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Cost-effectiveness of Universal and Targeted Newborn Screening for Congenital Cytomegalovirus Infection

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IMPORTANCE Congenital cytomegalovirus (cCMV) infection is a major cause of childhood deafness. Most cCMV infections are not diagnosed without newborn screening, resulting in missed opportunities for directed care.

OBJECTIVE To estimate the cost-effectiveness of universal and targeted newborn cCMV screening programs compared with no cCMV screening.

DESIGN, SETTING, AND PARTICIPANTS Models were constructed using rates and outcomes from prospective cohort studies of newborn cCMV screening in US postpartum care and early hearing programs. Costs of laboratory testing, treatment, and hearing loss were drawn from Medicaid data and published estimates. The benefits of cCMV screening were assumed to come from antiviral therapy for affected newborns to reduce hearing loss and from earlier identification of hearing loss with postnatal onset. Analyses were performed from July 2014 to March 2016.

INTERVENTIONS Models compared universal or targeted cCMV screening of newborns with a failed hearing screen, with standard care for cCMV infection.

MAIN OUTCOMES AND MEASURES The incremental costs of identifying 1 cCMV infection, identifying 1 case of cCMV-related hearing loss, and preventing 1 cochlear implant; the incremental reduction in cases of severe to profound hearing loss; and the differences in costs per infant screened by universal or targeted strategies under different assumptions about the effectiveness of antiviral treatment.

RESULTS Among all infants born in the United States, identification of 1 case of cCMV infection by universal screening was estimated to cost $2000 to $10 000; by targeted screening, $566 to $2832. The cost of identifying 1 case of hearing loss due to cCMV was as little as $27 460 by universal screening or $975 by targeted screening. Assuming a modest benefit of antiviral treatment, screening programs were estimated to reduce severe to profound hearing loss by 4.2% to 13% and result in direct costs of $10.86 per newborn screened. However, savings of up to $37.97 per newborn screened were estimated when costs related to functionality were included.

CONCLUSIONS AND RELEVANCE Newborn screening for cCMV infection appears to be cost-effective under a wide range of assumptions. Universal screening offers larger net savings and the greatest opportunity to provide directed care. Targeted screening also appears to be cost-effective and requires testing for fewer newborns. These findings suggest that implementation of newborn cCMV screening programs is warranted.

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Author Audio Interview

Supplemental content

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Cytomegalovirus (CMV) is the most common congenital infection and a leading cause of childhood hearing loss, cognitive deficits, and visual impairment. The prevalence of congenital CMV (cCMV) infection has been estimated to be 0.64% at birth, which translates into more than 20 000 neonates with congenital infection born annually in the United States.[1] Of these neonates, at least 3000 are estimated to develop permanent neurologic disabilities each year due to cCMV infection.[2,3] Approximately 10% to 25% of all childhood sensorineural hearing loss (SNHL) can be attributed to cCMV infection.[4,5] With an estimated annual cost of up to $4 billion in the United States, cCMV infection is an enormous public health concern.[2]

A minority of newborns with cCMV infection have clinically evident manifestations of disease at birth, which are largely nonspecific. As many as 50% of these symptomatic infants will experience neurologic sequelae, including SNHL. An additional 10% to 15% of the asymptomatic newborns will experience SNHL due to cCMV infection that can be present at birth or appear years later.[6,7] A definite diagnosis of cCMV requires direct viral detection in saliva, urine, or blood samples during the first 2 to 3 weeks of life; if detected later, postnatal CMV infection cannot be excluded. Polymerase chain reaction (PCR) analysis for CMV in saliva samples is sensitive, convenient, and amenable to large-scale screening.[8] At present, diagnosis of cCMV infection depends largely on clinical suspicion. However, only a small proportion of symptomatic cCMV infections (and essentially none of the asymptomatic ones) are diagnosed using this approach.[9-14] All infants with cCMV infection, symptomatic or asymptomatic, may benefit from early diagnosis for anticipatory guidance, early identification of late-onset hearing impairment, and appropriate support.[3] Treatment of newborns with symptomatic cCMV infection with the antiviral drug valganciclovir hydrochloride for 6 months also results in improved hearing and developmental outcomes.[15]

