Medical Research Archives

ESMED
European Society of Medicine

OPEN ACCESS

Published: July 31, 2022

Citation: Desloovere C, Van Overmeire B, et al., 2022. Influence of screening devices and protocol on audiological outcome of 25 years of universal neonatal hearing and vestibular screening in Flanders, Medical Research Archives, [online] 10(7). https://doi.org/10.18103/mra.v10i7.2897

DOI
https://doi.org/10.18103/mra.v10i7.2897

ISSN: 2375-1924

RESEARCH ARTICLE

Influence of screening devices and protocol on audiological outcome of 25 years of universal neonatal hearing and vestibular screening in Flanders

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ABSTRACT

Background: Congenital hearing loss has been linked with life-long deficits in speech and language abilities and children with vestibular deficits show delayed development of gross motor milestones.

Aim and scope of the research: To analyze if the universal neonatal hearing screening (UNHS) and vestibular screening program in Flanders meet the current guidelines and benchmarks of the position statements from the Joint Committee on Infant Hearing and how big the impact of screening devices and strategy is.

Methods: The UNHS is organized since 1997 by a Flemish public child care organization and performed by trained nurses. It is based on a two-step screening with Automated Auditory Brainstem Responses and in case of absent responses (named 'refer'), audiological and medical diagnostic are done in one of 21 certified centers. Vestibular screening started in 2018 around the age of 6 months with cervical Vestibular Evoked Myogenic Potentials (cVEMP) for all children with confirmed permanent hearing loss.

Results: The coverage of the UNHS from 1998 till 2020 was 96,3 % (range 91,1 – 98%). There was a bilateral refer for 0,27 % of the infants and unilateral refer for 0,37 %. A sensorineural or mixed hearing loss > 40 dB was diagnosed in 32 % of the referred infants, a conductive hearing loss which often resolved over time in 39 %, a normal hearing in 25% and 4,7 % were lost in follow-up for the diagnostic evaluation.

There was an effect of the screening device on the detection of conductive hearing losses and false-positive cases. The incidence was higher with the MAICO MB Classic® device compared to the ALGO® devices. The incidences of sensorineural or mixed hearing loss were independent of the screening device and remained relatively stable over the years.

A vestibular deficit was found in 9,5 % of all children with sensorineural hearing loss. The incidence was significantly higher in infants with severe or profound hearing loss (p=0,003)

Conclusion: The Flemish UNHS has a high coverage, low referral rate and low loss of follow-up rate. Strict monitoring and follow-up by a central organization are essential for optimal results. Long-term follow-up remains a challenge.

Keywords: Newborn hearing screening, vestibular screening

Introduction

Congenital hearing impairment is a common disability occurring in about 1-4 per 1000 newborns.[1] It has been linked with life-long deficits in speech and language abilities, poor educational performance and has an important social impact on both children and parents.[2] Under the impulse of the 1994 statement of the Joint Committee on Infant Hearing(JCIH)[3] who endorsed universal neonatal hearing screening (UNHS) before 3 months of age, as one of the first countries in the world, UNHS was initiated in 1997 in the whole region of Flanders, Belgium. It is organized by Opgroeien - Kind & Gezin (Grow up - Child and Family), a Flemish public child care organization and performed at the well-baby clinics by trained nurses. The screening program was conceived and implemented in collaboration with all Flemish university ENT departments and with 21 certified centers of expertise (the 21 referral centers).[4] The program integrates screening, referral, specialized investigation, rehabilitation, family guidance and reporting in a single protocol. Data are digitally collected in a central Opgroeien - Kind & Gezin database. The program is monitored by a dedicated team of Opgroeien - Kind & Gezin to prevent and track drop-outs.[5]

The 2000 position statement of the JCIH recommended that all infants should be screened before 1 month of age, diagnostics should be completed before the age of 3 months and in case of confirmed hearing impairment, intervention should be initiated before 6 months of age.[6] In the latest 2019 JCIH position statement a 1-2-3 benchmark was set with screening completed by 1 month of age, audiological diagnosis by 2 months of age and enrollment in early intervention by 3 months of age.[7]

The aim of this article is to analyze efficacy, coverage and diagnostic assessment of the UNHS and vestibular screening in Flanders. An important research problem is the impact of the different screening devices used over time on the detection and audiological characteristics of permanent childhood hearing loss. Additionally, because Flanders has one of the longest UNHS protocols, a thorough review on the specific trends, evolutions and challenges over 25 years was performed.

Methods

A retrospective database review was performed from 1997 to 2020 of a digitized database in which all infants born in Flanders were registered.

The screening protocol has been described before.[4] In short, the screening protocol is explained. The Flemish UNHS program is organized by Opgroeien - Kind & Gezin, a public child care organization and performed by a trained nurse. It is based on a two-step screening procedure with automated auditory brainstem response (AABR) devices. The referral level of the AABR is set at 35 dB nHL.

Every infant born in Flanders is offered a non-mandatory hearing screening test free of charge, within 3-6 weeks after birth at one of the well-baby clinics or at home. The screening is performed when the baby is in calm awake state or in natural sleep. In case of uni- or bilateral absent responses (named 'refer') a second screening session is scheduled within 1 week to reduce the number of false-positive cases due to temporary hearing impairment, if possible at another location to rule out technical disturbances. Infants who have been admitted to neonatal care or intensive care nurseries because of perinatal morbidity, complications, or prematurity, are usually screened before discharge from the neonatal intensive care unit, using AABR or diagnostic Auditory Brainstem Responses (ABR). These results are also integrated into the central database of Opgroeien - Kind & Gezin.

During the years the Flemish screening program has used several devices. From 1997 till 2006 the ALGO Portable® (Natus Medical Inc San Carlos CA, US) was used, based on AABR testing, and its successor the ALGO 3i® device from 2007 till 2012. From 2013 till 2018 the MAICO MB 11 classic® device (Maico diagnostics GmbH, Berlin, Germany) was used based on a combination of a fast AABR screening with the CE-Chirp® stimulus and a ASSR algorithm. From 2018 until now the MAICO MB 11 Classic® with an adapted software version has been used.

