

# Cost-effectiveness of newborn screening for congenital CMV infection

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# Disclosures

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- Off-label use of valganciclovir for treatment of congenital CMV infection will be discussed

# Congenital CMV infection

- Occurs in ~0.5% of live births in the U.S.
- Defined by detecting CMV at <3 weeks of life
- A major cause of sensorineural hearing loss (SNHL) and neurodevelopmental delay
- Without screening, most infections are not diagnosed
- 85-90% of cases are asymptomatic at birth
  - None are identified without screening
  - But hearing loss develops in 10-15% of these
- About half of symptomatic infants have sequelae
  - Symptoms at birth often subtle, unrecognized
  - 75%-90% of symptomatic infections are missed

# Benefits of CMV screening

- Early diagnosis allows directed care
  - Antiviral treatment of symptomatic newborns modestly improves hearing and developmental outcomes
  - Serial audiologic follow-up results in earlier detection of hearing loss with post-natal onset
- Often suspected too late to diagnose/treat
  - Dried blood spot PCR appears too insensitive
  - Best evidence for antivirals from trials that start treatment within 4 weeks of age

# CMV screening approaches

- “Targeted” screening increasingly performed
  - CMV testing of neonates with (suspected) SNHL now routine in parts of the US, UK, Australia, Belgium
  - Does not identify infants with late-onset hearing loss
- Universal newborn CMV screening not currently standard of care
  - Appears feasible and acceptable as well as beneficial
  - Identifies large numbers of infected children who won’t develop disease (and don’t benefit from screening)
- No comprehensive cost-effectiveness data for either approach

# Prior CMV screening models

- Cannon et al concluded that universal newborn CMV screening would benefit at least as many children as screening for other conditions
  - Costs/savings not estimated
- Economic analyses of targeted screening suggest the potential for cost-effectiveness
  - UK study estimated a cost of ~\$8,000 to identify 1 case of cCMV-related SNHL and ~\$18,000 to improve hearing in 1 case
  - Utah program estimated significant potential savings dependent on avoidance of cochlear implants

# Study objectives

- To determine the cost-effectiveness of universal or targeted newborn CMV screening compared to the current standard of care (no screening)
- Specifically, to estimate the:
  - Cost of identifying 1 case of cCMV infection
  - Cost of identifying 1 case of cCMV-related SNHL
  - Cost of preventing one cochlear implant
  - Total costs/savings associated with screening
  - Under a range of assumptions, for each strategy

# Case identification assumptions

- 2 screening models (universal and targeted), each compared with no screening
  - 1.5% of newborns fail stage the hearing screen
  - Of these, 10% have SNHL at birth
- Screen with saliva swab PCR
  - Assumed 97% sensitivity and 99% specificity
- cCMV rate = 0.5% based on CHIMES study
- 25% of symptomatic cases identified clinically
- Proportion of symptomatic cCMV and timing/severity of SNHL based on a universal screening study at UAB



# Prospective cohort data

- 551 children with cCMV identified by universal screening and followed for >5 years
- SNHL categories (based on worst ear):
  - Mild-moderate >20-70 dB
  - Severe-profound >70 dB
- SNHL occurred in 13% of all children with cCMV
  - 4% had hearing loss at birth
  - 9% with late-onset
  - 39% severe-profound
- 14% of all cases were “symptomatic” at birth
- Consistent with other cohort data

# Care and outcome assumptions

- All symptomatic infants receive laboratory testing, cranial ultrasound, ophthalmologic exam
- Evaluated 3 different treatment indications:
  - Symptomatic at birth only
  - Symptomatic or SNHL at birth
  - No treatment for any cases
- Treatment results in permanent improvement by 1 hearing category in 50% of cases
- cCMV cases without hearing loss at birth get audiology follow-up every 6 months until 6 years
- Cochlear implant for 50% of bilat. profound SNHL

# Cost estimates

- Medical costs obtained primarily from Medicaid
- Saliva CMV PCR = \$10 – \$50
- Cochlear implant = \$100,000
- Earlier identification of late-onset SNHL by screening reduces associated costs by 12%
  - Half the benefit of identifying hearing loss at birth through newborn hearing screening
- Loss of productivity due to SNHL in adults
  - Mild-moderate = none
  - Severe-profound = \$926,000

