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Effectiveness and Efficiency of a Universal Newborn Hearing Screening in Germany

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Key Words
Newborn hearing screening · Infant hearing · Universal newborn hearing screening · Hearing impairment

Abstract
The decision to mandate, finance, and implement a universal newborn hearing screening (UNHS) requires the evaluation of its therapy-directed benefit by comparing (1) a procedure employing a UNHS with (2) a targeted screening for at-risk babies for neonatal hearing disorders and (3) a procedure without systematic screening. In a cohort study the outcome of the UNHS program of Hessen in 2005 with 17,439 screened newborns was analyzed. Validity, effectiveness, and efficiency were evaluated and compared to a sample of 98 Hessian and 355 German children who were detected in 2005 as hearing-impaired but not by an UNHS. The UNHS group had a PASS rate of 97.0%. Forty-nine hearing-impaired children were diagnosed at a median age of 3.1 months and treated at a median age of 3.5 months. Corresponding values for the Hessian non-UNHS group were 17.8 and 21.0 months. For Germany the median age at diagnosis was 39.0 months. The age at therapy onset correlated negatively with parameters of speech/language and psychosocial development. A targeted screening would have resulted in a low sensitivity of 65.3%. Hence, a UNHS is the most effective way to an early therapy of neonatal hearing disorders with an optimal outcome.

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Introduction

About 1–2 per 1,000 children suffer from a neonatal bilateral permanent hearing loss that requires therapy [1]. For best therapy outcome infant hearing loss has to be treated as early as possible, before basal maturational processes of the auditory pathway are terminated [2]. Speech, language, and learning abilities correlate with early therapy onset, and late treatment leads to delayed speech and language development, learning disturbances, emotional and psychosocial disturbances, and negative consequences for the families [3]. Fifty-six percent of Hessian children treated with a cochlear implant between the ages of 3 and 6 years do not receive regular schooling but need special education for hearing-impaired children, but only 24% of the children treated before age 3 require special education [4].

For early detection and intervention of neonatal hearing disorders a universal newborn hearing screening (UNHS) has been recommended in several international position papers [5–8]. In many countries a UNHS is already implemented and mandated. In Europe, such a screening covers already over 90% of the newborns in 10 countries. In Germany legislative efforts are currently undertaken to make a universal hearing screening a regular procedure for each newborn. Recommendations for such a screening have recently been issued [9–11].

In the state Hessen a UNHS program has been developed which largely meets international quality criteria [12]. These criteria are: (1) coverage of at least 95% of the newborns, (2) use of a procedure with a REFER (positive result) rate of less than 4%, (3) referral of at least 95% of the REFER cases to confirming diagnostics (follow-up) by a tracking system, (4) structured organization of the follow-up, (5) diagnosis within 3 months of life, therapy onset within 6 months, and (6) quality control through a central database and by training and supervision of the screening staff.

Up to the end of 2005, in 49 of 86 Hessian birth institutions (maternity and neonatal clinics) an inpatient UNHS program was implemented including a daily data transfer from the screening devices to the database. In order to achieve a low referral rate, and considering that an increasing number of newborns is released within 24 h from the maternity wards, a two-stage transient evoked otoacoustic emission-automated auditory brainstem response (TEOAE-AABR) screening protocol is recommended for well babies without risk factors for neonatal hearing disorders, and an AABR for children on neonatal intensive care units (NICUs). Parents of babies who failed the screening are provided with address lists of follow-up institutions, a screening report, an identification number, and a notice in their baby-examination booklet. A tracking by a Hessian screening center ensures that parents who did not contact a follow-up institution within 2 weeks after a final REFER receive up to two reminder letters and – if necessary – one or more telephone calls. The screening staff gets a certified training and supervision by the screening center which also maintains a hotline.

For the decision to implement, mandate, and finance a UNHS, its therapy-related use has to be evaluated, e.g. by comparing (1) a procedure using a systematic UNHS with (2) a targeted screening of babies at risk for neonatal hearing disorders and (3) a procedure without systematic screening [13]. At-risk babies are mostly to be found in NICUs. Factors which increase the risk for a neonatal hearing disorder to 1–3% have been listed elsewhere [8, 14].

