

Early Detection of Congenital Cytomegalovirus – Universal Screening in the Neonatal Intensive Care Unit

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Introduction & Purpose

Introduction:

- Congenital cytomegalovirus (cCMV) is the most common congenital infection.¹
- It is a leading cause of neurodevelopmental delays and the leading non-genetic cause of sensorineural hearing loss (SNHL).²
- Infants are often asymptomatic at birth (up to 90%) but may develop neurodevelopmental delays and/or SNHL within six years of life.¹
- At age 4, CMV accounts for 25% of hearing loss in the pediatric population.³
- Antiviral therapy and timely interventions have improved outcomes, making early detection crucial.⁴
- Minnesota implemented universal cCMV screening state-wide in 2023, with other states (Connecticut starting in 2025) implementing targeted screening and/or introducing universal cCMV screening legislation.⁵
- No standardized universal cCMV screening protocol exists statewide in the Southeast.

Purpose: To describe the design and implementation of universal cCMV screening at a tertiary neonatal intensive care unit and present initial findings.

Methods

- Every infant admitted to the Duke University Hospital (DUH) or Duke Regional Hospital (DRH) neonatal intensive care units (NICUs) starting March 1, 2024 were tested for CMV within the first 21 days of life with saliva and/or urine CMC PCR.
- A positive saliva PCR was confirmed with urine PCR.
- Infants positive for cCMV underwent further evaluation for evidence of symptomatic disease (liver function tests, complete blood count, eye exam, head ultrasound, CMV blood PCR).
- Strategies for implementation are detailed in **Figure 1**.
- Infants <1500g were tested with urine and saliva and those >1500g were tested with saliva alone.
- We gathered patient-level data from retrospective chart review for cCMV+ infants, shown below in **Figure 2**.

