Newborn Hearing Screening Referrals:

The Importance of Congenital Cytomegalovirus Follow-Up

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Introduction:

- Congenital cytomegalovirus (cCMV) is the most common infectious cause of sensorineural hearing loss (SNHL).
- **Targeted screening** is defined as when all infants who "refer" on the newborn hearing screen (NHS) are tested for cCMV before hospital discharge.
- Targeted screening provides early detection of infants who have cCMV, to allow for prompt clinical follow-up, and ongoing surveillance for hearing loss and developmental delays in these high-risk newborns.
- We tested a targeted cCMV screening program from 2018-2022.

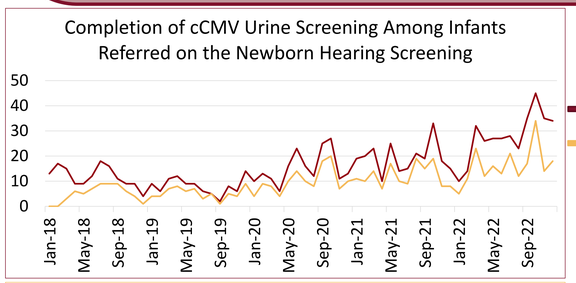
Aim Statement/Hypotheses:

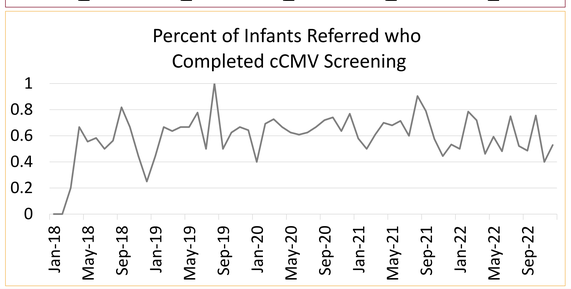
By implementing a targeted screening program for cCMV, we aim to increase:

1) Completed screening of at-risk babies
2) Detection of cCMV
3) Audiologic follow up, within 1 year

Methodology:

- **In Scope:** Babies born at seven M Health Fairview Hospitals who failed NHS.
- **Interventions:**
  Plan-Do-Study-Act (PDSA) 1. Urine PCR assay was recommended prior to hospital discharge.
  PDSA 2. Newborn order set was modified to obtain urine collection if failed NHS.
  PDSA 3. Multiple rounds of education completed for post partum nursing staff and clinicians.
- **Measures:**
  All NHS failures (outcome).
  Collection of urine for cCMV (process).
  Prevalence of cCMV identified by targeted screening (outcome).
  Referrals to outpatient audiology (process).
  Completion of ID clinic follow ups, cranial ultrasound, CMV viral load (processes).





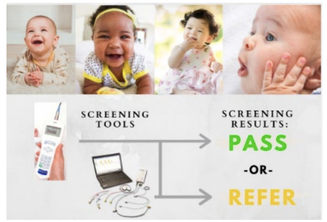


Image 1. Newborn hearing screening results in a "pass" indicating intact hearing, or a "refer" recommending formal audiologic evaluation.

Image 2. Example of a newborn hearing screening being conducted.

Results:

- **55,000 deliveries** occurred during the study period (1/1/18 to 12/31/22).
- **993 newborns** (1.8%) were referred on NHS. Overall, 592 (60%) had urine cCMV PCR testing obtained before discharge. Urine cCMV PCR testing rates varied between 50% - 100% across the seven hospital sites.
- **13 infants (2.2%) were identified with cCMV**. Clinical evaluation based on the Rawlinson criteria[1] indicated 4 had moderate-to-severe disease, 1 mildly symptomatic disease, 5 were asymptomatic with isolated SNHL, and 3 were asymptomatic. One infant who was mildly symptomatic and three infants who were moderately to severely symptomatic had SNHL; thus, surprisingly, one infant who had testing triggered by a "refer" on the NHS, and who had symptomatic disease based on the Rawlinson criteria, had a normal initial audiological evaluation. Two infants had cCMV-defining cranial ultrasound results.
- **10 (77%) have demonstrated SNHL to date** (7 unilateral, 3 bilateral). 3 infants who referred had normal hearing on follow-up.
- Viral loads ranged from < 137 IU/mL to >9,100,000 IU/mL.

