

Strategies for Early Congenital Cytomegalovirus Detection: Hearing Loss Driven Early CMV Testing

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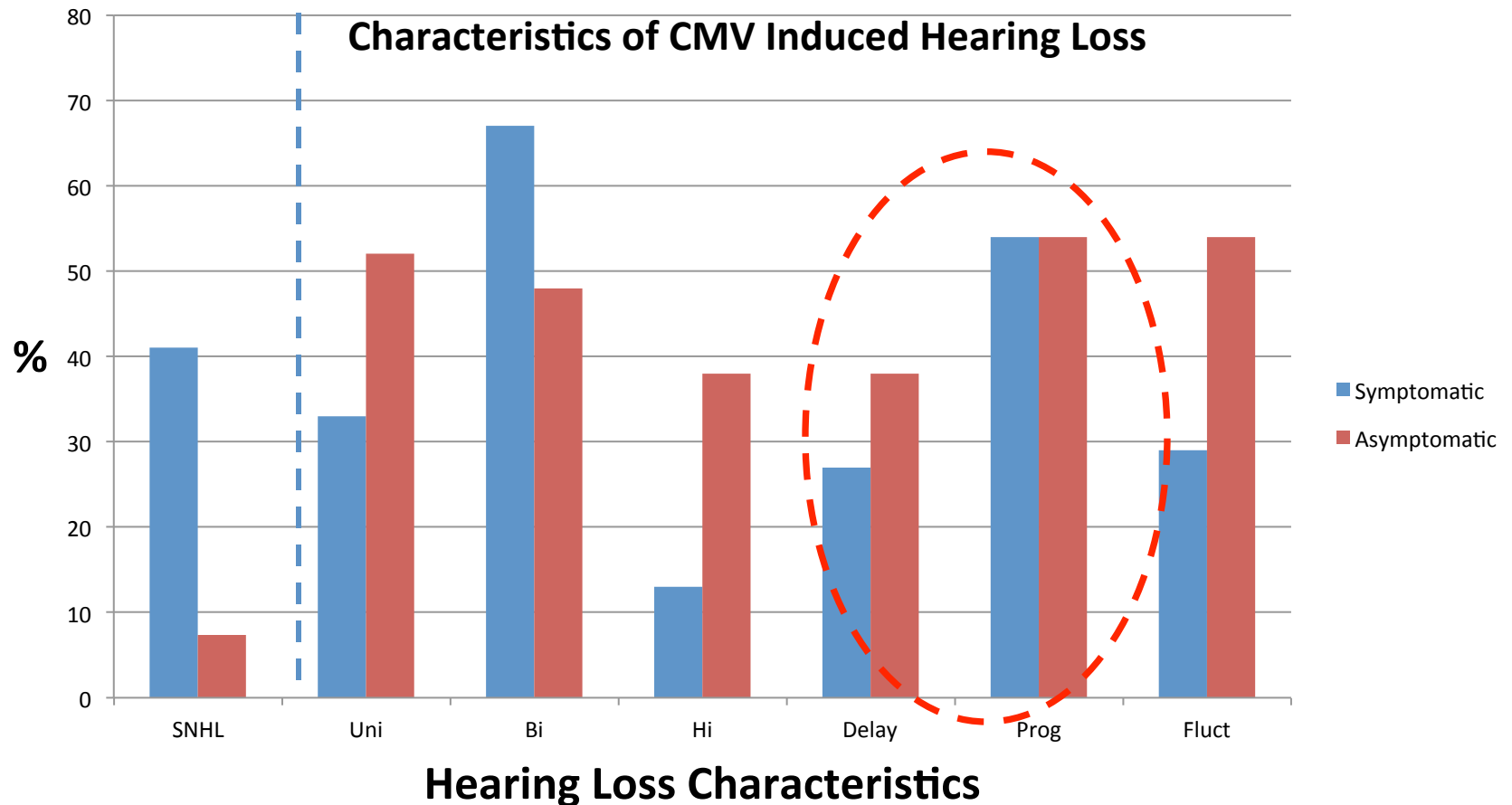
Disclosure:

- Triological Career Development Award-murine model of CMV induced SNHL (Park)
- Multi-institutional study CYP2D6 adenotonsillectomy clinical trial (Park)
- NIH- Magnetic Guidance for Improved Cochlear-Implant Insertion (Park)
- Textbook author (Bale)
- None of these are relevant to this presentation

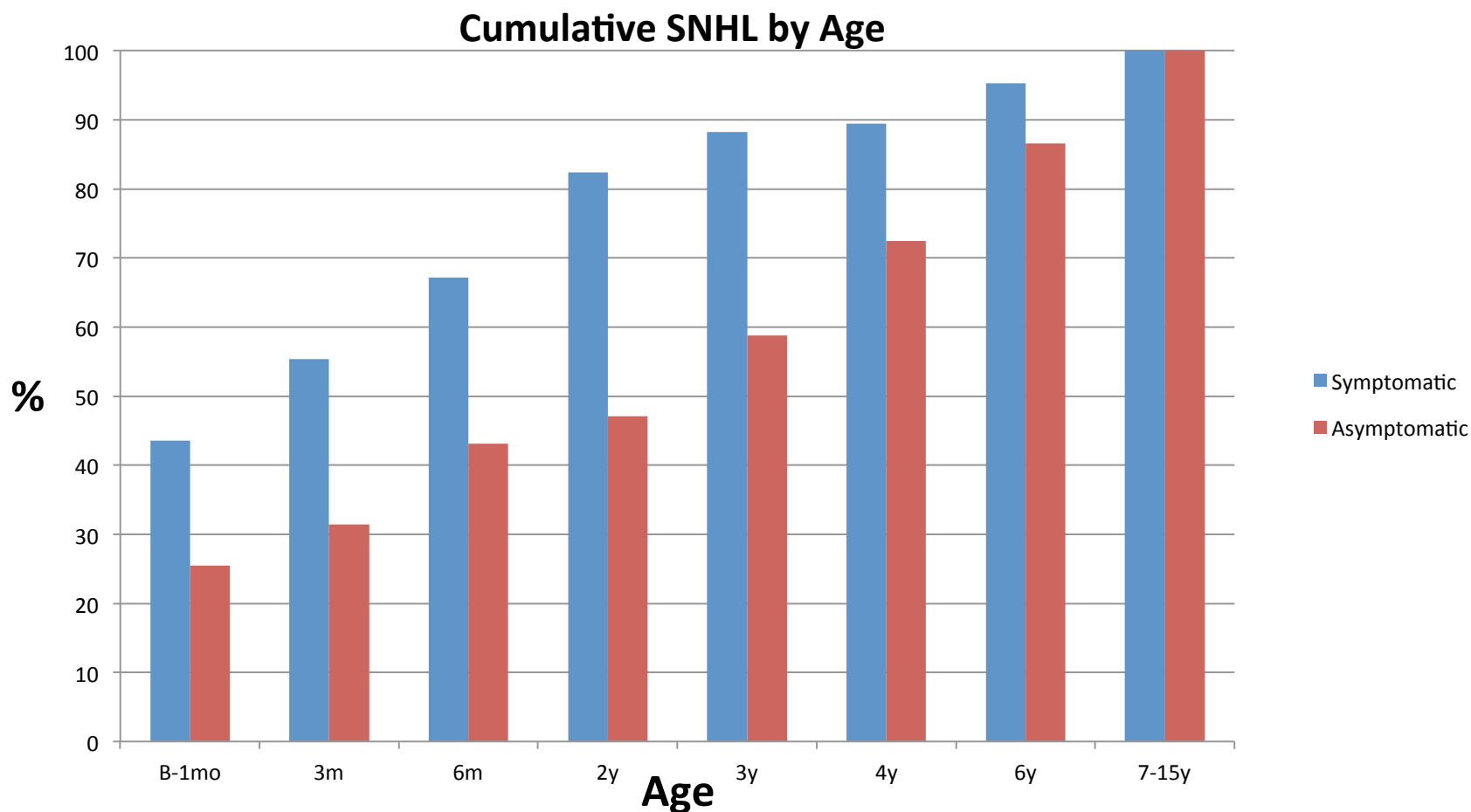
Objectives:

- Rationale Hearing Loss Driven Early CMV testing
- Novel approach towards pediatric hearing loss
- Daisy Doutre's story
- Hadlee Myer's story
- Early results after CMV law

Audiologic Sequelae of Congenital CMV Infection



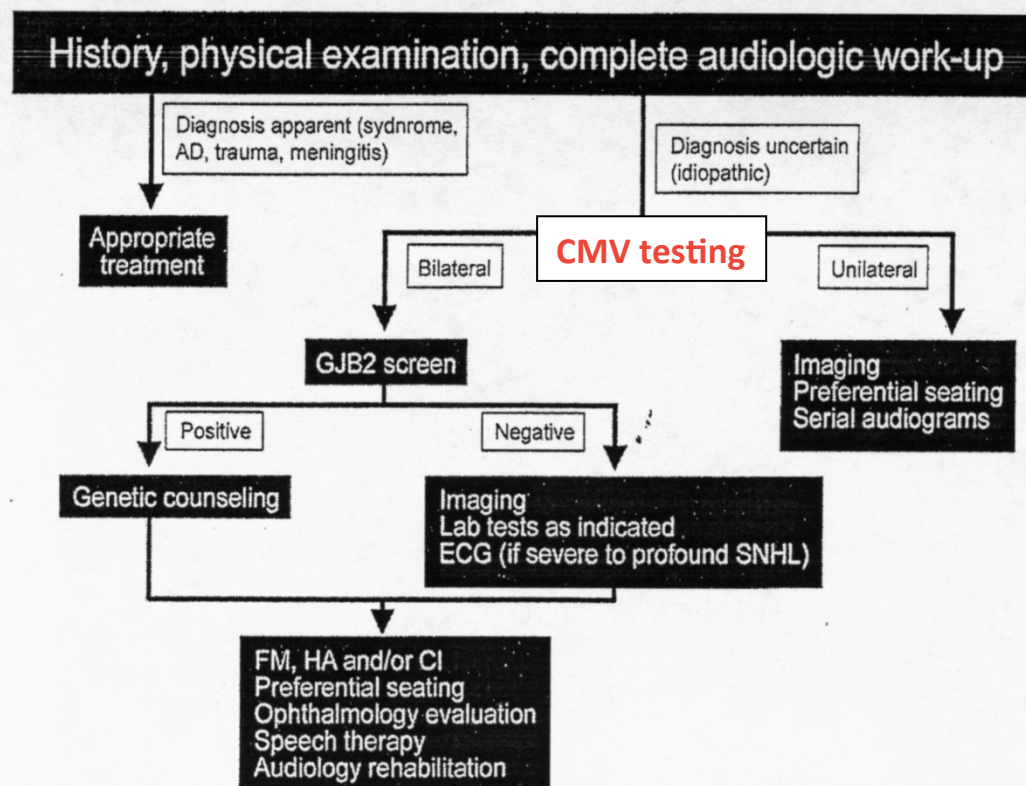
Nature of Progressive SNHL:



The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss – Utah Experience

- What happens if you look for CMV in children with hearing loss?
- In May 2008 we began rigorous CMV testing and a sequential diagnostic paradigm

“New Current” Approach to Pediatric SNHL



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METHODS

- May 2008-September 2013
- Children ≤ 3 yrs with hearing loss
- CMV testing performed by PCR of urine, saliva and/or blood spot
- Children with negative CMV testing underwent imaging, genetics evaluation +/- EKG

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- **Confirmed Diagnosis-** positive urine or saliva CMV PCR in an infant < 3 weeks OR positive CMV PCR in an infant > 3 weeks AND positive DBS
- **Suspected Diagnosis-** - positive urine or saliva > 3 weeks of age AND compatible CNS findings or progressive SNHL