Although universal newborn screening offers the benefit of identifying all infected infants, the low sensitivity of CMV testing reported using dried blood spots[8,16] (the sample used for all other universal newborn laboratory testing) means that an additional sample is required (ie, saliva or urine). In addition, most infants with cCMV infections (approximately 80%) will not develop CMV-related disability and therefore would not benefit from screening. Thus, cCMV screening strategies aimed at high-risk newborns have been evaluated, most commonly targeting infants with a failed newborn hearing screen.[17,18] Targeted cCMV screening based on failed newborn hearing screens would not capture infections that result in late-onset hearing loss. Although estimates have been calculated for the benefits of universal screening[3] and the cost of targeted screening programs,[19,20] formal cost-effectiveness analyses have not been performed for either strategy.

Key Points

Question Is newborn screening for congenital cytomegalovirus (cCMV) infection cost-effective?

Findings In a cost-effectiveness study that compared universal (for all newborns) or targeted cCMV screening (newborns with a failed universal newborn hearing screen) with no screening under a wide range of assumptions regarding the US costs of testing, treatment, and hearing loss related to cCMV infection, universal and targeted cCMV screening were relatively low cost, or cost saving if costs related to lost productivity were included.

Meaning Universal and targeted newborn screening programs for cCMV infection in the United States appear to be cost-effective.

Methods

Model Structure

We constructed the following 2 models to estimate the effect of cCMV screening programs on hearing loss and costs compared with standard care for most newborns (no screening): one to evaluate universal newborn screening and one for targeted screening (eFigure in the Supplement). Because this study used only secondary data in aggregate, it was exempted from human subjects protection review by the University of British Columbia.

Rates and Outcomes of cCMV Infection and Related Hearing Loss

The prevalence of cCMV infection at birth was assumed to be 0.5% based on the CMV and Hearing Multicenter Screening (CHIMES) study,[16] in which approximately 100 000 newborns were screened in 7 US sites. In the universal cCMV screening model, all newborns underwent testing for cCMV infection within 3 weeks of birth using PCR analysis of an oral swab, which has 97% sensitivity and 99% specificity.[8] With targeted screening, only newborns with failed hearing screens underwent testing for cCMV infection. Targeted cCMV screening was assumed to take place before a comprehensive audiologic evaluation given that this evaluation is typically only performed after 3 weeks of age. We assumed that 1.5% of newborns have a failed hearing screen and that, of these, 10% will have confirmed hearing loss.[21] Based on previous data,[4,5] we estimated that 13.3% of all infants with hearing loss at birth had cCMV infection. The prevalence of cCMV infection and the likelihood of late-onset hearing loss among infants with a false-positive hearing screen result (ie, newborns found to have normal hearing by auditory brainstem response evaluation) were assumed to be the same as for the general population. We conservatively assumed that 25% of symptomatic cCMV infections would be diagnosed clinically (ie, identified without screening) and treated with an antiviral.[3,9-14] Estimates for the timing and severity of hearing loss were based on 551 children with cCMV infection identified through a universal newborn screening program from 1980 to 2001 and evaluated prospectively as previously described.[22]

Assumptions and Statistical Analysis

Analyses were performed from July 2014 to March 2016. We used a real discount rate of 1%, which approximates the current interest rate on 30-year, inflation-protected US bonds. Medicaid reimbursement rates were used for all cost estimates unless otherwise specified. We estimated screening costs

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of $10 to $50 per newborn undergoing testing,[19,20] which includes the oral swab and CMV PCR analysis and a confirmatory urine PCR analysis for any newborns with a positive test result.[23] We did not include administrative costs; we acknowledge that start-up costs to add CMV screening to existing programs might increase costs, but these are expected to be one time and modest given the assumption that infrastructure already in place for newborn screening would be used. For example, all US states have established universal newborn screening programs for hearing loss by audiometry and for genetic diseases using dried blood spots.