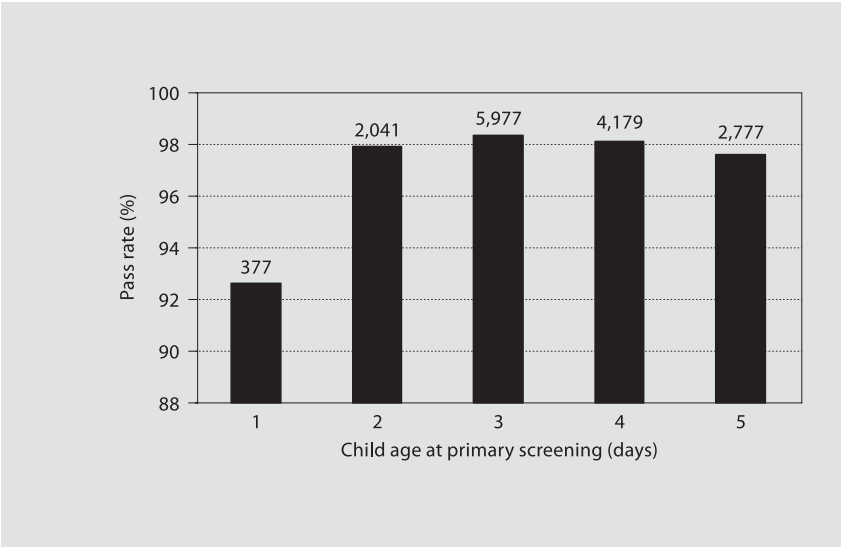

Fig. 1. PASS rates for day of life at screening (figures in columns: number of children screened).

To evaluate the validity, effectiveness, and efficiency of a German UNHS program, the 2005 outcome of the Hessian program was analyzed in a cohort study and compared to possible results of a targeted screening in Hessen. In addition, the Hessian outcome data were compared with Thuringian data (no UNHS) and with nationwide 2005 data from all states, most of them without a UNHS (German non-UNHS group). In order to quantify the effects of early detection and therapy onset, the age at therapy onset was correlated with parameters of speech/language, emotional, psychosocial, and cognitive development in a sample of hearing-impaired children who had not received a systematic screening. Furthermore, two subgroups of children with and without hearing screening were compared with respect to parental evaluation of the children's overall speech and language abilities.

Methods

Participants

This study included two groups, one which had received a UNHS (UNHS group), the other one with hearing-impaired children detected outside a UNHS (non-UNHS group). The UNHS group included all 17,439 screened children whose datasets had been sent to the UNHS database of Hessen in 2005 by 46 maternity clinics and three NICUs. The data of a total of 18,207 children born in these institutions were stored in the database of 2005. The screening was missed by 768 newborns because of early maternity ward discharge (n = 658) or parental refusal to screen (n = 110). Child age at screening (median 2.8 days, range 0–142) is given in figure 1.

Table 1. Mean and median ages at diagnosis and therapy of a bilateral infant hearing loss for the Hessian and the German-wide non-UNHS groups

Hearing loss	Hessian non-UNHS group			German non-UNHS group		
	n	mean (median) age[1] at		n	mean (median) age[1] at	
		diagnosis	therapy		diagnosis	therapy
All degrees	95	25.7 (17.8)	29.1 (21.0)	325	39.0 (33.0)	n.a.
Mild	11	44.1 (43.0)	49.4 (45.0)	96	72.0	73.0
Moderate	24	32.8 (31.0)	37.8 (43.0)	140	39.0	39.0
Severe	13	23.2 (17.5)	23.8 (19.0)	32	12.0	13.0
Profound	47	16.4 (13.0)	19.7 (13.8)	57	15.0	16.0

[1] Age in months.

The non-UNHS group consisted of 98 children (54 male, 44 female; median age 8;2 years, range 1;8–17;2) treated between 1991 and 2005 in our clinic for permanent hearing loss. These children were referred from roughly the same region as the UNHS group. Ninety-five children had a bilateral and 3 a unilateral hearing loss. The distribution of the bilaterally hearing-impaired children over the degrees of hearing loss, namely mild (pure-tone average hearing threshold for 0.5, 1, 2, and 4 kHz: ≤40 dB HL), moderate (40–69 dB HL), severe (70–94 dB HL), profound (>95 dB HL) are shown in table 1. For the monaurally hearing-impaired, the hearing loss was moderate in all 3 cases. In 88 cases the hearing loss was sensorineural, in 7 cases conductive, and in 3 cases mixed. From the children with binaural hearing loss, 60 wore air conduction hearing aids binaurally and 1 monaurally; 1 wore bone-anchored hearing aids binaurally; 25 had cochlear implants unilaterally, and 2 had undergone hearing-enhancing surgery on both ears.

Since the UNHS in Hessen has been implemented just recently, relevant developmental data of the children are not yet available. The developmental prognosis of the UNHS-detected hearing-impaired children can thus be estimated only indirectly on the basis of the developmental data from the non-UNHS group for which developmental data are available, assuming comparability of both groups. If it can be shown in the UNHS group that developmental achievements are correlated negatively with age at detection of hearing impairment, a case can be made for earliest possible detection. Additionally, within the non-UNHS group a subsample of all 15 children (median age 40.8 months, range 20–159) who had received a nonsystematic screening was compared with an age-matched sample of 84 children without a hearing screening (median age 101.3 months, range 27–206) with respect to developmental outcome. In order to compare the effectiveness of universal with targeted screening, the proportion of at-risk children with permanent hearing loss from all hearing-impaired children was calculated for both groups, UNHS and non-UNHS.

