REGELGEVING

COCHLEAIRE IMPLANTATEN

- GETOETST AAN DE PRAKTIJK –

"Horen is een recht"

VLOK-CI

IONICI

APEDAF
Association des Parents d'Enfants Déficients Auditifs Francophones

AHOSA VZW
Anders HOren Samen Aanpakken

onder ons

1. Voorstelling - "*wie zijn wij*"

Vanuit de verenigingen VLOK-CI vzw, ONICI, Ahosa vzw, Onder Ons vzw en Apédaf vwz [1] wensen we voor onze achterban van doven en slechthorenden enkele concrete voorstellen tot verbetering van de regels omtrent cochleaire implantaten aan te reiken.

Ongeveer 1 op de 1000 baby's wordt geboren met een ernstig bilateraal gehoorverlies en 6 op de 1000 beschikken niet over een goed gehoor aan beide oren. Van de ganse bevolking hoort 10% (of ruim 1 miljoen Belgen) niet goed.

Sinds de start van de vroege gehoorscreening in 1998, zijn er heel wat initiatieven genomen die zeer gunstig zijn voor de dove en slechthorende kinderen in België. Zo kan bijvoorbeeld vroeger gestart worden met behandeling van het kind en begeleiding van de ouders. En wanneer hoorapparaten onvoldoende spraakverstaan geven, kan reeds op jonge leeftijd overgeschakeld worden naar cochleaire implantaten.

Tot op heden hebben in België reeds meer dan 2500 kinderen een cochleair implantaat gekregen, met tal van positieve resultaten. Dit heeft als gevolg dat deze kinderen heel wat meer kansen en mogelijkheden kregen dan ooit voordien ingebeeld kon worden.

België en vooral Vlaanderen werd hiermee ook wereldwijd aanzien als een voorbeeld van goede hoorzorg.

Sindsdien is er spijtig genoeg niet meer veel veranderd en ondanks de positieve gevolgen van de vroege gehoorscreening, blijven er echter nog een aantal moeilijkheden bestaan, zowel voor kinderen als voor volwassenen met een gehoorverlies.

2. Algemene principes - "*wat vinden wij belangrijk*"

De algemene principes die wij vanuit onze verenigingen naar voren schuiven zijn de volgende:

1. **Horen is een recht.**

2. Horen doen we met twee oren. Elk oor met een gehoorverlies vraagt om behandeling.

3. Zodra een cochleair implantaat betere resultaten kan bieden dan een conventioneel hoortoestel, zou dit aangeboden en terugbetaald moeten worden.

4. We willen dat onze kinderen en volwassenen met een gehoorverlies maximaal kunnen participeren binnen de maatschappij die overwegend horend is.

   Via de nodige ondersteuning via technologische hulpmiddelen en/of tolken moeten ze kunnen participeren in de arbeidsmarkt en aan het sociaal leven.

5. België moet terug een koppositie innemen in Europa inzake hoorzorg!

Vanuit deze basisprincipes benaderen wij de dagelijkse praktijk en komen wij tot de vaststelling dat er binnen het kader van de huidige regelgeving heel wat zaken voor verbetering in aanmerking komen (lees: actualiseren, optimaliseren en harmoniseren van de wetgeving).

[1] zie de toelichting over de werking van deze verenigingen achteraan dit document

Hoewel de bovenstaande algemene principes voor ons essentiële uitgangspunten zijn, begrijpen wij zeer goed dat de praktische uitwerking van deze principes een bedachtzame investering van overheidsgeld behoeft. Wij baseren ons echter niet enkel op humanitaire inzichten, maar ook op **pragmatisch-financiële argumenten** die deze investeringen objectief verantwoorden.

Investeren in hoortechnologie verbetert immers niet enkel de kwaliteit van leven maar bespaart de maatschappij op termijn ook veel geld. Uit verschillende studies blijkt bijvoorbeeld dat personen met een ernstig gehoorverlies een verhoogd risico hebben op sociaal isolement, geestelijke gezondheidsproblemen, dementie, … hetwelk leidt tot een intensiever gebruik van medische en sociale diensten. Personen met een gehoorverlies zijn daarnaast ook frequenter werkloos of presteren onder hun niveau. [2]

Vanuit een positieve invalshoek zijn er dan weer verschillende studies die aantonen dat de investering in kinderen en cochleaire implantaten kan leiden tot betere studieresultaten, sociale integratie en meer kans op succes in de latere loopbaan.

Gezondheidssystemen moeten de reële kosten van gehoorverlies berekenen. Het niet tijdig voorzien van hoorapparaten en cochleaire implantaten moet gezien worden als een enorm risico. Het zorgt voor hoge extra kosten voor de gezondheidszorg en de welzijnsdiensten in de toekomst. We moeten ons denken hierover veranderen en zeker stellen dat we alle kosten meenemen in het geval gehoorverlies **niet** tijdig vastgesteld of aangepakt wordt.

3. Wetgeving in de praktijk - *"wat kan er beter"*

a. Actualiseren van de criteria (leeftijdsgrens, bilateraal, asymmetrisch, graad gehoorverlies)

Vooreerst zijn de in België gehanteerde criteria om in aanmerking te kunnen komen voor een cochleair implantaat de strengste criteria binnen de hele Europese Unie[3]. Deze criteria dateren nog steeds van 1992, het begintijdperk van de eerste cochleaire implantaties in België en zijn dan ook dringend aan actualisering toe conform de internationale wetenschappelijke kennis.

De leeftijdsgrens van 12 jaar voor terugbetaling voor een tweede implantaat bij bilaterale doofheid is achterhaald. Uit onderzoek en ervaring blijkt wel degelijk dat kinderen die aan beide zijden een implantaat dragen het beter doen dan zij die slechts één implantaat krijgen. Normaalhorenden horen ook met 2 oren, het is dan des te logischer dat dit ook voor doven en slechthorenden zo is.

Wij stellen de volgende **criteria** voor:

- gemiddelde drempels bepalen op 4 frequenties (ipv 3): nl. 500, 1000, 2000 en 4000 Hz
- gemiddelde drempels boven 70/75 dB
- spraakverstaan < 50% bij 70 dB

Ook voor de asymmetrische gehoorverliezen is de grens van 60 dB voor het beste oor een veel te streng criterium. Alle voorbereidende documenten in kader van dit dossier stelden 40 dB als grens. In het uiteindelijke document werd 60 dB gebruikt, waardoor een deel van de kinderen niet in aanmerking komt voor een cochleair implantaat maar er wel zeer dringend nood aan heeft.

Hier gaat kostbare tijd voor spraak- en taalontwikkeling verloren.

[2] Onderzoek van The Ear Foundation, oktober 2018.
[3] D. Vickers, L. De Raeve & J. Graham (2016) International survey of cochlear implant candidacy, Cochlear Implants International, 17:sup1, 36-41 (http://dx.doi.org/10.1080/14670100.2016.1155809).

b. Optimaliseren van administratie en levenslange terugbetaling in drie gevallen (doofblindheid (Usher), hersenvliesontsteking, auditieve neuropathie)

Voor 3 groepen zou levenslang tussenkomst moeten zijn voor 2 cochleaire implantaten, namelijk bij doofblindheid (Usher), hersenvliesontsteking en auditieve neuropathie.

Op heden is er geen tussenkomst voor de 2e cochleaire implantaat en moeten o.a. Usher-patiënten bovendien via het solidariteitsfonds om een tussenkomst te krijgen (zoals dit bijvoorbeeld ook het geval is voor een hersenstamimplantaat).

c. Harmoniseren terugbetaling fittings en medische follow-up

De technische instellingen van de spraakprocessor van een cochleair implantaat dienen regelmatig afgesteld te worden (*fitting* genaamd) teneinde de kwaliteit van het apparaat continu op te volgen en te verbeteren.

In de opstartperiode na implantatie kan dit enkele keren per maand zijn, maar eens afgeregeld is dit voor jongeren en volwassenen 1 per jaar en voor kinderen 2-3 keer (frequentie is afhankelijk van persoon tot persoon). Ook dient er jaarlijks een medische follow-up van de cochleaire implantaten te gebeuren.

Hierbij is er een onduidelijkheid voor jongeren en volwassenen die naar een ander revalidatiecentrum gaan voor therapie dan het CI-centrum waar de fitting gebeurt. Zij kunnen in een CI-centrum slechts 4 jaar in een revalidatiebilan een terugbetaling van deze fittingen en follow- up krijgen. Daarna moet dit via een andere manier bekostigd worden. Voor deze tussenkomst bestaat geen nomenclatuurnummer, wat maakt dat ieder CI-team er andere criteria op na houdt.

Dit zet bovendien ook een potentiële drempel bij bepaalde groepen van de bevolking. Onderzoek wijst namelijk uit dat doofheid meer voorkomt in kansarme gezinnen.

d. Terugbetaling vaccinatie hersenvliesontsteking

Omwille van een verhoogd risico op hersenvliesontsteking krijgen personen met een cochleair implantaat de medische aanbeveling om zich elke 5 jaar te laten vaccineren tegen hersenvliesontsteking.

Er is echter geen terugbetaling voorzien voor dit vaccin, hetgeen toch wenselijk zou zijn.

Ook hier resulteert dit in potentiële problemen bij kansarme gezinnen.

e. Hielprik – screening op CMV (Cytomegalovirus)

Tot slot vragen we om bij de bloedafname voor de hielprik pasgeborenen standaard te testen op een CMV-infectie.

Er is, enerzijds, namelijk geen algemene aanbeveling om CMV seroconversie tijdens de zwangerschap op te volgen, maar, anderzijds, bestaat er wel een belangrijk risico voor kinderen met een asymptomatische CMV-infectie dat zij later last krijgen van gehoor- en of evenwichtsstoornissen.

Deze kinderen worden niet gedetecteerd door de MAICO gehoortest van Kind en Gezin.

Een systematische screening op CMV-infectie bij de geboorte zou de ouders in dergelijk geval terecht kunnen informeren over de nood aan een periodieke opvolging en hen duidelijke *red flags* kunnen aanreiken voor het geval zij iets vreemd zouden opmerken in verband met visus, gehoor of motorische ontwikkeling.

In dit verband zijn er verschillende wetenschappelijke studies die een draagvlak bieden voor de standaardisering van deze test bij de pasgeborenen. [4] [5]

f. Betere terugbetaling andere hoorhulpmiddelen

Wij vragen ook om een betere terugbetaling te voorzien van andere hoorhulpmiddelen, zeker voor beengeleidingstoestellen (baha's) en middenoorimplantaten, maar ook voor de conventionele hoortoestellen (zeker voor volwassenen).

[4] Congenital Cytomegalovirus - A European Expert Consensus Statement on Diagnosis and Management, The Pediatric Infectious Disease Journal , Volume 36, Number 12, December 2017.
[5] Fowler KB, McCollister FP, Sabo DL, et al. A Targeted Approach for Congenital Cytomegalovirus Screening Within Newborn Hearing Screening. Pediatrics. 2017;139(2): e20162128.

De onderschrijvende verenigingen

1. VLOK-CI vzw (Vlaamse Ouders van Kinderen met een Cochleair Implant)

VLOK-CI vzw is een vereniging van en voor ouders van dove en slechthorende kinderen. Dit beperkt zich niet louter tot geïmplanteerde kinderen, ook ouders van slechthorende kinderen zijn bij ons welkom.

We trachten gezinnen bij elkaar te brengen en informatie uit te wisselen.

Dat doen we via 2 familiedagen per jaar. Via periodieke infodagen en een trimestriële nieuwsbrief trachten wij onze leden maximaal te informeren rond de problematiek van doofheid en slechthorendheid binnen de gezinscontext.

Tot slot proberen we ook via lobbywerk de belangen van onze leden te behartigen. Momenteel werken wij vooral rond volgende **thema's**:

- Niet alleen Vlaamse Gebarentaal, maar ook schrijftolken (omzetten van spraak naar tekst) en ondersteuning voor het dove of slechthorende kind zijn belangrijk.
- We onderhouden contacten met de VRT rond toegankelijkheid. Hierbij zetten we in op ondertiteling en clean audio.
- Toegankelijkheid Vlaamse film door het voorzien van ondertiteling.
- Wij komen op voor een eerlijke en transparante verhoogde kinderbijslag.
- Wij ijveren om de problemen, maar vooral de mogelijkheden van geïmplanteerde jongvolwassenen te promoten naar de arbeidsmarkt en werkgevers aan te moedigen om redelijke aanpassingen te voorzien zodat zij aan de slag kunnen.
- Wij ijveren om de implantatiecriteria bij te sturen.
- Wij ijveren om net zoals andere organisaties die het doofzijn meer benaderen vanuit een context van gebarentaal over gelijkaardige en gelijkwaardige middelen te kunnen beschikken.

Meer informatie is te vinden op www.vlok-ci.eu.

2. ONICI (ONafhankelijk Informatiecentrum over Cochleaire Implantatie)

ONICI werd in 2002 opgericht in België door Leo De Raeve, psycholoog in het Doveninstituut KIDS te Hasselt (B) en heeft als voornaamste doelstelling: up-to-date wetenschappelijke informatie verschaffen rond cochleaire implantatie en andere implanteerbare hoorapparaten, die zowel toegankelijk is voor gebruikers als voor professionelen.

Om deze doelstelling te bereiken richt ONICI zich op verschillende domeinen:

1. **INFORMATIE GEVEN** door:

   - de website www.onici.be
   - het verspreiden van een Nieuwsbrief via e-mail (6x/jaar) met reeds meer dan 1400 leden uit Nederland en België.
   - het geven van presentaties op studiedagen of congressen
   - het verspreiden van informatiebrochures van de verschillende CI-systemen

2. **WORKSHOPS en/of INFOSESSIES** organiseren zowel voor gebruikers als voor professionelen rond alles wat te maken heeft met de nazorg (revalidatie, begeleiding en onderwijs).