Infants with confirmed cCMV infection were assumed to undergo a medical evaluation. Those with a failed hearing screen were also assumed to have an expedited comprehensive audiologic evaluation within the first month of life (rather than by 3 months[24]) to guide the use of antiviral treatment. All cCMV-infected children without hearing loss at birth were assumed to have audiologic testing every 6 months to monitor for late-onset hearing impairment[24]; this follow-up was assumed to lead to earlier identification of hearing loss by a mean of 24 months. These follow-up costs end at the sixth birthday or when hearing loss is discovered. For infants with asymptomatic infection who have no hearing loss at birth, antiviral treatment is not recommended and no consensus exists on other testing. For infants with symptomatic infections at birth, with or without hearing loss, antiviral treatment with valganciclovir is indicated given evidence of improved hearing outcomes.[15] All infected newborns with symptoms and/or hearing loss at birth were also assumed to undergo basic laboratory testing, cranial ultrasonography, and ophthalmologic examination. We assumed that all infants with an abnormal finding on ultrasonography or on a neurologic examination would undergo brain magnetic resonance imaging and that these results would represent 20% of symptomatic and 1% of asymptomatic infants identified as a result of CMV screening. Identification of cCMV infection through screening was assumed to save the costs of testing for other common causes of hearing loss.[25]

For infants with infection and hearing loss at birth but no other apparent disease, equipoise exists among experts about whether antiviral therapy is indicated.[18,19,26,27] As such, the universal and targeted screening were modeled with and without antiviral treatment of this group. Costs of drugs and monitoring for toxic effects were included for all children treated with valganciclovir. Costs savings were based on a recent trial[26] that found improved outcomes at 24 months in 77% of newborns treated with 6 months vs 6 weeks of valganciclovir. Because approximately 22% of infants were observed to improve without treatment in an earlier trial,[28] we estimated that the current standard treatment improves hearing in approximately half of symptomatic infants. We therefore modeled the effect of antiviral treatment so that 50% of children in each hearing loss category were assumed to improve by 1 hearing loss category; that is, 50% of children who would have had profound hearing loss had severe hearing loss; 50% who would have had severe hearing loss had moderate hearing loss; 50% who would have had moderate hearing loss had mild hearing loss; and 50% who would have had mild hearing loss had normal hearing. We assumed that benefits are permanent and that this treatment has no effect on hearing loss with onset after 24 months. We applied this effect to all cases of hearing loss that developed within 2 years of birth for children with symptomatic infection. We assumed the same antiviral benefits if given to children who had hearing loss at birth but were otherwise asymptomatic. Although valganciclovir treatment of symptomatic cCMV infection may also result in improved neurocognitive outcomes,[26] these outcomes were not included owing to insufficient data to estimate the associated benefits and costs. We also modeled the cost-effectiveness of cCMV screening using higher and lower antiviral effectiveness and in the absence of antiviral treatment for any child.

Cost savings for children with asymptomatic cCMV infection without hearing loss at birth and for symptomatic children with onset of hearing loss beyond 24 months are assumed to result from earlier identification of hearing loss by virtue of repeated follow-up audiologic evaluations. Early identification has been found to reduce the functional impairments resulting from hearing loss.[29] Kennedy et al[30] found that early identification of hearing loss resulting from newborn hearing screens was associated with a 24% improvement in receptive language compared with no screening. We assumed that the impact of early intervention for late-onset hearing loss was one-half that for hearing loss present at birth, which is consistent with other estimates.[31] As such, we estimated a 12% reduction in the costs associated with any category of hearing loss owing to the earlier identification of hearing loss that results from cCMV screening and audiologic follow-up.

Once hearing loss was identified, costs of care were broken down into the following 4 categories: (1) medical, (2) audiologic, (3) equipment, and (4) therapy and special education programs. We assumed that only 50% of cases of bilateral profound hearing loss receive a cochlear implant[32-34] at a cost of $100 000.[20] We also estimated the costs related to loss of productivity as an adult. We assumed no loss of productivity for adults with mild or moderate hearing loss. For severe and profound hearing loss, the loss of productivity was estimated to be $926 000 in 2016 US dollars.[35] Life expectancy was assumed to be 79 years. Modeling estimates were generated using Excel software (version 2010; Microsoft Corp).

