.

Shamseer, L., D. Moher, M. Clarke, D. Ghersi, A. Liberati, M. Petticrew, P. Shekelle, et al. 2015. "Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) Elaboration and Explanation." BMJ 350: g7647. doi:10.1136/bmj.g7647.

Sloot, F., H. L. Hoeve, M. L. de Kroon, A. Goedegebure, J. Carlton, H. J. Griffiths, H. J. Simonsz, et al. 2015. "Inventory of Current EU Paediatric Vision and Hearing Screening Programmes." Journal of Medical Screening 22 (2): 55–64. doi:10.1177/0969141315572403.

Smith, A. W. 2008. "Demographics of Hearing Loss in Developing Countries." In Audiology in Developing Countries, edited by B. McPherson and R. Brouillette, 21–50. New York: Nova Science Publishers, Inc.

Smith, S. D., and R. T. Taggart. 2004. "Chapter 5. Genetic Hearing Loss with No Associated Abnormalities." In Hereditary Hearing Loss and Its Syndromes, edited by H.V. Toriello, W. Reardon, and R. J. Gorlin. New York: Oxford University Press.

Stevens, G., S. Flaxman, E. Brunskill, M. Mascarenhas, C. D. Mathers, and M. Finucane. 2013. "Global and Regional Hearing Impairment Prevalence: An Analysis of 42 Studies in 29 Countries." European Journal of Public Health 23 (1): 146–152. doi:10.1093/eurpub/ckr176.

Sun, X., X. Shen, D. Zakus, J. Lv, Z. Xu, H. Wu, W. Hsiao, et al. 2009. "Development of an Effective Public Health Screening Program to Assess Hearing Disabilities among Newborns in Shanghai: A Prospective Cohort Study." World Health and Population 11 (1): 14–23. PMID: 20039591.

Sutton, A. J., and K. R. Abrams. 2001. "Bayesian Methods in Meta-Analysis and Evidence Synthesis." Statistical Methods in Medical Research 10 (4): 277–303. doi:10.1177/096228020101000404.

Sutton, A. J., S. J. Duval, R. L. Tweedie, K. R. Abrams, and D. R. Jones. 2000. "Empirical Assessment of Effect of Publication Bias on MetaAnalyses." BMJ 320 (7249): 1574–1577. doi:10.1136/bmj.320.7249.1574.

Swanepoel, D., S. Ebrahim, A. Joseph, and P. L. Friedland. 2007. "Newborn Hearing Screening in a South African Private Health Care Hospital." International Journal of Pediatric Otorhinolaryngology 71 (6): 881–887. doi:10.1016/j.ijporl.2007.02.009.

Tajik, S., and M. Ahmadpour-Kacho. 2016. "Early Diagnosis and Intervention for Hearing Loss in Newborns Discharged from Intensive Care Units: A Four-Year Follow-up Study in North of Iran." International Journal of Pediatrics-Mashhad 4 (8): 3283–3291. doi:10.22038/IJP.2016. 7154.

Uus, K., and J. Bamford. 2006. "Effectiveness of Population-Based Newborn Hearing Screening in England: Ages of Interventions and Profile of Cases." Pediatrics 117 (5): e887–e893. doi:10.1542/peds.2005-1064.

Van Der Ploeg, C. P. B., N. N. Uilenburg, M. A. Kauffman-De Boer, A. M. Oudesluys-Murphy, and P. H. Verkerk. 2012. "Newborn Hearing Screening in Youth Health Care in The Netherlands: National Results of Implementation and Follow-up." International Journal of Audiology 51 (8): 584–590. doi:10.3109/14992027.2012.684402.

Van Dommelen, P., A. D. Mohangoo, P. H. Verkerk, C. P. Van Der Ploeg, H. L. Van Straaten, and The Dutch NICU Neonatal Hearing Screening Working Group. 2010. "Risk Indicators for Hearing Loss in Infants Treated in Different Neonatal Intensive Care Units." Acta Paediatrica 99 (3): 344–349. doi:10.1111/j.1651-2227.2009.01614.x.

Van Kerschaver, E., A. N. Boudewyns, F. Declau, P. H. Van de Heyning, and F. L. Wuyts. 2013. "Socio-Demographic Determinants of Hearing Impairment Studied in 103,835 Term Babies." The European Journal of Public Health 23 (1): 55–60. doi:10.1093/eurpub/cks010.

Van Straaten, H. L., E. T. Hille, J. H. Kok, P. H. Verkerk, and Dutch NICU Neonatal Hearing Screening Working Group. 2007. "Implementation of a Nation-Wide Automated Auditory Brainstem Response Hearing Screening Programme in Neonatal Intensive Care Units." Acta Paediatrica 92 (3): 332–338. doi:10.1111/j.1651-2227.2003.tb00555.x.

Viechtbauer, W. 2010. "Conducting Meta-Analyses in R with the metafor Package." Journal of Statistical Software 36 (3): 1–48. doi:10.18637/jss. v036.i03.

Vos, B., C. Senterre, R. Lagasse, G. Tognola, and A. Leveque. 2016. "Organisation of Newborn Hearing Screening Programmes in the European Union: Widely Implemented, Differently Performed." The European Journal of Public Health 26 (3): 505–510. doi:10.1093/eurpub/ ckw020.

Wang, C.-H., C.-Y. Yang, R. Lien, S.-M. Chu, J.-F. Hsu, R.-H. Fu, M.-C. Chiang, et al. 2017.

"Prevalence and Independent Risk Factors for Hearing Impairment among Very Low Birth Weight Infants." International Journal of Pediatric Otorhinolaryngology 93: 123–127. doi:10.1016/j.ijporl.2016.12. 029.

Watkin, P. M., and M. Baldwin. 1999. "Confirmation of Deafness in Infancy." Archives of Disease in Childhood 81 (5): 380–389. doi:10.1136/ adc.81.5.380.

Watson, D. R., R. J. McClelland, and D. A. Adams. 1996. "Auditory Brainstem Response Screening for Hearing Loss in High Risk Neonates." International Journal of Pediatric Otorhinolaryngology 36 (2): 147–183. doi:10.1016/0165-5876(96)01352-3.

Wells, G., B. Shea, D. O'Connell, J. Peterson, V. Welch, M. Losos, and P. Tugwell. 2018. "The Newcastle-Ottawa Scale (NOS) for assessing the quality of non-randomised studies in meta-analysis." Accessed 23 July 2019. http:// www.ohri.ca/programs/clinical_epidemiology/oxford.asp.

Wenjin, W., T. Xiangrong, L. Yun, L. Jingrong, C. Jianyong, W. Xueling, H. Zhiwu, et al. 2018. "Neonatal Hearing Screening in Remote Areas of China: A Comparison between Rural and Urban Populations." Journal of International Medical Research 46 (2): 637–651. doi:10.1177/ 0300060517706643.

Wolff, R., J. Hommerich, R. Riemsma, G. Antes, S. Lange, and J. Kleijnen. 2010. "Hearing Screening in Newborns: Systematic Review of Accuracy, Effectiveness, and Effects of Interventions after Screening." Archives of Disease in Childhood 95 (2): 130–135. doi:10.1136/ adc.2008.151092.

World Bank Group. 2018. "GNI per Capita, PPP (Current International $)." Accessed 22 November 2018. https://data.worldbank.org/ indicator/NY. GNP.PCAP.PP.CD.

World Health Organization. 2018. "Prevention of blindness and deafness – grades of hearing impairment." https://www.who.int/pbd/ deafness/hearing_impairment_grades/en/.

Wroblewska-Seniuk, K., G. Greczka, P. Dabrowski, W. Szyfter, and J. Mazela. 2017. "The Results of newborn hearing Screening by Means of Transient Otoacoustic Emissions – Has Anything Changed over 10 Years?" International Journal of Pediatric Otorhinolaryngology 96: 4–10. doi:10. 1016/j.ijporl.2017.02.021.

Yoshinaga-Itano, C., and M. L. Apuzzo. 1998a. "The Development of Deaf and Hard of Hearing Children Identified Early through the High-Risk Registry." American Annals of the Deaf 143 (5): 416–424. doi:10.1353/aad. 2012.0118.

Yoshinaga-Itano, C., and M. L. Apuzzo. 1998b. "Identification of Hearing Loss after Age 18 Months Is Not Early Enough." American Annals of the Deaf 143 (5): 380–387. doi:10.1353/ aad.2012.0151.

Zelante, L., P. Gasparini, X. Estivill, S. Melchionda, L. D'Agruma, N. Govea, M. Mila, et al. 1997. "Connexin26 Mutations Associated with the Most Common Form of Non-Syndromic Neurosensory Autosomal Recessive Deafness (DFNB1) in Mediterranean." Human Molecular Genetics 6 (9): 1605–1609. doi:10.1093/ hmg/6.9.1605.

Zuhair, M., G. S. A. Smit, G. Wallis, F. Jabbar, C. Smith, B. Devleesschauwer, and P. Griffiths. 2019. "Estimation of the Worldwide Seroprevalence of Cytomegalovirus: A Systematic Review and Meta-Analysis." Reviews in Medical Virology 29 (3): e2034. doi:10.1002/rmv.2034.

Chapter 3

Assessment of hearing screening programmes across 47 countries or regions I: Provision of newborn hearing screening

*Andrea ML Bussé**
*Allison R Mackey**
Hans LJ Hoeve
André Goedegebure
Gwen Carr
Inger M Uhlén
HJ Simonsz

the EUS€REEN Foundation

**Contributed equally and should be considered dual first authors*

ABSTRACT

Objectives

Newborn hearing screening (NHS) varies regarding number and type of tests, location, age, professionals and funding. We compared the provision of existing screening programmes.

Design

A questionnaire containing nine domains: demography, administration, existing screening, coverage, tests, diagnosis, treatment, cost and adverse effects, was presented to hearing screening experts. Responses were verified. Clusters were identified based on number of screening steps and use of OAE or aABR, either for all infants or for well and high-risk infants (dual-protocol).

Study Sample

Fifty-two experts completed the questionnaire sufficiently: 40 European countries, Russia, Malawi, Rwanda, India and China.

Results

It took considerable effort to find experts for all countries with sufficient time and knowledge. Data essential for evaluation are often not collected. Infants are first screened in maternity wards in most countries. Human development index and health expenditure were high among countries with dual protocols, three screening steps, including aABR, and low among countries without NHS and countries using OAE for all infants. Nationwide implementation of NHS took six years, on average.

Conclusion

The extent and complexity of NHS programmes are primarily related to health expenditure and HDI. Data collection should be improved to facilitate comparison of NHS programmes across borders.

INTRODUCTION

It has been 20 years since the first publications on the longstanding benefits of early detection of hearing impairment (HI) and intervention through newborn hearing screening (NHS) programmes (Yoshinaga-Itano and Apuzzo, 1998a, Yoshinaga-Itano and Apuzzo, 1998b, Yoshinaga-Itano et al., 1998). Prior to NHS, methods used to identify infants with HI included an inventory of risk factors or universal screening using the distraction test. The distraction test was not feasible until at least 7 months of age, and results were highly confounded by false positives and false negatives (Davis et al., 2001). In the 1990s, objective hearing tests such as otoacoustic emission (OAE) and automated auditory brain stem response (aABR) allowed screening to be performed at a much younger age. Using these tests reduced the cost per infant tested by half (Stevens et al., 1998, Uus et al., 2006). Reducing the age of hearing screening opened the possibility for earlier intervention, minimising the impact of HI on speech, language and general development and academic performance (Ching et al., 2018).

Many countries, regions and hospitals across the world have since implemented and sustained a universal NHS programme, in which infants eligible for screening are defined as all infants who are born in a certain country, region, or hospital. Variations exist across countries in how newborn hearing screening programs are implemented, which may make it difficult for policy makers and professionals in other locations to decide on best-practice protocols. International position statements provide some guidance for best practice (Joint Committee on Infant Hearing, 2007, World Health Organization, 2009, European Consensus Statement on Neonatal Hearing Screening., 1999). Furthermore, differences exist in health care environments across countries. Hearing screening experts or policy makers may need to adapt guidelines and construct protocols for the successful implementation of NHS in their local health care environment (World Health Organization, 2009). All NHS programmes aim to identify infants with HI early in life so that appropriate intervention may be provided, but different approaches are used to reach this shared goal (Sloot et al., 2015, World Health Organization, 2009, Vos et al., 2016).

Existing NHS programmes have been compared in a number of studies. These studies differed in the methods used, the countries or regions included, and the scope of the study (White, 2010, Sloot et al., 2015, Vos et al., 2016, Kanji et al., 2018, World Health Organization, 2009). These studies identified common screening sequences used across existing NHS programmes. An aABR protocol with multiple steps was most prominently used for infants with an increased risk for HI or retrocochlear dysfunction. An OAE protocol was most prominently used for infants without this risk. However, the central finding in these studies was that the choices made within NHS programme organisation and protocol design are diverse across countries. Within NHS, studies have not yet investigated the nature of the diversity of protocol design, the interaction of parameter choices, the country-specific factors behind the decisions that drive policy on NHS, and the possibility of harmonising best-practice guidelines within Europe.

A more detailed and essential overview of implemented NHS programmes is needed to inform policy makers on the considerations for planning and implementing NHS. When making the decision to implement an NHS programme, policy makers may consider the local (health care) circumstances, previous experiences, advice received from other programmes, or implementation research performed within the programme or elsewhere. The diversity between NHS programmes across regions and countries makes it difficult for policy makers to decide on how to optimise existing NHS programmes or how to implement a new NHS programme in their country.

The EUSCREEN study evaluates and compares the cost-effectiveness of vision and hearing screening programmes. A decision-analytic cost-effectiveness model is being developed to calculate the optimal, most cost-effective vision and hearing screening programme taking the local circumstances of a country into account. This model will be made available to health care policy makers to introduce, modify or disinvest screening programmes. For the development of this model, detailed information regarding hearing screening protocols, organisation of general preventive healthcare and local societal background was needed. We therefore carried out a comprehensive inventory of hearing screening in countries and regions, primarily in Europe.

This article and the accompanying article (Mackey et al., 2021) explore the results from this international inventory of hearing screening programmes. Specifically, these articles evaluate the existing approaches to NHS, its outcomes, and the possible features that influence NHS policy and performance. The current article inventories the provision, status and features of NHS in 45 countries to better understand the variability and the rationale for the diversity across programmes. The factors explored in this article include organisation, protocols, screening targets, referral pathway, infant age, location, screening professionals, and funding. The accompanying article (Mackey et al., 2021) details the effectiveness of NHS programmes from screening quality measures. In these articles, NHS is defined as hearing screening performed from birth to age 6 months. A description of childhood hearing screening programmes after the newborn period will be reported on in a separate article.

METHODS

Development of the questionnaire

A comprehensive questionnaire was developed to gather detailed information on general paediatric, vision and hearing screening programmes, following the success of a pilot study described in Sloot et al. (2015). Within this pilot study, a short questionnaire containing 25 questions was sent out to screening experts in 38 countries to measure their response, and almost all participated. A focus group of hearing and screening experts formulated 191 questions on hearing screening. An additional 126 questions were formulated on vision screening and 82 questions on general screening. Questions were categorised into nine domains: demography and epidemiology, administration and general background, existing screening programmes, coverage and attendance, tests and devices, follow up and diagnostic assessment, treatment options, costs and benefits and adverse effects.

Three types of questions were used: open-ended, multiple-choice and yes-no questions. Most of the questions were followed by a sub-question about the source of the information provided. A respondent could choose between (a) Data unavailable, (b) I don't know, (c) Rough estimate, (d) Real estimate from calculation, or (e) Actual data. The questionnaire then asked for the name and date of the data source if indicated.

The EUSCREEN questionnaire (Appendix 1) was converted to a web-based questionnaire, accessible through the EUSCREEN website (www.euscreen.org). As a separate consortium partner within the EUSCREEN study, the EUS€REEN foundation served to collect the data. So called Country Representatives (CRs) were elected by a tender procedure as prescribed by EU regulations, one for vision, one for hearing and one for general screening for each country. They were awarded a remuneration up to €2000 after they had sufficiently completed their part of the questionnaire. CRs registered online and progressed through the tender procedure, in which their role in the local screening programme and rights to data were assessed. Once accepted, the CR could log in using a unique username and password.

Formation of the Country-Committees Joint-Partnership of EUS€REEN Study Consortium

The Country-Committees Joint-Partnership of EUS€REEN foundation had been formed as an international collaboration of CRs in hearing, vision and general screening. In each of these countries, CRs on hearing screening were actively searched through screening organisations, publications in peer reviewed journals on the subject, national audiology and ENT societies, existing professional contacts and other CRs who had already registered. CRs representing countries or regions outside of the original selection were not actively searched, though they were welcome to participate. The CRs were contacted through e-mail, telephone calls and in-person meetings during conferences. When CRs were unable to complete the questionnaire, measures were taken to find additional CRs.

Collection of data

Preliminary efforts were made to collect data representing hearing screening for an entire country, but in many instances hearing screening programmes were organised and managed regionally. In these circumstances, the questionnaire was answered by a regional CR and these data were then considered representative only for that regional screening programme.

The questionnaire was originally accessible on the EUSCREEN website from March 2017 until December 2018. Several CRs required significant time for receiving approval, calculating results, and sharing outcomes from internal registries so the deadline for data submission was extended to June 30th 2019 (Figure 1, Appendix 2). CRs were encouraged to seek information and support from local contacts and resources in their home country or region to help fill in any unknown answers (e.g., costs of screening).

Multiple steps were taken to ensure the accuracy of the data. Firstly, CRs were asked to agree to an audit to validate responses. Secondly, when multiple CRs agreed to answer the questionnaire for the same programme, the same questions were asked to all CRs. Thirdly, the CRs were asked to cite the source of their answers in all relevant cases and provide a copy to the researchers if accessible, additional sources were searched for and accessed online. Source material was translated via Google Translate when necessary for verification purposes. In order to track any inconsistencies in the definitions of terms used in the questionnaire, a glossary was created and distributed (Appendix 3).

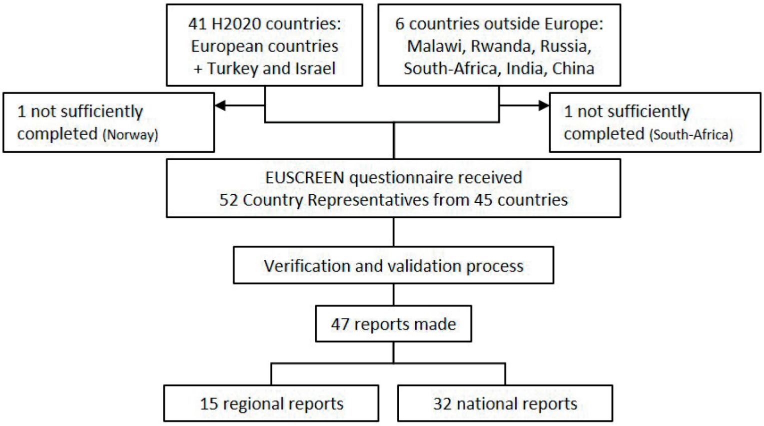


Figure 1. Flow chart displaying the number of participating countries, the number of reports made and the number of countries with NHS implemented. In some cases, multiple CRs filled out the questionnaire for the same country, in other cases, more reports were made for regions wihtin the same country

Validation of answers and clarification

Each survey response went through a verification and validation process (Figure 2, Appendix 2). Firstly, each response was checked for completeness and was cross-checked internally. In cases where multiple CRs completed the questionnaire for one programme, the consistency of each answer was evaluated between respondents. In all cases, answers were evaluated to other similar answers provided by the same respondent. Secondly, answers were cross-checked externally with source material provided and acquired through a programme-specific literature search. Thirdly, a list of clarification questions was prepared for each CR from any discrepancies noted in the verification process. This list contained any questions pertaining to: incomplete responses or inconsistencies noted during the verification stage, accessible source material that was not provided, responses based on a source that was not referenced, or responses of actual values or calculations where the details were not described or were inconsistent with the definition provided in the glossary. Finally, a report was drafted illustrating the current situation for childhood hearing screening in each participating country or region. Details of the definitions, source, and date of data collection were also described. The CRs were sent a copy of the report and provided their final comments and/or confirmed the final validity of the document.

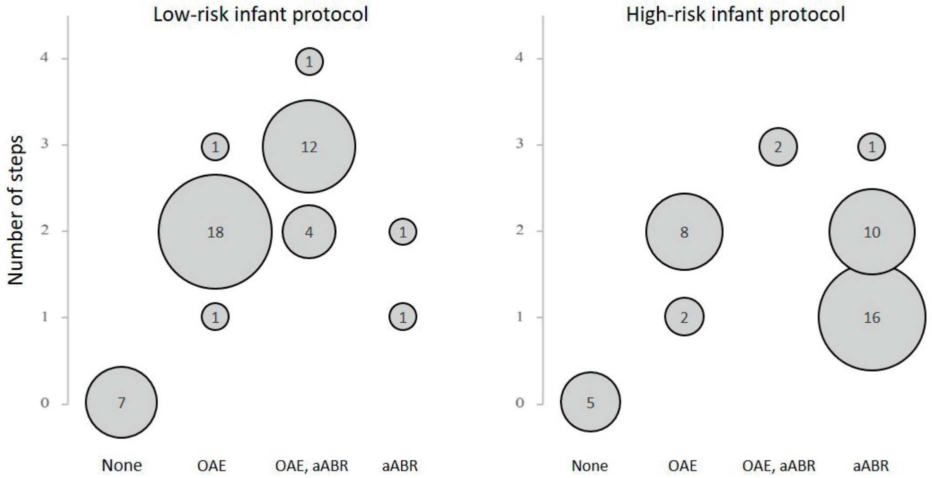


Figure 2. Type of protocol against number of steps. Protocols for low- and high-risk infants were combined with single-protocol design, in which the same protocol is used for both low- and high-risk infants. High-risk programmes that directly refer to diagnostic assessment without screening and programmes with varying protocols across a country or region were omitted. OAE, aABR: only the final step includes aABR, aABR for high-risk infants: aABR may be performed alone or together with OAE (OAE+aABR). A step is defined as that screening is performed and a result of pass or refer is obtained.

Data management

Demographic data such as World Bank classification, gross-domestic product (GDP) per capita, health expenditure and human development index (HDI) were added. The HDI uses life expectancy, education, and per capita income indicators to rank countries. (The World Bank, 2019, World Health Organization, 2019, United Nations Development Programme, 2019)

Programmes that use one test protocol to screen all eligible infants, are referred to as single-protocol design. A dual-protocol design is where a different protocol, which includes direct referral without screening, may be used for infants with an increased risk of HI. This group mainly consists of infants admitted to the neonatal intensive care unit (NICU); the other risk factors used are described in detail in Table 1, Appendix 2. Infants with an increased risk of HI are referred to as 'high-risk' infants, and all other infants, infants born well, are referred to as 'low-risk' infants. Programmes that only screen high-risk infants are defined as selective programmes.

Table 1. Programme reach and protocols described for low and high-risk infants in each country or region. The cluster analysis grouped countries or regions into five clusters based on five key variables of NHS programme design. The cluster number depicts the result of the cluster analysis, indicating to which cluster each country or region was assigned. The clusters are numbered as follow: 1=No NHS, 2=Selective NHS, 3=Single OAE-only, 4=Dual OAE-only, 5=Dual including aABR.

Country	Region represented	Programme organisation & reach		Test Sequence low-risk infants	Age step 1	Single/ Dual protocol	Test sequence high-risk infants	Cluster
Albania		No NHS programme						1
Kosovo		No NHS programme						1
Malawi		No NHS programme						1
Rwanda		No NHS programme						1
Montenegro		No NHS programme						1
Malta		Not nationwide	Selective				OAE, OAE	2
North Macedonia	Skopje Region	Not nationwide	Selective				OAE, OAE	2
Romania		Not nationwide	Universal	OAE°, OAE	24-72h	Dual	OAE	3
Bosnia Herzegovina	Tuzla Canton	Not nationwide	Universal	OAE, OAE	24-72h/>72h	Single	OAE, OAE	3
Latvia		Nationwide	Universal	OAE, OAE	>72h	Single	OAE, OAE	3
Lithuania		Nationwide	Universal	OAE, OAE	24-72h/>72h	Single	OAE, OAE	3
Serbia	Belgrade	Not nationwide	Universal	OAE, OAE	24-72h	Single	OAE, OAE	3
Moldova	Chisinau	Not nationwide	Universal	OAE, OAE	24-72h	Single	OAE, OAE	3
Faroe Islands		Nationwide	Universal	OAE, OAE, aABR	>72h	Single	OAE, OAE, aABR	3
Estonia		Nationwide	Universal	OAE°, OAE, aABR	24-72h	Single	OAE, OAE, aABR	3
Belgium	Wallonia-Brussels Federation	Nationwide	Universal	OAE, OAE	24-72h	Dual	Diagnostic assessment	4
Russia		Nationwide	Universal	OAE°	24-72h	Dual	OAE, diagnostic assessment	4
Austria	Upper Austria	Nationwide	Universal	OAE, OAE	24-72h	Dual	aABR, aABR	4
Croatia		Nationwide	Universal	OAE, OAE	24-72h	Dual	aABR/(OAE), aABR	4
Czechia	East Bohemia	Not nationwide	Universal	OAE°, OAE	24-72h	Dual	aABR, aABR	4
Poland		Nationwide	Universal	OAE, OAE	24-72h	Dual	OAE, OAE, diagnostic assessment	4
Luxembourg		Nationwide	Universal	OAE, OAE	24-72h	Dual	aABR, aABR	4

Table 1. Programme reach and protocols described for low and high-risk infants in each country or region. The cluster analysis grouped countries or regions into five clusters based on five key variables of NHS programme design. The cluster number depicts the result of the cluster analysis, indicating to which cluster each country or region was assigned. The clusters are numbered as follow: 1=No NHS, 2=Selective NHS, 3=Single OAE-only, 4=Dual OAE-only, 5=Dual including aABR. (continued)

Country	Region represented	Programme organisation & reach		Test Sequence low-risk infants	Age step 1	Single/ Dual protocol	Test sequence high-risk infants	Cluster
Spain	Aut. Comm. Valencia	Nationwide	Universal	OAE°, OAE	24-72h	Dual	aABR	4
Bulgaria		Nationwide	Universal	OAE°, OAE	24-72h	Dual	OAE+aABR	4
Portugal	Lisbon Region	Nationwide	Universal	OAE, OAE	24-72h	Dual	aABR	4
Slovakia		Nationwide	Universal	OAE, OAE	24-72h	Dual	OAE+aABR	4
Slovenia		Nationwide	Universal	OAE, OAE	24-72h	Dual	aABR	4
Switzerland		Nationwide	Universal	OAE, OAE	24-72h	Dual	aABR	4
Spain	Princip. Asturias	Nationwide	Universal	OAE, OAE, OAE	24-72h	Dual	OAE+aABR, (OAE, OAE)	4
Hungary		Nationwide	Universal	aABR°	24-72h	Single	aABR	5
China		Not nationwide	Universal	OAE, aABR	24-72h	Dual	OAE+aABR	5
Cyprus	Southern part	Nationwide	Universal	OAE, OAE, aABR	>72h	Dual	OAE+aABR	5
Israel		Nationwide	Universal	OAE°, aABR°	24-72h	Dual	OAE+aABR	5
Denmark		Nationwide	Universal	OAE/aABR, OAE+aABR	>72h	Dual	OAE+aABR	5
Belgium	Flanders	Nationwide	Universal	aABR, aABR	>72h	Single	aABR, aABR	5
France	Ile de France	Nationwide	Universal	OAE/aABR, OAE/aABR, (OAE/aABR)	24-72h	Dual	aABR, aABR, aABR	5
Germany	Westphalia-Lippe	Nationwide	Universal	OAE/aABR, aABR	<24h->72h	Dual	aABR, aABR	5
Greece	Attikon Hospital	Not nationwide	Universal	OAE, OAE, aABR	24-72h	Dual	OAE+aABR, aABR	5
Iceland		Nationwide	Universal	OAE, OAE, aABR	>72h	Dual	OAE+aABR, aABR	5
Netherlands		Nationwide	Universal	OAE, OAE, aABR	>72h	Dual	aABR, aABR	5
Italy	Veneto Region	Not nationwide	Universal	OAE, OAE, aABR	24-72h	Dual	OAE+aABR, OAE+aABR	5
Sweden	Stockholm Region	Nationwide	Universal	OAE, OAE, OAE, aABR	24-72h	Dual	OAE+aABR	5
Finland		Nationwide	Universal	OAE, OAE, aABR	24-72h	Dual	Varies (aABR included)	5
Ireland		Nationwide	Universal	OAE, OAE, aABR	<24-72h	Dual	OAE+aABR	5

Table 1. Programme reach and protocols described for low and high-risk infants in each country or region. The cluster analysis grouped countries or regions into five clusters based on five key variables of NHS programme design. The cluster number depicts the result of the cluster analysis, indicating to which cluster each country or region was assigned. The clusters are numbered as follow: 1=No NHS, 2=Selective NHS, 3=Single OAE-only, 4=Dual OAE-only, 5=Dual including aABR. (continued)

Country	Region represented	Programme organisation & reach		Test Sequence low-risk infants	Age step 1	Single/ Dual protocol	Test sequence high-risk infants	Cluster
England (U.K.)	S.E. London	Nationwide	Universal	OAE, OAE, aABR	<24h	Dual	OAE+aABR	5
Turkey		Nationwide	Universal	OAE°, OAE°, aABR°	24-72h	Dual	aABR	5
India		Not nationwide	Varies	Varies			Varies	-

° Multiple screens allowed within 1 step

Brackets indicate screening steps that are sometimes performed

/ either OAE or aABR may be used depending on the region or hospital

The age indicated is the time period in which the majority of infants are screened

Table 2. Results of the cluster analysis. Clusters of protocols in 46 countries or regions with similar approaches for NHS design were revealed. Five variables were used that most comprehensively represent the NHS protocols. Categories for NHS programme type are: no NHS programme is established, if NHS is selective (high-risk only), if a one protocol is used for all infants (single-design) or if seperate protocols are used for high-risk and low-risk infants (dual-design). India was excluded from the cluster analysis because insufficient information was available regarding the different protocols used, categories could not be assigned.

		No NHS (n=5)	*Selective NHS (n=2)*	*Single OAE-only (n=8)*	*Dual OAE-only (n=14)*	*Dual incl. aABR (n=17)*
NHS programme type (None / Selective /Single-design / Dual-design)		None (n=5)	Selective (n=2)	Single (n=7) Dual (n=1)	Single (n=0) Dual (n=14)	Single (n=2) Dual (n=15)
Low-risk infants	Tests used in protocol	N/A	N/A	OAE only (n=6)	OAE only (n=14)	aABR incl. (n=17)
	Number of steps	N/A	N/A	2 steps (n=6)	2 steps (n=11)	3 steps (n=10)
High-risk infants	Tests used in step 1	N/A	OAE only (n=2)	OAE only (n=8)	aABR incl. (n=14)	aABR incl. (n=17)
	Number of steps	N/A	2 steps (n=2)	2 steps (n=5)	1 step (n=8)	1 step (n=10)

Cluster analysis

A hierarchical agglomerative cluster analysis using a complete-linkage method was performed in SPSS (v.26.0), to identify groups of NHS programmes with similar protocol designs. Due to the relatively small sample, the number of variables that could be included in the cluster analysis were restricted. Factors such as screening location, professional, and infant age were not considered, as these decisions may be driven by the existing local structure of postnatal care. The diversity of decisions made on NHS protocol designs, however, was unexplained. Five variables were selected that comprehensively described the entire NHS protocol design: the programme type (no NHS programme, selective programme, single-protocol programme, or dual-protocol programme), the choice of using OAE only vs. including aABR in the protocol for low-risk infants, the number of steps for low-risk infants, the choice of using only OAE in step 1 (i.e., without aABR/ABR) for high-risk infants, and the number of steps for high-risk infants. The use of aABR technology in any step (low-risk) or step 1 (high-risk) was based on strategies recommended by the Joint Committee on Infant Hearing (2019). A category of "Not Applicable" was available for each protocol variable and was assigned to countries without an established NHS programme or with selective screening where appropriate. Note that the definition of a "step" is that screening is performed and a result (i.e., pass or refer) is obtained. When both OAE and aABR screening tests are performed to obtain one result (pass or refer), this is considered one step. Because insufficient information was provided regarding the different protocols used across India, assigning values for these variables was not possible and India was not included in the cluster analysis.

Clustering NHS programmes into groups, can reveal key factors that may be related to design choices. In an agglomerative method, clusters are built up into larger and larger groups until all cases are included. This is represented in a dendrogram (Table 2, Appendix 2). The dendrogram displays how closely countries or regions are linked together. The complete-linkage method was used to create links between countries or regions, as this method can be applied to categorical (nominal) data. In the complete-linkage method, the maximum distance between two clusters is calculated to determine the dissimilarity between all cases, resulting in a dissimilarity matrix for all pairwise comparisons. A chi-square measure was used to calculate this distance. The resulting distance between clusters is that between the furthest possible points (Defays, 1977). The optimal number of clusters was validated using the stopping rule with the agglomeration coefficients (indicating the heterogeneity between clusters) and a comparison of silhouette coefficients. Silhouette coefficients measure the strength of cluster cohesion and separation. To apply the stopping rule, the agglomeration coefficient chart was visually inspected across an increasing number of clusters to identify the point before a large drop in value. Finally, the dendrogram was inspected to consider the utility of the clustering.

Kruskal-Wallis tests (a non-parametric test to compare independent samples) were performed to evaluate measures of health expenditure per capita and HDI across clusters. Health expenditure per capita was selected as it represents the potential financial resources available for

NHS on a system level, and HDI was selected as it represents a broader measure of social and economic growth on an individual level (scale of 0 to 1). P-values were adjusted by Bonferroni correction for multiple pairwise comparisons where applicable.

RESULTS

Recruitment of hearing screening experts

Recruiting a local CR with knowledge about the local screening programme was the preferred option for sharing and aggregating data. However, the level of access to information of local CRs needed to be established. It took considerable effort to identify a single representative across all countries with the breadth of knowledge and equally importantly the time to fill out the full extensive questionnaire. For many programmes, CRs consulted other professionals with knowledge of the requested information to help them complete unknown answers. If the questionnaire could not be completed fully, additional CRs were engaged to complete the remainder of the questionnaire. This enabled data supply from multiple sources covering elements such as costs, prevalence and intervention options.

Even for some highly developed screening programs, some information was not recorded within the programme or was not accessible by the CR. This information was regularly unavailable for questions on intervention, quality indicators, costs, prevalence, and sensitivity/specificity of screening. For questions on NHS organisation, screening professionals, and target age and conditions, over 90% of the countries or regions provided complete answers (Figure 3, Appendix 2).

During the collection of information, regular contact was maintained with CRs to encourage the data completion. Furthermore, CRs were supported when technical difficulties occurred. When registered CRs encountered difficulties or did not have access to the requested information, new CRs had to be found. The first hearing CR registered on April 12th, 2017, the last complete questionnaire was submitted on June 30th, 2019. It took a considerable amount of time for CRs to collect all necessary information and fill out the questionnaire. It took a mean of 114 days between registration on the website and submission of the questionnaire (median of 44, range from 1 to 558 days) (Figure 1, Appendix 2).

Participating countries, regions and reporting CRs

The web-based questionnaire was completed sufficiently by a total of 52 CRs from 45 countries out of at least 85 CRs approached (Figure 1). CRs from Norway and South Africa did not fill out the questionnaire sufficiently for inclusion in the analysis. The participation of countries that were geographically located within or affiliated with Europe was actively sought. Out of all countries fully or partially geographically located in Europe, 39 were represented in

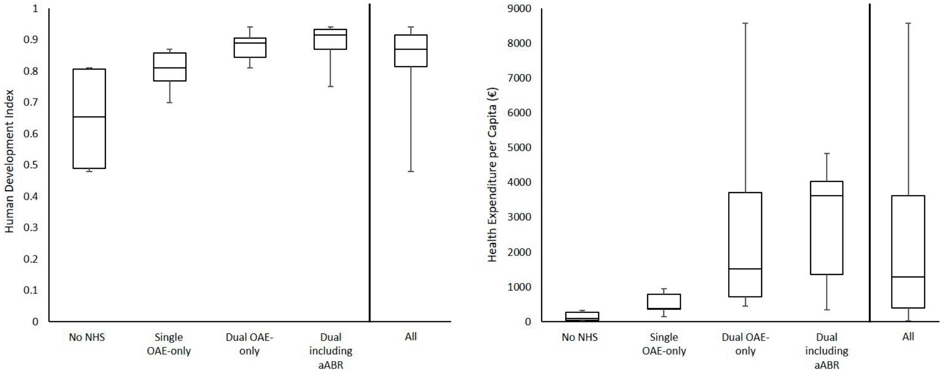


Figure 3. Box plots displaying the Human Development index and health expenditure per capita separately for each cluster expect the *Selective NHS* cluster and for all five clusters combined. The *selective NHS* cluster is not displayed because only two countries are included, Malta and North Macedonia. Health expenditure per capita and human development index for each country are available in Table 2, Appendix 2. The *No NHS cluster* contains countries without established NHS. *Single OAE only* contains mostly protocols that screen infants with low and high risk for HI with the same protocol (OAE only). In *Dual OAE-only* and *Dual including aABR* different protocols are used to screen infants with low and high risk for HI. For protocols in *Dual OAE-only,* only OAE is used to screen low-risk infants; protocols in *Dual including aABR* include aABR. The box plots represent the median (centre line), the 25th and 75th percentile (length of the box) with whiskers indicating the minimum and maximum values.

the analysis. Faroe Islands participated independently from Denmark. All member states of the European Union participated, in addition to Israel as an associated state.

Despite the predominance of participating countries in or affiliated with Europe, participation in this study was open to any country. The additional countries supplied information that could not be collected from within Europe, i.e., from very large or highly populated countries and from low-income countries.

The participating countries included two low-income, three lower-middle income, 10 upper-middle income, and 30 high-income countries, according to the World Bank classification system (The World Bank, 2019). The GDP per capita ranged from €195 to €92600 (median: €16560), and annual health expenditure per capita ranged from €30 to €8575 (World Health Organization, 2019). HDI ranged from 0.477 to 0.944 (median: 0.870) (United Nations Development Programme, 2019) (Table 2, Appendix 2).

CRs were predominantly medical professionals, of which the majority were otorhinolaryngologists. Of all CRs, 30 were involved in the organisation of the screening programme, two supervised screening, 18 were involved in diagnostic assessment and intervention of infants failing the screening and two were involved in other health care provision.

Current status and presence of NHS programmes

A total of 42 established NHS programmes were included in the analysis. A complete list of participating countries and regions with their corresponding NHS programme (if applicable) can be found in Table 1, including the variety of protocols, organisational authority and reach. Because of the multi-step verification and validation process performed, there is a high level of confidence in the information reported in this article.

Nationwide universal NHS is lacking in more low- and middle-income countries than high-income countries. For the 30 high-income countries surveyed, four do not have nationwide universal NHS, while for the 15 low- and middle-income countries surveyed, 12 lack nationwide universal NHS. These 12 countries are among the low- and middle-income countries with the lowest health care expenditure per capita and GDP per capita. Out of these 12 countries, five do not have an established NHS programme, however, most perform some sort of screening. NHS may be project-based, only performed in private hospitals or only some hospitals provide selective screening.

NHS in the EU was first implemented in the mid-1990s, and a sharp incline in NHS implementation can be observed in the mid-2000s. It took an average of six years (median of three years, range of 0 to 18 years) for countries to achieve nationwide reach after implementation (Figure 4, Appendix 2).

Programme features

A dual protocol is reported to be followed in 29 programmes, which means that high-risk infants are screened using a different protocol as compared to low-risk infants. For nine NHS programmes, the same protocol is used for all infants, i.e., a single-protocol design. In Finland a single or dual protocol may be used depending on the hospital. Malta and North Macedonia have selective programmes. All protocols are described in Table 1 for individual programmes and summarised in Figure 2.

Variability was found across the indicators used to classify risk among participating NHS programmes with dual-protocol designs (Table 1, Appendix 2). Admittance to the NICU is commonly used as an indicator for high risk, although, the minimum length of stay in the NICU varies. For many NHS programmes additional risk indicators were reported (range of 0 to 12, average of 6), which may cover the infants admitted to the NICU (e.g., assisted ventilation, infections) or not (e.g., family history, caregiver concern).

The type of test and the number of steps for both low and high-risk infants are displayed in Figure 2. Some protocols were grouped together for the purpose of this comparison. Among protocols used for low-risk infants, a two-step protocol or three-step protocol is most frequent (Table 1 and Figure 2). In Hungary and Russia, a one-step protocol is used, however, repeat screening is allowed prior to discharge (i.e., counted in the same step). Among protocols used for high-risk infants, a one-step protocol or two-step protocol is most common (Table 1 and Figure 2). In the Wallonia-Brussels Federation (Belgium), high-risk infants are referred to diagnostics without screening. In Poland and Russia, high-risk infants are referred to diagnostics regardless of screening outcome. Fewer steps tend to be used when screening for HI among high-risk infants than for low-risk infants. The screening protocol for high-risk infants more often includes aABR to screen for retrocochlear disorders.

Within all 29 dual-protocol design programmes participating, OAE is used in step 1 for all low-risk protocols, and aABR is used in step 1 for 24 high-risk protocols. An aABR screen may be performed alone or together with an OAE screen in the same step (i.e., OAE+aABR). There are only two participating single-protocol programmes in which all infants are screened with aABR using either one or two steps. For the remaining seven single-protocol programmes, all infants are screened using OAE for steps 1 and 2. Two of these also have a third step using aABR.

Other NHS programme features such as screening professionals, screening location and the age of the infant at each step of screening varied across participating programmes (Table 3, Appendix 2). A large array of professionals perform screening, including nurses, audiologists, midwives, otorhinolaryngologists, paediatricians, dedicated screeners, and health care workers or technicians. Infants in most NHS programmes typically complete step 1 in the hospital (maternity ward or NICU) before discharge. Low-risk infants typically leave the maternity hospital between 24h and 72h after birth, steps 2 and 3 are usually performed after discharge. High-risk infants stay in the NICU longer and step 2 and 3 can take place before discharge if needed.

All 42 programmes are funded by the government or health insurance except for Cyprus and Poland, where the national programme is funded predominantly by charity. All participating NHS programmes are free for parents except in the Wallonia-Brussels Federation in Belgium where a fee is billed to parents upon discharge from the maternity hospital to supplement the costs. When infants are delivered in private maternity hospitals, parents would be charged for NHS by the hospital.

Aim of screening programme and criteria for referral

The Joint Committee on Infant Hearing (2007) makes recommendations on target age: completion of screening by 1 month of age, completion of diagnostics by 3 months of age and initiation of intervention by 6 months of age. CRs from 36 programmes indicated that they follow an existing local guideline (Table 4, Appendix 2). The typical age for hearing aid fitting was reported to be 0-6 months of age for 35 out of 42 NHS programmes. However, typical age of hearing aid fitting was reported to be above 6 months for four programmes without universal NHS and not specified for three programmes.

In addition to age, target conditions are also reported for the severity of HI for both screening and intervention. However, it is important to realise that target conditions are specified as a hearing threshold (dB HL) while OAE and aABR are screening technologies that estimate the integrity of auditory function. For screening, over half of the reporting programmes described a target condition of 20 dB HL or greater. Bilateral and unilateral HI are the reported target conditions for 22 low-risk infant and 17 high-risk infant programmes. Bilateral HI only is reported as the target condition for nine low-risk infant programmes and four high-risk programmes (Table 4, Appendix 2).

In most cases, devices from one manufacturer are often selected for an entire NHS programme. A total of 13 different models across seven manufacturers were reported by 25 NHS programmes.

For most participating programmes, hearing aids are fit when a HI exceeds 30 to 40 dB HL (25 out of 41), though the range varied across programmes from ≥21 to ≥60 dB HL. For about half of the participating programmes, unilateral HI is fitted, even if on a case-by-case basis; for the other half, only bilateral HI is fitted. Despite this fact, most still refer infants that fail screening in one ear only.

Cluster analysis: Screening protocols

Five clusters were optimally generated for 45 protocols of included countries or regions, except India. Silhouette values for four, five and six clusters were calculated to be 0.37, 0.58 and 0.62. It was not clear from the silhouette values alone whether to select a five- or six-cluster solution. The stopping rule was applied, which signified a stopping point at five clusters. Further inspection of the dendrogram (Table 2, Appendix 2) confirmed this approach. The dendrogram revealed that, for a six-cluster solution, only two countries (Estonia and Faroe Islands) would form the sixth cluster. Because these two countries would ultimately be excluded from further analyses of health expenditure per capita and HDI in a six-cluster solution, the five-cluster solution was optimal for evaluation.

Table 2 describes each of the five clusters. All countries without an established NHS programme were grouped into the first cluster: No NHS. Countries with selective screening (Malta and North Macedonia) were grouped into the second cluster: Selective NHS. The cluster analysis grouped countries and regions with existing universal NHS programmes into the remaining three clusters. In the Single OAE-only cluster, all infants (including high-risk) are screened using only OAE in step 1, and a single protocol design for both high- and low-risk infants is used in seven out of the nine programmes. In the Dual OAE-only cluster, an OAE-only protocol is used for low-risk infants in all 14 programmes, eleven of which have two steps. An aABR is used in step 1 for high-risk infants. Similarly, in the Dual including aABR cluster, aABR is used for high-risk infants; however, aABR is also used for low-risk infants either for initial screening or for rescreening. Ten programmes have three steps. In general, the number of steps were greater for low-risk protocols than for high-risk protocols. This is also revealed in Figure 2, which displays the protocols for low- and high-risk infants across both single- and dual-protocol designs. It displays a preference for two-step OAE and three-step OAE, aABR protocols for low-risk protocols, while no obvious preference is revealed for high-risk protocols. All protocols are described in Table 1 for individual programmes.

