Cost-effectiveness of newborn screening for congenital CMV infection

Soren Gantt, Francois Dionne, Fred Kozak, Oran Goshen, David Goldfarb, Albert Park, Suresh Boppana, and Karen Fowler
Disclosures

• Research support from VBI Vaccines Inc, Boston

• Consulting fees from Omeros Corp, Seattle

• 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

Kimberlin *NEJM* 2015; Grosse *Volta Voices* 2007; Boppana *NEJM* 2011
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 identified 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

CDC EHDI program; Boppana *NEJM* 2011; Dahle *J Am Acad Audiol* 2000
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

Dahle J Am Acad Audiol 2000
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

<table>
<thead>
<tr>
<th>Cases</th>
<th>Number per 100,000 live births</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Universal screening</td>
</tr>
<tr>
<td>Newborns screened for cCMV</td>
<td>100,000</td>
</tr>
<tr>
<td>cCMV infections identified</td>
<td>500</td>
</tr>
<tr>
<td>Symptomatic cCMV at birth</td>
<td>70</td>
</tr>
<tr>
<td>Asymptomatic cCMV at birth</td>
<td>430</td>
</tr>
<tr>
<td>cCMV-related SNHL at birth</td>
<td>20</td>
</tr>
<tr>
<td>cCMV-related late-onset SNHL</td>
<td>44</td>
</tr>
</tbody>
</table>
Estimated costs of screening per case of cCMV and related SNHL

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Targeted screening</th>
<th>Universal screening</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$10 test</td>
<td>$50 test</td>
</tr>
<tr>
<td>Identify 1 cCMV infection</td>
<td>$566</td>
<td>$2,832</td>
</tr>
<tr>
<td>Identify 1 cCMV-related SNHL</td>
<td>$975</td>
<td>$3,916</td>
</tr>
<tr>
<td>Prevent 1 cochlear implant</td>
<td>$39,401</td>
<td>$271,947</td>
</tr>
</tbody>
</table>
## Estimated costs and savings from cCMV screening*

<table>
<thead>
<tr>
<th></th>
<th>Targeted screening</th>
<th>Universal screening</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Treat if symptoms</td>
<td>Treat if symptoms</td>
</tr>
<tr>
<td></td>
<td>at birth only</td>
<td>or SNHL at birth</td>
</tr>
<tr>
<td>Direct savings</td>
<td>$0.90</td>
<td>$4.95</td>
</tr>
<tr>
<td>(costs)</td>
<td>($2.01)</td>
<td>($10.86)</td>
</tr>
<tr>
<td></td>
<td>($6.83)</td>
<td>($14.16)</td>
</tr>
<tr>
<td>Net savings (costs)**</td>
<td>$10.66</td>
<td>$27.31</td>
</tr>
<tr>
<td></td>
<td>($1.80)</td>
<td>$21.34</td>
</tr>
<tr>
<td></td>
<td>$37.97</td>
<td>$1.67</td>
</tr>
</tbody>
</table>

* 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

Supported by awards from:
The Child & Family Research Institute
The National Institute on Deafness and Other Communication Disorders
The National Institute for Allergy and Infectious Diseases
## Estimated effect of screening on cCMV-related hearing loss

<table>
<thead>
<tr>
<th></th>
<th>Targeted screening</th>
<th>Universal screening</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Treat if symptoms at birth only</td>
<td>Treat if symptoms at birth only</td>
</tr>
<tr>
<td></td>
<td>Treat if symptoms or SNHL at birth</td>
<td>No treatment</td>
</tr>
<tr>
<td>Reduction in severe-profound cases</td>
<td>7.5%</td>
<td>NA</td>
</tr>
</tbody>
</table>

* Assumes $10/test

** Includes loss of productivity due to hearing loss