3. Deelname aan **(RESEARCH)PROJECTEN**

Vermits wij over heel wat ervaring beschikken op vlak van begeleiding en revalidatie van kinderen en volwassenen met een cochleair implantaat, wordt er ook meegewerkt aan onderzoeken op dit vlak.

Meer informatie is te vinden op www.onici.be en onze gratis ONICI-Nieuwsbrief.

3. AHOSA vzw (Anders HOren Samen Aanpakken)

AHOSA vzw is een non-profit organisatie die opkomt voor de inclusie van slechthorende/dove personen die communiceren in gesproken taal, in de brede samenleving.

10% van de bevolking is doof of slechthorend.

Ahosa vzw zorgt voor empowerment van dove en slechthorende personen en sensibiliseert de horende samenleving m.b.t. deze onzichtbare beperking.

Dit doet ze door een unieke werking van socio-culturele activiteiten en maatschappelijk gerichte acties met vrijwilligers en beroepskrachten.

Ahosa vzw biedt een deskundig en laagdrempelig aanbod, rekening houdend met innovatie en technologische en maatschappelijke ontwikkelingen.

Vertrekkend vanuit het principe van gelijkheid creëert Ahosa vzw kansen waardoor elke slechthorende/dove persoon greep krijgt op de eigen situatie.

Dit om als onafhankelijk volwaardig burger kwalitatief deel uit te maken van de samenleving.

Meer informatie is te vinden op www.ahosa.be.

4. **Onder ons vzw**

De werking van Onder Ons vzw steunt op drie pijlers die samen een aangepaste integratie van slechthorenden beogen: informatie, optimale communicatie en sensibilisatie.

Hiermee willen we de levenskwaliteit van de slechthorende optimaliseren.

Meer levenskwaliteit... door een aangepaste integratie voor slechthorenden

1. **Informatiekruispunt**

   Via allerlei kanalen informatie omtrent de gehoorproblematiek opvolgen, verzamelen en deze op maat doorgeven aan slechthorenden en hun naaste omgeving;

2. **Een optimale communicatie**

   De slechthorende of doofgewordene uit zijn/haar isolement halen en (opnieuw) in de maatschappij integreren.

   De problemen met de betrokkene en zijn/haar familie bespreken en samen zoeken naar een oplossing.We bieden cursussen liplezen, ook spraakafzien genoemd, aan als extra hulpmiddel in de communicatie.

3. **Sensibilisatie**

   De overheid gevoelig maken voor de problematiek van slechthorenden. De samenleving meer bewust maken voor de specifieke problemen en hen beter leren omgaan met deze groep mensen.

Meer informatie is te vinden op www.onder-ons.be.

4. Apédaf vzw

L'APEDAF est une association de parents d'enfants sourds et malentendants reconnue par l'Education permanente de la Fédération Wallonie-Bruxelles depuis 1984, et selon le nouveau décret de 2003. Depuis sa création, il y a plus de 35 ans, l'association a pour objectif l'épanouissement de l'enfant sourd et malentendant, et de sa famille. Elle y contribue au travers de **trois axes d'action** distincts :

1. Le soutien parental

Il s'articule autour de divers projets, tels que de l'aide sociale et le soutien psychologique des parents, le service de parents-relais, les rencontres familiales, les mini-conférences et les colloques.

2. Le soutien pédagogique de l'enfant sourd et malentendant dans l'enseignement ordinaire

L'APEDAF et ses aides pédagogiques soutiennent et suivent plus de 50 enfants partout en Fédération Wallonie-Bruxelles.

3. La sensibilisation du grand public

L'association réalise de nombreux ouvrages pédagogiques et brochures sur la surdité, qui œuvrent pour une meilleure compréhension de la différence. Nous contribuons ainsi à la construction d'une société plus tolérante, plus ouverte, solidaire et juste. Grâce aux actions menées, l'enfant sourd et malentendant peut et pourra, une fois adulte, devenir lui-même citoyen du changement.

- **Nu uitgeven om later te besparen**

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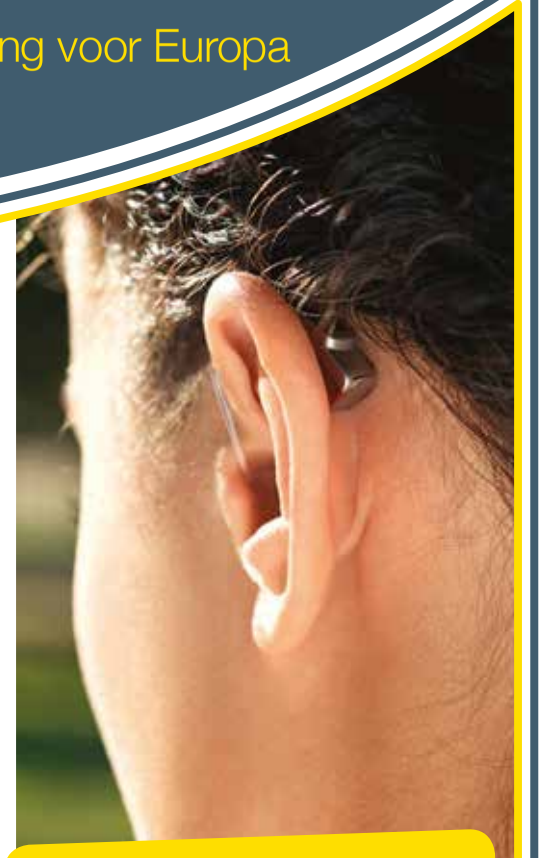
SAMENVATTING

Spend2Save: Investeren in hoortechnologie verbetert de kwaliteit van leven en bespaart de maatschappij veel geld

Gehoorverlies bij volwassenen: Een grote uitdaging voor Europa



Gehoorverlies is één van de meest uitdagende gezondheidsen sociale problemen waarmee Europa wordt geconfronteerd. Globaal gezien riep de Resolutie van de Wereldgezondheidsorganisatie *(WHO, 2016a; Mei 2017)* de landen op om hoorzorg meer te integreren in de gezondheidszorg en om hoorhulpmiddelen en communicatietechnologie te voorzien. Communicatie is immers van essentieel belang in onze hedendaagse maatschappij en ligt aan de basis van ons vermogen om te functioneren in de wereld: om relaties te hebben met familie, vrienden en collega's, om een job uit te oefenen, om een productief leven te hebben en om sociaal te kunnen functioneren.

Gehoorverlies ontneemt ons de mogelijkheid om te communiceren en beïnvloedt daardoor elk facet van het leven. En toch wordt gehoorverlies vaak niet tijdig opgemerkt en vastgesteld.

- **52 miljoen mensen** in heel Europa hebben gehoorverlies en dit aantal neemt jaarlijks nog toe *(EFHOH 2016, 2018, AEA 2017, EHIMA 2017)*
- Gehoorverlies is bij de **70-plussers** in West-Europa beperking nummer **één** *(Davis 2016)*
- Personen met een ernstig gehoorverlies hebben **5 X** meer risico op dementie dan normaalhorenden *(Lin & Ferrucci, 2012)*
- Verworven gehoorverlies is wereldwijd verantwoordelijk voor 9,1% van de vermijdbare dementie en is mogelijks een beïnvloedbare risicofactor voor dementie *(Livingston et al,2018)*
- Oudere mensen met een gehoorverlies hebben een verhoogd risico op **sociaal isolement en geestelijke gezondheidsproblemen** *(Shield 2006; Shield, 2018; Pichora-Fuller et al, 2015)*
- Ouderen met een gehoorverlies hebben **2.5 X** meer risico dan normaalhorenden om een depressie te ontwikkelen *(Mathews 2013)* en dragen een verhoogd risico van een ernstige depressie *(Amieva et al, 2015; Davis 2011)*
- **Sociaal isolement heeft een effect op de gezondheid** *(Cohen 1995)* en bij oudere mensen is er een sterk verband tussen gehoorverlies en cognitieve achteruitgang *(Lin 2013)*, psychische aandoeningen en dementie *(Lin 2011,2012)* en vroegtijdig overlijden *(Friburg 2014, Contrera 2015)*
- Gehoorverlies zorgt voor een intensiever **gebruik van medische en sociale diensten** *(Xiao, 2018, O'Neill 2016)*
- Personen met een gehoorverlies zijn **frequenter werkloos of presteren** onder hun niveau *(Kochkin 2007)*

"… je verliest je zelfvertrouwen, je zelfwaardegevoel en je wil niet meer communiceren in een groep als je gehoor je in de steek laat."

"Geen sociaal leven meer. Isolatie. Frustratie. Zelfs niet meer mogelijk om in het gezin vlot te functioneren."

"Het was angstaanjagend toen mijn gehoor achteruitging en ik ervoor vreesde mijn baan te zullen verliezen."

Een volwassene met gehoorverlies

The Ear Foundation®

Gehoorverlies is het grootste niet tijdig herkende gezondheidsprobleem in Europa, wat leidt tot extra kosten voor het individu en voor de maatschappij *(WHO, 2016a)*

Nochtans kunnen de huidige hoorapparaten en implantaten hier veel aan verhelpen:

- De recentste hoorapparaten en hoorimplantaten hebben duidelijk aangetoond dat zij het leven van mensen positief kunnen veranderen en kostenbesparend zijn *(Lamb et al, 2015; Morris, 2012; Bond, 2009)*
- Het effectief gebruik van hoorapparaten en hoorimplantaten is kosteneffectief en geeft zelfs een herinvestering van 10:1 *(Kervasdoue and Hartmann, 2016)*
- Het gebruik van hoorapparaten zorgt voor minder cognitieve achteruitgang *(Kochkin, 2010; Clinkard, 2015)*
- Hoorhulpmiddelen verbeteren de geestelijke gezondheid, de fysieke en cognitieve mogelijkheden en de werkgelegenheid *(Amieva et al, 2015; Contrera et al 2015; Kochkin 2012; Dept of Health/NHS England 2015; Cochrane review, Ferguson et al 2016; Mahmoudi et al al 2018)*
- Het gebruik van hoorapparaten zorgt voor minder cognitieve achteruitgang *(Deal, 2015; Amieva et al 2015; Mahmoudi et al, 2018)*
- Slechthorenden voelen zich vandaag minder gestigmatiseerd om hoorapparaten te dragen en ze zijn meer tevreden dan ooit te voren *(Shield, 2018; Eurotrak reports, from www.ehima.com/documents)*
- Hoorapparaat dragers geven ook aan dat zij hun hoorapparaten steeds meer dragen *(Eurotrak reports from www.ehima.com/documents, 2018)*
- CI verbetert bij volwassenen de kwaliteit van leven, vermindert depressie en verbetert het cognitief functioneren *(eg Mosnier et al 2015; Lamb and Archbold, 2014 and Ng et al, 2016)*
- In de Europese landen waar de meeste hoorapparaten gedragen worden, zoals in Denemarken, liggen de bijkomende kosten voor gebruik van medische en sociale diensten aanzienlijk lager dan in de andere landen *(Lamb, 2016)*
- Mensen met een ernstig gehoorverlies plaatsen een grote economische waarde voorop als het belangrijkste voordeel van een cochleair implantaat *(Ng et al 2016)*
- Criteria en vergoeding voor cochleaire implantaten kunnen van land tot land fel verschillen *(Archbold, 2014)* en veel minder mensen, dan voor wie het nuttig zou zijn, dragen een cochleair implantaat *(eg Raine, 2013;2016)*

"Ik voel dat ik vele taken uit mijn vorig leven weer kan hernemen. Ik heb mijn trots herwonnen en kan weer deelnemen aan de maatschappij op gelijke basis."

Een volwassene met een cochleair implantaat

Hoorapparaten en cochleaire implantaten zijn wetenschappelijk bewezen interventies die een significante verbetering teweeg brengen op vlak van communicatie en kwaliteit van leven, met minder risico op het ontwikkelen van dure gezondheidsproblemen zoals dementie, depressie, geestelijke gezondheidsproblemen, vallen en sociale isolatie.

Mensen met een gehoorverlies beschrijven grote veranderingen in hun leven, vooral op vlak van communicatie, zelfstandigheid en werkplezier en minder afhankelijk van medische en sociale diensten.

De echte kosten voor gehoorverlies …

Er zijn steeds meer bewijzen binnen Europa en vanuit heel de wereld over de enorme economische impact van gehoorverlies voor de samenleving en dit voornamelijk omwille van de toenemende medische en sociale kosten bij het niet tijdig herkennen en goed behandelen van gehoorverlies. Gehoorverlies dat niet wordt aangepakt kost de globale economie jaarlijks $750 miljard Dollar *(WHO,2016a)*.

De jaarlijkse economische kosten voor Europese landen wordt geraamd op:

DUITSLAND €30 MILJARD
FRANKRIJK €22 MILJARD
GROOT BRITTANIE €22 MILJARD
ITALIE €21 MILJARD
SPANJE €16 MILJARD
POLEN €14 MILJARD
NEDERLAND €6 MILJARD

(Duthey, 2013)

In een nog meer recente studie uit Engeland werden de kosten geassocieerd met gehoorverlies zelfs geraamd op £30.13 miljard per jaar, de medische en sociale kosten inbegrepen. *(Archbold, Lamb, O'Neil, 2014)* In Frankrijk, wordt in een recente studie gesproken over 23.4 miljard euro's. *(Kervasdoué, J. Hartmann, L. 2016)*

De kosten om **GEEN** hoorapparatuur te voorzien zijn aanzienlijk hoger dan de kosten om ze wel tijdig te voorzien. *(O'Neil et al., 2016; Kervasdoue and Hartmann 2016)*

Gezondheidssystemen moeten de reële kosten van gehoorverlies berekenen. Het niet tijdig voorzien van hoorapparaten en cochleaire implantaten moet gezien worden als een enorm risico. Het zorgt voor hoge extra kosten voor de gezondheidszorg en de welzijnsdiensten in de toekomst. We moeten ons denken hierover veranderen en zeker stellen dat we alle kosten meenemen in het geval gehoorverlies **NIET** tijdig vastgesteld of aangepakt wordt.

