

Viral causes of birth defects: Why we need to start talking about congenital cytomegalovirus (cCMV)

Kathleen M. Muldoon, Ph.D.

Associate Professor, Department of Anatomy
Arizona College of Osteopathic Medicine
Midwestern University
kmuldo@midwestern.edu

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Seth Dobson Ph.D., Gideon Dobson,
Janelle Sargent-Greenlee
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Viral causes of birth defects

Pregnant women with laboratory evidence of Zika infection = 400 (CDC, 7/21/2016)



- Status**
- Currently reporting
 - Has reported in past
 - Highly suitable but not yet reported
 - Limited suitability
 - Unsuitable



Viral causes of birth defects

ZIKA (ZIKA VIRUS)

Found in South and Central America



Transmitted by mosquito bite



Symptoms include fever, rash, joint pain, and conjunctivitis/red eyes

Can be transmitted from pregnant woman to unborn baby



Can cause baby to be born with microcephaly (small head/small brain)

No treatments or vaccine available

Prevent by wearing long sleeved shirts and pants, and use EPA-registered insect repellents

Liveborn infants with birth defects due to Zika = 12 (14 July 2016)

RUBELLA (RUBELLA VIRUS)

Found worldwide



Transmitted by contact with nasal or throat secretions infected individuals



Symptoms include fever, rash, headache, and conjunctivitis/red eye

Can be transmitted from pregnant woman to unborn baby



Can cause baby to be born with hearing loss, vision loss, microcephaly (small head/small brain), etc

Vaccine available

Prevent by vaccination

Liveborn infants with birth defects due to CRS = 0.75/yr (MMWR (2013) 62; 226-229)

CMV (CYTOMEGALOVIRUS)

Found worldwide



Transmitted by contact with bodily fluids of babies, toddlers, and small children



Symptoms include fever, fatigue, and joint pain

Can be transmitted from pregnant woman to unborn baby



Can cause baby to be born with hearing loss, cerebral palsy, seizures, microcephaly (small head/small brain), etc

Treatments and vaccine in development

Prevent by avoiding contact with saliva, urine, and other bodily fluids from babies, toddlers, and small children

Liveborn infants with birth defects due to cCMV = 8,000-10,000 (CDC)

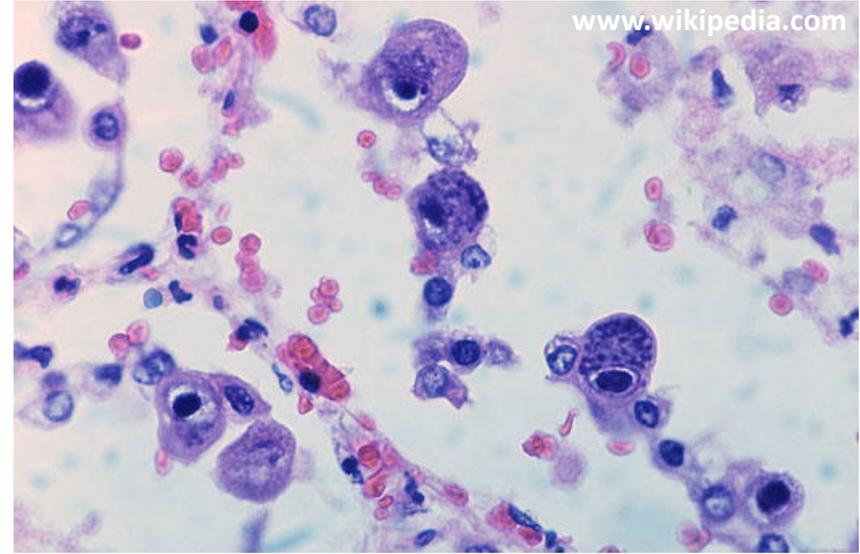
**Liveborn infants with birth defects
due to congenital cytomegalovirus
(cCMV) = 8,000-10,000/year
in the US**

Objectives

- Define congenital cytomegalovirus (cCMV) & provide new information about burden of cCMV disease
 - US seroprevalence and force of infection
 - Who is socially vulnerable? / disparities?
 - Clinical sequelae
 - Viable interventions?
- Discuss steps to undertake a public awareness campaign to increase knowledge of cCMV

What is cytomegalovirus (CMV)?