Procedure

UNHS Group

Of the 17,439 screened children, 17,383 were tested binaurally and 56 monaurally (34,822 screened ears). Seven hundred and thirty-nine newborns received a sole AABR screening (736 bilateral, 3 monaural test), 3,750 a sole TEOAE screening (3,741 bilateral, 9 monaural), and 12,950 a two-stage TEOAE-AABR screening, which involves an AABR screening only if the

child has failed an initial TEOAE screening (12,901 bilateral, 41 monaural). The screening devices used (Echo-Screen-TA Plus C®, Fischer-Zoth Diagnosesysteme GmbH) allowed both TEOAE and AABR measurements. Only one clinic had a sole TEOAE device. The screening protocol prescribed a binaural two-stage screening for well babies (mature babies without risk factors for neonatal hearing disorders) on maternity wards and at least an AABR screening for babies in NICUs. The 4.2% babies (739 out of 17,439) screened with AABR are roughly equivalent to the proportion of at-risk babies from the general population. From the babies who got a TEOAE test alone, time limitations prevented subsequent AABR in 3,627 cases, and 123 babies were screened by the institution that had a TEOAE device only. The tests were performed mostly by nurses or midwives.

Current hearing screening procedures employ statistical algorithms that deliver an automated PASS/REFER decision. Thus, test results are objective and not judged by the screening staff. In case of a PASS, no reference test was done, for a REFER after one or more tests, a confirming diagnostic including a frequency-specific auditory brainstem response (ABR) as a reference method was performed by pediatric audiologists.

The algorithm of the Echo-Screen TA uses a signal statistical procedure of averaging the positive and negative polarity of a signal curve which occur with the same probability for noise but not for a true signal like TEOAE. The predominance of one polarity is tested against random distribution with binomial statistics. For TEOAE, the measurement stops if a probability level of 99.7% is reached at eight positions in the polarity average (PASS criterion). The AABR algorithm uses template matching in addition to the binomial statistics. Both methods stop the test with a REFER if after a certain number of recorded test frames the PASS criterion is not reached (first cutoff criterion). The test is also stopped if after about half of maximum test time a lower level of significance is not reached. In this case it is assumed that a PASS would not have been reached within the rest of the maximum test time (second cutoff criterion). The maximum test time is also adjusted to noise level (TEOAE) or EEG level (AABR). Both methods use short transient stimuli, 75 dB SPL for TEOAE and 35 dB normalized hearing level (nHL) for AABR. The TEOAE procedure issues a REFER for hearing losses of more than 30 dB (detection threshold) between 1.5 and 4 kHz because with higher hearing losses TEOAE are not detectable any longer [15]. The frequency range of the AABR stimulus is 1–4 kHz. Because its level is 35 dB nHL, the detection threshold is <35 dB HL.

For the UNHS group the following parameters were evaluated: test duration; child age at screening, at follow-up onset, at diagnosis, and at therapy onset; PASS rate (proportion of negatively screened children); REFER rate (proportion of positively screened children); number of children detected with a hearing loss; lost to follow-up rate; positive and negative predictive value; sensitivity, specificity, likelihood ratio, Youden index, efficiency, and undesired side effects of the screening. Additionally, a cost-efficiency analysis was made.

Non-UNHS Group

To assess developmental outcome of therapy due to auditory skills, a criterion-based, close-format questionnaire was derived from various other existing questionnaires [15–18]. It considers speech/language (11 items), emotional (2 items), psychosocial (5 items), and cognitive/education-relevant development (2 items). For ease of understanding by parents, the response format of each item was traditional German school grades 1 (perfect) to 5 (very bad), with respect to the situation before therapeutic intervention and at present. The parents were questioned verbally by telephone.

Thuringian and Nationwide Non-UNHS Groups

Mean and median ages at diagnosis of 11 hearing-impaired children from the state of Thuringia (out of a sample with an estimated size of 5,500 children, assuming a prevalence of 2 per 1,000) and of 355 German hearing-impaired children (325 bilaterally and 30 unilaterally hearing-impaired, estimated sample of 177,500 children), both reported to the *Deutsches Zentralregister für kindliche Hörstörungen* (DZH) in 2005, were compared to corresponding values of the Hessian UNHS. Statistical analysis was done with BiAS version 8.2 [19], and SPSS 13.0.

Results

UNHS Group

In 2005 a total of 54,335 children were born in Hessen. For 18,207 a UNHS was available in 49 participating institutions with a screening coverage of 95.0% of the babies born there. From the 12,950 children who received a two-stage screening, 12,036 (92.9%) had a PASS by sole TEOAE measurements, 914 (7.1%) needed additional AABR tests. For the TEOAE screening, a median of 2.10 measurements per baby was necessary up to the final PASS or REFER result (one measurement means one ear), for the AABR screening 2.05 measurements, and for a two-stage TEOAE-AABR screening 2.27 measurements (2.15 OAE + 0.12 AABR).