"Het is erg verwarrend om tijdens vergaderingen niet te verstaan wat er verteld wordt. Ik voelde dat ik mijn job niet meer kon uitoefenen"

"Ik verloor mijn gehoor plots op de leeftijd van 24 jaar. Ik had juist een baby en was met zwangerschapsverlof. Plots veranderde mijn leven. Ik verloor mijn zelfvertrouwen en was bang om nog alleen te blijven. Ik kon onmogelijk terug mijn job als advocate gaan uitoefenen."

Een volwassene met gehoorverlies

Een toename in de herkenning en behandeling van gehoorverlies bij volwassenen zou vele levens veranderen en zou veel kosten besparen voor de maatschappij.

Het volledige Engelstalige rapport 'Spend to Save, a European strategy' kun je downloaden via de website van The Ear Foundation-Nottingham: **www.earfoundation.org.uk** en ONICI-Zonhoven **www.onici.be**

Aanbevelingen

Nog nooit hebben wij over zoveel mogelijkheden beschikt om gehoorverlies tijdig aan te pakken dan vandaag. Er is een enorme vooruitgang geboekt in hoorapparaten en cochleaire implantaten die zorgen voor een revolutionaire impact op de kwaliteit van leven van personen met een gehoorverlies. De kosteneffectiviteit van deze hoorapparatuur is duidelijk bewezen en neemt nog toe als de prijs van de apparaten afneemt en hun effectiviteit toeneemt.

Gehoorverlies heeft een enorme impact op de persoon en op de maatschappij, maar vandaag de dag kunnen wij hier iets aan doen, nu wij beschikken over goede gehoortechnologie:

- Nationale gehoorscreening voor volwassenen. Er moeten programma's ontwikkeld worden om mensen meer bewust te maken over de impact van gehoorverlies en om hen aan te zetten om er tijdig iets aan te doen om latere kosten te voorkomen
- Bij de berekening van de kosten voor hoortechnologie dient rekening gehouden te worden met de kosten als we er NIETS aan zouden doen
- Terugbetalingsschema's moeten dan ook rekening houden met de totale kosten op de gezondheids- en welzijnsdiensten, indien gehoorverlies niet zou worden aangepakt
- In elk land zou een gezondheidsbeleid moeten uitgewerkt worden, gebaseerd op het 'UK Action Plan on Hearing Loss' dit om gehoorverlies onder de aandacht te brengen van de publieke diensten voor gezondheidszorg
- De criteria voor hoorapparaten en cochleaire implantaten moeten herzien worden in die Europese landen met te strenge en achterhaalde criteria zoals in België
- Richt innovatieve diensten op om de optimale begeleiding te bieden nadat personen van hoortechnologie zijn voorzien en om kost-effectieve behandelingsmethodes (zoals tele-therapie vanop afstand) te ontwikkelen
- Een nieuwe EU standaard CI-patiënten dient uitgewerkt en geïmplementeerd te worden overeenkomstig het Engelse EN 15927: 2010 voor hoorapparaat dragers.

International survey of cochlear implant candidacy

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International survey of cochlear implant candidacy

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International survey of cochlear implant candidacy

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Background: The goal of this work was to determine international differences in candidacy based on audiometric and speech perception measures, and to evaluate the information in light of the funding structure and access to implants within different countries.
Method: An online questionnaire was circulated to professionals in 25 countries. There were 28 respondents, representing the candidacy practice in 17 countries.
Results: Results showed differences in the funding model between countries. Unilateral implants for both adults and children and bilateral implants for children were covered by national funding in approximately 60% of countries (30% used medical insurance, and 10% self-funding). Fewer countries provided bilateral implants routinely for adults: national funding was available in only 22% (37% used medical insurance and 41% self-funding). Main evolving candidacy areas are asymmetric losses, auditory neuropathy spectrum disorders and electro-acoustic stimulation. For countries using speech-based adult candidacy assessments, the majority (40%) used word tests, 24% used sentence tests, and 36% used a mixture of both. For countries using audiometry for candidacy (70–80% of countries), the majority used levels of 75–85 dB HL at frequencies above 1 kHz. The United Kingdom and Belgium had the most conservative audiometric criteria, and countries such as Australia, Germany, and Italy were the most lenient. Countries with a purely self-funding model had greater flexibility in candidacy requirements.

Keywords: cochlear implant candidacy, worldwide, international.

Introduction

The criteria for cochlear implant (CI) candidacy in both children and adults are known to have considerable variation between countries and also between some regions within countries. Recent UK research (Lovett *et al.*, 2015; Vickers *et al.*, 2015) looking at candidacy for bilateral implants in children suggests that the current audiometric candidacy criteria (equal to or greater than 90 dB HL at 2 and 4 kHz) may be too strict. Based on this research, it may be more appropriate to relax the criteria to be greater than or equal to 80 dB HL at 2 and 4 kHz. In countries such as Australia and Germany, there is a much more relaxed audiometric cut-off level that allows all potential candidates to be identified audiometrically. Subsequently, clinical observation and assessment of likely outcome are used to determine if individual candidates are making appropriate progress with their hearing aids, and whether they would be likely to gain more benefit with implants. Leigh *et al.* (2011) recommended that the audiometric criteria for Australia should be set at 70 dB HL four-frequency average (0.5, 1, 2, and 4 kHz) based on outcome comparisons with hearing aid users.

With technological improvements in implants in recent years, and changes in surgical techniques that have improved the preservation of residual hearing, implant outcomes have improved (Blamey *et al.*, 2013). All the CIs that are available today are able to provide additional acoustic amplification for any preserved natural hearing, together with the electrical delivery of sound through the implant itself, making implants a viable intervention for individuals with low-frequency residual hearing.

There is considerable variation at an international level, not only in the criteria for implantation, but also in access to CIs, including access to funding, both for adults and children (De Raeve and Wouters, 2013; Liang and Mason, 2013; Oliver, 2013; Raine, 2013; Sorkin, 2013), and this could be affected by the model of service delivery and funding as well as cultural and language aspects.

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The goal of this article was to evaluate the differences in CI candidacy for both adults and children across different regions of the world, in the context of the variation in approaches to funding and models of service delivery found in individual territories.

Method

A questionnaire was developed to gather information on the following four topics:

(1) Methods of funding for unilateral and bilateral implants;
(2) The presence or absence of specific guidelines, or criteria, to which teams are obliged to comply. The categories were based on evaluations and aetiological factors, for example: pure tone audiometry (PTA); speech perception tests (in quiet or in noise); duration of deafness; onset of deafness; age of the candidate; aetiology of deafness; presence of other disabilities; any other relevant factors;
(3) Specific factors that can exclude implantation;
(4) Whether there is flexibility within the system that might allow a centre to implant someone falling outside the programme's standard criteria.

The questionnaire was only available in English and was therefore written in a simple and clear way to aid understanding for those for whom English is not their first language. The questions used in the questionnaire are shown in Appendix.

The questionnaire went through two stages of validity review prior to circulation. Initially the members of the British Cochlear Implant Group (BCIG) working group on candidacy reviewed the first version of the questionnaire to ensure that the questions appropriately addressed the associated topic headings and could be analysed effectively to answer the research questions. The second stage was to send the questionnaire to a group of five experienced clinicians to determine if the questionnaire was clear and easy to complete.

The questionnaire was modified following the validation stages and then implemented as an online questionnaire in the University College London (UCL) OPINIO software. The link was sent out initially to 75 professionals working in CI clinics in 25 countries, and then further distributed to the member states of Euro-CIU the European CI Users association, for distribution to clinicians within their countries.

The questionnaire was open for completion for one calendar month.

Results

In total, 28 respondents completed the questionnaire, representing 17 countries: Argentina, Australia, Belgium, Bosnia Herzegovina, Brazil, Finland, Germany, India, Italy, The Netherlands, New Zealand, South Africa, Spain, Switzerland, Portugal, United Kingdom, and The United States of America. One centre was purely adult and another purely paediatric so they were unable to answer all of the questions relating to adult or paediatric guidelines. The results will be reported according to the four main subject areas.

Funding for unilateral and bilateral implants

Fig. 1 shows the primary source of funding for unilateral and bilateral CIs for adults and children. All territories had a mixed model of funding but this figure shows the main route for funding for the majority of implantations in the country.

A similar pattern is observed for adult and paediatric unilateral and paediatric bilateral implantation, the breakdown of the specific numbers by category are shown in Fig. 1. The results show that for approximately 60% of territories the funding was provided nationally. Approximately, 30% of countries receive funding from a local provision at a clinic or regional level or by private insurance, and in 10% of the countries implants are predominantly only available through self-funding with some local funding support (India and Bosnia Herzegovina).

The situation is rather different for adult bilateral CIs with only 22% of countries currently offering bilateral CIs to adults with national or local funding. However, private insurance does cover the costs in 37% of countries, but for approximately 40% of the countries bilateral CIs for adults are only available through a self-funding route.

Presence of obligatory guidelines or criteria

Fig. 2 shows the distribution of the use of guidelines and candidacy assessments and the numerical

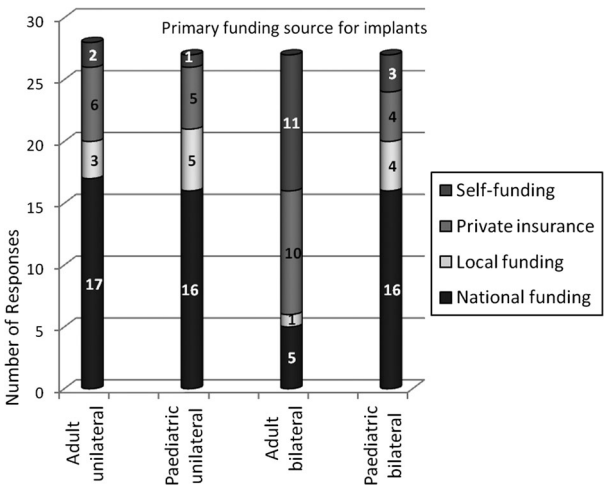

Figure 1 A stacked bar chart indicating the main source of funding for implants in a specific region, separated according to adult and paediatrics and also unilateral and bilateral implants. Each shaded section relates to the number of respondents that reported a specific outcome and the numbers indicate the exact number of respondents giving that response.

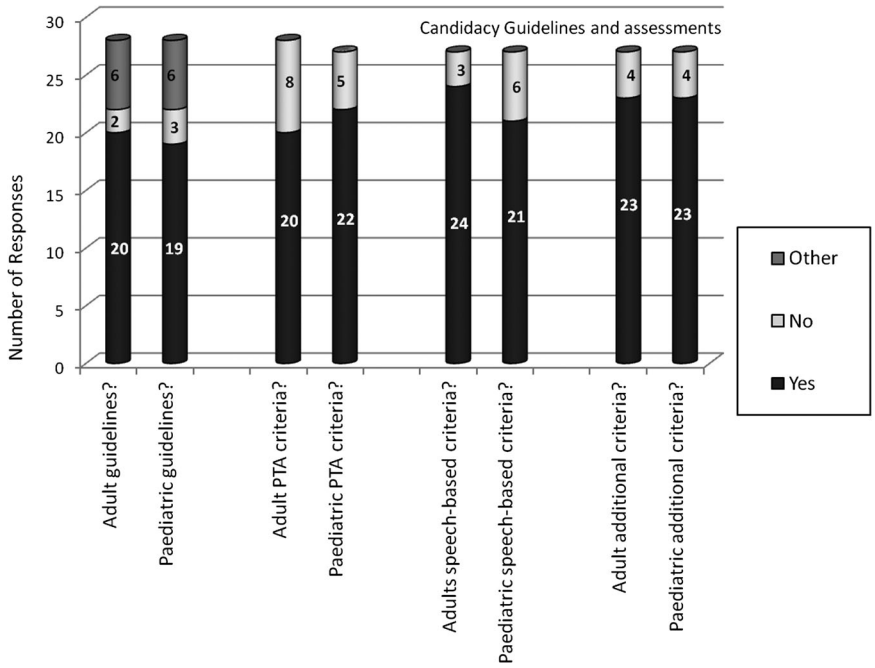

Figure 2 As for Fig. 1 but for the use of candidacy guidelines and assessments.

breakdown for each category. The findings show that around 70% of countries have national or local guidelines in place that govern candidacy for implantation, 10% do not have guidelines in place that they have to comply to, and 20% have guidelines but the decision about whether an individual is a candidate for implantation is down to the individual clinical team.

Approximately, 80% of countries have audiometric criteria in place for paediatric implantation, but only 70% of the respondents had audiometric guidelines for adult implantation. For the remaining clinics not using audiometric guidelines, the respondents reported that functional outcomes were a greater driving force for determining candidacy in their countries. For those reporting audiometric criteria, a range of candidacy rules were used; the responses ranged from the guidance in Australia which requires the average thresholds above 1500 Hz to be greater than 70 dB HL, to those in Belgium where the average thresholds should be greater than 85 dB HL at 500, 1000, and 2000 Hz bilaterally, or the UK guidance in which thresholds should be greater than 90 dB HL at both 2 and 4 kHz bilaterally. The most accepted pattern of audiometric candidacy used criteria in which the average thresholds should be greater than 75–80 dB HL at frequencies above 1 kHz for an individual to be considered a candidate. Eighty-five percent of countries have speech-based criteria for adults and approximately 60% have speech-based paediatric criteria, with assessments varying greatly dependent upon the developmental age of the child.