All babies without a bilateral 'pass' result after the two-step screening procedure are referred to one of the certified referral centers that committed to start standardized diagnostic evaluation within 2 weeks after referral. This is monitored by Opgroeien - Kind & Gezin. Diagnostics and follow-up are provided in specialized ENT departments and rehabilitation centers. At regular intervals, reports have to be sent to Opgroeien - Kind &

Gezin. The first report is due within one month after referral and includes data on birth weight, gestational age, neonatal risk factors, history of specialized neonatal care and audiological data (high-frequency tympanometry, otoacoustic emissions, air conduction and if applicable bone-conduction ABR-thresholds, Auditory Steady-State Response (ASSR) thresholds, cochlear microphonics), type of hearing loss (sensorineural, conductive, mixed type or auditory neuropathy spectrum disorder (ANSD)), referral of the child for family guidance or to a rehabilitation center.

Hearing loss is classified according to the BIAP criteria (International Bureau for Audiophonology: recommendations 02/1 bis May 1997) : ABR thresholds between 21 and 40 dB nHL: mild; between 41-70 dB nHL: moderate; between 71-90 dB nHL: severe and $\geq$ 91 dB nHL profound hearing loss.

The second report concerns etiology, the third report is about treatment/rehabilitation and both are due later. The first report is available for almost every child. Over the years it appeared that second and third reports were sent very irregularly notwithstanding the extra effort by Opgroeien – Kind & Gezin to obtain these within a reasonable time frame. For the analyses presented in this article, we retrieved data from the first reports obtained between 1998 and 2020 (2021 data were not yet completed at the time of submission).
Long-term follow-up data are available for the first 6 years of the UNHS-program because of missing a large proportion of reports 2 and 3.[4]

After confirmation of hearing loss the same standardized etiological work-up is performed by all centers with a clinical examination by a ENT specialist and in case of sensorineural hearing loss also examination by an ophthalmologist, clinical geneticist, testing for congenital cytomegalovirus infection (cCMV), genetic testing of Cx26/Cx30 and in recent years if negative targeted genome sequencing. More extensive investigations such as testing for other infections, imaging, urine analysis, electrocardiography or neurological evaluation are performed upon indication.
If audiological diagnostic workup confirms a sensorineural hearing loss, the child is also immediately referred to a rehabilitation center and/or family guidance to explore the need for hearing aid fitting and rehabilitation, in order to initiate treatment before the age of 2 months and not to wait till the medical diagnostic is complete.

Data on etiology are available for half of the referred children because of the insufficient return of report 2.

Initially all infants were screened at the age of 4 to 6 weeks. A prospective analysis in 2019 revealed that the referral rate was 3 to 7 times higher when infants were screened after the 21st day of life.[5,8] Therefore the protocol was adapted. From 2010 onward infants were screened preferably before the age of 3 weeks.

In addition to the neonatal hearing screening protocol, the Vestibular Infant Screening (VIS)-Flanders program was implemented since June 2018. It consisted of a basic vestibular screening of all infants diagnosed with uni- or bilateral permanent hearing impairment of $\geq$ 40 dB after neonatal hearing screening. The screening was performed with cervical Vestibular Evoked Myogenic Potentials (cVEMP) around the age of 6 months. The screening is completed in one of the 21 referral centers that are involved in the UNHS-program. In all centers the Neuro-Audio® commercial device and accompanying software (Neurosoft, Ivanovo, Russia) is used, presenting 500 Hz tone bursts with a rise/fall time of 1 ms and a 2 ms plateau time, intensity level of 59 dB nHL and a stimulation repetition rate of 5 Hz.[9]

Results

From 1998 to 2020 92,6% of all infants born in Flanders (n = 1.377.543) have been screened by Opgroeien - Kind & Gezin and 3,7 % (3,06 – 5,12 %) with a longer hospitalization were screened before discharge from a neonatal intensive care unit. This results in a coverage of 96,3 % (range 91,1 - 98 %) of all children born in the region of Flanders. During the first 3 years of the UNHS program 93,8 $\pm$ 2,5 % of the children were screened, during the last 3 years 96,9 $\pm$ 1,7 %.
A total of 5074 of the newborns (0,37 %) had a unilateral refer and 3664 (0,27 %) a bilateral refer. There was an unsuccessful screening for both steps for 220 children (0,02 %).

For all referred children the age at screening (the second test included) is shown in Figure 1. Most newborns finish the screening between the third and fifth week. There is a small increase over time in the

number of children referred before the age of 5 weeks (Figure 2).