Results

The net financial impact of universal or targeted cCMV screening was calculated as the sum of the screening-related costs (**Table 1**) and the difference between the hearing loss-related costs derived from the Special Education Expenditure Project[36] (**Table 2**) with and without screening. We assumed the following 2 screening effects: (1) an improvement in hearing owing to antiviral therapy for infants with clinical manifestations of cCMV infection at birth and (2) benefits resulting from earlier identification of hearing loss and earlier interventions. The proportion of infants with cCMV infection who developed hearing loss, categorized as mild to moderate or severe to profound, at a given age is shown in **Table 3**. The total proportion of symptomatic infections in this cohort was 14%, which is

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Table 1. Cost Assumptions Associated With Newborn cCMV Screening[a]

Screening Item	Cost, $	Comments
All screened newborns		
Collection and CMV PCR testing of oral swab	10-50 per test	Cost depends on volume and efficiencies[b]
All newborns with cCMV infection		
Medical evaluation	150.38	Pediatric clinic visit to follow up positive CMV test result and investigate signs of infection
Symtomatic newborns with cCMV infection and/or hearing loss at birth		
Laboratory testing	23	CBC count and serum chemistry panel
Cranial ultrasonography	82.03	To evaluate for brain abnormalities due to cCMV infection
Brain MRI	560.00	Performed on a proportion of infants (eg, those with abnormal findings of cranial ultrasonography)
Ophthalmology examination	115.44	To rule out CMV retinitis
All newborns with cCMV infection without hearing loss at birth		
Audiologic follow-up	152.76 per visit	Every 6 mo until the development of late-onset hearing loss or 6 y of age[c]; includes otoacoustic emission testing tympanometry and the cost of the audiologist's time
All treated newborns[d]		
Valganciclovir hydrochloride	4400	6-mo course, including dispensing fees
Laboratory monitoring	385	CBC count and serum chemistry panel performed 8 times during valganciclovir therapy

Abbreviations: CBC, complete blood cell; cCMV, congenital cytomegalovirus; MRI, magnetic resonance imaging; PCR, polymerase chain reaction.

[a] All costs are in current US dollars. Costs that would be incurred even in the absence of cCMV screening (eg, newborn hearing screening studies) are not included.

[b] The range of costs for CMV PCR is conservatively high and includes confirmation of positive swab results with a urine PCR analysis according to current estimates.[23]

[c] Late-onset hearing loss due to cCMV infection rarely occurs after 6 years of age; children older than 6 years are expected to receive routine hearing screening for school-aged children.[24]

[d] Different indications for treatment (eg, symptoms at birth or symptoms and/or hearing loss at birth) were modeled given the equipoise among experts.

similar to the mean proportion from published screening studies.[3] Among all 551 children with cCMV infection, 22 (4.0%) had hearing loss at birth (consistent with cCMV infection accounting for approximately 2 cases of SNHL per 10 000 population or 13.3% of all SNHL at birth), and 71 (12.9%) developed hearing loss at any time, which is again consistent with published estimates.[3,4,6,7]

The total costs to identify 1 case of cCMV infection and 1 case of cCMV-related hearing loss using the universal and targeted screening models and with a range of testing costs are shown in **Table 4**. The cost to prevent cochlear implantation for 1 child was estimated to be as little as $39 401, assuming antiviral treatment of symptomatic infants identified by targeted screening with a moderately inexpensive test. However, we estimated a cost ranging from $4 064 157 to $12 620 277 to prevent cochlear implantation for 1 child through universal screening depending on the cost of the test used.

Depending on assumptions related to antiviral treatment, the results of the universal and targeted screening models ranged from modest direct costs of $10.86 (sensitivity analysis, $6.97 to $14.73) to net savings of $37.97 (sensitivity analysis, $14.60 to $61.34) per newborn undergoing screening (**Table 5**). Both screening approaches were more cost-effective if antiviral therapy was assumed to be given and effective for isolated hearing loss at birth rather than just to newborns with clinically evident symptoms of cCMV infection. Even in the absence of any antiviral treatment, the direct costs of screening were modest, ranging from $2.01 per newborn undergoing targeted screening to $14.16 per newborn undergoing universal screening. Without treatment, the benefits of screening were derived exclusively from early identification of late-onset hearing loss. Under all assumptions, universal screening was slightly more cost-effective than targeted screening when the total lifetime functional cost of hearing loss was included.