Fig. 3 shows the categories of speech tests that are used for candidacy assessments in adults, based on 16 respondents.

Twenty-four percent of countries use purely sentence test based measures and approximately 40% use word test measures, the remaining 36% use combined sentence and word test criteria.

Over 80% of countries use additional assessments such as medical evaluation (i.e. scans indicating that the individual is appropriate for implantation and that they are sufficiently healthy to undergo surgery), mental health assessments to determine if individuals have appropriate expectations and are prepared for the process of implantation, effective previous hearing aid use and current lack of benefit from

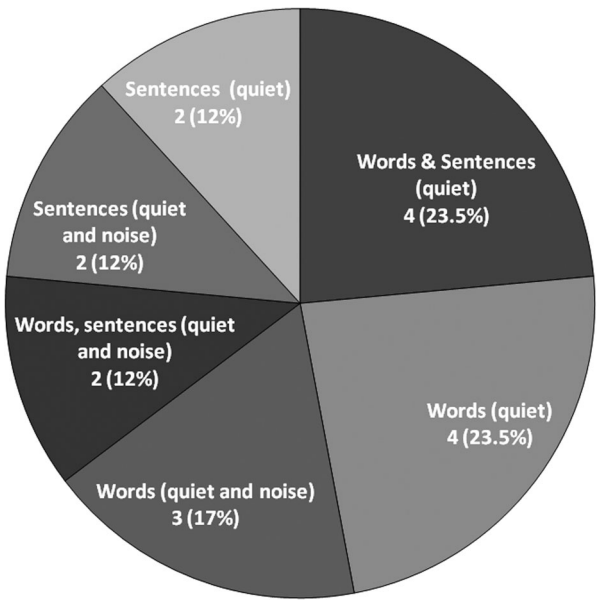

Figure 3 A pie chart showing the types of speech perception tests used for candidacy assessment in adults in different countries. The total of respondents was 17. Each shaded segment relates to a different measure as labelled.

appropriately fitted hearing aids for speech and language. In addition, 43% of centres reported utilizing questionnaire results to determine the impact of the hearing impairment and to determine the individual's functional use of hearing.

Specific exclusion factors

Only 10–20% of countries have specific exclusion factors within their candidacy assessments based on age, duration of deafness or aetiology. Paediatric age was the largest area for potential exclusion from implantation (see Fig. 4).

Flexibility allowing someone falling outside criteria to be offered an implant

In Germany, Italy, and Australia the teams have a great deal of flexibility and the clinical team determine if an individual is an appropriate candidate. The same is true for the clinics with a predominantly self-funding model. Some of the other countries, for example the UK, have occasional success on a case-by-case basis for obtaining funding for special cases outside criteria.

For subjects falling outside criteria the candidacy areas which are most effective at being funded are Auditory Neuropathy Spectrum Disorder (ANSD), in which the audiogram is often waived as a candidacy measure; Electro-Acoustic Stimulation (EAS, which has US Food and Drug Administration approval) and Single-Sided or asymmetric Deafness (SSD). For countries offering CIs to SSD cases, it is typical to undergo a contra-lateral routing of signal (CROS) or Bone-Anchored hearing aid trial, and one clinic was only able to implant if the individual suffered from tinnitus. Three respondents reported that their clinics were moving away from threshold requirements being bilaterally based and that as long as the ear to be implanted was within criteria it was acceptable, this was for both adults and children in two of the centres and just for adults in the third.

Discussion

The results of this study demonstrated that there are many common practices that are shared internationally, as well as highlighting the differences in the access to implants and the candidacy requirements in the different countries. Some countries do not work with the luxury of National or Health insurance funding, and only have the option to provide implants for individuals who can fund the implant themselves. These clinics often have greater flexibility in choosing whom they can consider to be an implant candidate. The majority of countries/clinics focus mainly on the functional outcomes and utilize questionnaires and a range of speech-based outcome assessments to determine candidacy, while the tonal audiogram itself is becoming less of a stringent requirement. For those countries/clinics that do still have an audiogram-based assessment, the UK and Belgium operate with the strictest audiometric cut offs, which are dramatically different from the 70 dB HL average thresholds at frequencies greater than 1500 Hz used in Australia. The majority of clinics with audiometric criteria use an average of 75–80 dB HL cut off for frequencies greater than 1 kHz, and this is in line with the recommendation that is being put forward in the UK to amend audiometric guidelines to be 80 dB HL at 2 and 4 kHz.

There is a general move away from requiring the candidacy cut off to be met in both ears, and in

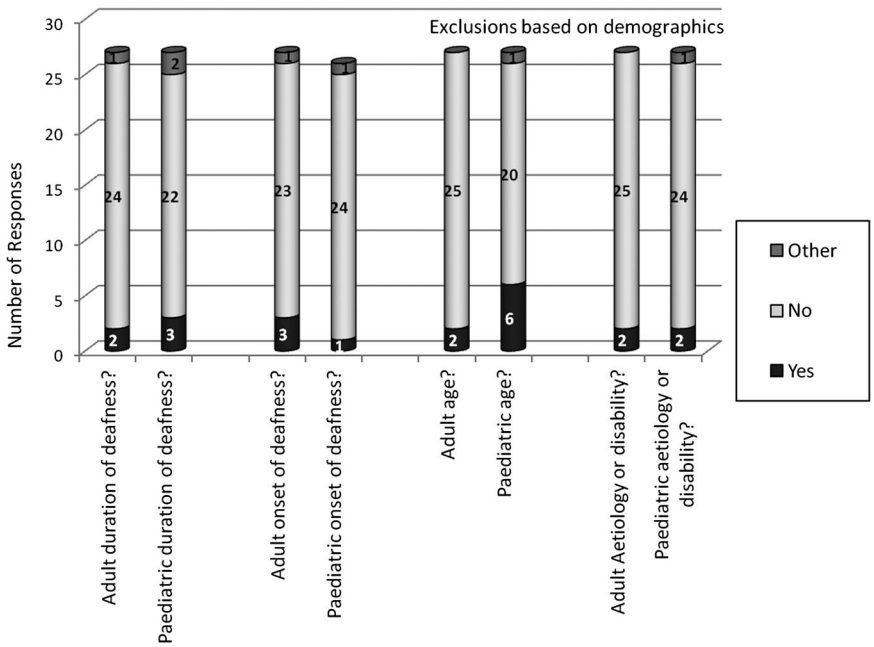

Figure 4 As for Fig. 1 but based on exclusion categories.

several countries cases with SSD are implanted. Individuals with residual hearing are routinely being provided with EAS systems in most countries and individuals with ANSD are commonly provided with implants. All of this suggests that these areas of candidacy are the natural development that should be incorporated into all candidacy guidelines.

What is clear from all of the respondents is that decisions about implantation are based upon the decision from a multi-disciplinary team, containing medical, surgical, audiological, educational, and rehabilitation professionals. There are many components used to determine if an individual would be appropriate for implantation and the goal of all professionals in the field is that they should provide the most appropriate intervention for optimizing the hearing abilities of each individual.

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Appendix: International Candidacy Criteria Questionnaire

Condensed layout of online questionnaire.

Dear colleague in the field of cochlear implantation

As you are no doubt aware, there are significant differences at an international level in relation to the criteria by which children and adults are able to qualify for cochlear implantation.

The purpose of this questionnaire is to increase awareness of the national and international differences and thus to maximize the chances of the appropriate children and adults being funded for and receiving cochlear implants.

We would therefore be very grateful if you could complete the following brief questionnaire.

(1) Please state how unilateral adult cochlear implantation is funded in your programme (e.g. national funding, local funding, private insurance, self-funding only)?
(2) Please state how unilateral paediatric cochlear implantation is funded in your programme (e.g. national funding, local funding, private insurance, self-funding only)?
(3) Please state how bilateral adult cochlear implantation is funded in your programme (e.g. national funding, local funding, private insurance, self-funding only)?
(4) Please state how bilateral paediatric cochlear implantation is funded in your programme (e.g. national funding, local funding, private insurance, self-funding only)?
(5) Are you required to comply with specific guidelines for the provision of cochlear implants for adults and/or children? If yes please provide details.
(6) Do you use guidelines based on the pure tone audiogram for adults and/or children? If yes please provide details.
(7) Do you have guidelines based on speech perception tests for adults and/or children? If YES, please provide following information for each speech test: (a) Name of speech test, (b) Presentation level, (c) Whether presented in quiet or noise (if so what type of noise), (d) The score that will allow the candidate to receive a CI (e.g. $\leq 50\%$).
(8) Do your guidelines prohibit implantation based on duration of deafness for adults and/or children? If yes please explain.
(9) Do your guidelines prohibit implantation based on onset of deafness for adults and/or children? If yes please explain.
(10) Do your guidelines prohibit implantation based on age of candidate for adults and/or children? If yes please explain.

(11) Do your guidelines prohibit implantation based on aetiology or disability criteria for adults and/or children? If yes please explain.

(12) Do you have other factors influencing CI candidacy for adults and/or children? e.g. use of questionnaires, hearing aid benefit? If yes please explain.

(13) Under what circumstances would you be able to provide a cochlear implant to individuals that fall outside your programme's criteria (e.g. Auditory Neuropathy Spectrum Disorders, Electro-acoustic Stimulation, Single-sided deafness, Progressive Hearing Loss, Visual or other Sensory Impairment. Please explain about special circumstances and state if special funding is required.

Thank you for completing this questionnaire, we appreciate your input

Congenital Cytomegalovirus - A European Expert Consensus Statement on Diagnosis and Management

Congenital Cytomegalovirus

A European Expert Consensus Statement on Diagnosis and Management

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Congenital cytomegalovirus (cCMV) is the most common congenital infection in the developed world. Reported prevalence varies between cohorts but is approximately 7 per 1000 births.[1] About half of cytomegalovirus (CMV)-infected babies with clinically detectable disease at birth are destined to have significant impairments in their development, and cCMV infection is implicated in approximately 25% of all children with sensorineural hearing loss (SNHL).[1,2] Meta-analysis shows that although long-term sequelae, especially SNHL, are more common in those with clinically detectable disease at birth, they are also found in 13% of those without clinical features attributable to CMV on initial examination.[1]

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Despite the significant long-term impact of cCMV infection, there is limited evidence on which to base many treatment decisions in clinical practice. In an era of enhanced perinatal screening, fetuses and newborns are increasingly tested for CMV after abnormalities were detected during routine ultrasonography or maternal serology. Furthermore, otherwise "asymptomatic", congenitally CMV-infected, newborns are being identified after detection of SNHL through newborn hearing screening programs. Because of earlier diagnosis, babies with cCMV now presenting to pediatricians differ from those primarily included in clinical trials of treatment reported in the literature.

A symposium was convened during the 2015 conference of the European Society of Paediatric Infectious Diseases to discuss the current management of cCMV. In attendance were clinicians from throughout Europe, many of whom are involved in policy for cCMV for their region/country.

This article summarizes the discussions at this meeting alongside the evidence informing them. A balanced perspective of the controversies in this area is presented and areas of consensus highlighted. Finally, where evidence is lacking, suggestions are made for future research efforts to address areas of unmet medical need.

The authors acknowledge the coexisting need for studies on the management of babies with symptoms consistent with cCMV, but in whom this diagnosis cannot be firmly established, and of those with symptomatic postnatal CMV infection; this article does not, however, address these groups.

The internationally accepted GRADE system for evaluating evidence has been used to illustrate points where relevant (Table 1).[3]

DEFINITIONS OF SYMPTOMATIC DISEASE

Classically, cCMV infection is categorized as "symptomatic" or "asymptomatic" at birth. Differing definitions and opinions on what constitutes "symptomatic" CMV infection, however, makes interpreting the literature challenging. Indeed, some of the largest cohort studies include babies with SNHL at birth in the group described as being "asymptomatic" because no "clinically apparent disease" was detectable during newborn examination.[4] In modern healthcare systems, whereby cCMV is increasingly detected through screening for other conditions, alongside increased accessibility of investigations, such as magnetic resonance imaging (MRI), the traditional dichotomy between clinically "apparent" and "inapparent" disease is becoming less meaningful. Table 2 summarizes the accepted clinical features of

TABLE 1. Grade System of Evaluating Evidence[3]

Quality Rating	Definition	Example Methodology	Depiction in Text
High	Further research is very unlikely to change our confidence in the estimate of effect	Randomized trials or double-upgraded observational studies	A
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate	Downgraded randomized trials or upgraded observational studies	B
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate	Double-downgraded randomized trials or observational studies.	C
Very low	Any estimate of effect is very uncertain	Triple-downgraded randomized trials, or downgraded observational studies, or case series/case reports	D

Strength of Recommendation	Definition	Depiction in Text
Strong recommendation for using (or not using) an intervention	Most informed patients would choose the recommended management and clinicians can structure their interactions with patients accordingly	1
Weak recommendation for using (or not using) an intervention	Patients' choices will vary according to their values and preferences and clinicians must ensure that patients' care is in keeping with their values and preferences	2

Strength of recommendations is determined by the balance between desirable and undesirable consequences of alternative management strategies, quality of evidence, variability in values and preferences and resource use.