Figure 1 Number of infants referred by age at the second screening step

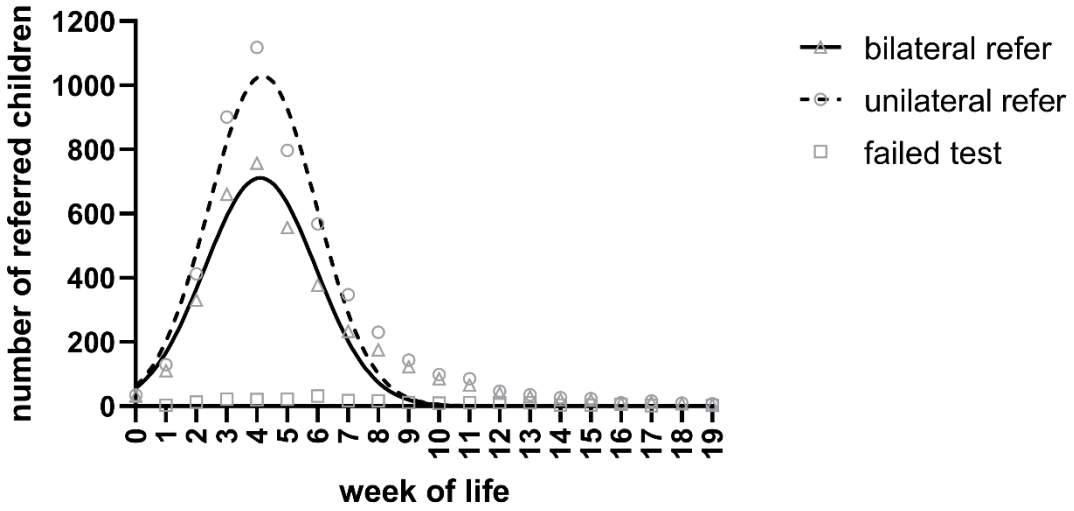
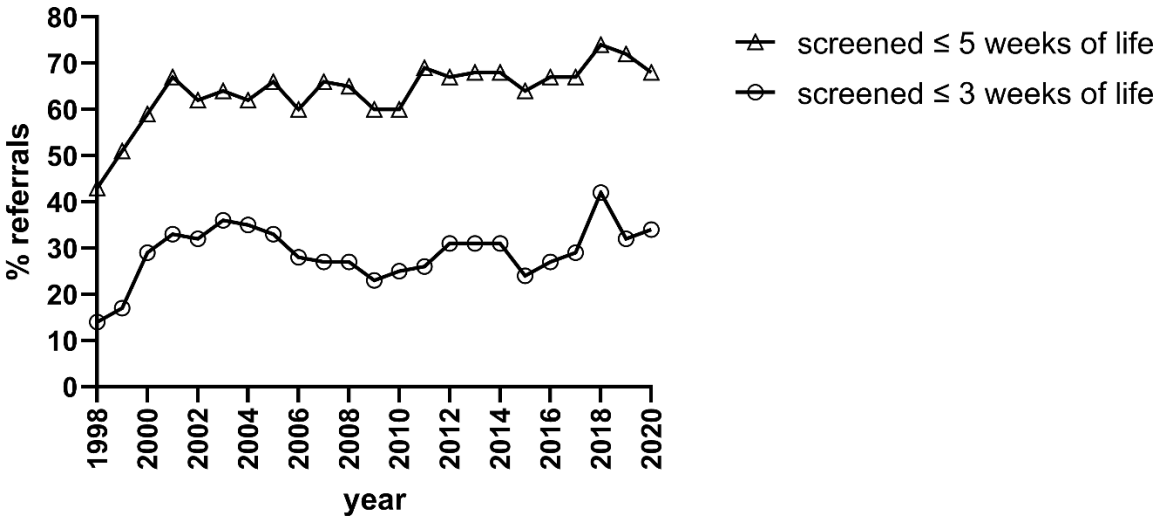


Figure 2: Percentage referred children after the second screening step within 3 and 5 weeks: evolution over time



When pooling the data for the different screening devices, with the ALGO Portable® device there was a unilateral refer of 0,13 % and a bilateral refer of 0,10 %. With the ALGO 3i® 0,4 % of the children had a unilateral and 0,26 % a bilateral refer. The referral rate with the first version of MAICO MB Classic® was 0,56 % (unilateral refer) and 0,44 % (bilateral refer) and with the second version 0,52 % and 0,39 % respectively.

The median time interval between referral after screening and diagnostic assessment was 7 days (n= 2887; range: 0-161). Report 1 with data on the audiological diagnostic workup was available for 95,3 % of the infants, the loss of follow-up for the diagnostic step was 4,7 %.

After referral to the ENT-departments, a sensorineural or mixed hearing loss > 40 dB was confirmed in 2845 infants (incidence 0,2%), a conductive hearing loss in 3503 infants (incidence 0,25%) and 2277 infants had a normal hearing. Of all the referred infants 25 % had a normal hearing, 39 % a conductive hearing loss and 32 % had a

sensorineural or mixed hearing loss. The overall positive predictive value to have a permanent child hearing loss, sensorineural of conductive (PCHL) > 40 dB was 39,3 %.

Table 1 shows detailed results of unilateral, bilateral referral and screening failures over time, as well as the distribution of the confirmed diagnoses (normal hearing, conductive hearing loss, sensorineural/mixed hearing loss and unknown or inconclusive results).

There was no effect of the screening device on the confirmed incidence of unilateral (median 0,6 per 1000; range 0,4 - 0,8) and bilateral sensorineural hearing loss > 40 dB (median 1,3 per 1000; range 0,6 - 2,3), which remained relatively stable over the years (Figure 3). The same goes for the incidence of permanent conductive hearing loss > 40 dB (Figure 4). When looking at the incidence of transient conductive hearing loss ≤ 40 dB there was a 4-fold increase with the ALGO 3i® in comparison to the ALGO Portable® and a doubling with the first version of MAICO MB Classic® (Figure 4).

Table 1: Referred children after screening and outcome of the audiological diagnostic

Year	**N screened**	**N referred (incidence %)**			**N confirmed**			
		Unilateral	***Bilateral***	***Failed***	***Normal***	***Con-ductive***	***Sensorineural or mixed***	***Unknown or inconclusive***
1998	38048	43 (0.11)	20 (0.05)	-	7	-	47	9
1999	57047	71 (0.12)	44 (0.08)	-	15	4	93	3
2000	55900	64 (0.11)	51 (0.09)	-	15	3	91	6
2001	55291	83 (0.15)	50 (0.09)	-	29	1	96	7
2002	58875	72 (0.12)	53 (0.09)	-	20	1	95	9
2003	54349	67 (0.12)	86 (0.16)	-	18	18	115	2
2004	58359	82 (0.14)	64 (0.11)	18 (0.03)	40	7	112	5
2005	58870	97 (0.16)	58 (0.10)	17 (0.03)	21	3	132	16
2006	62365	99 (0.16)	80 (0.13)	22 (0.04)	32	14	129	26
2007	63843	300 (0.47)	165 (0.26)	18 (0.03)	58	174	186	65
2008	65947	310 (0.47)	170 (0.26)	19 (0.03)	80	224	186	9
2009	65087	300 (0.46)	198 (0.30)	11 (0.02)	73	237	196	3
2010	65922	301 (0.46)	223 (0.34)	11 (0.02)	109	282	144	-
2011	65037	298 (0.46)	179 (0.28)	8 (0.01)	108	243	132	2
2012	64602	219 (0.34)	174 (0.27)	7 (0.01)	56	204	139	1
2013	62846	316 (0.50)	196 (0.31)	8 (0.01)	145	252	123	-
2014	62326	318 (0.51)	240 (0.39)	11 (0.02)	156	275	120	18
2015	61250	314 (0.51)	256 (0.42)	7 (0.01)	168	287	114	8
2016	61929	380 (0.61)	343 (0.55)	17 (0.03)	254	326	133	27
2017	59899	401 (0.67)	317 (0.53)	18 (0.03)	272	309	125	30
2018	59531	366 (0.61)	284 (0.48)	15 (0.03)	238	273	126	28
2019	60521	319 (0.53)	230 (0.38)	8 (0.01)	200	213	118	26
2020	59699	254 (0.43)	183 (0.31)	5 (0.01)	163	153	102	24
Total		**5074 (0.37)**	**3664 (0.27)**	**220 (0.02)**	**2277**	**3503**	**2845**	**324**