Figure 1. Implementation Strategies

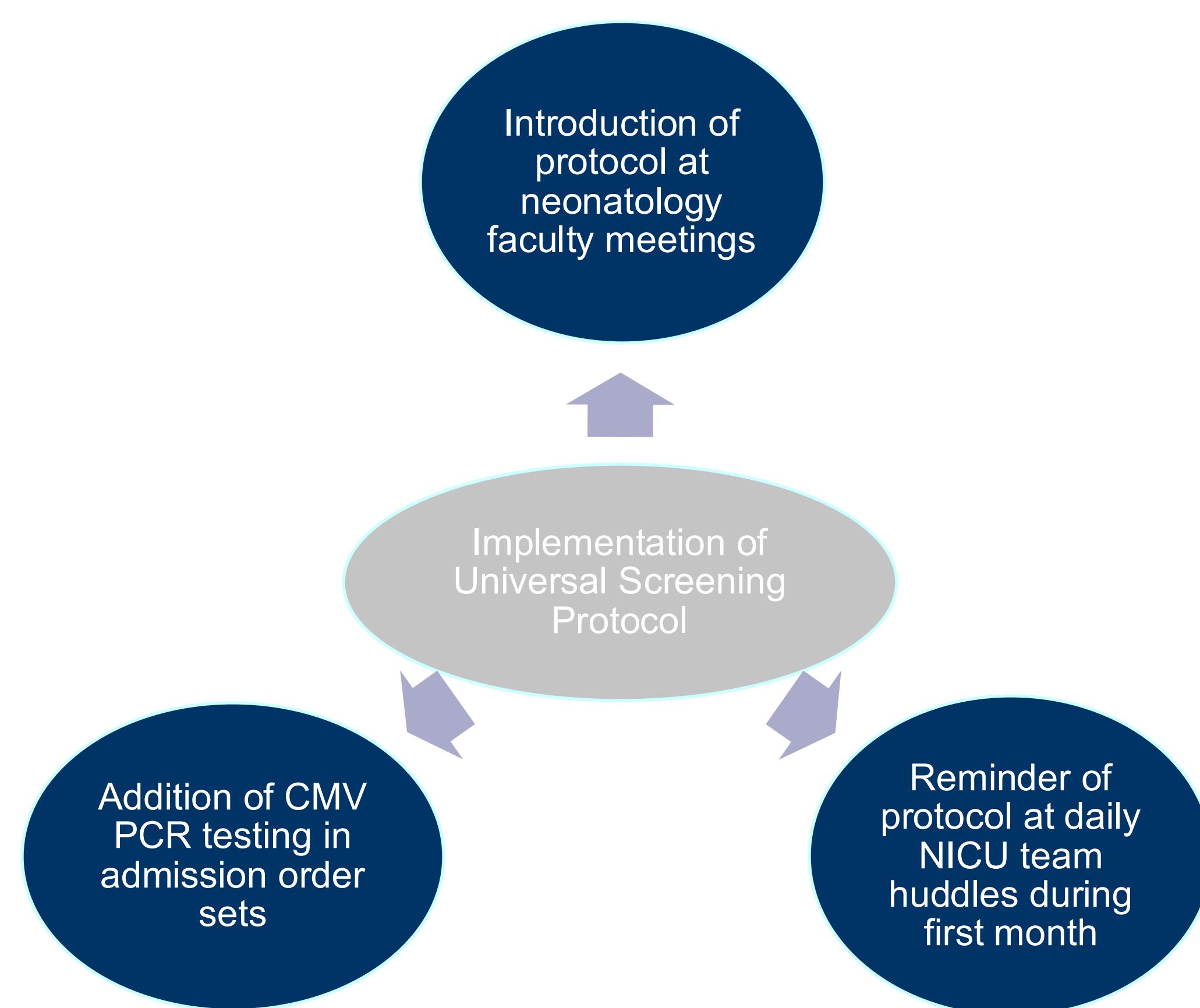