TABLE 2. Possible Signs and Symptoms in Children With Congenital CMV[5–8]

Clinically detectable symptoms/signs
Physical Examination
Small for gestational age (birth weight <–2 SD for gestational age)
Microcephaly (head circumference <–2 SD for gestational age)
Petechiae or purpura (usually found within hours of birth and persist for several weeks)
Blueberry muffin rash (intra dermal hematopoiesis)
Jaundice*
Hepatomegaly
Splenomegaly
Neurologic physical examination
Microcephaly (head circumference <–2 SD for gestational age)
Neurologic signs (lethargy, hypotonia, seizures, poor sucking reflex)
Abnormalities detected incidentally or through subsequent investigation/specialist examination
Laboratory results
Anemia
Thrombocytopenia (occurs in the first week but platelets often increase spontaneously after the second week)
Leukopenia, isolated neutropenia
Elevated liver enzymes (ALT/AST)
Conjugated hyperbilirubinemia
Cerebrospinal fluid
Abnormal cerebral fluid indices, positive CMV DNA
Neuroimaging
Calcifications, periventricular cysts, ventricular dilatation, subependymal pseudocysts, germinolytic cysts, white matter abnormalities, cortical atrophy, migration disorders, cerebellar hypoplasia, lenticulostriatal vasculopathy
Hearing test
Sensorineural hearing loss uni- or bilaterally
Visual examination
Chorioretinitis, retinal hemorrhage, optic atrophy, strabismus, cataracts

*CMV-associated jaundice can be present at the first day after birth and usually persists longer than physiologic jaundice.

ALT indicates alanine aminotransferase; AST, aspartate aminotransferase; SD, standard deviations.

cCMV disease with those symptoms detectable on newborn examination listed separately to those detectable only if specific investigations are conducted, for example, when cCMV is already suspected.[5–8]

Full Consensus Within This Expert Group Was That

1. For the purposes of research and publication, newborns identified as having cCMV disease after abnormal clinical examination at birth (such as microcephaly, small for gestational age (SGA), widespread petechiae, hepatosplenomegaly) should be differentiated from those babies identified through screening or investigation for other disorders, for example, those tested for CMV after known/likely maternal infection or abnormal newborn hearing screening. This differentiation would allow for more accurate assessment of the prognostic value of individual manifestations of "symptomatic" disease on longer-term outcomes as already shown in other publications.[9]
2. "Symptomatic" cCMV should be considered as "severe," "moderate" or "mild" disease.
   a. "Mild" disease includes those with isolated (1 or 2 at most), otherwise, clinically insignificant or transient findings, such as petechiae, mild hepatomegaly or splenomegaly or biochemical/hematologic abnormalities (such as thrombocytopenia, anemia, leukopenia, borderline raised liver enzyme abnormalities or conjugated hyperbilirubinemia) or SGA (defined as weight for gestational age <−2 standard deviations) without microcephaly.
   b. "Severe" disease includes those with central nervous system (CNS) involvement (abnormal neurologic or ophthalmologic examination, microcephaly or neuroimaging consistent with cCMV disease [such as calcifications, moderate to severe ventriculomegaly, cysts, white matter changes, cerebral or cerebellar hypoplasia, hippocampal dysplasia, neuronal migration abnormalities])[10] or with life-threatening disease.

The Majority Agreed That

2b. "Severe" disease also includes babies with evidence of severe single-organ disease (including those with clinically significant liver enzyme abnormalities [liver "failure"] and marked hepatosplenomegaly) or those with significant multiorgan involvement. Babies with transient or otherwise clinically insignificant abnormalities (ie, the babies are not "sick") that resolve spontaneously over a few weeks are not included in this group even if these abnormalities are multiple.

2c. A further group exists that may be considered to have "moderate" disease. This group is heterogeneous and includes, for example, those with persistent (eg, more than 2 weeks duration) abnormalities of hematologic/biochemical indices or more than 2 "mild" disease manifestations (as listed earlier). Because of lack of evidence, full consensus could not be reached on how to approach this group, and treatment decisions are currently made on a case by case basis. Development of a validated clinical scoring system for disease severity at presentation and risk of sequelae would be beneficial for both counseling parents and informing treatment decisions.

3. Defining CNS involvement
   a. It remains uncertain whether some, nonspecific findings detected on cranial ultrasound (CrUSS) and MRI (particularly isolated lenticulostriatal vasculopathy [LSV]) constitute clinically significant CNS disease. LSV has been detected in 0.4%–5.8% of all neonates undergoing an ultrasound, and only 5% has been associated with cCMV.[11,12] Some have suggested isolated LSV as a marker of risk for SNHL.[11] Others have found only more extensive neuroimaging abnormalities to be of prognostic value.[13,14] The majority at this meeting would not consider LSV in isolation to be a notable CNS manifestation of disease. It is suggested that neuroradiologic abnormalities not known to be clearly associated with CMV disease and adverse outcomes are discussed with a suitably experienced neuroradiologist, particularly, if the results of these discussions might influence treatment decisions.
   b. The exact pathophysiology of SNHL is not clear but is likely secondary to infection and degradation of sensory structures within the inner ear.[15,16] It is therefore debated whether isolated SNHL should truly be considered a CNS manifestation of infection and, as a consequence, whether such children should be considered comparable to those with CNS disease included in published clinical trials. No studies have addressed this specific population, but a nonrandomized cohort study observing the effects of valganciclovir in isolated SNHL is in progress (clinicaltrials.gov NCT02005822). The majority of experts at this meeting would categorize babies with isolated, confirmed SNHL in the "severe"/CNS group because bilateral SNHL is not only associated with likely long-term impairments but was also included in the criteria for recruitment in the only randomized controlled trials (RCTs) in cCMV. However, consensus was not reached because the spectrum of hearing loss is wide, and treatment of isolated SNHL has not been evaluated in any RCTs.

WHEN SHOULD TESTING FOR CONGENITAL CMV BE CONSIDERED?

Indications for testing for cCMV are based on the presence of one or more of the most frequently observed clinical features (Table 3).[17] Unfortunately, predictive values for each of these features are not available.

Full Consensus Within This Expert Group Was That Testing for cCMV Should be Performed in

1. Fetuses with ultrasound/MRI imaging consistent with cCMV disease (by appropriately timed antenatal testing of amniotic fluid).[18] (Quality C, Level 1)
2. Newborns where there is a maternal history of suspected primary CMV infection during pregnancy. If antenatal testing of amniotic fluid has been conducted, it is suggested that cCMV infection should still be confirmed at birth because both false-positive and -negative results have been reported.[18] (Quality C, Level 1)
3. Newborns with signs/symptoms consistent with cCMV disease (see Table 2; including those with findings consistent with cCMV on antenatal imaging). (Quality B, Strength 1)
4. Children with confirmed SNHL.[16] Systems need to be established to ensure testing for cCMV occurs, where possible, in the first 21 days of life because dried blood spot (DBS) are not always readily available for testing (see below). (Quality B, Strength 1)

The Majority Agreed That

5. Newborns who are SGA should not routinely be tested. Studies in SGA newborns have shown the prevalence of cCMV to be 0%–5.2%.[19–22] However, the majority of

TABLE 3. Clinical Features That Should Lead to Testing for Congenital CMV

Neonates
Physical examination
Hepatosplenomegaly
Petechiae, purpura or blueberry muffin rash in a newborn
Jaundice (prolonged or conjugated hyperbilirubinemia)
Microcephaly (head circumference <–2 SD for gestational age)
Consider if symmetrically small for gestational age (<–2 SD for gestational age)
Neurology
Seizures with no other explanation
Laboratory parameters
Prolonged jaundice with transaminitis
Conjugated hyperbilirubinemia
Unexplained thrombocytopenia, *consider if leucopenia or anemia*
Neuroimaging
Intracranial calcification (often periventricular)
Intracranial ventriculomegaly without other explanation
Consider in the case of periventricular cysts, subependymal pseudocysts, germinolytic cysts, white matter abnormalities, cortical atrophy, migration disorders, cerebellar hypoplasia, lenticulostriate vasculopathy
Visual examination
Abnormal findings on ophthalmologic examination consistent with congenital CMV (eg, chorioretinitis)
Consider if congenital cataracts
Failed neonatal hearing screen
Maternal serology
Evidence of maternal seroconversion*
*Consider in women with known CMV infection (known IgG seropositive at start of pregnancy), particularly, if symptoms or virologic examination consistent with suspected CMV reactivation/reinfection**
Prematurity†
Older children
Sensorineural hearing loss: new diagnosis

Features in bold are those where there is consensus for testing. Features in italics are those that might lead to testing in individual circumstances and depending on local practice.

*Seek expert clinical virology advice for interpretation of virologic investigations in pregnancy.

†Baseline screening to differentiate between congenital and postnatal CMV infection is helpful for extremely premature infants (<28 weeks gestational age) who are at increased risk of symptomatic postnatal infection.

SD indicates SD indicates standard deviations.

studies report a prevalence of 1.4%–1.8%, which is not significantly higher than the prevalence of cCMV in the general population. Therefore, evidence is insufficient to justify screening all newborns with isolated SGA for cCMV. None of these studies distinguish between asymmetrical (with normal head circumference) and symmetrical SGA, but when head circumference was mentioned, most SGA babies with cCMV had microcephaly (head circumference <−2 standard deviations).[21,22] Because of this, and the poor prognostic outcome of children with cCMV and microcephaly, many present at this meeting test those babies with symmetrical SGA but not those with preserved head growth.[14](Quality C, Strength 2)

6. Prematurity. Evidence that premature babies have a higher incidence of cCMV is limited.[20,23] Testing extremely premature babies (<28 weeks gestational age) at birth does, however, assist in differentiating between congenital and postnatal infection. This may be very helpful in guiding the management of these babies that are particularly vulnerable to symptomatic postnatal infection. However, consensus was not reached regarding practice in this area, with cost being a factor among other considerations.[24] (Quality C, Strength 2)
7. Testing of babies born to mothers who are known to be CMV seropositive at the establishment of pregnancy. Although maternal nonprimary CMV infection is known to be important when considering the overall burden of cCMV disease, testing all babies born to these women, particularly in populations with high maternal seroprevalence, is tantamount to universal neonatal screening.[25,26] Identifying women with nonprimary CMV who are at highest risk of transmitting infection to their fetus remains elusive. It was agreed that individual case discussion and local policy should therefore dictate practice in this area. Further research is clearly needed.

LABORATORY DIAGNOSIS OF CONGENITAL CMV INFECTION

Testing for cCMV using CMV polymerase chain reaction (PCR) in urine is highly reliable: sensitivity is 100% and specificity 99%.[27] One negative urine specimen in a neonate is therefore sufficient to exclude infection, and repeat sampling is not necessary. After 21 days, a urine positive for CMV could be because of CMV acquired postnatally from, for example, passage through the birth canal or through breast milk. As CMV PCR techniques are becoming more sensitive, earlier testing, before the age of 14 days, is recommended.[27]

CMV PCR testing of saliva is an alternative and is easy to perform. Samples should be taken immediately before feeding in breastfed newborns, and confirmed with urine, as false-positive results have been reported.[28–31]

PCR assay of neonatal DBS can be performed retrospectively in an attempt to diagnose cCMV after the first 21 days of life. Sensitivity is around 84% in meta-analysis but is highly variable depending on the laboratory techniques used and the population being tested; a negative DBS PCR cannot, therefore, be used to definitively exclude a diagnosis of cCMV.[32]

Full Consensus Within This Expert Group Was That

1. Testing for cCMV should be performed using a single CMV PCR of urine obtained within 21 days of birth but ideally within 14 days of birth (Quality B, Strength 1).
2. Saliva PCR testing can be an alternative, but a positive result should be confirmed using urine (Quality B, Strength 1).
3. After the age of 21 days, CMV DNA PCR of stored DBS can be used to diagnose cCMV retrospectively; sensitivity is relatively low, and a negative test cannot be used to definitively exclude a diagnosis of cCMV (Quality B, Strength 1).

RECOMMENDED INVESTIGATIONS AFTER CONFIRMING A DIAGNOSIS OF CONGENITAL CMV INFECTION

After a virologic diagnosis of cCMV infection has been made, additional investigations are necessary to evaluate the extent of disease and to assist with discussions regarding prognosis and treatment.

Full Consensus Within This Expert Group Was That

1. The investigations below are conducted in any baby in whom a diagnosis of cCMV is confirmed, looking specifically for the manifestations of disease (Table 2):
   - Complete blood count, liver enzymes, (conjugated) bilirubin
   - Renal function (before initiating therapy)

- CrUSS. (Quality A, Strength 1)
- Audiologic testing (brainstem-evoked response; some screening tests such as otoacoustic emissions are not sufficient to detect central auditory hearing loss in cCMV). (Quality A, Strength 1)
- Ophthalmic assessment. (Quality A, Strength 1)

2. If additional imaging to CrUSS is felt to be indicated, then MRI is the preferred neuroimaging modality. MRI can be successfully performed in neonates without the need for sedation and is, therefore, both highly sensitive and free of the risks of radiologic exposure, which accompany computed tomography. (Quality C, Strength 1)
3. MRI should be performed in babies with clinically detectable neurologic findings or CrUSS abnormalities.

The Majority Agreed That

4. Cranial MRI should be performed in any babies with cCMV and evidence of CMV disease (see Table 2). (Quality C, Strength 1)
5. CMV PCR quantitation should be performed in blood at baseline. Several studies have shown the absence of CMV viremia to be associated with better long-term outcomes, and this may be reassuring when evaluating babies without any other manifestations of cCMV disease.[33–35] Blood CMV PCR should not, however, be used to rule out cCMV infection because, paradoxically, the absence of CMV in blood has been described even in babies with severe cCMV disease.[33,36] (Quality C, Strength 2)
6. Examination of cerebrospinal fluid (CSF): No current evidence supports examination of CSF as part of routine diagnostic work up. Studies have shown detectable CMV DNA in CSF, and elevated biomarkers such as β2-microglobulin suggest a poor prognosis.[13,37] However, others have shown no additional prognostic value from CSF specimens obtained in the clinical setting.[37] Despite this lack of evidence, there was a majority view that although a possible area of interest for future research, lumbar puncture should not be performed routinely in babies with cCMV infection (Quality C, Strength 1).

