Considering adding congenital cytomegalovirus (cCMV) to the Washington State Newborn Screening Panel

A narrative of an economic analysis for the Department of Health, State Board of Health, and technical advisory committee

October 2022

Proposed Rule and Brief History

The State Board of Health (Board) is authorized by RCW 70.83.050 to adopt rules and regulations relating to congenital newborn screening (NBS). The Board established rules under Chapter 246-650 WAC regarding which conditions to include on the NBS panel. RCW 70.83.020 grants the Board authority to identify which screening the Department of Health (Department) is required to perform for all infants in the state. RCW 70.83.030 tasks the Board with adopting rules related to the reporting of heritable and metabolic disorders to the Department.

In February 2021, the Washington CMV Project petitioned the Board to mandate targeted congenital cytomegalovirus (cCMV) screening for infants who fail newborn hearing screening. After reviewing available evidence in October 2021, the Board directed Department staff to convene a multidisciplinary technical advisory committee (TAC) to consider adding cCMV to the list of mandated NBS conditions in WAC 246-650-010 and WAC 246-650-020. The TAC evaluated cCMV against five Board-approved criteria for potential inclusion in the NBS panel in September 2022.

Overview and Background - Congenital Cytomegalovirus

Cytomegalovirus (CMV) is the most common cause of viral congenital infections and non-genetic sensorineural hearing loss (SNHL) in newborns. CMV is a DNA virus that can be transmitted via two pathways: horizontal and vertical transmission. Horizontal transmission of CMV can occur postnatally via exchange of bodily fluids, e.g., saliva, blood, tears, and urine; these are known as acquired CMV infections. Vertical transmission of CMV can occur between pregnant persons and a fetus prenatally across the placenta (congenital infections) or perinatally during birth or breastfeeding. There is a higher risk of adverse outcomes if a fetus is infected during the first trimester of pregnancy but a higher risk of disease transmission during the third trimester of pregnancy.

CMV can remain dormant and reactivate throughout life. CMV infections are common in adults and many adults may be unaware of their infection status. However, untreated cCMV infections in infants can present serious complications on newborn development, notably hearing loss. Unfortunately, early identification and intervention does not prevent severe disability and death. Early identification of cCMV can allow an infant to receive antiviral treatment for symptoms and intervention services for late onset hearing loss (LOHL); this may improve their language and developmental outcomes later in life.

cCMV is present in approximately 1 in 200 babies, which is a higher prevalence compared to other conditions on NBS panels (1, 2). In 2011, Misono et al. calculated that CMV was present

in 1.4 in 100 babies in Washington State (3). At present, one state (Minnesota) and two Canadian provinces (Ontario and Saskatchewan) universally screen newborns for CMV at birth. Ten states (Utah, Connecticut, Illinois, Iowa, New York, Virginia, Florida, Kentucky, Pennsylvania, and Maine) require targeted CMV testing be offered or conducted after failed newborn hearing screens.

Currently in Washington, there are no state mandates on cCMV education, screening, or reporting (4). CMV testing is up to a provider's discretion and results are not reported to the Department.

While cCMV disease presents as a spectrum, the following categories are commonly used to describe cCMV infections.

- *Moderately to severely symptomatic disease*: numerous visible congenital anomalies or central nervous system involvement
- *Mildly symptomatic disease*: few mild, isolated, observable congenital anomalies
- *Asymptomatic with SNHL*: only observable congenital anomaly is hearing loss
- *Asymptomatic*: no observable congenital anomalies

Most infants with cCMV are asymptomatic and will not develop long-term sequelae. Clinical diagnosis of cCMV is imperfect and relies on a provider recognizing clinical signs and symptoms of cCMV infections, many of which are non-specific. Clinical manifestations of symptomatic cCMV can include small-for-gestational age, microcephaly, hepatosplenomegaly, petechiae, retinitis, and thrombocytopenia. Long-term outcomes differ among symptomatic and asymptomatic infants, with symptomatic infants having higher risk of developing permanent sequelae; sequelae can include SHNL, intellectual disability, vision loss, cerebral palsy, seizures, and death.