cCMV Disease Classification Definitions:

Moderately to severely symptomatic cCMV:

- Multiple manifestations: thrombocytopenia, petechiae, hepatomegaly, splenomegaly, intrauterine growth restriction, hepatitis (raised transaminases or bilirubin), *or*
- Central nervous system involvement such as microcephaly, radiographic abnormalities consistent with CMV central nervous system disease, abnormal cerebrospinal fluid indices, chorioretinitis, sensorineural hearing loss, or the detection of CMV DNA in cerebrospinal fluid.

Mildly symptomatic cCMV:

- One or two isolated manifestations of cCMV infection that are mild and transient (eg, mild hepatomegaly or a single measurement of low platelet count or raised levels of alanine aminotransferase).

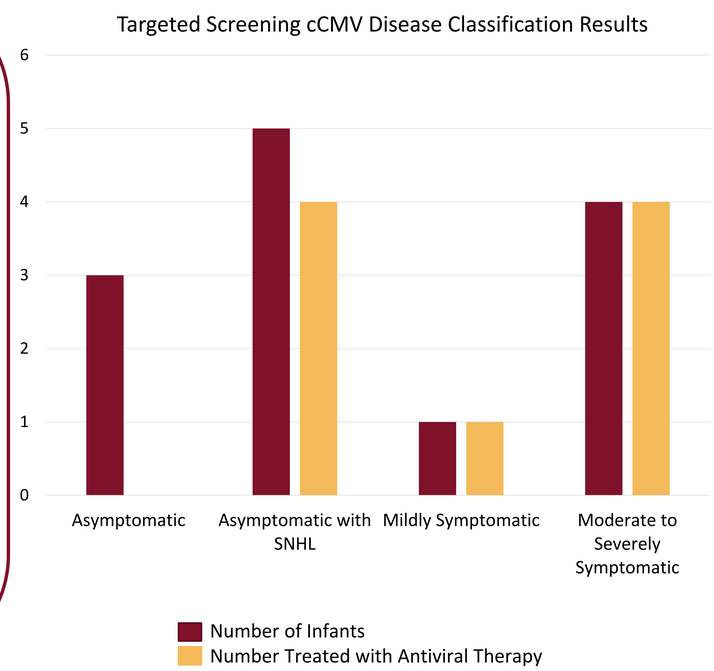
Asymptomatic cCMV infection with isolated SNHL:

- No apparent abnormalities to suggest cCMV disease, but sensorineural hearing loss (≥21 decibels).

Asymptomatic cCMV:

- No apparent abnormalities to suggest cCMV disease, and normal hearing.

[1]Rawlinson, W. et al. Congenital cytomegalovirus infection in pregnancy and the neonate: consensus recommendations for prevention, diagnosis, and therapy. *The Lancet Infectious Diseases*, Volume 17, Issue 6, 2017, Pages e177-e188



Conclusions:

- Challenges to diagnostic PCR for cCMV prior to nursery discharge included difficulty obtaining urine specimens, parental refusal, and declination of testing at the discharging provider's discretion.
- **60% of NHS "refer" infants underwent cCMV testing**, despite a nursery discharge order set requirement. Among infants in the NHS refer group, 2.2% had cCMV infection.
- **Most infants had proven SNHL on follow-up, allowing for early diagnosis, commencement of antivirals, and screening for evolution of SNHL**. Some infants that "referred" on NHS had normal audiological evaluation on follow-up but had cCMV infection. In 62% of infants, the diagnosis of cCMV was not clinically suspected.
- Quality improvement approaches are needed to improve compliance. Targeted cCMV screening for NHS referrals after Minnesota begins universal cCMV testing in 2023 will require optimization.