Only a Minority Agreed That

7. Cranial MRI should be performed in all CMV-infected babies. Although there is no conclusive evidence that performing MRI gives additional prognostic information to CrUSS in those without evidence of CMV disease at birth, some argued that it is desirable to conduct MRI in all cCMV-infected babies because additional pathology can be identified as compared with CrUSS[38–40] (Quality D, Strength 2).

TREATMENT

No antiviral drugs are currently licensed for the treatment of cCMV. Although many case reports and cohort studies have reported on treatment for cCMV, there are results from only 2 RCTs.[7,41–44] The first of these studies evaluated 6 weeks' intravenous ganciclovir treatment in neonates (<1 month of age), gestational age ≥32 weeks and clinically apparent disease in the newborn period with evidence of CNS disease (including microcephaly, intracranial calcification, abnormal CSF indices for age, hearing deficit and chorioretinitis).[7] Improved hearing and neurodevelopmental outcomes were shown, but there was significant loss to follow-up.[7,44] A more recent trial compared 6-week to 6-month treatment with oral valganciclovir and included babies with any evidence of symptomatic (including non-CNS) cCMV disease.[41] Few babies enrolled, however, had isolated, mild clinical features, and none in the 6-month treatment group had isolated SNHL (D Kimberlin 2015, personal email correspondence, 28 April). A modest benefit on both 2-year hearing and neurodevelopmental outcomes was shown with the 6-month treatment course. The longer treatment course improved likelihood of better hearing outcomes most notably in those with preexisting CNS involvement. Longer duration of therapy was only statistically significant, however, for "total ear" hearing as opposed to "best ear" hearing (which is of greater functional significance) and only once adjusted for baseline CNS involvement. Given the natural resolution of some features of cCMV disease in published cohorts, alongside the delayed onset of hearing loss and fluctuations in SNHL reported in cCMV, it is even more challenging to draw any conclusions regarding treatment effect from uncontrolled studies.[7,16,45]

Clinical trials to date do not, therefore, provide good evidence on which to base treatment decisions for many of the infants presenting to clinicians in everyday clinical practice.

Table 4 provides guidance on which infants should be offered treatment after a risk versus benefit discussion with the family. This table and associated text indicate areas where consensus was reached. Much discussion focused around the treatment of babies with less severe cCMV disease and whether the minimal additional benefit shown in the 6-month treatment course was sufficient to justify such a prolonged course of treatment. Although clinical findings such as SGA and petechiae have been shown in historical cohorts to predict risk for SNHL, more recent reanalysis of data indicates that these findings in isolation are generally associated with disease-free outcomes in babies presenting without other manifestations of symptomatic disease.[9,46] Opinion on the severity, or number, of symptoms justifying antiviral treatment remains divided, and it is therefore strongly recommended that clinicians discuss treatment initiation and duration with an expert in this area.

Full Consensus Within This Expert Group Was That

1. Babies with evidence of CNS disease should receive antiviral treatment (Quality A, Strength 1). Treatment should be preferably for 6-months duration (Quality B, Strength 2).
2. Babies with no clinical/laboratory findings consistent with CMV disease should not receive treatment because no evidence exists to support treatment in this group (Quality D, Strength 1 [not to treat]).
3. Babies with evidence of life-threatening disease or severe single-organ disease or multiorgan involvement should receive treatment. Although evidence is limited, particularly for life-threatening disease, consensus was that treatment should be considered in this group (Quality B, Strength 1). Consensus could not be reached on duration of treatment in this group.
4. Oral valganciclovir is now the drug of choice. Intravenous ganciclovir should be used in babies unable to tolerate oral drug or where gastrointestinal absorption is uncertain (Quality A, Strength 1).

The Majority Agreed That

5. Babies with "mild" cCMV disease (as defined earlier) should not receive treatment. No studies have clearly addressed treatment in this group. Most present at this meeting would not, therefore, treat babies with 1 or 2 isolated or transient, clinically insignificant, manifestations of disease (Quality C, Strength 2).
6. Babies with "moderate" cCMV disease (as defined earlier). Evidence for treating babies with multiple, but not severe, manifestations of disease (including jaundice, hepatosplenomegaly without significantly raised liver enzymes, SGA) is limited. It is, therefore, recommended that these cases are discussed on a case-by-case basis with a clinician with experience of managing babies with cCMV (such as a pediatric infectious disease specialist) (Quality B, Strength 2).

TABLE 4. Summary of Treatment Recommendations

Disease Manifestation	Treatment Recommendation	Level of Evidence
Consensus		
CNS disease Microcephaly, CNS calcification, chorioretinitis White matter changes (or other abnormalities on MRI consistent with CMV disease)†	Ganciclovir/valganciclovir: duration 6 months*	Treatment: Quality A, Strength 1 (to treat) Duration: Quality B, Strength 2
Other "severe" disease (includes life-threatening or severe single-organ or multiorgan non-CNS disease)	Ganciclovir/valganciclovir: minimum of 6 weeks, up to 6 months*‡	Treatment: Quality B, Strength 1 Duration: Quality B, Strength 2
"Mild" disease: isolated or transient disease (eg, jaundice, Petechiae, SGA in isolation; max 2 abnormalities)	No treatment	Treatment: Quality C, Strength 2 (for no treatment)
No clinical or biochemical findings of disease (± detectable CMV viremia)	No treatment	Treatment: Quality D, Strength 1 (for no treatment)
Majority opinion: but not consensus		
Isolated hearing deficit*§	Ganciclovir/valganciclovir: Duration 6 months*	Treatment: Quality C, Strength 1 Duration: Quality C, Strength 2
"Moderate" disease (see text for definition; eg, multiple minor findings consistent with CMV disease)*	Consider treatment after discussion with specialist Duration: Minimum of 6 weeks and up to 6 months*	Treatment: Quality C, Strength 2 Duration: Quality B, Strength 2

There is currently only evidence for starting treatment in the first month of life.

*Limited evidence without full consensus: see text for further description.

†In the case of isolated, nonspecific MRI findings that are not consistent with cCMV disease, it was agreed that treatment is not necessarily indicated.

‡It was suggested (without consensus) that treatment might continue in this group until the underlying clinical manifestation of disease (eg, hepatitis) resolved because benefit of 6 months treatment is unclear.

§No studies address this particular group, although they were included in eligibility criteria for treatment in both published RCTs of treatment.

7. Treatment of isolated SNHL: The majority at this meeting would include SNHL at birth in their indications for treatment because this was in the inclusion criteria for treatment in previous RCTs. Furthermore, the main benefit of treatment is in preserving hearing rather than improving hearing once damage exists, with good outcomes reported in observational studies (with likely bias).[7,41,47] There was not, however, consensus, and it is acknowledged that no RCTs have specifically addressed treatment effect in this group of babies who are usually now identified through newborn hearing screening programs (Grade C, Strength 1).
8. Drug dose and formulation: Although oral valganciclovir is now first-line treatment in most cases, it is currently unknown whether valganciclovir reaches target areas as effectively as ganciclovir or, indeed, where drug should be targeted (eg, CNS or inner ear) because no studies have directly compared the 2 drugs. In those with severe disease, particularly if absorption is uncertain, intravenous ganciclovir is, therefore, preferred by some in early stages of treatment until oral therapy can be reliably tolerated (Quality C, Strength 1).
9. Treatment duration in cases without CNS involvement: In those infants in whom the decision is taken to give antiviral treatment, the majority would treat for 6 months. However, there was no consensus on this point in light of the modest benefit shown for longer treatment courses in the only RCT (Quality B, Strength 2).
10. Treating babies older than 28 days: Treatment of older children has not been addressed in any RCTs, although it is acknowledged that the 28-day cutoff is also not evidence based. Retrospective case series of small numbers of babies treated outside the newborn period have reported good outcomes.[48,49] Babies found to have SNHL after hearing screening at birth often do not have a diagnosis of cCMV confirmed until outside the 1-month "window of evidence" for treatment. No consensus was reached on how late it might be acceptable to start treatment in this scenario, or in the eventuality of hearing deterioration. Two RCTs are currently evaluating the use of treatment in older children with cCMV and SNHL (clinicaltrials.gov NCT01649869 and NCT02606266), which may clarify this debate. (Evidence for treating outside the newborn period Quality D, Strength 2.)

SIDE EFFECTS OF ANTIVIRAL TREATMENT

Much of the debate around treating less severely affected babies relates to the potential side effects of currently available antiviral drugs.

Significant neutropenia is frequently observed during antiviral treatment in infants. This is reported less commonly with valganciclovir than with ganciclovir (21% compared with 65%).[7,41,44,50] Neutropenia generally occurs during the first month of treatment, with no increased toxicity observed after 6 weeks in those randomized to receive 6-month treatment compared with placebo in the only RCT evaluating this.[41] The oral administration of valganciclovir also removes the burden of hospitalization and risk of nosocomial infections and central line complications observed during treatment with ganciclovir. Hepatotoxicity has been reported in up to 30% of those treated with ganciclovir and thrombocytopenia in a similar proportion.[51] In the most recent study of treatment with valganciclovir, deranged liver function was observed, but this was neither clinically nor statistically significant when compared with placebo. In all studies, abnormal biochemical and hematologic parameters resolved after drug discontinuation.

Long-term side effects have not been evaluated in neonates treated with ganciclovir or valganciclovir. Animal studies raise the theoretical risk of gonadotoxicity and carcinogenicity.[52,53] Although this has not been observed in humans to date, parents should be counseled about these potential risks, particularly when considering treatment in those groups in which benefit has not been clearly shown. No adverse long-term effects have been documented in a small cohort of babies treated in early neonatal studies and followed up to puberty (NCT00031421, unpublished data).

MONITORING OF BABIES DURING TREATMENT

Table 5 summarizes a proposed monitoring strategy for babies treated for cCMV. These recommendations are based on the safety monitoring and data obtained from the published RCTs.[7,41]

TABLE 5. Monitoring and Follow-Up According to Treatment Status

No Treatment Given	Treatment Given
—	Investigations whilst on treatment*
—	FBC,* LFT† and U&E suggested weekly for first 4 weeks and then at least monthly until completion of treatment course (ganciclovir/valganciclovir)‡ (Quality B, Strength 2)
	Weight measurement and drug dose review at time of blood sampling
—	Viral load at baseline (Quality C, Strength 2).
	Consider Viral load 2–4 weekly whilst on antiviral therapy (not consensus; Quality D, Strength 2)§
—	Consider therapeutic drug monitoring if: Viral load increase >1.0 $\log_{10}$ during treatment¶ Toxicity is suspected There is an increased risk of toxicity: eg, prematurity <36 weeks, abnormal renal function (Quality D, Strength 2)
Follow up	Follow up
Audiology assessment every 3–6 months in the first year, then every 6 months until 3 years of age and then every 12 months until 6 years old‖ (Quality C, Strength 1)	
Pediatric infectious disease clinic review (or general pediatric clinic after consultation with a specialist) until at least 1 year, and ideally 2 years, of life. (Quality D, Strength 1)	Pediatric infectious disease clinic as soon as possible in the first month, then annual review until at least age 2 years (specialist or general clinic with pediatric infectious diseases input depending on local agreements). (Quality D, Strength 1)
Monitor development. (Quality D, Strength 1)	Monitor development with neurodevelopmental assessment at 1 year in a child development service. (Quality D, Strength 1)
Ophthalmic assessment as directed by ophthalmologist, but baseline and annual review up to age 5 years in those with clinically detectable symptoms/signs at birth recommended.** (Quality D, Strength 2)	Ophthalmic assessment directed by ophthalmologist, but baseline and annual review up to age 5 years recommended.** (Quality D, Strength 2)

FBC indicates full blood count; LFT, liver function tests; U&E, urea, creatinine and electrolytes.

*Interrupt treatment or consider granulocyte colony stimulating factor (GCSF) if absolute neutrophil count $<0.5 \times 10^9$/L. Decreasing dose may be considered for less severe neutropenia.

†LFT monitoring monthly is sufficient if sampling difficulties.

‡Increase frequency or seek advice if there is deterioration.

§Measuring viral load is not evidence based but offers some evaluation of virus response and enables detection of possible viral resistance.

¶Consider CMV resistance testing (sequencing) in unexplained elevations/breakthrough of viremia.

‖According to current United Kingdom newborn hearing screening guidelines.

**There is limited evidence on late ocular manifestations of cCMV. They are rare and include visual impairment and strabismus.[6,53]

There are no data to support therapeutic drug monitoring.[54] Therapeutic drug monitoring may, however, have a role when toxicity is a concern (eg, in those with impaired renal function) or where there are concerns about treatment response.

Full Consensus Within This Expert Group Was That

1. Where treatment is given, babies should have regular weight measurement and safety monitoring to enable appropriate dose adjustment of medication (see Table 5).(Quality A, Strength 1)
2. Where treatment is given, parents should be fully counseled about both the known and potential side effects of treatment with current antivirals. (Quality A, Strength 1 for short-term side effects; Long-term, no published studies)
3. Although there are theoretical risks of longer term treatment toxicity, no large cohorts have been followed up to enable this to be fully evaluated in humans treated during early life. Where possible, children receiving antiviral treatment should, therefore, be entered into a registry to enable ongoing pharmacovigilance.

Only a Minority Agreed That

1. Viral load monitoring: Some centers report monitoring viral load to assist in decisions regarding adequate drug dosing and detection of potential drug resistance; however, most experts at this meeting do not conduct this routinely. Treatment duration is not altered by any viral parameters, and rebound of virus after treatment discontinuation is well documented with no demonstrable association with long-term outcomes (Quality D, Strength 2). If viral load is checked after discontinuing drug, it is suggested that parents are forewarned of the likelihood that virus will be detectable and that this is of unknown significance.