Kruskal-Wallis tests revealed significant differences in health expenditure per capita ($p<0.001$) and HDI ($p=0.001$) across all clusters except the Selective NHS cluster. These differences, including the percentiles for each metric across clusters are illustrated in Figure 3. Because the Selective NHS cluster contained only two countries (Malta and North Macedonia), it was excluded from the analysis. Post hoc pairwise comparisons for health expenditure per capita revealed significant differences between the Single OAE-only and the Dual including aABR cluster ($p=0.016$), between the No NHS and Dual including aABR cluster ($p<0.001$), and between the No NHS and Dual OAE-only cluster ($p=0.006$). Significant and near significant differences were also found for HDI between the Single OAE-only and Dual including aABR cluster ($p=0.013$), between the No NHS and Dual including aABR cluster ($p=0.003$) and between the No NHS and Dual OAE-only cluster ($p=0.055$). Although some of the reported protocols were region-specific, health expenditure per capita and HDI were only available for the whole country. Values were not available for Faroe Islands, so this country was excluded from the Kruskal-Wallis analyses.

DISCUSSION

Results of this study show that, in most participating countries, the first screening step takes place 24-72 hours after birth, before discharge from the maternity hospital. Countries with the lowest health expenditure and HDI do not have NHS yet. Among countries with NHS programmes, those with the lowest health expenditure and HDI use OAE only to screen all infants and use fewer screening steps. Screening is performed by a diversity of screening professionals. Implementation of NHS takes six years on average to scale up to nationwide screening.

In this study, a comprehensive survey was undertaken investigating all aspects of childhood hearing screening, from its organisation, protocol, intervention, outcomes and costs. The extensive international network of screening experts covered almost all countries in Europe. The information received was verified and validated ensuring high accuracy of the data reported. The original purpose of this study was to gather data about hearing screening programmes to populate a cost-effectiveness model, which is the main product of the EUSCREEN project. This model compares the cost-effectiveness of hearing screening programmes across countries, taking local circumstances into account.

However, much of the data essential for evaluation of cost-effectiveness, particularly the prevalence of HI, hearing screening outcomes, and costs, were not provided even by some countries with highly developed hearing screening programmes (Mackey et al., 2021). Data were sometimes not compiled in a central database, or data governance regulations prevented CRs from accessing or sharing the required information. Moreover, in some cases, CRs were well informed about one part of the hearing screening programme (e.g., screening low-risk infants) but were less familiar with other parts. It was a considerable time commitment to gather the requested information, both for the CRs and the researchers. Regular phone and email reminders, engagement with additional experts, and full-time technical support were needed to complete a study of this scale across countries where sustainable methods for quality control were often lacking. The lack of data that can be compared across countries may perpetuate the lack of uniformity of hearing screening programmes in Europe. In the future, a cross-border exchange of data can only be feasible if data collection, monitoring and quality control exist across all programmes.

From our data, we can derive at least five essential questions with which policy makers are faced. First, they must decide on the location of screening, which may be connected to the age at which an infant is screened. Screening can take place before discharge from the maternity hospital within the first days after birth or later, e.g., in the hospital, healthcare centre or at home. Next, the professional performing the screening should be decided on; this could be someone already employed at the screening location (e.g., nurse, midwife or physician) or someone specially hired and trained to only perform screening. Third, the type of screening device(s), either OAE, aABR or a combination of both, and fourth, the number of steps, make up the screening protocol. Finally, policy makers must decide if a separate protocol will be used for high-risk infants. It is unclear and debatable if one set of guidelines for NHS implementation would be ideal or even beneficial among countries with high variability across postnatal care, resources available and health care organisation, as certain decisions on NHS policy are made based on local circumstances.

In countries where the majority of infants are born in a maternity hospital, performing the first step of screening before discharge ensures high coverage. Completing all screening steps in the maternity hospital can avoid loss to follow-up that could otherwise occur between screening steps. However, residual amniotic fluid in the middle ear reduces the number of infants that pass screening when screening is performed within the first days after birth (Berninger and Westling, 2011). In some countries, screening professionals are already involved in postnatal care, ranging from nurses to physicians, whereas other countries use dedicated screeners for NHS. Although professionals with a medical background may require less initial training, which lowers initial costs, combining screening with other work can result in less practice and higher overall referral rates, compared to dedicated screeners (Vohr et al., 2001).

This study found that the provision of NHS and the screening protocol – the use of both OAE and aABR, the number of screening steps, and screening high-risk infants with a separate protocol – are related to health expenditure and HDI. In middle- or low-income countries with fewer resources available for preventive healthcare, a single screening protocol using only OAE may be chosen because of initial cost savings. The cost for aABR screening, including the device, consumables, screening time and training, is up to two times higher than the cost for OAE screening (Vohr et al., 2001, Boshuizen et al., 2001). Policy makers should be aware that excluding aABR from the protocol for both low- and high-risk infants, may put these countries at a long-term disadvantage. Screening with aABR is less influenced by middle ear fluid, and including aABR in the protocol reduces the total number of false positives (Caluraud et al., 2015). Reducing the number of referrals eases the burden on diagnostic centres and can reduce the number of infants lost to follow-up (Mackey et al., 2021). Thereby, the overall effectiveness of the NHS programme may be higher when including aABR, particularly in countries where loss to follow-up is a concern. Furthermore, because of the higher prevalence of retrocochlear disorders among high-risk infants, aABR is the recommended technology for screening among the high-risk population (Joint Committee on Infant Hearing, 2019, EFCNI et al., 2018). Despite these points, an NHS programme with OAE screening may be the preferred choice for low- and middle-income countries with limited resources particularly during early stages of implementation.

It proved to be difficult to gather detailed data, and in many countries essential data on NHS needed for evaluation could not be reported on a regional or national scale. When screening outcomes are not collected on a programme-wide level, a screening programme cannot be evaluated, nor can it be compared to screening programmes of other countries. This lack of monitoring and evaluation likely perpetuates the diversity in screening protocols across countries and regions. To be able to exchange information routinely and reliably, NHS programmes need good, sustainable monitoring systems.

Acknowledgments

Members of the EUS€REEN foundation contributed information from their local screening programmes. The following are members of the EUS€REEN Foundation contributing to this work: B. Qirjazi; D. Holzinger; L. Stappaert; B. Vos; F. Brkić   P. Rouev; X. Peng; M. Velepic; C. Thodi; J. Drsata; T. Ovesen; M. Bambus; M. Lepplaan; B. Ellefsen; R. Niemensivu; T. Willberg; F. Denoyelle; P. Matulat; T. Nikolopoulos; A. Gáborján; I. Hinriksdóttir; Z. Chaudhurri; G. Norman; L. Rubin; A. Martini; D. Spanca; M. Audere; S. Kušķe; N. Drazdiene, E. Lesinskas; J.M. Hild; M. Cakar; T. Fenech; W. Mulwafu; D. Chiaburu; T. Kujundžić; E. Zvrko; A. Meuwese; A. Goedegebure; H. Hoeve; V. Nagaraj; G. Greczka; L. Monteiro; M. Georgescu; G. Tavartkiladze; L. Gouma; S. Filipovic; G. Jokovic; L. Langova; I. Sebova; S. Battelino; D.W. Swanepoel; F. Núñez-Batalla, J.M. Sequi-Canet; I. Uhlén; B. Nora; M. Baydan; J. McCall.

REFERENCES

BERNINGER, E. & WESTLING, B. 2011. Outcome of a universal newborn hearing-screening programme based on multiple transient-evoked otoacoustic emissions and clinical brainstem response audiometry. Acta Oto-Laryngologica, 131, 728-739.

BOSHUIZEN, H. C., VAN DER LEM, G. J., KAUFFMAN-DE BOER, M. A., VAN ZANTEN, G. A., OUDESLUYS-MURPHY, A. M. & VERKERK, P. H. 2001. Costs of different strategies for neonatal hearing screening: a modelling approach. Archives of Disease in Childhood - Fetal and Neonatal Edition, 85, F177-F181.

CALURAUD, S., MARCOLLA-BOUCHETEMBLE, A., DE BARROS, A., MOREAU-LENOIR, F., DE SEVIN, E., REROLLE, S., CHARRIERE, E., LECLER-SCARCELLA, V., BILLET, F., OBSTOY, M. F., AMSTUTZ-MONTADERT, I., MARIE, J. P. & LE-ROSEY, Y. 2015. Newborn hearing screening: analysis and outcomes after 100,000 births in Upper-Normandy French region. Int J Pediatr Otorhinolaryngol, 79, 829-33.

CHING, T. Y. C., DILLON, H., LEIGH, G. & CUPPLES, L. 2018. Learning from the Longitudinal Outcomes of Children with Hearing Impairment (LOCHI) study: summary of 5-year findings and implications. International Journal of Audiology, 57, S105-S111.

DAVIS, A., BAMFORD, J. & STEVENS, J. 2001. Performance of neonatal and infant hearing screens: sensitivity and specificity. Br J Audiol, 35, 3-15.

DEFAYS, D. 1977. An Efficient Algorithm for a Complete Link Method. Comput. J., 20, 364-366.

EFCNI, OUDESLUYS-MURPHY, A. M., VAN WASSENAER-LEEMHUIS, A., WOLKE, D. & VAN STRAATEN, H. L. M. 2018. European Standards of Care for Newborn Health: Hearing screening [Online]. Available: https://newborn-health-standards.org/hearing-screening/ [Accessed December 5 2019].

EUROPEAN CONSENSUS STATEMENT ON NEONATAL HEARING SCREENING. 1999. European Consensus Statement on Neonatal Hearing Screening. Finalized at the European Consensus Development Conference on Neonatal Hearing Screening. Acta Paediatr, 88, 107-8.

JOINT COMMITTEE ON INFANT HEARING 2007. Year 2007 position statement: Principles and guidelines for early hearing detection and intervention programs. Pediatrics, 120, 898-921.

JOINT COMMITTEE ON INFANT HEARING 2019. Year 2019 Position Statement: Principles and Guidelines for Early Hearing Detection and Intervention Programs. The Journal of Early Hearing Detection and Intervention, 4, 1-44.

KANJI, A., KHOZA-SHANGASE, K. & MOROE, N. 2018. Newborn hearing screening protocols and their outcomes: A systematic review. Int J Pediatr Otorhinolaryngol, 115, 104-109.

MACKEY, A. R., BUSSÉ, A. M. L., HOEVE, H. L., GOEDEGEBURE, A., CARR, G., SIMONSZ, H. J. & UHLÈN, I. M. 2021. Assessment of hearing screening programmes across 47 countries or regions II: Coverage, referral, follow-up and detection rates from newborn hearing screening Submitted for publication.

SLOOT, F., HOEVE, H. L., DE KROON, M. L., GOEDEGEBURE, A., CARLTON, J., GRIFFITHS, H. J. & SIMONSZ, H. J. 2015. Inventory of current EU paediatric vision and hearing screening programmes. J Med Screen, 22, 55-64.

STEVENS, J., HALL, D. M. B., DAVIS, A., DAVIES, C. M. & DIXON, S. 1998. The costs of early hearing screening in England and Wales. Archives of disease in childhood, 78, 14-19.

THE WORLD BANK. 2019. World Bank Country and Lending Groups [Online]. The World Bank. Available: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-

world-bank-country-and-lending-groups [Accessed 03-06-2019 2019].

UNITED NATIONS DEVELOPMENT PROGRAMME. 2019. Global Human Development Indicators [Online]. United Nations Development Programme. Available: http://hdr.undp.org/en/countries [Accessed 12-09-2019 2019].

UUS, K., BAMFORD, J. & TAYLOR, R. 2006. An analysis of the costs of implementing the National Newborn Hearing Screening Programme in England. Journal of medical screening, 13, 14-19.

VOHR, B. R., OH, W., STEWART, E. J., BENTKOVER, J. D., GABBARD, S., LEMONS, J., PAPILE, L. A. & PYE, R. 2001. Comparison of costs and referral rates of 3 universal newborn hearing screening protocols. J Pediatr, 139, 238-44.

VOS, B., SENTERRE, C., LAGASSE, R., TOGNOLA, G. & LEVEQUE, A. 2016. Organisation of newborn hearing screening programmes in the European Union: widely implemented, differently performed. Eur J Public Health, 26, 505-10.

WHITE, K. R. 2010. Universal Infant Hearing Screening: Successes and Continuing Challenges.

WORLD HEALTH ORGANIZATION. 2009. Newborn and infant hearing screening [Online]. WHO. Available: https://www.who.int/blindness/publications/Newborn_and_Infant_Hearing_Screening_Report.pdf?ua=1 [Accessed 13-03-2019 2019].

WORLD HEALTH ORGANIZATION. 2019. Global Health Expenditure Database [Online]. World Health Organisation. Available: http://apps.who.int/nha/database/Select/Indicators/en [Accessed 03-06-2019 2019].

YOSHINAGA-ITANO, C. & APUZZO, M. L. 1998a. The development of deaf and hard of hearing children identified early through the high-risk registry. Am Ann Deaf, 143, 416-24.

YOSHINAGA-ITANO, C. & APUZZO, M. L. 1998b. Identification of hearing loss after age 18 months is not early enough. Am Ann Deaf, 143, 380-7.

YOSHINAGA-ITANO, C., SEDEY, A. L., COULTER, D. K. & MEHL, A. L. 1998. Language of early- and later-identified children with hearing loss. Pediatrics, 102, 1161-71.

Chapter 4

Assessment of hearing screening programmes across 47 countries or regions II: Coverage, referral, follow-up and detection rates from newborn hearing screening

*Allison R Mackey**
*Andrea ML Bussé**
Hans LJ Hoeve
André Goedegebure
Gwen Carr
Huibert J Simonsz
Inger M Uhlén

the EUS€REEN Foundation

**Contributed equally and should be considered dual first authors*

ABSTRACT

Objectives

To assess the performance of newborn hearing screening (NHS) programmes, through selected quality measures and their relationship to protocol design.

Design

NHS coverage, referral, follow-up and detection rates were aggregated. Referral rates were compared to age at screening step 1, number of steps, and test method: OAE or aABR.

Study sample

A questionnaire on existing hearing screening was completed by experts from countries in Europe, plus Russia, Malawi, Rwanda, India and China.

Results

Out of 47 countries or regions, NHS coverage rates were reported from 26, referral rates from 23, follow-up from 12 and detection rates from 13. Median coverage rate for step 1 was 96%. Referral rate from step 1 was 6%-22% where screening may be performed <24 hours from birth, 2%-15% for >24 hours, and 4% for >72 hours. Pooled referral rates to diagnostic assessment were 2.1% after one to two steps using OAE only, 1.7% after two steps including aABR, and 0.8% after three to four steps including aABR. Median detection rate for bilateral permanent hearing impairment ≥40dB was 1 per 1000 infants.

Conclusion

Referral rates were related to age, test method and number of screening steps. Quality measures were not available for many NHS programmes.

INTRODUCTION

To achieve early identification and intervention for infants with permanent hearing impairment (HI), programmes for newborn hearing screening (NHS) have been widely implemented. The goal is to detect all infants with HI while maintaining low false positives to avoid unnecessary costs and parental worry. A sustained data collection process allows decision makers and programme managers to monitor and evaluate the performance of their NHS programme. According to the World Health Organisation (2015), implementing a procedure for monitoring and evaluation is a key step in the development of a national strategy for ear and hearing care (including early detection). Without it, success cannot be distinguished from failure.

Quality measures and benchmarks (i.e., performance targets) provide a framework for evaluating the performance of screening. In this study, coverage rate, referral rate, and follow-up rate are the quality measures assessed. These measures were previously described in literature and are used in local screening programmes and position statements from around the world (Joint Committee on Infant Hearing, 2007, Neumann et al., 2019, Patel and Feldman, 2011, Wood et al., 2015, Olusanya et al., 2007). Benchmarks for quality measures used in NHS have been recommended by the Joint Committee on Infant Hearing (2007) and are used directly or as a starting point for local policy makers to predefine alternative benchmarks.

Coverage is the quality measure that ensures NHS is available to all eligible infants who are born in the administering hospital, or who live in the administering region or country. In some literature, coverage rate has been defined as the percentage of eligible infants that complete the entire screening pathway within a specific timeframe (e.g., Wood et al., 2015). In other studies, coverage has been defined as the number of eligible infants that complete step 1 (e.g., Olusanya et al., 2007). Notwithstanding the different definitions, coverage rate reflects the quality of NHS access and its uptake. Several screening programmes and guidelines have defined a benchmark coverage rate of 95% to 97% (Joint Committee on Infant Hearing, 2007, Neumann et al., 2019, Patel and Feldman, 2011, Januario et al., 2015).

Referral rate is the percentage of infants that do not pass the screening, for each individual step or after all screening steps. A screening step is when screening is performed, and a result (pass or fail) is obtained. Infants that fail a screening step may be referred to the next step. Infants that fail all steps in the sequence are referred to diagnostic assessment. Approximately 0.1 to 0.2% of all infants are born with a permanent HI (Bussé et al., 2020, Kennedy et al., 1998). The infants with a permanent HI make up only a part of the infants referred for diagnostic assessment. Other infants referred may have normal hearing, a transient HI (e.g., temporary fluid in the middle ear) or a permanent HI that was missed if best-practice diagnostic protocols were not followed. Referral rates should therefore be low, signifying a low false positive rate. The benchmark for final referral to diagnostic assessment is commonly 4% for low-risk or all infants combined (Joint Committee on Infant Hearing, 2007, Neumann et al., 2019, Patel and Feldman, 2011, Januario et al., 2015). In this study, high-risk infants are defined as having an increased risk for HI or retrocochlear dysfunction and the remaining infants are defined as low risk.

Follow-up rate is the percentage of infants whose families attend either the rescreening step or the diagnostic assessment, after having been referred in a previous step. Follow-up rate could inversely be described as loss to follow-up (LTFU), which identifies the percentage of infants referred who are not followed up (or documented) at a rescreening step or diagnostic assessment. A benchmark of 90-97% is often used for a target follow-up rate (Joint Committee on Infant Hearing, 2007, Neumann et al., 2019, Patel and Feldman, 2011, Januario et al., 2015).

Within the EUSCREEN project, the cost-effectiveness of vision and hearing screening programmes will be compared. A model is being developed to calculate the most cost-effective screening programme in any country given its local circumstances. For this purpose, a large-scale international aggregation of information on childhood hearing and vision screening was completed. In the preceding article, we described the various NHS protocols, in terms of the number of screening steps, the choice of test (otoacoustic emissions [OAE] and/or automated auditory brainstem response [aABR]), and the age of the infant at step 1 (Bussé et al., 2021). Our results suggested that the level of health care spending may influence decisions on protocol design, as more countries with lower health spending had OAE-only programmes. Yet OAE screening is highly sensitive to transient obstructions of the middle ear, such as amniotic fluid, which may lead to a high number of false positive results (van Dyk et al., 2015). Increasing the number of screening steps, using aABR instead of OAE, and/or delaying step 1 may help reduce the overall referral rate (Benito-Orejas et al., 2008, Caluraud et al., 2015, Clemens and Davis, 2001, Berninger and Westling, 2011). Lower referral rates reduce the subsequent burden and costs on diagnostic services, and may also lead to a reduction of LTFU (Finitzo et al., 1998). Given the significant diversity in protocol design across countries (Sloot et al., 2015, Bussé et al., 2021), a systematic evaluation of the effectiveness of NHS is essential to better understand the consequences of protocol choice and the current barriers to effective NHS.

In the present study, we evaluated the quality measures reported by NHS programmes. This study also examined the relationship between referral rates to the protocol features across multiple screening programmes. Specifically, the minimum age and location for step 1, the number of screening steps, and the use of aABR and/or OAE were investigated. The quality measures described in this study are the coverage of the NHS programme, the referral rates per step and to diagnostic assessment, the follow-up rates between steps 1 and 2 and from all screening steps to diagnostic assessment, the detection rates, specificity and the positive predictive value (PPV). Sensitivity and negative predictive value are difficult to assess and were not included in this study. Decisions made by policymakers when selecting or revising an NHS protocol design may be influenced by previous findings on its effectiveness, in combination with the current state of newborn health care in the country. This is addressed in the present study. Results are particularly valuable to areas still in the phase of NHS implementation, where few local reports on NHS effectiveness may be available.

METHODS

The web based EUSCREEN questionnaire was developed by a panel of hearing and screening professionals and contained 191 questions across nine domains on hearing screening. Questions on the organisation, protocol, pathways for referral, quality measures, and costs were included. Most questions were followed by a five-choice sub-question on the level of evidence of the answer supplied, which composed the options (a) Data unavailable, (b) I don't know, (c) Rough estimate, (d) Real estimate from calculation, (e) Actual data. If the response was composed using data from a source, the name and date of this source was requested. Publicly available sources, such as annual screening reports, were also requested via email when available.

Respondents were local screening experts, so called Country Representatives (CRs). CRs of the originally selected countries were recruited via professional organisations, existing contacts, and recent publications. Participation was open to experts from any country, regardless of the status of their NHS programme or data availability. Screening experts from countries outside the original selection were welcome to register to fill out the questionnaire but were not actively sought. Upon registration, the qualifications of the CRs were checked, and the CRs had to confirm their expertise in relation to the NHS data they provided. CRs accessed the questionnaire between March 2017 and June 2019 via the EUSCREEN website (www.euscreen.org) with a unique username and password. After the questionnaire was submitted, it was checked for completeness. The verification procedure is summarised in Figure 1. An internal cross-checking procedure was performed between CRs representing the same country or region and between questions asking for similar answers. External literature and source material, supplied by the CR or searched and accessed online, were translated via Google Translate and cross-checked with answers provided. CRs were asked to clarify their answers when original answers were unclear, when answers were inconsistent with other answers within the same questionnaire, or when answers were inconsistent with supplementary materials. After completion, the list of clarification questions was returned by the CRs. A report was developed for each programme based on the combined collected information and sent to the CR for final confirmation. Countries were excluded from the study if answers were not sufficiently completed to generate a descriptive report.

To describe the current health care status for newborn care, data on universal newborn care were aggregated from established sources (Unicef, 2019, World Health Organization, 2019) and from responses in the questionnaire. The measures evaluated were the percentage of infants born in health facilities, the percentage of infants undergoing a post-natal check-up by 2 days of age, and the immunisation coverage of the first dose of diphtheria toxoid, tetanus toxoid and pertussis vaccine.

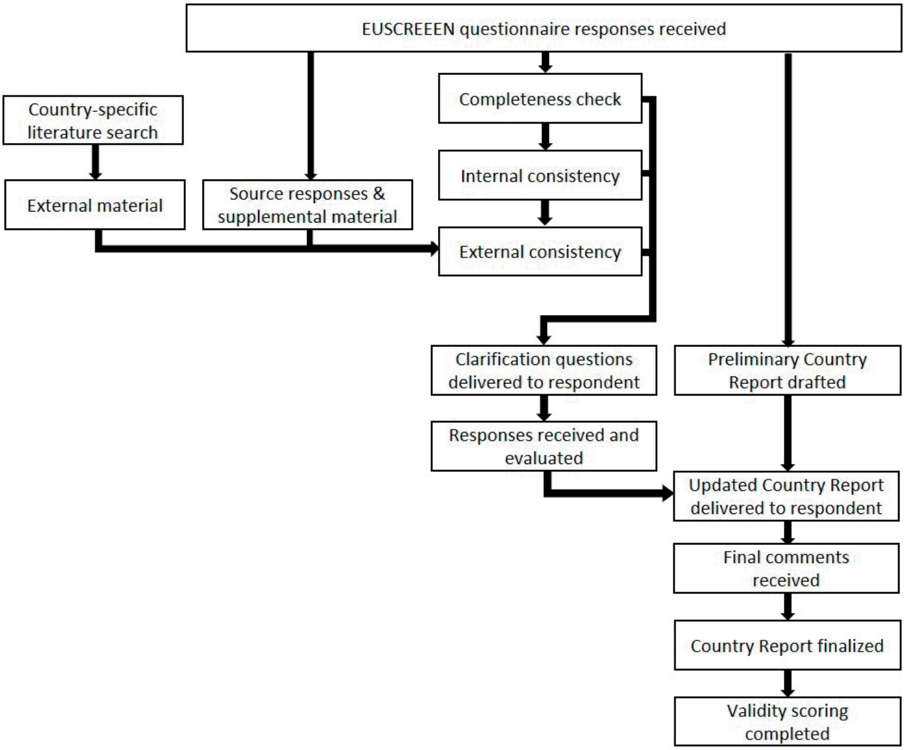


Figure 1. Flow chart of the verification and validation process.

Selection and validation of quality measures

The quality measures described in this study were selected based on previously defined measures used in NHS guidance documents, international position statements, and literature describing NHS performance across countries from various income levels (Wood et al., 2015, Olusanya et al., 2007). Quality measures were the coverage, referral between screening steps, referral from screening to the diagnostic assessment, and follow-up rate to screening steps. Detection rates reveal the outcome of the screening programme (i.e., the number of children with permanent HI).

Among established NHS programmes, the validation of responses was based on the level of evidence provided by the CRs. It was the CRs' responsibility as collaborators to provide high quality and valid data where available. The quality of the responses they provided were self-rated in the sub-question following each main question. The data supplied were classified as 'not valid' if the CR indicated that they were based on a rough estimation. In cases where answers were provided based on calculations of data, responses were considered 'valid' if source data were recent (collected from 2014 or later), representative of the target population, and consistent with the source or external literature. The method used to collect the raw data, including the data management system, may affect the validity and accuracy of the figures provided, though this was not evaluated in this study. This made it possible for answers to be included across all data collection and management systems. Minimum sample size criteria varied based on the outcome measure: coverage rates were not dependent on the sample size; referral rates were valid if sample size was 1000 or more; detection rates were valid when the sample size was >5000. The exception was for countries or regions where birth rates were under these values.

Evaluation of valid quality measures

Data considered valid as a result of the validity scoring were analysed further. A null value was assigned for any data not scored as valid or where annual birth rates were under 1000. Descriptive statistics were calculated for all selected quality measures. To calculate pooled rates, the reported rates for each programme were transformed to estimated counts using the number of live births in the country or region for a one-year birth cohort (Table 1) due to the differences in population size.

The CRs filled out the questionnaire for an individual NHS programme, which was organised either nationally or regionally. For regionally organised programmes, the quality measures reported represented only the participating region, and other regions within the country were not represented. For nationally organised programmes, the rates represented the entire country.

Referral and follow-up rates were evaluated between individual steps and from the entire screening programme to diagnostic assessment. Costs were evaluated for screening (in euro per infant screened), screening devices, screener salaries, and intervention.

Analyses of quality measures and protocol design

The reported referral rates (where provided) were compared across the age of the infant at step 1 and screening protocols for low-risk infants. Formation of groups were based on the results of Bussé et al (2021). Age was categorised based on the minimum age of screening: <24 hours, 24 hours, or 72 hours. Programmes that perform screening after 72 hours performed screening outside the maternity hospital, either in a child health care centre or at home; all remaining programmes screen in the maternity hospital (before or after discharge). Protocol groups were formed based on the screening devices used (OAE versus aABR) and the number of steps (i.e., screens and repeat screens) in the protocol. For protocols using OAE only, all steps are performed using OAE. The category of OAE could include either transient-evoked OAE or distortion-product OAEs, although transient-evoked OAEs are used in the majority of programmes. For one- to two-step protocols including aABR, one programme uses aABR for step 1 (no step 2), one programme uses aABR for steps 1 and 2, and the others use OAE for step 1 and aABR for step 2. For three- or four-step protocols including aABR, the final step is performed with aABR and earlier steps are performed with OAE. A list of technologies for OAE and aABR showing the diversity across manufacturer and passing criteria is available in Bussé et al. (2021).

Table 1. Annual births for each country or region, validity of selected quality measures, and data collection process for each participating country or region. Countries or regions are sorted to match the sequence in the accompanying article (Bussé et al., 2021), which is arranged by protocol-design cluster. Five countries did not have established NHS programmes at time of data aggregation (Albania, Kosovo, Malawi, Rwanda, and Montenegro). Some countries were represented on a national level in this study, and a lack of data cannot be presumed (particularly for large countries), as regional data may be available that were not reported. Responses were considered valid (V) if source data were recent, representative of the target population, consistent with the source or external literature, and over the minimum sample size. Responses provided that did not meet these criteria were coded as not valid (X). The remaining blank fields indicate data not provided. Two items in the questionnaire are described on whether data collection is performed and mandated: yes (+), no (-), or limited to only some hospitals.

		Screening quality measures								
Country	Region represented	Annual number of births	Coverage	Final referral to diagnostic	Referral to step 2	Follow-up to step 2	Follow-up to diagnostic	Detection	Quality assurance by government	Outcome measures collected
Albania		31733								
Kosovo		23416								
Malawi		663000								
Rwanda		352052								
Montenegro		7386								
Malta		4308	V	X			X		-	-
N. Macedonia	Skopje Region	8466						X	-	-
Romania		191694	V	X	X		X		-	+
Bosnia & Herzegovina	Tuzla Canton	3727	V	V	V	V	X		-	+
Latvia		21646	X	X	X		X		-	-
Lithuania		30623	V	V				V	-	+
Serbia	Belgrade	64587		X	X		X		-	Limited
Moldova	Chisinau	37394	X	X	X		X		-	-
Faroe Islands		686	X	V*	X		X			-
Estonia		14053	X					V	-	-
Belgium	Wallonia-Brussels Federation	57500	V	V	V	V	V		+	+
Russia		1888729	V	V			V	V	-	+
Austria	Upper Austria	15394	V	V	V		V	V	-	+
Croatia		37503	V	V	V	V	X	X	-	+
Czechia	East Bohemia	11074	V	X	X	V	V	V	-	+
Poland		382300	V	V			V	V	+	+
Luxembourg		7128	V	V	V*	V	V		-	+
Spain	Aut. Comm. Valencia	43450	V	V	V	V	V	V	-	+

Table 1. Annual births for each country or region, validity of selected quality measures, and data collection process for each participating country or region. (continued)

Country	Region represented	Annual number of births	Screening quality measures							
			Coverage	Final referral to diagnostic	Referral to step 2	Follow-up to step 2	Follow-up to diagnostic	Detection	Quality assurance by government	Outcome measures collected
Bulgaria		63955		X	X		X	X	-	+
Portugal	Lisbon Region	86154	V	V	V	X			+	Limited
Slovakia		57969							-	Limited
Slovenia		20641	V	X	V			X	-	+
Switzerland		87381	X	X	X		X	X	-	Limited
Spain	Princip. Asturias	6600	V	V	V	V	V	V	-	+
Hungary		91577							-	-
China		15.2 mil	X	X	X		X	X	-	Limited
Cyprus	Southern part	9229	X	V	V		X	X		+
Israel		181351	V	V	V		X	X	+	+
Denmark		61476	V	V	X			X	-	+
Belgium	Flanders	88691	V	V	V			X	+	+
France	Ile de France	174439	V				X	X	+	+
Germany	Westphalia-Lippe	792131	V	V	V	X	X	X	+	+
Greece	Attikon Hospital	94134	X	X	V*		X	X	-	-
Iceland		4071	V	V				X	-	+
Netherlands		169836	V	V	V	V	V	V	+	+
Italy	Veneto Region	36587	X	V	V	X	V		+	Limited
Sweden	Stockholm Region	28805	V	V	V		V	V	-	+
Finland		52814	X					X	-	
Ireland		65607	V	V	V			V	+	+
England (U.K.)	S.E. London	26000	V	V	V		V	V	+	+
Turkey		1309771	V	V				V	+	+
India		27 mil								

*Although considered valid, these data were not included in calculations or analyses due to the diversity of data collection parameters (e.g., sample size was low due to low annual birth rate, sourced from one hospital only, or incorporated a large percentage of infants who were not previously screened).

Next, a comparison between referral rate and follow-up rate was performed. For the analyses, the estimated counts for referrals were derived from the number of births across a one-year cohort, and the estimated counts for follow-up were derived from the number of referrals.

Risk ratios were calculated in SPSS (v.26.0) with 95% confidence intervals to show the increased risk of referral between two conditions (in this case protocol choices). Because of the large population-based estimates used, risk ratios with confidence intervals provided a more clinically applicable result than p-values when comparing conditions (Cumming, 2013).

RESULTS

Questionnaires were sufficiently completed by CRs from 40 European countries plus five additional CRs with interest in participating: Russia, Malawi, Rwanda, India, and China (Appendix 2). Two regions from Spain and two regions from Belgium participated, for a total of 47 participating countries or regions (Table 1). The questionnaires from South Africa and Norway were not sufficiently completed to generate a descriptive report and were excluded.

Newborn health care

Thirty high-income countries (HICs), 13 middle-income countries (MICs) and two low-income countries (LICs) were included, according to the World Bank classification system (2019). Data on hospital births from the questionnaire and UNICEF's Maternal and Newborn Database (2019) were available for all but eight HICs. The percentage of deliveries in a health facility was >90% for all but three countries. In India, Flanders (Belgium) and the Netherlands, 79%, 83% and 81% of deliveries take place in a hospital. Data from some participating MICs and LICs were available regarding the percentage of infants that undergo a postnatal check-up after delivery (up to 2 days of age). Rates varied from 19% in Rwanda and 27% in India to 86% in Albania, 96% in Kosovo and 99% in Montenegro (Unicef, 2019). Immunisation coverage for the first dose of diphtheria, tetanus, & acellular pertussis (around 2 months of age) was available for all except nine countries (seven HICs and two MICs) and ranged from 89% to 99%, according to statistics from the World Health Organisation (2019).

Validation of quality measures

A list of all participating countries and regions and the corresponding validation results are presented in Table 1. Valid responses to the selected performance measures could not be provided by all countries or regions. Sixteen were unable to provide valid outcome data of which five (Albania, Malawi, Montenegro, Kosovo, and Rwanda) did not have a permanently established NHS programme at the time of data aggregation.

Figure 2 displays that valid coverage rate was reported by the most NHS programmes and valid follow-up and detection rates were reported by the fewest programmes. CRs typically acquired valid quality measures from internal databases or registries, quality assessment reports, or studies published in local journals, local media, or student theses. Data were collected from 2014 to 2017, and most represented a one-year birth cohort, although some data were collected over a longer period. The sources used to cross-check the survey responses or when cited by the CR are listed in Appendix 1.

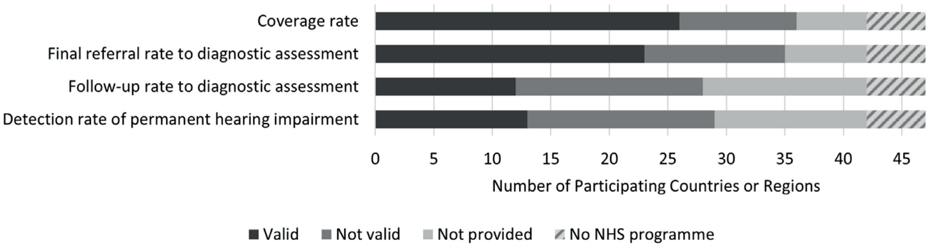


Figure 2. Results of the validation scoring for coverage rate, referral rate to diagnostic assessment, follow-up rate to diagnostic assessment, and detection rate of permanent hearing impairment. Data were considered valid when source data were recent, representative of the target population, met the minimum sample size criteria, and consistent with the source or external literature. Out of the 47 participating countries or regions, the number are displayed with valid data, not valid data, or none provided. Five countries did not have a permanently established NHS programme. Note that the exact definition of each measure may vary across programmes, as NHS programmes could only report on the values that they themselves calculate. Notably, more valid data could be provided on coverage and referral rates compared to follow-up or detection rates.

Quality measures and costs

The following paragraphs present descriptive results of the performance of NHS programmes. As described previously, pooled rates were calculated from estimated counts from each programme. Programmes reported either for all infants irrespective of risk group or for low- and/or high-risk infants separately. Table 1 lists the NHS programmes (national or regional) with valid data for each selected quality measure.

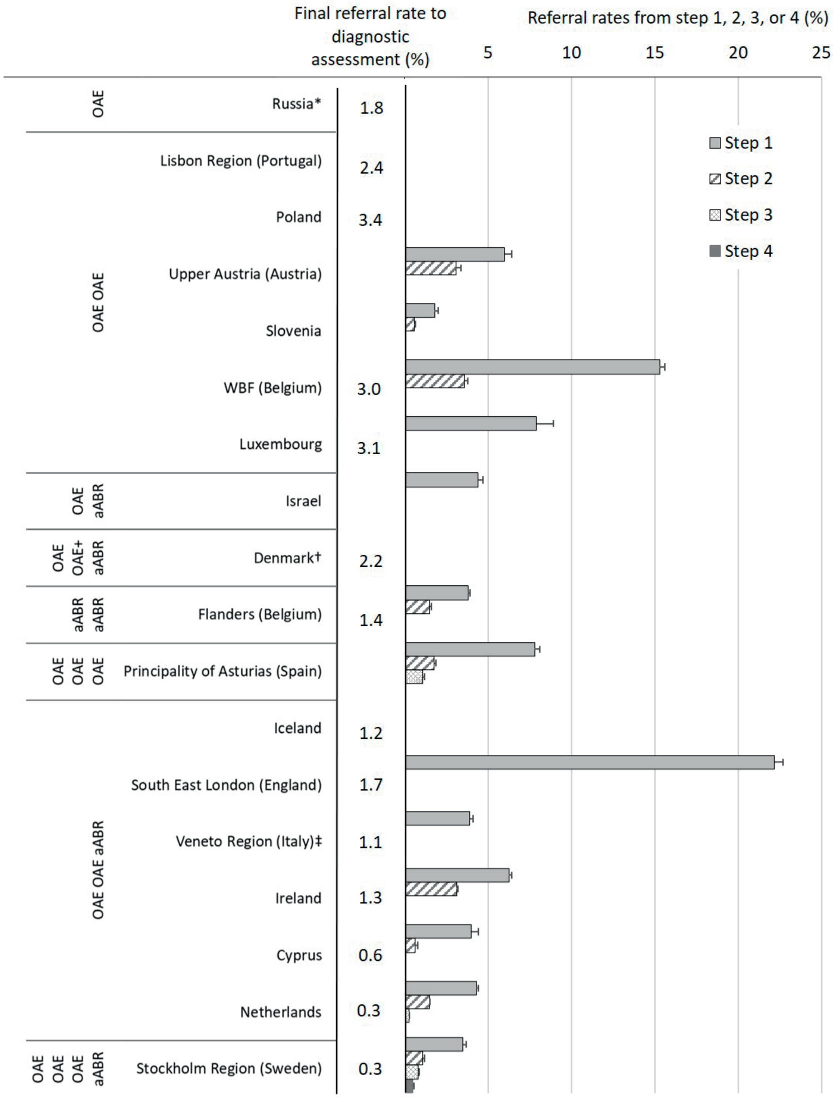
Coverage rates. The definition of coverage varied slightly across the 26 NHS programmes that reported valid coverage rate data. For four programmes, coverage rate was defined as the percentage of infants that completed the entire screening sequence, and for the remaining 22 coverage was defined as the infants who completed step 1. For the four programmes where coverage rate was defined as the percentage of infants that completed the entire sequence, one had a rate of 93% and the other three had rates of 98-99%. Out of the 22 programmes where coverage of step 1 was reported, 17 had ≥95% coverage. The pooled coverage rate for step 1 (all infants, high plus low-risk) was 97.9% and the median was 96% (range: 79 to 100%). Romania (coverage of 18%) was not included in this calculation, as it has a national programme in the process of scaling up. Besides Romania, step 1 coverage rates of 79, 96 and 98% were reported from three MICs. The remaining programmes were from HICs (median: 96.7%, range: 85 to 100%).

Referral rates. For 18 programmes, separate referral rates were reported for low-risk infants, which are displayed in Figure 3 according to protocol design. Figure 3 shows the decremental referral rates from each step of screening (step 1, 2, etc.) and the final referral rate to diagnostic assessment out of the total number of infants screened. The pooled final referral rate to diagnostic assessment for low-risk infants was 1.9% (median 1.5%, range 0.27-3.4%). For seven programmes, referral rates were reported for high-risk infants, for which the pooled referral rate to diagnostic assessment was 8.0% (median 6.8%, range 4.0-10.2%). For ten programmes, referral rates for all infants irrespective of risk group were reported, for which the pooled referral rate from step 1 was 9.0% (median 8.4%, range 3.5-12.1%) and the pooled final referral rate from screening to diagnostic assessment was 2.6% (median 1.5%, range 0.3-3.5%). All final referral rates to diagnostic assessment for programmes reporting on low-risk or all infants were less than 4%; all final referral rates for high-risk infants were 4% or higher.

Follow-up rates. For programmes where all infants were reported on, irrespective of risk group, the pooled follow-up rate to step 2 out of those referred from step 1 was 81% (median 81%, range 27-97%, n=9). All programmes were from HICs except for one MIC where a 27% follow-up rate to step 2 was reported. The pooled follow-up rate to diagnostic assessment out of those referred from the final screening step was 72% (median 89%, range 19-97%, n=12). For programmes where low- and high-risk infants were reported separately, pooled follow-up rates to diagnostic assessment were 77% for low-risk infants (median: 74%, range 71-97%) and 90% for high-risk infants (median 90%, range 64-95%). However, this contrast between high- and low-risk infants was not consistent across individual programmes. All countries where follow-up rate to diagnostic assessment was reported were HICs except for one MIC, which had 76 and 89% follow-up rates for low- and high-risk infants. Overall, out of a total of 12 participating NHS programmes where valid follow-up rates were reported to diagnostic assessment for all infants and high- and low-risk infants combined, follow-up rates were under 80% for six, between 80 and 90% for two, and 90% or higher for four.

For programmes where the referral rate from step 1 was higher, follow-up rates to step 2 were lower. For only five programmes figures for both measures were provided. Referral rates from step 1 were 4%, 4%, 8%, 8%, and 15%. Corresponding follow-up rates to step 2 were 99%, 95%, 92%, 91% and 87%. Furthermore, loss to follow-up between steps can also affect the final referral rate, such as in Tuzla Canton (Bosnia and Herzegovina), where the final reported referral rate for all infants to a diagnostic assessment (0.35%) was highly influenced by a low follow-up rate between screening steps 1 and 2 (27%).

Detection rates. The detection rates (or prevalence rate after detection by NHS) varied between 0.7 and 3 per 1000 births (median: 1.16 per 1000, n=10) for bilateral permanent HI ≥ 40 dB HL and between 0.28 and 0.72 per 1000 births (median: 0.42 per 1000, n=9) for unilateral permanent HI ≥ 40 dB HL. For eight programmes (seven from HIC and one from a MIC), additional data were provided on bilateral or unilateral permanent HI ≥ 80 dB HL. Detection rates varied between 0.2 and 1.16 per 1000 (median: 0.32 per 1000, n=8) for bilateral



*Multiple OAE tests can be performed before maternity ward discharge
†aABR is performed as the first screening test in Central region Denmark
‡ Data collected from Province of Padua only

Figure 3. Percentage of infants referred out of the total population screened from each step and to diagnostic assessment, grouped by the reported NHS protocol for low-risk infants. For some programmes data for all steps could not be reported. Low-risk infants are defined as infants without an increased risk for HI or retrocochlear dysfunction as per the risk factors specified by each NHS protocol. Error bars represent 95% confidence intervals. Because most infants without hearing impairment pass step 1, a large reduction of referral rate is seen between steps 1 and 2. Programmes with more steps and using aABR had lower final referral rates.

permanent HI ≥ 80 dB HL and between 0.1 and 0.6 per 1000 (median: 0.16 per 1000, n=6) for unilateral permanent HI ≥ 80 dB HL. All detection rates provided were from HICs except one from a MIC, where a detection rate of 0.6 per 1000 was reported for bilateral permanent HI >80 dB HL. No clear trends were observed between detection rates of permanent HI and measures of follow-up rates to diagnostic assessment.

For only a few participating NHS programmes valid data were provided on detection or prevalence rates of auditory neuropathy spectrum disorder (ANSD), a type of retrocochlear dysfunction, among infants. In the Netherlands, a prevalence rate was reported of 2.7 per 1000 infants admitted to the NICU. Prevalence rates of ANSD for all infants were reported for the Principality of Asturias (Spain) (0.07 per 1000 births) and Ireland (0.02 per 1000 births). All other ANSD figures were rough estimations or absolute counts of ANSD cases on file.

Specificity and positive predictive value. The specificity of the entire protocol was defined as the percentage of infants with normal hearing who pass screening at any step within the sequence. Valid specificity was only reported from Westphalia-Lippe (Germany), Ireland, and Flanders (Belgium) for low-risk or all infants: 97.1%, 98.4% and 99.7%. Data on sensitivity and negative predictive value were not available.

PPV was defined as the percentage of infants referred from screening to a diagnostic assessment who have a confirmed hearing impairment that was targeted by the NHS programme. PPV is presented for each NHS programme in brackets. The only valid data on the PPV for an entire NHS programme for all infants were from Germany (6), Ireland (10), Poland (5) and the Autonomous Community of Valencia (Spain) (14). Programmes providing a PPV for low-risk infants were East Bohemia (Czechia) (10), Flanders (Belgium) (65), Upper Austria (Austria) (4), Wallonia-Brussels Federation (Belgium) (10) and the Netherlands (39). Out of these, the Netherlands also provided a PPV for high-risk infants (64.6). The protocols used by these countries can be observed in Figure 3.