PASS rates were only 92.6% on the first day of life but reached 98% by the second day and thereafter (fig. 1). From the 17,439 screened newborns, 526 (3.0%) finished the screening with a REFER. The REFER rates were 2.45% for the two-stage TEOAE-AABR screening, 1.9% for the sole AABR screening, and 5.2% for the sole TEOAE screening. From these REFER cases, 41 children were not referred to a follow-up (lost to follow-up rate 7.8%). These children were either not found with the tracking under their given address (majority of cases), or their parents refused further diagnostics. From the remaining 485 babies who received further diagnostics, 49 children (25 male, 24 female) were diagnosed as being hearing-impaired at a median age of 3.1 months (mean age 4.5 months). In addition to these 49 UNHS babies, 27 children without screening were diagnosed in 2005 with a permanent hearing loss in our clinic. Thus, almost two thirds of the newly detected hearing-impaired children in 2005 were filtered out by the UNHS. Due to skewed age distributions, means and medians may differ considerably. The median age at diagnosis of these 27 non-screened children was 49.5 months (mean age 50.6 months). The median age at diagnosis of all hearing-impaired children detected in south and middle Hessen in 2005 was 6.3 months (mean age 21.5 months) and thus 32.7 months below the median value for Germany, which was 39.0 months (mean age 42 months).

Thirty-nine of the 49 hearing-impaired UNHS children had a bilateral hearing loss, 10 a unilateral one. For the monaurally hearing-impaired children the hearing loss was mild in 4 cases, moderate in 3, severe in 1, and profound in 2 cases. The bilateral hearing loss was mild on the better ear in 9 cases, moderate in 16, severe in 4, and profound in 10 cases. Forty-four babies had a sensorineural hearing loss, 5 a conductive one. Six of the children with monaural hearing loss did not get a therapy because their hearing loss was larger than 60 dB HL, but remained under supervision for a later therapy trial. In 2 cases delayed maturation of the auditory system occurred which did not need therapy because hearing abilities improved over the next months up to normality. One bilateral hearing loss at high frequencies could not be treated sufficiently at baby age yet. The remaining children were treated with hearing aids at a median age of 3.5 months (mean age 4.8 months). Of the binaurally hearing-impaired babies, 34 got air conduction hearing aids binaurally, 1 bilateral cochlear implants, and 2 underwent hearing-improving surgery. The prevalence of neonatal hearing disorders in the whole cohort is 2.7 per 1,000 if the monaurally hearing-impaired children but not those with delayed maturation are also taken into consideration. If only a permanent bilateral hearing loss is considered, the prevalence is 2.1 per 1,000.

Table 2. Validity parameters evaluated for the UNHS group

Parameter	Value (95% CI)
Sensitivity[1], % (correct positive)	100.0 (93.3–100.0)
Specificity, % (correct negative)	97.3 (97.0–97.5)
Rate false positive, %	2.7 (2.5–3.0)
Rate false negative, %	0.0 (0.0–6.7)
Positive predictive value, % (correct positive/total positive)	10.1 (7.6–13.0)
Negative predictive value, % (correct negative/total negative)	100.0 (99.98–100.0)
Efficiency, % (rate of correct decisions)	97.3 (97.0–97.5)
Youden index, % (Y = sensitivity + specificity – 100)	97.3 (97.0–97.5)
Likelihood ratio positive, % [LR_{pos} = sensitivity/(1 – specificity)]	36.7568 'very good'
Likelihood ratio negative, % [LR_{neg} = (1 – sensitivity)/specificity]	0.0000 'very good'

[1] Sensitivity calculation described in 'Methods' section; see also Hoth and Neumann [20].

The validity parameters of the UNHS are presented in table 1. Internal validity considers quality criteria within the context of a study, whereas external validity its practical applicability. The specificity given here, however, contains components of both internal and external influences. The internal specificity is calculated on the basis of the PASS and REFER decisions of the devices only. The external specificity takes also environmental conditions into account, such as incomplete measurements of agitated babies needing retests. Because the devices transfer only data of complete measurements to the database, only internal data are available. The number of REFER cases referred to follow-up, however, results also from external influences. Therefore, only an overall specificity can be calculated. This specificity was 97.2% for the whole program (table 2), for the sole TEOAE screening 95.0% (95% confidence interval 94.3–95.7%), for the sole AABR screening 98.8% (97.7–99.4%), and for the two-stage screening 97.8% (97.6–98.1%).

In a previous study with the Echo-Screen TA device, a sensitivity estimate from diagnosed hearing-impaired children did not reveal any false-negative result in 132 ears (TEOAE) and 94 ears (AABR), respectively [20]. Thus, and despite a bias discussed below, the internal sensitivity in the study presented here was set at 100%.