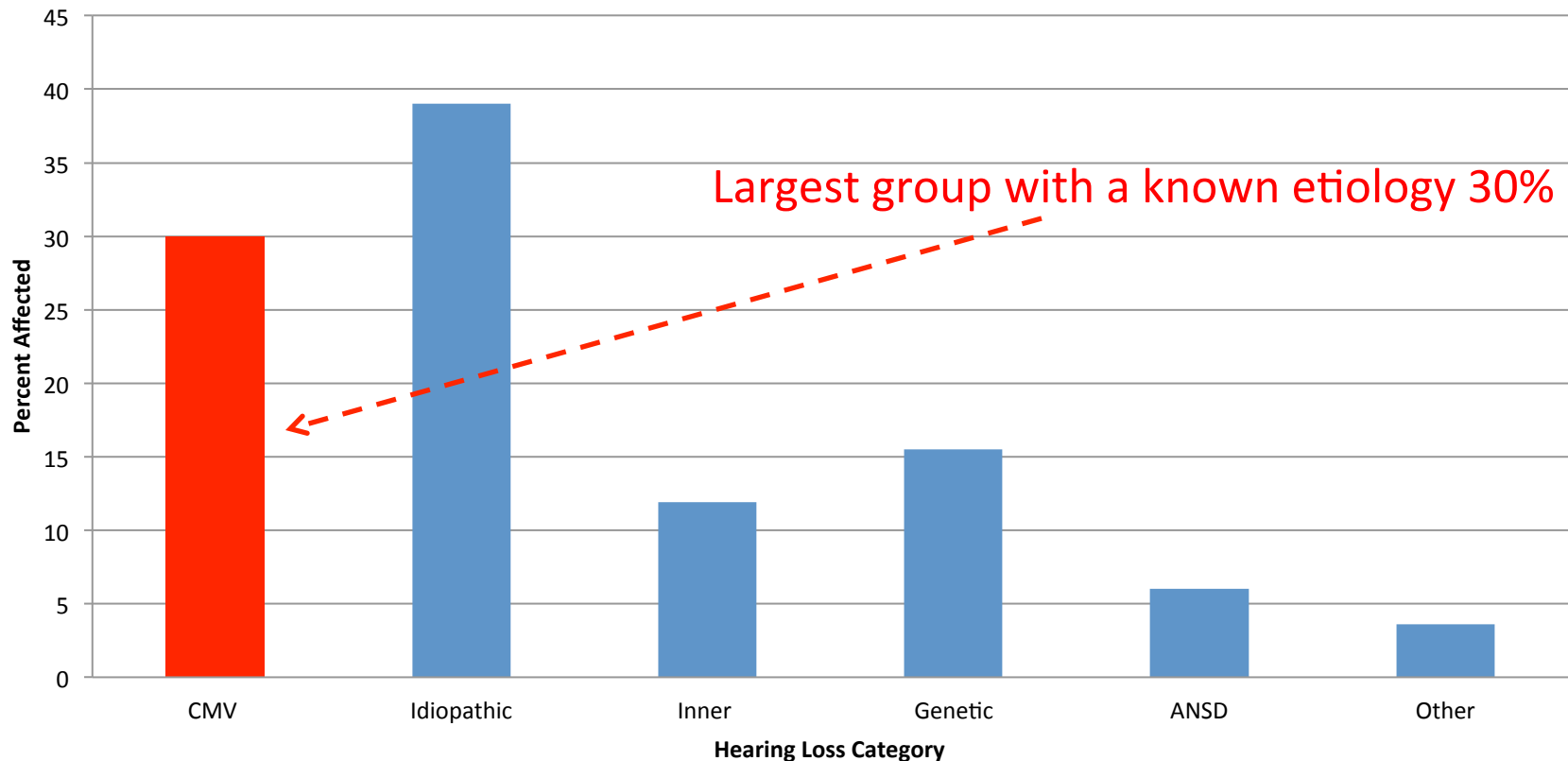
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RESULTS

- N=83 children w SNHL underwent CMV evaluation (2008-2013)
- Cost of the diagnostic testing (Multihospital Standardized Cost Accounting System):
 - MRI (temporal bone) \$1591
 - GJB2 testing \$611
 - CMV PCR saliva or urine \$66

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SNHL Etiology Based on CMV, Imaging and Genetic Evaluation



Most common non-genetic cause of pediatric SNHL!

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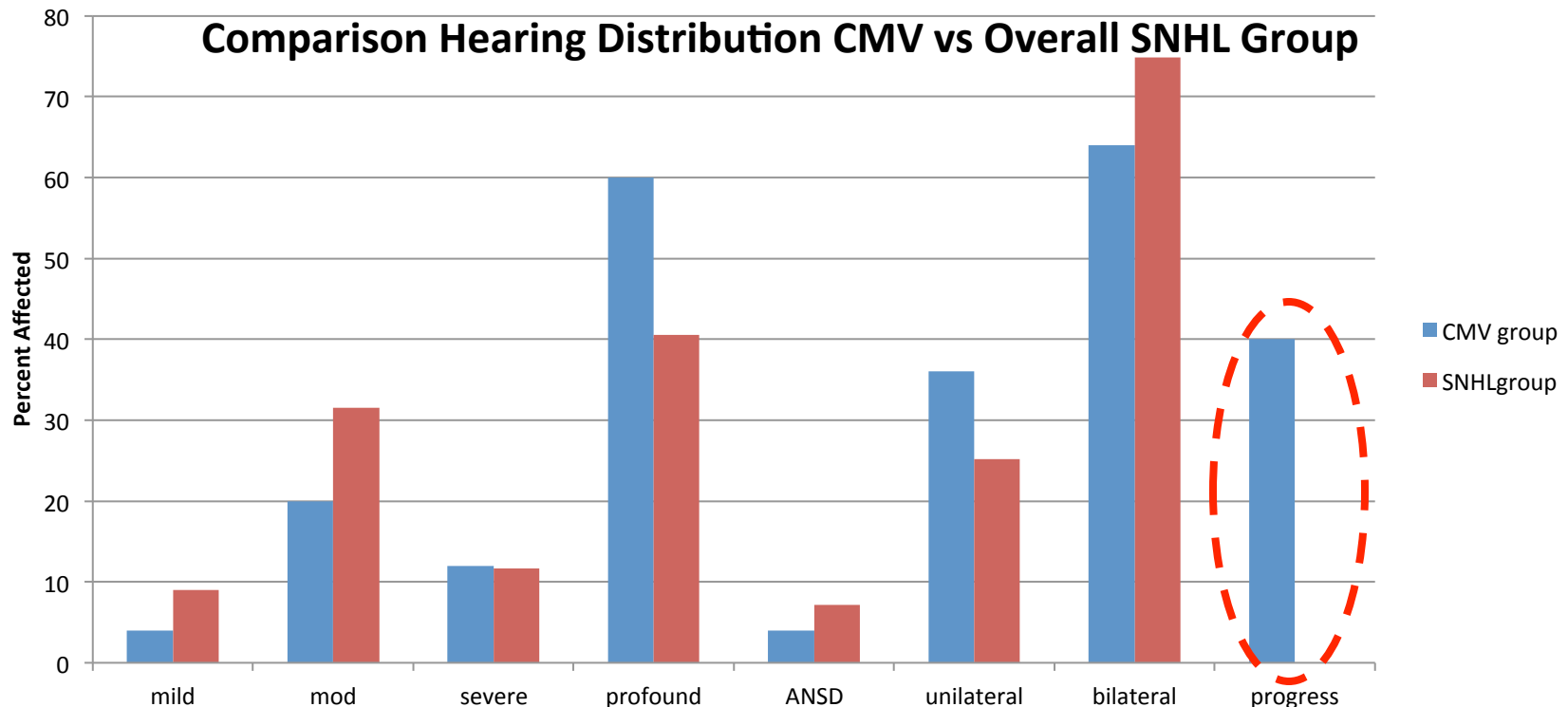
- Summary of Children with CMV
 - N = 25
 - Sixteen (64%) – confirmed CMV
 - Six of sixteen diagnosed via **DBS** testing
 - Nine (36%) – suspected CMV