Discussion

Newborn cCMV screening strategies have been increasingly recognized for their potential medical benefits.[3,17,18,27] Debate about these programs has increased as a result of recent advances in diagnosis and treatment. Convenient, accurate, and inexpensive testing for cCMV in newborns with the use of oral swabs is now available.[8,23] In addition, randomized clinical trial data indicate that oral antiviral therapy for symptomatic cCMV infection is safe and effective.[26] Available evidence indicates that current approaches to identification of newborns with cCMV-related disease are inadequate, and most infants with a cCMV infection will not receive timely and appropriate care in the absence of some type of screening program.[3,13,14]

Targeted cCMV screening, triggered by suspected newborn hearing loss, has been shown to be feasible in the United States and United Kingdom.[17,18] Notably, offering cCMV testing for newborns with hearing loss is mandated by law in some US states.[37] Preliminary reports of the cost of these programs are comparable to those of other screening programs.[19,20] Although universal newborn screening could benefit thousands of children per year in the United States,[3] it has not been adopted for cCMV infection, in part because of questions regarding cost-effectiveness. We find that universal and targeted screening programs appear to reduce total costs under most assumptions.

The major strength of this study is a comprehensive analysis of all of the costs related to newborn cCMV screening using data derived from large prospective cohorts. Net savings from universal screening were estimated to be greater than those from targeted screening, although screening costs are higher. Savings from screening strategies are derived from improved hearing with antiviral treatment of affected newborns but also from earlier detection of late-onset hearing loss. One impor-

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Table 2. Annual Cost Assumptions for Care of Children With Hearing Loss Due to cCMV Infection[a]

Age Group by Severity of Hearing Loss	Service and Cost				Total Cost per Infant, $
	Medical[b]	Audiology[c]	Equipment[d]	Therapy[e]	
From identification of hearing loss to <6 y					
Mild to moderate	ENT yearly ($100 first visit; $66 each subsequent visit)	OAE, tympanometry, and VRA every 6 mo ($305.52)	Hearing aids ($1144), FM system ($334)	0	$1850 ($1884 the first year)
Severe to profound	ENT yearly ($100 first visit; $66 each subsequent visit)	OAE, tympanometry, and VRA every 6 mo ($305.52)	Hearing aids ($858), FM system ($668)	$6907	$8805 ($8839 the first year)
6 to <13 y					
Mild to moderate	ENT every 2 y ($22 per year)	OAE, tympanometry, and play audiometry yearly ($178.55)	Hearing aids ($1001), FM system ($334)	0	$1536
Severe to profound	ENT every 2 y ($22 per year)	OAE, tympanometry, and play audiometry yearly ($178.55)	Hearing aids ($751), FM system ($668)	$19 151	$20 771
13 to <18 y					
Mild to moderate	ENT once ($13.20)	OAE, tympanometry, and conventional audiometry yearly ($178.55)	Hearing aids ($1001), FM system ($334)	0	$1527
Severe to profound	ENT once ($13.20)	OAE, tympanometry, and conventional audiometry yearly ($178.55)	Hearing aids ($751), FM system ($668)	$19 151	$20 762
≥18 y					
Mild to moderate	None	None	$948	0	$948
Severe to profound	None	None	$948	0	$948

Abbreviations: cCMV, congenital cytomegalovirus; ENT, ear, nose, and throat; FM, frequency modulation; OAE, otoacoustic emissions; VRA, visual reinforcement audiometry.

[a] All costs are in 2016 US dollars. All hearing loss due to cCMV infection is assumed to occur by 6 years of age.

[b] Otolaryngology (ENT) visits are estimated to occur at the frequency shown to evaluate changing hearing loss or other issues identified by audiologic follow-up. Visits are expected to be rare beyond 18 years of age and are therefore excluded.

[c] Costs include audiologist time. The cost of auditory brainstem response required to confirm audiometry results for a small minority of children is excluded.

[d] We assumed that 50% of children with mild to moderate and all with severe to profound hearing loss receive FM systems; that all children with hearing loss receive hearing aids; and that 50% of children with severe to profound hearing loss receive cochlear implants at a 1-time cost of $100 000, after which they no longer incur hearing aid costs. The yearly cost for FM systems have been calculated based on binaural fitting with replacement every 5 years, including estimated costs for maintenance, repair, and replacement parts using a representative retail price. The yearly costs for hearing aids have been calculated based on binaural amplification with replacement every 4 years, including ear molds, batteries, and fitting fees.