Costs. It was difficult for CRs to make a valid estimation of the costs of their screening programme. Overall screening costs, costs of screening devices, salary costs, hearing aid fitting and cochlear implant fitting included different aspects for each programme. The variability within the costs provided made any comparison between programmes impossible.

Analyses of quality measures and protocol design

The following paragraphs describe the results of the comparisons between quality measures and protocol features (minimum age of the infant at step 1, number of screening steps, and the inclusion of aABR in the protocol).

Referral rate from step 1 across age. For 13 programmes, the referral rate was reported from step 1 for low-risk infants. Step 1 is often performed in the maternity hospital before discharge. Subsequent steps may be performed before or after discharge. For most programmes, step 1 is performed in the maternity ward after 24 hours of age. For these programmes, the pooled referral rate from step 1 was 7.5% (median: 5.2%, range: 1.8% to 15.3%). In South East London

(England) and Ireland, step 1 screening may be performed less than 24 hours after birth. In England, the average length of stay in the maternity ward for deliveries without complications was 1.4 days (OECD, 2019). Referral rate from step 1 in the maternity hospital was 22%, a figure consistent across England (23%; NHS Newborn Hearing Screening Programme, 2019). In Ireland, the length of stay averaged 2.4 days (OECD, 2019), and referral rate from step 1 was 6%. In Flanders (Belgium), the Netherlands and Cyprus, step 1 is performed after 72 hours of age in a child health centre or home visit. Referral rates from step 1 were 4% for all three programmes. Out of the 13 programmes, aABR for step 1 is only used in Flanders. No difference in step 1 referral rate was observed between Flanders and the Netherlands or Cyprus where OAE is used for step 1.

Referral rate from all steps to diagnostic assessment across test method and steps. Table 2 displays the referral rates and risk ratios across groups of programmes with similar low-risk protocols. Not all protocols were represented. Referral rate information was not available for countries that performed a one-step aABR protocol or a three-step protocol using only OAE. From the eight protocol categories displayed in Figure 3, protocols were grouped into: protocols with one or two steps using OAE only; protocols with two steps using aABR in one or both steps; and protocols with three or four steps using aABR in the final step. Referral rates were highest for one- to two-step protocols with OAE only and lowest for a three- to four-step protocols including aABR. This trend can also be observed for individual programmes, displayed in Figure 3.

Table 2. Pooled final referral rates (%) to diagnostic assessment for groups of programmes based on protocol design for low-risk infants (middle column). Low-risk infants are defined as all infants not considered at-risk for hearing impairment by the individual programmes surveyed. Referral rates for each group (based on protocol design) were pooled based on the number of births per year in each country or region. Risk ratios compare the referral rates pairwise between groups of programmes with a similar protocol design (steps and test method). The increased risk of a referral occurrence between two groups (along with the 95% confidence intervals) is displayed. Also displayed is the total number of infants that would require diagnostic assessment to detect one infant with permanent hearing impairment of 40 dB HL or worse. If a prevalence of 0.1 to 0.2% is assumed, the pooled final referral rate is between 4 and 21 times the prevalence.

Protocol design for low-risk infants		Pooled final referral rate (95% confidence intervals)	Number of infants requiring diagnostic assessment to detect one infant with permanent HI (prevalence 0.1-0.2%)	Risk ratio for refer result (95% confidence intervals)	
Steps	Test method			vs. 1 or 2 steps OAE-only	vs. 2 steps incl. ABR
1 or 2 steps	OAE only	2.10% (2.09-2.12%)	11 to 21		
2 steps	incl. aABR	1.66% (1.60-1.73%)	8 to 17	1.26 (1.21-1.32)	
3 or 4 steps	incl. aABR	0.80% (0.78-0.83%)	4 to 8	2.62 (2.53-2.71)	2.07 (1.97-2.19)

DISCUSSION

Of the 42 countries or regions with an NHS programme, 26 reported coverage rates, of which 22 reported only the coverage rate for screening step 1; 23 reported rates of referral from screening to diagnostic assessment; 12 reported the percentage of children who followed up from screening to diagnostic assessment; and 13 reported the percentage of infants detected with permanent HI. The percentage of infants referred from screening step 1 is related to the infants' age when screened. For programmes that use aABR, referral rate from screening to diagnostic assessment was lower compared to those that use only OAE. Programmes also had lower referral rates to diagnostic assessment if they have more screening steps. Across the few countries where follow-up rates were reported, 81% of infants referred from step 1 followed up to step 2, and 72% of infants referred from all screening steps followed up to the diagnostic assessment.

Results of this study can be compared to benchmarks for NHS, as described by the Joint Committee on Infant Hearing (2007). Firstly, there were differences noted in the definition of coverage rate. The definition presented in the benchmark is the completion of screening before one month of age. In contrast, most programmes reported only the coverage rate of step 1, which neither reflects the LTFU between screening steps nor the timeliness of screening. However, it may be argued that the definition should be determined by the programme, so long as the same definition is applied to the benchmark. Despite differences in the definition of coverage rate, 20 out of 26 programmes reported good coverage (95% or higher). All reported referral rates to diagnostic assessment (for low-risk or all infants combined) achieved the benchmark (4% or lower), indicating high specificity. However, the referral rate can also be influenced by LTFU between screening steps. Unfortunately, follow-up rates were scarcely reported, and out of 12 programmes where follow-up rates were reported from screening to diagnostic assessment, only four reached the benchmark of 90% or higher, suggesting that LTFU remains a barrier to effective NHS in many countries. In the current study, detection rates of bilateral permanent HI for high- and low-risk infants combined ranged from 0.7 to 3 per 1000 infants, consistent with a previous review of the literature that showed a pooled prevalence rate of 2.2 per 1000 with a range across studies from 1 to 6 per 1000 infants (Bussé et al., 2020a).

When an NHS programme is implemented in a country, healthcare policy makers must make a few essential decisions. First, they must decide on the location where screening takes place, which is closely related to the age of the infant when screened. Screening is typically performed before discharge from the maternity hospital among countries with a high percentage of hospital births. This offers a major advantage, as it results in inherently high coverage. However, screening within 24 hours after birth can result in a high referral rate from step 1 because of residual amniotic fluid in the middle ear. In this study, programmes performing step 1 after 24 hours reported a range of referral rates from 2 to 15%. It is possible to achieve low referral rates when screening closely after birth with highly trained professionals (Vohr et al., 2001) and quiet test environments. For programmes with step 1 at 72 hours of age or later, step 1 referral rates were 4%. Although low false positive rates are achieved, this strategy may be more expensive, and coverage may be lower. Still, high coverage after discharge from the maternity hospital has been obtained by programmes in this study and others, by combining step 1 with an existing postnatal health visit (Olusanya et al., 2009, Khoza-Shangase and Harbinson, 2015). Second, a screening professional should be selected and trained. The decision on screening professional is described in more detail in the accompanying article (Bussé et al., 2021).

Next, the screening device and the number of steps should be established, plus whether a separate protocol is used for high-risk infants. In this study, aABR screening was related to lower referral rates to diagnostic assessment. An aABR may be used as the primary method for all infants or only infants that refer from earlier steps. The costs for aABR screening are up to double the costs of OAE screening, and aABR may be more complicated to use; however, lower referral rates will reduce the burden on diagnostic services, which may consequently reduce total costs (Vohr et al., 2001, Boshuizen et al., 2001). Screening effectiveness also depends on the device performance and passing criteria, listed in the accompanying article (Bussé et al., 2021). Given the lack of standardisation in screening equipment and the diversity of manufacturers, the decision of which device to select for a screening programme is difficult and may come down to cost and ease of use. Next, this study shows that NHS programmes with more screening steps had lower referral rates to diagnostic assessment. However, the requirement that families return one or multiple times for rescreening increases the risk that they do not return, which lowers the sensitivity of the screening programme. Finally, the decision should be taken whether to use a separate protocol for high-risk infants, which is discussed in the accompanying article (Bussé et al., 2021).

The overall efficacy of NHS is reduced if infants with a hearing impairment are not ultimately identified. Although sensitivity or negative predictive value were not reported in this study, poor follow-up rates between steps and to the diagnostic assessment show that LTFU is clearly an area in need of great improvement, according to both this quality investigation and other studies (Deem et al., 2012, Gaffney et al., 2010). It is a particular barrier in LICs and MICs (Olusanya et al., 2007). Reducing referral rates may improve LTFU. NHS programmes that have gained more experience with the devices and management of care across a large population may have successfully streamlined both the screening and follow-up processes (Finitzo et al., 1998, Mehl and Thomson, 2002). Furthermore, the confidence in the screen and perceived importance of follow-up for both the screener and parents may be strengthened by the saliency of a screening failure.

In conclusion, coverage, referral, follow-up and detection rates were aggregated across 42 NHS programmes. Our results show that screening protocol design influences the effectiveness of the NHS programme. The referral rate for step 1 was related to the age of the infants screened. Programmes had lower referral rates from screening to diagnostic assessment if they used aABR or had more screening steps. Many NHS programmes could not provide recent data representing their country or region for these quality measures. Among the reported figures, there was surely inherent variability in the quality and validity of the data supplied, despite working closely with the CRs, verifying all data where possible, and only accepting data that were considered valid. Still, the results of this study relied heavily on the CRs to provide accurate figures based on data from their local programmes, and the quality of the data management system (paper-based, digital, etc.) was not evaluated. Some programmes may collect this data in local hospitals, yet data are not shared nor evaluated on a regional or national level. Most concerningly is that many, even mature programmes, do not monitor or evaluate the performance of their NHS programme. For countries implementing NHS, the only method of ensuring effective use of resources is by collecting data, monitoring and evaluating the performance of the screening programme. Methods to identify areas for improvement, evaluate the selected protocol design, and ensure the effective use of resources should be essential components in all NHS programmes.

Acknowledgments

Members of the EUS€REEN foundation contributed information from their local screening programmes. The following are members of the EUS€REEN Foundation contributing to this work: B. Qirjazi; D. Holzinger; L. Stappaert; B. Vos; F. Brkić; P. Rouev; X. Peng; M. Velepic; C. Thodi; J. Drsata; T. Ovesen; M. Bambus; M. Lepplaan; B. Ellefsen; R. Niemensivu; T. Willberg; F. Denoyelle; P. Matulat; T. Nikolopoulos; A. Gáborján; I. Hinriksdóttir; Z. Chaudhurri; G. Norman; L. Rubin; A. Martini; D. Spanca; M. Audere; S. Kušķe; N. Drazdiene, E. Lesinskas; J.M. Hild; M. Cakar; T. Fenech; W. Mulwafu; D. Chiaburu; T. Kujundžić; E. Zvrko; A. Meuwese; A. Goedegebure; H. Hoeve; V. Nagaraj; G. Greczka; L. Monteiro; M. Georgescu; G. Tavartkiladze; L. Gouma; S. Filipovic; G. Jokovic; L. Langova; I. Sebova; S. Battelino; D.W. Swanepoel; F. Núñez-Batalla, J.M. Sequi-Canet; I. Uhlén; B. Nora; M. Baydan; J. McCall.

REFERENCES

BENITO-OREJAS, J. I., RAMIREZ, B., MORAIS, D., ALMARAZ, A. & FERNANDEZ-CALVO, J. L. 2008. Comparison of two-step transient evoked otoacoustic emissions (TEOAE) and automated auditory brainstem response (AABR) for universal newborn hearing screening programs. Int J Pediatr Otorhinolaryngol, 72, 1193-201.

BERNINGER, E. & WESTLING, B. 2011. Outcome of a universal newborn hearing-screening programme based on multiple transient-evoked otoacoustic emissions and clinical brainstem response audiometry. Acta Oto-Laryngologica, 131, 728-739.

BOSHUIZEN, H. C., VAN DER LEM, G. J., KAUFFMAN-DE BOER, M. A., VAN ZANTEN, G. A., OUDESLUYS-MURPHY, A. M. & VERKERK, P. H. 2001. Costs of different strategies for neonatal hearing screening: a modelling approach. Archives of Disease in Childhood - Fetal and Neonatal Edition, 85, F177-F181.

BUSSÉ, A. M. L., HOEVE, H. L. J., NASSERINEJAD, K., MACKEY, A. R., SIMONSZ, H. J. & GOEDEGEBURE, A. 2020. Prevalence of permanent neonatal hearing impairment: systematic review and Bayesian meta-analysis. International Journal of Audiology, 59, 475-485.

BUSSÉ, A. M. L., MACKEY, A. R., HOEVE, H. L., GOEDEGEBURE, A., CARR, G., UHLÈN, I. M. & SIMONSZ, H. J. 2021. Assessment of hearing screening programmes across 47 countries or regions I: Provision of newborn hearing screening. Submitted for publication.

CALURAUD, S., MARCOLLA-BOUCHETEMBLE, A., DE BARROS, A., MOREAU-LENOIR, F., DE SEVIN, E., REROLLE, S., CHARRIERE, E., LECLER-SCARCELLA, V., BILLET, F., OBSTOY, M. F., AMSTUTZ-MONTADERT, I., MARIE, J. P. & LEROSEY, Y. 2015. Newborn hearing screening: analysis and outcomes after 100,000 births in Upper-Normandy French region. Int J Pediatr Otorhinolaryngol, 79, 829-33.

CLEMENS, C. J. & DAVIS, S. A. 2001. Minimizing false-positives in universal newborn hearing screening: a simple solution. Pediatrics, 107, E29.

CUMMING, G. 2013. The New Statistics: Why and How. Psychological Science, 25, 7-29.

DEEM, K. C., DIAZ-ORDAZ, E. A. & SHINER, B. 2012. Identifying quality improvement opportunities in a universal newborn hearing screening program. Pediatrics, 129, e157-64.

FINITZO, T., ALBRIGHT, K. & O'NEAL, J. 1998. The newborn with hearing loss: detection in the nursery. Pediatrics, 102, 1452-1460.

GAFFNEY, M., GREEN, D. R. & GAFFNEY, C. 2010. Newborn hearing screening and follow-up: are children receiving recommended services? Public Health Rep, 125, 199-207.

JANUARIO, G. C., LEMOS, S. M., FRICHE, A. A. & ALVES, C. R. 2015. Quality indicators in a newborn hearing screening service. Braz J Otorhinolaryngol, 81, 255-63.

JOINT COMMITTEE ON INFANT HEARING 2007. Year 2007 position statement: Principles and guidelines for early hearing detection and intervention programs. Pediatrics, 120, 898-921.

KENNEDY, C., KIMM, L., DEES, D. C., CAMPBELL, M. & THORNTON, A. 1998. Controlled trial of universal neonatal screening for early identification of permanent childhood hearing impairment. The Lancet, 352, 1957.

KHOZA-SHANGASE, K. & HARBINSON, S. 2015. Evaluation of universal newborn hearing screening in South African primary care. African journal of primary health care & family medicine, 7, 769.

MEHL, A. L. & THOMSON, V. 2002. The Colorado newborn hearing screening project, 1992–1999: on the threshold of effective population-based universal newborn hearing screening. Pediatrics, 109, e7-e7.

NEUMANN, K., CHADHA, S., TAVARTKILADZE, G., BU, X. & WHITE, K. R. 2019. Newborn and Infant Hearing Screening Facing Globally Growing Numbers of People Suffering from Disabling Hearing Loss. International Journal of Neonatal Screening, 5, 7.

NHS NEWBORN HEARING SCREENING PROGRAMME 2019. Newborn hearing screening data tables 1 April 2017 to 31 March 2018.

OECD. 2019. Health at a Glance 2019: OECD Indicators. Average length of stay in hospitals. [Online]. Available: https://doi.org/10.1787/888934017804 [Accessed October 20 2020].

OLUSANYA, B. O., EBUEHI, O. M. & SOMEFUN, A. O. 2009. Universal infant hearing screening programme in a community with predominant non-hospital births: a three-year experience. Journal of Epidemiology & Community Health, 63, 481-487.

OLUSANYA, B. O., SWANEPOEL, D., CHAPCHAP, M. J., CASTILLO, S., HABIB, H., MUKARI, S. Z., MARTINEZ, N.V., LIN, H.-C. & MCPHERSON, B. 2007. Progress towards early detection services for infants with hearing loss in developing countries. BMC Health Services Research, 7, 14.

PATEL, H. & FELDMAN, M. 2011. Universal newborn hearing screening. Paediatr Child Health, 16, 301-10.

SLOOT, F., HOEVE, H. L., DE KROON, M. L., GOEDEGEBURE, A., CARLTON, J., GRIFFITHS, H. J. & SIMONSZ, H. J. 2015. Inventory of current EU paediatric vision and hearing screening programmes. J Med Screen, 22, 55-64.

THE WORLD BANK. 2019. World Bank Country and Lending Groups [Online]. The World Bank. Available: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups [Accessed 03-06-2019 2019].

UNICEF 2019. Maternal and Newborn Health Coverage Database. November 2019 ed.

VAN DYK, M., SWANEPOEL, D. W. & HALL, J. W. 2015. Outcomes with OAE and AABR screening in the first 48h—Implications for newborn hearing screening in developing countries. International Journal of Pediatric Otorhinolaryngology, 79, 1034-1040.

VOHR, B. R., OH, W., STEWART, E. J., BENTKOVER, J. D., GABBARD, S., LEMONS, J., PAPILE, L. A. & PYE, R. 2001. Comparison of costs and referral rates of 3 universal newborn hearing screening protocols. J Pediatr, 139, 238-44.

WOOD, S. A., SUTTON, G. J. & DAVIS, A. C. 2015. Performance and characteristics of the Newborn Hearing Screening Programme in England: The first seven years. Int J Audiol, 54, 353-8.

WORLD HEALTH ORGANIZATION 2015. Ear and hearing care: planning and monitoring of national strategies: a manual. Geneva, Switzerland.

WORLD HEALTH ORGANIZATION. 2019. First dose of diphtheria toxoid, tetanus toxoid and pertussis vaccine [Online]. Available: https://apps.who.int/immunization_monitoring/globalsummary/timeseries/tscoveragedtp1.html [Accessed April 28 2020].

Chapter 5

Assessment of hearing screening programmes across 47 countries or regions III: Provision of childhood hearing screening after the newborn period

*Andrea ML Bussé**
*Allison R Mackey**
Hans LJ Hoeve
André Goedegebure
Gwen Carr
Inger M Uhlén
HJ Simonsz

the EUS€REEN Foundation

**Contributed equally and should be considered dual first authors*

ABSTRACT

Objective

To inventory provision and features of childhood hearing screening after the newborn period (CHS), primarily in Europe.

Design

From each participating country or region, experts provided information through an extensive questionnaire: implementation year, age at screening, test method, pass criteria, screening location, screener profession, and quality indicators: coverage, referral, follow-up and detection rates, supplemented by literature sources.

Study sample

Forty-two European countries or regions, plus Russia, Malawi, Rwanda, India and China.

Results

CHS was performed universally with pure-tone audiometry screening (PTS) in 17 countries or regions, whereas non-universal CHS was performed in eight with PTS or whisper tests. All participating countries with universal PTS had newborn hearing screening. Coverage rate was provided from three countries, detection rate from one, and referral and follow-up rate from two. In four countries, universal PTS was performed at two ages. Earliest universal PTS was performed in a (pre)school setting by nurses (n=9, median age: 5 years, range: 3-7), in a healthcare setting by doctors and nurses (n=7, median age: 4.5 years, range: 4-7), or in both (n=1).

Conclusions

Within universal CHS, PTS was mostly performed at 4-6 years by nurses. Insufficient collection of data and monitoring with quality indicators impedes evaluation of screening.

INTRODUCTION

Early detection of a hearing impairment (HI) and subsequent intervention have a positive effect on language, cognitive and social outcomes in children (Yoshinaga-Itano et al., 1998, Moeller, 2000). To reach this goal, several guidelines and position statements recommend screening for HI among infants and children (Skarzynski and Piotrowska, 2012, European Consensus Statement on Neonatal Hearing Screening, 1999). Childhood hearing screening after the newborn period (CHS) uses a variety of methods. The distraction test (Ewing and Ewing, 1944) was widely used in high-income countries to screen children for HI around the age of 7 to 9 months; however, it has since been replaced by universal newborn hearing screening (NHS). In a universal hearing screening programme, screening is provided to all children, regardless of their risk for HI. The whisper test can be administered to children from age 3 years and requires no equipment and little training, thereby making it feasible for lower-income settings (Pirozzo et al., 2003). Though, due to its poor reliability and a sensitivity of only 70 to 87% in children, its use is of limited value for CHS (Pirozzo et al., 2003). Pure-tone audiometry screening (PTS) can be performed with a frequency sweep or a limited series of frequencies and intensities which results in a pass or fail result. The earliest report of using PTS for children was published in 1955 (Ewing, 1955). It has since become the standard practice for screening children aged 3 years and older (Yong et al., 2020b) because of its high sensitivity and reliability (Fortnum et al., 2016). PTS requires calibrated equipment, trained personnel, and a behavioural response from the child. Including tympanometry to evaluate middle ear function in the screening session can determine the appropriate referral pathway (i.e., medical or audiological) after a failed hearing test (American Academy of Audiology, 2011). Automated methods are currently under development that will allow screening with, for example, speech stimuli to be performed via a smartphone or tablet (Denys et al., 2019, De Sousa et al., 2020).

The prevalence of permanent HI increases from 1-2 per 1000 at birth to 2-3 per 1000 by the age of 9 years (le Clercq et al., 2017, Fortnum et al., 2001). Without screening, some children with a HI may remain undetected and lack appropriate intervention throughout important developmental and educational years (Watkin and Baldwin, 2011). Children with a congenital HI may not be detected due to issues related to the NHS programme such as false negatives, loss to follow-up, parental refusal, or because they were not offered screening (Fortnum, 2003, Prieve et al., 2015). Even a well-executed NHS programme may not be designed to target mild or unilateral HI, of which negative effects may become apparent particularly in early school years (Bess et al., 1998, Winiger et al., 2016). Many countries have targeted surveillance programmes after NHS, where children with risk factors are regularly scheduled for audiological assessment; however, there are limitations to this system, particularly the high loss to follow-up among children being monitored (Beswick et al., 2012).

Hearing impairment may be conductive or sensorineural, congenital or acquired, and permanent or transient. Most sensorineural HI detected after the newborn period is a delayed-onset HI. Delayed-onset HI has a prevalence of around 0.7 per 1000 children aged 3 to 7 (Lü et al., 2011) and may be caused by hereditary factors or pre- or perinatal infections, the most common being cytomegalovirus. Acquired sensorineural HI may be caused by ototoxic medications, trauma, or postnatal infection (Smith et al., 2005). The most common type of HI that is found among children is an acquired conductive HI caused by otitis media, a condition of the middle ear. Two types of otitis media are chronic suppurative otitis media (CSOM) and otitis media with effusion (OME).

CSOM is characterised by a discharge of fluid from the middle ear through a perforation in the tympanic membrane. The prevalence rate is approximately 2 to 2.5% in children aged 1 to 10 years, with no major differences across age (Monasta et al., 2012). CSOM is considered to be a particular burden for developing countries, and the most common cause of mild to moderate HI among children in these countries, with at least half the cases of CSOM resulting in associated HI (World Health Organization, 2004). If left untreated, CSOM can cause permanent HI in over 90% of cases (Jensen et al., 2013).

OME is characterised by the presence of fluid behind an intact tympanic membrane. OME is extremely common among young children. Prevalence rates range from 1% to 30% in children aged 1 to 8 years worldwide, with a peak at age 3 to 4 years (Casselbrant and Mandel, 2003, Mandel et al., 2008). At least half of the children with OME will have an associated HI (Gravel, 2003). Although most OME resolves within 3 months, up to 40% of affected children will have recurrent or longstanding OME requiring intervention (Rosenfeld et al., 2016). It is unclear whether targeting cases of OME in a CHS programme is cost-effective (Rosenfeld et al., 2016).

The EUSCREEN study compares the cost-effectiveness of vision and hearing screening programmes across participating countries, given the local circumstances in a country or region. In combination with our previous studies on NHS (Bussé et al., 2021, Mackey et al., 2021), results of this article will aid the development of a decision-analytic cost-effectiveness model produced within the EUSCREEN study. Unlike NHS, the importance of CHS has not been universally established. High quality information that is needed to make a conclusive judgement on the cost-effectiveness of CHS is currently lacking. This hampers the ability of policy makers and professionals to decide which programmes should be implemented and how. This study reports on the current provision, protocols, and outcomes of CHS for children after the newborn period via an international inventory of hearing screening programmes. It also compares its practice against local healthcare and school structure. This article evaluates the provision of CHS, funding source, age at which children are screened, test method, year of implementation, pass criteria, screening location, screener profession, quality measures (coverage, referral, follow-up and detection rate), and costs, supplemented by literature sources.

METHODS

From each of the originally selected countries primarily in Europe, hearing screening experts, so called Country Representatives (CR), were recruited via professional networks, scientific journal articles, or existing professional connections. CRs from countries in Europe or with affiliated research programmes were actively sought. Participation in the study was open to any country, and experts from five non-European countries expressed interest in participation. Involvement of countries outside of Europe, such as from large, highly populated countries or low-income countries, could add information that would not be available from within a European-only context. CRs with the time available to complete the questionnaire were required to confirm their role and expertise in relation to their hearing screening programme. They formed the Country-Committee Joint-Partnership of EUS€REEN Foundation and were remunerated up to €2000 for completing the questionnaire sufficient to formulate a country- or region-specific report detailing the strategies for screening.

Data collection

The EUSCREEN questionnaire contained 191 hearing questions, 51 of which related specifically to CHS. The remaining questions related to NHS or general early detection and intervention practice. Questions were a combination of multiple choice, yes-no, and open-ended questions and were subdivided into nine domains: demography and epidemiology, administration and general background, existing screening programmes, coverage and attendance, tests and devices, follow up and diagnostic assessment, treatment options, costs and benefits and adverse effects. A sub-question typically followed each question, asking the respondent to state the source of the information. Possible answers were (a) Data unavailable, (b) I don't know, (c) Rough estimate, (d) Real estimate from calculation, or (e) Actual data. The name and date of the data source, in addition to source materials were requested if relevant. The questionnaire was made accessible to the CR through the EUSCREEN website (www.euscreen.org) via a unique username and password.

After submission, the questionnaire was checked for completeness and all answers went through a verification and validation process (Figure 1, Appendix). Answers were evaluated for completeness and cross-checked across similar questions. Any material provided by the CR or acquired via an online search were cross-checked to the provided answers. All discrepancies were sent to the CR for clarification. A country-specific report was written which was delivered back to the CR for final confirmation. Information on CHS after the newborn period was then extracted from the reports for evaluation.

Quality indicators

Screening performance should be evaluated through predetermined quality measures. Data on four key quality measures were collected to assess CHS programmes (American Academy of Audiology, 2011): coverage rate, referral rate, follow-up rate, and detection rate. Coverage rate was the percentage of children screened out of all eligible children. Referral rate was the percentage of children referred from screening, either to a rescreening step or to diagnostic assessment, out of all children screened. Follow-up rate was the percentage of children who attend the diagnostic assessment out of all children referred. Detection rate was the percentage of children detected with a HI (targeted by the programme), out of all children screened. Additional measures may also be used to evaluate screening (e.g., sensitivity and specificity), but these are not reported in this article.

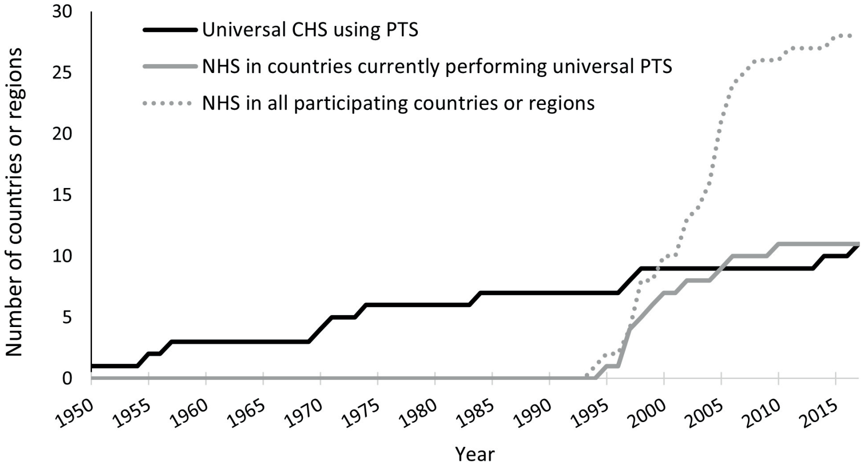


Figure 1. The cumulative number of participating countries or regions implementing newborn hearing screening (NHS) and universal childhood hearing screening (CHS) with pure-tone audiometry screening (PTS) according to the reported year of implementation. Information on implementation year was available for 28 NHS and 11 universal CHS programmes. All programmes with universal CHS used PTS. PTS started as early as 1950 with a slow spread across participating countries or regions. Only four implemented new programmes since 2000. Two programmes implemented PTS after NHS. No information was included about the use of other methods for CHS (e.g., the distraction test) in these countries. The first NHS programme was implemented in 1994 with a rapid increase from 1995 to 2010.

Assessment of CHS

The questions on the status of CHS included whether it was provided, the year it was first implemented, and the funding source (e.g., parents, health insurance, state). Questions on the protocol covered the age at screening (open-ended), the test method (e.g., pure-tone screening, whisper test), the pass criteria, and the number of rescreening tests performed prior to referral for audiological or ENT assessment if pass criteria were not met. Pass criteria for PTS were defined as a valid response at a minimum intensity (dB HL) across specified frequencies, in either one ear or both ears.

An open-ended question on screener profession (e.g., nurse, audiologist) was evaluated, in addition to a multiple-choice question on the screening location (e.g., child health clinic, school, kindergarten), where several options may be selected including an open choice, under the heading of 'other'. The term for early education prior to primary school varied across countries and for children of different ages. For this article, preschool was defined as all pre-primary school systems up to primary-school start. The questions on costs included both the total cost of the screening programme and the cost per child screened.

Supplemental literature data on coverage for CHS

High coverage of CHS can be ensured by combining screening with school attendance, healthcare appointments or with vaccination. Data from supplemental literature were aggregated to investigate the context for ensuring high coverage rates for CHS for all countries and regions that participated in data collection, including those without CHS. Indicators of school and routine child healthcare during childhood were compiled from the following databases: European Commission/EACEA/Eurydice (2015), UNESCO (2020), UNICEF (2012), and World Health Organisation (2020, 2019a, 2019b). These included the age, location, and coverage rate of the second dose of measles-containing vaccine; the out-of-school rate for primary school-age children; and the participation rate in preschool.

RESULTS

Out of 49 countries or regions, the questionnaire was sufficiently completed in 47, which were included in the overall study. Two countries were excluded because the information supplied was not sufficient to complete a descriptive report (South Africa and Norway). Among the included countries were 30 high income (HIC), 10 upper-middle income, three lower-middle income and two low income, according to the World Bank classification system (2019) (Table 1, Appendix).

Provision of CHS

Table 1 and 2 provide an overview of the provision of CHS in 17 participating countries or regions with universal CHS and 8 countries or regions that offer non-universal or non-routine CHS. In all 25 countries or regions where CHS is offered, NHS is also performed. CRs from the remaining 22 countries or regions indicated that their country did not offer CHS. In twenty programmes, the type of funding for CHS was reported: 14 were funded by either the regional or national government and six by health insurance.

The distraction test at 7 to 9 months of age was not reported to be used by any programme. The whisper test was used by three countries or regions for children aged 5 to 8 years of which one also used PTS. PTS was used for screening children aged 3 to 8 years in 20 countries or

Table 1. Age at screening, test methods, pass criteria, screening profession and location for the 17 countries or regions performing universal childhood hearing screening with pure-tone audiometry screening (PTS). PTS was accompanied by other tests in two countries. In countries where the test method indicated a rescreen, children who do not meet pass criteria would return for a rescreening test, and if pass criteria are still not met, they would then be referred for diagnostic assessment. Pass criteria for PTS were described in terms of the intensity (dB HL), the screening frequencies (Hz), and whether responses were required in only one or both ears. With two exceptions, responses were required for all specified frequencies at the corresponding intensity to qualify a pass. Abbreviations: SLT (speech-language therapist); GP (general practitioner); ENT (ear, nose, throat specialist); PTS (pure-tone audiometry screening); tymp (tympanometry).

			Pass criteria				
Country and region	**Age (yrs)**	**Test methods**	**Intensity**	**Frequencies**	**Ears**	**Screener profession**	**Location**
Austria, Upper Austria	4-5	PTS	25 dB	500-4000 Hz	Both	SLT	Kindergarten
Belgium, Flanders	5-6	PTS	30 dB	1000 & 4000 Hz	Both	Nurse	Preschool
Bulgaria	7	PTS	40 dB	Not indicated	Both	Various	Child health clinic
England (U.K.)	4-5	PTS	25 dB 30 dB	1000-4000 Hz & 500 Hz	Both	Nurse, Audiologist	Kindergarten, School
Faroe Islands	7	PTS	20 dB	Not indicated	Both	Nurse	School
Finland	4-5 / 6★	PTS	20 dB	250-4000 Hz	Both	Nurse	Child health clinic
France	3-4 / 6★	PTS	30 dB	500-4000 Hz	Both	School physician	School
Germany	4	PTS	30 dB	500-6000 Hz†	Both	Paediatrician's staff	Child health clinic
Hungary	5	PTS	25 dB	Not indicated	Both	Nurse	Kindergarten
Ireland	4-5	PTS (rescreen)	25 dB	1000-4000 Hz	Both	Nurse	School
Israel	6	PTS	20 dB 25 dB	1000-4000 Hz & 500 Hz	Both	Nurse, Audiologist	School
Latvia	5-6	PTS+speech	20 dB	Not indicated	One	GP, ENT	Child health clinic
Luxembourg	5-6	PTS (rescreen)	20 dB	Not indicated	Both	SLT	Kindergarten
Netherlands	5-6	PTS (rescreen)	30 dB	500-4000 Hz	Both	Nurse, Assistant	School, Health clinic
Serbia	6-7	PTS+tymp+ tuning fork	25 dB	Not indicated	Both	Audiologist	Child health clinic
Sweden, Stockholm	4 / 6★	PTS (rescreen)	25 / 20★ dB	500-4000 Hz†	Both	Nurse	Child health clinic / School★
Switzerland	4 / 6★	PTS (rescreen)	30 dB	Not indicated	Both	GP, Paediatrician	Child health clinic

★ The second screen in countries where screening is performed at two different ages.

†A referral is made if pass criteria are not met in 2 or more frequencies

regions, alone or in combination with tympanometry, speech test or a tuning fork test (Table 1). The test method was unknown for three countries.

In eight countries or regions, limited or variable screening was reported, which took place during short periods (i.e., project-based), during paediatric doctors' appointments (i.e., non-systematic), or intermittently during screening camps (Table 2). In 17 countries or regions, there was universal screening, all using PTS (Table 1). With the exception of Bulgaria and Serbia, all were high-income countries. The following sections provide findings from these 17 programmes with universal CHS, all performing PTS.

Table 2. Description of childhood hearing screening after the newborn period among 8 countries or regions that offered non-routine or non-universal screening. A dash indicates that the Country Representative did not supply information. Test methods were the whisper test or pure-tone audiometry screening (PTS). Pass intensity for PTS, indicated in brackets (in dB HL) were provided by three countries or regions. PTS was accompanied by tympanometry in one country. All other participating countries not listed in Tables 2 or 3 reported that childhood hearing screening was not performed. Abbreviations: SLT (speech-language therapist); GP (general practitioner); ENT (ear, nose, throat specialist); PTS (pure-tone screening); tymp (tympanometry).

Country and region	Age (yrs)	Test methods	Screener profession	Location	Details of non-universal childhood hearing screening
Czechia	-	-	-	-	No nationally regulated programme; differences in provision and protocol across regions.
Estonia	6-8	Whisper	Physician	Child health clinic	No nationally regulated programme; screening by physician may be performed based on parental concern.
India	-	Screening camps	-	-	No routine screening; screening camps have been performed in some states during which all children and adults of any age are being offered screening. Some ENT specialists screen children when there is a suspicion of hearing loss.
Moldova, Chisinau	6-8	PTS+tymp (30-35 dB)	GP, ENT	Kindergarten, school	No routine screening; screening is organised through projects that are carried out within a limited timeframe on a limited number of children.
N. Macedonia, Skopje	5-6	PTS (30 dB)	SLT	ENT/hearing clinic	Children in Skopje may come into the ENT or hearing clinic for testing.
Poland	-	-	-	-	No centralised information; screening exists only in some regions or local areas.
Romania	6	Whisper	School physician	School	No nationally regulated programme; screening may be performed as a school-entry test.
Slovenia	5-6	PTS (30dB), whisper, other	Paediatrician, Nurse	Child health clinic	No nationally regulated programme; differences in provision and protocol across regions.

Implementation of PTS

Universal PTS started in 1950, well before NHS (Figure 1). In 2016, the Flanders region of Belgium stopped screening universally at age 3, and instead, screening was only performed on children with risk factors for delayed-onset HI. Universal screening is still performed at age 5-6. In 2015 in England, expansion of screening in other health care districts was not recommended while existing CHS could continue to operate. In 2012, Iceland terminated their CHS programme.

Quality indicators of PTS

Coverage rates were only provided by CRs in three out of the 17 countries or regions with universal screening. Referral rates from screening and follow-up rates to the diagnostic assessment were only provided by CRs from two countries. Data on detection rate after PTS were reported from one country.

Coverage rates were provided from Israel, Luxembourg and Serbia. A 97% coverage rate was reported from Israel, based on a 2015 audit, and 99% from Luxembourg based on data from 2018. In Serbia, the coverage rate in 2017 was 45% for the entire country and 92% for the Belgrade Region. CRs from four additional programmes reported rough estimations of their coverage rates, ranging from 90 to 100%.

Referral rates from screening and follow-up rate to the diagnostic assessment were reported from Luxembourg and Israel. In Luxembourg, 10% did not pass the first screening and were invited to rescreening, after which 7.6% of all infants first screened were referred to diagnostic assessment in 2018. Out of these children, 58% followed up to diagnostic assessment. In Israel, 7.9% were referred from screening to diagnostic assessment in 2015. A follow-up rate of 77% was found by a survey among parents.

The detection rate after PTS was only reported from Israel; 0.012% of infants screened were diagnosed with a previously undetected permanent HI ≥25 dB HL. Little information was provided on OME or CSOM. Five CRs provided estimated prevalence rates; however, the estimated rates varied dramatically (3.5% of all children to 35% of preschool-age children).

Protocol for PTS

Across the 17 universal PTS programmes, universal screening was performed at two different ages in four programmes: at 3 to 5 years and again at 6 to 7 years. The age of children at the earliest screen was 3 to 4 years (4 programmes), 4 to 5 years (5 programmes), 5 to 6 years (4 programmes), and 6 to 7 years (4 programmes).

In all 17 programmes with universal PTS, both ears were screened. In all programmes except for that in Latvia, children were referred for diagnostic assessment if suspected with a unilateral or bilateral HI. In 12 programmes, children who did not pass initial PTS were referred to an audiology or ENT clinic for diagnostic testing. In the other five programmes one or two rescreening tests were offered before referral to diagnostic testing. The intensity (in dB) used as a pass criterion for PTS was available for all 17 programmes and ranged from 20 to 40 dB. In most programmes the frequencies 500 to 4000 Hz were used. In two programmes 500 Hz was excluded, and in two others there is higher pass intensity at 500 Hz. The median pass intensity was 30 dB for PTS performed on children aged 3 to 4 years, and 25 dB for PTS on children over age 4.

Professionals and locations for PTS

CRs from all 17 universal PTS programmes provided information on location and professionals (Table 1). For nine programmes, nurses screened children aged 3 to 7 years (median: 5) in a (pre)school setting. For seven programmes, doctors and nurses screened children aged 4 to 7 years (median: 4.5) in a healthcare setting. In the Netherlands, nurses performed screening in either a healthcare or school setting.

Costs of PTS

Most CRs could not report on costs of screening. The reported cost per child screened ranged from 5 to 45 euros; the specific costs included in each estimation were not specified (e.g., equipment, disposables, salary). Therefore, these values may have included varying aspects of the screening programme.

Supplemental literature data on coverage for CHS

Table 1 in the Appendix lists the enrolment in preschool and primary school education together with economic status, age and coverage of measles-containing vaccine. The median participation rate in the final year of preschool education for 10 low- and middle-income countries (LMIC) was 83% compared to 98% for 31 HICs (UNESCO, 2020). In contrast, the median participation rate for primary school differed only slightly between participating LMICs (95%) and HICs (98%). Twenty-five participating countries (16 HICs and nine LMICs) offered the second dose of the measles-containing vaccine during the pre-school or school-entry years (3 to 7 years) (World Health Organization, 2020). According to the World Health Organisation, out of these nine LMICs, five offered the vaccine in schools (The European Observatory on Health Systems and Policies, 2018, World Health Organization, 2019b).

DISCUSSION

This study revealed that PTS is performed only in some countries that also have NHS, and most are high-income. The distraction test at 9 months was not reported to be used in any participating country. The whisper test, easy to perform but with low sensitivity, is only performed by three countries or regions. In 20 countries or regions, PTS is used alone or in combination with tympanometry, speech testing, or tuning fork tests, 17 of which are universal programmes.

Universal PTS is performed by nurses in a (pre)school setting in nine programmes for children at a median age of 5 years (range 3-7 years), in a healthcare setting by nurses and doctors in seven programmes for children at a median age of 4.5 years (range: 4-7 years), and in both for one programme.

Although we originally aimed to compare the effectiveness of CHS programmes in this study, coverage rates could only be provided by three programmes, referral and follow-up rates by two and detection rates by one. It is apparent that data are not routinely collected and that monitoring and quality control are not performed in the majority of screening programmes. This makes it impossible to compare the effectiveness of hearing screening programmes and perpetuates the variety in screening programmes.

When implementing a CHS programme, healthcare policy makers have to make some key decisions within the context in their country, including the screening location, the professional performing the screening, the test method, and the age at which a child is eligible for screening. The location of screening may be a healthcare centre or school. A (pre)school setting is a viable place for routine health services to ensure high coverage if enrolment rates are favourable and lack disparity, which may not be the case in some countries in Europe (UNICEF, 2012). Integrating screening with other healthcare services, such as immunisation, also leads to high coverage rates and equitable care (Okwo-Bele, 2012). The screening professionals could typically be nurses, nurse assistants, doctors, audiologists or speech-language therapists. When deciding on a screening professional, costs of experienced professionals and extensive training may be justified if it ensures high specificity of the screening.

When deciding on the test method, policy makers must consider that the feasibility of various hearing screening tests for CHS depends on the age of the child and the costs. Before 3 years, PTS is typically not possible, as many children this age are not mature enough to learn the task in a short time or maintain attention throughout the screening. From 3 years onward, PTS is the most commonly used method for CHS, because it has high sensitivity and specificity under ideal conditions (Fortnum et al., 2016). PTS will detect both sensorineural and conductive HI, including conductive HI caused by OME or CSOM. Tympanometry supplements PTS in two programmes and provides an indication of the presence or absence of fluid in the middle ear. PTS requires a quiet location, best realised through a sound-proof room. PTS also requires well-trained screeners and a screening audiometer, which needs regular calibration. All of these prerequisites may be especially scarce in lower income or more remote areas (Yong et al., 2020b). The whisper test is still performed in some countries in this study, which requires no equipment and little training; however, reliability and sensitivity are poor (Pirozzo et al., 2003). None of the participating countries reported use of new automated technologies for performing CHS with speech stimuli via a smartphone or tablet, that are based on hearing screening tests for adults using speech perception in noise (Denys et al., 2019, De Sousa et al., 2020).

After choosing the test method, the age at which screening is provided and the pass criteria must be decided upon. The advantage of screening from age 3 to 4 is so that intervention can be supplied as early as possible. However, sensitivity and specificity may be lower when screening is performed at 3 to 4 years because of difficulty with sustained attention and less reliable responses to a low intensity tone in the presence of background noise (Browning, 2000). This may also explain the 5 dB difference in the reported pass criterion between younger and older ages. Additionally, OME is highly prevalent at this age (Browning, 2000) which will lead to higher referral rates of children with a conductive HI. Although not consistent across all studies (e.g., Fitzpatrick et al., 2014), permanent mild HI may have a negative effect on speech and language development and school performance (Bess et al., 1998, Winiger et al., 2016). It may be crucial to identify children with mild permanent HI and persistent OME before or soon after they start school, so that audiological intervention and accommodation in the classroom can be provided (McKay et al., 2008).

With PTS, a lower pass intensity will increase the number of cases detected with mild HI, while a higher pass intensity may more efficiently identify the more severe cases, which could be particularly resourceful in countries with limited resources (Mahomed-Asmail et al., 2016). The use of a low-frequency tone (250 and 500 Hz) was not consistent practice across participating programmes. Lower pass intensity and inclusion of low frequencies will also capture many children with CSOM or OME, which often presents as a mild HI in the lower frequencies (Silman et al., 1994). Environmental noise may interfere with a low-frequency tone, which can result in a higher number of false positives (McPherson et al., 2010). The decision to include low frequencies may depend on local circumstances, including the likelihood of environmental noise interference in the chosen screening locations, the existing intervention pathways, and the local prevalence rates of OME and CSOM at the age when screening is performed. Including low frequencies in the test protocol improves the sensitivity of the screen, capturing children with a low-frequency HI (McPherson et al., 2010).