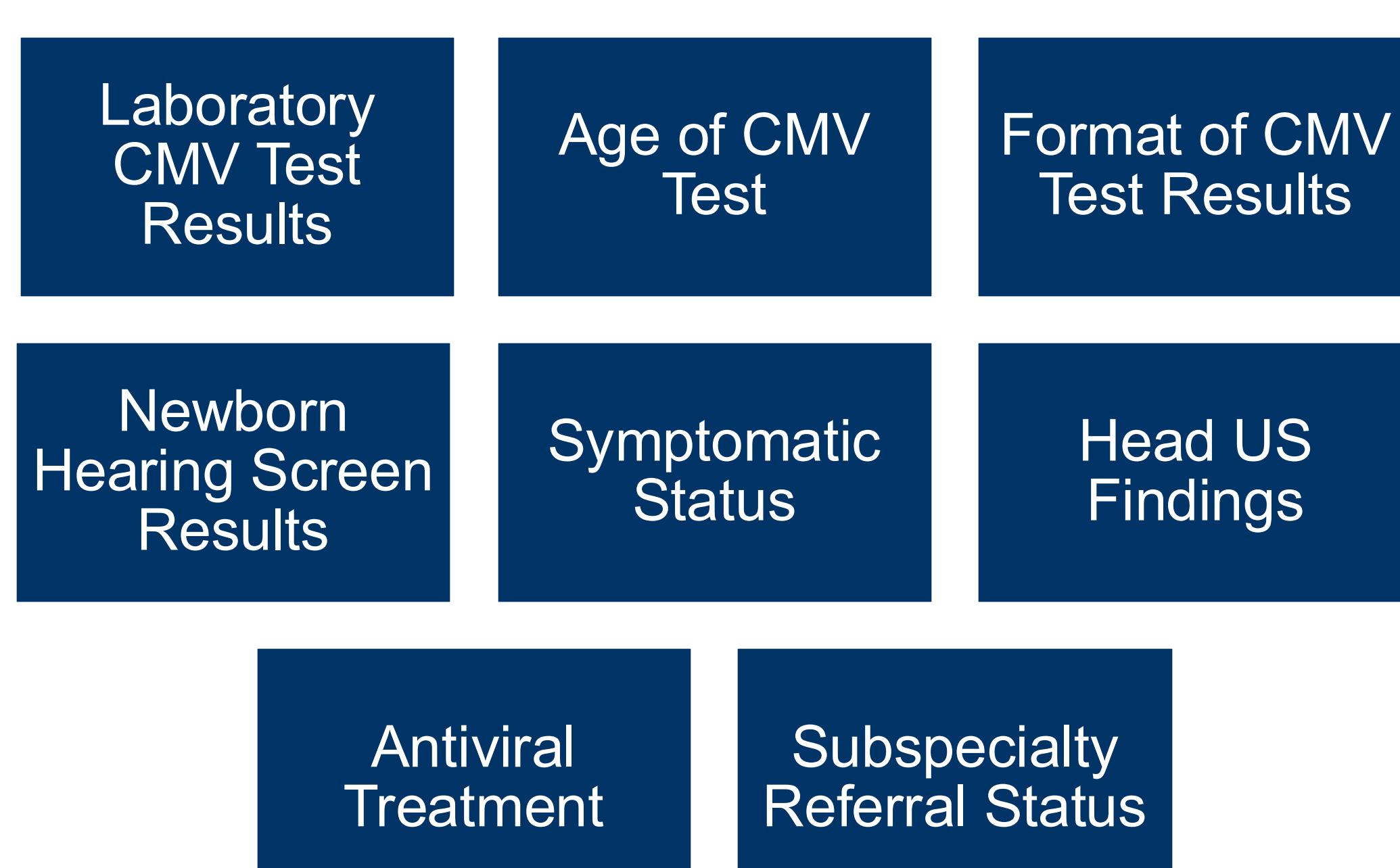