Figure 3 Confirmed incidence of unilateral and bilateral sensorineural hearing loss (SNHL) > 40 dB in relation to the screening devices

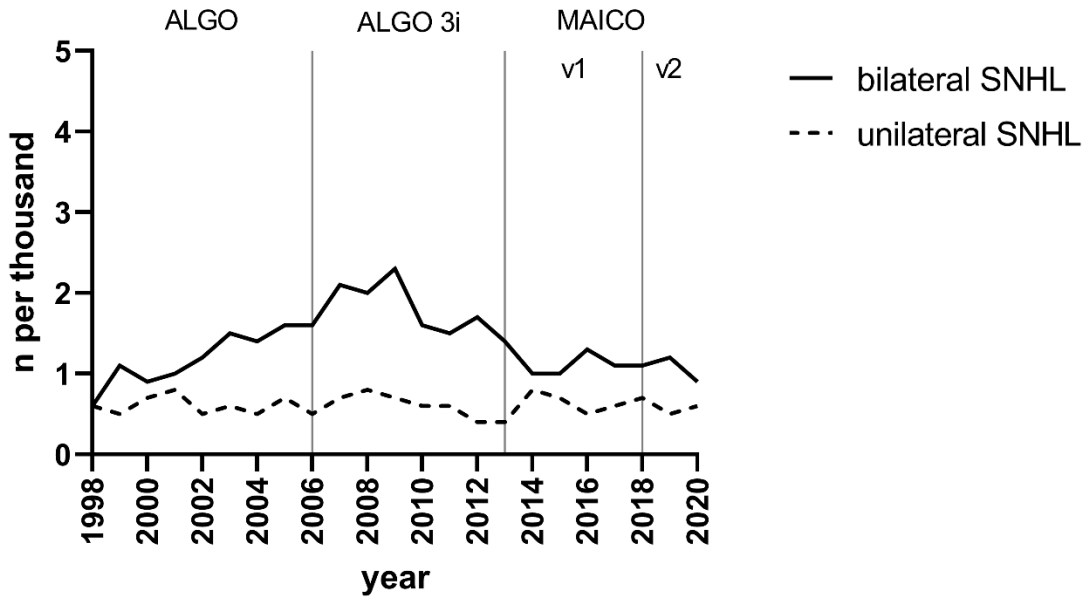
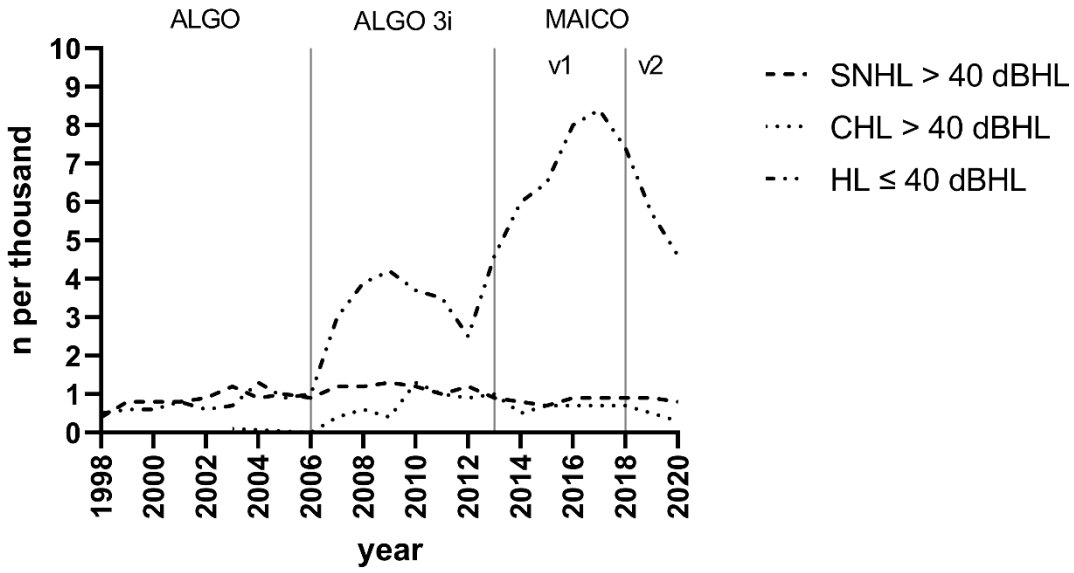
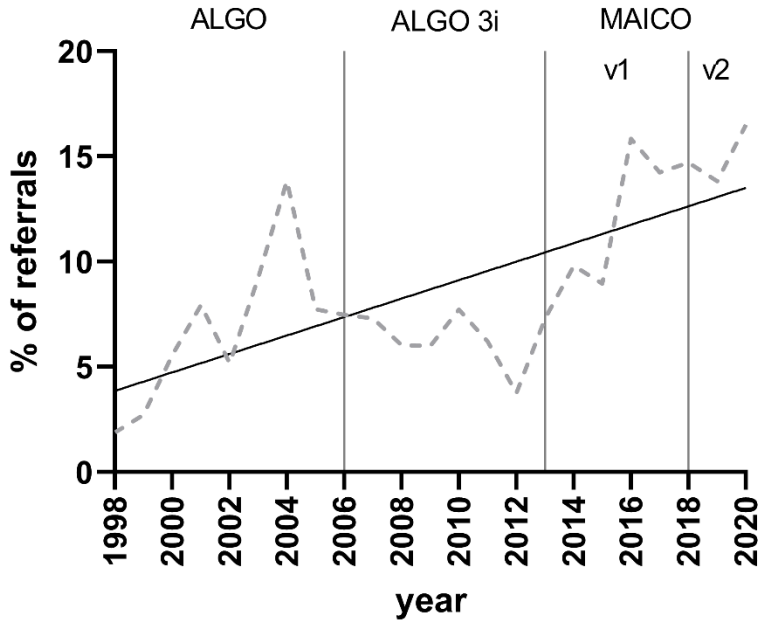