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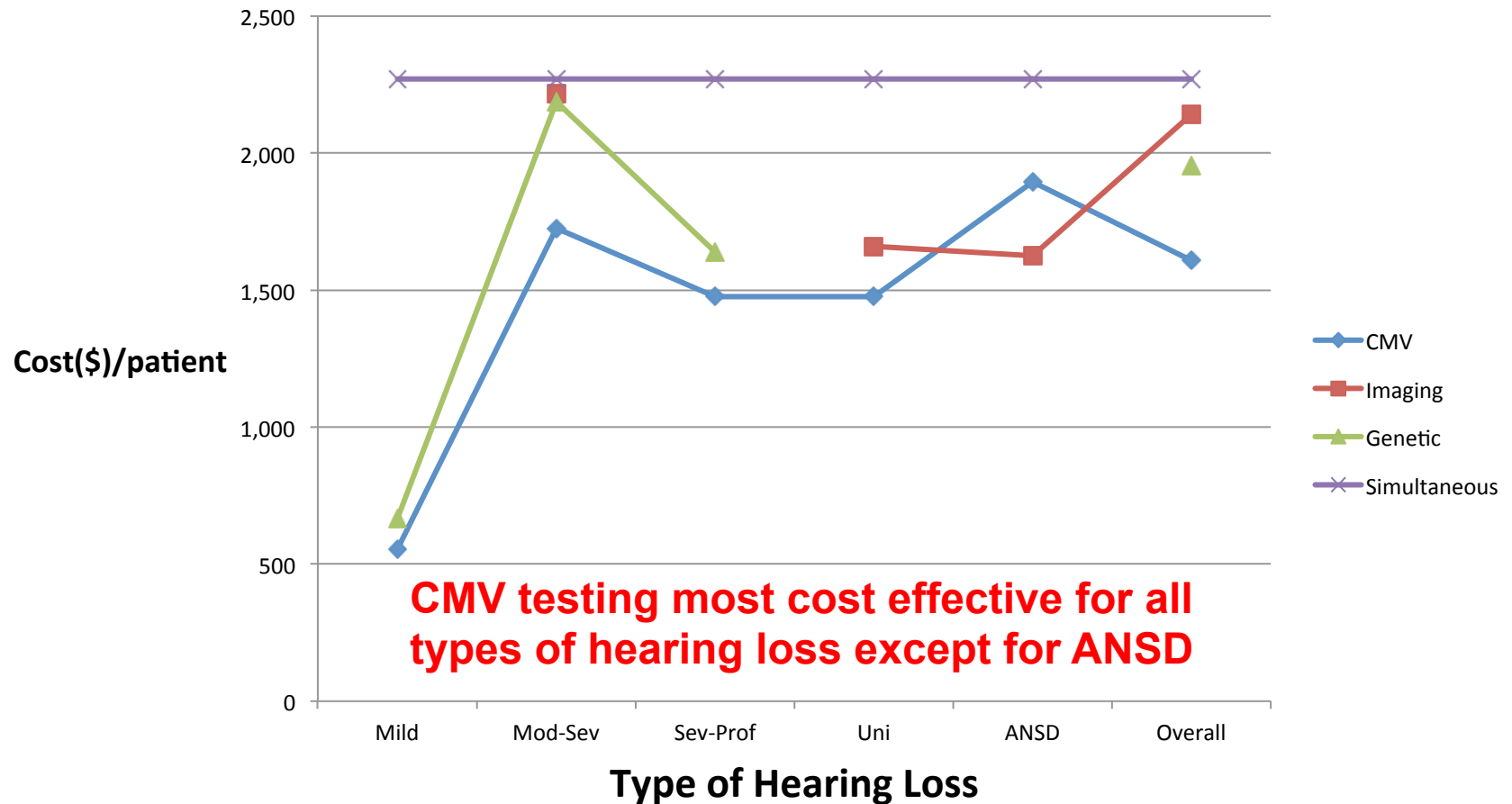
- Timing of Evaluation in Children with CMV-Induced SNHL
 - Average age initial evaluation for CMV 352 days (range 24-1387 days)!
 - Only 5 infants were evaluated for CMV at one month of age or less

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- Distribution of CMV vs SNHL Groups:



Cost Estimates Using Different Approaches for SNHL Evaluation



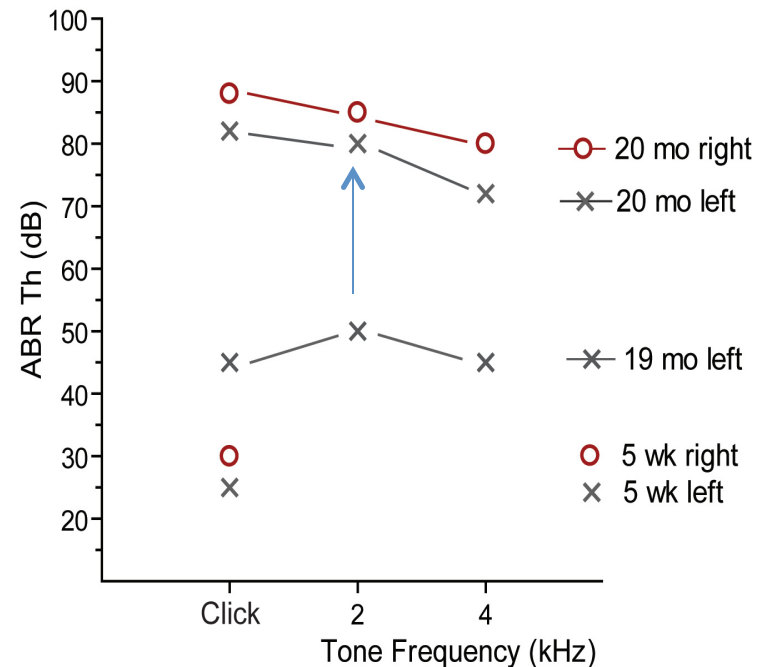
Rationale for Hearing Loss Driven Screening

- 19 mo with progressively hearing
- Failed newborn hearing screen and automated ABR at 3 weeks
- Click ABR at 3 weeks: 30 dB nHL right and 25 dB nHL left
- Recommended FU 9 mo.
- U/S at birth- “germinolytic” cystic changes- compatible with an in utero insult