Figure 2. Values Gathered During Retrospective Chart Review



Results

- Out of 1401 admitted infants to the DUH and DRH NICUs, 1362 infants (97.2%) were tested for CMV through the universal screening protocol. **Figure 3.**
- Of the 26 missed infants, 4 patients died on their birth date and thus were untested.
- For the 207 admitted infants that weighed less than 1500 grams at birth, 203 (98.1%) received saliva and urine CMV tests.
- Saliva was the most used modality for screening, at 1422 of 1800 total tests (79%).
- 6 infants tested positive for cCMV, with 5 receiving a cCMV diagnosis. 1 had a false positive saliva result.
- cCMV+ Infant profiles are shown in **Table 1**.
- Differences between gestational age and birthweight between the two cohorts is shown in **Table 2**. No significant difference ($P > 0.05$) was found for both markers.

Figure 3. Total Screened and Missed Infants

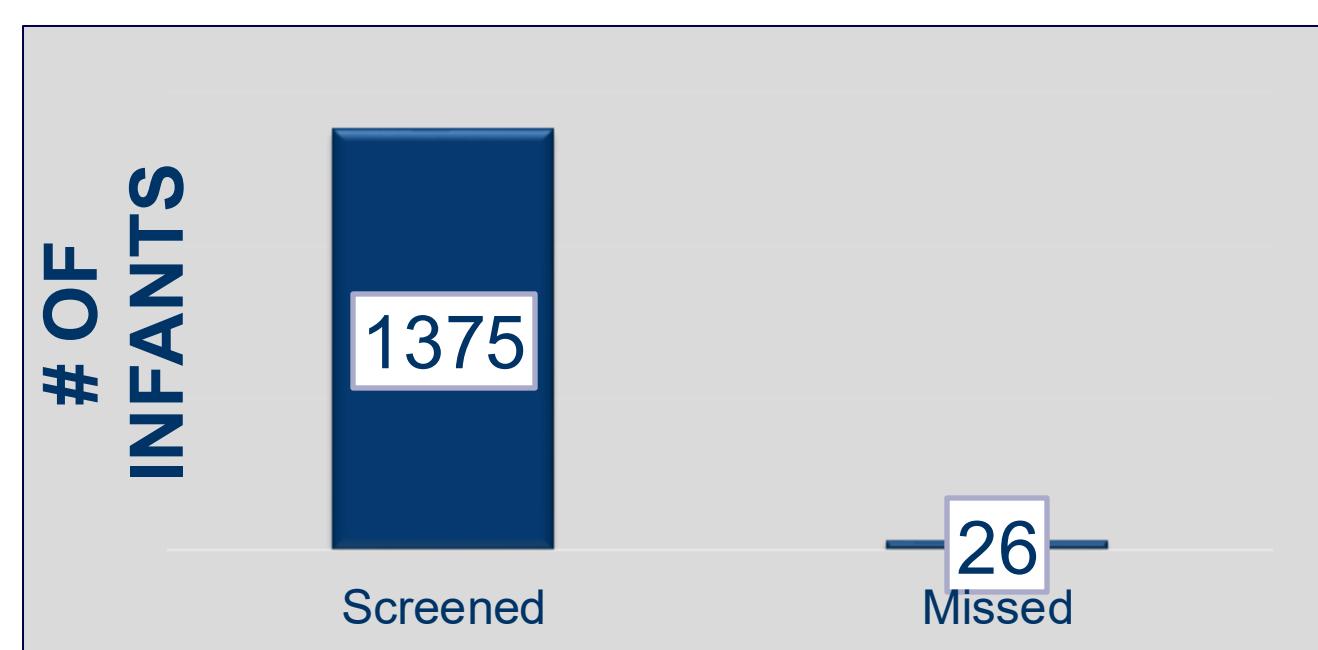


Table 1. cCMV Positive Infant Profiles

cCMV + Infants	1	2	3	4	5
Newborn Hearing Screen	Pass	Pass	Bilateral Refer	Pass	Bilateral Refer
Would Have Been Detected Through Targeted Screen	N	N	Y	Y	Y
Symptoms Present At Birth	N/A	N/A	Hearing Loss	Microcephaly	Hearing Loss, Abnormal Liver Function Testing
Head US?	Y	Y	Y	Y	Y
Head US Findings	Small cyst in germinal matrix	Choroid plexus cyst on right	Bilateral grade 1 germinal matrix hemorrhages	Normal	Cystic enlargement of bilateral germinal matrices
Antiviral?	Valganciclovir	Valganciclovir	Valganciclovir	Valganciclovir	Valganciclovir

Referral Status	1	2	3	4	5
Audiology	X	X	X	X	X
Speech/Feeding Therapy	X	X	X	X	X
Occupational Therapy		X		X	
Physical Therapy		X	X	X	X
Ophthalmology	X	X	X	X	X
Otolaryngology		X			X
Special Infant Care Clinic (SICC)		X	X	X	X
Infectious Disease	X	X	X	X	X

Table 2. Gestational Age and Birthweight

	cCMV +	cCMV -
# Infants	5	1359
Birthweight Mean (g)	2211	2443.4
Gestational Age (wks)	34.6	34.5