Figure 4: Incidence of sensorineural hearing loss (SNHL), conductive hearing loss (CHL) > 40 dB and mild hearing loss (HL) in relation to the screening devices



The percentage of referred children with the final diagnosis of normal hearing or mild hearing loss ≤ 40 dB (false positive) is shown in Figure 5. There is an increase with MAICO MB Classic®.
The positive predictive factor (PPV) to have a PCHL (sensorineural of conductive) > 40 dB was 66 % with the ALGO Portable®, 46,7 % with the ALGO 3i®, 28,1 % with the first version of the MAICO MB Classic® and 29,9 % with the second version.

Figure 5: Evolution of false-positive results after referral (normal or mild hearing loss ≤ 40 dB) over the years



A permanent sensorineural hearing loss was diagnosed in 2951 children, 48,4 % of them had a symmetrical hearing loss > 40 dB, in 20 % there was a bilateral hearing loss > 70 dB and 11,6 % had a profound bilateral hearing loss. The distribution of the asymmetrical sensorineural/ mixed hearing losses is shown in Table 2. In the group of 3480 children with conductive hearing loss, 58,6 % had a mild and 39,4 % a moderate unilateral or bilateral hearing loss.

Table 2 Distribution of sensorineural/mixed hearing loss (n=2921)

		Left ear				
		Normal	***Mild***	***Moderate***	***Severe***	***Profound***
Right ear	***Normal***	-	2.6%	5.5%	2.7%	4.2%
	Mild	3.0%	9.7%	3.3%	0.9%	1.0%
	Moderate	5.8%	4.1%	22.0%	2.4%	1.0%
	Severe	2.6%	1.4%	1.8%	6.5%	0.8%
	Profound	3.6%	1.3%	1.2%	1.1%	11.6%

An etiological workup was already published by 3 university ENT departments responsible for 48 % of the referred infants from the UNHS-program, n=569 referred to Leuven[10] between 1997 and 2011, n=802 to Gent[11] between 2007 and 2019 and n=1002 referred to Antwerp[12] between 1998 and 2019.

The pooled data showed a loss of follow-up for 110 infants (4,6%). After diagnostic work-up 1404 infants (59%) finally had a normal hearing, 36,4 % of them after a temporary hearing loss. A PCHL ≥ 40 dB was bilateral in 59 % of the cases and unilateral in 41 %. 1365 infants were diagnosed with PCHL, 8,4 % of them had a conductive hearing loss due to an anomaly of the outer and/or middle ear. Genetic causes were responsible for 31,3 % of PCHL, 18,2 % syndromic, 9,8 % non-syndromic due to a mutation in the GJB2-gene. ASND was diagnosed in 5,3 % and non-genetic disorders of the inner ear and cochlear nerve in 6,1 %. No etiology could be found in 38,8 % of infants with PCHL.

Long-term results of the UNHS and treatment on language development and education level are available for 229 out of 280 children (81,7%) with a bilateral referral within the first 6 years of the UNHS program (1998 - 2003).[4,8] In 177 children a PCHL ≥ 40 dB was diagnosed, 52 had a normal or

mild hearing loss. 108 children were fitted with hearing aids and 67 received cochlear implants. 70 children had additional disabilities. As the number of additional disabilities increased, there was a statistically significant decrease in the odds of being in mainstream education. Analysis showed that 85,4 % of the children with moderate, severe or profound hearing loss and without additional disability, older than 5,5 years, reached mainstream education. Of all cochlear implant children above 5,5 years, without additional disabilities, 78,9 % attended mainstream education. Data on language development were available for 80 % of the children and showed a normal language development in 34,5 % of the children, a slight delay in 18,5 %, a moderate delay in 15,7 % and a severe delay in 12,2 %.[4,8]

The first results of 1,5 year Vestibular Infant Screening (VIS)-Flanders[9] were published in 2020. A total of 210 infants were detected with a PCHL in that period, 169 (91,8 %) of the infants had a permanent uni- or bilateral sensorineural and 15 a permanent uni- or bilateral conductive hearing loss. A vestibular screening was performed in 182 (86,7 %) infants. All infants with conductive hearing loss passed the test. For the infants diagnosed with sensorineural hearing loss there was a referral rate of 9,5 %. Unilateral or bilateral refer after vestibular screening occurred significantly more in infants with uni- or bilateral severe to profound hearing loss (> 71 dB) compared to infants with unilateral mild to moderate hearing loss (21-70 dB) (p=0,003).[9] The 3-year results are currently analyzed and will be published later this year.

Discussion

In the 2007 position statement of the JCIH several benchmarks were set for UNHS programs. It is recommended that more than 95 % of all newborns are screened before the age of 1 month. The benchmark for referral after screening is less than 4 %. After referral the recommended benchmark for audiological evaluation is 90 % and for those with confirmed bilateral hearing loss who need amplification 95 % to receive it within one month after confirmation of the hearing loss.[13] As already mentioned an initial benchmark for screening, audiological diagnosis and intervention timing was 1-3-6 months and later 1-2-3 months.[7]

In Flanders around 93 % of the children are screened by Opgroeien Kind & Gezin and about 3,7 % are screened in a hospital, resulting in a coverage of 96,3 % (range 91,1 – 98%), meeting the benchmark of the JCIH. The coverage was already high during the first years and remained relatively stable over the years, with a slight increase during the last years.

Neuman et al, 2021 assessed the hearing screening protocols around the world for 158 countries, representing 95 % of the world's population.[14] They showed that less than one-third of the world's newborns were enrolled in UNHS programs covering at least 85 % of all babies.[14] In the EUSCREEN project[15] the pooled coverage range for all children (high and low-risk) was 97,9 % and the median 96 % (range 79-100 %) for 26 European NHS programs plus Russia, Malawi, Rwanda, India and China.[16] Moreover 20 out of 26 programs had a coverage of 95 % or higher.