There are two common approaches to screening: universal NBS and hearing targeted NBS. Typically, universal screening utilizes dried blood spots (DBS) to screen all infants regardless of presentation of symptoms; less common specimen types for mass newborn screening include saliva and urine. Targeted screening involves testing infants who do not pass their newborn hearing screen(s); targeted screening will not detect infants with asymptomatic cCMV who pass their newborn hearing screen and develop late-onset hearing loss.

Diagnostic laboratory testing for cCMV is a quantitative polymerase chain reaction (qPCR) test on a urine specimen to confirm the presence and quantity of viral DNA. Infants must be tested within the first three weeks of life for a CMV infection to be considered congenital; otherwise, a CMV infection could be acquired from hospitals, nursing parent(s), or other places. Infants who

fail their hearing screen are referred for diagnostic audiologic evaluation, which commonly takes place outside of this critical three-week window in the early infant period (5).

Infants can be treated with antivirals, such as intravenous ganciclovir and/or oral valganciclovir. Current clinical guidelines recommend 6 months of oral valganciclovir for moderately to severely symptomatic infants (6, 7). Initiation of treatment within the first month of life has been shown to improve hearing and developmental outcomes, though long-term effects of antiviral therapy are less clear. Treatment for pregnant persons and asymptomatic infants with or without isolated hearing loss is not currently recommended.

Overview of Cost-Benefit Analysis

The following summary explains the benefit-cost analysis performed for potentially adding cCMV to the mandatory NBS panel. The calculations for this analysis were done in a spreadsheet (available upon request) and describes the medical model for comparing the status quo, or a "No Screening Model" (upper section) with a "Universal Screening Model" (middle section) and a "Hearing Targeted Screening Model" (lower section) (Figure 1). For this analysis on cCMV, the universal screening model is based on DBS testing and the hearing targeted screening model is based on testing infants after two failed hearing screens. The analysis is from the health sector perspective, in which all costs for providing services are estimated, regardless of who pays the costs.

Point estimates and ranges for input variables were derived from primary literature, data from NBS programs piloting cCMV screening, and consultations with expert scientists and clinicians. The universal model predicts a benefit-cost ratio of 0.35 and the hearing targeted model predicts a benefit-cost ratio of 0.00. This means that for every dollar of costs for universal or hearing targeted NBS for cCMV, there will be approximately $0.35 or $0.00, respectively, worth of benefit. The model structure was developed during 2022 by the Washington NBS program and presented to the cCMV NBS TAC on September 21, 2022. It will be presented to the State Board of Health on October 12, 2022.

There are adequate screening tests for finding newborns with cCMV. One of the tricky things about cCMV is that a positive screen cannot predict the onset and severity of disease. Some babies with cCMV will be missed by universal screening because of lower analytical sensitivity using DBS. Similarly, many babies will be missed by hearing targeted screening because they are asymptomatic and pass their hearing screens. Based on current guidelines from the American Academy of Pediatrics, moderate to severely symptomatic infants with cCMV that meet clinical criteria may receive oral valganciclovir.

We constructed an economic model to estimate the benefits and costs of two NBS models for cCMV (Universal Screening Model and Hearing Targeted Screening Model). The analysis compares these costs to what is happening now (No Screening Model).

The first step is to estimate the number of newborns with cCMV. We used information from the Centers for Disease Control and Prevention (CDC) to estimate the number of babies with cCMV born in Washington State this year. We chose to use one year of babies born for this analysis.

The next step is to find out which newborns will be diagnosed early and benefit from intervention. In the No Screening Model, a small percentage of newborns will be diagnosed early because they will be symptomatic at birth (early identification due to onset symptoms). We use the sensitivity of the screening test to estimate the number of newborns diagnosed early in the Universal Screening Model and the prevalence of congenital hearing loss in infants with cCMV to estimate the number of newborns diagnosed early in the Hearing Targeted Screening Model. The sensitivity is the ability of the test to correctly identify newborns with cCMV. Our model predicts that each year there will be about 315 babies with cCMV identified early through universal screening and 52 babies identified through targeted screening, compared to identification through early onset symptoms alone without screening (estimated 52 babies identified).