Bergevin *Int J Ped Oto* 2015; Kennedy *NEJM* 2006; Mohr *Policy Anal Brief H Ser* 2000

# Estimated numbers of children screened and cCMV cases identified

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| <b>Cases</b>                 | <b>Number per 100,000 live births</b> |                           |
|------------------------------|---------------------------------------|---------------------------|
|                              | <b>Universal screening</b>            | <b>Targeted screening</b> |
| Newborns screened for cCMV   | 100,000                               | 1,500                     |
| cCMV infections identified   | 500                                   | 27                        |
| Symptomatic cCMV at birth    | 70                                    | 10                        |
| Asymptomatic cCMV at birth   | 430                                   | 17                        |
| cCMV-related SNHL at birth   | 20                                    | 20                        |
| cCMV-related late-onset SNHL | 44                                    | <1                        |

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# Estimated costs of screening per case of cCMV and related SNHL

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| Outcome                      | Cost per outcome   |           |                     |              |
|------------------------------|--------------------|-----------|---------------------|--------------|
|                              | Targeted screening |           | Universal screening |              |
|                              | \$10 test          | \$50 test | \$10 test           | \$50 test    |
| Identify 1 cCMV infection    | \$566              | \$2,832   | \$2,000             | \$10,000     |
| Identify 1 cCMV-related SNHL | \$975              | \$3,916   | \$27,460            | \$90,038     |
| Prevent 1 cochlear implant   | \$39,401           | \$271,947 | \$4,064,157         | \$12,620,277 |

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# Estimated costs and savings from cCMV screening\*

## Savings (costs) per newborn screened

|                        | Targeted screening              |                                    |              | Universal screening             |                                    |              |
|------------------------|---------------------------------|------------------------------------|--------------|---------------------------------|------------------------------------|--------------|
|                        | Treat if symptoms at birth only | Treat if symptoms or SNHL at birth | No treatment | Treat if symptoms at birth only | Treat if symptoms or SNHL at birth | No treatment |
| Direct savings (costs) | \$0.90                          | \$4.95                             | (\$2.01)     | (\$10.86)                       | (\$6.83)                           | (\$14.16)    |
| Net savings (costs)**  | \$10.66                         | \$27.31                            | (\$1.80)     | \$21.34                         | \$37.97                            | \$1.67       |

\* Assumes \$10/test

\*\* Includes loss of productivity due to hearing loss

# Summary

- Newborn cCMV screening appears cost-effective under a wide range of assumptions
- Even assuming no antiviral treatment, screening is essentially cost-neutral when costs related to loss of productivity are included
  - Earlier identification and directed care for late-onset hearing loss results in large savings
- When modestly effective antiviral treatment is assumed, screening results in cost savings
- Universal screening incurs greater direct costs, but greater net savings, than targeted screening under all scenarios

# Limitations

- Sensitivity analyses performed for selected parameters but assumptions may be inaccurate
- Costs might be higher if health care utilization due to screening is greater than expected
  - Indiscriminate testing (e.g., brain MRI) or treatment
- Savings might be substantially higher
  - Only costs related to SNHL were included
  - If costs related to cognitive impairment or other cCMV-related morbidity were included
  - Antiviral treatment may become more effective
  - Diagnostic assays are increasingly less expensive



# Policy implications

- In addition to fulfilling the other required criteria for newborn screening, cCMV screening also appears to be cost-effective
- In the absence of an effective way to prevent cCMV infection, current targeted screening programs appear warranted
  - Universal screening provides greater benefits and is estimated to be more cost-effective
- Ongoing and planned cCMV screening programs should evaluate real-world cost-effectiveness among their quality metrics



# Thank you

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# Estimated effect of screening on cCMV-related hearing loss

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|                                    | Targeted screening              |                                    |              | Universal screening             |                                    |              |
|------------------------------------|---------------------------------|------------------------------------|--------------|---------------------------------|------------------------------------|--------------|
|                                    | Treat if symptoms at birth only | Treat if symptoms or SNHL at birth | No treatment | Treat if symptoms at birth only | Treat if symptoms or SNHL at birth | No treatment |
| Reduction in severe-profound cases | 7.5%                            | 13%                                | NA           | 4.2%                            | 9.7%                               | NA           |

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\* Assumes \$10/test

\*\* Includes loss of productivity due to hearing loss