The likelihood ratio indicates how much more frequent a positive test result occurs in subjects with a certain disorder compared with subjects without this disorder. With values of larger than 10 for positive test results, and smaller than 0.1 for negative ones, the likelihood ratios are very good according to convention. The Youden index of 97.3% is good according to convention. Thus, all validity parameters estimated for the UNHS program except the lost to follow-up rate meet international quality criteria.

The mean test duration for each procedure was composed of the mean durations for preparation, measurement, documentation, travel, talking to parents, screening organization, and transmitting data and were estimated, with due caution, from the times measured in our own department. These times obviously vary with situational conditions in different departments. The mean durations for an AABR were 18 min (binaural) and 14 min (monaural), for a TEOAE 13 and 11 min. For a two-stage

Table 3. Improvement of developmental parameters and correlation with age at therapy onset

Item	Mean		Paired t test				Correlation of improvement with age at therapy onset
	before therapy (n)	at present (n)	t	d.f.	p	d	
Speech and language development							
Speech overall	4.09 (47)	2.31 (64)	12.92	46	0.000	1.63	–0.51***
Speech perception							
In quiet environment	4.04 (49)	2.19 (64)	15.33	48	0.000	1.87	NS
In noise	4.58 (48)	3.16 (63)	11.11	47	0.000	1.64	NS
Listening to stories	4.07 (43)	2.53 (59)	9.18	42	0.000	1.14	–0.33*
Familiar persons	3.96 (47)	1.98 (62)	13.16	46	0.000	1.81	–0.41**
Unfamiliar persons	4.18 (44)	2.81 (62)	10.71	43	0.000	1.43	NS
Speech production							
Vocabulary	3.86 (44)	2.27 (64)	9.04	43	0.000	1.32	NS
Grammar	3.88 (43)	2.37 (64)	8.49	42	0.000	1.05	NS
Articulation	4.41 (41)	2.55 (64)	3.99	40	0.000	0.85	NS
Speech intelligibility	4.00 (39)	2.71 (62)	8.48	38	0.000	1.07	NS
Emotional development							
Contentedness	3.70 (53)	1.85 (55)	10.49	52	0.000	1.89	NS
Aggression	3.50 (46)	2.57 (60)	5.80	45	0.000	0.76	NS
Psychosocial development							
Social behavior in peer group	2.98 (45)	2.03 (60)	5.63	43	0.000	0.83	–0.41*
Integration in family	2.26 (43)	1.61 (61	4.28	42	0.000	0.67	NS
Self-confidence in talk to unfamiliar persons	3.44 (41)	2.49 (59)	5.67	40	0.000	0.76	NS
Ease in making friends	3.18 (44)	2.29 (62)	6.35	43	0.000	0.84	–0.30
Communication with unfamiliar persons	3.72 (32)	2.52 (56)	4.64	31	0.000	0.80	NS
Cognitive/educational development							
Following working instructions	3.58 (36)	2.04 (57)	7.79	34	0.000	1.24	–0.34
Concentration ability	3.66 (41)	2.75 (59)	6.19	40	0.000	0.88	NS

d = Effect size. Correlation coefficients: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. NS = $p > 0.10$.

screening it was 22 min (TEOAE and AABR binaural), 20 min (TEOAE monaural, AABR binaural), 19 min (TEOAE binaural, AABR monaural), and 17 min (TEOAE and AABR monaural).

Per detected case of hearing impairment, the cost of screening amounted to EUR 5,711 (sole TEOAE), EUR 4,837 (sole AABR), and EUR 4,268 (two-stage TEOAE-AABR). For the fully implemented Hessian program, EUR 2.95 per case have been estimated roughly. Hence, the two-stage screening is the most cost-efficient procedure.

UNHS vs. Targeted Screening

Of the 49 hearing-impaired babies detected with UNHS, 32 (65%) had a risk factor (predominantly parental consanguinity, 33%) for a neonatal hearing loss. The non-UNHS group included 68% at-risk children (67 of 98). A targeted screening of only the at-risk babies of the UNHS group would have resulted in a sensitivity of 65.3%, compared with a 100% sensitivity for the UNHS group.

Screening for Different Degrees of Hearing Loss

Mean and median ages at diagnosis and therapy of the bilaterally hearing-impaired children detected without an UNHS in 2005 in Hessen and nationwide are shown in table 1 for the various degrees of hearing loss. Both datasets are roughly comparable. With no UNHS the detection and treatment ages depend on the degree of hearing loss and are considerably higher than the ages of the UNHS group, which are independent of the degree of hearing loss.

Non-UNHS Group: Correlation between Therapy Onset and Developmental Parameters

The analysis of the parental responses to the questionnaire is shown in table 3. All developmental parameters improved from before therapy to the present. Effect size d indicates the magnitude of improvement (small effect: $d > 0.2$, $d > 0.5$ moderate, $d > 0.8$ large). For all items, strong and medium effects could be observed, the strongest effects with $d > 1.0$ for all items of speech/language development, contentedness, and transfer of working instructions.