In contrast to universal NHS for which cost-effectiveness has largely been established (Sharma et al., 2019), that of CHS is not clear (Fortnum et al., 2016). NHS has seen rapid widespread implementation since 1995. However, children with a HI that develops after the neonatal period or a mild HI that was not detected by NHS, may subsequently remain undetected if no additional screening or risk factor surveillance is done (Lü et al., 2011). Whereas universal CHS has been implemented in 17 countries since 1950, the CHS programme in Flanders (Belgium) was scaled down in 2016 and terminated in Iceland in 2012. Similarly, in 2015, national expansion of CHS was no longer recommended in England until more information would become available on its cost-effectiveness.

For parts of the world where NHS is not available, CHS could be cost-effective when it is the first screening or the only screening available. CHS may also be cost-effective when local circumstances are taken into account. In countries where CSOM is prevalent and not detected or treated at a young age, CHS may contribute to its detection (Yong et al., 2020a). Therefore, the World Health Organisation (2004) recommends performing CHS in developing countries to reduce the burden of CSOM. Surgical and medical treatment can be provided to mitigate hearing problems as well as prevent permanent HI and its associated costs (Nguyen et al., 2015). In sub-Saharan Africa and South East Asia, a modelling study showed that PTS in combination with the provision of hearing aids among school-aged children would be cost effective. NHS was not included in that model, however (Baltussen and Smith, 2012).

This study set out to compare the cost-effectiveness of CHS by evaluating screening quality indicators: coverage, referral rate, follow-up rate and detection rate across programmes. Unfortunately, most Country Representatives could not report these data. One may argue that the lack of available data may have been due to limited access of the participating Country Representatives who were predominantly involved in NHS. However, in several countries, data were not sufficiently collected or shared across district or regional programmes.

Consequently, when basic determinants like coverage, referral rate, follow-up rate and detection rate are not collected, cost-effectiveness cannot be calculated or compared with that of other countries and, hence, the large diversity between screening programmes remains. It would be advantageous if all systems for data collection, monitoring and evaluation of screening were uniform across regions of a nation and across countries. When the data collected and reported from CHS programmes can be compared across borders, it will be possible to calculate whether CHS would be cost-effective (alone or in combination with NHS), and optimal conditions like choices on location, personnel, test method and age of testing can be formulated.

Acknowledgments

Members of the EUS€REEN Foundation contributed information from their local screening programmes. The following are members of the EUS€REEN Foundation contributing to this work: B. Qirjazi; D. Holzinger; L. Stappaert; B. Vos; F. Brkić; P. Rouev; X. Peng; M. Velepic; C. Thodi; J. Drsata; T. Ovesen; M. Bambus; M. Lepplaan; B. Ellefsen; R. Niemensivu; T. Willberg; F. Denoyelle; P. Matulat; T. Nikolopoulos; A. Gáborján; I. Hinriksdóttir; Z. Chaudhurri; G. Norman; L. Rubin; A. Martini; D. Spanca; M. Audere; S. Kušķe; N. Drazdiene, E. Lesinskas; J.M. Hild; M. Cakar; T. Fenech; W. Mulwafu; D. Chiaburu; T. Kujundžić; E. Zvrko; A. Meuwese; A. Goedegebure; H. Hoeve; V. Nagaraj; G. Greczka; L. Monteiro; M. Georgescu; G. Tavartkiladze; L. Gouma; S. Filipovic; G. Jokovic; L. Langova; I. Sebova; S. Battelino; D.W. Swanepoel; F. Núñez-Batalla, J.M. Sequi-Canet; I. Uhlén; B. Nora; M. Baydan; J. McCall.

REFERENCES

AMERICAN ACADEMY OF AUDIOLOGY. 2011. Childhood Hearing Screening, Clinical Practice Guidelines [Online]. American Academy of Audiology. Available: https://audiology-web.s3.amazonaws.com/migrated/ChildhoodScreeningGuidelines.pdf_5399751c9ec216.42663963.pdf [Accessed 16/11/2020 2020].

BALTUSSEN, R. & SMITH, A. 2012. Cost effectiveness of strategies to combat vision and hearing loss in sub-Saharan Africa and South East Asia: mathematical modelling study. Bmj, 344, e615.

BESS, F. H., DODD-MURPHY, J. & PARKER, R. A. 1998. Children with minimal sensorineural hearing loss: prevalence, educational performance, and functional status. Ear Hear, 19, 339-54.

BESWICK, R., DRISCOLL, C., KEI, J. & GLENNON, S. 2012. Targeted surveillance for postnatal hearing loss: A program evaluation. Int J Pediatr Otorhinolaryngol, 76, 1046-1056.

BROWNING, G. G. 2000. Influence of Age, Type of Audiometry and Child's Concentration on Hearing Thresholds. British Journal of Audiology, 34, 231-240.

BUSSÉ, A. M. L., MACKEY, A. R., HOEVE, H. L., GOEDEGEBURE, A., CARR, G., UHLÈN, I. M. & SIMONSZ, H. J. 2021. Assessment of hearing screening programmes across 47 countries or regions I: Provision of newborn hearing screening. Submitted for publication.

CASSELBRANT, M. L. & MANDEL, E. M. 2003. Chapter 10 Epidemiology. In: ROSENFELD, R. M. & BLUESTONE, C. D. (eds.) Evidence-Based Otitis Media. 2nd ed. London: BC Decker Inc Hamilton.

DE SOUSA, K. C., SWANEPOEL, D. W., MOORE, D. R., MYBURGH, H. C. & SMITS, C. 2020. Improving Sensitivity of the Digits-In-Noise Test Using Antiphasic Stimuli. Ear and Hearing, 41, 442-450.

DENYS, S., DE LAAT, J., DRESCHLER, W., HOFMANN, M., VAN WIERINGEN, A. & WOUTERS, J. 2019. Language-Independent Hearing Screening Based on Masked Recognition of Ecological Sounds. Trends in Hearing, 23, 2331216519866566.

EUROPEAN COMMISSION/EACEA/EURYDICE 2015. Early Childhood Education and Care Systems in Europe. National Information Sheets - 2014/15. In: EURYDICE FACTS AND FIGURES (ed.). Luxembourg: Publications Office of the European Union.

EUROPEAN CONSENSUS STATEMENT ON NEONATAL HEARING SCREENING 1999. European Consensus Statement on Neonatal Hearing Screening. Finalized at the European Consensus Development Conference on Neonatal Hearing Screening. Acta Paediatr, 88, 107-8.

EWING, A. W. 1955. The sweep-frequency method of making screening tests of the hearing of schoolchildren. Br Med J, 1, 41-2.

EWING, I. R. & EWING, A. W. G. 1944. The Ascertainment of Deafness in Infancy and Early Childhood. The Journal of Laryngology & Otology, 59, 309-333.

FITZPATRICK, E. M., WHITTINGHAM, J. & DURIEUX-SMITH, A. 2014. Mild bilateral and unilateral hearing loss in childhood: a 20-year view of hearing characteristics, and audiologic practices before and after newborn hearing screening. Ear Hear, 35, 10-8.

FORTNUM, H. 2003. Epidemiology of permanent childhood hearing impairment: Implications for neonatal hearing screening. Audiological Medicine, 1, 155-164.

FORTNUM, H., UKOUMUNNE, O. C., HYDE, C., TAYLOR, R. S., OZOLINS, M., ERRINGTON, S., ZHELEV, Z., PRITCHARD, C., BENTON, C. & MOODY, J. 2016. A programme of studies including assessment of diagnostic accuracy of school hearing screening tests and a cost-effectiveness model of school entry hearing screening programmes. Health Technology Assessment, 20.

FORTNUM, H. M., SUMMERFIELD, A. Q., MARSHALL, D. H., DAVIS, A. C. & BAMFORD, J.

M. 2001. Prevalence of permanent childhood hearing impairment in the United Kingdom and implications for universal neonatal hearing screening: questionnaire based ascertainment study. BMJ, 323, 536-40.

GRAVEL, J. S. 2003. Hearing and Auditory function. In: ROSENFELD, R. M. & BLUESTONE, C. D. (eds.) Evidence-Based Otitis Media. 2nd ed. London: BC Decker Inc Hamilton.

JENSEN, R. G., KOCH, A. & HOMØE, P. 2013. The risk of hearing loss in a population with a high prevalence of chronic suppurative otitis media. International Journal of Pediatric Otorhinolaryngology, 77, 1530-1535.

LE CLERCQ, C. M. P., VAN INGEN, G., RUYTJENS, L., GOEDEGEBURE, A., MOLL, H. A., RAAT, H., JADDOE, V. W. V., BAATENBURG DE JONG, R. J. & VAN DER SCHROEFF, M. P. 2017. Prevalence of Hearing Loss Among Children 9 to 11 Years Old: The Generation R Study. JAMA Otolaryngol Head Neck Surg, 143, 928-934.

LÜ, J., HUANG, Z., YANG, T., LI, Y., MEI, L., XIANG, M., CHAI, Y., LI, X., LI, L., YAO, G., WANG, Y., SHEN, X. & WU, H. 2011. Screening for delayed-onset hearing loss in preschool children who previously passed the newborn hearing screening. International Journal of Pediatric Otorhinolaryngology, 75, 1045-1049.

MACKEY, A. R., BUSSÉ, A. M. L., HOEVE, H. L., GOEDEGEBURE, A., CARR, G., SIMONSZ, H. J. & UHLÈN, I. M. 2021. Assessment of hearing screening programmes across 47 countries or regions II: Coverage, referral, follow-up and detection rates from newborn hearing screening Submitted for publication.

MAHOMED-ASMAIL, F., SWANEPOEL, D. W. & EIKELBOOM, R. H. 2016. Referral criteria for school-based hearing screening in South Africa: Considerations for resource-limited contexts. Health SA Gesondheid, 21, 96-102.

MANDEL, E. M., DOYLE, W. J., WINTHER, B. & ALPER, C. M. 2008. The incidence, prevalence and burden of OM in unselected children aged 1-8 years followed by weekly otoscopy through the "common cold" season. Int J Pediatr Otorhinolaryngol, 72, 491-9.

MCKAY, S., GRAVEL, J. S. & THARPE, A. M. 2008. Amplification Considerations for Children With Minimal or Mild Bilateral Hearing Loss and Unilateral Hearing Loss. Trends in Amplification, 12, 43-54.

MCPHERSON, B., LAW, M. & WONG, M. 2010. Hearing screening for school children: comparison of low-cost, computer-based and conventional audiometry. Child: Care, Health and Development, 36, 323-331.

MOELLER, M. P. 2000. Early intervention and language development in children who are deaf and hard of hearing. Pediatrics, 106, E43.

MONASTA, L., RONFANI, L., MARCHETTI, F., MONTICO, M., VECCHI BRUMATTI, L., BAVCAR, A., GRASSO, D., BARBIERO, C. & TAMBURLINI, G. 2012. Burden of disease caused by otitis media: systematic review and global estimates. PLoS One, 7, e36226.

NGUYEN, K.-H., SMITH, A. C., ARMFIELD, N. R., BENSINK, M. & SCUFFHAM, P. A. J. P. O. 2015. Cost-effectiveness analysis of a mobile ear screening and surveillance service versus an outreach screening, surveillance and surgical service for indigenous children in Australia. PloS One, 10.

OKWO-BELE, J. M. 2012. Integrating immunization with other health interventions for greater impact: the right strategic choice. J Infect Dis, 205 Suppl 1, S4-5.

PIROZZO, S., PAPINCZAK, T. & GLASZIOU, P. 2003. Whispered voice test for screening for hearing impairment in adults and children: systematic review. BMJ, 327, 967.

PRIEVE, B. A., SCHOOLING, T., VENEDIKTOV, R. & FRANCESCHINI, N. 2015. An Evidence-Based Systematic Review on the Diagnostic Accuracy of Hearing Screening Instruments for Preschool- and School-Age Children. Am J Audiol, 24, 250-67.

ROSENFELD, R. M., SHIN, J. J., SCHWARTZ, S. R., COGGINS, R., GAGNON, L., HACKELL, J. M., HOELTING, D., HUNTER, L. L., KUMMER, A. W., PAYNE, S. C., POE, D.

S., VELING, M., VILA, P. M., WALSH, S. A. & CORRIGAN, M. D. 2016. Clinical Practice Guideline: Otitis Media with Effusion (Update). Otolaryngology–Head and Neck Surgery, 154, S1-S41.

SHARMA, R., GU, Y., CHING, T. Y. C., MARNANE, V. & PARKINSON, B. 2019. Economic Evaluations of Childhood Hearing Loss Screening Programmes: A Systematic Review and Critique. Appl Health Econ Health Policy, 17, 331-357.

SILMAN, S., SILVERMAN, C. & ARICK, D. S. 1994. Pure-tone assessment and screening of children with middle-ear effusion. Journal of the American Academy of Audiology, 5, 173-173.

SKARZYNSKI, H. & PIOTROWSKA, A. 2012. Screening for pre-school and school-age hearing problems: European Consensus Statement. Int J Pediatr Otorhinolaryngol, 76, 120-1.

SMITH, R. J., BALE, J. F., JR. & WHITE, K. R. 2005. Sensorineural hearing loss in children. Lancet, 365, 879-90.

THE EUROPEAN OBSERVATORY ON HEALTH SYSTEMS AND POLICIES 2018. The organization and delivery of vaccination services in the European Union, United Kingdom, World Health Organisation.

THE WORLD BANK. 2019. World Bank Country and Lending Groups [Online]. The World Bank. Available: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups [Accessed 03-06-2019 2019].

UNESCO. 2020. UNESCO Institute for Statistics [Online]. UNESCO. Available: http://data.uis.unesco.org/ [Accessed 05-06-2020 2020].

UNICEF. 2012. The Right of Roma Children to education, Position Paper [Online]. UNICEF. Available: https://www.unicef.org/eca/reports/right-roma-children-education [Accessed 05-06-2020 2020].

WATKIN, P. M. & BALDWIN, M. 2011. Identifying deafness in early childhood: Requirements after the newborn hearing screen. Arch Dis Child, 96, 62-66.

WINIGER, A. M., ALEXANDER, J. M. & DIEFENDORF, A. O. 2016. Minimal Hearing Loss: From a Failure-Based Approach to Evidence-Based Practice. American journal of audiology, 25, 232-245.

WORLD HEALTH ORGANIZATION 2004. Chronic suppurative otitis media: Burden of Illness and Management Options. Geneva, Switzerland: World Health Organization.

WORLD HEALTH ORGANIZATION. 2019a. Measles, 2nd dose (MCV2), Immunization coverage estimates by country [Online]. World Health Organization. Available: https://apps.who.int/gho/data/node.main.MCV2n [Accessed 05-06-2020 2020].

WORLD HEALTH ORGANIZATION. 2019b. Vaccines and immunization, Measles and rubella country profile [Online]. World Health Organization. Available: http://www.euro.who.int/en/health-topics/disease-prevention/vaccines-and-immunization/publications/surveillance-and-data/measles-and-rubella-elimination-country-profiles/2019 [Accessed 05-06-2020 2020].

WORLD HEALTH ORGANIZATION. 2020. WHO vaccine-preventable diseases: monitoring system. 2019 global summary [Online]. World Health Organization,. Available: https://apps.who.int/immunization_monitoring/globalsummary/schedules [Accessed 05-06-2020 2020].

YONG, M., LIANG, J., BALLREICH, J., LEA, J., WESTERBERG, B. D. & EMMETT, S. D. 2020a. Cost-effectiveness of School Hearing Screening Programs: A Scoping Review. Otolaryngol Head Neck Surg, 194599820913507.

YONG, M., PANTH, N., MCMAHON, C. M., THORNE, P. R. & EMMETT, S. D. 2020b. How the World's Children Hear: A Narrative Review of School Hearing Screening Programs Globally. OTO Open, 4, 2473974X20923580.

YOSHINAGA-ITANO, C., SEDEY, A. L., COULTER, D. K. & MEHL, A. L. 1998. Language of early- and later-identified children with hearing loss. Pediatrics, 102, 1161-71.

Chapter 6

Cost-Effectiveness of Neonatal Hearing Screening Programs: A Micro-Simulation Modeling Analysis

Mirjam L. Verkleij
Eveline A.M. Heijnsdijk
Andrea M.L. Bussé
Gwen Carr
André Goedegebure
Allison R. Mackey
Birkena Qirjazi
Inger M. Uhlén
Frea Sloot
Hans L.J. Hoeve
Harry J. de Koning

Country-Committees Joint-Partnership of EUSCREEN Study Consortium

ABSTRACT

Objectives

Early detection of neonatal hearing impairment moderates the negative effects on speech and language development. Universal neonatal hearing screening protocols vary in tests used, timing of testing and the number of stages of screening. This study estimated the cost-effectiveness of various protocols in the preparation of implementation of neonatal hearing screening in Albania.

Design

A micro-simulation model was developed using input on demography, natural history of neonatal hearing impairment, screening characteristics and treatment. Parameter values were derived from a review of the literature and expert opinion. We simulated multiple protocols using otoacoustic emissions (OAE) and automated auditory brainstem response (aABR), varying the test type, timing and number of stages. Cost-effectiveness was analysed over a life-time horizon.

Results

The two best protocols for well infants were OAE followed by aABR (i.e., two-stage OAE-aABR) testing in the maternity ward and single-aABR testing. Incremental cost-effectiveness ratios were €4181 and €78,077 per quality-adjusted life-year gained, respectively. Single-aABR screening led to more cases being detected compared to a two-stage screening program. However, it also resulted in higher referral rates, which increased the total costs of diagnostics. Multi-staged screening decreased referral rates but may increase the number of missed cases due to false-negative test results and nonattendance.

Conclusions

Only the 2-stage OAE-aABR (maternity ward) protocol was below the willingness-to-pay threshold of €10,413 for Albania, as suggested by the World Health Organization, and was found to be cost-effective. This study is among the few to assess neonatal hearing screening programs over a life-time horizon and the first to predict the cost-effectiveness of multiple screening scenarios.

INTRODUCTION

About 32 million children worldwide experience disabling hearing impairment (WHO 2013).

Before the widespread implementation of hearing screening, permanent hearing impairment among infants typically went undetected until signs of the hearing impairment were evident to caregivers. Early detection of neonatal hearing impairment can lead to earlier interventions that improve language development (Pimperton et al. 2016; Yoshinaga-Itano et al. 2017). Studies have repeatedly shown that, by introducing universal neonatal hearing screening (UNHS), more infants with hearing impairment are referred for audiological assessment and at a younger age (Thompson et al. 2001; Wood et al. 2015). A United Kingdom controlled trial found that with UNHS, 62 more infants with hearing impairment per 100,000 were referred for audiological assessment before 6 months of age compared to the study cohort without UNHS (Wessex Universal Neonatal Hearing Screening Trial Group 1998).

UNHS has been implemented in the US and in many European countries, but screening protocols vary in the type of screening test used, the timing of testing, and the number of screening rounds (Arehart et al. 1998; Joint Committee on Infant Hearing guidelines 2007; Sloot et al. 2015). When a screening program is either in development or being evaluated, comparing the cost-effectiveness of various screening protocols is useful to support the decision-making processes. However, the evidence supporting UNHS as a cost-effective program is scarce. A recent systematic review by Sharma et al. (2019) updated the previous systematic reviews by Colgan et al. (2012) and Langer et al. (2012). They concluded that only a few publications included quality of life, estimates over the entire lifetime, or distinction of the severity of hearing impairment.

The design of UNHS protocols includes the test method(s), the location, and the number of rescreening stages. The screening tests used may be otoacoustic emissions (OAE), automated auditory brainstem response (aABR), or a combination of the two. A screening test may result in either "pass" or "refer." The first stage aims to screen all infants. In a one-stage protocol, infants that do not pass the screen will be referred for a full audiological diagnostic assessment. In a protocol with multiple stages, infants that do not pass initial screening are referred for a second (and possible third) stage for rescreening before referral for diagnostic assessment. Screening may take place in the maternity hospital before discharge or after discharge during an outpatient visit.

It is not feasible to compare multiple screening protocols in a controlled trial, simply because of the expense and time required to recruit and follow-up an appropriately large study sample micro-simulation models, in which individuals' lives are simulated, use data resources from multiple studies, which enable calculations of the life-time costs and effects of a variety of screening protocols. Local circumstances, such as health care infrastructure, screening participation, treatment opportunities, and costs, could all influence the effectiveness of a screening program. For example, if the test is performed when the infant is still in the maternity ward, the participation rates for the first hearing test are likely to be high. Long travel distances—especially in poorer, rural regions—could result in lower participation rates for follow-up screening tests and audiological assessments.

Part of the EUSCREEN project included implementation of UNHS in Albania. This study aimed to estimate the most cost-effective UNHS protocol. We developed a micro-simulation model. Then, we simulated multiple UNHS protocols for the example of Albania and calculated the most cost-effective protocol for the country. The model was built to analyze screening protocols for full term, well babies excluding those admitted to the neonatal intensive care unit.

MATERIALS AND METHODS

We developed a microsimulation model using the MIcrosimulation SCreening ANalysis framework to simulate the costs and effects of various UNHS programs. MIcrosimulation SCreening ANalysis is a microsimulation model developed for the evaluation of screening and has been used previously to estimate the harms, benefits, and cost-effectiveness of various cancer screening programs (de Kok et al. 2012; van Hees et al. 2014; Heijnsdijk et al. 2015; Sankatsing et al. 2015). In this model, the lives of 10 million individuals were simulated from birth to death in a situation without a NHS program. Next, the model simulates for the same population a situation in which a screening program identifies the hearing impairment. With this approach, the population health outcomes of various screening programs can be compared.

Figure 1 describes the first part of the model. Permanent hearing impairment can be congenital or acquired later on in life. Hearing impairment can worsen in the first years of life or it can progress from unilateral to bilateral. Directly after birth, the hearing impairment is undetected (pre-clinical states in Fig. 1). Without a screening program, this hearing impairment will be detected later in life, by the parents, caregivers, or teachers. The age of clinical detection depends on the age of onset and degree of hearing impairment (ref Fortnum). With a screening program, the hearing impairment can be either detected or missed by the screening test. Detected hearing impairment can be left untreated (especially mild or unilateral hearing impairment) or treated with hearing aids or cochlear implantation. Depending on the severity of the hearing impairment and the effect of interventions, quality of life will be affected. Supplement I in Supplemental Digital Content 1, http://links.lww.com/TP/C32 provides more detailed information about the micro-simulation modelling techniques used for this analysis.

We defined a set of input parameters and selected their values based on data from the literature and multiple expert meetings. Next, we defined a general model for hearing screening. Finally, as an example, we altered several parameters to the circumstances within the context of Albanian health care. An overview of all input parameter values is provided in Table 1.

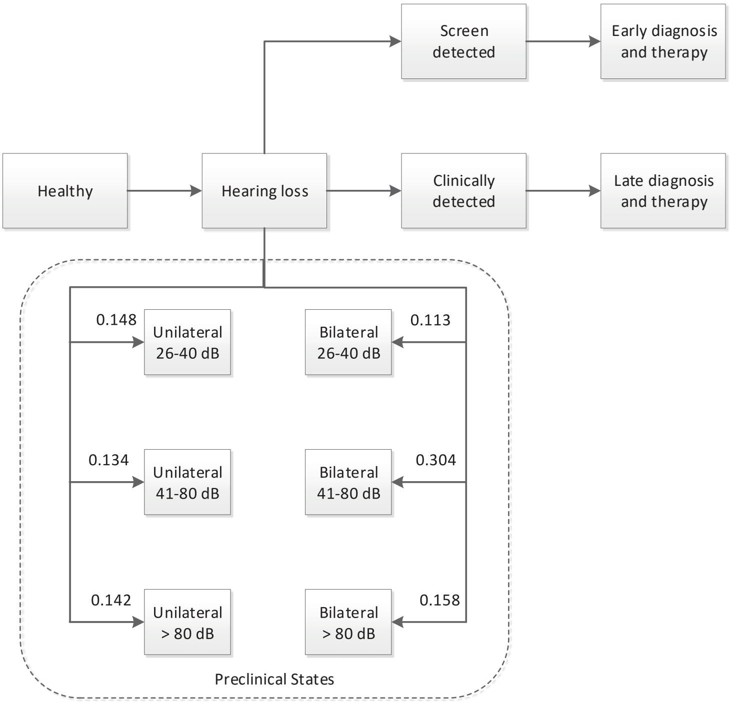


Figure 1. General MISCAN-Hearing model structure including possible hearing impairment states. In the model an infant can get hearing impairment at birth or any at any time in life. The proportions unilateral and bilateral and level of severity are indicated in the figure. Also progression to a more severe state or from unilateral to bilateral is possible (not shown in the figure). Hearing loss can be detected clinically (for example by parents' concerns), or by neonatal hearing screening. When hearing loss is detected by screening, the infants probably have a higher quality of life.

Natural History of Hearing Impairment

Permanent hearing impairment can be unilateral or bilateral, categorized into three levels of severity, based on the World Health Organization (2017) classification: mild hearing impairment (26 to 40 decibel [dB]), moderate and severe hearing impairment (41 to 80 dB), and profound hearing impairment (more than 80 dB). Input from multiple large cohort studies was used to model this natural history (Fortnum & Davis 1997; Cone-Wesson et al. 2000; Berninger & Westling 2011; Watkin & Baldwin 2011).

Accurate data on the onset and progression of hearing impairment are scarce (Fortnum et al. 2001; Barreira-Nielsen et al. 2016). Barreira-Nielsen et al. (2016) followed children identified with hearing impairment in the neonatal period until 4 years of age. Their results showed that 23% of the children had a deterioration of 20 dB within the 4 years period. In our model, we assumed that 10% of infants with mild hearing impairment will progress to moderate/ severe and 10% of infants with moderate/ severe hearing impairment will progress to profound across an average of 4 years. Similarly, we assumed that 10% of infants with unilateral hearing

Table 1. Input parameters and baseline values for MISCAN hearing screening model.

Input parameter	Baseline value
Demography	Life table Albania (Eurostat, 2017)
Time before clinical detection	**Average (s.d.)** Weibull distribution
Unilateral	4 years (1)
Bilateral, 26-40 dB	3 years (1)
Bilateral, 41-80 dB	2 years (1)
Bilateral, >80 dB	1 year (0.5)
Test device	**Sensitivity per test**
OAE	0.95
aABR	0.97
Treatment by hearing impairment category	**Probability**
Unilateral 26-40 dB	0.5 no treatment 0.5 family education
Unilateral 41-80 dB	0.3 no treatment 0.6 family education 0.1 hearing aid
Unilateral >80 dB	0.3 no treatment 0.65 family education 0.05 hearing aid
Bilateral 26-40 dB	0.35 no treatment 0.35 family education 0.3 hearing aid
Bilateral 41-80 dB	0.1 no treatment 0.1 family education 0.8 hearing aid
Bilateral >80 dB	0.05 no treatment 0.05 family education 0.9 hearing aid
Health-related Quality of Life by hearing impairment category	
Unilateral mild (26-40 dB)	1.0
Unilateral moderate, severe, profound (>40 dB)	0.85
Bilateral mild (26-40 dB)	0.85
Bilateral moderate, severe (41-80 dB)	0.661
Bilateral profound (>81 dB)	0.467
Average unit costs	**EUROs**
Invitation per child	1
OAE screening test	10
aABR screening test	20
Diagnostic consultation	60
Early family education (first year)	94
Hearing aid (per side)	110
Fitting hearing aids (per side)	290
Repair of hearing aids (yearly)	23
Extra costs due to late treatment (age 1 to 16)	**EUROs**
Unilateral >80 dB loss	500
Bilateral 41-80 dB loss	1000
Bilateral >80 dB loss	1500

impairment will develop bilateral hearing impairment within an average of 4 years. Using these proportions as input parameters, the model estimated 22.7 per 10,000 neonates with unilateral or bilateral hearing impairment >25 dB at birth. At age 3, a total prevalence of 28.3 per 10,000 children was estimated. This increases to 37.6 per 10,000 children at age 9.

Health-Related Quality of Life

Health-related quality of life (HR-QoL) is described by using utility values, where the value zero corresponds to death and one corresponds to being perfectly healthy (Drummond et al. 2005). For the purpose of the model, utility values were derived from Barton et al. (2006), who used a version of the Health Utilities Index Mark 3 for children with bilateral hearing impairment greater than 40 dB. Utility values for bilateral hearing impairment 26 to 40 dB and unilateral hearing impairment greater than 40 dB were assumed to be 0.85 and no utility loss was assumed for unilateral mild hearing impairment (Table 1).

With the assumption that interventions were successful, we simulated an improvement in quality of life expressed by a higher utility value. For example, a child having bilateral hearing impairment between 41 and 80 dB and successfully treated with hearing aids and follow-up support, will have a utility of 0.85 instead of 0.66 for the rest of his/her lifetime.

Model Adjustments for Albania

Multiple screening protocols were defined with a variation in test method, age of the infant during testing, and the number of stages of screening. For each stage in each protocol, the test sensitivity, referral rate, and participation rates were defined (Table 2). We used screening test sensitivities of 97% for aABR and 95% for OAE for detecting hearing impairment >40 dB, based on the findings of a controlled trial study in the United Kingdom (Kennedy et al. 2005), see Supplement I in Supplemental Digital Content 1, http://links.lww.com/TP/C32.

For the referral rate, we used 9.7% when screening was performed with OAE on day 2 (24 to 48 hours) after birth, based on a previous pilot study in Albania (Hatzopoulos et al. 2007). When OAE testing was performed within the first 24 hours after birth, we used a higher referral rate (20%), due to increased likelihood of fluid in the middle ear directly after birth (Hergils 2007). For testing with aABR on day 2, a referral rate of 7% was used (Hofmann et al. 2012).

Participation rates were estimated to be 95% for all inpatient screens. This was the case in all first stages and in some second stages, if performed while infants were still in the maternity ward. When second (and third) stages occur after hospital discharge, we estimated a 70% participation rate based on expert opinion from the members of the EUSCREEN study.

Treatment

For the example of Albania, each treatment intervention can include family education, sign language, speech therapy, and special education throughout childhood. The probability of each treatment type was based on the Bamford et al. (2007) report, updated with Albanian expert

Table 2. Screening protocols and attendance rates per screening stage for Albania.

				Stage 1		Stage 2		Stage 3		
Screening protocol	**Day of testing after birth (per screening stage)**	**Program sensitivity (100% attendance assumed)**	**Positive Predictive Value**	**Attend***	**Refer****	**Attend**	**Refer**	**Attend**	**Refer**	**Overall attendance**
OAE OAE aABR	2 – 10 – 30	88%	17.7%	95%	10%	70%	30%	70%	30%	47%
OAE OAE aABR (maternity)	1 – 2 – 10	88%	8.9%	95%	20%	95%	30%	70%	30%	63%
OAE aABR	2 – 10	92%	6.1%	95%	10%	70%	30%	N/A	N/A	67%
OAE aABR (maternity)	2 – 2	92%	5.6%	95%	10%	95%	30%	N/A	N/A	90%
aABR aABR	2 – 10	94%	8.2%	95%	7%	70%	30%	N/A	N/A	67%
aABR	2	97%	2.5%	95%	7%	N/A	N/A	N/A	N/A	95%

Overview of all screening protocols tested in the model. All programs assume first round testing at the maternity ward. Both programs labelled 'maternity' involve screening while still admitted to maternity ward for the first two stages.

Attend*: Attendance rate; number of children attending specified screening stage, as a percentage of all children invited for that particular round. Refer**: Referral rates; number of children referred to next stage or diagnostic follow-up, as a percentage of all children screened in that particular stage.

opinion. Currently, there is little opportunity for pediatric cochlear implantation in Albania. Although cochlear implantation may be adopted as usual care in the future, we assumed that all patients eligible for cochlear implantation were offered amplification via hearing aids. We estimated the probability of success (i.e., significant improvement of HR-QoL) to be 80% if infants were treated before their first birthday. The success rate declines linearly to 0% if initiated at age 6 years of age or older.

Costs of Screening and Treatment

The costs per screen were estimated based on the screening test device used, nurses' salary, and room rental. The costs for treatment were divided into costs for initial treatment (first year), costs for life-time usage of hearing aids, and additional costs for special education and early family intervention (Bamford et al. 2007). Infants treated with hearing aids were assumed to have their hearing aids replaced every 5 years on average for the rest of their lives. Most likely, each infant detected after the age of one would require extra investments on special education and early family intervention. These costs were obtained from local expert opinion and were included in the model for the ages of 1 to 16 years. Prices were converted from 2007 pound (£) to 2017 euro (€). Both direct and downstream health care costs were included (Table 1).

Cost-Effectiveness

For each protocol, the quality-adjusted life years (QALYs) gained were calculated by multiplying the increase in HR-QoL for each child by the remaining life-years based on the life expectancy for Albania. Next, the sum of all costs (screening, diagnosis, and treatment) and the sum of all QALYs were calculated for all 10 million infants in the micro-simulation. Cost-effectiveness was calculated by dividing the total net costs by the QALYs gained. We used a 3% discount rate for both costs and QALYs, that is, the costs and QALYs were valued 3% less each year to reflect uncertainty in the future, as is common practice in health economic studies. Cost-effectiveness was analysed from a health care perspective, meaning that societal costs (e.g., travel costs for the parents) and benefits (e.g., increased work productivity later in life due to successful amplification with hearing aids in early childhood) were not included.

To compare the screening protocols, we determined the average cost-effectiveness ratio (ACER) and the incremental cost-effectiveness ratio (ICER). The ACER is calculated as the net costs per QALY gained compared with no screening. The ICER is calculated as the incremental net costs per incremental QALY gained compared with the previous cost-effective protocol.

One-way sensitivity analyses were performed by varying each selected parameter of the model individually. These additional model simulations aimed to evaluate the effect of specific parameters on the simulation results. The results of the sensitivity analyses can reflect variation across countries.

RESULTS

Effects

About 23 infants (per 10,000 population) were expected to be born with hearing impairment. Table 3 shows the average number of infants participating and referred and the number of cases detected per 10,000 infants for each screening protocol. The 2-stage screening protocol, OAE-aABR (maternity), referred 271 infants for audiological diagnostic testing, to detect an average of 15.2 infants with hearing impairment. When the second stage of the same protocol (OAE-aABR) was performed at day 10 after birth, 200 infants were referred for diagnostic testing, which resulted in an average of 11.1 infants with hearing impairment detected. Here, fewer infants were detected due to lower participation at the second stage. If a multi-stage screening protocol is implemented, infants were lost to follow-up between test rounds and fewer infants were detected. For a single-stage aABR screening protocol with minimal lost to follow-up, a relatively high numbers (average of 16.8 infants) were detected. However, in this protocol, a large number (665 infants) was referred for audiological diagnostics, which substantially increased the expense.

Table 3. Predicted number of participation, referrals, cases detected and cost-effectiveness for various screening protocols for Albania per 10,000 children.

	OAE aABR (maternity)	OAE aABR	OAE OAE aABR	OAE OAE aABR (maternity)	aABR	aABR aABR
Stage 1 participation	9,500	9,500	9,500	9,500	9,500	9,500
Stage 1 referrals[a]	950	950	950	1900	665	665
Stage 2 participation	903	665	665	1805	n/a	466
Stage 2 referrals[a]	271	200	200	542	n/a	140
Stage 3 participation	n/a	n/a	140	379	n/a	n/a
Stage 3 referrals[a]	n/a	n/a	42	114	n/a	n/a
Cases detected due to UNHS, age < 6 months[b]	15.2	11.1	7.4	10.2	16.8	11.5
Bilateral > 40dB cases detected due to UNHS, age < 6 months[c]	8.6	6.3	4.2	5.8	9.6	6.5
Discounting 3%						
Total extra costs (€)	€45,915	€61,976	€71,568	€74,874	€135,968	€147,067
Total QALYs gained	10.98	8.05	5.39	7.48	12.14	8.40
ACER[d] **(€/QALYs)**	€4,182	€7,700	€13,273	€10,013	€11,204	€17,511
ICER[e] **(Δ€ / ΔQALYs)**	€4,182	Inefficient	Inefficient	Inefficient	€78,077	Inefficient

[a] Referrals from screening to diagnostic consultation in the grey cells.

[b] Predicted total cases of hearing impairment at birth: 22.7 / 10,000.

[c] Predicted total cases of bilateral hearing impairment > 40dB at birth: 10.4 / 10,000.

[d] ACER: Average cost-effectiveness ratio: Total costs / total QALYs gained compared with no NHS (rounded).

[e] ICER: Incremental net costs per incremental QALY gained compared with the previous cost-effective protocol (rounded).

Cost-Effectiveness

Table 3 shows the total life-time costs, QALYs gained, ACER, and ICER for each screening protocol for a cohort of 10,000 children. OAE-aABR (maternity) was estimated to cost €45,915 for 11 QALYs gained compared to no screening program. This resulted in €4181 per QALY gained (ACER). The single-stage aABR protocol was estimated to cost €135,968 for 12.1 QALYs gained compared to no screening protocol. This resulted (rounded) in €11,204 per QALY gained (ACER).

Figure 2 provides another overview of the total life-time costs and QALYs gained for each screening protocol. The two protocols using only aABR were more expensive than the protocols using only OAE or a combination of OAE and aABR. The OAE-aABR (maternity) protocol and aABR protocol gained the most QALYs, but the differences between the protocols were very small (one QALY per 10,000 children).

In Figure 2, the efficiency frontier is the line that connects the cost-effective screening protocols. All protocols that fall beneath this line are inefficient. For example, implementing a three-stage screening protocol would cost more than a two-stage protocol and would also result in fewer QALYs gained. After excluding the inefficient protocols, only two protocols remained: OAE-aABR (maternity) and aABR. ICERs were calculated by dividing the difference in net costs by the differences in QALYs gained. The cheapest protocol was OAE-aABR (maternity). When comparing a situation without NHS to OAE-aABR (maternity), the resulting ICER was (rounded) €4181 per QALY gained (€45,915/11.0-0). When comparing OAE-aABR (maternity) to aABR, the resulting ICER (rounded) was €78,077 per QALY gained ([135,968 to 45,915]/[12.1 to 11.0]).

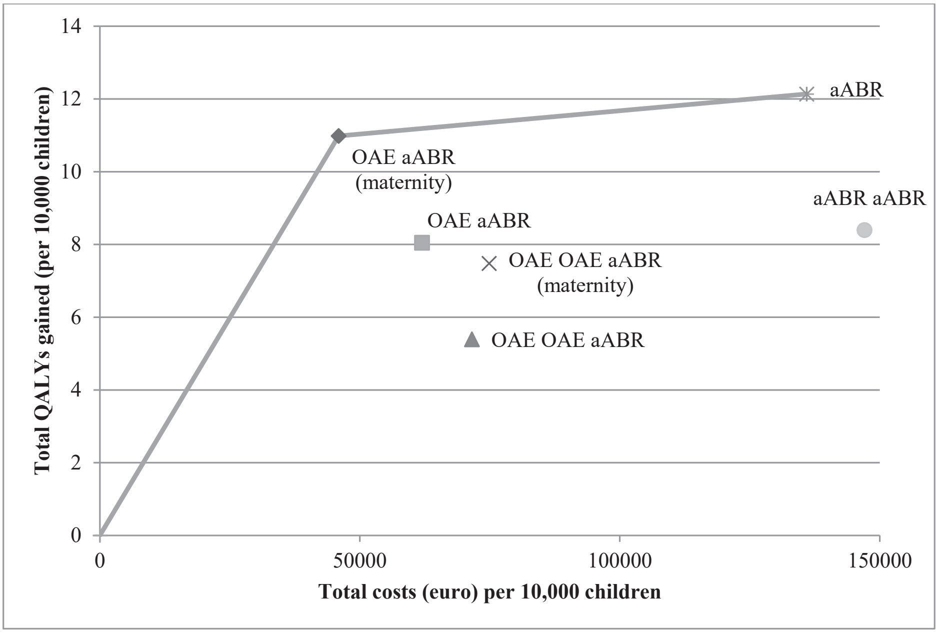


Figure 2. The total costs and total QALYs gained for each strategy for Albania (at 3% discount rate).

Sensitivity Analyses

One-way sensitivity analyses were performed for input parameters on the distribution of severity categories of hearing loss; the age of clinical detection; screening participation rates; costs of diagnosis and quality of life. Sensitivity analyses showed that the two-stage OAE-aABR (maternity) screening protocol using different assumptions was still preferred overall other protocols tested in the model (Supplement II in Supplemental Digital Content 1, http://links.lww.com/TP/C32).

DISCUSSION

The model revealed substantial differences in number of infants detected by screening and cost-effectiveness between different screening methods. Overall, performing a multistage screening program will decrease the number of refers to diagnostic assessment. A two-stage OAE-aABR protocol resulted in over four times as many referrals for diagnostic testing compared to the three-stage OAE-OAE-aABR protocol. Many extra referrals will lead to unnecessary health care costs and is a burden for infants and their caregivers. Contrary, performing multiple screening stages may lead to an increased number of missed cases of hearing impairment in each screening stage, either caused by infants that don't attend the next stage of the protocol or by having false negative test results.

Another example of a choice in the screening program is about the day of screening. Ensuring all tests are performed while the infant is still in the maternity ward will increase the uptake and may lead to fewer cases lost in between stages. However, performing the first screening test too soon after birth will increase the number of false-positive tests due to the high likelihood of fluid in the middle ear directly after birth. Differences in health care system structure and child health care utilization between countries have to be taken into consideration when designing the most optimal screening program.

The willingness-to-pay threshold is a benchmark for health care policymakers to practically apply cost-effectiveness analyses to their decision-making processes. A new health care intervention can be considered cost-effective if the ICER between the new and current intervention is no more than three times the gross domestic product per capita (World Health Organization 2016). For Albania, the willingness-to-pay threshold is € 10,413 (3 times €3471) per QALY gained (World Bank Group 2017). Only the two-stage OAE-aABR (maternity) protocol (ICER = €4181) fell under the willingness-to-pay threshold for Albania. Therefore, the two-stage OAE-aABR (maternity) protocol is the cost-effective protocol for this country. Sensitivity analyses showed our model predictions are robust. The cost-effective ratio of this protocol remained below the Albanian willingness-to-pay threshold when we assumed an increasing age of clinical detection (ICER €2371) or a decreasing screening participation rate (ICER €6071). However, the cost-effectiveness ratio of the OAE-aABR (maternity) protocol exceeded the willingness-to-pay threshold when we assumed that the distribution of the prevalence of hearing impairment was shifted towards milder hearing losses (ICER €12,159) or when we assumed that effects of early hearing impairment identification on quality of life were smaller (ICER €24,895).

To our knowledge, our model is the first that compared multiple hearing screening protocols where most studies compared only two to three screening programs (Keren et al. 2002; Grill et al. 2005; Burke et al. 2012; Colgan et al. 2012). Keren et al. (2002) concluded that UNHS could be cost-saving under the assumption that early detection substantially decreases future costs and productivity losses. Burke et al. (2012) concluded that costs of screening and baseline prevalence are the most influential factors in the cost-effectiveness of hearing screening protocols.

The model predictions in this study assessed quality-adjusted life-years over a lifetime horizon, which facilitates comparison between cost-effectiveness studies and interpreting results for decision-makers (Sanders et al. 2016). In contrast, most other studies estimated only the effects in the first years of life or reported on costs per case screened/detected, making it difficult to compare with other health interventions. Furthermore, the natural history component of our model was populated using multiple large cohort-studies, providing more certainty for the data used as model input. Finally, this model includes both unilateral and bilateral hearing impairment as well as mild hearing impairment.

There are some limitations to emphasize. First, our model incorporates hearing screening for well babies only. Infants admitted to the neonatal intensive care unit are often screened with a separate protocol due to the increased prevalence of auditory neuropathy. Second, we performed an economic evaluation from a health care perspective. We excluded societal costs such as loss of income by the caregivers when traveling for screening and treatment appointments. This was, however, our conscious decision. Scarcity of evidence on life-time productivity losses (e.g., income) due to hearing impairment would increase uncertainty regarding model outcomes. Thirdly, the exact relationship between the severity of neonatal hearing impairment, timeliness of early intervention and HR-QoL is unclear. A systematic review (41 studies) and meta-analysis (included 4 out of the 41 studies) found that HR-QoL was generally lower for children with hearing impairment compared to their normally hearing peers, but not all included studies supported that conclusion (Roland et al. 2016). However, to compare UNHS with other health care interventions, it is necessary to calculate costs per QALY gained. We aimed to cover the uncertainty of the utility values by imposing higher utilities (compared to baseline analysis) for hearing impairment in the sensitivity analysis.

Several assumptions had to be made for the model input. The participation rate, referral rate, sensitivity, specificity, and prevalence may turn out differently from our estimates. For example, true prevalence of hearing impairment in children is often unknown and varies between countries (Wilson et al. 2017; Bussé, 2020). Also, differences in socioeconomic background of the target population may lead to different health care utilization (Andersen 1995). Citizens of rural areas may experience difficulties in access to care caused by longer travel times for screening and follow-up diagnostics. Furthermore, referral rates are highly variable and have been shown to depend on the training of staff conducting the screening, the day of testing, the type of test used, and the referral criteria (unilateral/bilateral, hearing impairment threshold) (Vohr et al. 2001). Referral rates have been shown to be high in the first years of screening implementation and decrease as experience increases among the screeners (De Ceulaer et al. 2001; Wood et al. 2015). More accurate parameter values for the specified Albanian setting will become available after the first few years of implementation.