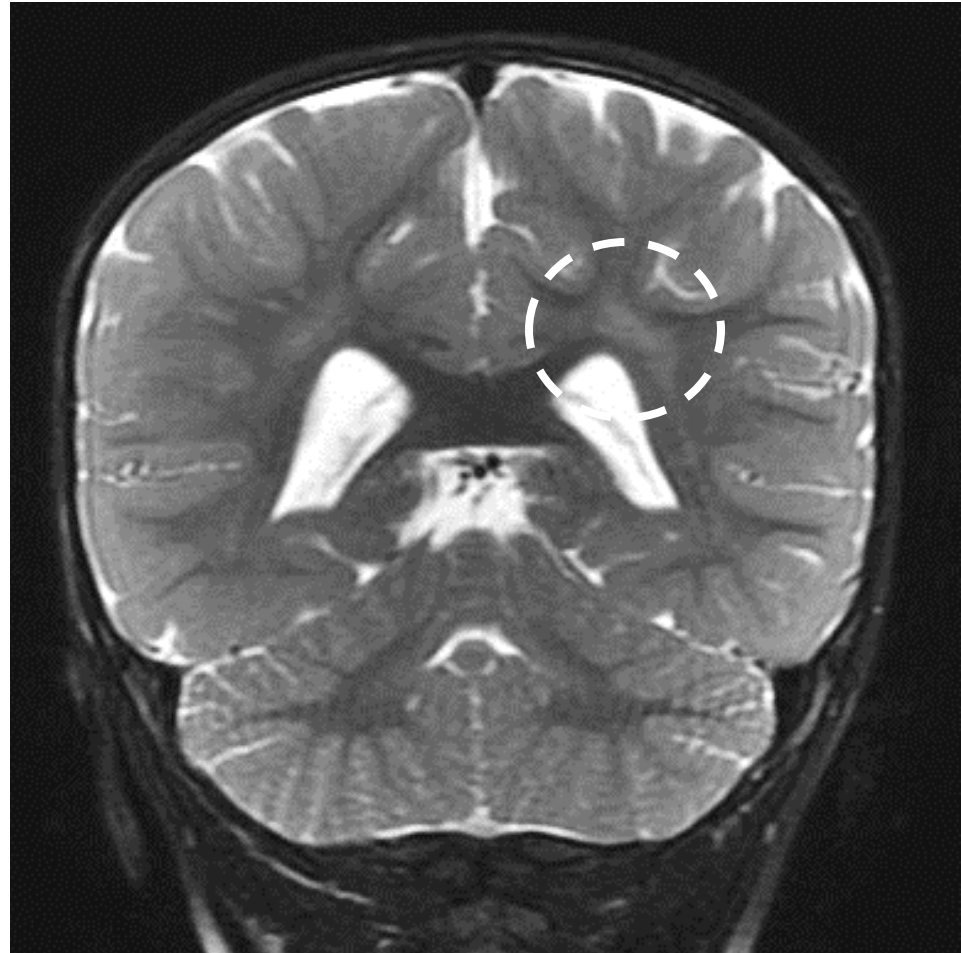
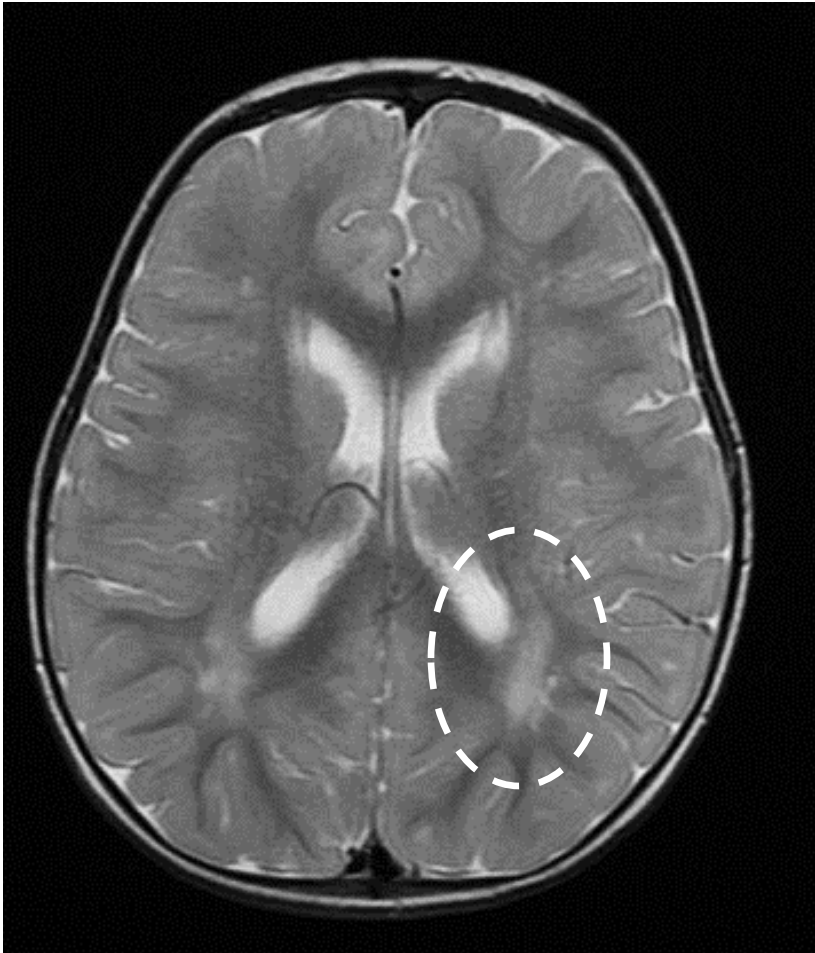


Rationale for Hearing Loss Driven Screening

- Normal Otologic examination
- Repeat ABR right profound and left moderate SNHL
- Saliva CMV PCR- positive
- Neonatal Dry Blood Spot PCR-
positive
- 6 week course of valganciclovir
- Left ear worsened to profound
- Bilateral Cochlear Implantation