- **common** and ubiquitous virus
- evolved alongside humans
- herpesvirus = lifelong infection
 - salivary glands, brain, liver
 - **latent** – allows immune evasion by inhibiting proinflammatory cytokine synthesis (= suppression of cell-mediated immune response, natural killer cell response)
 - **lytic** – can reactivate throughout lifetime after initial infection

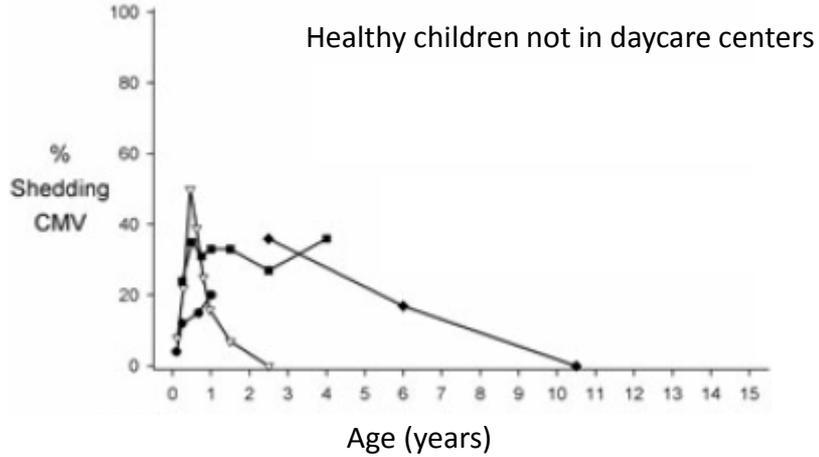
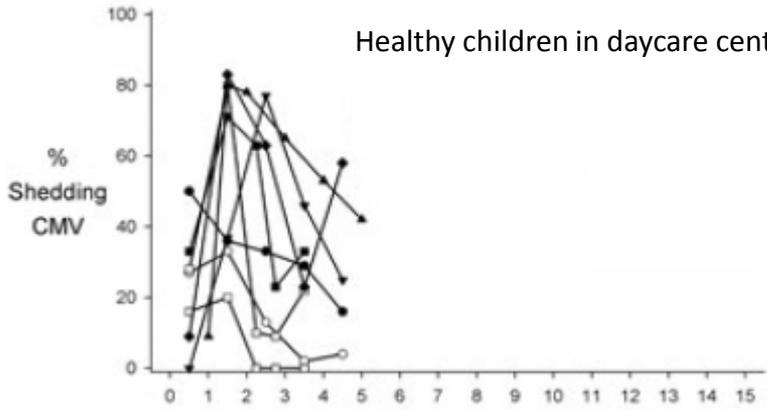


Usually **ASYMPTOMATIC** in immunocompetent (e.g., healthy) host
“The STEALTH Virus”

How is CMV transmitted?

- CMV is spread by close personal contact through saliva, urine, mucous, tears, blood, and other bodily fluids
- up to 80% of **healthy** children between 1-3 years of age have CMV

Cannon,
Hyde,
Schmid
(2011)



How easy is it to contract CMV?

Table 3: Comparison of force of infection for different viruses for selected* age ranges.

| Virus | Force of infection (per 100 persons per year) | Ages modeled |
|-------------|---|--------------|
| Measles | 20 | 11-17 |
| Mumps | 12 | 11-17 |
| Rubella | 10 | 11-17 |
| Varicella | 6 | ≥ 10 |
| CMV | 1.8 | 12-49 |
| Dengue | 0.9 | 5-64 |
| HSV-2 | 0.84 | ≥ 12 |
| Hepatitis B | 0.15 | 6-39 |
| HIV | 0.0001 | 13-44 |