The referral rate after screening is depending on several factors, e.g. the timing of screening, the screening method and the number of screening steps. The goal is to achieve a low referral rate, but also not to miss children with PCHL.
Lower referral rates reduce subsequent burden and costs of audiological and medical diagnostic and may lead to a reduction of the loss of follow-up.[16] False-positive results are mainly due to temporary conductive hearing loss.[16] The positive predictive value of PCHI after referral should be as high as possible.

A variety of objective screening measures are used to conduct UNHS. These include transient evoked otoacoustic emissions (TEOAEs), distortion product otoacoustic emissions (DPOAEs), automated auditory brainstem response (AABR) or a combination of both. The otoacoustic emissions are generated from the outer hair cells in the cochlea and can only provide information on the cochlear function. The AABR gives information on the peripheral auditory pathway from the ear to the brainstem.

TEOAEs are the most commonly used screening method in NHS programs worldwide as they are easier to conduct, have a shorter test time and are considered less expensive in terms of the need for consumables[15]. The inclusion of AABR or diagnostic ABR decreases the false positive rates as well as the referral rates. With exclusive use of OAE babies with auditory neuropathy spectrum disorders (ANSD) may be missed.[6] The reported incidence of

ASND in universal newborn screening is 0,027–0,06%, for NICU babies an incidence of 5,3-14,8 % was found.[7,12,18] The pooled incidence of ASND in our UNHS program was 5,3 % of all referred cases, but this may be an underestimation.

The percentage of deliveries in a health care facility was > 90 % in most countries in the EUSCREEN project, assessing hearing screening programs across 47 mainly European countries, in Flanders 81 % of the deliveries take place in a hospital.[10,16] In most UNHS programs step 1 screening is done in the hospital (maternity ward or NICU). Out of 39 screening programs 3 performed the first step within 24 hours after birth, 29 between 42 and 72 hours and 7 more than 72 hours after birth.[15]
Different screening protocols are being applied with 1 to 3 steps using OAE, AABR or a combination of both. In some programs a dual-protocol is followed, which means that high-risk infants in NICU are screened using a different protocol as compared to low-risk infants. In Flanders the NICU children are tested with the same protocol (AABR or diagnostic ABR) and the results are also integrated into the database of Opgroeien Kind & Gezin. In the EUSCREEN project 20 programs only use OAE for UNHS in a 1-3 steps procedure, 15 use a combination of OAE en AABR in a 2 to 4 step procedure and only 2 use AABR in a 1 or 2 step procedure.[15] For high-risk infants AABR is used by 27 programs in 1 to 3 steps. In a worldwide evaluation of 158 countries Neumann et al 2021 showed that OAE was the preferred method in 57% of the countries, followed by OAE-AABR (30 %) and AABR only (11 %).[14] We use a two-step procedure with AABR on both occasions > 72 h and before 3-6 weeks after birth.

Data on referral rates are available for the different steps in the EUSCREEN project.[16] For ten programs, the pooled referral rate from step 1 was 9% (median 8,4%, range 3,5-12,2%) and the pooled final referral rate from screening to diagnostic assessment was 2,6 % (median 1,5%, range 0,3-3,5 %). They also made an analysis of final referral rates in relation to the study design. For low-risk infants the final referral rate was 2,1 % (2,09-2,12) for programs with OAE only in 1 or 2 steps and 1,66 % (1,60-1,73 %) for 2 steps including AABR and 0,8 % (0,78-0,83%) for 3-4 steps including AABR. Increasing the number of screening steps, using AABR instead of OAE and/or delaying step 1 may help to reduce the overall referral rate.[16,17] Screening within 24 hours after birth may result in a high referral rate because of amniotic fluid in the middle ear. In the EUSCREEN project the referral rate was 6-22 % when screening was performed < 24 h from birth, 2-15 % between 24 and 75 h after birth and 4 % > 72 h.[14] From our program only data on the second step are available with referral rates corresponding to the results of 3-4 steps screening including AABR in the literature.

Within our UHNS program the actual goal is to screen before the age of 3 weeks. A retrospective analysis of the data from 2003 till 2007 showed that the later the screening was performed, the higher the incidence of referral was.[5] This was confirmed in a prospective study in 2009, the percentage of referrals after the second test was 3,7 times higher for screening after 21 days of age than in earlier screening. The higher incidence is probably due to temporary hearing impairment caused by secretory otitis media.[5]

In our program a two-step AABR protocol is used with a detection level set at > 35 dB. Despite the same detection level and same screening strategy differences could be found across different screening devices used over time. With the change from the ALGO portable® device to the ALGO 3i® device, the referral rate increased from 0,31 % to 0,76 % with a sixfold increase of false positives, mainly consisting of children with mild temporary conductive hearing impairment.[19] Analysis of both devices showed a mean stimulus level of 59,2 dBSPL(A) (SD= 0,5 dB) for the Algo Portable® and 55,6 dBSPL(A)(SD 0,3 dB) for the ALGO 3i® device. The decrease in stimulus level of 4,6 dB with the ALGO 3i® device results in an increased sensitivity and is the main reason for the additional detection of mild temporary hearing impairments along with a different stimulus spectrum and unexplained irregularities during 4 % of the stimulation time.[19] The ALGO 3i was replaced by the MAICO MB 11 classic® device in 2013 which uses a combination of AABR and ASSR. The CE-Chirp® stimulus has an intensity of 35 dBnHL. This again resulted in a doubling detection of temporary mild conductive hearing loss. The broader frequency range of the combined AABR/ASSR approach with detection of more low- frequency hearing loss may explain the difference.

Our referral percentage increased from 0,13 % to 0,52 % for unilateral refer and from 0,10% to 0,39% for bilateral refer.