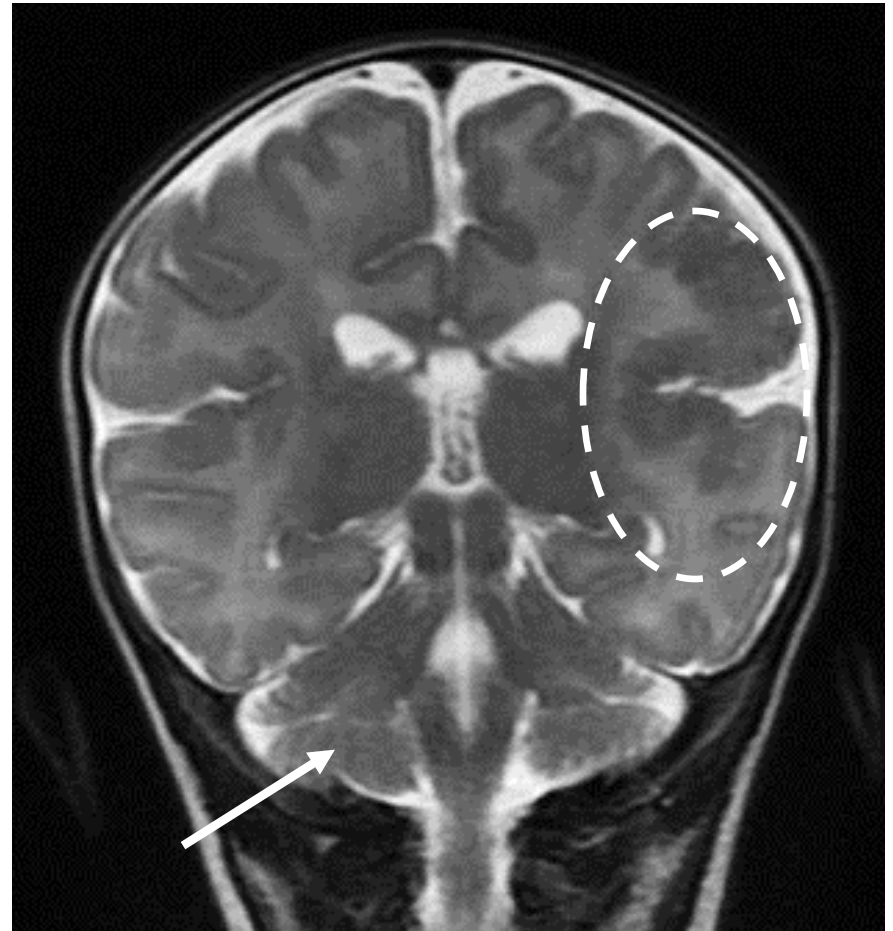
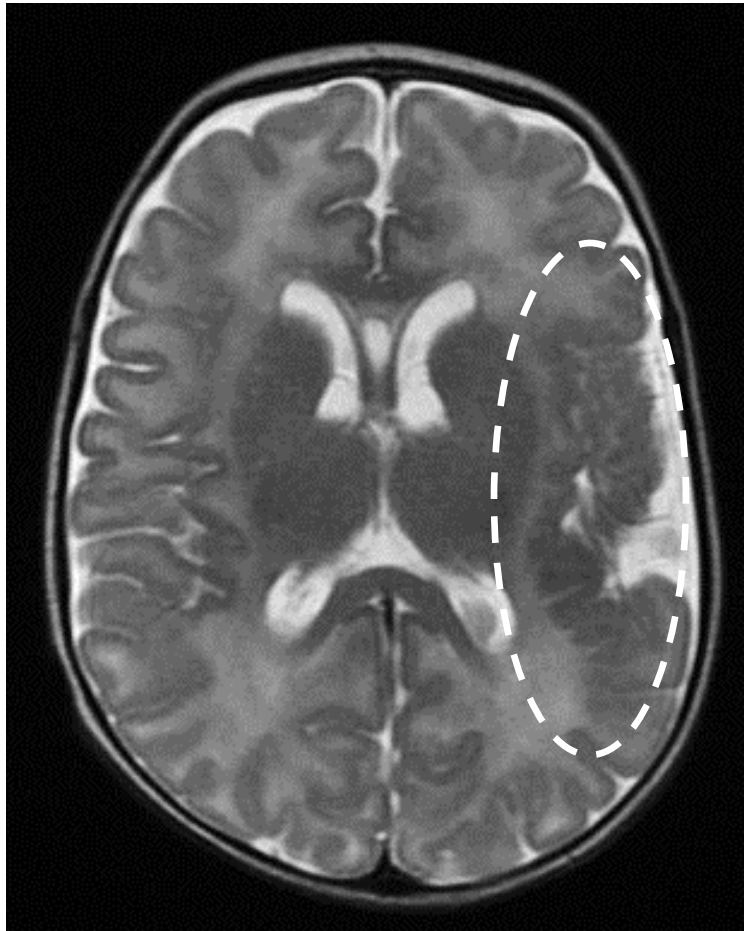
Neurodiagnostic Evaluation



Rationale for Hearing Loss Driven Screening

- 26 day old infant presented with CMV induced SNHL (born before July 2013)
- Failed NBHS
- Saliva CMV PCR @ 3 wks age- **positive**
- ABR- normal right and left profound SNHL
- MRI: bilateral perisylvian cortical dysplasia
- Ophthalmology exam- normal

Neurodiagnostic Evaluation



Rationale for Hearing Loss Driven Screening:

- VGC x 6 weeks
- FU audio 18 mo after rx-stable hearing
- Speech progressing well



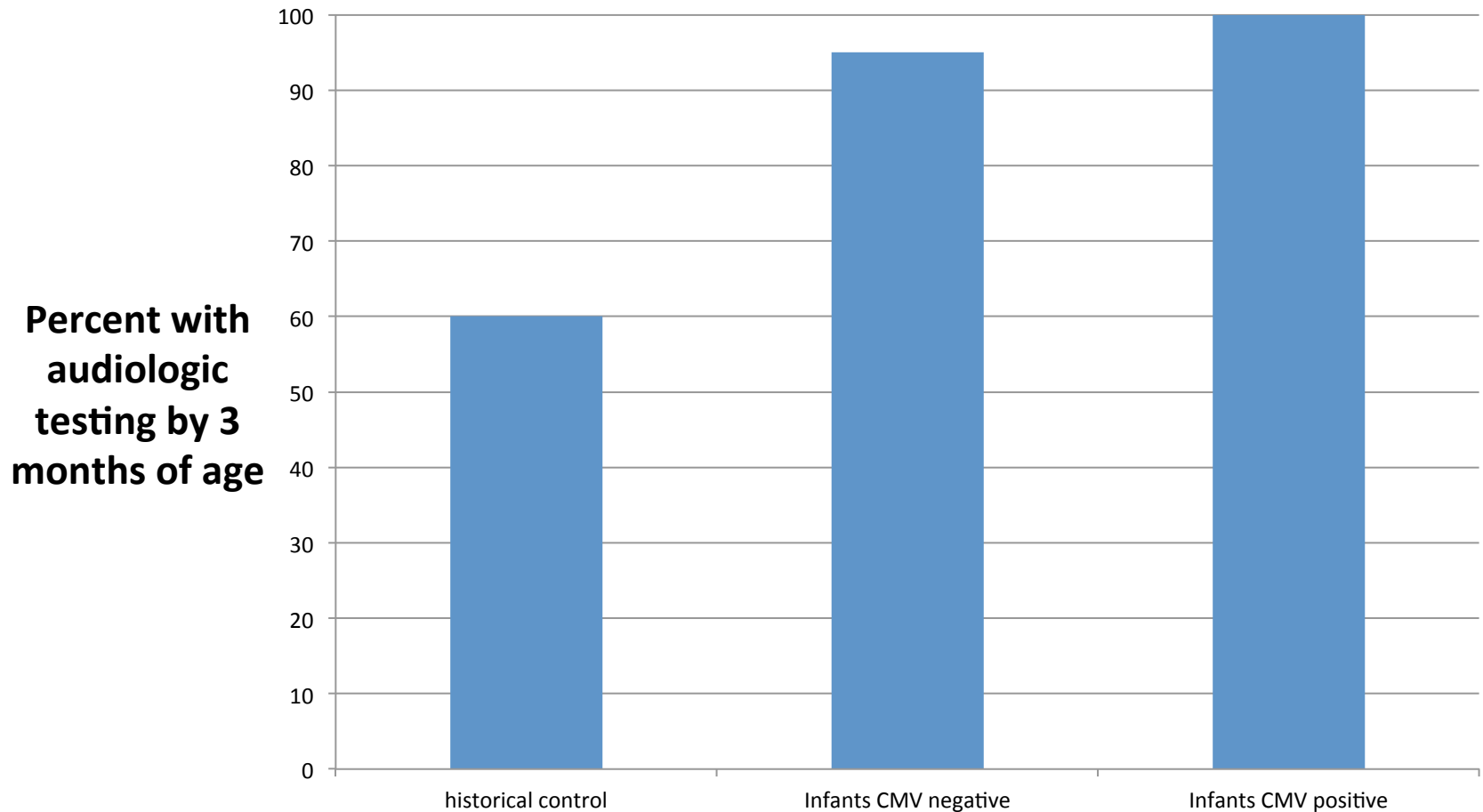
House Bill 81 (July 2013)