easier to catch

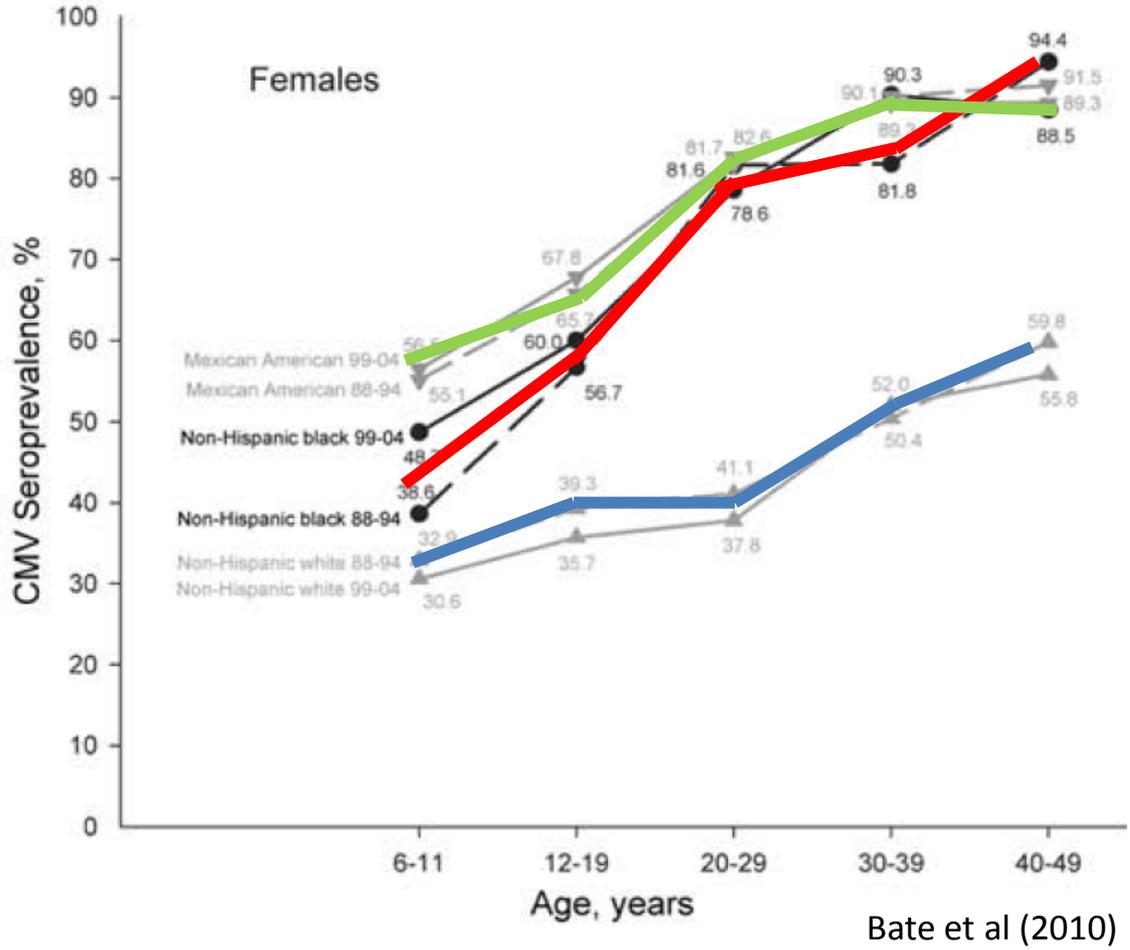


harder to catch

Colugnati et al (2007)
CDC HIV statistics (2014)
Castanha et al (2012)

Seroprevalence higher in females, older people, certain ethnic groups

How common is CMV among women?