The median age at therapy onset was 21 months (range 2–132 months). Age at therapy onset correlated negatively with parental rating of improvement in overall speech/language abilities, in speech perception during listening to stories, in understanding speech of familiar persons, and in adjustment to peer groups. The correlation between age at therapy onset and parental evaluation of overall speech/language progress was highly significant ($r = -0.51$, $p = 0.001$). The scatter plot in figure 2 indicates a linear inverse proportionality between both parameters.

Screened Children vs. Nonscreened Children

In order to compare within the non-UNHS group those children who had received a nonsystematic screening ($n = 15$) with the children who had not received such a screening with respect to development status after therapeutic intervention, age-matched comparisons could not be made because the former group was considerably younger than the latter. Therefore, a partial correlation was calculated between the variable 'no screening/nonsystematic screening' (coded as 0 or 1) and parental evaluation of overall speech status after therapeutic intervention, with age at therapy onset held constant between both groups. The resulting partial correlation coefficient was $r = 0.24$ ($n = 58$, one-tailed $p = 0.035$). This amounts to an effect size of $d = 0.48$.

UNHS Group vs. Hessian, Thuringian, and German Non-UNHS Groups

The median age at diagnosis for the UNHS group was 3.1 months and for the non-UNHS groups 17.8 months (Hessen), 52.0 months (Thuringia), and 39.0 months (Germany). The median age at therapy was 3.5 months for the UNHS group and 21.0 months for the Hessian non-UNHS group. From the positive correlation between

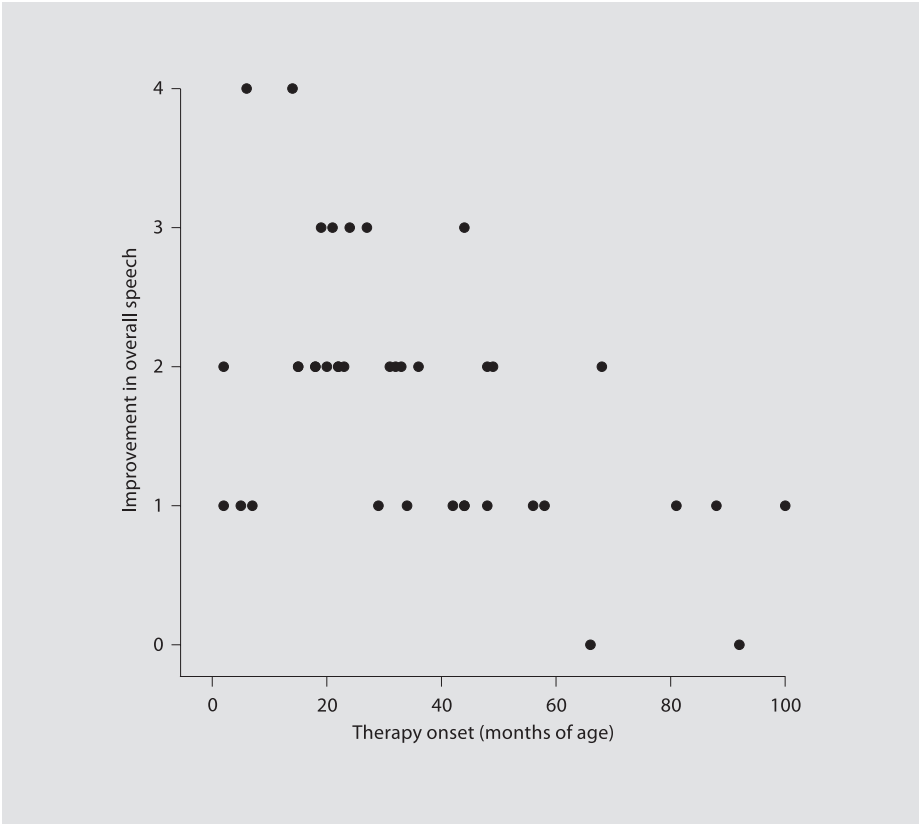

Fig. 2. Improvement in overall speech and language as related to the age of therapy onset.

early therapy and parental evaluation of speech/language and psychosocial developmental progress in the Hessian non-UNHS group, and from the medium effect of being screened or not on the parental evaluation of overall speech and language progress, it can be concluded that an early detection and therapy of an infant hearing loss, as in the 49 UNHS cases, will have a positive influence on the therapy outcome.

Discussion

This study has shown that the Hessian UNHS program fulfills almost all quality criteria. Early therapy correlates positively with the speech/language and psychosocial development. In a sample of hearing-impaired children, having been screened correlated positively with speech/language progress. Because UNHS detects hearing impairments early, independently of the degree of impairment, and allows a therapy start within the first 6 months of life, it is the most effective procedure to detect hear-

ing impairments of all degrees. A targeted screening yields a lower external sensitivity than a UNHS.