CONCLUSION

We developed a model that evaluated costs and effects of multiple UNHS protocols for well infants over a life-time horizon. The model estimations for Albania supported that a two-stage screening protocol (OAE-aABR maternity) was cost-effective for implementation. Because our model is readily adjustable, future possibilities for model development can include predictions for other countries and settings. This may be useful to decision-makers when designing the most optimal screening program for their country.

Acknowledgments

The following members of the Country-Committees Joint-Partnership of EUSCREEN Study Consortium are non-author contributors—Austria: Daniel Holzinger; Belgium (Flanders): Luc Stappaert; Belgium (Wallonia): Bénédicte Vos; Bosnia and Herzegovina: Fuad Brkic; Bulgaria: Petar Rouev; China: Xiangyue Peng; Croatia: Marko Velepic; Cyprus: Chryssoula Thodi; Czech Republic: Jakub Drsata; Denmark: Therese Ovesen; Estonia: Made Bambus, Maret Lepplaan; Faroe Islands: Bjarki Ellefsen; Finland: Riina Niemensivu, Tytti Willberg; France: Francoise Denoyelle; Germany: Peter Matulat; Greece: Thomas Nikolopoulos; Hungary: Anita Gaborjan; Iceland: Ingibjörg Hinriksdóttir; India: Zia Chaudhurri; Ireland: Gary Norman; Israel: Lisa Rubin; Italy: Alessandro Martini; Kosovo: Dugagjin Spanca; Latvia: Mareta Audere, Sandra Kuske; Lithuania: Nijole Drazdiene, Eugenijus Lesinskas; Luxembourg: Jean Marc Hild; Macedonia: Marina Cakar; Malta: Tony Fenech; Malawi: Wakisa Mulwafu; Moldova: Doina Chiaburu; Montenegro: Tarik Kujundžić, Elvir Zvrko; Netherlands: Anneke Meuwese; Norway: Vinay Swarnalatha Nagaraj; Poland: Grażyna Greczka; Portugal: Luisa Monteiro; Romania: Madalina Georgescu; Russia: George Tavartkiladze; Serbia: Snezana Andric Filipovic, Galina Jokovic; Slovakia: Lenka Langova, Irina Sebova; Slovenia: Saba Battelino; South-Africa: DeWet Swanepoel; Spain: Faustino Nunez-Batalla (Asturia), Jose Miguel Sequi-Canet (Valencia); Switzerland: Buser Nora; Turkey: Mine Baydan; United Kingdom (England): Jolanta McCall.

REFERENCES

Andersen, R. M. (1995). Revisiting the behavioral model and access to medical care: does it matter? J Health Soc Behav, 36, 1–10.

Arehart, K. H., Yoshinaga-Itano, C., Thomson, V., et al. (1998). State of the states: the status of universal newborn hearing screening, assessment, and intervention systems in 16 states. Am J Audiol, 7, 101–114.

Bamford, J., Fortnum, H., Bristow, K., et al. (2007). Current practice, accuracy, effectiveness and cost-effectiveness of the school entry hearing screen. Health Technol Assess, 11, 1–168, iii.

Barreira-Nielsen, C., Fitzpatrick, E., Hashem, S., et al. (2016). Progressive hearing loss in early childhood. Ear Hear, 37, e311–e321.

Barton, G. R., Stacey, P. C., Fortnum, H. M., Summerfield, A. Q. (2006). Hearing-impaired children in the United Kingdom, IV: cost-effectiveness of pediatric cochlear implantation. Ear Hear, 27, 575–588.

Berninger, E., & Westling, B. (2011). Outcome of a universal newborn hearing-screening programme based on multiple transient-evoked otoacoustic emissions and clinical brainstem response audiometry. Acta Otolaryngol, 131, 728–739.

Burke, M. J., Shenton, R. C., Taylor, M. J. (2012). The economics of screening infants at risk of hearing impairment: an international analysis. Int J Pediatr Otorhinolaryngol, 76, 212–218.

Bussé, A. M. L., Hoeve, H. L. J., Nasserinejad, K., et al. (2020). Prevalence of permanent neonatal hearing impairment: systematic review and Bayesian meta-analysis. Int J Audiol, 59, 475–485.

Colgan, S., Gold, L., Wirth, K., et al. (2012). The cost-effectiveness of universal newborn screening for bilateral permanent congenital hearing impairment: systematic review. Acad Pediatr, 12, 171–180.

Cone-Wesson, B., Vohr, B. R., Sininger, Y. S., et al. (2000). Identification of neonatal hearing impairment: infants with hearing loss. Ear Hear, 21, 488–507.

De Ceulaer, G., Daemers, K., Van Driessche, K., et al. (2001). Neonatal hearing screening with transient evoked otoacoustic emissions—retrospective analysis on performance parameters. Scand Audiol Suppl, 109– 111. doi: 10.1080/010503901300007245.

de Kok, I. M., van Rosmalen, J., Dillner, J., et al. (2012). Primary screening for human papillomavirus compared with cytology screening for cervical cancer in European settings: cost effectiveness analysis based on a Dutch microsimulation model. BMJ, 344, e670.

Drummond, M. F., Sculpher, M. J., Torrance, G. W., et al. (2005). Methods for the Economic Evaluation of Health Care Programme (3rd ed.). Oxford, United Kingdom: Oxford University Press.

Fortnum, H., & Davis, A. (1997). Epidemiology of permanent childhood hearing impairment in Trent Region, 1985-1993. Br J Audiol, 31, 409–446.

Fortnum, H. M., Summerfield, A. Q., Marshall, D. H., et al. (2001). Prevalence of permanent childhood hearing impairment in the United Kingdom and implications for universal neonatal hearing screening: questionnaire based ascertainment study. BMJ, 323, 536–540.

Grill, E., Hessel, F., Siebert, U., et al. (2005). Comparing the clinical effectiveness of different newborn hearing screening strategies. A decision analysis. BMC Public Health, 5, 12.

Hatzopoulos, S., Qirjazi, B., Martini, A. (2007). Neonatal hearing screening in Albania: results from an ongoing universal screening program. Int J Audiol, 46, 176–182.

Heijnsdijk, E. A., de Carvalho, T. M., Auvinen, A., et al. (2015). Costeffectiveness of prostate cancer screening: a simulation study based on ERSPC data. J Natl Cancer Inst, 107, 366.

Hergils, L. (2007). Analysis of measurements from the first Swedish universal neonatal hearing screening program. Int J Audiol, 46, 680–685.

Hofmann, M., Luts, H., Poelmans, H., Wouters, J. (2012). Investigation of a significant increase in referrals during neonatal hearing screening: a comparison of Natus ALGO Portable and ALGO 3i. Int J Audiol, 51, 54–57.

Joint Committee on Infant Hearing guidelines. (2007). Year 2007 position statement: principles and guidelines for early hearing detection and intervention programs. Pediatrics, 120, 898–921.

Kennedy, C., McCann, D., Campbell, M. J., et al. (2005). Universal newborn screening for permanent childhood hearing impairment: an 8-year follow-up of a controlled trial. Lancet, 366, 660–662.

Keren, R., Helfand, M., Homer, C., et al. (2002). Projected cost-effectiveness of statewide universal newborn hearing screening. Pediatrics, 110, 855–864.

Langer, A., Holle, R., John, J. (2012). Specific guidelines for assessing and improving the methodological quality of economic evaluations of newborn screening. BMC Health Serv Res, 12, 300.

Pimperton, H., Blythe, H., Kreppner, J., et al. (2016). The impact of universal newborn hearing screening on long-term literacy outcomes: a prospective cohort study. Arch Dis Child, 101, 9–15.

Roland, L., Fischer, C., Tran, K., et al. (2016). Quality of life in children with hearing impairment: systematic review and meta-analysis. Otolaryngol Head Neck Surg, 155, 208–219.

Sanders, G. D., Neumann, P. J., Basu, A., et al. (2016). Recommendations for conduct, methodological practices, and reporting of cost-effectiveness analyses: second panel on cost-effectiveness in health and medicine. JAMA, 316, 1093–1103.

Sankatsing, V. D., Heijnsdijk, E. A., van Luijt, P. A., et al. (2015). Costeffectiveness of digital mammography screening before the age of 50 in The Netherlands. Int J Cancer, 137, 1990–1999.

Sharma, R., Gu, Y., Ching, T. Y. C., et al. (2019). Economic evaluations of childhood hearing loss screening programmes: a systematic review and critique. Appl Health Econ Health Policy, 17:331–357.

Sloot, F., Hoeve, H. L., de Kroon, M. L., et al.; EUS€REEN Study Group. (2015). Inventory of current EU paediatric vision and hearing screening programmes. J Med Screen, 22, 55–64.

Thompson, D. C., McPhillips, H., Davis, R. L., et al. (2001). Universal newborn hearing screening: summary of evidence. JAMA, 286, 2000–2010.

van Hees, F., Habbema, J. D., Meester, R. G., et al. (2014). Should colorectal cancer screening be considered in elderly persons without previous screening? A cost-effectiveness analysis. Ann Intern Med, 160, 750–759.

Vohr, B. R., Oh, W., Stewart, E. J., et al. (2001). Comparison of costs and referral rates of 3 universal newborn hearing screening protocols. J Pediatr, 139, 238–244.

Watkin, P. M., & Baldwin, M. (2011). Identifying deafness in early childhood: requirements after the newborn hearing screen. Arch Dis Child, 96, 62–66.

Wessex Universal Neonatal Hearing Screening Trial Group. (1998). Controlled trial of universal neonatal screening for early identification of permanent childhood hearing impairment. Lancet, 352, 1957–1964.

Wilson, B. S., Tucci, D. L., Merson, M. H., O'Donoghue, G. M. (2017). Global hearing health care: new findings and perspectives. Lancet, 390, 2503–2515.

Wood, S. A., Sutton, G. J., Davis, A. C. (2015). Performance and characteristics of the Newborn Hearing Screening Programme in England: the first seven years. Int J Audiol, 54, 353–358.

World Bank Group. (2017, November 20). Albania country overview. http:// www.worldbank.org/en/country/albania/overview. World Health Organization. (2016, August 22). Cost-effectiveness and strategic planning. http://www.who.int/choice/en/.

World Health Organization. (2017, December 5). Grades of hearing impairment. http://www.who.int/deafness/hearing_impairment_grades/en/.

Yoshinaga-Itano, C., Sedey, A. L., Wiggin, M., et al. (2017). Early hearing detection and vocabulary of children with hearing loss. Pediatrics, 140, e20162964.

Chapter 7

Implementation of a neonatal hearing screening programme in three provinces in Albania

Andrea ML Bussé
Birkena Qirjazi
André Goedegebure
Martijn S Toll
Hans LJ Hoeve
Ervin Toçi
Enver Roshi
Gwen Carr
Huibert J Simonsz

ABSTRACT

Objectives

The EUSCREEN study compares the cost-effectiveness of paediatric hearing screening programmes and aims to develop a cost-effectiveness model for this purpose. Alongside and informed by the development of the model, neonatal hearing screening (NHS) is implemented in Albania. We report on the first year.

Methods

An implementation plan was made addressing objectives, target population, screening protocol, screener training, screening devices, care pathways and follow up. NHS started January 1st, 2018 in four maternity hospitals: two in Tirana, one in Pogradec and one in Kukës, representing both urban and rural areas. OAE-OAE-aABR was used to screen well infants in maternity hospitals, whereas aABR-aABR was used in neonatal intensive care units and in mountainous Kukës for all infants. Screeners' uptake and attitudes towards screening and quality of screening were assessed by distributing questionnaires and visiting the maternity hospitals. The result of screening, diagnostics, follow up and entry into early intervention were registered in a database and monitored.

Results

Screeners were keen to improve their skills in screening and considered NHS valuable for Albanian healthcare. The number of "fail" outcomes after the first screen was high initially but decreased to less than 10% after eight months. In 2018, 11,507 infants were born in the four participating maternity hospitals, 10,925 (94.9%) of whom were screened in the first step. For 486 infants the result of screening was not registered. For the first screen, ten parents declined, eight infants died and one infant was discharged before screening could be performed. In 1115 (10.2%) infants the test either could not be performed or the threshold was not reached; 361 (32.4%) of these did not attend the second screen. For the third screen 31 (34.4%) out of 90 did not attend. Reasons given were: parents declined (124), lived too far from screening location (95), their infant died (11),had other health issues (7), or was screened in private clinic (17), no reason given (138).

Conclusions

Implementation of NHS in Albania is feasible despite continuing challenges. Acceptance was high for the first screen. However, 32.4% of 1115 infants did not attend the second screen, after a "fail" outcome for the first test.

INTRODUCTION

The EUSCREEN study [1] compares the cost-effectiveness of paediatric vision and hearing screening programmes and aims to develop a cost-effectiveness model for this purpose. When completed, the model can be used to assist introduction, modification or disinvestment of a screening programme in a country or region, taking into account the local circumstances such as professionals available to screen and existing screening pathways. Alongside the development of the model and informed by its preliminary predictions, neonatal hearing screening (NHS) is being implemented in Albania, where hearing screening is not yet routinely performed. The implementation of NHS is being evaluated in three provinces in Albania: Tirana, Pogradec and Kukës. Information gathered by the implementation study will be used to validate and calibrate the model to improve its predictions.

Studies that report on implementation of NHS can be retrospective [2–4] or prospective [5–12] cross-sectional studies. They mainly report on the outcomes related to the screening programme, such as coverage, referral rates and attendance rates. Only a few describe the actual implementation process and describe their experiences with requisites and barriers for implementation [8, 9, 12]. In most countries where NHS has been implemented, most of the infants are born in maternity hospitals. Acceptance of the first screen has been found to vary between 90.85% (China [11]) and 99.8% (Singapore [8]) (Table 1), however, out of all infants screened in the first screen, the percentage that was invited fora second screen varied between 1.7% [7] and 14.3% [9], whereas nonattendance for the second screen varied between 0.1% in France [2] and 51.6% in Nigeria [9]. Out of all infants who attended the second screen, between 10.75% [10] and 31.3% [2] received a "fail" outcome (the test could not be performed or the threshold was not reached). Between 4.6% [2] and 64.6% [5] did not attend diagnostic assessment.

Table 1. Studies on implementation of NHS in other countries, their protocol, attendance and referral rates.

Author	**Country**	**Protocol**	**Attendance screen 1**	**Invited screen 2**	**Non-attendance screen 2**	**Referral diagnostic assessment**
Augustine, 2014[5]	India	aABR, aABR	97.70%	9.10%	17.40%	
Bouillot, 2019[2]	France	aABR, aABR, (aABR)	99.50%	10.30%	0.10%	2.20%
Caluraud, 2015[7]	France	OAE+aABR, aABR	99.40%	1.70%	7.90%	0.20%
Chen, 2017[3]	China	OAE, OAE	93.60%	11.30%	31.30%	0.80%
Low, 2005[8]	Singapore	OAE/aABR, OAE/aABR	99.80%			6.00%
Olusanya, 2008[9]	Nigeria	OAE, aABR		14.30%	51.60%	4.10%
Saki, 2017[10]	Iran	OAE+aABR, OAE+aABR		11.68%	4.23%	1.25%
Sun, 2009[11]	China	OAE, OAE	90.85%	12.16%	34.32%	7.30%
Uilenburg, 2009[12]	The Netherlands	OAE, OAE, aABR	94.00%	7.60%	6.30%	2.20%
Wood, 2015[4]	UK	OAE+aABR	97.54%			< 3.00%

The Joint Committee on Infant Hearing (2007, 2019) [13, 14] defined benchmarks to evaluate the implemented NHS programmes. They recommend to cover 95% of eligible infants and to refer less than 4% of infants to diagnostic assessment. They also recommend for an infant to complete screening within the first month after birth, to complete diagnostic assessment within 3 months after birth and to initiate intervention within 6 months after birth.

Albania has a population of 2.9 million inhabitants and an annual birth rate of about 30,869 [15]. Assuming a prevalence between 1 and 3 per 1000 neonates [16–18], in Albania approximately 30–90 out of the 30,869 infants are born with a permanent sensorineural hearing impairment (HI) of more than 40 dB HL. Without a screening programme, hearing disorders usually are not detected or treated until infants are one to three years old [19,20]. Delays in detection and treatment of childhood hearing impairments have serious consequences for speech, language, cognitive and socio-emotional development [21, 22] which can be prevented or significantly reduced by neonatal hearing screening, timely diagnosis and effective early intervention.

Albania is one of the few European countries currently without established NHS. White (2010) [23] reported that of the countries that have an NHS programme, seven screened over 90% of neonates, nine countries screened 25–89% of neonates and 46 countries screened less than 25% of neonates. Sloot et al. (2015) [24] reported that 33 of 38 European countries had a nationwide NHS programme.

An Albanian-Italian study, conducted in 2003–2004 by Hatzopoulos et al. (2007) [25] and an Italian study, conducted in 2009–2012 and funded by MAGIS by Beqiri and Nika (2015) [26] previously studied implementation of NHS in Albania. Hatzopoulos et al. (2007) [25] used a screening programme with two examinations in which infants who failed the first otoacoustic emission (OAE) screen performed in the maternity hospital 2–3 days after birth, underwent a second OAE after four weeks. Infants who failed the second OAE were asked to return a third time after 4–6 weeks for diagnostic assessment using click-auditory brainstem response (ABR). They screened 463 well babies (WB; healthy infants without any overt diseases) and 1098 infants admitted to the neonatal intensive care unit (NICU). The programme had an attendance of 98.5% for the initial OAE. However, 40–50% of infants did not attend the second OAE. Two (0.18%) NICU infants of the 1098 and none of the 463 WB were diagnosed with a bilateral hearing impairment. Beqiri and Nika (2015) [26] screened 47,341 infants in the three main cities of Albania (Tirana, Shkodra and Fier) with an OAE-ABR protocol for WB and a single ABR for NICU infants. Of the infants screened, 93 had a bilateral hearing impairment. These NHS programmes were not continued. At the time the studies ended, the Albanian government and its Ministry of Health did not consider continuation of NHS to be a priority, resulting in no programme implementation at that time.

We report on the first year of implementation of a NHS programme as part of the EU-SCREEN project in three provinces in Albania (Tirana, Pogradec and Kukës) that started on January 1st, 2018.

METHODS

In what follows, we describe the prediction of the cost-effectiveness model, the demography, the screening protocol and methods to assess outcome of implementation.

Prediction of the cost-effectiveness model for Albania

A micro-simulation model has been developed using the MIcrosimulation SCreening ANalysis (MISCAN) model structure [27]. This model was originally developed to simulate the natural history of diseases and to evaluate screening programmes such as for cancer. It was provisionally adapted to evaluate neonatal hearing screening programmes.

In the preparation phase in 2017, the cost-effectiveness model was used to evaluate several possible NHS programme approaches, taking into account local circumstances in Albania such as demography and geography, natural history of hearing impairment in Albania and costs. It proved to be impossible to make accurate predictions as the data needed for the calculation were insufficient or unknown. Since the model was still in the process of being developed, it was a challenge for the preliminary version of the model to take all of the local circumstances into account to calculate the most cost-effective NHS programme.

Demography

NHS was implemented in Tirana, Pogradec and Kukës in Albania (Fig. 1) because they offer an appropriate representation of the general population of Albania with respect to provision of health care in both urban and rural areas and a range of socio-economic circumstances. The NHS programme has been implemented in two maternity hospitals in Tirana: Mbretëresha

Figure 1. Map of Albania marked for Tirana, Pogradec and Kukës.

Map: Philippe Rekacewicz, Emmanuelle Bournay, UNEP/GRID-Arendal (http://www.grida.no/resources/5360)

Geraldine (MG) and Koço Gliozheni (KG), each having their own NICU department. It has also been implemented in the maternity hospital in Pogradec and the maternity hospital in Kukës. The maternity hospitals in Pogradec and Kukës provide limited NICU care. In Albania the majority of the deliveries (>97%) take place in a hospital [28]. Deliveries at home are rare and occur mainly in remote areas, where no adequate transport is available.

Whereas both Pogradec and Kukës are located in rural and mountainous regions, Kukës is one of the poorest regions in Albania and the inhabitants of the Kukës province are more spread out across the countryside. Parents have to travel far from remote places to reach the maternity hospital and roads are often blocked by snow in winter. Pogradec is situated in the South-East of Albania near the border with Macedonia and Kukës is situated near the border with Kosovo in the North-East of Albania.

Location and timing of screening

The total number of births per year in the maternity hospitals in the selected regions is approximately 11,500. The majority of deliveries (approximately 10,000) take place in the two maternity hospitals in Tirana. The maternity hospitals in Pogradec and Kukës each account for 400–600 births annually.

In Tirana and Kukës, mothers are discharged within 24 h after delivery. In Pogradec, discharge takes place within 48 h after delivery. Unless infants are delivered by a caesarean section, mothers do not return for routine follow up appointments after they have left the maternity hospital. To reach high coverage, the best option was to perform the first screen in the period the mother and the infant were still in the maternity hospital. However, when screening shortly after birth, residual amniotic fluid in the neonates' middle ear has been shown to cause a higher rate of failed tests [29, 30]. OAE measures the reactive sound emitted by the outer hair cells in the cochlea to a tone or click produced by the screening device and played in the ear canal. The residual amniotic fluid causes the middle-ear to be less sound-conductive and increases the number of "fail" outcomes during screening. Amniotic fluid disappears when the middle ear is aeriated and more optimal screening conditions may be reached between the third and fifth day after birth [29]. An aABR detects the change in brain wave activity of the auditory brainstem as a reaction to a tone or click. Screening tests performed with aABR are less sensitive to transient conditions such as amniotic fluid in the middle ear, which results in fewer false-positive results [31].

Most existing NHS programmes commonly use a combination of OAE and aABR in a screening protocol that consists of 2 or 3 subsequent screening steps [24, 32]. Sensitivity and specificity are between 90% and 100% for both tests [33–35]. Although aABR is more sensitive and specific, less sensitive to transient conditions in the middle and external ear and more likely to detect auditory neuropathy, aABR may be more expensive and time consuming than OAE. Both OAE and aABR can be performed by a wide range of practitioners, provided that they are appropriately trained and have gained sufficient experience.

The Ministry of Health was consulted by the local study coordinator (BQ) to receive approval for the study and to decide on the maternity hospitals that participate in the study. Agreements were made between the Tirana University Hospital Centre (TUHC) and the maternity hospitals in Tirana, Pogradec and Kukës. All infants born healthy as well as all infants admitted to NICU in one of the four maternity hospitals were eligible for NHS.

Screening personnel and training

The first screen was performed in the maternity hospital after delivery and before discharge. Nurses and midwives who were already employed in the maternity hospitals were considered most suited to be trained to perform the screening. Other NHS programmes have trained a wide range of professionals for NHS such as health care professionals, paediatricians, speech language therapists, audiologists or dedicated screeners.

During the autumn of 2017 a training course of three days was set up for screening nurses and midwives participating in the programme. During the first course screeners were taught theoretical information regarding anatomy and physiology of hearing, hearing impairment, hearing (screening) tests, diagnostic assessment, factors influencing the testing, etc. In the second course, screeners were taught about the screening devices, and screeners were able to use the devices. In the last course, screeners were taught about communication skills. They were given information on how to approach and inform parents regarding their participation in the screening programme, how screening can affect the parents, how to explain the test they are performing, and how to explain the result to the parents. After the course, the knowledge of the participants was assessed by administering a test and their screening skills were evaluated.

During screening the screeners were supervised by a team from the University of Tirana supported by technical staff of the manufacturers. After several months of screening a refresher course was organised so screeners could exchange experiences, get help with problems identified and have questions answered.

An additional one-day course was set up for health care professionals from Tirana, Pogradec and Kukës that did not perform screening: personnel (nurses and general practitioners (GP)) from health centres in the villages, midwifes from maternity hospitals that did not perform screening, paediatricians from child consultancy centres and public health workers. During this course these health care professionals were informed about the purpose of the screening programme, how screening is performed, how infants are followed up and what kind of rehabilitation is provided. Furthermore, information on NHS was included in the continuing education courses provided for GP's nationwide. GPs will be informed on the screening outcome through the 'baby book' each infant receives in the maternity hospital. In this book, medical information such as birthweight is recorded, a page was added to document the result of hearing screening.

Information for parents of screened children

The awareness of parents about the importance of early detection and intervention and their acceptance of NHS is of great importance for the success of the programme [36,37]. This has previously been reported for NHS programmes in Albania [25, 26]. Leaflets and posters were developed to inform parents about hearing impairment and the effect of hearing impairment on the development of their infants. One leaflet was developed about the existence, rationale for and the course of the screening programme. Another leaflet was developed about what happens when an infant is referred for diagnostic assessment. Information campaigns and interviews were broadcast on television and radio. Furthermore, information videos were produced and played on screens in the waiting rooms of the maternity hospitals.

Outcome criteria for implementation of the screening programme

In this ongoing implementation study, the following criteria for implementation of screening are to be assessed: acceptability, adoption, appropriateness, feasibility, fidelity, costs, coverage and sustainability of the screening programme [38, 39]. These criteria can only be assessed after the implementation study has ended in 2020. The definitions and appraisal methods of acceptability, adoption, appropriateness, feasibility, fidelity, costs, coverage and sustainability of the screening programme are presented in the supplemental material (Appendix 1).

A questionnaire was used to measure the screeners' uptake and the acceptability of hearing screening, their level of responsibility, and their attitudes towards parents. It consisted of 155 multiple choice questions in seven domains: general information, attitudes of the screener towards hearing screening, hearing loss, parents of infants screened and subcultures, individual features of the screener and additional questions. This questionnaire was distributed amongst screeners at the start of the screening programme and after one year of screening. They will be asked to fill out the questionnaire again after two years of screening. On-site visits and observations were made to determine the adoption and adherence to the programme, to get an indication of the commitment, understanding and the skills of the screeners. The workflow in the maternity hospitals and the collaboration within the screening teams in the maternity hospitals was studied: how the teams experienced the training courses, how much they remembered after training, how well they used and handled the devices. Additionally, interviews with 8 parents and all 21 nurses who perform screening in each maternity were conducted. In these interviews, parents were asked how they experienced the screening and what information they received. Nurses were asked about their experiences and opinions regarding the screening programme.

At the end of the implementation study in 2020, the acceptability, adoption, appropriateness, feasibility, fidelity, costs, coverage and sustainability of the screening programme will be assessed.

Database of screened infants

To collect data about the screened infants, a database was developed for the implementation study. Data were filled out by local screeners and the database was monitored by the Erasmus Medical Centre in Rotterdam. All four maternity hospitals were assigned an account in the database. Screeners were able to create their own account that was linked to one of the maternity hospitals. Each eligible neonate was registered in the database by one of the screeners and was assigned an anonymous and unique number. Screeners filled out medical information about the neonates screened such as date of birth, duration of the pregnancy and possible risk factors for hearing impairment. They also registered the date and results of screening as well as the reasons given by parents to decline screening. All three screening outcomes were registered as well as subsequent diagnostics, follow up and hearing-aid fitting. The overall coverage of the programme was estimated from the number of eligible infants screened.

Care pathway and follow up strategies

Following referral from completion of screening, infants received diagnostic assessment at the TUHC or Child Centre for Rehabilitation (CCR) in Tirana. An audiometric booth was built in the TUHC. This room was equipped with one diagnostic ABR device that can be used for both diagnostic ABR and auditory steady state response testing. Another diagnostic ABR device was installed in the CCR.

Because Albania had no formal neonatal hearing screening programme to date, there was little experience with hearing aid fitting in very young infants. In the spring of 2018, a team consisting of speech language therapists, psychologists and paediatricians was trained to help guide parents through the care pathway and provide early intervention. This has helped to create a pathway for children with various levels of hearing impairment and to ensure that the families experience between detection of hearing impairment and appropriate follow up is streamlined.

RESULTS

Screening protocol

It had been our intention to have the model predict the best screening protocol for the three provinces in Albania. However, the development of the model had to be completed within 7 months and it was not sufficiently finished when the decision on the protocol had to be made and the training of screeners began. Furthermore, because of the sparse and not very detailed data on demographics, current provision of healthcare, follow up and costs, it proved to be difficult to adapt the model specifically for the situation in Albania and to make differentiated regional predictions for Tirana, Pogradec and Kukës. For example, because of the lack of experience with NHS, the margin of error in the estimation of the costs for screening and diagnostic assessment was very large. This information is difficult to collect, even in countries with established NHS programmes.

As a consequence, decisions made for the screening programme relied much on sound clinical judgement, experience of implementation of NHS in other countries and conclusions made after the previous attempts to implement NHS in Albania. Based on these considerations, local circumstances, expected expenses associated with the screening programme and expected costs for the parents a multi-step programme including aABR was chosen to improve the specificity of the programme and to reduce the number of infants that have to travel to Tirana for full diagnostic assessment. The sequence of the tests, the location, choice of screening regime and postnatal age at the first screen and the age at repeat screening were considered to be relevant to decide on the NHS programme implemented in Tirana, Pogradec and Kukës. This led to the use of a different protocol in the mountainous region of Kukës as this could reduce the need for repeat screening in recognition of the long journey parents have to undertake to reach the maternity hospital [40]. In anticipation of this problem, the number of steps were reduced and a more specific screening test was expected to result in lower referral rates.

The protocol for WB in Tirana and Pogradec was decided to be an OAE-OAE-aABR test sequence. This protocol was used in both maternity hospitals in Tirana and in the maternity hospital in Pogradec. This sequence was chosen because a three-step programme and the use of an aABR screen offers high sensitivity and specificity. A two- or three-step screening programme and a combination of both OAE and aABR are commonly used across Europe, and higher sensitivity and specificity are beneficial when high numbers of infants do not attend repeat screening. In hindsight, more in-depth consideration about factors influencing low attendance rates would have been advantageous.

For neonates admitted to NICU a sequence of aABR-aABR was chosen to enable detection of auditory neuropathy. Neonates who had a "fail" outcome after the final screen were referred to the ENT department of the TUHC for diagnostic assessment.

To ensure maximum attendance and minimal costs for the first screen, tests were performed in the maternity hospital immediately before discharge. When a "fail" outcome was obtained for one or both ears, a repeat screen was scheduled, after the result of the test was explained to the parents. Within the current programme, infants who lived outside Tirana were not tracked. When parents did not attend repeat screening, they were contacted by the screeners by telephone. When required, the second screen took place in the maternity hospital approximately two weeks after the first screen and the third screen took place in the maternity hospital approximately one week after the second screen. As with WB, the first screen for NICU infants took place before they left the maternity hospital. Parents who lived outside the Tirana area were given the possibility to return for repeat screening in Tirana, however, these parents were not actively reminded. These infants may have been followed up elsewhere.

Screening location and devices

A room was prepared in all maternity hospitals exclusively for hearing screening. A small bed for the neonates was installed as well as screening devices with consumables and a computer with internet connection to upload all screening data and fill out the case record form in the database. Initial problems were that there was too much environmental noise and some screening rooms were too cold for the neonates. No constructional acoustical improvements could be made in any of the maternity hospitals. Therefore, a room was chosen in a quieter part of the maternity hospital and measures were taken to improve screening conditions. Broken doors and windows were replaced to diminish environmental noise and electric heaters were installed to make infants more comfortable during winter months.

Nine Natus Echo-Screen III devices were obtained to perform OAE testing. These devices were distributed between the maternity hospitals in Tirana and Pogradec and the university hospital. Six Interacoustics Titan ABRIS devices to perform aABR testing were obtained for all maternity hospitals. Equipment to perform these tests is calibrated and validated regularly by the supplier to ensure sensitivity and specificity.

Screening personnel and training

Both teams in Tirana consisted of six screeners and an administrator. The local administrators were in charge of organising the screening programme. They made sure sufficient consumables such as probe tips and electrodes were available. Furthermore, the strategy used to track all infants depended mainly on the local administrator organising the follow up. In Pogradec, four nurses and one administrator took care of screening. The Kukës team consisted of four screeners who alternated shifts to ensure there was always someone present to perform the screening.

The screeners who participated in the project were paid approximately €150 per month by the study in addition to their salary, €400–500 on average. Screening as well as administration took place in overtime. All staff members selected to perform screening attended the training courses and passed the assessment. Screeners were supervised during the first screens and were only allowed to screen independently after they became sufficiently skilful.

Information for parents of screened children

Before the screening test was done, parents were informed about how the hearing screening test works and were able to ask questions before giving written informed consent. After screening, the result was explained. When the infant got a "fail" outcome for the screening test, screeners made an appointment for the next screen one or two weeks later in the maternity hospital.

Most parents were interested in participating in screening when asked to participate in the maternity hospital. Only a few parents declined screening based on their belief that their child could hear or that the test might hurt their child. Screeners reported that the better parents were informed about the project, the less they declined. This is consistent with the wider literature [36, 37].

On-site observations

Albania was visited four times by the authors (AB, HH, AG): during the preparation phase, when screening had just started, a few months after screening had started and after one year of screening. Questionnaires were distributed to observe the implementation and to determine the adoption of the programme. During the first two visits and during the last visit all maternity hospitals were visited. During the intermediate visit only the two maternity hospitals in Tirana were visited. Screeners were interviewed. They expressed their ideas and concerns about the programme. Only a few interviews with parents were conducted, because the language barrier prevented an in-depth conversation and translators were not always available. A follow up visit will be made again after 24 months of screening.

During the first months of the screening programme, equipment failures such as malfunctioning OAE devices and broken OAE probes disturbed the screening process. The broken probes and devices were sent back to the manufacturer for replacement but it took several weeks for the equipment to be repaired. This did not delay screening since back-up screening devices were available. Steps were taken to ensure more care when handling the probes and transporting the devices.

Initially, it was difficult for the screeners to place the probe and make sure all conditions were right for screening. Many tests were paused and restarted when screeners experienced difficulties placing the probe, when the probe fell out of the infants' ear, the probe got obstructed or when the infant was restless during the test. Initially "fail" outcomes occurred often when screeners had not yet gained sufficient experience in screening. These problems resulted in high failure rates (50–80%) for the first screen. In Pogradec, 78% of infants were referred for repeat screening in the first month. For most maternity hospitals the failure rates for the first screen decreased to less than 10% after eight months. The more neonates were being screened, the better the test seemed to be executed and the lower the failure rate was (Fig. 2).

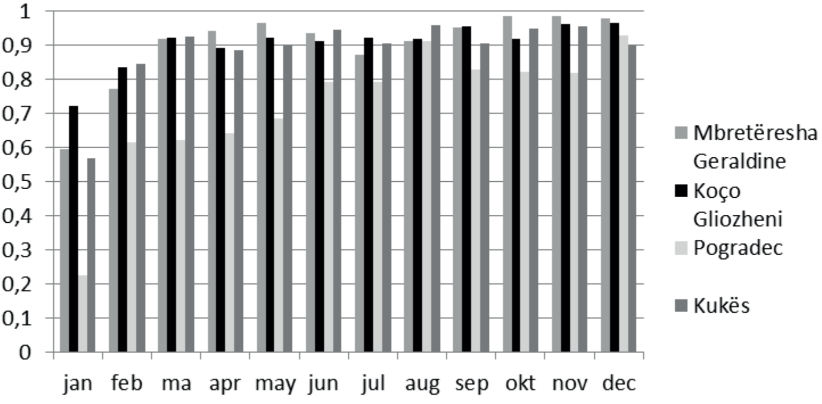


Figure 2. Pass rate of the first screen for each maternity hospital per month.

Differences were noted between the two maternity hospitals in Tirana. The number of infants born in MB was 1.74 times higher than in KG while the number of screeners was the same. This resulted in different outcomes. In KG, screening was organised in a more efficient way resulting in a lower referral rate and less infants not attending repeat screening.

Screening outcome

All infants born in one of the four maternity hospitals involved in the study were eligible for screening. In 2018, 9583 infants were born in the Tirana province, 1634 in the Korçe province, in which Pogradec is located, and 952 in the Kukës province [15]. In the participating maternity hospitals, a total of 11,507 eligible infants were born. In principle, all infants were invited to participate in screening. For 11,430 infants a record was made in de database but for 486 infants no result of screening was registered. Out of the 10,944 remaining infants, 19 did not participate in the first screen because parents refused screening (7), the infants died (8), or the infant was discharged before screening could be performed (4). Out of all infants who participated in the first screen, an additional 392 (3.4%) did not reach screen completion. Reasons given were: the infant died (21) or had other health issues (8), parents were convinced their child could hear and did not think repeat screening was necessary (9), parents went to a private clinic for screening (17), parents lived too far away from the location where screening took place and were unable to return (61), parents declined screening but no further reason was given (157) or parents did not attend without giving a reason (138). The distribution of reasons given per maternity is shown in Table 2. In the first year, 97.28% of infants completed screening within the first month after birth.

Of the 10,925 (94.9%) infants participating in the first screen, 1115 (10.2%) infants had a "fail" outcome. Six were referred to Tirana for diagnostic assessment and all 1109 remaining infants were invited for the second screen. Out of the 1109 infants invited, 361 (32.6%) did not participate of whom 124 did not provide a reason. The remaining 748 (67.4%) were screened in the second screen, 90 (12%) of whom received a "fail" outcome. Out of these 90 infants, ten were referred to Tirana for diagnostic assessment and 31 did not participate in the third screen, of which 14 did not provided a reason. Forty-nine infants participated in the third screen. A total of 33 (0.30%) infants were referred for full diagnostic assessment in Tirana (Fig. 3). The low referral rate in general and the low referral rates for each screener were looked at in more detail during the second year of screening. Results from the diagnostic assessment will be reported after the implementation study has ended in December 2019.

Despite the use of a different protocol, the proportion of infants referred in the Kukës maternity hospital was much higher than should be anticipated [40]. This implies that further training may be needed. This inconsistency has given rise to more in-depth exploration of the situation in Kukës and what is required to maintain screener quality.

Table 2. The number of infants screened in the first, second and third screen in four maternity hospitals in Albania. The table shows the number of ”Pass” and “Fail” results per screen, the number of infants referred for full diagnostic assessment and the number of infants who did not attend follow up screening including the reasons given. “Fail” results include tests that failed or did not reach threshold.

	Mbretëresha Geraldine			**Koço Gliozheni**			**Pogradec**			**Kukës**	
	First screen	Second screen	Third screen	First screen	Second screen	Third screen	First screen	Second screen	Third screen	First screen	Second screen
Total	6615	584	32	3795	353	40	442	118	8	578	54
Unknown	352 (5.3%)			61 (1.6%)			62 (14%)			11 (1.9%)	
Did not attend	14 (0.2%)	270 (46.2%)	13 (40.6%)	5 (0.1%)	57 (16.1%)	16 (40%)		18 (15.3%)	2 (25%)		16 (29.6%)
Reason Unknown	*-*	*73*	*1*	*-*	*19*	*12*	*-*	*16*	*1*	*-*	*16*
No parental consent	*5*	*117*	*7*	*5*	*18*	*2*	*-*	*2*	*1*	*-*	*-*
Infant lives in different city	*1*	*40*	*1*	*-*	*17*	*2*	*-*	*-*	*-*	*-*	*-*
Infant screened in private hospital	*-*	*15*	*2*	*-*	*-*	*-*	*-*	*-*	*-*	*-*	*-*
Parents convinced infant can hear	*-*	*6*	*1*	*-*	*2*	*-*	*-*	*-*	*-*	*-*	*-*
Infant died	*8*	*13*		*-*	*-*	*-*	*-*	*-*	*-*	*-*	*-*
Other health issues	*-*	*6*	*1*	*-*	*1*	*-*	*-*	*-*	*-*	*-*	*-*
Infants screened	6249 (94.5%)	314 (53.8%)	19 (59.4%)	3729 (98.3%)	296 (83.9%)	24 (60%)	380 (86%)	100 (84.7%)	6 (75%)	567 (98.1%)	38 (70.4%)
Pass	5663 (90.6%)	281 (89.5%)	14 (73.7%)	3376 (90.5%)	248 (83.8%)	18 (75%)	262 (68.9%)	91 (91%)		509 (89.8%)	38 (100%)
Fail	584 (9.3%)	32 (10.2%)		353 (9.5%)	40 (13.5%)		118 (31.1%)	8 (8%)		54 (9.5%)	
Fail + refer to diagnostics	2 (0.1%)	1 (0.3%)	5 (26.3%)		8 (2.7%)	6 (25%)		1 (1%)	6 (100%)	4 (0.7%)	

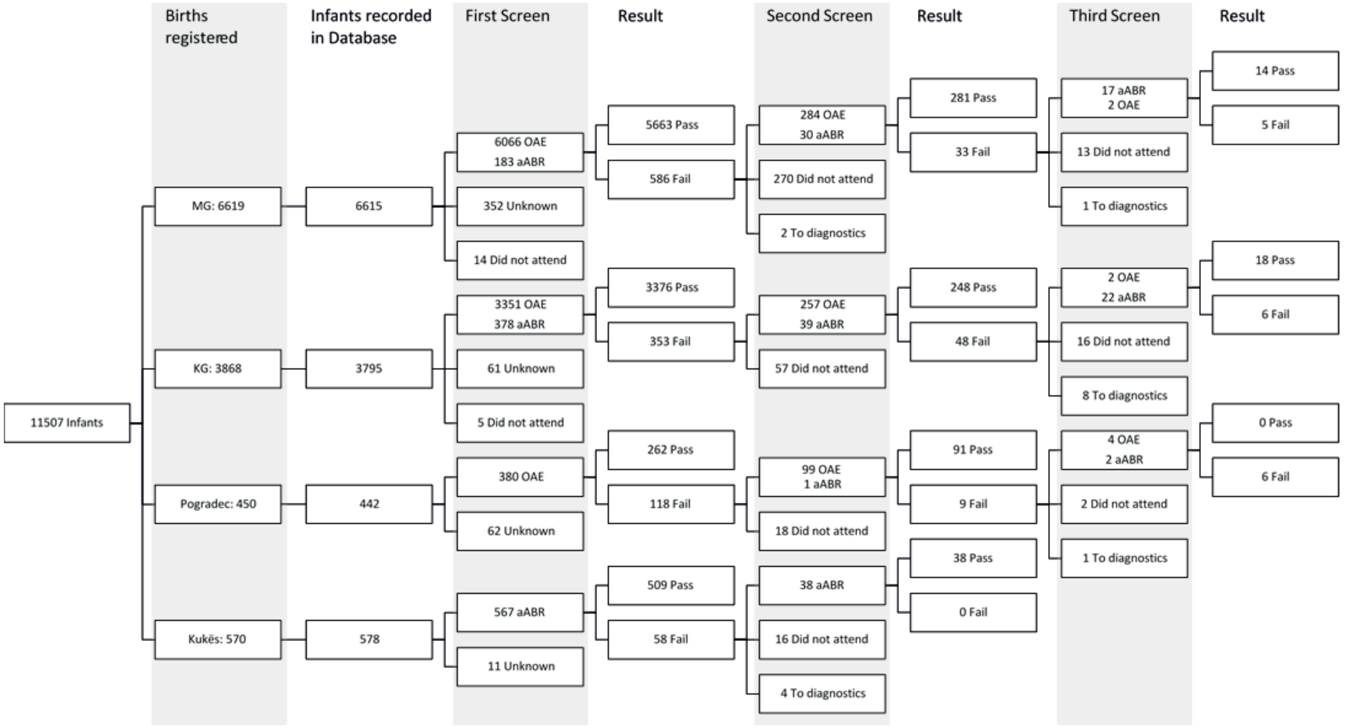


Figure 3. The number of infants screened is depicted for the first, second and third screen in the four maternity hospitals in Albania.

The figure shows the number of "Pass" and "Fail" results per screen, the number of infants referred for full diagnostic assessment and the number of infants who did not attend follow up screening. "Fail" results include tests could not be performed or did not reach threshold.

'MG': Mbretëresha Geraldine, maternity hospital in Tirana; 'KG': Koço Gliozheni, maternity hospital in Tirana; 'OAE': number of infants screened with OAE; 'aABR': number of infants screened with aABR; 'unknown': infants for whom no results were recorded in the database; "Pass": infants who reached threshold on the screening test; "Fail": infants for whom the test failed or did not reach threshold; 'Refer to diagnostics'; refer for diagnostic assessment in Tirana; 'Did not attend': Infants who did not participate in screening due to various reasons.

Assessment of screening implementation

Acceptability and adoption by the screeners were assessed by means of the questionnaire. Nineteen of the twenty-one screeners returned a completed questionnaire at the start of the screening programme. The questionnaire identified a positive attitude from the screeners towards the programme. They indicated their belief screening should be provided to all Albanian citizens. Screeners feel confident and able to participate in the programme, they were ready to take on extra screening tasks because they strongly believed in this screening programme. They found the training course to be very informative but would like to have more follow up training.

After 12 months the questionnaire was distributed again and all twenty-one screeners returned a filled-out questionnaire. The answers provided by the screeners after one year of screening were similar to the previous questionnaire in relation to attitudes and general feelings towards hearing screening. After one year, the screeners felt more confident, did not have to spend as much time preparing for screening and considered screening to be an obvious part of their daily work. Screeners spent more time on informing the parents about hearing screening and noticed parents understood the aim of the screening programme better because of their explanation. The screeners indicated their interest in expanding their knowledge on hearing and screening. The questionnaire will be filled out again after 24 months of screening.