- Department of Health (DOH) public education program to inform caregivers about CMV
- DOH education for providers and other organizations offering children's programs
- Medical practitioners to test infants < 3 wks of age who fail two newborn screening tests for CMV and inform the parents regarding results and interventions

First Year Results

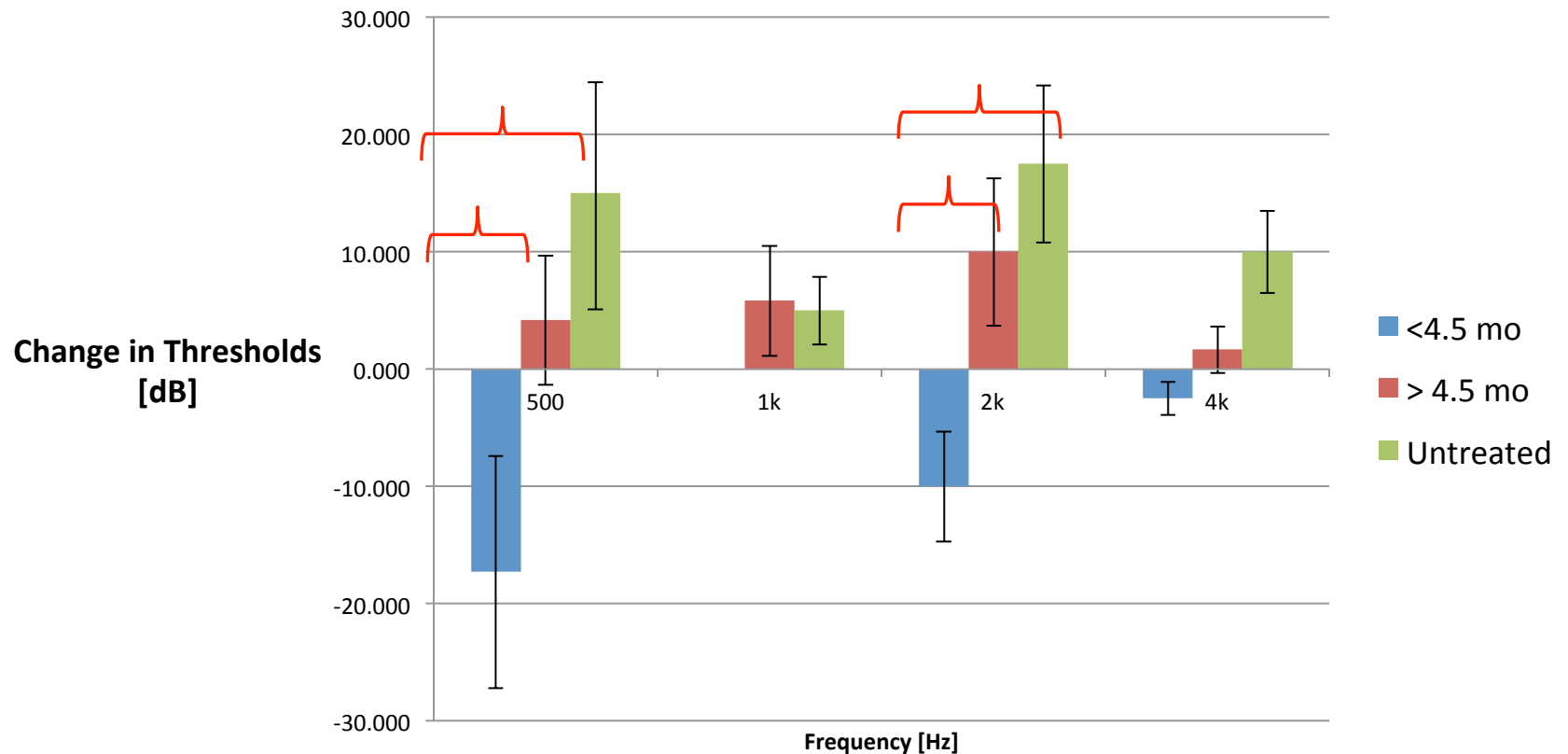
- July 2013-June 2014
- N=42,336 newborns underwent newborn hearing screening (NBHS)
- 245 failed NBHS birth hospital and @ FU
- 163 CMV testing (67%)
- 17 CMV positive infants (10%)