For most UNHS programs the level for referral is set at ≥ 35 or ≥ 40 dB HL.[16] Neumann et al, 2021 have defined permanent childhood hearing loss (PCHL) as a permanent hearing loss of ≥ 20 dB HL in the better ear for bilateral hearing loss or in the worse ear for unilateral hearing loss.[14] This is in line with the new classification published by the WHO[20] in the World Report on Hearing in 2021. In the study by Butcher et al, 2019 it was defined as ≥ 26 dB HL.[21] In the study of Mackey et al, 2021 PCHL was defined as ≥ 40 dB.[16] Since the detection levels for most screening programs are ≥ 35 or ≥ 40 dB HL, mild hearing losses between 20 and 40 dB may be missed and also for our screening program it is only possible to present reliable data on permanent hearing losses ≥ 40 dB. Our results showed an increase in the referral rate from 0,31 % to 0,76 % with the change from ALGO Portable® to ALGO 3i® with a sixfold increase in false positives due to temporary hearing loss by lowering the detection threshold with 4,6 dB, but an unchanged prevalence of permanent sensorineural hearing loss. Further studies are necessary to establish the optimal detection threshold for AABR devices to optimize the detection of permanent mild hearing losses but also to control the burden of audiological diagnostic caused by temporary hearing loss and false-positive results.

An important issue is the loss of follow-up between hearing screening and the audiological diagnostic step. Depending on the screening program, patients are referred to a diagnostic center or need to make an appointment themselves. Strict case management and monitoring of the screening and diagnostic process are very important, but sometimes time-consuming. In our program this is done by a dedicated team of Opgroeien Kind & Gezin.[5]

A benchmark of 90% is set by the JCIH for the diagnostic step.[13] In a review of 53 articles published between 2005 and 2015 the observed overall rate of loss to follow-up after UNHS was 21 % (11,5 – 41,4 %) in multicenter studies.[22] In the EUSCREEN project the pooled rate of diagnostic assessment after referral was 72 % (median 89 %, range 19-97 %) for 12 programs with sufficient data. In one-third of the programs the referral rate was 90 % or higher.[16] A median of 93 % (86-100%) of screen-positive children attended diagnostic testing in 21 studies from highly developed countries.[21] In our study there is only a loss of follow-up of 4,7 % due to the dedicated team of Opgroeien Kind & Gezin with tracking of loss of follow-up resulting in a referral rate for the diagnostic step of 95,3 %, in accordance with the benchmark of the JCIH.

Butcher et al, 2019 analyzed the positive predictive value (PPV) for UNHS studies from very high developed countries.[21] For all studies the positive predictive value to have a bilateral PCHL ≥ 26 dB ranged between 2 % and 84 %.[21] They looked at the PPV for studies that only used OAE (n=7), only ABR (n=4) or a combination of both (n=14). For OAE median PPV was 7 % (1,6 - 22,2), for ABR it was 13,3 % (4,9-27,9) and for the combination 24,8 % (range 2,3-83,5). Because of the large variation no statistical analysis was performed.[21] Our results confirm the dependence on the screening device used with a PPV to have a PCHL > 40 dB of 66 % with the ALGO Portable®, 46,7 % with the ALGO 3i®, 28,1 % with the first version of the MAICO MB Classic® and 29,9 % with the second version.

The pooled prevalence of bilateral PCHL ≥ 26 dB was 1,1 (0,9 - 1,3) per 1000 screened children for 41 studies. There was no association between screening protocol type and detected prevalence of bilateral PCHL, indicating that the reported variation in referral rates has little impact on the number of detected cases.[21]
In the EUSCREEN project the detection rate of PCHL ≥ 40 dB varied between 0,7 and 3 per 1000 births (median 1,16) for bilateral hearing loss and between 0,28 and 0,72 (median 0,43) for unilateral hearing loss ≥ 40 dB. In our UNHS program the prevalence was 1,3 per 1000 for bilateral sensorineural hearing loss > 40 dB and 0,6 per 1000 for unilateral sensorineural hearing loss.

Hearing type loss is categorized as sensorineural, mixed, ANSD, transient conductive or permanent conductive. There are only scarce reports on the type of hearing loss. In our program 25 % of the referred children had a normal hearing, 39 % a conductive hearing loss and 32 % a sensorineural or mixed hearing loss. The screening program in Queensland Australia is comparable with our program (two-step AABR screening with ALGO 3® and 3i® devices from Natus, California). Between 2006 and 2017 they reported a referral rate of 1,1 %.[23] On a total of 6735 hearing impaired children a uni- or bilateral PCHL of > 25 dB HL was detected in 20,30 % of the children, a normal hearing or transient conductive hearing loss in 67,88

% of the cases and there was no diagnostic outcome in 11,82 % of the children.[23] Although they defined PCHL > 25 dB we found a higher incidence of PCHL, the number of children with normal and transient conductive hearing loss is comparable.

The vestibular screening with cVEMP was started in 2018 for all children diagnosed with a uni- or bilateral permanent hearing impairment of ≥ 40 dB after neonatal hearing screening and performed around the age of 6 months. As far as we know this is the first general vestibular screening reported. Previous studies mainly focused on older children with severe to profound hearing losses, incidences of vestibular dysfunction in children with hearing loss are reported between 20 and 85 %.[24] Children with vestibular dysfunction show delayed development of gross motor milestones, which is an important reason for early detection and treatment.[9] The incidence of vestibular dysfunction measured by cVEMP was 9,5 % in the first 3 years but significantly higher in children with severe or profound hearing loss in accordance with the literature.[9,24] Since cVEMP only tests the sacculus, further testing at a later age is necessary to confirm the results and test the other parts of the vestibular system.

Conclusion

The UNHS-program in Flanders is running since 1997 with a high coverage, low referral rate and a low percentage of loss to follow-up. The screening is conducted and monitored by the Flemish public child care organization with a two-step AABR screening procedure mainly at an outpatient base. Central organization of monitoring and follow-up have proven to be essential for the program's success. Over the years screening shifted progressively towards an earlier age and mainly before 3 weeks. Different screening devices have been used over time and had a major effect on the detection of temporary conductive hearing losses and false-positive cases. The incidence of permanent sensorineural hearing loss was independent of the screening device and in line with published results. Further studies are necessary to establish the optimal detection threshold for AABR devices to optimize the detection of permanent mild hearing losses but also to control the burden of audiological diagnostic caused by temporary hearing loss and false-positive results. A big challenge is the long-term follow-up of the children with confirmed PCHI till through school age, since the follow up of the children by Opgroeien - Kind & Gezin ends at the age of 2,5 years.