Force of Infection

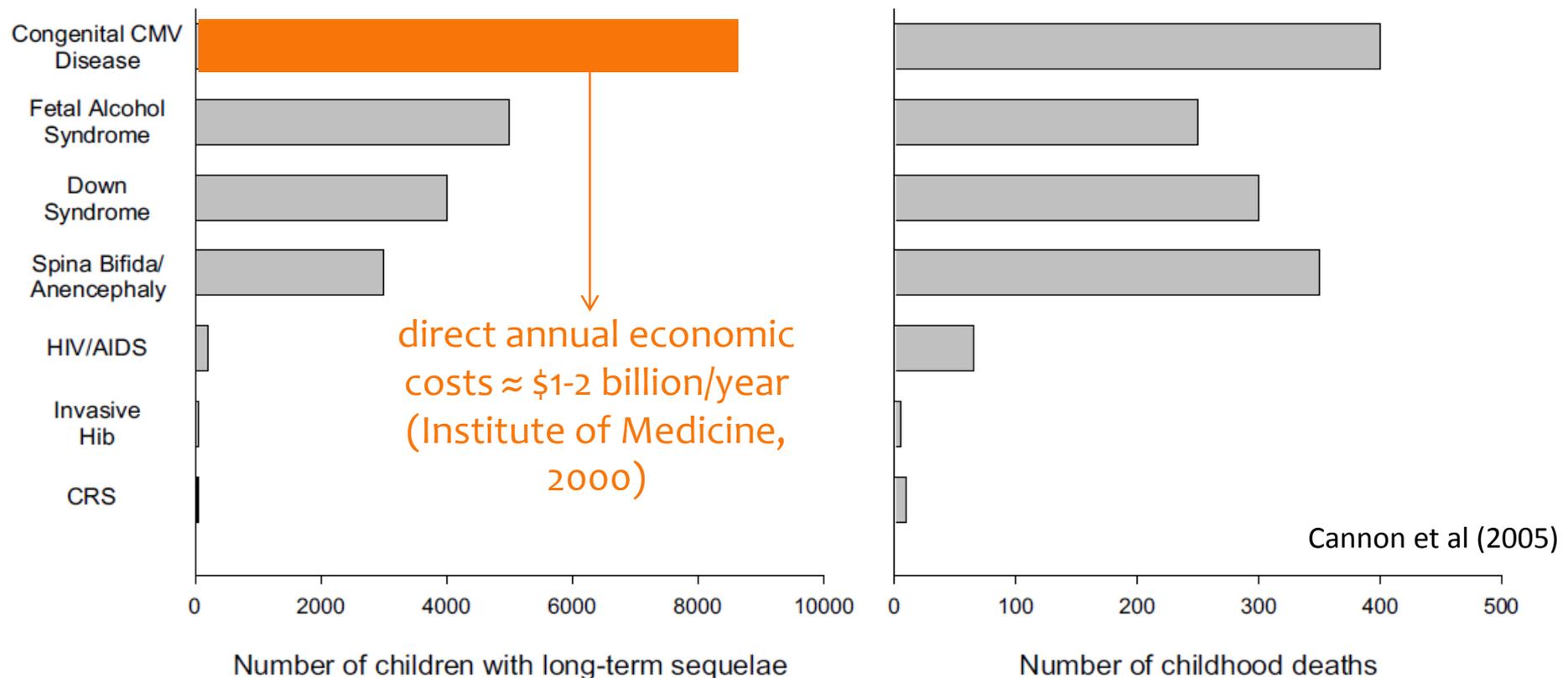
- general seronegative population = 1.8
- NH white = 1.4
- NH black = 5.7
- Mexican American = 5.1

- In women of child-bearing age, infection rates for seronegative childcare employees are between 10-20%/year