Conclusions

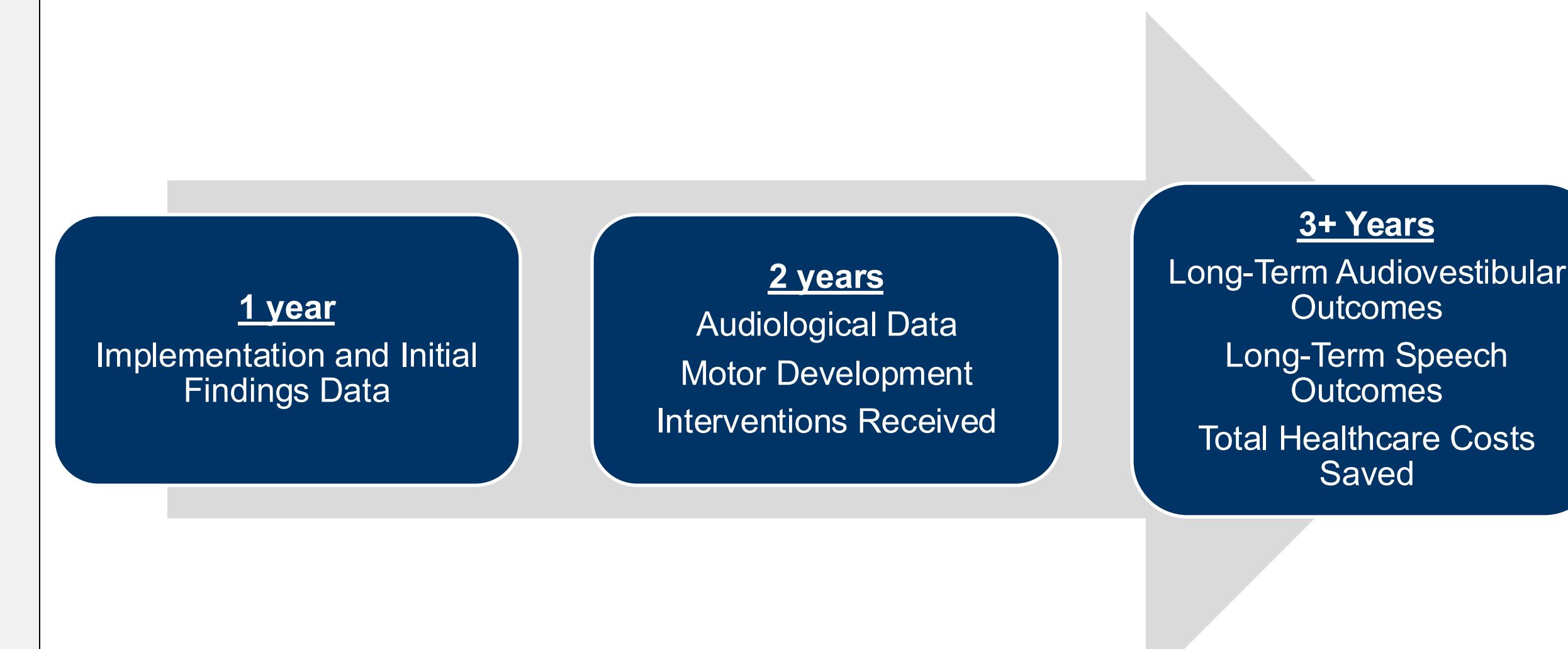
- Overview**
 - With an overall screening rate of 97.2%, Duke's new universal screening protocol has diagnosed 5 patients with cCMV in the first 12 months of implementation.
 - We used saliva testing as our primary modality. Saliva testing is cheaper but does require a unique sample – other newborn screens use DBS.
 - Saliva testing also tends to have false positives, as seen in this cohort.⁷
- The cCMV+ cohort was very small, so it was not powered to detect differences.
- Two of the five (40%) infants were asymptomatic but ended up having positive head ultrasound findings. They would have been missed with targeted screening and would not have received appropriate and timely antiviral treatment.

Limitations

- Small cCMV positive sample size.
- Difficult to replicate a universal screening program at all hospitals, Duke has the unique ability to fund this program.
- CMV incidence varies year to year, so difficult to compare results with targeted screening.

Future studies:

- Future studies are detailed below.
- Our goal is that this program serves as a gateway for universal screening in North Carolina, and the Southeastern United States as a whole.



References

- Adler SP, Marshall B. Cytomegalovirus infections. *Pediatr Rev*. 2007 Mar;28(3):92-100. doi: 10.1542/pir.28-3-92. PMID: 17332168.
- Dppard SC, Grosse SD, Ross DS. New estimates of the prevalence of neurological and sensory sequelae and mortality associated with congenital cytomegalovirus infection. *Rev Med Virol*. 2007 Sep-Oct;17(5):355-63. doi: 10.1002/rmv.544. PMID: 17542052.
- Morton CC, Nance WE. Newborn hearing screening--a silent revolution. *N Engl J Med*. 2006 May 18;354(20):2151-64. doi: 10.1056/NEJMra050700. PMID: 16707752.
- Kimberlin DW, Jester PM, Sánchez PJ, et al.; National Institute of Allergy and Infectious Diseases Collaborative Antiviral Study Group. Valganciclovir for symptomatic congenital cytomegalovirus disease. *N Engl J Med*. 2015 Mar 5;372(10):933-43. doi: 10.1056/NEJMoa1404599. PMID: 25738669; PMCID: PMC4401811.
- Kaye T, Dufort EM, Rosenthal SD, et al. *Notes from the Field: Universal Newborn Screening and Surveillance for Congenital Cytomegalovirus—Minnesota, 2023–2024*. *MMWR Morb Mortal Wkly Rep* 2024;73:703–705. DOI: <http://dx.doi.org/10.15585/mmwr.mm7332a2>.
- Exler S, Daiminger A, Grothe M, Schalasta G, Enders G, Enders M. Primary cytomegalovirus (CMV) infection in pregnancy: Diagnostic value of CMV PCR in saliva compared to urine at birth. *Journal of Clinical Virology*. 2019;117:33-6.