DISCUSSION

In the first year of implementation of a NHS programme in four maternity hospitals in urban and rural areas in Albania, both the uptake by the screeners and the acceptance by the parents for the first screen was good. Screeners were keen to improve their skills in screening and considered NHS valuable for Albanian health care. The number of "fail" outcomes - the test could not be performed or the threshold was not reached - on the first screen was high in the beginning but decreased to less than 10% after eight months. Devices and probes initially broke often. However, after a "fail" outcome of the first screen, a high number of infants did not attend the second (32.4%) and third (34.4%) screen, thereby forming the most important obstacle for implementation of NHS in Albania. Possible reasons for not attending the second screen were: not enough information given to parents, administrative problems such as incorrect contact information and the parents could not be reminded of repeat screening, follow up examination took place at another location, the health condition of the infant, parents assumed their infant could hear, travel distances, time between rescreens and costs.

The first screen had high acceptance (94.9%), comparable to acceptance rates in Turkey [6], Italy [41], Poland [42] and Greece [43]. However, 32.4% of infants with a "fail" outcome in the first screen did not attend the second screen for all four maternity hospitals. Non-attendance was especially high in the MG maternity hospital in Tirana and in the maternity hospital in Kukës. For all maternity hospitals together, 34.4% of the infants with a "fail" outcome in the second screen did not attend the third screen. In retrospect, planning all screening steps before discharge, reducing the time between screening steps or choosing a protocol with fewer steps may have prevented these high non-attendance rates.

The aABR-aABR protocol in Kukës resulted in a lower proportion of "fail" outcomes compared to Pogradec, similarly rural but less mountainous and more affluent. This may indicate that the use of a two-step aABR protocol has a higher specificity and reduces the number of "fail" outcomes. The proportion of infants that did not attend the second screen was, however, similar to results found in the other maternity hospitals. The advantage of better specificity for aABR screening may be offset by larger travel times in mountainous areas.

High non-attendance rates were previously found in newly implemented NHS programmes in Italy (29.9% for the second screen) [44], Nigeria (43.1% for the second screen) [45] in Turkey (30%) [46] and in Shanghai (34.32% for the second screen) [11]. Other newly implemented NHS programmes have reported non-attendance rates that are much lower as for example 0.2–0.4% in France [2,7] 4.23% in Iran [10] and 6% in the Netherlands [12]. Three studies previously reported that non-attendance reduced when experience in screening was gained. In Greece non-attendance reduced from 72.2% to 58.2% after three years of screening. In Colorado 52% of infants did not attend repeat screening between 1992 and 1996 compared to 24% in 1999 [43, 47]. More recently, a non-attendance rate of 19% was reported for infants born in Colorado in 2005 and 18% for WB born between 2007 and 2012 [48]. Similar rates of non-attendance have been reported for referral to diagnostic assessment. During the early phase of the UK implementation the target of diagnostics within four weeks of screen completing was not met in 60% of cases. However, after seven years this improved to 17.5% [4].

Acceptance is usually high when the first screen is performed in the maternity hospital before discharge. In contrast to the first screen, attendance to repeat screens may be much lower when parents have to overcome practical problems such as larger travel distances and costs [3, 11, 12, 25, 46]. Other reasons for non-attendance described in previous research were also similar to reasons given by parents and screeners in Albania: parents did not understand the importance of screening [49], negative attitudes and lack of awareness in parents or screeners [25, 43], programme organisation [43], cultural reasons [26] and type of health insurance [50]. Another possible explanation may be that parents did not receive an invitation for repeat screening after their infant received a "fail" outcome or that the health condition of the infant did not allow for screening to be performed yet. In the Netherlands, attendance was found to be higher when NHS was combined with other health care measures thereby also improving the cost-effectiveness of NHS [12]. In developing countries mothers often do not give birth in regular maternity hospitals [45], and screening in combination with other mother or infant health care services has proven to be more efficient in these countries [45,51]. Similarly, when NHS is organised within an existing maternal and infant health programme and the professionals involved are more successful in explaining the importance to the parents, the number of infants not attending is reduced [2]. To further reduce the number of non-attendants in

Albania, the number of screening steps may be reduced or repeat screening may be combined with existing maternal or infant health care services such as vaccination. When NHS will be implemented in the whole of Albania, multiple screening locations will be set up across the country so parents do not have to travel as far.

In previous implementation studies results indicated that parental awareness is very important to increase the acceptance of screening [36, 37, 45, 52]. Therefore, the local study coordinator (BQ) developed leaflets and informative videos that were played in hospital waiting rooms to inform parents. Furthermore, she appeared in several national television and radio shows to explain the importance of NHS. The efforts made to inform parents improved their willingness to participate.

The number of "fail" test results in Albania was high initially. This may have been caused by the early timing of screening or the inexperience in screeners. As is described by Berninger and Westling (2011)[30],amniotic fluid that is present in the neonates' middle ear in the first days of life may cause increased failure rates when performing OAE screening before the third post-natal day. Despite the fact that a more optimal timing for the first screen may be five days after birth [30], most NHS programmes perform the first screen in the maternity hospital before discharge because high attendance can be achieved. A number of experienced screening programmes (in the UK, USA and Italy) have reported low repeat rates despite screening within 48 h after birth [4, 41, 42]. Lack of experience with screening may have contributed to high screening repeat rates in Albania, in areas with low birth numbers like Pogradec and Kukës in particular.

Out of 10,925 infants that participated in the first screen, 411 (3.8%) did not complete screening and for 486, no results were registered. This may be an issue with database records not being completed. The proportion of infants that did not reach screen completion was 4.8% in MG, 2.1% in KG, 5.3% in Pogradec and 2.8% in Kukës. Only 33 infants of the 10,925 who started screening were referred for a full diagnostic assessment. The outcomes of the screening programme show that more than 95% of eligible infants were covered and lessthan4% of infants were referred, according to the JCIH recommendations. Low referral rates to full diagnostic assessment may be associated with a high number of false positives (for example due to multiple screens within one step), high numbers of infants lost to follow up and high-quality screening resulting in very low repeat rates between steps. The referral rates for each screener revealed that a number of screeners did not refer any infants. Screeners may choose to repeat screening within one step to be able to give good news to the infants' parents. This is an issue that may be addressed in further training. Both the high number of infants that did not reach screen completion and the low number of infants referred to diagnostic assessment remain areas of concern. These issues will be followed up in the second year of screening. Low referral rates to diagnostic assessment were previously found in Turkey (0.01%) [6], France (0.2%) [7] and China (0.8%) [3]. The number of infants lost to follow up varied between studies: Caluraud et al. (2015) [7] reported 0.2% for both screening steps while 10% was reported for the same number of steps by Chen et al. (2017) [3]. Infants lost to follow up were not reported by Bolat et al. [6]. Another difference found was the protocol used in these studies. In the study performed by Caluraud et al. (2015) [7], aABR is used in the first step, Bolat et al. [6] uses aABR only in the second step and Chen et al. (2017) [3] does not use aABR in any of the screening steps.

Based on what we have learned from the first year of implementation, both the successes and the continuing challenges, an implementation plan is being developed to extend NHS to the whole country. This plan will take into account the areas in which the programme is still experiencing difficulties. It will combine current experiences with the experiences from previous implementation, that still need to be addressed such as the number of infants that do not complete screening.

In a country where previous implementations of NHS were not continued because NHS was not considered a priority at that time, significant successes were achieved in the number of infants reached in the first screen, improving the awareness in parents and developing a care pathway. However, the number of infants that do not attend repeat screening and consequently, the number of infants that does not completescreeningremainstoohigh.Thisissuewillbefurtherexploredand addressed in the second year of screening and in the plan for nationwide implementation. Additionally, information gathered during this implementation study will be fed back into the model to improve its prediction for a nationwide NHS programme in Albania.

Acknowledgments

We thank the parents and children, nurses, administrators, the diagnostic team of the TUHC, the team in the CCR, the local organising team and all those participating.

REFERENCES

[1] CORDIS Europa, Implementation of Cost-Optimized Childhood Vision and Hearing Screening Programmes in Middle-Income Countries in Europe, European Commision, City, 2018.

[2] L. Bouillot, M.Vercherat, C. Durand, Implementing universal newborn hearing screening in the French Rhone-Alpes region. State of affairs in 2016 and the 1st half of 2017. 2019, Int. J. Pediatr. Otorhinolaryngol. 117 (2019) 30–36.

[3] X. Chen, M. Yuan, J. Lu, Q. Zhang, M. Sun, F. Chang, Assessment of universal newborn hearing screening and intervention in Shanghai, China. 2017, Int. J. Technol. Assess. Health Care 33 (2017) 206–214.

[4] S.A. Wood, G.J. Sutton, A.C. Davis, Performance and characteristics of the newborn hearing screening programme in england: the first seven years, Int. J. Audiol. 54 (2015) 353–358 2015.

[5] A.M. Augustine, A.K. Jana, K.A. Kuruvilla, S. Danda, A. Lepcha, J. Ebenezer, R.R. Paul, A. Tyagi, A. Balraj, Neonatal hearing screening - experience from a tertiary care hospital in Southern India. 2014, Indian Pediatr. 51 (2014) 179–183.

[6] H. Bolat, F.G. Bebitoglu, S. Ozbas, A.T. Altunsu, M.R. Kose, National newborn hearing screening program in Turkey: struggles and implementations between 2004 and 2008, Int. J. Pediatr. Otorhinolaryngol. 73 (2009) 1621–1623 2009.

[7] S.Caluraud,A.Marcolla-Bouchetemble, A.deBarros,F.Moreau-Lenoir,E.deSevin, S. Rerolle, E. Charriere, V. Lecler-Scarcella, F. Billet, M.F. Obstoy, I. AmstutzMontadert, J.P. Marie,Y. Lerosey, Newborn hearing screening: analysis and outcomes after 100,000 births in Upper-Normandy French region, Int. J. Pediatr. Otorhinolaryngol. 79 (2015) 829–833 2015.

[8] W.K. Low, K.Y. Pang, L.Y. Ho, S.B. Lim, R. Joseph, Universal newborn hearing screening in Singapore: the need, implementation and challenges, Ann. Acad. Med. Singapore 34 (2005) 301–306 2005.

[9] B.O. Olusanya, S.L. Wirz, L.M. Luxon, Community-based infant hearing screening for early detection of permanent hearing loss in Lagos, Nigeria: a cross-sectional study, Bull. World Health Organ. 86 (2008) 956–963 2008.

[10] N. Saki, A. Bayat, R. Hoseinabadi, S. Nikakhlagh, M. Karimi, R. Dashti, Universal newborn hearing screening in southwestern Iran, Int. J. Pediatr. Otorhinolaryngol. 97 (2017) 89–92 2017.

[11] X. Sun, X. Shen, D. Zakus, J. Lv, Z. Xu, H. Wu, W. Hsiao, Development of an effective public health screening program to assess hearing disabilities among newborns in Shanghai: a prospective cohort study, World Health Popul. 11 (2009) 14–23 2009.

[12] N. Uilenburg, M. Kauffman-de Boer, K. van der Ploeg, A.M. Oudesluys-Murphy, P. Verkerk, An implementation study of neonatal hearing screening in The Netherlands, Int. J. Audiol. 48 (2009) 108–116 2009.

[13] Joint Committee on Infant Hearing, Year 2007 position statement: principles and guidelines for early hearing detection and intervention programs, Pediatrics 120 (2007) 898–921 2007.

[14] Joint Committee on Infant Hearing, Year 2019 position statement: principles and guidelines for early hearing detection and intervention programs, J. Early Hearing Detect. Interv. 4 (2019) 1–44 2019.

[15] Republic of Albania Institute of statistics, Regional statistical yearbook, INSTAT, 2018 City.

[16] J.A. Mason, K.R. Herrmann, Universal infant hearing screening by automated auditory brainstem response measurement, Pediatrics 101 (1998) 221–228 1998.

[17] A.B. Maxon, K.R. White, B.R. Vohr, T.R. Behrens, Using transient evoked otoacoustic emissions for neonatal hearing screening, Br. J. Audiol. 27 (1993) 149–153 1993.

[18] A.L. Mehl, V. Thomson, Newborn hearing screening: the great omission, Pediatrics 101 (1998) E4 1998.

[19] K. Neumann, M. Gross, P. Bottcher, H.A. Euler, M. Spormann-Lagodzinski, M. Polzer, Effectiveness and efficiency of a universal newborn hearing screening in Germany, Folia Phoniatrica Logop. 58 (2006) 440–455 2006.

[20] D.L. Stewart, A. Pearlman, Newborn hearing screening, J. Ky. Med. Assoc. 92 (1994) 444–449 1994.

[21] C. Yoshinaga-Itano, M.L. Apuzzo, The development of deaf and hard of hearing children identified early through the high-risk registry, Am. Ann. Deaf 143 (1998) 416–424 1998.

[22] C. Yoshinaga-Itano, M.L. Apuzzo, Identification of hearing loss after age 18 months is not early enough, Am. Ann. Deaf 143 (1998) 380–387 1998.

[23] K.R. White, Universal Infant Hearing Screening: Successes and Continuing Challenges, (2010) 2010.

[24] F. Sloot, H.L. Hoeve, M.L. de Kroon, A. Goedegebure, J. Carlton, H.J. Griffiths, H.J. Simonsz, Inventory of current EU paediatric vision and hearing screening programmes, J. Med. Screen 22 (2015) 55–64 2015.

[25] S. Hatzopoulos, B. Qirjazi, A. Martini, Neonatal hearing screening in Albania: results from an ongoing universal screening program, Int. J. Audiol. 46 (2007) 176–182 2007.

[26] E. Beqiri, D. Nika, Universal neonatal hearing screening in Albania, 2009-2012, Mater. Soc. Med. 27 (2015) 13–14 2015.

[27] J.D. Habbema, G.J. van Oortmarssen, J.T. Lubbe, P.J. van der Maas, The MISCAN simulation program for the evaluation of screening for disease, Comput. Methods Progr. Biomed. 20 (1985) 79–93 1985.

[28] D. Bali, G. Kuli-Lito, N. Ceka, A. Godo, Maternal and child health care services in Albania, J. Pediatr. 177S (2016) S11–S20 2016.

[29] E. Berninger, B. Westling, Outcome of a universal newborn hearing-screening programme based on multiple transient-evoked otoacoustic emissions and clinical brainstem response audiometry, Acta Otolaryngol. 131 (2011) 728–739 2011.

[30] A. Erenberg, J. Lemons, C. Sia, D. Trunkel, P. Ziring, Newborn and infant hearing loss: detection and intervention.American academy of pediatrics. Task force on newborn and infant hearing, 1998- 1999, Pediatrics 103 (1999) 527–530 1999.

[31] M. van Dyk, W. Swanepoel de, J.W. Hall 3rd, Outcomes with OAE and AABR screening in the first 48 h–Implications for newborn hearing screening in developing countries, Int. J. Pediatr. Otorhinolaryngol. 79 (2015) 1034–1040 2015.

[32] B. Vos, C. Senterre, R. Lagasse, G. Tognola, A. Leveque, Organisation of newborn hearing screening programmes in the European Union: widely implemented, differently performed, Eur. J. Publ. Health 26 (2016) 505–510 2016.

[33] H.M. Bantock, S. Croxson, Universal hearing screening using transient otoacoustic emissions in a community health clinic, Arch. Dis. Child. 78 (1998) 249–252 1998.

[34] B.S. Herrmann, A.R. Thornton, J.M. Joseph, Automated infant hearing screening using the ABR, Am. J. Audiol. 4 (1995) 6–14 1995.

[35] Institute for Quality and Efficiency in Health Care: Executive Summaries, Neonatal Screening for Early Detection of Hearing Impairment Executive Summary of Final Report S05-01, Version 1.0, City: Institute for Quality and Efficiency in Health Care (IQWiG), Cologne, Germany, 2005 2005–2007, February.

[36] V. Weichbold, K. Welzl-Mueller, E. Mussbacher, The impact of information on maternal attitudes towards universal neonatal hearing screening, Br. J. Audiol. 35 (2001) 59–66 2001.

[37] M.Y.Y. Lam, E.C.M. Wong, C.W. Law, H.H.L. Lee, B. McPherson, Maternal knowledge and attitudes to universal newborn hearing screening: reviewing an established program, Int. J. Pediatr. Otorhinolaryngol. 105 (2018) 146–153 2018.

[38] D.H. Peters, T. Adam, O. Alonge, I.A. Agyepong, N. Tran, Implementation research: what it is and how to do it, BMJ 347 (2013) f6753 2013.

[39] E. Proctor, H. Silmere, R. Raghavan, P. Hovmand, G. Aarons, A. Bunger, R. Griffey, M. Hensley, Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda, Adm. Policy Ment. Health 38 (2011) 65–76 2011.

[40] B.R. Vohr, W. Oh, E.J. Stewart, J.D. Bentkover, S. Gabbard, J. Lemons, L.A. Papile, R. Pye, Comparison of costs and referral rates of 3 universal newborn hearing screening protocols, J. Pediatr. 139 (2001) 238–244 2001.

[41] L. Bubbico, G. Tognola, F. Grandori, Evolution of Italian universal newborn hearing screening programs, Ann Ig 29 (2017) 116–122 2017.

[42] G. Greczka, M. Wrobel, P. Dabrowski, K. Mikolajczak, W. Szyfter, Universal neonatal hearing screening program in Poland–10-year summary, Otolaryngol. Pol. 69 (2015) 1–5 2015.

[43] S.G. Korres, D.G. Balatsouras, T. Nikolopoulos, G.S. Korres, E. Ferekidis, Making universal newborn hearingscreening asuccess, Int. J. Pediatr. Otorhinolaryngol. 70 (2006) 241–246 2006.

[44] F. Cianfrone, F. Mammarella, M. Ralli, V. Evetovic, C.M. Pianura, G. Bellocchi, Universal newborn hearing screening using A-TEOAE and A-ABR: the experience of a large public hospital, J. Neonatal Perinat. Med. 11 (2018) 87–92 2018.

[45] B.O. Olusanya, A.A. Okolo, Early hearing detection at immunization clinics in developing countries, Int. J. Pediatr. Otorhinolaryngol. 70 (2006) 1495–1498 2006.

[46] M.M. Tatli, M. Bulent Serbetcioglu, N. Duman, A. Kumral, G. Kirkim, B. Ogun, H. Ozkan, Feasibility of neonatal hearing screening program with two-stage transient otoacoustic emissions in Turkey, Pediatr. Int. 49 (2007) 161–166 2007.

[47] A.L. Mehl, V. Thomson, The Colorado newborn hearing screening project, 19921999: on the threshold of effective population-based universal newborn hearing screening, Pediatrics 109 (2002) E7 2002.

[48] V. Thomson, C. Yoshinaga-Itano, The role of audiologists in assuring follow-up to outpatient screening in early hearing detection and intervention systems, Am. J. Audiol. 27 (2018) 283–293 2018.

[49] A. Abdullah, M.Y. Hazim, A. Almyzan, A.G. Jamilah,S. Roslin, M.T. Ann,L. Borhan, A. Sani, L. Saim, N.Y. Boo, Newborn hearing screening: experience in a Malaysian hospital, Singap. Med. J. 47 (2006) 60–64 2006.

[50] C.L. Liu, J. Farrell, J.R. MacNeil, S. Stone, W. Barfield, Evaluating loss to follow-up in newborn hearing screening in Massachusetts, Pediatrics 121 (2008) e335–343 2008.

[51] W. Swanepoel de, R. Hugo, B. Louw, Infant hearing screening at immunization clinics in South Africa, Int. J. Pediatr. Otorhinolaryngol. 70 (2006) 1241–1249 2006.

[52] B.O. Olusanya, L.M. Luxon, S.L. Wirz, Infant hearing screening: route to informed choice, Arch. Dis. Child. 89 (2004) 1039–1040 2004.

Chapter 8

Implementation of newborn hearing screening in Albania

Andrea ML Bussé
Birkena Qirjazi
Allison R Mackey
André Goedegebure
Hans LJ Hoeve
Ervin Toçi
Enver Roshi
Gwen Carr
Martijn S Toll
Huibert J Simonsz

ABSTRACT

Objectives

Newborn hearing screening was implemented in Albania in two maternity hospitals in rural provinces and two maternity hospitals in the urban province of Tirana in 2018 and 2019. Implementation outcome, screening outcome and screening quality measures were evaluated to determine barriers and facilitators relevant to the screening programme implemented in Albania.

Methods

Infants were first screened before discharge from the maternity hospital with a 3-step OAE-OAE-aABR protocol or a 2-step aABR-aABR protocol, by midwifes and nurses who were trained to perform screening with OAE and aABR. Acceptability, appropriateness, feasibility, adoption, fidelity, coverage, attendance, stepwise and final referral rate were studied by on-site observations in maternity hospitals, by interviews with screeners, parents and supervisors, by questionnaires for screeners and parents, and with a database comprising all infants participating in the study. A post-hoc analysis was performed to identify reasons for loss to follow-up (LTFU) in a multivariate logistic regression.

Results

In 2018 and 2019, 22,818 infants were born of which 22,051 (96.6%) were first screened. In the first screening step, 1,559 (7.1%) infants received a fail outcome, including 13 who were referred to diagnostic assessment. Out of 1,546 infants invited for the second screening step, 519 (33.6%) did not attend, 146 (14.2%) received a second fail outcome and 42 were referred for diagnostic assessment. Out of 104 infants invited for the third screening step, 42 (40.4%) did not attend, 26 (25%) received a third fail outcome and 39 were referred for diagnostic assessment. Out of 81 infants referred for diagnostic assessment, 29 (35.8%) did not attend and 22 (0.1%) were diagnosed with hearing loss (HL) of ≥40dB, six unilateral. Acceptance of NHS by parents and screeners was high. Adoption of NHS by screeners was good and organisation of screening and screening skill improved throughout the implementation. Some screeners repeated the test multiple times to obtain a pass result. Excessive workload in the largest urban maternity hospital led to high LTFU rates. Travel duration from family home to maternity hospital was a significant predictor of LTFU.

Conclusions

Newborn hearing screening was successfully implemented in four maternity hospitals in Albania and was considered feasible in both rural and urban provinces. NHS performed by nurses and midwifes before discharge from the maternity hospitals worked very well. Initial screening coverage was high. However, LTFU was 33.6% to the second screening step, 40% to the third

screening step and 35.8% to diagnostic assessment. It is imperative that a good database is in place to supervise the screeners and track infants through screening, diagnostic assessment and intervention.

INTRODUCTION

Newborn hearing screening (NHS) programmes have been successfully implemented in countries across the world to detect infants with a hearing loss and to provide them with subsequent intervention. These programmes seem to be lacking more often in countries with lower health expenditure and human development index [1, 2]. Without an effective NHS programme in place, children with a hearing loss (HL) remain undetected until delays in speech and language development are noticed by observant caregivers [3]. Children with a HL that remains untreated during early childhood can experience delays in speech and language development which can affect academic performances and social development [4, 5].

Albania has a total area of 28,748 km2 and a population of 2,845,955 inhabitants [6]. Almost 40% of the Albanian population lives in rural areas [7]. Each year, nearly 30.000 infants are born in Albania [8], of which 1 to 3 out of every 1000 infants may be born with a permanent sensorineural HL ≥40dB [9-11]. Two previous attempts were made to implement NHS in Albania. In the first study, by Hatzopoulos et al (2007) [12], 40% of well babies (WB) and 53% of infants admitted to the neonatal intensive care unit (NICU) did not follow up after a referral from screening. In total, 0.18% of the NICU infants were diagnosed with a HI. In the second study, by Beqiri and Nika (2015) [13], only 1.6% of the infants did not follow up with screening or diagnostic assessment and 0.21% of all infants were diagnosed with a HI. Both screening programmes were not continued after the end of the project.

In most countries, NHS is performed immediately after birth and the first screening step is usually performed before discharge from the maternity hospital. The average length of stay in the maternity hospital in Europe is 3.1 days after giving birth (range: 1.5-4.9 days) [14]. Screening before discharge ensures high coverage, but residual fluid and debris in the ear after birth may cause some infants to receive a false fail outcome after the first screen [15, 16].

A high proportion of infants lost to follow-up (LTFU) is a serious obstacle for successful implementation of NHS. It was reported to be even more challenging in developing countries [17]. Reasons for LTFU between screening steps include travel times and costs, parental educational level, parental awareness, organisation of NHS, religion, ethnicity, premature birth, low birth weight, APGAR score, and NICU admission [12, 18-22]. To minimise the proportion of infants LTFU, parents, screeners and hospital staff were better informed about the consequences of a newborn HL which improved their attitudes towards NHS [20, 23]. Low LTFU was found among a well organised national NHS programme with clear protocols [24] and programmes that offered rescreening at local mother-child health centres [25]. In addition to LTFU, referral rates were reported to be higher after the first screen when NHS was just implemented. It decreased when screeners gained more experience [20, 26, 27]. Efforts made to lower referral rates included repeating the test multiple times [20], screening at a later age, and additional training for screeners [26].

Within the EUSCREEN study the cost-effectiveness of paediatric vision and hearing screening programmes are being compared in Europe and beyond. A cost-effectiveness model is being developed to compare the cost-effectiveness of hearing screening programmes across borders. It can assist in the introduction and modification of or disinvestment from screening programmes in countries or regions while taking local circumstances into account such as demography and geography [28]. Alongside the development of the model, NHS was implemented in four maternity hospitals in Albania during 2018 and 2019 [29]. The outcomes of previous implementation studies in Albania were considered, and the Albanian government was consulted regarding the continuation of NHS and nationwide implementation.

Data were collected from the Albanian experience with implementation of an NHS programme as part of the EUSCREEN project. NHS was implemented in two maternity hospitals in two rural provinces and two maternity hospitals in the urban province of Tirana in Albania between January 1st, 2018 and December 31st, 2019. Experiences with the implementation of NHS were described as well as feasibility of NHS in both rural and urban provinces. Implementation outcomes and screening quality measures were evaluated to determine facilitators and barriers for implementation of NHS in Albania.

METHODS

Preparation and screening protocol

NHS was implemented in Albania in four maternity hospitals. Two maternity hospitals were situated in Tirana: Mbretëresha Geraldine (MG) and Koço Gliozheni (KG), one in Pogradec and one in Kukës (Figure 1). The maternity hospitals were located in three different provinces that were chosen because they appropriately represented the distribution of the Albanian population. They include both rural and urban areas and covered a range of socio-economic circumstances. A total of 9,583 infants were born in 2018 and 9,321 in 2019 in the Tirana province; 1,634 in 2018 and 1,750 in 2019 in the Korçe province (where Pogradec is located); and 952 in 2018 and 1,103 in 2019 in the Kukës province [30]. Within the current observational study, all infants born in one of the four maternity hospitals during the time of implementation (2018-2019) were eligible for screening.

Implementation was organised, coordinated and facilitated by a local internal programme lead (BQ). During the preparatory phase the programme lead made arrangements with the maternity hospitals. She acquired the screening devices, provided equipment to prepare a screening room and hired screeners. Before and during the preparations, the programme lead explored possibilities to expand screening to nationwide reach. The screening protocol and the objectives for the NHS programme that was implemented in Albania were described in detail before implementation started [29]. The protocol also included details on screening organisation, the professionals invited to perform screening, screener training, screening location, screening devices and possible expansion of the programme country-wide.

Figure 1. Map of Albania. ⊕ marks the four maternity hospitals: two in Tirana, one in Pogradec and one in Kukës. The striped area marks the region around each maternity hospital within a travel time of 30 min by car. The grey area marks the region around each maternity hospital within a travel time of 60 min by car.

Written informed consent was sought from parents before screening. Screening was performed in the maternity hospital by nurses who were selected by the head of the maternity hospital or NICU department and who had been trained to perform screening. Parents were informed through leaflets, posters, informational videos on television screens in the maternity hospital and interviews on national television and radio.

The first screening step took place before discharge from the maternity hospital because the majority of infants are born in a maternity hospital in Albania [31]. Most infants are discharged within 24 hours after birth. Infants stayed in the maternity hospital longer when they were born by caesarean section or when complications in either the mother or the infant occurred. Infants who received a fail outcome for the first screening step had to return to the maternity hospital for subsequent screening steps. When applicable, the second screening step was scheduled two weeks after the first screening step and the third screening step was scheduled two weeks after the second screening step. All healthy infants (well babies; WB) who were born in Tirana and all infants born in Pogradec were screened with a three-step OAE-OAE-aABR protocol. All infants born in Kukës were screened using a two-step aABR-aABR to limit the number of follow-up screens and thus limit the expected LTFU rate caused by long travel times for parents [28]. Infants admitted to the NICU in one of the maternity hospitals in Tirana, were screened using a two-step aABR-aABR to also detect retrocochlear HI [29]. Parents were reminded of these appointments by a telephone call. Infants who did not receive a pass result on completion of screening were sent to Tirana for diagnostic audiological assessment and subsequent intervention. This took place at the Tirana University Hospital Centre (TUHC) or Child Centre for Rehabilitation (CCR).

Organisational changes made to improve follow-up in 2019 based on experiences in 2018

The main problem that was experienced during the first year of screening was the high number of infants that did not attend follow-up screening [29]. Consequently, a high number of infants who failed the first screen did not complete the entire screening protocol. Based on observations made in the first year, some changes were made to increase follow-up in the second year. All infants with a fail outcome on the first screen received an appointment to return for follow-up screening two weeks later. Screeners emphasised the importance of this follow-up screening and possible effects for the infant. Parents were reminded to return for follow-up screening by a telephone call a few days before the appointment.

Small changes were made in the teams that conducted screening. In the MG maternity hospital, screeners had to deal with a high workload. One screener, who resigned, was replaced by two new screeners to manage the high number of infants born each day. In Pogradec only a small number of infants were screened using aABR so one screener was put in charge of aABR screening to provide consistent screening quality. After the first training course, two refresher courses were organised. During these refresher courses, the screeners could share experiences and ask each other for help with the difficulties they encountered. The screeners kept in contact with each other throughout the two years of implementation. They continued to share experiences and ask questions through phone calls and text messages.

Database with screening outcome

Screeners filled out infant data and the anonymised results of screening of each infant on a paper form. Additionally, the screeners administered a socio-economic questionnaire (described previously [32]). The forms were transferred to a secure digital database. Each screener had their own username and password. They were responsible for uploading the information for each screening step of all the infants they screened. All eligible infants received an anonymised code in the database. Each maternity also kept a register of all the infants that was designed by the head nurse in collaboration with the screeners. The data that were recorded included date of birth, the date on which screening took place, location, admission to NICU, possible medical factors and the outcome of screening. The database was checked for inconsistencies, obvious mistakes such as typing errors were corrected.

From this database, the following screening quality measures were calculated for eligible infants in the study for each maternity hospital and for each screener: coverage, attendance, stepwise and final referral rates (Table 1). Attendance rates were calculated for each screening step. Infants for whom no follow-up screening was registered were considered LTFU. Infants who were registered as LTFU were phoned by the local screening team to record reasons for LTFU. The database was compared to the local register in each maternity hospital to assess and improve accuracy. The screening data that were uploaded in the database, could be accessed by the local programme lead (BQ) who also performed most of the diagnostic assessments. LTFU was analysed in more detail in a post-hoc analysis of the screening data collected in the database.

Outcomes from implementation of the screening programme

To evaluate the barriers and facilitators of NHS implementation in Albania, implementation outcomes were evaluated, defined in Table 1 based on framework by Proctor et al. [33]. Within this implementation study, the acceptability, appropriateness, feasibility, adoption and fidelity of NHS were evaluated in Albania [33, 34]. Stakeholders are defined as parents of the infants eligible for screening, screeners, audiologists, doctors, rehabilitation workers and policy makers. These outcomes were evaluated using observations of screening during on-site visits, interviews with screeners and parents, screener questionnaires, a socio-economic questionnaire for the parents, screening outcome data collected through the database and follow-up phone calls with parents of infants LTFU.

On-site visits and screening observations

Three authors (BQ, ET, ER) organised and facilitated the local NHS programme. Three authors (AB, AG, HH) visited Albania a total of five times for on-site visits and screening observa-

Table 1. Implementation outcomes and screening quality measures that were used to evaluate barriers and facilitators relevant to the screening programme implemented in Albania, their definition and operationalisation for Albania [33].

Implementation outcomes	Definition	Operationalisation
Acceptability	The extent to which the programme is considered agreeable, palatable or satisfactory by staff or other stakeholders.	*How important do screeners, parents, doctors, audiologists, healthcare administrators and policymakers think NHS is for Albania?*
Appropriateness	The perceived fit and relevance for stakeholders and the setting in which it is implemented.	*Is NHS relevant in current healthcare in Albania when compared to other healthcare priorities?* *Is audiological diagnostic assessment and intervention available to all infants screened positively or referred?*
Feasibility	The extent to which it can be successfully used or carried out within a given setting, its practicality.	*Can NHS be practiced successfully in maternity hospitals by nurses and midwifes?*
Adoption	The intention of the stakeholders to participate in the programme.	*How many parents of infants invited for screening agreed to participate in the programme? Did screeners integrate NHS in their daily routine? How important are infants with a HL for the screeners? Do screeners want to put in more effort to detect infants with a HL by extending their knowledge and skills? Did screeners change their attitude towards NHS?*
Fidelity	The extent to which the agreements and prescribed protocols were followed during the implementation.	*Was screening carried out as prescribed in the screening protocol? How was the screening programme monitored/supervised? How accurate was administration performed? Were all infants invited and did all infants attend follow-up screening in subsequent screening steps?*
Coverage	The proportion of eligible infants invited for screening.	*What proportion of eligible infants has been screened as intended during the implementation?*
Attendance	The proportion of the invited infants that have been screened.	*How many infants attended the first screening step and subsequent screening steps after having been invited?*
Stepwise referral rate ***Final referral rate to diagnostics***	The proportion of screened infants that were referred to the next step after a fail outcome. The proportion of screened infants that were referred to diagnostic assessment after a fail outcome.	*What proportion of eligible infants was referred for follow-up screening to the second and third screening step after a fail outcome?* *What proportion of eligible infants was referred for diagnostic assessment?*

tions. These visits took place before, during and at the end of implementation. The maternity hospitals were visited to observe the screeners, to evaluate their screening skills and to inspect the devices. Additionally, the diagnostic assessment and intervention clinics were visited before and during implementation. Based on the observations made during the first year of screening, some changes were made to improve screening outcome in the second year. During these visits, screeners and parents were interviewed and the screening questionnaires were distributed.

Interviews with screeners and parents

All screeners who were available at the time of the on-site visit were interviewed. During the interviews, screeners were asked about their experiences with the screening protocol, the devices, the database and their interactions with the parents. They were asked to estimate referral and follow-up rates in their maternity hospital and screeners expressed their ideas about continuation of the programme. A few interviews were conducted with parents who were present in the maternity hospital at the time of the visit after consent for the interview was obtained. They were asked how they experienced screening and how they were informed about the screening programme. The number of available screeners and parents varied between maternity hospitals and between visits.

Questionnaire for screeners and parents

All screeners received a questionnaire containing 155 multiple choice questions, covering seven domains: general information, attitudes of the screener towards hearing screening, hearing loss, parents of infants screened and subcultures, individual features of the screener and additional questions. The questionnaire was distributed three times: during the on-site visits at the beginning of screening, after one year and at the end of the second year. The answers were compiled and compared across screeners, maternities and the time when the questionnaire was filled out. Screeners conducted a short questionnaire among parents that contained 13 questions on socio-demographic and socio-economic subjects. Answers were collected in the study database and used in the post-hoc analysis to identify reasons for LTFU.

Post-hoc analysis of the database to identify reasons for LTFU

To get more insight into possible reasons for LTFU, a post-hoc analysis was performed based on infant screening outcome registered in the database. The outcome variable was LTFU between screening steps 1 and 2 (yes/no).

Infants and their families have individual characteristics that may predict their likelihood to be LTFU. Infants are grouped by screener, and screener characteristics may also influence whether infants are LTFU. Two levels of analysis were thus considered, the individual level and the screener level. At the individual level, the predictor variables applied to either the mother/family or to the infant. Some maternal/family variables were collected through the socio-economic questionnaire, and these variables included the family's economic status (5-point scale: very bad to very good), the mother's overall health status (5-point scale: very bad to very good) and the mother's age. Other family variables were the location of the family's home as reported by the parents (urban or rural) and the duration of time needed to travel from the family's home to the screening facility (in hours) calculated through a spatial analysis. Infant variables were registered in the database by the screeners and included the year of birth (2018 or 2019), the gender, the duration of pregnancy (in weeks), the number of risk factors for HL (zero or at least one), and whether the infant failed screening in one or both ears.

At the screener level, the predictor variables were the protocol used by the screener, the total number of infants screened, and the referral rate for each screener. Additionally, a median odds ratio was calculated to translate the variance of the screener into an interpretable odds ratio, which describes the increase in likelihood of being LTFU if screened by a screener with an overall higher LTFU rate [35].

Geocoding travel time

To maintain anonymity, exact residential addresses were not obtained from the family apart from their hometown. A total of 392 hometowns were listed in the database, out of which 95 hometowns were listed among infants who were referred from screening step 1. The geographic information system (GIS) software QGIS v. 3.14 was used for geocoding and to perform the spatial analysis. All hometowns and four screening institutions were geocoded to spatial coordinates (x,y). Fastest travel time by car in hours was calculated from each family's hometown to their respective screening institution using the Open Route Service plugin function for road network analyses.

Analysis

To investigate the variables that significantly predict which infants will be LTFU between screening steps 1 and 2, a hierarchical multivariate logistic regression analysis was performed in SPSS (v. 27). This type of analysis is most appropriate to perform when individuals are grouped by another factor, such as screener. Using this approach, the variance between screeners can also be considered within the analysis. The final model contains the variables that best predict which infants are LTFU between screening steps 1 and 2 at a significance level less than 0.05.

To select the variables for inclusion in the multivariate logistic regression analysis, univariate analyses using likelihood ratios were performed for each predictor variable. Predictor variables with a significance level less than 0.1 in the univariate analysis were accepted into the multivariate model. Categorical variables with more than two categories were dummy coded. Categories were merged in two instances of quasi-complete separation of categorical variables due to the low number of infants in each group. The categories of very bad and bad were merged for the variables mother's economic situation (n=2 and n=9) and health status (n=3 and n=125).

Infants were excluded from the analysis if they passed screening (i.e., not required to attend rescreening) or if they referred from screening directly for a diagnostic assessment. Missing covariate data were imputed using multiple imputation with chained equations.

RESULTS

During 2018-2019, NHS was implemented in four maternity hospitals in Albania using OAE-OAE-aABR or aABR-aABR. In the results of this study, screening outcome is described for all infants who participated in screening. Furthermore, this study reports on the outcomes from implementation and investigates possible reasons for LTFU.

Screening outcome

The results of screening are reported based on data obtained through the study database. Several issues occurred with the registration of screening outcome in the database, some were caused by technical problems such as duplicate files and others were caused by mistakes that were made when filling out the database forms. For example, for some infants, no follow-up screen was registered, while parents indicated to have attended this screen. Some screeners indicated to not complete the database when parents did not attend the follow-up appointment after two weeks but returned for screening at another time. All infants with a 'ail outcome in the first or second screening step for whom no follow-up screen was registered in the second or third screening step were considered LTFU. The database was checked for inconsistencies and obvious mistakes were corrected.

Because it was unclear which infants had been admitted to the NICU based on information collected through the database, data are reported for all infants, both WB and infants admitted to the NICU, combined. All 22,818 infants born were invited for screening and 22,051 infants participated in the first screening step. Coverage in the first screening step (96.6%) was high throughout the two years of implementation (Figure 2). Out of the infants who participated in the first screen, 21,490 (97.5%) infants completed the entire screening protocol. Sixty-one percent of all infants who received a fail outcome after the first screening step were LTFU. Of the infants screened in the first screening step, 7.2% were referred to the second screening step; 14.2% of the infants screened in the second screening step were referred to the third screening step and 40% of the infants screened in the third screening step were referred to diagnostic assessment. LTFU was 33.6% between the first and second screening step and 40% between the second and third screening step. Of the 81 infants who were referred for a diagnostic assessment, 52 attended. Twenty-two infants (0.1% of the total population) were diagnosed with a HL of 40 dB or greater, of which 6 had a unilateral HI.

In the first screening step parents of 28 infants declined, 519 infants were LTFU to the second screening step and 42 to the third screening step. Reasons for not attending a screening step were registered in the database. They include health issues (11), the infant died (24), the infant was discharged before screening took place (2), the infant was screened in another location (21), travel distance (88), economic reasons (5), parental refusal (147, of which 39 parents believed their infant could hear), parents could not be contacted (47) and for a number of infants this reason remained unknown (244). Parents who had not attended screening without providing a

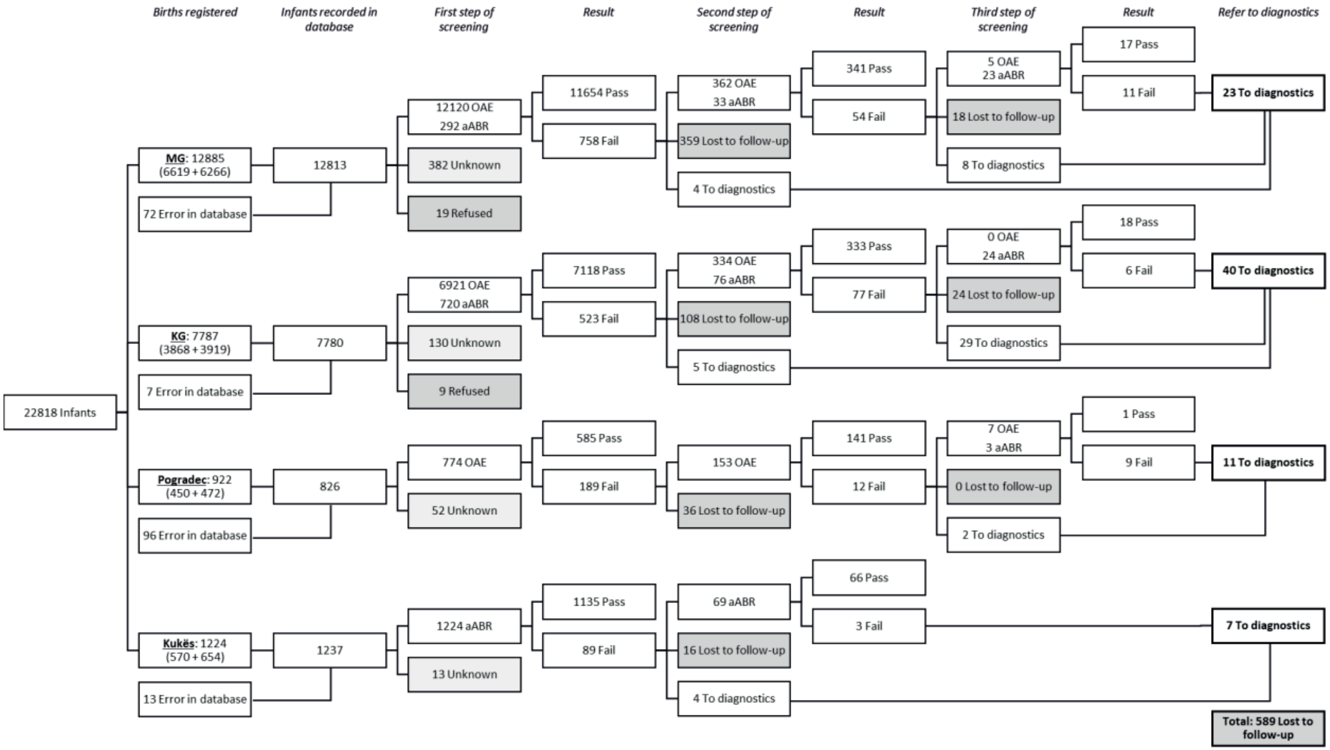


Figure 2. Flow chart depicting the number of infants screened for each screening step, the number of infants with a pass and fail result, the number of infants referred to diagnostic assessment and the number of infants lost to follow-up in all four maternity hospitals in Albania.

'MG': Mbretëresha Geraldine, maternity hospital in Tirana; 'KG': Koço Gliozheni, maternity hospital in Tirana; 'OAE': number of infants screened with OAE; 'aABR': number of infants screened with aABR; 'unknown': infants for whom no results were recorded in the database; 'Pass': infants who reached threshold on the screening test; 'Fail': infants for whom the test failed or did not reach threshold; 'Refer to diagnostics'; refer for diagnostic assessment in Tirana; 'Lost to follow up': Infants who did not participate in screening due to various reasons.

reason (unknown category) were phoned. In addition to reasons listed above, reasons provided during these telephone calls were: religious reasons, not understanding the purpose of the screening programme, no contact information, parents moved away, parents said they were not invited for screening or that no screening staff were present in the hospital when they brought their infant for screening.

Outcomes from implementation of the screening programme

Results for each implementation outcome measure are summarised in Table 2. NHS in Albania was considered acceptable. Both parents and screeners considered NHS to be important and wanted to participate in the programme. Despite having experienced several difficulties while setting up NHS, screeners reported that NHS was important, that it was suitable for Albania. NHS was considered appropriate because it could be implemented within the existing organisation of neonatal preventive healthcare in Albania. Audiological diagnostic assessment was made available for all infants who failed screening and early intervention for all infants who were diagnosed with HL.

It was feasible to employ nurses and midwifes to screen infants before discharge from the maternity hospital. However, it was more difficult to find a quiet room to perform screening in the MG hospital.

Adoption was good, all nurses who were invited to participate in the screener training agreed and all performed screening. Observations of the screeners showed that organisation of screening and individual screening skills improved throughout the two year of implementation.

Regarding fidelity, most screeners kept to the screening protocol; however, some screeners repeated the test multiple times during a step to obtain a pass result. The protocol prescribed that the test could be repeated twice after an initial fail outcome. This issue was addressed during the yearly refresher training course and can be monitored using the database.