FOLLOW-UP

Table 5 summarizes recommended follow-up of babies with cCMV (both treated and untreated).

The recommendation for audiologic follow-up is based on long-term surveillance studies of SNHL in cCMV.[4,16] Frequent follow-up is suggested during the first 2 years of life because this is the period of highest risk for development of cCMV-associated hearing loss and a critical period for language development. Early detection of SNHL during this period is also most likely to improve long-term outcomes.[55] Monitoring should continue into early childhood, however, because deterioration in hearing continues throughout early life[55] (Quality B, Strength 1).

Neurodevelopmental follow-up is suggested at 1 and 2 years of age ideally with formal neurodevelopmental assessment. This is not, however, routinely conducted in all centers, and there is no evidence-based benefit in this particular group, although early detection of functional impairments is generally agreed to be beneficial.

Ophthalmic follow-up is recommended annually at least until children can talk in those with clinically detectable disease at birth, but not in those without, because deterioration in vision has been observed in this group (Quality C, Strength 1).[6]

Families should be given information for local/national support groups where these exist (see acknowledgements). Where cCMV parent groups are not easily accessible, parents of children with hearing loss may find support from groups for those with hearing impairment.

RECOMMENDATIONS FOR FUTURE PEDIATRIC RESEARCH

1. Clinical trials addressing treatment of those with more "minor" manifestations of disease/no clinically detectable disease at birth and those with isolated SNHL.
2. Clinical studies of antenatal therapies to decrease transmission of infection and cCMV disease once infection is established.
3. Publications relating to cCMV should make it clear how those included were identified (ie, babies presenting with clinically detected "symptoms" vs "screened" babies identified through existing antenatal or postnatal screening pathways including hearing screening programs), or after further investigation of abnormalities, such as thrombocytopenia, found incidentally when blood sampling is performed for other indications.
4. Development of clinical prediction models to better categorize severity of disease (CNS vs non-CNS and babies with single vs multiple findings of disease) and associated outcomes to assist counseling of parents.
5. Studies of neuroimaging, particularly MRI, and added value with regards to predicting long-term impairments particularly in those without clinically detectable disease at birth through studies involving unselected cCMV cohorts.
6. Clinical trials of alternative treatment durations and new anti-CMV therapies when available.
7. Biomarkers. It seems unlikely that a predefined duration of treatment will be similarly beneficial in babies with such varying clinical manifestations of disease and likely variable viral burden and host immune function. The development of both host and virologic biomarkers of long-term outcomes would greatly enhance design of future RCTs and enable more accurate counseling and resource allocation.
8. All children receiving treatment should be captured in a registry to enable ongoing pharmacovigilance for any long-term effects of antiviral medication.
9. Identification of risk factors for maternal virus transmission, particularly, in those mothers with previous known exposure to CMV (CMV IgG seropositive).

CONCLUSIONS

As stated at the outset, this article represents the consensus opinion of a group of professionals with a particular interest in cCMV. It highlights that much of our practice is based on limited data but identifies areas where there is nonetheless consensus amongst experts. Recent publications have shown potential cost effectiveness of screening at birth for cCMV, although these calculations are constrained by the issues raised in this article regarding true quantification of benefits of treatment and agreed treatment duration in certain patient groups.[56,57] It will be challenging to address many of the research questions raised through RCTs, given the significant resources and long-term follow-up required alongside potential difficulties in recruiting into such studies when treatment is anecdotally being offered more freely. Collecting accurate data on disease manifestations and treatment outcomes in different patient groups alongside maternal demographics can, however, inform treatment strategies as previously shown very effectively for the management of pediatric human immunodeficiency virus. This requires a unified approach to initial diagnostic tests, definitions of symptomatology and follow-up which is currently being addressed by a network of clinicians with an interest in this area through both national and European initiatives such as Paediatric European Network for Treatment of AIDS - Infectious Diseases, the European Congenital CMV Initiative and European Society of Paediatric Infectious Diseases and European Society for Clinical Virology (ESCV). It should also be reiterated that this article focuses on postnatal aspects of diagnosis and treatment. There is an associated and simultaneous need for work alongside obstetric and fetal medicine colleagues to address similar uncertainties in aspects of antenatal care. It is hoped that through such collaborations, progress will be made in decreasing infection and disease in fetuses, newborns and subsequently older children with cCMV.

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The CMV-infected children and their parents/carers who we have cared for and who challenge us on a daily basis to provide evidence-based and consistent care including those parents who are involved with supporting other parents through local or national support groups including (but not exclusively) CMV Action (www.cmvaction.org.uk); https://www.stopcitomegalovirus.org.

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A Targeted Approach for Congenital Cytomegalovirus Screening Within Newborn Hearing Screening

A Targeted Approach for Congenital Cytomegalovirus Screening Within Newborn Hearing Screening

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abstract

BACKGROUND AND OBJECTIVE: Congenital cytomegalovirus (cCMV) infection remains a leading cause of childhood hearing loss. Currently universal CMV screening at birth does not exist in the United States. An alternative approach could be testing infants who do not pass their newborn hearing screening (NHS) for cCMV. This study was undertaken to evaluate whether a targeted approach will identify infants with CMV-related sensorineural hearing loss (SNHL).

METHODS: Infants born at 7 US medical centers received NHS and were also screened for cCMV while in the newborn nursery. Infants who tested positive for CMV received further diagnostic audiologic evaluations to identify or confirm hearing loss.

RESULTS: Between 2007 and 2012, 99 945 newborns were screened for both hearing impairment and cCMV. Overall, 7.0% of CMV-positive infants did not pass NHS compared with 0.9% of CMV-negative infants ($P < .0001$). Among the cCMV infants who failed NHS, diagnostic testing confirmed that 65% had SNHL. In addition, 3.6% of CMV-infected infants who passed their NHS had SNHL confirmed by further evaluation during early infancy. NHS in this cohort identified 57% of all CMV-related SNHL that occurred in the neonatal period.

CONCLUSIONS: A targeted CMV approach that tests newborns who fail their NHS identified the majority of infants with CMV-related SNHL at birth. However, 43% of the infants with CMV-related SNHL in the neonatal period and cCMV infants who are at risk for late onset SNHL were not identified by NHS.

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WHAT'S KNOWN ON THIS SUBJECT: Congenital cytomegalovirus (CMV) infection is a leading cause of childhood hearing loss. Although CMV saliva screening of newborns for CMV identifies infected infants for monitoring and early intervention, routine CMV screening does not occur in the United States.

WHAT THIS STUDY ADDS: A targeted CMV testing approach identifies infants with CMV-related hearing loss at birth. However, 43% of the infants with CMV-related hearing loss and congenital CMV infants who are at risk for late onset hearing loss will not be identified.

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Congenital cytomegalovirus (cCMV) infection is found worldwide and contributes to thousands of children each year being born with or developing permanent disability such as hearing loss, vision loss, cerebral palsy, cognitive impairment, and developmental delay. In the United States, Canada, Western Europe, and Australia, cCMV is estimated to occur in ~0.5% to 0.7% of all live births.[1–3] In other parts of the world, such as Latin America, Africa, and most countries in Asia, cCMV rates are even higher at ~1% to 2% of all births.[4–8] Approximately 10% of infants with cCMV will have clinical findings at birth (symptomatic infection). The vast majority of infected infants (≈90%), however, will have no clinical manifestations present during the newborn period (asymptomatic infection).[9] Approximately 40% to 60% of symptomatic infants will manifest permanent sequelae, with sensorineural hearing loss (SNHL) being the most common, followed by cognitive impairment, retinitis, and cerebral palsy.[2,10–12] Asymptomatic infants are also at risk for CMV-related disabilities, and ~10% to 15% of asymptomatic infants will develop SNHL.[2,11–15] Disabilities from symptomatic and asymptomatic cCMV infection are more common in children in the United States than other more recognized diseases such as Down syndrome, fetal alcohol syndrome, or spina bifida.[16]

cCMV infection significantly contributes to permanent childhood hearing loss, with CMV-related SNHL being second only to genetic causes both at birth and during the early years of life.[14,17] SNHL after cCMV may be present at birth or occur later in childhood (late onset). Children with SNHL after cCMV may also have further worsening or progression of their losses.[11–13,15]

Although cCMV is a leading cause of SNHL in children and is more common than any of the other screened newborn conditions in the United States, routine newborn CMV screening does not occur in the United States. Limited CMV awareness by both providers and parents, the difficulty in confirming the diagnosis of cCMV after the newborn period, the inability to predict which children with cCMV will have sequelae, the lack of effective treatments to prevent or ameliorate the effects of the virus, and the absence of an inexpensive and rapid screening test have been some of the obstacles preventing the implementation of widespread CMV screening in the past. Recent advances in the development of a rapid, high-throughput method for detecting CMV in saliva,[18] success with antiviral treatment in symptomatic infants,[19] and the recognition that early identification for targeted monitoring and intervention during critical stages of speech and language acquisition improves outcomes[20,21] have led to renewed interest in both targeted and universal approaches to screening newborns for cCMV. As part of the CMV and Hearing Multicenter Screening (CHIMES) study, ~100 000 infants were tested for CMV and received a newborn hearing screening (NHS) while in the hospital nursery, thus allowing us to examine the effectiveness of a targeted approach in identifying infants with CMV-related hearing loss where only newborns who did not pass NHS would be tested for cCMV.

METHODS

Study Population

Between March 2007 and March 2012, 100 607 infants born at 7 US medical centers (University of Alabama at Birmingham Hospital, Birmingham, AL; The University of Mississippi Medical Center, Jackson, MS; Saint Peter's University Hospital, New Brunswick, NJ; Carolinas Medical Center, Charlotte, NC; Good Samaritan Hospital, Cincinnati, OH; Magee Womens Hospital, Pittsburgh, PA; and Parkland Memorial Hospital, Dallas, TX) were consented and enrolled prospectively in the CHIMES Study. All live-born infants were eligible for participation. Mothers were approached postpartum to obtain written informed consent for their infant's enrollment in the study. Upon enrollment, saliva specimens were collected from the newborn and additional dried blood spots were obtained at the time of routine newborn metabolic screening and tested for CMV as previously described.[18,22] Infants with positive saliva or dried blood spots screening specimens were enrolled in the follow-up component of the study to confirm cCMV and to monitor their hearing outcome. Newborn medical records were reviewed for infants with cCMV to determine if the infants had clinically apparent disease. An a priori definition of symptomatic cCMV was established at the beginning of the CHIMES study by study investigators. Infants were considered to have symptomatic cCMV if they had any of the following symptoms in the newborn period: generalized petechial rash, purpuric rash, hepatomegaly, splenomegaly, jaundice with direct bilirubin of 3 mg/dL or greater, unexplained neurologic/CNS abnormalities (eg, microcephaly, seizures, focal or generalized neurologic deficits), or chorioretinitis. Clinical decisions about further evaluations and possible treatment of the CMV-infected infants were made by the physicians at each study site. The CHIMES study did not include treatment of cCMV infants. Local institutional review board approval was obtained at each site.

NHS

NHS results and any additional outpatient hearing screens or diagnostic follow-up audiologic testing results were collected from

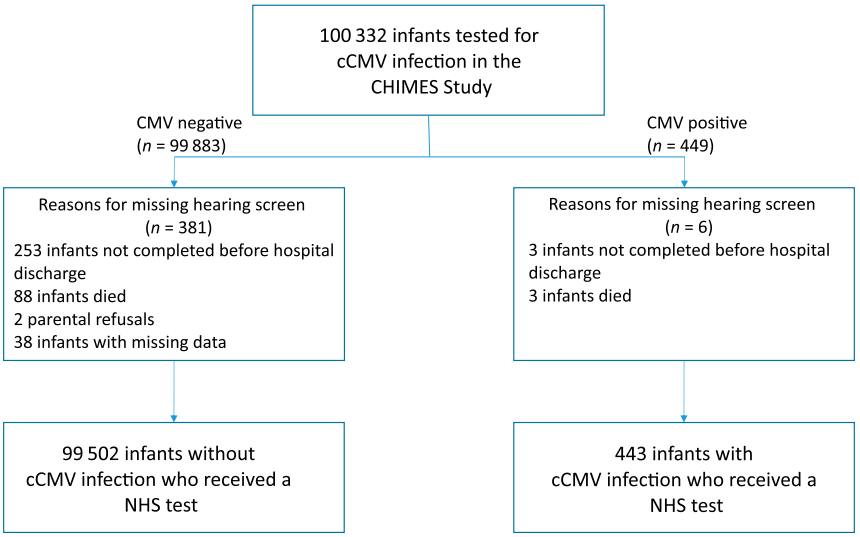

FIGURE 1
Study cohort for the CHIMES study.

the individual hospital's audiology program for each infant enrolled in the study. Each study site followed the NHS protocol designed for their hospital. Most of the hospitals used a 2-stage protocol where infants who did not pass in the hospital were scheduled for an additional outpatient hearing screen, and infants not passing their outpatient hearing screen were scheduled for a follow-up diagnostic audiologic evaluation. Infants with cCMV, regardless of hearing screen status, received a diagnostic audiologic assessment at 3 to 8 weeks of age as part of the CHIMES study. The CHIMES study diagnostic audiology protocol included a tone burst Auditory Brainstem Response with thresholds at 0.5, 1.0, 2.0, and 4.0 kHz and Distortion Product Otoacoustic Emissions for each ear. Bone conduction, tympanometry, and ipsilateral acoustic reflexes were performed with a 1000-Hz probe tone if hearing loss was suspected. CMV-negative infants who referred (ie, did not pass) on NHS were audiologically managed per their hospital's and state's recommendations for a diagnostic audiologic assessment by 3 months of age for the identification of possible hearing loss in the infants.[21] CMV-negative infants did not receive their audiological assessments as part of the CHIMES study.