Next, we compare the medical outcomes for early versus late onset of symptoms. The morbidity estimates are the percentages of infants we expect will develop LOHL from cCMV. These estimates differ among infants depending on their presentation of symptoms at birth. The mortality rates are the percentages of newborns we expect will die from cCMV. There is a larger chance for death in symptomatic cases compared to asymptomatic cases.

We have constructed what is called a decision tree. The next step is to walk through each branch of the decision tree. To do this, we multiply the rates by the number of newborns affected to find out how many newborns have each of the medical outcomes. In the end, we will have estimates for the number of newborns that fall into each category.

Now is the time to compare each of the outcomes. First, we add each of the death estimates together. We subtract the numbers of deaths in each screening model (Universal and Hearing Targeted) from the No Screening Model to find the shift in numbers; this is the difference made by screening. However, screening newborns for cCMV does not have an impact on infant mortality. We also calculate the additional infants identified in both models that will receive diagnostic testing, be treated with antivirals, develop LOHL and receive early intervention, and not develop LOHL but receive extended surveillance for hearing loss.

Next, we assign a value to saving a life. The Federal Government makes estimates for the value of saving a life. We used an estimate of $11.6 million to estimate the value of a life saved through NBS. We also included the annual benefit of $44,200 for early identification for hearing loss.

We need to estimate how much each NBS program costs. Based on information from the Washington NBS program, we estimated that the costs for universal NBS are $31.10 per baby and the costs for hearing targeted NBS are $4.03 per baby. Screening tests are not perfect. This means that some babies who do not have cCMV will have false positive NBS results and some babies with cCMV will have false negative (normal) NBS results. Babies with false positive results need diagnostic testing to rule out CMV (their follow-up diagnostic urine CMV test will be normal).

The next step is to add up all the benefits and the costs (lives saved, LOHL intervention, NBS and diagnostic testing costs, antiviral treatment costs, and cost of surveillance for hearing loss). We divide the benefits by the costs to get a benefit/cost ratio. Our final results are 0.35 for universal screening and 0.00 for hearing targeted screening. This means that for every dollar of costs to provide universal or hearing targeted cCMV screening, there will be $0.35 or $0.00, respectively, worth of benefits. The net benefits for universal and hearing targeted cCMV screening are -$2,249,458.18 and -$744,120.53, respectively. Negative net benefits represent a cost to the overall system.

Technical Explanation of Model Parameters

We chose numbers for a base case analysis: if we had several estimates from the published data, we either used an average or the middle value. Note: the spreadsheet we used calculates the percentages and estimates, which have in some instances been rounded for simplicity. Subsequent calculations are unaffected by this rounding, so sometimes the numbers appear to not match perfectly.

- ***Birthrate.*** This analysis is for a hypothetical birth cohort of **84,000** babies (cells B13, B50, and B92) which is the number of babies expected to be screened per year in Washington State. This number is based on the number of births projected in Washington in 2022.
- ***Prevalence.*** The prevalence used was **0.5% or 1 cCMV case per 200 births** (cells D13, D37, and D79), which is the prevalence reported by the CDC (1). This predicts **420** babies (cells E13, E37, and E79) born with cCMV in Washington each year. Of note, one pilot universal screening program reported 1 cCMV case per 224 births, which is the prevalence found among 12,554 babies (Minnesota).