Finally, regarding fidelity, it was important to find the right balance in workload for the screeners. In rural maternity hospitals the number of infants was low and experience was gained slowly. On the other hand, mistakes were made when the workload was too high, resulting in a higher LTFU rate. After an additional screener was hired for the second year in the MG maternity hospital, the screeners were better able to handle the workload.

It was anticipated that in Kukës and Pogradec, where population density is low, long travel times between the home and the maternity hospital would negatively influence the parents' willingness to return for follow-up screening. During the study it became clear that even parents residing in Tirana had to travel for many hours to reach the maternity hospital, as mothers from all over Albania give birth in Tirana, which made it very difficult for them to travel back for screening once they have returned home. This was further explored in a post-hoc analysis.

Table 2. Implementation outcomes and screening quality measures that were used to evaluate barriers and facilitators relevant to the screening programme implemented in Albania, how each criterion was measured and our findings.

Implementation criteria	Sources	Outcome
Acceptability	Screener interviews (1) Screener questionnaire (2) Parental interviews (3)	Screeners considered hearing screening important so that hearing loss in infants is detected early. (1, 2) Screeners indicated that all infants in Albania should have access to NHS. (1, 2) Parents thought hearing screening was important for their child after having received information on screening. (3) Parents sometimes felt anxious about screening. (3)
Appropriateness	Screener interviews (1) Screener questionnaire (2) On-site observation of screening (3) On-site observation of diagnostics (4) On-site observation of intervention (5)	NHS can be implemented within the existing organisation of neonatal preventive healthcare. (1, 2, 3) Most births in Albania take place in a maternity hospital, which facilitates the first screen performed before infants are discharged. (3) Audiological diagnostic assessment in two locations, was available for infants who were referred from screening. (4) Intervention with hearing aids was available to all infants with a confirmed permanent HL; furthermore, family intervention was made available by training a multidisciplinary team that included speech therapists, psychologists and paediatricians. (5)
Feasibility	Screener interviews (1) Screener questionnaire (2) On-site observations of screening (3)	Performing NHS in the maternity hospital provides easy access to the infants because in Albania the majority of infants are born in the maternity hospitals. (1, 3) Nurses and midwifes who were already employed by the maternity hospital were able to perform screening in addition to other tasks. (1, 2, 3) Screening rooms were available at the maternity hospitals. (1, 3) It was challenging to find a quiet room for screening in the maternity hospital with the largest number of births (MG). (1, 3) When screening is continued, budget should be made available to acquire additional devices. (3) Fragility of the OAE probes and aABR electrode cables made them vulnerable for inexperienced handling. (1, 3)

Table 2. Implementation outcomes and screening quality measures that were used to evaluate barriers and facilitators relevant to the screening programme implemented in Albania, how each criterion was measured and our findings. (continued)

Implementation criteria	**Sources**	**Outcome**
Adoption	Screener interviews (1) Screener questionnaire (2) Parental interviews (3) On-site observations of screening (4) Database with infant screening outcome (5)	Maternity hospitals facilitated NHS by providing a screening room, logistic support and time for the screeners to participate in the programme. (1, 4) All screeners, who were trained during the project, performed screening. (1, 2, 4) Screeners wanted to improve their screening skills. (1, 2) Throughout the two years of implementation, referral rates decreased steadily reflecting increased screening skills. (5) Parents agreed with screening. (3) Database administration went reasonably well given that the programme had just started. (5)
Fidelity	Screener interviews (1) On-site observations of screening (2) Database with infant screening outcome (3) Follow-up phone calls with parents of infants lost to follow-up (4)	The screening protocol was followed. (1, 2, 3) However, in the MG maternity hospital, screeners repeated OAE screening several times during the first screening step to obtain a pass result. (1, 2) Some infants of mothers who experienced complications during the delivery were admitted to the NICU, these infants were not screened with the NICU protocol. (1, 3) Mistakes were made while filling out the study database forms: for example the day of birth or the day of screening. (3) Contact information was not registered for a number of infants, making it impossible for the screeners to contact these parents for follow-up. (3, 4) The largest maternity hospital did not have enough screeners or too few working hours for the number of births each day, and supervision was insufficiently strict. (2, 3, 4) Two screeners accounted for 46.5% of infants lost to follow-up in the MG maternity hospital. (3)
Screening quality measures	**Sources**	**Outcome**
Coverage	Database with infant screening outcome (1)	All infants born in 2018 and 2019 in one of the four maternity hospitals in Tirana, Pogradec and Kukës, were invited for screening. (1)

Table 2. Implementation outcomes and screening quality measures that were used to evaluate barriers and facilitators relevant to the screening programme implemented in Albania, how each criterion was measured and our findings. (continued)

Implementation criteria	Sources	Outcome
Attendance	Database with infant screening outcome (1) Post-hoc analysis of database (2) Follow-up phone calls with parents of infants lost to follow-up (3)	96.6% of all eligible infants were screened in the first screening step. (1) 94.2% of all eligible infants completed the entire screening protocol. (1) Loss to follow-up after the first and towards the second screening step was 33.5%, to the third screening step 41% and to diagnostic assessment 36%. (1) Variety was observed between screeners regarding loss to follow-up, for some screeners, loss to follow-up was exceptionally high (described in fidelity). (1) Parents indicated that they experienced difficulties to return to the maternity hospital because of long travel times, because they thought their infant could hear or because the infant had other health issues. (3) Infants of parents who had to travel longer (not necessarily in rural areas) were more likely to be lost to follow-up. (2)
Stepwise and final referral rate	Screener interviews (1) On-site observations of screening (2) Database with infant screening outcome (3)	After the first screening step, 1,546 (7%) infants were referred to the second screening step. (3) After the second screening step, 107 (10.2%) infants were referred to the third screening step. (3) After the third screening step, 26 (43.5%) infants were referred to diagnostic assessment. (3) From all three screening steps, 81 (0.35%) infants were referred to audiological diagnostic assessment; 13 after the first screening step, 42 after the second and 26 after the third. (3) Referral rates decreased steadily when experience was gained, in maternity hospitals where more infants were born referral rates decreased more rapidly in the first 6 months. (1, 2, 3)

Follow-up rates between screeners and maternity hospitals

Over the course of two years, 22 screeners were involved in the implementation study (Table 3). Each screener screened an average of 1574 infants in the MG maternity hospital (range: 624-2620), an average of 1110 in the KG maternity hospital (range: 523-1467), an average of 206 in Pogradec (range: 182-234) and an average of 412 in Kukës (range: 298-595). The average referral rates and LTFU varied across screeners as is displayed in Figure 3. The proportion of infants LTFU between the first and second screening step ranged from 0% to 93%. LTFU was highest for two screeners in the MG maternity hospital, one of whom resigned within the first year. These two screeners accounted for 46.5% of all infants LTFU from the MG maternity hospital.

Table 3. The number of infants registered for each screener and the outcome of screening for screening step 1: the number of infants who failed screening, were referred to screening step 2, and the number of infants lost to follow-up. For some infants, no screener was registered, they could not be included in the table. 'MG': Mbretëresha Geraldine, maternity hospital in Tirana; 'KG': Koço Gliozheni, maternity hospital in Tirana; 'LTFU': Lost to follow up, Infants who did not participate in screening due to various reasons.

		Total screened	Fail screening step 1	Refer to screening step 2	LTFU 2
MG	MG1	2337	128 (5.5%)	122	96 (78.7%)
	MG2	693	30 (4.3%)	30	19 (63.3%)
	MG3	2620	182 (6.9%)	181	35 (19.3%)
	MG4	886	19 (2.1%)	19	8 (42.1%)
	MG5	1400	63 (4.5%)	57	29 (50.9%)
	MG6	624	71 (11.4%)	71	66 (93.0%)
	MG7	2338	201 (8.6%)	201	63 (31.3%)
	MG8	1695	64 (3.8%)	60	32 (53.3%)
KG	KG1	523	42 (8.0%)	42	2 (4.8%)
	KG2	1467	187 (12.7%)	187	43 (23.0%)
	KG3	1357	31 (2.3%)	31	14 (45.2%)
	KG4	1167	90 (7.7%)	90	22 (24.4%)
	KG5	1301	85 (6.5%)	84	17 (20.2%)
	KG6	1031	16 (1.6%)	14	2 (14.3%)
	KG7	924	72 (7.8%)	71	9 (12.7%)
P	P1	234	61 (26.1%)	61	17 (27.9%)
	P2	194	41 (21.1%)	41	7 (17.1%)
	P3	182	46 (25.3%)	46	8 (17.4%)
	P4	215	42 (19.5%)	42	5 (11.9%)
K	K1	595	42 (7.1%)	40	10 (25.0%)
	K2	343	19 (5.5%)	19	0 (0%)
	K3	298	28 (9.4%)	26	6 (23.1%)

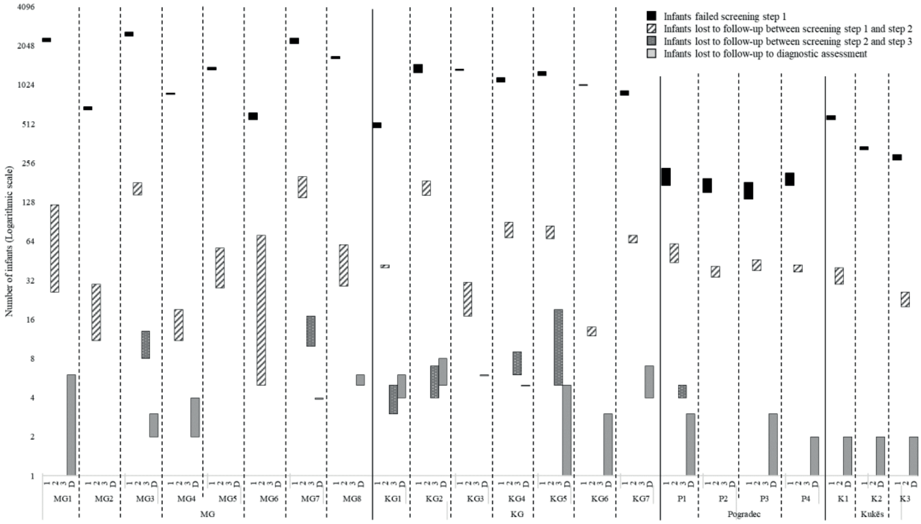


Figure 3. In this figure screening outcome for each of the 22 screeners in the four maternity hospitals is shown. Proportions are given on a logarithmic scale for the first, second and third screening step. The first bar (black) extends from the number of infants first screened by this nurse to the number of infants who passed the first screen. The second bar (striated) extends from the number of infants that should have been screened a second time to the number of infants that were screened a second time. The third bar (spotted) extends from the number of infants that should have been screened a third time to the number of infants that were screened a third time. The fourth bar (grey) represents the number of infants that should have been referred to diagnostic assessment and the number of infants who attended diagnostic assessment.

Average referral rates across maternity hospitals were not correlated to LTFU. Although the number of infants born in Pogradec and Kukës were similar, average referral rate was much higher in Pogradec (24.4% of infants screened were referred to screening step 2 and 1.4% of all infants were referred to diagnostics) than in Kukës (7.3% of infants were referred to screening step 2 and 0.6% of all infants were referred to diagnostics). Follow-up rates for screening step 2 were high in both Pogradec (81%) and Kukës (82%).

Post-hoc analysis of the database to identify reasons for LTFU

Out of the total of 22,051 infants screened, 1559 failed the first screening step, 13 were referred directly to diagnostics and 1546 were referred to the second screening step. Five hundred and nineteen infants did not follow up with the second screening step, and 1027 infants were screened of which 881 passed and 146 failed.

Results of the univariate analyses for LTFU between screening steps 1 and 2 showed that the following variables were significant predictors: region (urban/rural) and duration of travel from the family home to the hospital (Table 4). These predictors were incorporated into the hierarchical multivariate logistic regression model. Out of the 1546 infants eligible for inclusion in the multivariate analysis, predictor variable data were missing for 95 infants, these data

Table 4. Univariate and multivariate logistic regression analyses showing the individual and screener-level predictors of loss to follow-up between screening steps 1 and 2. Predictors significant at p<0.1 in the univariate analysis were included in the multivariate analysis. Odds ratios are presented with 95% confidence intervals. The reference category or continuous variable unit is indicated in brackets.

Variable	**Univariate analysis**		**Multivariate analysis**	
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Individual-level predictors				
Family economic status (ref: Very good)	--			
Good	0.81 (0.45-1.45)	0.47	--	
Moderate	0.77 (0.44-1.33)	0.35	--	
Bad/Very bad	0.94 (0.45-1.45)	0.87	--	
Mother's health status (ref: Very good)	--			
Good	1.0 (0.69-1.44)	1.0	--	
Moderate	1.35 (0.80-2.28)	0.27	--	
Bad/Very bad	0.97 (0.25-3.87)	0.97	--	
Mother's age (Years)	1.00 (0.98-1.03)	0.54	--	
Region of family home (ref: Rural)	--			
Urban	0.78 (0.60-1.02)	0.07	0.89 (0.68-1.17)	0.41
Travel time (Family home to screening institution, hours)	1.62 (1.41-1.87)	<0.001	1.61 (1.39-1.86)	<0.001
Infant sex (ref: Girl)	--			
Boy	0.96 (0.75-1.22)	0.73	--	
Screening year (ref: 2019)	--			
2018	1.11 (0.84-1.49)	0.45	--	
Duration of pregnancy (Weeks)	0.99 (0.93-1.06)	0.80	--	
Risk factors (ref: Yes)	--			
No	1.15 (0.74-1.79)	0.54	--	
Screen 1 result (ref: Unilateral fail)	--			
Bilateral fail	1.05 (0.82-1.35)	0.69	--	
Screener-level predictors				
Test method (ref: Both OAE, aABR)	--			
aABR only	0.33 (0.06-1.74)	0.19	--	
Infants screened (Total number)	1.00 (1.00-1.00)	0.14	--	
Referral rate (%)	0.96 (0.89-1.03)	0.27	--	

were imputed. In the multivariate model, region (urban/rural) was not significant (p=0.41). The analysis did not show a significant difference in LTFU between the first and second year of screening. The changes made after the first year of screening did not target specific screeners with high LTFU. The only significant predictor variable was the travel duration from the family home to the hospital (p<0.001). Infants of parents who had to travel longer were more likely to be LTFU (odds ratio 1.61, 95% CI 1.39-1.86). For every additional minute of travel the likelihood of LTFU for screening step 2 increased with 1%.

Table 4. Results of the multivariate logistic regression analysis for loss to follow-up from steps 1 and 2. The odds ratios for the two remaining significant variables in final the logistic regression and the explanation of the result are described.

Variable	p-value	Adjusted odds ratio (95% CI)	p-value	Explanation
Individual-level predictors				
Travel time from family home to screening institution (hours)	<0.001*	1.64 (1.41-1.90)	<0.001*	Infants are 64% more likely to be lost to follow-up for each hour increase in travel time.
Region (urban vs. rural)	0.362			
Screener-level predictors				
Screener performance (ref: high)	<0.001*			Infants screened by poor performing screeners were over 9x more likely to be lost to follow-up compared to infants screened by high performing screeners
moderate		2.27 (0.98-5.25)	0.05	
poor		9.19 (4.20-20.11)	<0.001*	

Although none of the screener-level predictor variables were significant, the variability between the screeners was significant (p=0.005), indicating that there is a significant effect of the screener on LTFU (p=0.005). To translate the variance into an odds ratio that can be compared to the odds ratios in Table 4, the median odds ratio for the screener was calculated. The median odds ratio was 3.12 which indicates that the likelihood of LTFU (median) was more than 200% higher for infants screened by screeners with higher overall LTFU compared to screeners with lower overall LTFU.

DISCUSSION

NHS has been implemented in four maternity hospitals in Albania in 2018 and 2019. Screening performed by nurses and midwifes before discharge from maternity hospitals, shortly after birth worked well. LTFU between screening steps and to diagnostic assessment was the main problem during the implementation of NHS in Albania. Coverage in the first screening step was high throughout the implementation study. Referral rates decreased steadily when screeners gained experience. In maternity hospitals with a low number of births, screeners needed more time to gain experience. In the largest maternity hospitals in Tirana screeners struggled with the high workload which resulted in errors, primarily reflected in a high LTFU rate.

High coverage was achieved by performing the first screening step before discharge from the maternity hospital. In this study, the programme lead was a well-respected professor in ENT and audiology who had been involved in previous attempts to implement NHS in Albania. She played an integral role in the facilitation of NHS, such as training, supporting the screeners and informing stakeholders on the existence and importance of screening, which in turn led to high participation. Facilitation is a widely used strategy to implement evidence-based programmes in a health care setting [36]. These efforts resulted in motivated screeners and well-informed parents who were willing to participate in the programme. Screeners indicated that parents who were better informed and who understood why their infant was screened, were more likely to accept screening and to return for follow-up screening after a fail outcome.

Referral rates after the first screening step were high initially but decreased as screeners gained more experience. In the first year of screening, it took more time for the screeners in Pogradec and Kukës to decrease referral rates after the first screening step. This can be related to the low number of births in both Pogradec and Kukës, causing the screeners to take more time to gain the same experience as the screeners in the maternity hospitals in Tirana. At the end of 2019, referral rates after the first screening step in Kukës were comparable to MG and KG in Tirana, but referral rates in Pogradec remained higher throughout the two years of implementation. This can be related to a number of factors including training and the fact that screeners in Pogradec were responsible for learning both OAE and aABR techniques which may have contributed to the continuously high referral rates across the two years. In Tirana, it was reported that some of the screeners started repeating the test multiple times within one screening step to obtain a pass result, which can partly explain the decrease in referral rate in that location. This issue was addressed, screeners could repeat the test a maximum of three times. Going forward, it will be incorporated in training as well as in the yearly refresher course.

LTFU was the main problem throughout the two years of screening and was related to the screener and travel time between the infants' home and the maternity hospital. Out of all infants who received a fail outcome in screening step 1, only 39% reached screen completion, which means that some infants with a HL were not diagnosed and did not receive intervention. Higher follow-up rates were achieved because of efforts made by the screeners throughout the study to emphasise the importance of completing the screening programme and by the fact that screeners reminded parents of their appointment a few days in advance. Despite these efforts the number of infants LTFU remained high. Follow-up rates varied greatly between screeners, in particular in the MG maternity hospital in Tirana. Results from the multivariate analysis showed that, even considering a wide range of infant and family variables including travel distance, the screener was the greatest predictor of an infant being LTFU.

Screeners in maternity hospitals with higher birth rates can gain more experience; however, due to increased pressure from the high workload LTFU can remain high. The workload in the MG maternity hospital was excessively high and an additional screener was hired in 2019. This finding emphasises the importance of sufficient screeners and good supervision. Some infants may not have been invited for follow-up screening. When a follow-up appointment was made but parents did not attend, parents may not have received sufficient information on the importance of screening, practical issues such as travel distances, time or other priorities prevented these parents from following up with screening. Another explanation may be that parents had more confidence in certain screeners or maternity hospitals than in others.

Incomplete data fields in the database may have also contributed to higher LTFU (in this case, loss to documentation). In the future, LTFU could be further reduced by monitoring the screeners more closely and by highlighting the importance of parental information and data entry during training.

Travel time between the hometown and the maternity hospital was a significant predictor for infants LTFU between the first and second screening step even when the variation in screener performance was taken into account. When screening is continued and extended to nationwide reach, LTFU can be further reduced by combining screening with other health care appointments, planning screening steps closer together, reducing the number of screening steps or performing two screening steps during the same appointment. However, this would reduce the specificity of the second test. This was also reflected in the predictions of the cost-effectiveness model that was developed within the EUSCREEN study [28]. This model calculated an OAE-aABR protocol for WB in which both screening steps are performed before discharge from the maternity hospital to be the more cost-effective than five other protocols. When screening is implemented nationwide, more locations will be available closer to the family's home for parents to go to, which can reduce LTFU.

A total of 22 of the 22,051 infants were diagnosed with a HL of 40 dB or greater of which 6 had a unilateral HI. Although more infants with a HL were expected to be found based on the literature [12, 13, 37, 38] this may be explained by the high proportion of infants lost to follow-up between screening steps and to diagnostic assessment. Some of the information on the results of diagnostic assessment and early intervention with hearing aids or through family support was missing. Because different institutions and professionals were involved in follow-up after screening, it was difficult to gather data from all infants who were referred after screening. This may have led to infants being lost to documentation. This can be resolved by using a database that can track infants through both screening, diagnostic assessment and intervention.

The results of this study rely to a great extent on data that were collected in the study database. Screening results of some infants may not have been registered in the database. For other infants, inconsistencies were found in the database that may have influenced the screening outcome that was reported in this article. A reliable database is essential when screening is continued in Albania. This database should be easy to use by the screeners, the professionals involved in diagnostic assessment and the team organising the screening programme. Clear instructions on how to use the database should be available so that all infants can be tracked and followed up. A good database can also assist in monitoring outcome for each screener. Screeners that have high referral rates or low follow-up rates can be monitored and asked to follow additional training courses.

The implementation of screening as part of the EUSCREEN study ended on December 31st, 2019. Efforts were made to improve screening outcomes throughout the two years of implementation. Progress was made, however some issues remained at the end of the study. It takes time for a screening programme to run effectively especially when setting up a new programme. Plans were made to gradually extend NHS throughout Albania. However, because of the COVID-19 pandemic, money that was allocated for the extension of NHS had to be used elsewhere. The plan to extend NHS nationwide will be continued when priorities can shift from controlling the global pandemic to other healthcare interventions.

When screening will be continued and extended nationwide, screening will be performed in all 37 maternity hospitals in Albania to obtain high coverage and to provide a screening location closer to the family's home to reduce travel distance. It could be beneficial to implement a single-device protocol in maternity hospitals with a low number of births to improve screener experience and achieve low referral rates. This could be further improved by hiring a dedicated screener for each or several maternity hospitals. The results of this study emphasise the importance of a good monitoring system to keep track of all eligible infants and their screening outcomes, to monitor the screening programme, to assure quality of the screening, to document the results and to adjust protocols based on context to improve the outcomes of the screening programme.

Acknowledgments

We thank the parents and children, nurses, administrators, the diagnostic team of the TUHC, the team in the CCR, the local organising team and all those participating.

REFERENCES

1. Bussé, A.M.L., et al., Assessment of hearing screening programmes in 47 countries or regions I: Provision of newborn hearing screening. Submitted for publication, 2020.
2. Mackey, A.R., et al., Assessment of hearing screening programmes across 47 countries or regions II: coverage, referral, follow-up and detection rates from newborn hearing screening. International Journal of Audiology, 2021: p. 1-10.
3. Watkin, P.M. and M. Baldwin, Identifying deafness in early childhood: Requirements after the newborn hearing screen. Arch Dis Child, 2011. 96(1): p. 62-66.
4. Yoshinaga-Itano, C. and M.L. Apuzzo, The development of deaf and hard of hearing children identified early through the high-risk registry. Am Ann Deaf, 1998. 143(5): p. 416-24.
5. Yoshinaga-Itano, C. and M.L. Apuzzo, Identification of hearing loss after age 18 months is not early enough. Am Ann Deaf, 1998. 143(5): p. 380-7.
6. Albanian Institute of Statistics (INSTAT). Population of Albania. 2020; Available from: http://www.instat.gov.al/media/6850/population-on-1-january-2020___.pdf.
7. Bank, T.W. Rural population (% of total population). 2018 [cited 2020 15-07-2020]; Available from: https://data.worldbank.org/indicator/SP.RUR.TOTL.ZS?locations=AL.
8. INSTAT. Demography and Social Indicators. 2020 [cited 2020 16-06-2020]; Available from: http://www.instat.gov.al/en/themes/demography-and-social-indicators/.
9. Mason, J.A. and K.R. Herrmann, Universal infant hearing screening by automated auditory brainstem response measurement. Pediatrics, 1998. 101(2): p. 221-228.
10. Maxon, A.B., et al., Using transient evoked otoacoustic emissions for neonatal hearing screening. Br J Audiol, 1993. 27(2): p. 149-53.
11. Mehl, A.L. and V. Thomson, Newborn hearing screening: the great omission. Pediatrics, 1998. 101(1): p. E4.
12. Hatzopoulos, S., B. Qirjazi, and A. Martini, Neonatal hearing screening in Albania: results from an ongoing universal screening program. Int J Audiol, 2007. 46(4): p. 176-82.
13. Beqiri, E. and D. Nika, Universal neonatal hearing screening in Albania, 2009-2012. Mater Sociomed, 2015. 27(1): p. 13-4.
14. Oecd and U. European, Health at a Glance: Europe 2018. 2018.
15. Berninger, E. and B. Westling, Outcome of a universal newborn hearing-screening programme based on multiple transient-evoked otoacoustic emissions and clinical brainstem response audiometry. Acta Otolaryngol, 2011. 131(7): p. 728-39.
16. Erenberg, A., et al., Newborn and infant hearing loss: detection and intervention. American Academy of Pediatrics. Task Force on Newborn and Infant Hearing, 1998- 1999. Pediatrics, 1999. 103(2): p. 527-30.
17. Olusanya, B.O., et al., Progress towards early detection services for infants with hearing loss in developing countries. BMC Health Services Research, 2007. 7(1): p. 14.
18. Chen, X., et al., Assessment of Universal Newborn Hearing Screening and Intervention in Shanghai, China. Int J Technol Assess Health Care, 2017. 33(2): p. 206-214.
19. Abdullah, A., et al., Newborn hearing screening: experience in a Malaysian hospital. Singapore Med J, 2006. 47(1): p. 60-4.
20. Korres, S.G., et al., Making universal newborn hearing screening a success. Int J Pediatr Otorhinolaryngol, 2006. 70(2): p. 241-6.
21. Olusanya, B.O., Follow-up default in a hospital-based universal newborn hearing screening programme in a low-income country. Child: Care, Health and Development, 2009. 35(2): p. 190-198.
22. Thomson, V. and C. Yoshinaga-Itano, The Role of Audiologists in Assuring Follow-Up

to Outpatient Screening in Early Hearing Detection and Intervention Systems. Am J Audiol, 2018. 27(3): p. 283-293.

23. Mehl, A.L. and V. Thomson, The Colorado newborn hearing screening project, 1992-1999: on the threshold of effective population-based universal newborn hearing screening. Pediatrics, 2002. 109(1): p. E7.
24. Wood, S.A., G.J. Sutton, and A.C. Davis, Performance and characteristics of the Newborn Hearing Screening Programme in England: The first seven years. Int J Audiol, 2015. 54(6): p. 353-8.
25. Hunter, L.L., et al., Influence of the WIC Program on Loss to Follow-up for Newborn Hearing Screening. Pediatrics, 2016. 138(1): p. e20154301.
26. De Ceulaer, G., et al., Neonatal hearing screening with transient evoked otoacoustic emissions: a learning curve. Audiology, 1999. 38(6): p. 296-302.
27. van der Ploeg, C.P., et al., Newborn hearing screening in youth health care in the Netherlands: National results of implementation and follow-up. Int J Audiol, 2012. 51(8): p. 584-90.
28. Verkleij, M.L., et al., Cost-Effectiveness of Neonatal Hearing Screening Programs: A Micro-Simulation Modeling Analysis. Ear Hear, 2020.
29. Bussé, A.M., et al., Implementation of a neonatal hearing screening programme in three provinces in Albania. Int J Pediatr Otorhinolaryngol, 2020. 134: p. 110039.
30. Republic of Albania Institute of statistics, Regional statistical yearbook, INSTAT, Editor. 2018: www.instat.gov.al.
31. Bali, D., et al., Maternal and Child Health Care Services in Albania. J Pediatr, 2016. 177S: p. S11-S20.
32. Qirjazi, B., et al., Mothers' perceptions of universal newborn hearing screening in transitional Albania. PLoS One, 2020. 15(8): p. e0237815.
33. Proctor, E., et al., Outcomes for implementation research: conceptual distinctions, measurement challenges, and research agenda. Adm Policy Ment Health, 2011. 38(2): p. 65-76.
34. Peters, D.H., et al., Implementation research: what it is and how to do it. Bmj, 2013. 347: p. f6753.
35. Merlo, J., et al., A brief conceptual tutorial of multilevel analysis in social epidemiology: using measures of clustering in multilevel logistic regression to investigate contextual phenomena. J Epidemiol Community Health, 2006. 60(4): p. 290-7.
36. Dogherty, E.J., M.B. Harrison, and I.D. Graham, Facilitation as a role and process in achieving evidence-based practice in nursing: a focused review of concept and meaning. Worldviews Evid Based Nurs, 2010. 7(2): p. 76-89.
37. Neumann, K., et al., A Survey on the Global Status of Newborn and Infant Hearing Screening. 2020. 5: p. 63-84.
38. Bussé, A.M.L., et al., Prevalence of permanent neonatal hearing impairment: systematic review and Bayesian meta-analysis. International Journal of Audiology, 2020. 59(6): p. 475-485.

Chapter 9

GENERAL DISCUSSION

Several factors need to be considered when organising a hearing screening programme that affect the outcome of screening. These factors include the target condition (degree of the hearing impairment (HI), type of HI and unilateral or bilateral HI), the prevalence of the target condition, the population that is eligible for screening, screening location, age at screening, screening devices, screening protocols, screening professionals, diagnostic assessment, intervention after screening, quality measures, benchmarks, data collection and quality monitoring. In this study, first the literature was reviewed to determine the prevalence of neonatal permanent hearing impairment. The reported prevalence rate of permanent unilateral and bilateral hearing impairment worse than 40 dB in neonates varied from 1 to 6 per 1000, with an overall prevalence rate of 2.21 per 1000 (credible interval: [1.71, 2.8]). Next, existing hearing screening programmes were inventoried in a large survey with the intention to compare the cost-effectiveness of hearing screening programmes across Europe. Local hearing screening experts provided information on current hearing screening programmes through an extensive questionnaire that was developed within the EUSCREEN study. It was completed by representatives from 40 European countries plus representatives from Russia, Malawi, Rwanda, India and China.

In newborn hearing screening (NHS), the definition of the target condition of the screening programme plays a crucial role in the way screening is organised. Firstly, the target condition can be permanent or transient HI and sensorineural or conductive HI. All NHS programmes include permanent sensorineural and conductive HI in the newborn period in the target condition but transient conductive HI is not included. However, an NHS programme will detect all types of HI, both transient and permanent. Conductive HI during the first days after birth is often caused by residual fluid in the middle ear. Moreover, otitis media with effusion can occur a few weeks after birth. These conditions of the middle ear can resolve over time. Secondly, the degree of HI that is included in the target condition should be determined. In our survey, participating countries with an NHS programme reported a unilateral and bilateral permanent HI of between 20 and 40 dB as target condition. Most of these reported a HI of between 30 and 40 dB as target condition. Additionally, the choice of a threshold between 30 and 40 dB depends on the consequences related to the degrees of HI and the follow-up and intervention that is available in a country. A HI of at least 30 or 40 dB particularly affects speech and language development. In our survey, hearing aids were fitted in children when their HI exceeded thresholds that varied between 25 and 40 dB. Finally, the target condition may be defined as bilateral or as both unilateral and bilateral HI. Unilateral HI affects speech and language development less than a bilateral HI but it may evolve into a bilateral HI. In our survey, most screening programmes have both unilateral and bilateral HI as target condition. Nevertheless, in almost all countries, both ears are routinely screened.

An NHS programme can be practiced in a (maternity) hospital, in a region or nationwide. Our survey revealed that 31 of the 42 programmes had a nationwide programme of which 11 reported to organise screening regionally. The remaining 11 programmes provided screening that was project-based, performed in private hospitals or only provided in some hospitals. Universal NHS implies that all infants of the defined population are eligible for screening, while selective NHS targets only infants with an increased risk for HI (high-risk infants), based on a number of risk factors. About 50% of infants with a HI do not have any known risk factors [1-3]. In our survey, risk factors for HI included having been admitted to a neonatal intensive care unit (NICU) in 32 of the 42 NHS programmes but the minimal length of NICU stay varied across countries. Other known risk factors for HI reported in our survey included: a family history of HI, pre- or postnatal infections, craniofacial anomalies, syndromes associated with HI, adverse perinatal conditions and neurodegenerative disorders [4]. When NHS is implemented universally, one single protocol can be used to screen all infants, or separate protocols can be used for infants without known risk factors (low-risk) and infants with an increased risk for HI (high-risk) in a dual-programme. Within our survey, a dual protocol was reported to be used in 29 programmes.

When the majority of deliveries take place in a maternity hospital, high coverage can be obtained by performing the first step of screening before discharge of mother and child. The average length of stay in the maternity hospital in Europe is 3.1 days after giving birth (range: 1.4-4.9 days) [5]. Therefore, screening will usually be performed within 72 hours after birth. In our survey, 39 of the 42 NHS programmes performed the first screening step in the maternity hospital before discharge. Screening can also be performed during post-natal healthcare appointments (e.g., newborn blood-spot screening) or vaccinations if attendance to these appointments or vaccinations is high. Notably, the two countries in Europe that reported the lowest percentage of infants born in the maternity hospital – the Netherlands and Belgium (Flanders) – performed the first screening step outside the maternity hospital. Combination of the first screening step of NHS with postnatal healthcare visits resulted in high attendance at the first screen in two NHS programmes in Nigeria and South Africa [6, 7]. While screening in the maternity hospital ensures high attendance for the first screen, screening close to birth has its drawbacks. Amniotic fluid, that is present in the middle ear after birth, reduces the number of infants that pass screening [8]. Referral rates for the first step of screening as reported in our survey were higher when screening took place within 24 hours after birth (6-22%) than when screening took place at least 24 hours after birth (2-15%). The difference was even larger when screening took place at least 72 hours after birth (4%). This result was confirmed by a study that reported the lowest pass rate when screening within the first 24 hours after birth and the highest pass rate when screening was performed at five days after birth [8].

NHS can be performed with otoacoustic emission (OAE) and/or automated auditory brain stem response (aABR) devices. An OAE screen measures the reaction of the outer hair cells in the cochlea to the tone or click that is produced by the screening device. An aABR screen measures changes in brain wave activity in the auditory brainstem as a reaction to the tone or click that is produced by the screening device. Screening with aABR has the advantage that it is less affected by middle ear effusion and has a higher specificity [9]. Additionally, in contrast to OAE, screening with aABR can detect retrocochlear disorders, which are more prevalent in high-risk infants, making it the recommended type of screening for infants with an increased risk for HI [10]. On the other hand, OAE devices are less expensive than aABR devices [11, 12], OAE screening takes less time to perform and requires less training of the screener. Therefore, OAE is usually the preferred method for the first screening step in the general population.

Our study showed that almost all programmes screen low-risk infants with OAE in the first screening step. Including aABR in the screening protocol improves the specificity [9, 13, 14]. Accordingly, in our survey referral rates to diagnostic assessment were lower when programmes included aABR and when programmes used more screening steps. Referral rates to diagnostic assessment were 2.1% for programmes with one or two steps using only OAE, 1.7% for programmes with two steps including aABR, and 0.8% for programmes with three or four steps including aABR. Because of the higher sensitivity and specificity of aABR, it may be cost-effective to use only aABR even in countries with less available resources [15]. In the implementation study in Albania, different protocols were implemented in the maternity hospitals in Kukës and Pogradec. Both are located in a mountainous region, and Kukës is one of the most rural areas of Albania. An aABR-aABR protocol was implemented in the maternity hospital in Kukës and an OAE-OAE-aABR screening protocol was used to screen infants born in Pogradec. Screeners in Kukës using aABR-aABR obtained lower referral rates than screeners in Pogradec using OAE-OAE-aABR. Both maternity hospitals had low birth numbers because of their rural nature.

A screening protocol consists of the type of test(s) used, the number of screening steps and the timing of these screening steps. Our survey showed that the choices made with regards to the screening protocol – type of screening programme, numbers of steps, devices used – were related to socio-economic circumstances: health expenditure and Human Development Index (HDI). Health expenditure is the amount of money spent by a country on healthcare [16]. HDI is a measure that averages the outcome of four key dimensions of human development: life expectancy, expected years of schooling, mean years of schooling and gross national income [17]. In general, participating countries in the EUSCREEN study, with lower health expenditure and HDI were more likely to not perform NHS or to have a selective screening programme. Countries with lower health expenditure and HDI that had an NHS programme in place used one single protocol to screen all infants, used two screening steps for low-risk infants and screened with OAE only more often than countries with high health expenditure and HDI. Countries with high health expenditure and HDI more often used different protocols for low- and high-risk, used three screening steps for low-risk infants and included aABR in the protocol, in at least one screening step for low-risk infants and in the first step for high-risk infants.

High specificity can be achieved by increasing the number of screening steps [14, 18-20]. However, each additional step also reduces the programme sensitivity, especially when the proportion of infants lost to follow-up is high. Different screening steps can be combined in one visit, or can be performed during multiple contact moments. Combining screening steps in one visit has advantages and disadvantages. On the one hand, parents do not have to return to the maternity hospital which increases the follow-up at the next step. When travel times are long and travel costs are high, following up with subsequent screening steps may be particularly difficult. On the other hand, specificity of the second step may be low when the reason for a fail outcome such as fluid in the middle ear persists in the subsequent screening step. This affects the next screening step, whereas it may resolve when more time is allowed between screening steps.

When screening is performed in the maternity hospital, nurses and midwifes, who are already working in the maternity hospital and have experience with newborns, form a very good choice to perform the screening. Other screening programmes will choose to train specialised screeners to perform only NHS or to train professionals who can screen the infants in combination with other healthcare appointments or vaccinations. Initial costs may be lower when professionals with a medical background are hired because they require less initial training; however, when they perform screening in addition to other work, experience with screening is accumulated less rapidly which can lead to higher referral rates as compared to dedicated screeners [11]. Screeners should be trained, have gained experience with screening and follow predetermined standards of care. A good monitoring system that tracks all screening outcomes assists in evaluating screening performance and reveals irregularities in a screeners' performance that may warrant additional training. Furthermore, screeners should be able to explain the purpose of NHS to parents and make clear how the infant benefits from screening, from early detection of a HI and from treatment. They should be able to reassure anxious parents after a 'fail' outcome while stressing the importance of attending subsequent screening steps [21, 22].

An essential factor to consider within an NHS programme is access to diagnostic assessment and early intervention for all infants who are referred after screening. Screening is only the first step towards helping children with a HI. To provide screening without appropriate diagnostic assessment and intervention is considered unethical [23]. In an ideal situation, a follow-up pathway is in place before NHS is implemented, but in practice, the follow-up pathway is often developed in parallel with the NHS programme.

The EUSCREEN study was designed to calculate and compare the cost-effectiveness of the very diverse hearing screening programmes in Europe. This diversity between hearing screening programmes is caused only in part by the different circumstances in these countries like differences in healthcare infrastructure, availability of screening professionals, etcetera. In our survey we found that even in countries with well-developed screening programmes, the data essential for comparative cost-effectiveness analysis are insufficiently collected, even the quality measures as formulated by the Joint Committee on Infant Hearing [24]. Our survey showed that not all countries or regions collect quality measures, monitor screening, or perform research on the cost-effectiveness of the screening programmes. Many even well-established screening programmes could not report on quality measures of their screening programme. Our survey showed that these data are often not collected nationally or that they are not accessible, although, in some cases, the experts filling out the questionnaire may not have been able to find the right source. Data on quality measures can help to ensure the effective use of resources when setting up NHS or to detect where current problems lie when improving existing hearing screening programmes. When all hearing screening programmes collect data, monitor the screening and control the quality of the programme, it will become much easier to share data and compare the cost-effectiveness across borders. This shared data can be used to compare cost-effectiveness within a country or between countries and, subsequently, the diversity amongst screening programmes will decrease.

Experiences with implementation of NHS in Albania

In preparation of implementation of NHS in Albania, a cost-effectiveness model was developed within the EUSCREEN study in which demography, natural history of HI, screening characteristics, treatment, costs and quality of life were used to estimate the cost-effectiveness of a screening programme. This model was used to compare the cost-effectiveness of six different screening protocols for well infants in Albania. The protocol that was considered most cost-effective in the Albanian context was an OAE-aABR protocol in which both steps were to be performed before discharge from the maternity hospital. However, the model was not sufficiently finished when preparations for the implementation of NHS in Albania started. Therefore, the decision on what screening protocol to implement in Albania was mostly based on sound clinical judgement, conclusions made after the previous attempts, experience of implementation of NHS in other countries, local circumstances, and expected costs for both the programme organisation and parents to implement NHS in Albania.

In Albania, screening was implemented in both urban and rural maternity hospitals. Screening outcome was monitored through an online screening database that was filled out by the screeners. Out of 22,818 infants born, 22,051 (96.7%) underwent the first screening step. Referral rates were 7.1% for the first step, 14.1% for the second step, 43.5% for the third step and 0.35% of all infants that participated in the first screening step were referred to diagnostic assessment. Follow-up rates were 66.5% for the second step, 59% for the third step and 66.7% to diagnostic assessment. A total of 21,493 (94.2%) infants completed the entire screening protocol of which 78 infants were referred for a diagnostic assessment, 52 attended and 22 (0.1%) were diagnosed with a HI of 40 dB or worse, of which 6 had a unilateral HI. While it took more time for screeners in rural areas to gain experience in screening because of the low number of births in the rural maternity hospitals, coverage rates, referral rates and follow up rates were similar to urban maternity hospitals once experience was gained. In the large maternity hospitals in Tirana, where the number of births was high, efficient organisation of screening proved to be essential. In all four maternity hospitals combined, a large number of infants (34%) did not attend follow-up screening after having received a 'fail' outcome in the first step. Consequently, a high number of the infants who failed the first screening step did not complete the entire screening protocol (61%). Loss to follow-up between step 1 and step

2 was correlated to the screener and travel time to the maternity hospital. Both the successes and continuing challenges from all four locations were evaluated to look into the possibility to extend NHS to nationwide reach.

The following criteria for implementation of NHS were evaluated in Albania in 2018-2019: acceptability, adoption, appropriateness, coverage and follow-up, feasibility, and fidelity. These criteria were evaluated based on on-site observations in the maternity hospitals, interviews with screeners and parents, a questionnaire in which screeners were asked about their opinions on the hearing screening programme in more detail and a socio-economic questionnaire distributed amongst parents. Screening outcome data as well as reasons for not following up with screening were collected through a database. Both screeners and parents considered it important that all infants in Albania had access to NHS. All screeners who were trained participated in the NHS programme. Screeners were eager to improve their screening skills, referral rates, one of the collected quality measures, decreased steadily. All infants who were screened positively were offered diagnostic audiological assessment and therapeutic intervention. Screening performed by nurses and midwifes in maternity hospitals before discharge of mother and child led to high coverage. However, a large number of infants did not attend follow-up screening. Screeners needed more time to gain experience when the number of births were low and screeners struggled with the high workload when the number of births were high. The number of infants lost to follow-up varied per screener. The largest clinic had the largest loss to follow-up and had nurses with high loss to follow-up. In this clinic with the highest number of births the workload was high and supervision, hence, had difficulty coping from time to time. This underscores the need of sufficient screeners and good supervision and quality control.

Childhood hearing screening after the newborn period

Childhood hearing screening after the newborn period (CHS) is not commonly provided across countries participating in the survey. Universal CHS is performed mainly in high-income countries using pure tone audiometry screening (PTS). For CHS, considerations similar to NHS can be made for factors that are important for the organisation of CHS. These factors include the target condition, the population, location, age at screening, screening test, screening professionals, quality measures and monitoring.

In addition to a unilateral or bilateral permanent HI of a certain degree, the target condition for CHS programmes can also include (transient) conductive HI such as HI caused by otitis media. Screening can either include all children or exclude children with a known HI or ear problem. To reach high attendance, CHS can be performed at a location with an implicit high attendance such as (pre)school or in combination with other child healthcare exams or vaccination. Screening can be performed by PTS, speech (in noise) tests, whisper test, tympanometry, OAE, a combination of different tests or by questionnaires filled out by the parent or teacher of the child. The choice of test and screening protocol used (e.g., frequencies tested and passing criteria) depend on the age and developmental level of the target population. Our survey showed that in Europe CHS was offered to children between the ages of 3 and 7. CHS programmes mainly used PTS. The threshold used for passing PTS ranged from 20 to 40 dB and depended to some degree on the age of the child. CHS programmes used a median passing criterion of 30 dB for children aged 3 to 4 years and 25 dB for children aged 4 and older. The choice of threshold may be based on the inability of younger children to reliably respond to PTS and the high prevalence of otitis media at that age [25].

In our survey, only a few countries could provide data on quality measures such as coverage rate, referral rate and follow-up rate. When quality measures are not collected, the effectiveness of CHS cannot be calculated or compared across countries. CHS is able to detect children with a HI that were missed during NHS or who developed a HI after NHS was performed. These children may remain undetected without additional screening or risk factor surveillance programme [26]. CHS may be cost-effective in countries where no NHS is available or where otitis media is particularly prevalent. However, no data was available for such countries. Until such data becomes available, the cost-effectiveness of CHS cannot be reliably calculated. Interestingly, across all countries and regions participating in our survey, none indicated that both NHS and CHS are organised through the same institution. In many countries, NHS runs as an independent programme or is integrated with maternal and newborn healthcare while CHS is often incorporated into childhood health services or the education system. One system to monitor screening outcome throughout childhood can assist healthcare personnel in helping and following up children with a HI.