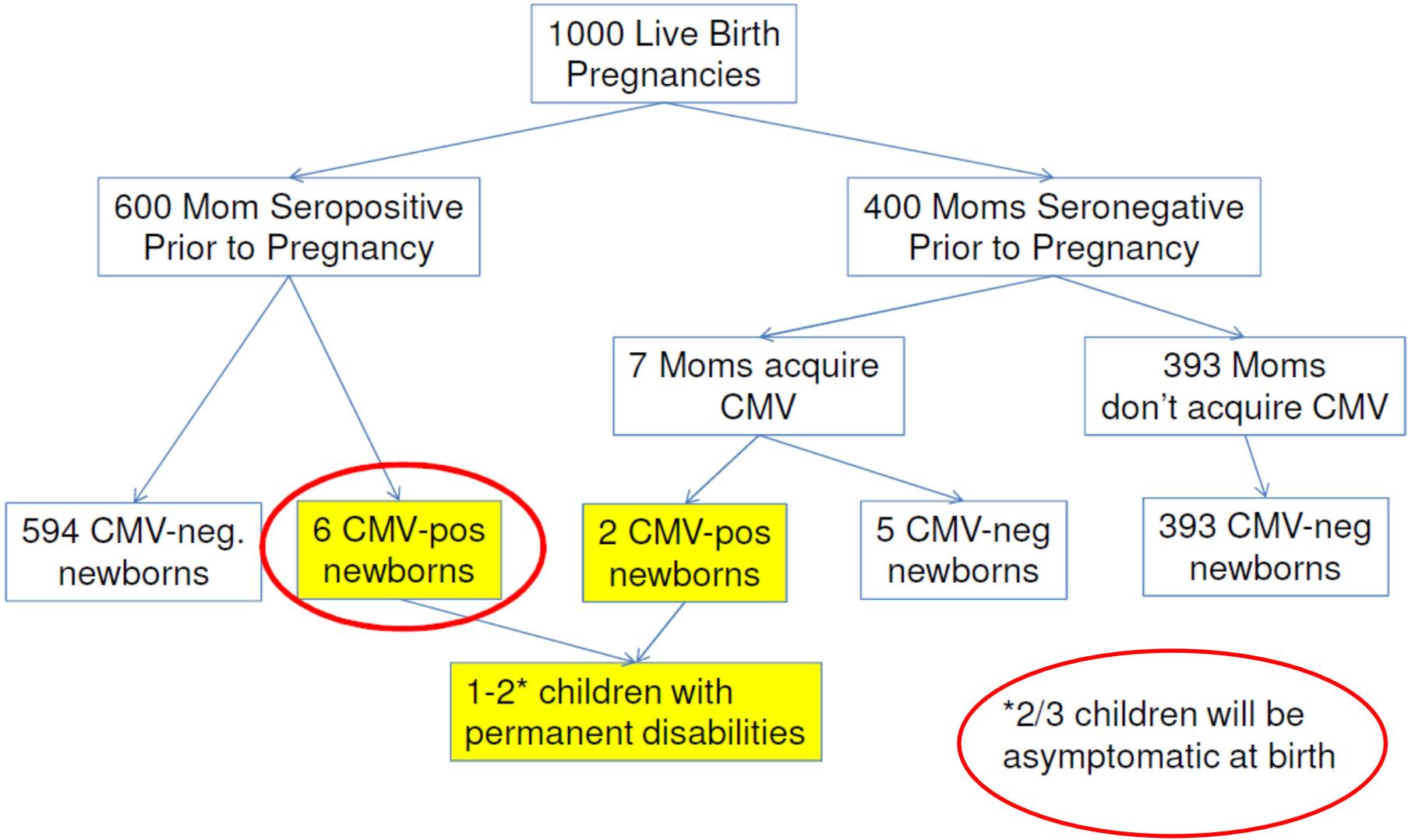
**CMV is the most common virus
transmitted from a mother to her
unborn baby**

What is congenital CMV (cCMV)?

- 1:150 children is born with cCMV infection in the US ($\approx 40\,000/\text{yr}$)
- Of those, $\sim 20\%$ will suffer permanent disability due to CMV disease ($\approx 8000-10,000$), 1% will die within 1 year (≈ 400)



Disease burden of cCMV



Possible Outcomes of cCMV disease

- 10% of congenitally infected infants* are symptomatic at birth

TRANSIENT OUTCOMES

- hepatosplenomegaly
- jaundice
- petechiae and purpura
- fetal growth restriction
- seizures

Possible Outcomes of cCMV disease

- 10% of congenitally infected infants* are symptomatic at birth
- Of the 90% who are asymptomatic*, 10-15% will develop symptoms

PERMANENT OUTCOMES

- microcephaly
- wide range of brain anomalies
- vision loss (chorioretinitis)*
- sensorineural hearing loss (SNHL)*
- intellectual disability
- autism
- motor disability *
- seizures
- death

* children with hearing loss alone are considered asymptomatic

* vision loss does not include children with cortical visual impairment (CVI)

* congenital infections are **THE LEADING CAUSE** of cerebral palsy (CP) in full-term infants; CP secondary to cCMV is often severe - involving all 4 limbs with associated epilepsy, hearing and/or vision loss (Smithers-Sheedy, 2014)

**90% of babies born with cCMV will
appear healthy at birth**

How can cCMV be prevented?

- Wash hands and toys with soap and water. After cleansing, no viable virus was recovered using: water (0/22), plain soap (0/20), antibacterial soap (0/20), hand sanitizer (0/22) (Stowell et al 2013)



- Avoid kissing babies and young children on the mouth or face while pregnant.