- ***Percent of babies with cCMV with early-onset clinical symptoms.*** These babies will be treated early because of the presentation of visible clinical symptoms at birth recognized by the provider. The estimate for this parameter (**12.5%**, cells G4, J47, and J89) was derived from primary literature (1, 2).
- ***Sensitivity***. The sensitivity, or the ability of the screen to correctly identify babies with cCMV is estimated at **75%** (cell G34) for universal screening and **12.5%** (cell G76) for hearing targeted screening. The values used are from a pilot universal cCMV study in Minnesota and prevalence estimates of congenital hearing loss in infants with cCMV from primary literature (8-11). The universal sensitivity value predicts **315** true positives (cell H34) identified early and **105** false negatives (cell H48) or missed cases of cCMV per year. The hearing targeted sensitivity value predicts **52.50** true positives (cell H76) identified early and **367.50** false negatives (cell H90) or missed cases of cCMV per year. True positive babies will need diagnostic CMV testing to determine the presence of CMV.
- ***Specificity.*** The specificity, or the ability of the screen to correctly identify babies who do not have cCMV, is estimated at **99.88%** (cell G62) for universal screening and **99.1%** (cell G104) for hearing targeted screening. The values used are from the pilot study in Minnesota and primary literature (10, 12). The specificity values predict **100.19** false positives per year (cell H55) from universal screening and **752.22** false positives per year (cell H97) from hearing targeted screening. False positive babies will also need diagnostic CMV testing to determine the presence of CMV.
- ***Difference in mortality.*** The mortality estimates for symptomatic cases of cCMV (**7%**, cells J3, N45, and N87) and asymptomatic cases of cCMV (**0%**, cells J14, N56, and N98) are from primary literature and expert opinion (13-15). Typically, the benefit for babies identified early is decreased mortality. However at present, there are no reported long-term mortality estimates for infants with cCMV after identification and/or treatment (16). Long-term outcome studies reporting mortality attribute death to non-cCMV causes (9). An estimate for the mortality rate after screening (**0.88%**, cells J27 and J69) was created to show a net zero benefit for mortality between the models.
- ***Percent of babies with cCMV receiving antiviral treatment.*** Antiviral treatment is recommended for infants with moderately to severely symptomatic cCMV. Treatment has been shown to be modestly beneficial, but more studies are needed to assess long-term benefits (9, 15). The estimate for infants not identified through screening (**71%**, cells N5, S47, and S89) was derived from primary literature (8). Preliminary findings from the pilot universal screening study in Minnesota and trends on valganciclovir use in cCMV infants report a lower percentage of infants receiving antivirals in practice (**21%**, cells N29 and N71) (10, 17).
- ***Percent of babies who develop LOHL.*** Some infants in the group of babies who do not receive antiviral treatment will still develop LOHL, regardless if symptoms are present at birth. The estimate for symptomatic cCMV infants with LOHL (**35%**, cells S11 and

W55) was derived from primary literature (18). The upper end of the range for this parameter (**40%**, cell W97) was used for the hearing targeted model in order to show no difference in the number of infants with LOHL between the hearing targeted and no screening models. The estimate for asymptomatic infants with LOHL **12.5%**, cells N17, S36, S59, and S101) was also derived from primary literature (8, 18).

The next step is to evaluate the differences between the models to quantify the benefits and costs of screening. This is done by determining the sum of the following outcomes per model and calculating the differences made between no screening and each screening model.

- ***Deaths Averted.*** There are **3.68** deaths in the no screening Model (cell AD2), universal model (cell AD25), and hearing targeted model (cell AD67); therefore, **0** deaths (cells AD33 and AD74) are averted per year in both screening models. This is based on there being no described improvement in mortality rates from early intervention (13, 16, 19).
- ***Shift in babies with diagnostic testing.*** The number of infants that will require diagnostic testing is **52.50** (cell AD3) in the no screening model, **415.19** (cell AD26) in universal NBS, and **804.72** (cell AD68) in hearing targeted NBS. The additional number of infants needing diagnostic testing annually in universal and hearing targeted NBS is **362.69** (cell AD34) and **752.22** (cell AD75), respectively. Early identification through hearing targeted NBS identifies a higher number of false positive infants when compared to universal NBS.
- ***Shift in babies treated with antivirals.*** The number of infants that will receive antiviral treatment is **34.67** (cell AD4) in the no screening model, **74.24** (cell AD27) in universal NBS, and **41.26** (cell AD69) in hearing targeted NBS. The additional number of infants needing antiviral treatment annually in universal and hearing targeted NBS is **39.57** (cell AD35) and **6.60** (cell AD76), respectively.
- ***Shift in babies surviving with LOHL and early intervention.*** The number of surviving asymptomatic infants that will develop LOHL and receive early intervention for hearing loss is **4.96** (cell AD5) in the no screening model, **32.07** (cell AD28) in universal NBS, and **4.96** (cell AD70) in hearing targeted NBS. The additional number of infants annually with LOHL and early intervention in universal and hearing targeted NBS is **27.12** (cell AD36) and **0** (cell AD77), respectively.
- ***Shift in babies surviving without hearing loss receiving 6 years of surveillance.*** There is a subset of asymptomatic infants with cCMV in the universal screening model that, if identified early, can be placed into 6 years of surveillance to monitor for signs of hearing loss. The number of surviving infants that will not develop hearing loss but receive 6 years of surveillance is **9.20** (cell AD6) in the no screening model and **215.84** (cell AD29) in universal NBS. The number of infants identified through universal NBS that will undergo surveillance for hearing loss is **206.63** (cell AD37).