Coverage and Loss to Follow-Up

A coverage of 95% for an UNHS, that is not yet implemented nationwide, meets the quality criteria and documents the acceptance of the screening program. Parental refusal rate was only 0.6%, and these refusals were mostly not due to parents' anxiety but to their trust that the baby is well. The obtained low REFER rate and high specificity are assumed to be due to high acceptance of the program by a well-trained staff as well as appropriate screening protocol and technique. Since each screening person is identifiable in the database, person-related quality controls and retrainings are possible. The program allows for rescreening, which was not performed regularly, however.

To decrease the lost to follow-up rate, efforts are currently undertaken to establish identification numbers which are valid for the whole of Germany. This would facilitate to locate parents who have moved to another state.

Procedure

This study confirmed that a two-stage screening protocol is the most effective and efficient one for well babies. Such a protocol has been recommended already in 1993 by the National Institutes of Health for the USA [6]. The protocol combines the TEOAE advantage of short measurement duration, sensitive detection threshold of 30 dB HL, and low costs for disposables with the AABR advantage of higher specificity and coverage of a larger part of the auditory pathway. More than 90% of the screened babies passed the TEOAE in this study (specificity 95%), and the remaining babies received an AABR test. This combined procedure led to an improvement of the specificity to over 97%. Advantages of a two-stage procedure have also been reported elsewhere [21]. For years, two-stage protocols have been considered the most cost-efficient ones, as confirmed also in this study. The costs calculated here are in the range of other German UNHS cost calculations [22, 23], except for AABR techniques the costs of which decreased recently. The high specificity and sensitivity reached in the UNHS program indicate that the equipment used in this study (Echo-Screen-TA Plus C) is well suited for a UNHS.

A two-stage protocol leaves the rare auditory neuropathy (AN) undetected. AN subsumes hearing disorders with a profoundly reduced speech perception and detectable TEOAE because of intact outer hair cells but absent or abnormal ABR because of disturbed temporal responses of the nerve to acoustic stimuli and anomalous transmission to the brainstem. About half of AN children have been reported to be at risk for neonatal hearing disorders [24] and are therefore found on NICUs. During a NICU screening, in 24% of all cases TEOAE were detectable but no ABR [25]. An AABR screening in NICUs is therefore recommended [26]. Only well AN babies would thus remain undetected by a two-stage screening, a disadvantage of this method. On the other hand, TEOAE measurement is fast, easy to perform, detects a majority of hearing impairments, and is more sensitive to slight hearing loss than AABR (detection threshold 30 dB HL vs. 35–40 dB HL). In a recent multicenter study 1,524 babies failed the TEOAE in a UNHS but passed a subsequent AABR [27]. Extensive diagnostics after on average 9.7 months with 64% of these children identified 21 children (30 ears) with a therapy-relevant hearing impairment. The authors

calculated that with a nontracking of TEAOE REFERs or with a sole AABR screening, 23% of all children with mostly mild sensorineural hearing loss would remain undetected. This number is higher than the prevalence of expected AN cases, given as 3 per 1,000 among at-risk children or about 1 in 10 hearing-impaired children [24], which suggests the following implications.

Considering the late age of first diagnosis for mild infant hearing losses, a screening program seems to make sense which includes TEOAE and recommends follow-up diagnostics also in case of a TEOAE REFER and an AABR PASS. To meet both factors – AN and higher sensitivity of TEOAE method for mild hearing impairments – a screening seems to be advisable which always employs both TEOAE and AABR, possibly with a time-saving simultaneous registration of both signals [28]. Additionally, a second screening later in childhood involving speech development has been proposed [27]. Such extended screening programs, however, have to be affordable and to show a reasonable cost-benefit ratio. For well babies a two-stage TEOAE-AABR screening seems therefore to be suitable at present, and for at-risk babies a screening that involves AABR. A low-cost AABR screening is also advisable if the higher detection threshold is taken into account [29]. The option of several retests would increase the specificity of a TEOAE procedure and make it suitable. Occasionally, also distortion product otoacoustic emission (DPOAE) is used for an NHS. However, because DPOAEs are detectable up to threshold elevations of 50 dB HL [30], they are not recommended for screening purposes.

Best PASS rates are obtained from the second day of life on [9, 20]. Because of debris in the ear canal or fluid in the middle ear, usually less than 90% of babies pass a TEOAE screening on the first day of life. However, a two-stage screening improves the PASS rate also on this day [31], as can be seen in figure 1.