LIST OF ABBREVIATIONS:

HI	Hearing impairment
NHS	Newborn hearing screening
CHS	Childhood hearing screening
HDI	Human Development Index
NICU	Neonatal intensive care unit
OAE	Otoacoustic emission
aABR	Automated auditory brain stem response
PTS	Pure-tone audiometry screening

REFERENCES

1. Davis, A. and S. Wood, The epidemiology of childhood hearing impairment: Factors relevant to planning of services. British Journal of Audiology, 1992. 26(2): p. 77-90.
2. Davis, A., et al., A critical review of the role of neonatal hearing screening in the detection of congenital hearing impairment. Health Technol Assess, 1997. 1(10): p. i-iv, 1-176.
3. Mehl, A.L. and V. Thomson, Newborn hearing screening: the great omission. Pediatrics, 1998. 101(1): p. E4.
4. Joint Committee on Infant Hearing and American Academy of Pediatrics, Year 2007 position statement: Principles and guidelines for early hearing detection and intervention programs. Pediatrics, 2007. 120(4): p. 898-921.
5. OECD. Health at a Glance 2019: OECD Indicators. Average length of stay in hospitals. 2019 9-November-2020 [cited 2020 October 20]; Available from: https://doi.org/10.1787/888934017804.
6. Olusanya, B.O., O.M. Ebuehi, and A.O. Somefun, Universal infant hearing screening programme in a community with predominant non-hospital births: a three-year experience. Journal of Epidemiology & Community Health, 2009. 63(6): p. 481-487.
7. Khoza-Shangase, K. and S. Harbinson, Evaluation of universal newborn hearing screening in South African primary care. African journal of primary health care & family medicine, 2015. 7(1): p. 769.
8. Berninger, E. and B. Westling, Outcome of a universal newborn hearing-screening programme based on multiple transient-evoked otoacoustic emissions and clinical brainstem response audiometry. Acta Otolaryngol, 2011. 131(7): p. 728-39.
9. Ngui, L.X., et al., Comparison of distortion product otoacoustic emission (DPOAE) and automated auditory brainstem response (AABR) for neonatal hearing screening in a hospital with high delivery rate. Int J Pediatr Otorhinolaryngol, 2019. 120: p. 184-188.
10. Joint Committee on Infant Hearing, Year 2007 position statement: Principles and guidelines for early hearing detection and intervention programs. Pediatrics, 2007. 120(4): p. 898-921.
11. Vohr, B.R., et al., Comparison of costs and referral rates of 3 universal newborn hearing screening protocols. J Pediatr, 2001. 139(2): p. 238-44.
12. Boshuizen, H.C., et al., Costs of different strategies for neonatal hearing screening: a modelling approach. Archives of Disease in Childhood - Fetal and Neonatal Edition, 2001. 85(3): p. F177-F181.
13. Benito-Orejas, J.I., et al., Comparison of two-step transient evoked otoacoustic emissions (TEOAE) and automated auditory brainstem response (AABR) for universal newborn hearing screening programs. Int J Pediatr Otorhinolaryngol, 2008. 72(8): p. 1193-201.
14. Gravel, J., et al., New York State universal newborn hearing screening demonstration project: effects of screening protocol on inpatient outcome measures. Ear & Hearing, 2000. 21(2): p. 131-140.
15. van Dyk, M., W. Swanepoel de, and J.W. Hall, 3rd, Outcomes with OAE and AABR screening in the first 48 h--Implications for newborn hearing screening in developing countries. Int J Pediatr Otorhinolaryngol, 2015. 79(7): p. 1034-40.
16. OECD. Health spending. 2019 [cited 2020 19-08]; Available from: https://data.oecd.org/healthres/health-spending.htm#:~:text=Health%20spending%20measures%20the%20final,services%20as%20well%20as%20health.
17. UNITED NATIONS DEVELOPMENT PROGRAMME. Human Development Reports. Human Development Index (HDI). 2020 [cited 2020 19-08-2020]; Available from: http://hdr.undp.org/en/content/human-development-index-hdi.
18. Caluraud, S., et al., Newborn hearing screening: analysis and outcomes after 100,000

births in Upper-Normandy French region. Int J Pediatr Otorhinolaryngol, 2015. 79(6): p. 829-33.

19. Clemens, C.J. and S.A. Davis, Minimizing false-positives in universal newborn hearing screening: a simple solution. Pediatrics, 2001. 107(3): p. E29.
20. Berninger, E. and B. Westling, Outcome of a universal newborn hearing-screening programme based on multiple transient-evoked otoacoustic emissions and clinical brainstem response audiometry. Acta Oto-Laryngologica, 2011. 131(7): p. 728-739.
21. Weichbold, V., K. Welzl-Mueller, and E. Mussbacher, The impact of information on maternal attitudes towards universal neonatal hearing screening. Br J Audiol, 2001. 35(1): p. 59-66.
22. Lam, M.Y.Y., et al., Maternal knowledge and attitudes to universal newborn hearing screening: Reviewing an established program. Int J Pediatr Otorhinolaryngol, 2018. 105: p. 146-153.
23. Wilson, J.M.G., G. Jungner, and O. World Health, Principles and practice of screening for disease / J. M. G. Wilson, G. Jungner. 1968, World Health Organization: Geneva.
24. Joint Committee on Infant Hearing, Year 2019 Position Statement: Principles and Guidelines for Early Hearing Detection and Intervention Programs. The Journal of Early Hearing Detection and Intervention, 2019. 4(2): p. 1-44.
25. Browning, G.G., Influence of Age, Type of Audiometry and Child's Concentration on Hearing Thresholds. British Journal of Audiology, 2000. 34(4): p. 231-240.
26. Lü, J., et al., Screening for delayed-onset hearing loss in preschool children who previously passed the newborn hearing screening. International Journal of Pediatric Otorhinolaryngology, 2011. 75(8): p. 1045-1049.

Chapter 10

ENGLISH SUMMARY

Hearing impairment is a common health problem during childhood, affecting 2 out of every 1000 newborns. When a hearing impairment remains untreated during childhood, it may affect speech, language and general development. Screening for hearing impairment and subsequent intervention may prevent these negative outcomes. Hearing screening during childhood can be performed in the newborn period or at (pre)school age. Newborn hearing screening (NHS) usually takes place within the first days after birth and is performed by either an otoacoustic emission (OAE) screen or an automated auditory brainstem response (aABR) screen. The protocol can include multiple repeat screening steps after a fail outcome before infants are referred to full audiological diagnostic assessment. An infant that fails screening is referred to diagnostic assessment to confirm if a permanent hearing impairment is present and to determine its type and degree. Infants with a permanent hearing impairment are referred for subsequent intervention. This intervention includes amplification through hearing aids, cochlear implants or bone conductive hearing aids. Additionally, speech language therapy and family intervention can be provided. In addition to NHS, some countries also perform childhood hearing screening after the newborn period (CHS). This type of screening usually takes place between 3 and 7 years using pure tone audiometry screening. This thesis inventories and evaluates strategies for hearing screening programmes that are performed during childhood.

The EUSCREEN study compares the cost-effectiveness of vision and hearing screening programmes in countries in Europe and beyond. Large variation exists in vision and hearing screening programs across Europe with regards to age and frequency of testing, tests used, uptake, screening professionals, referral pathway and funding. A model was developed to compare the cost-effectiveness of screening programmes across countries, taking local circumstances into account.

For comparison of the cost-effectiveness of NHS programmes, insight in the natural history and prevalence of hearing impairment is essential. In a systematic literature review, 35 out of 7520 studies met the inclusion criteria and were analysed, 25 of which were from high-income countries. Twenty-seven reported on the general infant population, three reported only on healthy infants and five reported only on infants admitted to the neonatal intensive care unit (NICU). The prevalence rate of permanent unilateral and bilateral hearing impairment worse than 40 dB in neonates varied from 1 to 6 per 1000, with an overall prevalence rate of 2.21 per 1000 (credible interval: [1.71, 2.8]). Approximately one-third was unilateral permanent hearing impairment. Reported prevalence among infants admitted to the NICU averaged 15.77 per 1000. Higher prevalence rates were reported by studies from countries with lower gross national income and from countries in Asia compared to countries in Europe, but this did not reach statistical significance. Reported percentage of infants lost to follow-up was higher in countries with lower gross national income but this did not reach statistical significance (p=0.07). (**Chapter 2**)

A large survey was carried out by developing an extensive questionnaire that was distributed amongst hearing screening experts in all countries in Europe. The information that was collected was used to inventory the provision and performance of existing screening programmes. This questionnaire covered nine domains: demography and epidemiology, administration and general background, existing screening programmes, coverage and attendance, tests and devices, follow up and diagnostic assessment, treatment options, costs and benefits and adverse effects. The information gathered from the questionnaire was supplemented with demographic data to better understand the variability and the rationale for the diversity across programmes. The questionnaire was completed by representatives from 40 European countries plus Russia, Malawi, Rwanda, India and China.

Nationwide universal NHS was offered in 26 of 30 high-income countries and in three out of 15 low- and middle-income countries. Out of a total of 42 NHS programmes, 39 performed the first screening step of NHS in the maternity hospital before discharge. Within screening programmes different decisions were made for five variables related to protocol design. A single protocol can be used to screen all infants or a separate protocol can be used for infants with an increased risk for hearing impairment, including infants admitted to NICU (high-risk) in a dual-programme. A screening protocol has a number of screening steps in which screening is repeated after a fail outcome before referral to diagnostic assessment. Finally, the protocol can consist of OAE and/or aABR screening, aABR is more sensitive and specific but also more expensive than OAE. This study showed that these choices were related to local socio-economic factors: health expenditure and human development index (HDI). Health expenditure and HDI were high in countries with a dual protocol, using three screening steps including aABR and low in countries with a two-step OAE-only protocol for all infants. (**Chapter 3**)

Figures for quality measures of screening, as defined by the Joint Commission on Infant Hearing: coverage rate, referral rate and follow-up rate, could not be provided by many NHS programmes within the survey. Median coverage rate was 96% for the first screening step, mostly performed in the maternity hospital after birth. Referral rates were lower for programmes that first screened later than 24 hours after birth (2-15%) than when screening took place within 24 hours after birth (6-22%). Referral rates were even lower when screening was performed later than 72 hours after birth (4%). Screening programmes that referred less infants after the first step of screening, had higher attendance rates for follow-up screening. Programmes with one or two steps using only OAE referred 2.1%, programmes with two steps including aABR referred 1.7% and programmes with three or four steps including aABR referred 0.8% of infants to diagnostic assessment. Median detection rate for bilateral permanent hearing impairment ≥40dB was 1.16 per 1000 (range: 0.7 to 3 per 1000). (**Chapter 4**)

While NHS was performed in most participating countries and regions, only a few performed screening after the newborn period. All participating countries with CHS also performed NHS. All 17 countries and regions that performed universal CHS used pure tone audiometry screening. Eight countries with non-universal CHS used pure tone screening or whisper tests. Almost half of the universal programmes performed the first step of screening in a (pre)school setting, where nurses performed screening on children aged 3 to 7 years (median: 5). The other programmes performed the first screen in a healthcare setting, where doctors or nurses performed screening on children aged 4 to 7 (median: 4.5). One programme screened children in both. Median intensity for passing the screen were 30 dB at 3 to 4 years and 25 dB for children over 4 years. Similar to NHS, few programmes could provide quality measures of screening for CHS. (**Chapter 5**)

The estimated prevalence rates of permanent newborn hearing impairment and the information gathered through the extensive EUSCREEN questionnaire were used to develop the EUSCREEN cost-effectiveness model. This model calculates the cost-effectiveness of a hearing screening programme in a country, taking the local circumstances into account including healthcare infrastructure, demography, natural history of newborn hearing impairment, screening characteristics, treatment and costs. It permits comparison of the cost-effectiveness of hearing screening programmes across countries in Europe. In preparation of implementation of NHS in Albania, six NHS programmes were compared. The analysis was limited to well babies, screened with either OAE, aABR or a combination of both in the maternity hospital at different ages after birth. The model made a distinction in severity of hearing impairment (26-40dB, 40-80dB, >80dB) and took local circumstances in Albania into account. Assumptions were made for sensitivity (97% for aABR and 95% for OAE), referral rate (9.7% when screening was performed with OAE between 24 and 48 hours after birth and 20% when performed within 24 hours) and attendance rate (95% for inpatient screens and 70% after discharge). The model calculated a two-step OAE-aABR protocol, both performed in the maternity hospital before discharge to be most cost-effective in Albania. A single aABR protocol detected more cases but resulted in higher referral rates, which increased costs. Multiple-step screening decreased referral rates but increased the number of missed cases caused by false-negative results and a high number of infants lost to follow-up. (**Chapter 6**)

Finally, NHS was implemented in three provinces in Albania, where no NHS existed, during 2018-2019. Over the course of two years 22,818 infants were born of which 22,051 (96.7%) were screened. In the first step, 1,561 (7.1%) infants received a fail outcome, including 13 who were referred to diagnostic assessment. Out of 1,547 infants invited for the second step, 519 (33.5%) did not attend and 145 (9.4%) received a second fail outcome. Thirty-eight were referred for diagnostic assessment. For the third step, 105 infants were invited of which 43 (40.2%) did not attend and 27 (25.2%) received a fail outcome. A total of 21,493 (94.2%) infants completed the entire screening protocol of which 78 (0.36%) infants were referred for a diagnostic assessment, 52 attended and 22 (0,1%) were diagnosed with a hearing impairment of 40 dB or worse, of which 6 had a unilateral HI. The greatest concern during the implementation study was the high proportion of infants lost to follow-up after screening yielded a ‘fail’ result. Loss to follow-up between step 1 and step 2 was correlated to the screener and travel time to the maternity hospital.

The following criteria for implementation were evaluated in Albania: acceptability, adoption, appropriateness, feasibility, fidelity, coverage and attendance. Implementation criteria were evaluated based on on-site observations in the maternity hospitals, interview with screeners and parents, a screener questionnaire and a screening database in which screening outcome data were collected. Screening was considered acceptable, both screeners and parents considered NHS to be important. Adoption was good, all screeners who were trained participated in the NHS programme and parents accepted screening. Other preventive paediatric healthcare interventions may be considered more important, but NHS was considered appropriate in Albania. Screening performed by nurses and midwifes in maternity hospitals was considered feasible but screeners needed more time to gain experience when the number of births were low and screeners struggled with the high work load when the number of births were high. A more specific screening protocol and a good monitoring system could help in this regard. Coverage was high but a large number of infants did not attend follow-up screening. The screening programme was updated based on the experiences gained during the implementation and a plan was made to extend NHS to nationwide reach. (**Chapter 7 and 8**)

Chapter 10

NEDERLANDSE SAMENVATTING

Slechthorendheid is een vaak voorkomend gezondheidsprobleem tijdens de kindertijd. 2 op de 1000 kinderen worden slechthorend geboren. Als slechthorendheid tijdens de kindertijd niet wordt behandeld, kan dit invloed hebben op de ontwikkeling van spraak, taal en de algemene ontwikkeling van het kind. Door kinderen te screenen op slechthorendheid én vroeg te behandelen kunnen deze problemen vermeden worden. Neonatale gehoorscreening (NGS) vindt meestal plaats in de eerste dagen na de geboorte. Dit gebeurt met behulp van een otoakoestische emissie (OAE) of een automatische 'auditory brainstem response' (aABR). Het screeningsprotocol kan uit verschillende stappen bestaan. Behaalt een kind onvoldoende resultaat in de eerste stap? Dan wordt de screeningtest herhaald in een volgende stap. Is ook in het volledige screeningsprotocol het resultaat onvoldoende? Dan wordt het kind doorverwezen voor een diagnostisch onderzoek. Hierin wordt nagegaan of het gaat om permanente slechthorendheid. Ook wordt vastgesteld om welk type en welke mate van de slechthorendheid het gaat. De behandeling van slechthorende kinderen bestaat uit het versterken van het geluid via hoorapparaten, cochleaire implantaten of beengeleider hoortoestellen. Verder kan de behandeling ook bestaan uit logopedie en gezinsbegeleiding.

Kinderen kunnen ook op latere leeftijd gescreend worden. Gehoorscreening in de kindertijd na de neonatale periode (KGS) vindt meestal plaats als het kind tussen 3 en 7 jaar oud is. Dit gebeurt met behulp van toonaudiometrie. Dit proefschrift inventariseert en evalueert verschillende strategieën voor gehoorscreening tijdens de kindertijd.

De EUSCREEN-studie vergelijkt de kosteneffectiviteit van oog- en gehoorscreeningsprogramma's in landen binnen en buiten Europa. In Europa bestaat grote variatie tussen deze screeningsprogramma's in leeftijd, het aantal testmomenten, de gebruikte testen, de achtergrond van de screeners, diagnostiek, interventie en financiering van de screening. Het kosteneffectiviteitsmodel is ontwikkeld om screeningsprogramma's te vergelijken waarbij rekening wordt gehouden met de lokale omstandigheden.

Bij de vergelijking van de kosteneffectiviteit van NGS-programma's is informatie over het verloop en de prevalentie van slechthorendheid belangrijk. Een systematisch literatuuronderzoek vond 7.520 studies, waarvan er 35 voldeden aan de inclusiecriteria. Deze 35 studies werden opgenomen in de analyse. Hiervan kwamen 25 studies uit hoge-inkomenslanden. 27 studies bespraken de algemene populatie. Drie bespraken enkel kinderen die niet op een neonatale intensive care unit (NICU) waren opgenomen, 5 studies bespraken enkel NICU-kinderen. De prevalentie van permanente slechthorendheid van minimaal 40 dB in de neonatale populatie varieerde tussen 1 en 6 kinderen per 1.000 met een gemiddelde prevalentie van 2.21 per 1.000 (credible interval: [1.71, 2.8]). Bij ongeveer een derde van de kinderen was de slechthorendheid enkelzijdig. Voor NICU-kinderen werd een gemiddelde prevalentie van 15.77 per 1.000 gevonden. De prevalentie van neonatale slechthorendheid was hoger in lage-inkomenslanden dan in hoge-inkomenslanden en hoger in Azië dan in Europa. Echter, deze verschillen waren niet statistisch significant. Het gerapporteerde percentage kinderen dat niet kwam opdagen voor vervolg screening was hoger in lage-inkomenslanden, maar ook dit verschil was niet statistisch significant (p = 0.07). (**Hoofdstuk 2**)

In een grootschalig onderzoek werd een uitgebreide vragenlijst ontwikkeld om informatie te verzamelen over gehoorscreeningsprogramma's. Deze vragenlijst werd ingevuld door gehoorscreeningsdeskundigen uit voornamelijk Europese landen. Op basis van deze informatie werd onderzocht welke factoren mogelijk van invloed zijn op de organisatie en de uitkomsten van gehoorscreening. De vragenlijst bestond uit 9 onderdelen: demografie en epidemiologie, administratie en algemene achtergrond, bestaande screeningsprogramma's, dekking van de screening en opkomst, tests en apparatuur, follow-up en diagnostiek, behandelingsmogelijkheden, kosten en de voordelen en nadelen van screening. Bijkomende demografische informatie werd verzameld om de verschillen tussen programma's beter te begrijpen. Deze vragenlijst werd ingevuld door vertegenwoordigers uit 40 Europese landen en uit Rusland, Malawi, Rwanda, India en China.

Universele NGS-programma's zijn nationaal ingevoerd in 26 van de 30 hoge-inkomenslanden en in 3 van de 15 lage- of midden-inkomenslanden. Van de 42 NGS-programma's screenden 39 programma's kinderen de eerste keer voor hun ontslag uit het ziekenhuis. Screeningsprogramma's namen verschillende beslissingen voor 5 aan het protocol gerelateerde variabelen. Als universele NGS wordt ingevoerd kan ervoor gekozen worden om alle kinderen met 1 protocol te screenen. Ook kan een apart protocol gebruikt worden voor kinderen met een verhoogd risico op slechthorendheid (hoge-risico kinderen). Vervolgens wordt het aantal screeningsstappen in het programma bepaald. Als er meer screeningsstappen zijn, wordt de kans op een vals positief resultaat kleiner. Ten slotte wordt de soort screening test bepaald: OAE en/of aABR. Deze keuzes waren gerelateerd aan de gezondheidsuitgaven en de ontwikkelingsindex van een land. De gezondheidsuitgaven en de ontwikkelingsindex waren hoger in landen met een apart protocol voor hoge-risico kinderen en waarbij 3 screeningsstappen met minstens 1 aABR gebruikt werden. Ze waren lager in landen die een OAE-protocol met 2 stappen gebruikten voor alle kinderen. (**Hoofdstuk 3**)

Uitkomstmaten van screening zoals gedefinieerd door de 'Joint Commission on Infant Hearing' – dekkingsgraad, verwijspercentage en follow-up percentage – worden gebruikt om de effectiviteit van screening te evalueren. Deze waren voor een groot aantal NGS-programma's niet beschikbaar. In de eerste screeningstap was de mediaan voor het gerapporteerde dekkingspercentage 96%. De gerapporteerde verwijspercentages waren lager voor programma's waarin kinderen na 24 uur na de geboorte werden gescreend (2-15%) dan binnen 24 uur na de geboorte (6-22%). Verwijspercentages waren nog lager wanneer pas na 72 uur na de geboorte werd gescreend (4%). Screeningprogramma's die na de eerste screeningsstap minder kinderen doorverwezen, hadden een hogere opkomst voor de vervolgscreening. Programma's met 1 of 2 stappen die enkel OAE gebruikten, verwezen 2.1% van de kinderen voor een diagnostisch onderzoek. Dit was 1.7% voor programma's met 2 stappen waarbij ook aABR gebruikt werd, en 0.8% voor programma's met 3 of 4 stappen met minstens 1 aABR. Bilateraal permanente slechthorendheid ≥40dB werd gevonden in 1.16 kinderen per 1.000 (mediaan) en varieerde tussen 0.7 en 3 kinderen per 1.000. (**Hoofdstuk 4**)

Terwijl NGS wordt uitgevoerd in de meeste landen binnen de EUSCREEN-studie, screenen maar enkele landen het gehoor in de kindertijd na de neonatale periode. Alle landen met KGS hebben ook een NGS-programma. De 17 landen met een universeel KGS-programma maken gebruik van toonaudiometrie. 8 landen met niet-universele KGS maken gebruik van toonaudiometrie of fluistertests. Ongeveer de helft van de KGS-programma's vindt plaats in een schoolomgeving, waar verpleegkundigen kinderen tussen 3 en 7 jaar screenen (mediaan: 5). De andere programma's vinden plaats in een zorgomgeving, waar artsen of verpleegkundigen kinderen tussen 4 en 7 jaar screenen (mediaan: 4,5). Een KGS-programma screent kinderen in beide locaties. De intensiteit die gebruikt wordt om de grenswaarde voor een voldoende gehoor te bepalen is afhankelijk van de leeftijd van het kind. Dit is 30 dB voor kinderen van 3 tot 4 jaar en 25 dB voor kinderen van 4 jaar en ouder. Ook voor KGS waren voor weinig programma's uitkomstmaten van screening beschikbaar. (**Hoofdstuk 5**)

Met behulp van de prevalentiecijfers van permanente slechthorendheid in de neonatale populatie en de informatie die werd verzameld via de EUSCREEN-vragenlijst, werd een kosteneffectiviteitsmodel ontwikkeld. Dit model kan voor een land het meest kosteneffectieve gehoorscreeningsprogramma berekenen. Hierbij wordt rekening gehouden met de lokale omstandigheden, waaronder de infrastructuur van de gezondheidszorg, demografie, het natuurlijk beloop van slechthorendheid bij pasgeborenen, behandeling en kosten. Aan de hand van dit model kan ook de kosteneffectiviteit van gehoorscreeningsprogramma's in verschillende landen in Europa vergeleken worden. Ter voorbereiding van de implementatie van NHS in Albanië werden 6 NHS-programma's voor gezonde kinderen vergeleken. Deze protocollen verschilden in het aantal screeningsstappen, de leeftijd van het kind per screeningsstap en het gebruik van OAE en/of aABR. Het model maakte een onderscheid tussen verschillende mate van slechthorendheid (26-40dB, 40-80dB,> 80dB) en hield rekening met de lokale omstandigheden in Albanië. Aannames werden gedaan voor de sensitiviteit (97% voor aABR en 95% voor OAE), het verwijzingspercentage (9,7% voor screening met OAE tussen 24 en 48 uur na de geboorte en 20% wanneer screening werd uitgevoerd binnen 24 uur) en opkomstpercentage (95% voor ontslag uit het ziekenhuis en 70% na ontslag). Volgens de berekeningen van het model was het OAE-aABR protocol, waarbij beide stappen worden uitgevoerd in de kraamkliniek vóór ontslag uit het ziekenhuis, het meest kosteneffectieve screeningsprogramma voor de situatie in Albanië. Een aABR-protocol met 1 stap detecteerde meer slechthorende kinderen, maar het aantal verwezen kinderen was hoger waardoor de kosten hoger waren. In een protocol met meerdere stappen werden enerzijds minder kinderen doorverwezen. Anderzijds werden meer slechthorende kinderen niet gedetecteerd door een fout-negatief resultaat en ging een groot aantal kinderen verloren tussen de screenings stappen. (**Hoofdstuk 6**)

Ten slotte werd NGS in 2018-2019 in 3 provincies in Albanië geïmplementeerd. Gedurende deze implementatie werden 22.818 kinderen geboren, waarvan 22.051 (96,7%) werden gescreend. In de eerste stap hadden 1.561 (7,1%) kinderen een onvoldoende resultaat, waarvan 13 meteen werden verwezen voor een diagnostisch onderzoek. Van de 1.547 kinderen die voor een tweede test moesten komen, kwamen er 519 (33,5%) niet en kregen er 145 (9,4%) opnieuw een onvoldoende resultaat. 38 kinderen werden verwezen voor diagnostisch onderzoek. Van de 105 kinderen die werden uitgenodigd voor de derde stap, kwamen er 43 (40,2%) niet en kregen 27 (25,2%) een onvoldoende resultaat. Het volledige screeningsprogramma werd doorlopen door 21.493 (94,2%) kinderen. 78 (0,36%) werden verwezen voor een diagnostisch onderzoek, van wie er 52 werden onderzocht. Bij 22 (0,1%) kinderen werd een slechthorendheid van 40 dB of slechter ontdekt, van wie er 6 een eenzijdige slechthorendheid hadden. Het grootste probleem tijdens de implementatie van NGS in Albanië was het hoge percentage kinderen dat niet terugkwam voor een vervolgafspraak na een ‘onvoldoende’ resultaat. Dit hing samen met de screener en de reistijd tussen het ziekenhuis en de woonplaats.

De ‘acceptability’, ‘adoption’, ‘appropriateness’, ‘feasibility’, ‘fidelity’ en ‘coverage and attendance’ werden geëvalueerd tijdens de implementatie van NGS in Albanië. Dit gebeurde op basis van observaties in de kraamklinieken, interviews met screeners en ouders, een vragenlijst voor de screeners en een database waarin de uitkomst van de screening werd geregistreerd. Zowel screeners als ouders vonden NGS belangrijk, screening was acceptabel. Alle screeners die de cursus volgden, voerden ook screening uit, en ouders waren bereid om deel te nemen aan de screening, ‘adoption’ was goed. Binnen de gezondheidszorg kunnen andere interventies voor kinderen als belangrijker worden beschouwd, toch werd NGS in Albanië beschouwd als ‘appropriate’. Het was mogelijk om screening te laten uitvoeren door verpleegkundigen en verloskundigen in het ziekenhuis (‘feasibility’). In ziekenhuizen met weinig geboortes hadden screeners meer tijd nodig om voldoende ervaring op te doen; in ziekenhuizen met veel geboortes was de werkdruk te hoog. Een specifieker screeningsprotocol bij een laag aantal geboortes en een goede database om screening te monitoren bij een hoog aantal geboortes kunnen hierbij helpen. Het dekkingspercentage van het NGS-programma was hoog, maar een aantal kinderen kwam niet terug voor het vervolgonderzoek (‘coverage and attendance’). Het screeningsprogramma in Albanië werd aangepast op basis van de ervaringen die zijn opgedaan tijdens de implementatie. Er werd een plan gemaakt om NGS nationaal uit te rollen. (**Hoofdstuk 7 en 8**)

Chapter 11

Dankwoord/Acknowledgements

List of publications

Co-authors and their affiliations

About the author

PhD Portfolio

DANKWOORD/ACKNOWLEDGEMENTS

Promoveren doe je niet alleen en zoals het gezegde gaat, vele handen maken licht werk. Daarom wil ik hier graag de tijd nemen om iedereen te bedanken wiens handen dit proefschrift direct of indirect mee lichter hebben gemaakt. Bedankt allemaal, zonder jullie had ik hier nooit gestaan!

Allereerst, aan mijn promotoren en begeleiders:

Harry, bedankt voor je begeleiding, je kritische blik, de steun, de adviezen en de rustige manier waarop jij met de stress van dit project wist om te gaan. Bedankt dat je deur altijd voor me open stond ondanks je drukke agenda.

Huib, bedankt voor alle mogelijkheden die je voor het EUSCREEN-project en voor mij hebt gecreëerd de afgelopen jaren. Jij zorgde ervoor dat alles wat er geschreven werd ook leesbaar was voor de leek.

Hans, bedankt voor je geduld, je hulp bij het uitspitten van de oneindige artikels voor ons prevalentie artikel, de lessen epidemiologie en je geweldige oog voor detail. Bedankt om me de kneepjes van het vak te leren en om me eraan te blijven herinneren altijd kritisch te blijven.

André, bedankt voor je wetenschappelijke en audiologische inzichten, je hulp bij het uitzoeken van statistiek, het nalezen van de artikels en je hulp bij presentaties. Bedankt ook voor je luisterende oor, je steun en geloof in mijn kunnen (ook en misschien vooral wanneer ik het zelf even niet zag).

Martijn, bedankt om altijd de tijd te nemen voor besprekingen, je kritische blik en je gestructureerde manier van werken.

Bedankt allemaal ook voor de leerzame maar vooral ook enorm gezellige en geweldige tripjes die we samen hebben mogen maken. Dit boekje was er nooit geweest zonder jullie als mijn begeleiders!

Ik zou nooit aan PhD traject begonnen zijn zonder een bron van inspiratie die ik zelfs al mee kreeg van vóór ik begon aan mijn studie ‘logopedische en audiologische wetenschappen’ aan de KU Leuven. Bedankt Prof. Astrid van Wieringen en Prof. Jan Wouters, voor jullie enthousiasme en toewijding, bedankt om me de liefde voor onderzoek en het vak mee te geven tijdens de opleiding.

Bedankt Kazem, om me wegwijs te maken in de Bayesian statistiek, om altijd geduldig te blijven wanneer we iets niet helemaal snapten de eerste keer en wanneer we toch weer een studie wouden toevoegen.

Bedankt aan de (ex)collega’s van Ee1667 en Ee1664, Elisabeth, Jan, Annelies, Aveen, Emily, Frea, Marieke, Sjoukje, Aya, Tanya. Bedankt ook aan de collega’s van maatschappelijke gezondheidszorg, Mirjam en Eveline. Bedankt allemaal voor de gezellige tijden die we samen hebben beleefd en om wanneer het nodig was, samen elkaars stress te proberen verlichten met praatjes, koffie, thee en chocolade.

In het bijzonder, Mandy, bedankt voor alles, want ik kan het hier niet allemaal benoemen. Bedankt voor de steun, de koffiepauzes, de middagwandelingetjes, de gezellige lunches, het blijven hangen na werk. Bedankt voor het nalezen, het kritisch beoordelen van mijn ideeën en de frisse blik op mijn onderzoek. Bedankt ook voor alle keren dat ik bij jou terecht kon voor alles wat niets te maken had met werk. Wat mij betreft is dit boekje voor een groot deel ook aan jou te danken.

The Rotterdam-team was only a part of the EUSCREEN study. We would not have been able to perform this study without the help of all our 'Country Representatives', thank you for filling out our questionnaire! This project would never have been able to achieve everything that it did without the help of all the EUSCREEN consortium partners. A warm thank you to: Cristina, Simona, Daniela, Mihai, Monica, Alin (Romanian team in Cluj-Napoca); to Anna; to Maria; and to Jill and Hellen.

I would especially like to thank the Albanian team. Thank you to all the nurses who contributed to our study and to all the parents and their infants who participated in our study. Thank you Enver, Edi, Ervin and Birkena, for your hospitality, the translations, for accompanying us on every visit we made. For making the implementation of hearing screening in this study possible and for never giving up, no matter how difficult it was to get the NHS programme running in Albania. Thank you for the lovely lunches, dinners and conversations we had. Thank you so much for showing me your beautiful country and teaching me Albanian dancing!

Dear Gwen, thank you so much for our many talks, your support, your ever wise advice, for reading through every manuscript multiple times, for correcting my English, for teaching me everything I know about NHS and EHDI programmes, thank you for your mentorship. I really hope we can continue to work together in the future!

To the Stockholm team. Dear Inger, even though you were not officially my supervisor, you did help me a lot during my PhD, both in person and through Allison. Thank you for the fun times we had while I was visiting Stockholm and for always reminding me not to work too hard, but to also enjoy life!

My dearest Allison, words cannot describe how thankful I am for having been able to share most of my PhD time with you, even though we did so about a 1000km away from each other. I can only feel honoured to have been able to work and write with you. I know that you will accomplish great things. Thank you for your hospitality, your kindness, your patience and most of all your friendship!

Aan mijn vrienden/to my friends, I want to thank all of my friends, both in the Netherlands and Belgium, for believing in me and supporting me throughout the past 4 years, for their patience and tolerance. To accept me both as how I am usually and as the silent/tired/stressed out version of myself. For brightening up my life, for making me forget, for all of your help! I am also so very happy for all the babies that have been born over the past years. Even though, living in the Netherlands and working on my PhD meant I could not always visit as soon or as often as I may have wanted. Congrats to you all and thank you all for answering my endless questions about how their hearing screening went ;).

In particular, I would like to thank my 'Dutch Family group' for being my main support system since the beginning, I could not have wished for a better one, and for always having my back, thank you Dani, Erin, Sara, Janet, Helena, Ira. In het bijzonder ook bedankt Sarah en Dorien, om in me te geloven, me op weg te helpen en me te steunen in deze keuze, bedankt Silke, om te luisteren wanneer ik het nodig had, bedankt Elien, voor de vele bezoekjes en uitstapjes, thank you Ira, for the amazing food and our regular 'decompression' sessions, thank you Helena, for the walks, the talks, the laughs, the movie nights and yoga sessions, bedankt Lien, voor de avondjes weg en de pintjes, bedankt Katrien, voor je bezoekjes, bedankt Nadia, voor de goede raad, bedankt Koen & Amani voor de gezellige avondjes samen, bedankt Justine, voor de wijntjes. Hier kan helaas niet alles gezegd worden, daarom aan iedereen, enorm bedankt voor alles wat jullie voor mij hebben gedaan en hoeveel jullie voor mij hebben betekend de afgelopen jaren!

Liefste familie, zowel in Nederland als in België.

Ik had nooit gedacht dat toen ik naar Nederland verhuisde, ik een tweede thuis zou vinden. Dat ik hier ook de familiale gezelligheid zou vinden die ik soms zo hard moest missen. Bedankt Ruud, Marijke, Leon en Lisa (en natuurlijk ook Laika) om me hier ook 'thuis' te doen voelen, om me mee op te nemen en vooral om me te aanvaarden in jullie familie, ook wanneer ik soms met mijn hoofd even ergens anders zat.

Liefste broertje, liefste zusje, er is de afgelopen jaren van alles gebeurd in jullie leven. Groot en klein. Ik had hier tijdens graag dichter bij jullie willen kunnen zijn. Dat weten jullie wel, maar ik wil het hier nog een keertje gezegd hebben. Ondanks dat waren jullie er altijd voor me, ook van op afstand. Daarvoor, oneindig hard bedankt! Liefste Anke, ook jij bedankt, om altijd te doen waar je zo goed in bent en te zorgen voor alles en iedereen rond je, ook voor mij, ik ben heel blij dat jij een deel bent van onze familie!

Liefste mama, liefste papa, ten eerste, ik hoop dat ik ondertussen eindelijk kan zeggen dat ik het schrijven van alinea's onder de knie heb! Bij deze nog eens bedankt voor alle uren die jullie van in het begin van mijn schooltijd naast me hebben moeten zitten om me te helpen met schrijven, goede zinnen vormen en me te leren hoe een alinea juist werkt. Bedankt voor jullie engelengeduld met mij. Bedankt om dit allemaal mogelijk te maken en ons zo op te voeden dat we geen schrik hebben om te vertrekken. Want we weten goed genoeg waar we altijd weer terecht kunnen en zullen dankzij jullie ook altijd de weg naar huis weer weten te vinden, hoe ver dat ook mag zijn.

Als laatste, maar zoals het gaat, zeker niet de minste, Eric. Van alle mensen die hun schouders mee onder dit boekje hebben gezet, werden die van jou misschien wel het zwaarste belast. Toch was je er telkens opnieuw met een overvloed aan onvoorwaardelijke liefde, steun en begrip. Woorden schieten te kort om je te bedanken voor alle gezonde maaltijden, met ongezondere dessertjes en oneindige theetjes die onverwachts voor me klaar stonden, je begrip wanneer ik weer eens veel te vroeg ging opstaan, je kritische blik op komma's, je onverwachtse bloemen, koekjes en chocolaatjes wanneer ik het nodig had. Toch zegt dit nog niet genoeg, dus ik hou het hierbij: Jij ben mijn noorden, want zoals het zo mooi bij ons om de hoek staat, *zonder noorden komt niemand thuis*.

LIST OF PUBLICATIONS

Bussé A.M.L., Hoeve H.L.J., Nasserinejad K., Mackey A.R., Simonsz H.J., Goedegebure A. Prevalence of permanent neonatal hearing impairment: systematic review and Bayesian meta-analysis. Int J Audiol. 2020 Jun; 59(6):475-485. doi: 10.1080/14992027.2020.1716087. Epub 2020 Feb 3. PMID: 32011197.

Bussé A.M., Qirjazi B., Goedegebure A., Toll M., Hoeve H.L., Toçi E., Roshi E., Carr G., Simonsz H.J. Implementation of a neonatal hearing screening programme in three provinces in Albania. Int J Pediatr Otorhinolaryngol. 2020 Jul; 134:110039. doi: 10.1016/j.ijporl.2020.110039. Epub 2020 Apr 8. PMID: 32304854.

Verkleij M.L., Heijnsdijk E.A.M., **Bussé A.M.L.**, Carr G., Goedegebure A., Mackey A.R., Qirjazi B., Uhlén I.M., Sloot F., Hoeve H.L.J., de Koning H.J.; Country-Committees Joint-Partnership of EUSCREEN Study Consortium. Cost-Effectiveness of Neonatal Hearing Screening Programs: A Micro-Simulation Modeling Analysis. Ear Hear. 2020 Nov 30; Publish Ahead of Print. doi: 10.1097/AUD.0000000000000981. Epub ahead of print. PMID: 33306547.

Bussé, A.M.L.*, Mackey, A.R.*, Hoeve H.L.J., Goedegebure A., Carr G., Uhlén I.M., Simonsz H.J.; Country-Committees Joint-Partnership of EUSCREEN Study Consortium. Assessment of hearing screening programmes across 47 countries or regions I: Provision of newborn hearing screening. doi: 10.1080/14992027.2021.1886350. Accepted for publication in International Journal of Audiology, 2021.

Mackey, A.R.*, **Bussé, A.M.L.***, Hoeve H.L.J., Goedegebure A., Carr G., Simonsz H.J., Uhlén I.M.; Country-Committees Joint-Partnership of EUSCREEN Study Consortium. Assessment of hearing screening programmes across 47 countries or regions II: Coverage, referral, follow-up and detection rates from newborn hearing screening. doi: 10.1080/14992027.2021.1886351. Accepted for publication in International Journal of Audiology, 2021.

Bussé, A.M.L.*, Mackey, A.R.*, Hoeve H.L.J., Goedegebure A., Carr G., Uhlén I.M., Simonsz H.J.; Country-Committees Joint-Partnership of EUSCREEN Study Consortium. Assessment of hearing screening programmes across 47 countries or regions III: Provision of childhood hearing screening after the newborn period. doi: 10.1080/14992027.2021.1897170. Accepted for publication in International Journal of Audiology, 2021.

Bussé A.M.L., Qirjazi B., Toll M., Mackey, A.R., Goedegebure A., Hoeve H.L., Toçi E., Roshi E., Carr G., Simonsz H.J. Implementation of newborn hearing screening in Albania. Submitted for publication.

*These authors contributed equally to the respective manuscripts ans should be considered dual first authors

CO-AUTHORS AND THEIR AFFILIATIONS

Andrea M.L. Bussé	Department of Otorhinolaryngology and Head and Neck Surgery Department of Ophthalmology, Erasmus University Medical Center, Rotterdam, The Netherlands
Gwen Carr	Independent Consultant in Early Hearing Detection, Intervention and Family Centered Practice, London, United Kingdom
André Goedegebure	Department of Otorhinolaryngology and Head and Neck Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands
Eveline A.M. Heijnsdijk	Department of Public Health, Erasmus MC University Medical Center Rotterdam, Rotterdam, the Netherlands
Hans L.J. Hoeve	Department of Otorhinolaryngology and Head and Neck Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands
Harry J. de Koning	Department of Public Health, Erasmus MC University Medical Center Rotterdam, Rotterdam, the Netherlands
Allison R. Mackey	Department of Clinical Intervention and Technology (CLINTEC), Karolinska Institutet, Stockholm, Sweden
Kazem Nasserinejad	Amsterdam University Medical Center, Amsterdam, The Netherlands
Birkena Qirjazi	University of Medicine of Tirana, Department of Ear, Nose and Throat Diseases - Ophthalmology, Tirana, Albania
Enver Roshi	University of Medicine of Tirana, Department of Public Health, Tirana, Albania
Huibert J. Simonsz	Department of Ophthalmology, Erasmus University Medical Center, Rotterdam, The Netherlands
Frea Sloot	Department of Ophthalmology, Erasmus University Medical Center, Rotterdam, The Netherlands

Ervin Toçi	University of Medicine of Tirana, Department of Public Health, Tirana, Albania
Martijn S. Toll	Department of Otorhinolaryngology and Head and Neck Surgery, Erasmus University Medical Center, Rotterdam, The Netherlands
Inger M. Uhlén	Department of Clinical Intervention and Technology (CLINTEC), Karolinska Institutet, Stockholm, Sweden
Mirjam L. Verkleij	Department of Public Health, Erasmus MC University Medical Center Rotterdam, Rotterdam, the Netherlands

ABOUT THE AUTHOR

Andrea Bussé was born on February 14th, 1988 – a sunny Sunday – in Leuven where she grew up. She obtained her Bachelor and Master of Science in Speech Therapy and Audiology Sciences at the Catholic University of Leuven in 2012 and subsequently her Postgraduate Studies in Audiology and Hearing Aid Fitting in 2013. She worked as an intern at the National MS Centre in Melsbroek for speech therapy and at the Glasgow Royal Infirmary for Audiology during her master years. For her master thesis she compared two setups to determine hearing thresholds using auditory steady-state responses. While studying for her postgraduate, she held internships at the University Hospital in Leuven and the Audionova hearing centre in Leuven. In 2015, she started culinary school to study the French-Belgian cuisine.

After her graduation she worked for Amplifon, a hearing retail company, where she helped hearing impaired patients by finding the best solution for their problem. In 2016 the opportunity arose to go into research. In 2017 she started her PhD at the Erasmus Medical Centre in Rotterdam under the supervision of dr. L.J. Hoeve, dr. ir. A. Goedegebure, prof. dr. H.J. Simonsz, and prof. dr. H.J. de Koning. She conducted her PhD as part of the EUSCREEN study, which is described in this thesis.

PHD PORTFOLIO

Summary of PhD training and teaching

Name PhD student:	Andrea Bussé
Erasmus MC Department:	Department of Otorhinolaryngology and Head and Neck Surgery Department of Ophthalmology
PhD period:	May 2017 – April 2021
Promotor(s):	Prof. Dr. H.J. de Koning; Prof. Dr. H.J. Simonsz
Copromotor:	André Goedegebure
Supervisor:	Hans Hoeve

	Year	Workload (Hours/ECTS)
General courses		
- Systematic literature and Endnote medical library	2017	2.0
- Biomedical English Writing and Communication	2019	3.0
- Research Integrity	2020	0.3
- Biostatistical Methods I: Basic Principles Part A	2018	2.0
	2019	
(Inter)national conferences, seminars and workshops		
- European Union for School and University Health and Medicine (EUSUHM) congress 2017, Leuven, Belgium	2017	1.0
- EFAS 2017	2017	1.0
- ORL-HNS 2017	2017	1.0
- HEAL 2018	2018	1.0
- WCA 2018	2018	1.0
- EFAS 2019	2019	1.0
- EUSCREEN conference 2019	2019	1.0
Presentations at (international) conferences		
- Oral presentation at EUSUHM 2017, Leuven: EUSCREEN: the evaluation of vision and hearing screening programs in Europe	2017	1.0
- EFAS 2017	2017	1.0
- ORL-HNS 2017	2017	1.0
- HEAL 2018	2018	2.0
- WCA 2018	2018	1.0
- EFAS 2019	2019	2.0
- EUSCREEN conference 2019	2019	1.0
Other presentations		
- Research bespreking communicatie Audiologie	2019	1.0
Other		
- EUSCREEN H2020 international and EU progress reports	Continuing	15.0
- Organisation EUSCREEN Conference Poznan 2019	2019	5.0
- EUSCREEN manual and model development	Continuing	5.0