Benefits are estimated next.

- ***Value of Lives Saved.*** The value of a statistical life is estimated at **$11,600,000.00**; this is per the U.S. Department of Transportation (20). The value of lives saved by screening is the number of deaths averted multiplied by the monetary value of a statistical life. Since newborn screening for cCMV does not prevent infant death, the universal and hearing targeted models estimate yearly benefits of **$0.00** (cells AE42 and AE82) for saving lives of babies with cCMV.
- ***Value per baby with early identification for hearing loss.*** Per Grosse et al. 2018, the value of early intervention services for hearing loss is estimated to be **$44,200** per child. This is the estimated reduced costs for schooling per infant identified by universal newborn hearing screening that received intervention for hearing loss (21). The total value of LOHL intervention is the number of infants identified in the shift (additional babies surviving with LOHL and early intervention) multiplied by the value of early intervention for hearing loss (**$1,198,583.21** (cell AE44) for universal NBS and **$0.00** (cell AE84) for hearing targeted NBS).
- ***Total benefits of Newborn Screening Models.*** The total annual benefits of universal screening (**$1,198,583.21**, cell AE45) and hearing targeted screening (**$0.00**, cell AE85) are the sum of the value of lives saved and the total value of LOHL intervention.

Then, costs are estimated.

- ***Cost of screening.*** The estimated costs of CMV NBS testing are **$31.10** (cell AD49) per baby for universal screening and **$4.03** (cell AD89) per baby for hearing targeted screening. Costs for universal newborn screening includes staffing for laboratory and follow-up services, new instrumentation and kits, and clinical support. Costs for targeted newborn screening includes staffing for follow-up services and clinical support. The total costs for cCMV newborn screening are the birthrate multiplied by cost per baby (**$2,612,121.22** (cell AE50) for universal NBS and **$338,707.97** (cell AE90) for hearing targeted NBS).
- ***Costs of diagnostic testing.*** True and false positive babies are counted for diagnostic testing costs. The estimated cost for diagnostic testing is **$487.50** per baby (cells AD51 and AD91); this is the outpatient cost for CMV qPCR testing for a urine specimen at the Mayo Clinic Laboratories. The total costs of diagnostic testing annually are the number of additional babies identified in the shift (additional babies with diagnostic testing) multiplied by the cost of diagnostic testing (**$176,812.25** (cell AE52) for universal NBS and **$366,707.25** (cell AE92) for hearing targeted NBS).
- ***Costs of antiviral treatment.*** A subset of symptomatic babies receive antiviral treatment. The 6-month cost associated with oral valganciclovir and monitoring laboratory tests is **$4,785.00** per Gantt et al. 2016; monitoring labs include complete blood counts and

chemistry tests to monitor signs of toxicity from antiviral therapy (22). Other symptomatic care costs added to the treatment costs for symptomatic individuals include initial laboratory testing, audiologic follow-up, ophthalmologic examination, cranial ultrasonography, brain magnetic resonance imaging, and a medical evaluation; therefore, the total treatment costs are estimated to be **$5,868.61** (cells AD53 and AD93). The total costs of antiviral treatment annually are the number of additional babies identified in the shift (additional babies treated with antivirals) multiplied by the cost of antiviral treatment (**$232,231.90** (cell AE54) for universal NBS and **$38,705.32** (cell AE94) for hearing targeted NBS).