Validity

The sensitivity of a UNHS can be calculated by two methods. (1) A retrospective search for false-negative cases in a screened cohort large enough to ensure acceptable confidence interval with only 1–2 permanent hearing impairments per 1,000 children; such a retrospective search, however, is biased because several infant hearing disorders develop late or progressively, or fluctuate and may not be present during the screening [9]. (2) The examination of children previously diagnosed as hearing-impaired with the screening device. Biases are here that the examiner is informed about the hearing impairment and hence is not free from expectations, and that the examination is not performed under screening conditions. However, compared to retrospective search this bias is considered to be small and would anyhow reduce the probability of false PASS. Because no reference examination is feasible for the many PASS cases, the procedure to screen cases already diagnosed as positive was used here. This sensitivity calculation seems to be sufficiently valid, considering available options.

The internal validity is evaluated by searching for sources of bias, like screening method, device, algorithm, PASS/REFER criteria, and day of life at screening. Antibias procedures like randomization or examiner blindness are impractical and unethical here. The variety of institutions involved, the large number of datasets, and the staggered arrival of the data in the database are assumed to somewhat reduce biases which may be nonrandom in a small study but tend to cancel each other out in a large study with multiple sources. The external validity cannot be evaluated by criteria as clear as those for internal validity. External validity, among others, re-

quires experience of the test administrators and appropriate testing conditions. A less than complete coverage of the screening and a certain number of cases lost to follow-up reduce external sensitivity. For instance, with a lost to follow-up rate of 7.8%, an additional 4 hearing-impaired children who are no-shows in the Hessian follow-up institutions can be expected among the 526 REFER cases, given sample comparability, but could not be included in the validity estimate here.

UNHS vs. No UNHS and Targeted Screening

Compared with the nonsystematically screened cohorts of Hessen, Thuringia and the whole of Germany, the UNHS reduced the median ages at diagnosis and therapy considerably and is thus more efficient than a nonsystematic screening or no screening.

A targeted screening program has a lower sensitivity than a UNHS. Among the hearing-impaired children registered in the DZH, 46.2% were at risk for infant hearing loss [32], which would make the sensitivity of a targeted screening even lower than the one reported here. Thus, a UNHS is more efficient than a targeted screening.

The comparatively large proportion of at-risk children in this study may be partially caused by parental consanguinity, which is high in the Frankfurt and Rhine-Main region due to a high proportion of immigrants from certain traditional cultures.

Bilateral vs. Unilateral Screening

A bilateral UNHS is recommended in Germany [9] because of evidence that an overlooked unilateral hearing loss may influence the social development as well as cognitive, language, and auditory abilities, and that unilaterally hearing-impaired children have a significantly higher risk for academic failure than normal-hearing children [33].

Improvement in Quality of Life

The analysis of the parental responses to the questionnaire in the non-UNHS group revealed improvement from before therapy to the present on all items. For some items this is to be expected due to natural developmental progress, for instance ability to concentrate on tasks. For other items it seems rather due or partially due to therapy, for instance the increase in contentedness or the ability to listen to stories. A bias might be that parents, who after all have invested time, financial, and emotional resources in the therapy, rate their child's improvement unduly positive due to a self-justification effect. It should finally be considered that several correlations between therapy onset and parental evaluation of developmental progress are considerable in magnitude, yet insignificant due to small sample size (e.g. item 'following working instructions': $r = -0.34$, $p = 0.072$).

The yield expected from an NHS is early detection and treatment of hearing-impaired children, which leads to improved communication, higher educational achievement, and better quality of life. Financial public savings can be expected in the educational domain, because hearing-impaired children treated early have a higher chance to succeed with regular schooling, which is less costly than special education. Savings per child and year were estimated at EUR 4,500 [34]. The biggest savings, however, come from reduced later income loss.

Without a UNHS, neonatal hearing disorders are in most cases detected late. In Germany of 1998, such disorders were diagnosed on average at 31 months of age and treated at 36 months [32, 35]. Several previous German pilot projects of spontaneous or regional hearing screening had been unable to reduce the age at diagnosis [36]. Only after the initiative in several federal states to implement a UNHS, the mean age at diagnosis decreased to 24 months (median 18 months) in 2004 [37] but rose again in 2005 (table 1). Just 5% of the babies with hearing impairment who were reported to the DZH between 1997 and 2004 were detected by an NHS, but this number increased to 33% in 2004. Thus, the implementation of a UNHS makes progress and has already led to earlier diagnosis of neonatal hearing loss and to a reduced time lag between diagnosis and therapy.

Conclusion

This study provides evidence that a UNHS is the most effective and efficient way for early detection and successful therapy of neonatal hearing impairments, also in Germany. A UNHS is more sensitive than a targeted or a nonsystematic screening, and is independent of the degree of hearing loss. A positive correlation of early therapy with speech/language and psychosocial development has been confirmed. An increasing number of infants with permanent hearing disorders are identified by a UNHS, in the Hessian program already two thirds of all hearing-impaired children. This improvement has led to a desired reduction of age at diagnosis and therapy.

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