Conflicts of Interest Statement

The authors have no conflicts of interest to declare.

References

1. Morton CC, Nance WE. Newborn hearing screening – a silent revolution. *N Engl J Med*. 2006;354(20):2151-2164.
2. Willems PJ. Genetic causes of hearing loss. *N Engl J Med*. 2000;342:1101-1109.
3. Joint Committee on Infant Hearing. 1994 Position Statement. *Int J Pediatr Otorhinolaryngol*. 1995;32 :265-74. doi: 10.1016/0165-5876(95)90066-7.
4. Verhaert N, Willems M, Van Kerschaver E, Desloovere C. Impact of early hearing screening and treatment on language development and education level: evaluation of 6 years of universal newborn hearing screening (ALGO) in Flanders, Belgium. *Int J Pediatr Otorhinolaryngol*. 2008;72(5):599-608. doi: 10.1016/j.ijporl.2008.01.012. Mar 4, 2008.
5. Van Kerschaever E. Universal neonatal hearing screening in Flanders reveals socio-demographic risk factors for hearing impairment. *B-ENT*. 2013;9 Suppl.21:3-8.
6. Joint committee on infant hearing. Year 2000 position statement: principles and guidelines for early hearing detection and intervention programs. *Am J Audiol*. 2000;9:9-29.
7. Joint Committee on Infant Hearing. Year 2019 position statement: principles and guidelines for early hearing detection and intervention programs. JEHDI.2019;4(2):1-44.
8. Desloovere C, Verhaert N, Van Kerschaver E, Debruyne F. Fifteen years of early hearing screening in Flanders: impact on language and education. *B-ENT*. 2013;Suppl 21:81-90.
9. Martens S, Dhooge I, Dhondt C et al. Vestibular Infant Screening (VIS)-Flanders: results after 1.5 years of vestibular screening in hearing-impaired children. *Sci Rep*. 2020;10(1):21011. doi: 10.1038/s41598-020-78049-z. Dec 3, 2020
10. Lammens F, Verhaert N, Devriendt K, Debruyne F, Desloovere C. Aetiology of congenital hearing loss: a cohort review of 569 subjects. *Int J Pediatr Otorhinolaryngol*. 2013;77(9):1385-91. doi: 10.1016/j.ijporl.2013.06.002. Jul 5, 2013.
11. Acke FR, De Vriese C, Van Hoecke H, De Leenheer EM. Twelve years of neonatal hearing screening: audiological and etiological results. *Eur Arch Otorhinolaryngol*. 2021 doi: 10.1007/s00405-021-07060-5. Aug 31, 2021.
12. Boudewyns A, van den Ende J, Declau F et al. Etiological work-up in referrals from neonatal hearing screening: 20 years of experience. *Otol Neurotol*. 2020;4:1240-1248. doi: 10.1097/MAO.0000000000002758
13. Joint committee in infant hearing. Year 2007 position statement: Principles and guidelines for early hearing detection and intervention programs. *Pediatrics*. 2007;120(4):898-921. doi: 10.1542/peds.2007-2333.
14. Neumann K, Mathmann P, Chadha S, Euler HA, White KR. Newborn hearing screening benefits children, but global disparities persist. *J Clin Med*. 2022;11:271.doi: 10.3390/jcm11010271. Jan 5, 2022.
15. Bussé AM, Mackey AR, Hoeve HL et. Assessment of hearing screening programmes across 47 countries or regions I: provision of newborn hearing screening. *Int J Audiol*. 2021;60(11):821-830. doi: 10.1080/14992027.2021.1886350. Mar 10, 2021.
16. Mackey AR, Bussé AM, Hoeve HL et al. Assessment of hearing screening programmes across 47 countries or regions II: coverage, referral, follow-up and detection rates from newborn hearing screening. *Int J Audiol*. 2021;60(11):831-840. doi: 10.1080/14992027.2021.1886351. Mar 9, 2021.
17. Kanji A, Khoza-Shangase K, Moroe N. Newborn hearing screening protocols and their outcomes: a systematic review. *Int J Pediatr Otorhinolaryngol*. 2018;115:104-109. doi: 10.1016/j.ijporl.2018.09.026. Sep 25, 2018.
18. Korver AM, van Zanten GA, Meuwese-Jongejeugd A, van Straaten HL, Oudesluys-Murphy AM. Auditory neuropathy in a low-risk population: a review of the literature. *Int J Pediatr Otorhinolaryngol*. 2012;76(12):1708-11. doi: 10.1016/j.ijporl.2012.08.009. Aug 31, 20212.
19. Hofmann M, Luts H, Poelmans H, Wouters J. Investigation of a significant increase in referrals during neonatal hearing screening: a comparison of Natus ALGO Portable and ALGO 3i. Int J Audiol.2012;51(1):54-57.
20. World Health Organization. World Report on Hearing; World Health Organization: Geneva, Switzerland, 2021. Available online:

https://www.who.int/publications/i/item/world-report-on-hearing

21. Butcher E, Dezateux C, Cortina-Borja M, Knowies RL. Prevalence of permanent childhood hearing loss detected at the universal newborn hearing screen: systematic review and meta-analysis. *PLoS ONE*. 2019;14(7):e0219600. doi: 10.1371/journal.pone.0219600. eCollection 2019 Juli 11, 2019.
22. Ravi R, Gunjawate DR, Yerraguntla K, Lewis LE, Driscoll C, Rajashekhar B. Follow-up in newborn hearing screening - A systematic review. *Int J Pediatr Otorhinolaryngol*. 2016;90:29-36. doi: 10.1016/j.ijporl.2016.08.016. Aug 26, 2016.
23. Fitzgibbons EJ, Driscoll C, Myers J, Nicholls K, Beswick R. Predicting hearing loss from 10 years of universal newborn hearing screening results and risk factors. *Int J Audiol*. 2021;60:1030-1038. doi: 10.1080/14992027.2021.1871975. Feb 16, 2021.
24. Verbecque E, Marijnissen T, De Belder N et al. Vestibular (dys)function in children with sensorineural hearing loss: a systematic review. *Int J Audiol*. 2017;56(6):361-381. doi: 10.1080/14992027.2017.1281444. Feb 13, 2017.