- ***Costs of surveillance for hearing loss.*** Based on recommendations from the Utah Early Hearing Detection and Intervention Program, a six-year surveillance system was created for asymptomatic infants with cCMV to monitor for signs of hearing loss (23). Type and frequency of audiology tests were recommended by the Washington EHDDI Program. Costs for audiologic services were based on average Medicaid payments per McManus et al. 2010 (24). The total cost for 6 years of hearing surveillance for asymptomatic cCMV infants is estimated to be **$1,826.19** (cells AD55 and AD95); this includes varying audiologic services conducted every 3 months until age 3, then every 6 months until age 6. The total costs for surveillance for hearing loss are the number of additional babies identified in the shift (additional babies without hearing loss but 6 years of surveillance) multiplied by the cost of 6 years of surveillance (**$426,876.02** (cell AE56) for universal NBS and **$0.00** (cell AE96) for hearing targeted NBS).
- ***Total costs of Newborn Screening Models.*** The total annual costs of cCMV screening are the sum of the costs of screening, diagnostic testing, antiviral treatment, and surveillance for hearing loss. The total annual costs for universal and hearing targeted screening are estimated to be **$3,448,041.39** (cell AE57) and **$744,120.53** (cell AE97), respectively.

Finally, the ratio of benefits to costs is calculated. Any ratio greater than 1 signifies that the benefits outweigh the costs.

- ***Benefit/Cost Ratio.*** For universal screening, **$1,198,583.21** of benefits divided by **$3,448,041.39** of costs yields a benefit/cost ratio of **0.35** (cell AE60). For hearing targeted screening, **$0.00** of benefits divided by **$744,120.53** of costs yields a benefit/cost ratio of **0.00** (cell AE100).
- ***Net Benefit.*** The net benefit is the amount of money saved each year by adding screening, and is the total costs subtracted from the total benefits. For universal screening, **$1,198,583.21** minus **$3,448,041.39** gives a net benefit of **-$2,249,458.18** (cell AE62). For hearing targeted screening, **$0.00** minus **$744,120.53** gives a net benefit of **-$744,120.53** (cell AE102). The negative net benefits associated with universal and hearing targeted screening are costs to the public health system.

After completing the base case benefit-cost ratio, we performed a one-way sensitivity analysis to evaluate how the benefit-cost ratio changes when estimates for the parameters are individually varied and all others remain constant.

- ***Sensitivity analysis.*** Table 1 contains three estimates for each parameter, the estimate used in the base case followed by conservative and liberal estimates. Only one parameter was changed at a time to generate unique benefit/cost ratios for each of the scenarios compared to the base case benefit/cost ratio for universal NBS (0.35). The model proved to be very robust and was somewhat sensitive to four parameters: birth prevalence, cost of universal NBS, the percent of asymptomatic infants with LOHL, and the value per baby with early identification for LOHL.

Table 1. Sensitivity analysis

Parameter	Conservative estimate	Base case	Liberal estimate	Benefit/cost ratio swing
Birthrate	73,000	84,000	95,000	No change
Prevalence	1:250	1:200	1:71	0.29 to 0.69
Sensitivity	73.2%	75%	85.7%	0.34 to 0.38
Specificity	99.76%	99.88%	100%	0.34 to 0.35
Cost of universal NBS	$15.55	$31.10	$46.65	0.56 to 0.25
Cost of diagnostic test	$243.75	$487.50	$4,875.00	0.36 to 0.24
Cost of antiviral treatment	$0.00	$5,868.61	$58,686.10	0.37 to 0.22
Cost of surveillance for hearing loss	$792.89	$1,826.19	$2,516.07	0.37 to 0.33
% symptomatic surviving with antiviral treatment	10.5%	21%	42%	0.42 to 0.23
% asymptomatic surviving with late onset hearing loss	6.25%	12.5%	25%	0.15 to 0.74
Value per baby with early identification for late onset hearing loss	$22,100	$44,200	$88,400	0.17 to 0.70

Of the four parameters that have a modest impact on the model, two base case estimates are strongly supported in the literature (birth prevalence and percent asymptomatic with LOHL) (1,

8, 18). The base case value for the cost of universal NBS was estimated by the Department and similar to the cost for universal NBS calculated by the Minnesota Department of Health ($43 per baby) (25). The value per baby with early identification for LOHL comes from one estimate in the literature; however, this point estimate is from a reliable source in health economics (21).