[e] For those younger than 6 years, includes any program designed to optimize the development of language, speech, and communication for preschoolers. Therapy for school-aged children includes speech therapy and assistance with schooling, such as note taking. Costs are derived from the Special Education Expenditure Project.[36]

tant limitation is that the precise long-term benefits of antiviral therapy, an important component of our models, are not well defined.[15] As such, we performed sensitivity analyses across a wide range of valganciclovir efficacy. Under the extreme assumption that no effective antiviral therapy is available, we found that universal and targeted screening would still be nearly neutral with respect to net costs. However, strong evidence suggests that inhibitors of CMV replication improve the outcomes of children with cCMV infection.[15,27] Furthermore, the benefits of antiviral therapy may well increase as a result of longer treatment courses and/or regimens that include more effective agents.[38-41]

The impact of earlier identification of late-onset hearing loss due to cCMV infection is also not well defined, and different estimates would affect the cost-effectiveness of screening, particularly using the universal approach. We did not estimate the effects of screening or treatment on cognitive outcomes owing to insufficient information on which to base costs and effect despite evidence that antiviral therapy appears to improve developmental outcomes.[15] If antiviral treatment does reduce intellectual disability, cost savings of cCMV screening would likely increase dramatically.[42]

Other limitations include our estimates of the costs of screening, costs associated with hearing loss, and assumptions about the impact of early intervention. As such, we evaluated a range of CMV PCR costs that include recent estimates.[19,20] Even if testing costs were as high as $50, universal screening would still be roughly cost neutral under some scenarios in our model. These estimates are highly conservative given experience with per-sample PCR costs of less than $10 in other newborn screening programs.[43] Newborn PCR-based screening programs for other diseases have already demonstrated the possibility for cost savings,[43,44] and the costs of high-throughput molecular diagnostics will likely continue to decrease. Other efficiencies might further increase savings. For example, improving the specificity of screening for hearing or timeliness of confirmatory audiologic evaluation could reduce the number of CMV tests using a targeted screening strategy. Identification of infants with cCMV infection could result in costs for use of health care resources that exceed our estimates (eg, excessive use of magnetic resonance imaging of the brain), which would reduce the savings associated with screening. On the other hand, although we assumed some cost savings from

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Table 3. Timing and Severity of Hearing Loss Among Children With cCMV Infection

Timing of Onset by Severity of Hearing Loss[a]	All Children With cCMV Infection, No. (%)		
	Symptomatic[b]	Asymptomatic	Total
At birth			
Mild to moderate	4 (0.7)	6 (1.1)	10 (1.8)
Severe to profound	6 (1.1)	6 (1.1)	12 (2.2)
≤12 mo			
Mild to moderate	3 (0.5)	6 (1.1)	9 (1.6)
Severe to profound	5 (0.9)	8 (1.5)	13 (2.4)
>12 to 24 mo			
Mild to moderate	2 (0.4)	1 (0.2)	3 (0.5)
Severe to profound	0	0	0
>24 to 36 mo			
Mild to moderate	2 (0.4)	1 (0.2)	3 (0.5)
Severe to profound	0	1 (0.2)	1 (0.2)
>36 to 48 mo			
Mild to moderate	0	5 (0.9)	5 (0.9)
Severe to profound	0	0	0
>48 to 60 mo			
Mild to moderate	0	3 (0.5)	3 (0.5)
Severe to profound	0	0	0
>60 mo			
Mild to moderate	5 (0.9)	5 (0.9)	10 (1.8)
Severe to profound	1 (0.2)	1 (0.2)	2 (0.4)
None identified	49 (8.9)	431 (78.2)	480 (87.1)
Total	77 (14.0)	474 (86.0)	551 (100)

Abbreviation: cCMV, congenital cytomegalovirus.

[a] Mild to moderate severity indicates greater than 20 to 70 dB; severe to profound severity, greater than 70 dB (based on worst ear).

[b] Indicates symptoms at birth, not including hearing loss.

Table 4. Estimated Mean Incremental Costs per Newborn to Identify Cases of cCMV Infection and Related Hearing Loss

Cost	Screening Strategy, $[a]			
	Universal		Targeted	
	10/Test	50/Test	10/Test	50/Test
Cost to identify 1 cCMV infection	2000	10 000	566	2832
Cost to identify 1 cCMV-related hearing loss	27 460	90 038	975	3916
Cost to prevent 1 cochlear implant[b]	4 064 157	12 620 277	39 401	271 947

Abbreviation: cCMV, congenital cytomegalovirus.