Even CMV-negative newborns benefit from early CMV testing



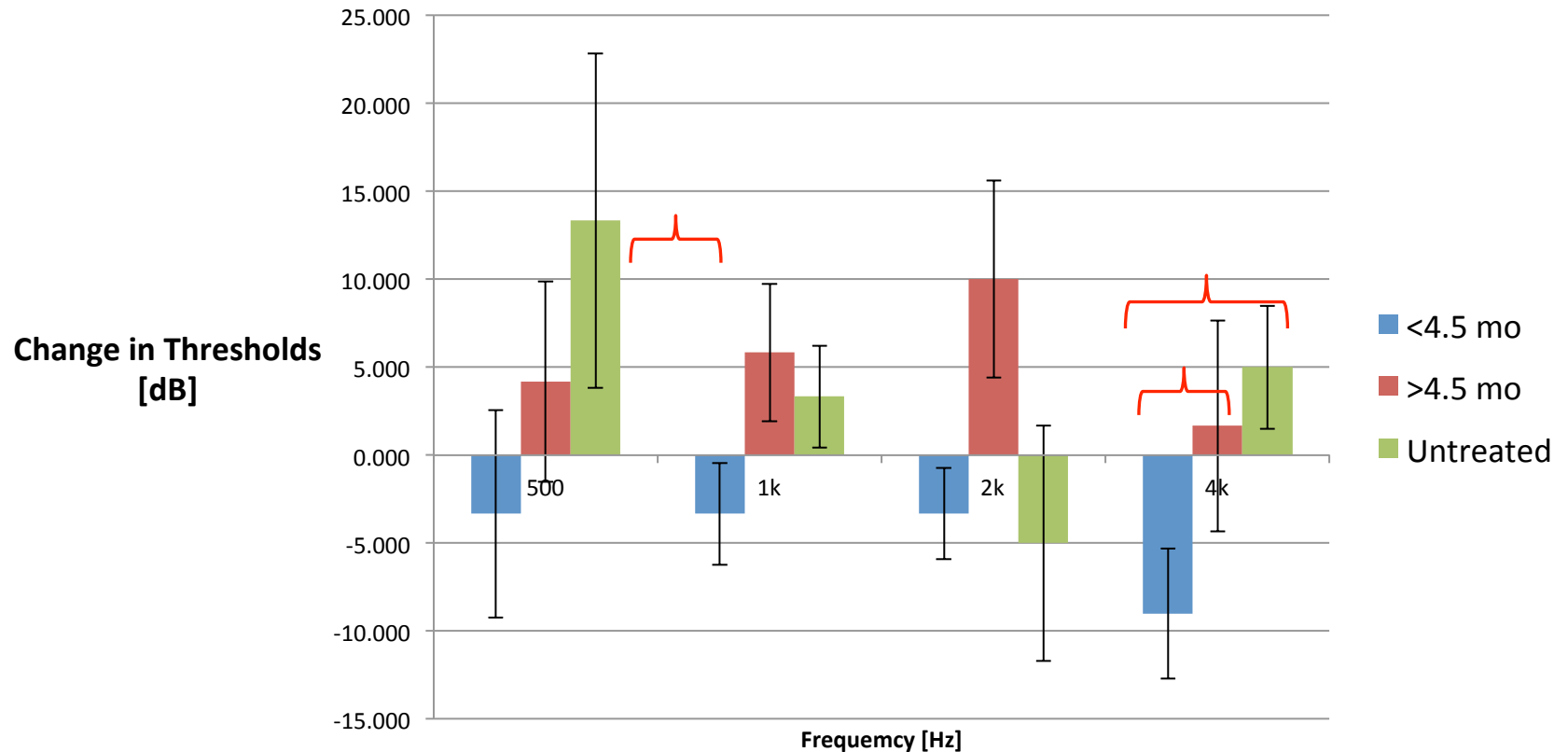
Preliminary Results from VGC in Utah (n=19)

Mean Change Between Pre- and Post-Treatment (Right)



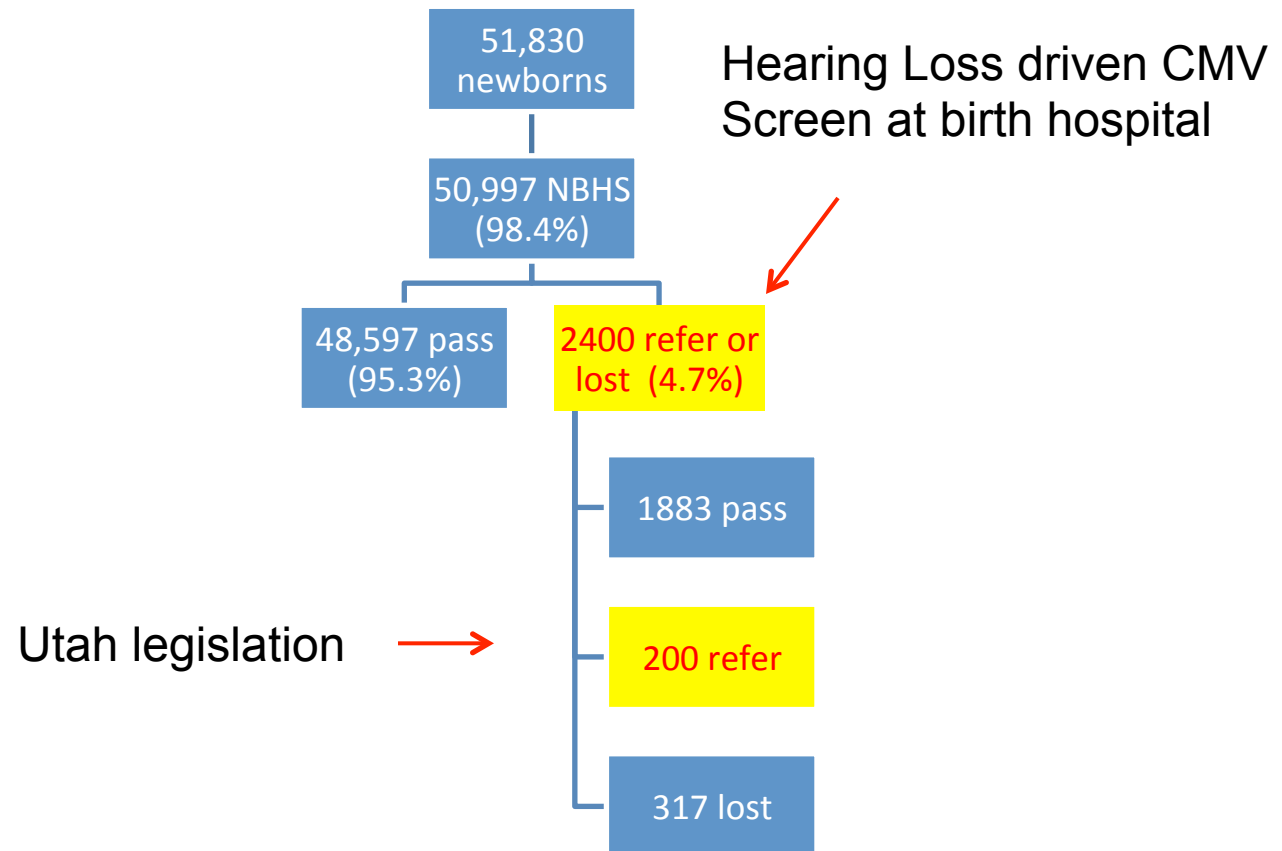
Preliminary Results from VGC in Utah (n=19)

Mean Change Between Pre- and Post-Treatment (Left)



Future Directions:

- Early CMV testing before newborn leaves the hospital



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CONCLUSIONS

- Diagnostic Paradigm incorporating early CMV testing has high yield (30%)
- CMV testing has substantially lower cost than imaging or genetic testing
- Detecting CMV stimulates additional clinical evaluation, such as brain MRI, and provides opportunities for intervention.
- Utah legislation promotes early evaluation and intervention

Acknowledgements:

BASIC SCIENCE

Mark Schleiss

Matt Firpo

Elaine Hillas

Ali Almishaal

Robert Harrison (Toronto)

Mattia Carrero (Toronto)

Wayne Yokoyama (St. Louis)

Ed Hsu

Richard Rabbit

Kuby Balagurunihan

Xiao Rui Shi (Oregon)

CLINICAL

Cathleen Zick

Marissa Diener

Richard Nelson

Jim Bale

Krow Ampofo

Xiaoming Sheng

Tom Greene

Jaewhan Kim

Christina Yoshinaga-Itano (Colorado)

Karen Fowler (UAB)

Beth Prieve (Syracuse)

Lisa Hunter (Cincinnati)