Statistical Analysis

All statistical analyses were performed by using SAS software, version 9.3 (SAS Institute, Inc, Cary, NC).

The results of CMV screening were compared with the newborn hearing results. Binomial 95% confidence intervals (CIs) were calculated for point estimates. Statistical significance was determined by using a 2-tailed χ^2 or Fisher's exact test with a 5% level of significance, where appropriate.

RESULTS

Of the 100 332 enrolled infants with a CMV test result, 99 945 (99.6%) had an NHS result (Fig 1). Reasons for not having NHS results included the following: hearing screen not completed before discharge from the nursery; infant death; or parental refusal. Of the 6 CMV-positive infants who did not have an NHS result, 3 symptomatic preterm infants died before a hearing screen was obtained, and 2 infants did not enroll in the follow-up component, so no follow-up information is available about whether these infants had hearing loss or normal hearing. The other infant did not have any evidence of hearing loss at birth confirmed by a diagnostic audiologic assessment when the infant enrolled in the follow-up component of the CMV study. Of the 99 945 infants who received an NHS, 443 (0.4%) were diagnosed with cCMV infection. Study characteristics of the 99 945 infants are seen in Table 1.

The NHS referral (did not pass) rate for the study population was 1.0% (95% CI, 0.9%–1.0%). However, 7.0% of CMV-positive infants did not pass their hearing screen compared with 0.9% of CMV-negative infants who did not pass their hearing screen ($P < .0001$). The same pattern remained in both the well-infant and the NICU nurseries, where the CMV-positive infants were significantly more likely to fail their hearing screen compared with CMV-negative infants (Table 2). Among infants with asymptomatic cCMV, 20/403 (5%, 95% CI, 3.1%–7.6%) failed NHS. In the well-infant and the NICU nurseries, 15/375 (4%, 95% CI, 2.3%–6.5%) and 5/28 (18%, 95% CI, 6%–37%) asymptomatic infants did not pass NHS, respectively. Symptomatic cCMV infants had a much higher referral rate of 11/40 (28%, 95% CI, 15%–44%), and had similar referral rates in both the well-infant (7/25; 28%, 95% CI, 12%–49%) and the NICU (4/15; 27%, 95% CI, 8%–55%) nurseries.

Of the 31 (7%) CMV-positive infants who did not pass NHS, 20 (65%) were confirmed to have SNHL by diagnostic audiologic evaluations. The other 11 (35%) who failed NHS were confirmed to have normal hearing by diagnostic evaluation. An additional 15 (3.6%) CMV-positive infants who passed NHS had SNHL confirmed by a diagnostic hearing evaluation in the first 3 to 8 weeks of life. The severity of

the hearing loss in cCMV infants is seen in Table 3. Those infants who failed NHS were more likely diagnosed with bilateral loss (60%) and also were diagnosed with at least moderate hearing loss (65%). Of the 15 CMV-positive infants who passed their hearing screen but were diagnosed with SNHL during infancy, 9 (60%) had mild loss and 4 of these 9 infants had bilateral loss. The other 6 (40%) of 15 infants were diagnosed with at least a moderate to severe SNHL and 3 of these 6 infants had bilateral loss. None of the 31 CMV-positive infants who failed NHS nor the 15 additional infants who had SNHL were diagnosed as having syndromes or other malformations associated with hearing loss, or had a family history of hearing loss.

TABLE 1 Study Characteristics for the 99 945 Newborns Who Underwent NHS and CMV Testing at the 7 Sites

Characteristic	% (no.)
Infant sex	
Girl	49.2 (49 160)
Boy	50.8 (50 784)
Infant race/ethnicity	
Asian	4.1 (4160)
Black	24.0 (23 946)
White, Hispanic	32.3 (32 269)
White, non-Hispanic	37.1 (37 048)
Multiracial	2.5 (2527)
Insurance status for hospital stay	
Private	35.2 (35 156)
Public or no insurance	64.8 (64 783)
Maternal age, mean (SD), y	27.4 (6.1)
Hospital site	
Birmingham, Alabama	12.0 (12 015)
Jackson, Mississippi	6.3 (6346)
New Brunswick, New Jersey	10.7 (10 706)
Charlotte, North Carolina	15.1 (15 081)
Cincinnati, Ohio	14.1 (14 071)
Pittsburgh, Pennsylvania	19.1 (19 103)
Dallas, Texas	22.6 (22 623)
Hospital nursery	
Well-infant	96.5 (96 735)
NICU	3.5 (3209)

Overall, NHS identified 20/35 (57%, 95% CI, 39%–74%) infants who had CMV-related SNHL in the newborn period leaving 43% not identified with hearing loss. In asymptomatic infants, NHS identified only 9/19 (47%, 95% CI, 24%–71%) of the CMV-related SNHL in these infants, missing 53% with hearing loss. Among symptomatic infants, NHS identified CMV-related hearing loss in 11/16 (69%, 95% CI, 41%–89%) infants.

CMV-positive infants with SNHL identified by NHS and those who passed their hearing screen but had SNHL in the neonatal period comprised 7.9% (95% CI, 5.6%–10.8%) of all infants with cCMV. As expected when infants were categorized by the presence of clinical findings at birth, those with symptomatic infection had a significantly higher rate of hearing loss than those with asymptomatic cCMV at birth. SNHL occurred in 38.1% (95% CI, 23.6%–54.4%) of the symptomatic infants compared with 4.7% (95% CI, 2.9%–7.3%) of the asymptomatic infants ($P < .0001$).

TABLE 2 Newborn Hearing Screen Referral Rates for Infants by CMV Status, Overall and by Nursery

CMV Screen	No. Screened	No. Referred	Hearing Screen Referral Rates, % (95% CI)	*P*
CMV positive	443	31	7.0% (4.8%–9.8%)	<.0001
CMV negative	99 502	930	0.9% (0.8%–1.0%)	
Well-Infant Nursery				
CMV positive	400	22	5.5% (3.5%–8.2%)	<.0001
CMV negative	96 336	768	0.8% (0.7%–0.9%)	
NICU				
CMV positive	43	9	20.9% (10.0%–36.0%)	<.001
CMV negative	3166	162	5.1% (4.4%–5.9%)	

TABLE 3 SNHL Severity by Newborn Hearing Screen Status for Infants With cCMV Infection

	Did Not Pass Hearing Screen, No. (%)	Passed Hearing Screen, No. (%)	Total, No. (%)
Unilateral loss	8 (40)	8 (53)	16 (46)
Bilateral loss	12 (60)	7 (47)	19 (54)
Mild loss (21–40 dB HL)	7 (35)	9 (60)	16 (46)
Moderate or greater loss (>40 dB HL)	13 (65)	6 (40)	19 (54)
Total SNHL	20 (57)	15 (43)	35 (100)

DISCUSSION

Our large study of almost 100 000 infants revealed that a targeted CMV screening approach that only tests newborns who do not pass NHS identified the majority of infants with CMV-related SNHL at birth. However, this approach failed to identify a significant number of infants with CMV-related SNHL (43%) during infancy. Among infants with asymptomatic cCMV, 53% of those with CMV-related SNHL at birth will not be identified by a targeted approach. In addition, only testing infants who failed their hearing screen will miss the CMV-positive infants who are without symptoms at birth, pass NHS, and who go on to develop late onset hearing loss. A previous retrospective study in Texas revealed 6% of hearing impairment in newborns was attributable to CMV when they used a targeted CMV screening approach.[23] Another study in Italy revealed that 10% of infants with SNHL detected <2 months of age had cCMV infection.[24] Although these studies indicated that testing infants who fail NHS for CMV could identify CMV-related SNHL, both studies were retrospective and did not include CMV screening of all infants. Our study included both CMV and hearing screening of all infants and provides reliable estimates of the effectiveness of a targeted CMV screening approach in identifying infants with CMV-related SNHL.

An important finding of our study is that newborns with cCMV have a significantly higher NHS referral rate (7%) than CMV-negative infants. These results indicate that newborns who do not pass their hearing screen and have no other known etiology for their possible hearing loss should be screened for CMV infection. In fact, existing clinical guidelines from the 2007 Statement by the Joint Committee on Infant Hearing recommend that infants with confirmed hearing loss and an uncertain etiology after an initial medical evaluation should have an expanded multidisciplinary evaluation protocol that includes testing for CMV.[21] However, by the time permanent hearing loss is confirmed by the diagnostic audiologic evaluation and the initial medical evaluation is completed, it will be too late to confirm cCMV. Testing of infants who refer on NHS for CMV by saliva or urine polymerase chain reaction before hospital discharge or by 2 to 3 weeks of age by the pediatric medical home provider will provide confirmation of CMV as the cause of any suspected congenital hearing loss. After 3 weeks of age, cCMV cannot be reliably diagnosed as the etiology for infants with SNHL.

NHS programs have been successful in identifying congenital hearing loss but do have some limitations because of the sensitivity and specificity of hearing screen tools and testing protocols.[25] In many programs, the majority of infants who fail NHS will not have permanent hearing loss.[26,27] Although it would be expected that more infants with cCMV who failed their hearing screen would have permanent loss, our finding that 64% of the infants had SNHL was a higher confirmation rate than expected on the basis of other studies.[26,27]

It is unclear why 43% of all CMV-positive infants and 53% of asymptomatic cCMV infants passed NHS but were confirmed to have CMV-related SNHL in the newborn period. A previous multicenter study estimated that ~23% of infants who passed a 2-stage hospital screening protocol had permanent hearing loss at 9 months of age; however, it is estimated that their protocol missed up to 70% of all cases of mild unilateral and bilateral hearing loss.[28,29] At another center, one-third of the pediatric cochlear implant population had previously passed NHS.[30] The percentage of CMV-positive infants with SNHL who passed their hearing screen was higher than these previously reported studies. It is possible that some of the infants who passed NHS but were confirmed to have SNHL were missed because of limitations of the NHS algorithms that were unable to reliably detect mild or isolated frequency region hearing losses. However, this does not explain the infants who had moderate to severe hearing loss identified on their diagnostic evaluation. It is also possible that the hearing loss occurred after the first week after birth or progressed to a measurable level by 6 to 8 weeks after birth. However, this is speculative and no previous data exist to suggest that CMV-related hearing loss is unstable in the neonatal period.

In addition to the fact that NHS failed to detect 43% of CMV-positive infants who had SNHL in the newborn period, the progressive nature of CMV-related hearing loss in ~50% of children with SNHL underscores the limitations of the targeted CMV screening approach.[12,13] The rate of hearing loss progression in cCMV infection seems to be similar regardless of whether a child has an asymptomatic or a symptomatic infection, although the symptomatic infants have a greater degree of severity and also earlier progression of their hearing loss.[12] With current pediatric newborn screening practices, CMV-positive infants who pass NHS but have CMV-related SNHL, whether stable or progressive loss, will be missed by any targeted screening program and otherwise will remain unidentified because routine CMV screening does not occur.

There are limitations in our study in that although all live-born infants were eligible to participate at the hospitals not all were enrolled in the study. Infants who were in the NICU were less likely to be approached by study staff because of the fragility of the infant and to not place any additional burdens on their families.

Infants who were discharged early or who were delivered on weekends or evenings may have been missed if study personnel were not available to obtain consent. It is possible that we missed cCMV infants, especially asymptomatic infants, and underestimated the rate of cCMV infection for our hospital sites. Our study revealed a 0.4% cCMV rate that is lower than some previously reported studies,[2,3] although not lower for other large studies of cCMV.[31,32] However, the lower cCMV rate should not impact the observed difference in the hearing referral rates between CMV-positive and CMV-negative infants, because there is no evidence to suggest the missed cCMV infants would have had a different hearing referral rate than those infants diagnosed. Also, the rates of CMV-related SNHL in the study were similar to previous reports, so it is not likely that the study missed a significant number of CMV-positive infants at the sites.[11,12]

Targeted CMV screening will minimize the diagnostic etiology odyssey for some of the infants with suspected hearing loss because cCMV can only be reliably diagnosed within the first few weeks after birth. Also, infants identified with CMV-related hearing loss through targeted screening will have the opportunity for more focused audiologic monitoring, early intervention, and antiviral treatment. However, the limitations of a targeted CMV screening approach are the failure to identify all CMV-related SNHL in the newborn period and missing the cCMV infants who pass NHS but are at risk for late onset hearing loss.

CONCLUSIONS

A targeted CMV screening approach does identify the majority of infants with CMV-related SNHL in the newborn period. However, this method fails to identify a significant number of infants with CMV-related SNHL during infancy highlighting the need to develop approaches to improve detection of CMV-related hearing loss at birth. Strategies to identify all infants with cCMV who remain at risk for late onset and progressive hearing losses are needed.

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ABBREVIATIONS

cCMV: congenital cytomegalovirus
CHIMES: CMV and Hearing Multicenter Screening
CI: confidence interval
CMV: cytomegalovirus
NHS: newborn hearing screening
SNHL: sensorineural hearing loss

data and coordinated and supervised audiology data collection at the Alabama site and critically reviewed the manuscript; Dr Cox assisted in the development of the CHIMES audiology protocols, collected audiology data at the North Carolina site, and coordinated and supervised the collection of audiology data; Dr Mohamed collected audiology data at the North Carolina site and critically reviewed the manuscript; Dr Choo contributed in the development of the CHIMES audiologic protocols, advised on the collection of audiologic data at the Ohio site, and critically reviewed the manuscript; Dr Boppana conceptualized and designed the study, actively participated in the conduct of the study, and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

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