[a] All costs are in 2016 US dollars.

[b] Assumes valganciclovir hydrochloride treatment of only symptomatic newborns, calculated as the number of newborns who needed to be screened to prevent 1 cochlear implant case multiplied by the incremental cost of screening, follow-up, and valganciclovir per newborn screened.

Table 5. Estimated Mean Savings of Newborn cCMV Screening Strategies[a]

Outcome	Screening Strategy[b]					
	Universal			Targeted		
	Treat cCMV-Infected Symptomatic Newborns Only	Treat cCMV-Infected Symptomatic Plus Asymptomatic Newborns With Hearing Loss at Birth	No Treatment	Treat cCMV-Infected Symptomatic Newborns Only	Treat cCMV-Infected Symptomatic Plus Asymptomatic Newborns With Hearing Loss at Birth	No Treatment
Reduction in severe to profound cases enabled by screening, %	7.5 (2.5 to 12.6)	13 (5.3 to 21)	NA	4.2 (1.4 to 7)	9.7 (4.1 to 15.2)	NA
Costs/savings per newborn excluding loss-of-productivity costs, $	−10.86 (−14.73 to −6.97)	−6.83 (−12.98 to −0.68)	−14.16	0.90 (−0.82 to 3.51)	4.95 (0.50 to 9.15)	−2.01
Net costs/savings per newborn including loss-of-productivity costs, $	21.34 (6.54 to 36.17)	37.97 (14.60 to 61.34)	1.67	10.66 (2.57 to 19.67)	27.31 (10.21 to 43.59)	−1.80

Abbreviations: cCMV, congenital cytomegalovirus; NA, not applicable.

[a] Assumes a screening test cost of $10 per newborn. All costs/savings are in 2016 US dollars.

[b] Treatment consists of valganciclovir hydrochloride. Values shown are derived using the estimated benefit of valganciclovir on hearing loss as described in the Methods section, with a sensitivity analysis shown in parentheses in which the estimated benefit is 50% lower or higher.

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decreased use of diagnostic testing for other common causes of hearing loss among newborns diagnosed with cCMV infection, other costs might be saved by avoiding "the diagnostic odyssey."[3(p293)] The true proportion of newborn hearing loss due to cCMV infection is also uncertain[4,5] but has implications for the cost-effectiveness of targeted CMV screening.

Limited information is available about the costs associated with hearing loss. We estimated total lifetime costs of $280 000 for children with severe or profound hearing loss, plus an estimated productivity loss of $926 000, for a total cost of approximately $1.2 million, which is consistent with other estimates.[35,45] We also provide results with and without costs related to the loss of productivity. A major contributor to these costs is educational assistance. Our estimate of the cost of educational assistance for severe and profound hearing loss with onset before age 6 years is approximately $230 000. Although estimates vary in other studies from about $135 000[46] to $290 000,[35] using the extremes of this range of educational assistance cost does not have a major effect on the model. For example, if educational assistance costs of $135 000 are used, the savings estimate of universal cCMV screening with antiviral treatment for symptomatic newborns and for newborns with hearing loss at birth falls from $37.97 per newborn to approximately $30. Because hearing loss has lifetime effects, the discount rate used in calculations is an important consideration. Varying the discount rate from 1% to 3% increases the present value net cost estimate by approximately $3 per newborn for universal screening and by approximately $1.50 per newborn for targeted screening.

Conclusions

We found that screening newborns for cCMV infection is generally associated with cost savings, or is essentially cost neutral from the perspective of net public spending, across a wide range of assumptions. These results, combined with the reported clinical benefits[3,15] and high parental acceptance,[19,47,48] appear to satisfy accepted criteria for newborn screening.[49] Thus, in the absence of a vaccine or other effective methods to prevent cCMV infection, newborn cCMV screening appears warranted in the United States.

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Concept and design: Goshen, Park.
Acquisition, analysis, or intepretation of data: Gantt, Kozak, Goldfarb, Park, Boppana, Fowler.
Drafting of the manuscript: Gantt, Dionne, Goshen, Boppana.
Critical revision of the manuscript for important intellectual content: Gantt, Kozak, Goldfarb, Park, Boppana, Fowler.
Statistical analysis: Gantt, Dionne.
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Study supervision: Park.

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