- ***Break even points.*** Table 2 contains the break-even point for each parameter. This is what the estimate would need to be, holding all other parameters constant, to increase the benefit/cost ratio to 1 (meaning it is now beneficial). Of note, the cost for universal NBS would need to be significantly lower than the base case estimate to be influential on the model.

Table 2. Break even points.

Parameter	**Base case**	**Break even point**
Birthrate	84,000	Impossible
Prevalence	1:200	1:31
Sensitivity	75%	Impossible
Specificity	99.88%	Impossible
Cost of universal NBS	$31.10	$4.30
Cost of diagnostic test	$487.50	Impossible
Cost of antiviral treatment	$5,868.61	Impossible
Cost of surveillance for hearing loss	$1,826.19	Impossible
% symptomatic surviving with antiviral treatment	21%	Impossible
% asymptomatic surviving with late onset hearing loss	12.5%	33%
Value per baby with early identification for late onset hearing loss	$44,200	$127,000

Intangible Benefits and Costs

This economic analysis does not address several benefits and costs associated with screening that are difficult to quantify. The majority of infants with cCMV have clinically inapparent infections and diagnosis through newborn screening may or may not be viewed by families as beneficial. Hypothetical and retrospective studies on parental attitudes regarding cCMV NBS show high

acceptability, as parents valued the information in light of heightened anxiety from screening (26-28). Early diagnosis of asymptomatic infants creates an emotional impact on individuals and families affected by cCMV. The establishment of a six-year surveillance system for these asymptomatic infants/children aims to provide more frequent follow-ups and monitoring for signs of LOHL. There is an opportunity to intervene in a critical period of learning and language development for infants who undergo the proposed surveillance and develop LOHL. For families in this situation, the surveillance program will be beneficial. However, the vast majority of asymptomatic infants under surveillance (87.5%) will never develop hearing loss; these families will experience financial and nonfinancial costs associated with surveillance without receiving any benefits.

The adverse psychosocial impact of newborn screening, specifically false-positive results, is well-documented (29). The variability of cCMV infections amplifies these concerns because unlike heritable conditions, a positive cCMV result does not shed light on disease severity or onset. For some families, the value of knowing this result is a benefit; for others, the uncertainty of cCMV infections further complicates the diagnostic odyssey. The value of this knowledge is also contingent upon the severity of symptoms since antiviral treatment is not warranted in all cases of cCMV.

Antiviral treatment, specifically 6 months of valganciclovir, is generally recommended for infants with moderately to severely symptomatic disease or central nervous system involvement (6, 7). It is not currently recommended that mildly symptomatic infants or asymptomatic infants with isolated SNHL receive antiviral treatment (7). Overall, the effects of antiviral therapy may be favorable but there is insufficient evidence of its enduring benefit (9).

The impact of cCMV prevention strategies for pregnant persons is another intangible benefit. The ability to reduce the prevalence of cCMV during pregnancy has the potential to save lives. Some states mandate public health education programming for cCMV to ensure healthcare practitioners, families, and expectant parents receive up-to-date and evidence-based information on cCMV.

Conclusion

Early identification of babies with cCMV is generally regarded as being beneficial to the babies, their families, and the medical professionals caring for them. Although screening newborns for cCMV does not prevent death or disability, it does create an opportunity for monitoring for LOHL in babies with asymptomatic cCMV and providing early language services for those developing hearing loss.

This analysis used data from primary literature, NBS programs piloting screening for cCMV, and expert opinion to quantify benefits and costs for asymptomatic babies with cCMV who may

benefit from early surveillance for hearing loss. Using our best estimates for parameters, the benefit-cost ratio for universal and hearing targeted screening was 0.35 and 0.00, respectively. For every dollar of costs to provide cCMV screening, we predict that there will be $0.35 worth of benefits from universal screening and $0.00 worth of benefits from hearing targeted screening. The net benefits from universal and hearing targeted screening are -$2,249,458.18 and -$744,120.53, respectively. The sensitivity analysis showed that the model is very robust because the benefit-cost ratio did not change much when more conservative or liberal estimates for parameters were made in the model.

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Figure 1. Washington State Benefit-Cost Analysis for potentially adding NBS for cCMV