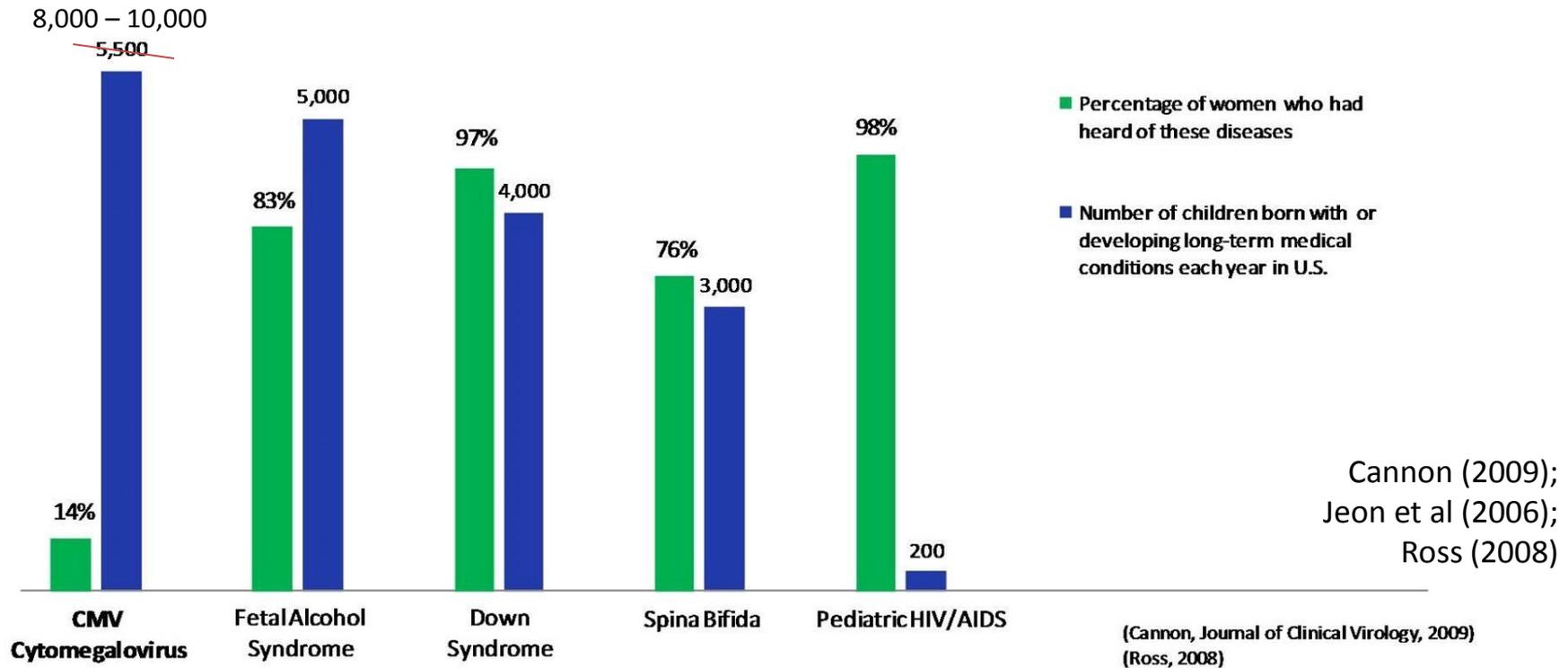
- Do not share food, drinks, utensils or toothbrushes with babies or young children while pregnant.



Adler et al (1996),
Picone et al (2009),
Vauloup-Fellous et al (2009)

cCMV awareness gap

- ~ 14% of women in the US have heard of CMV (CDC, 2010)



- This awareness gap has serious public health implications because cCMV is more **common** than other congenital conditions, is **preventable** through behavioral modifications, and recent studies show it is likely **treatable** in utero (Adler, 2011)

cCMV in medical practice (OB/GYNs)



THE AMERICAN COLLEGE OF OBSTETRICIANS AND GYNECOLOGISTS
WOMEN'S HEALTH CARE PHYSICIANS

PRACTICE BULLETIN

CLINICAL MANAGEMENT GUIDELINES FOR OBSTETRICIAN—GYNECOLOGISTS

- “Perinatal Viral and Parasitic Infections”
(No 20, September 2000, 2008)

- Some groups of women at higher risk for acquisition of CMV infection

“**Women with young children** or **those who work with young children** should be advised that the **risk of infection** can be reduced significantly by safe-handling techniques, such as the use of latex gloves and rigorous hand-washing after handling diapers or after exposure to respiratory secretions”

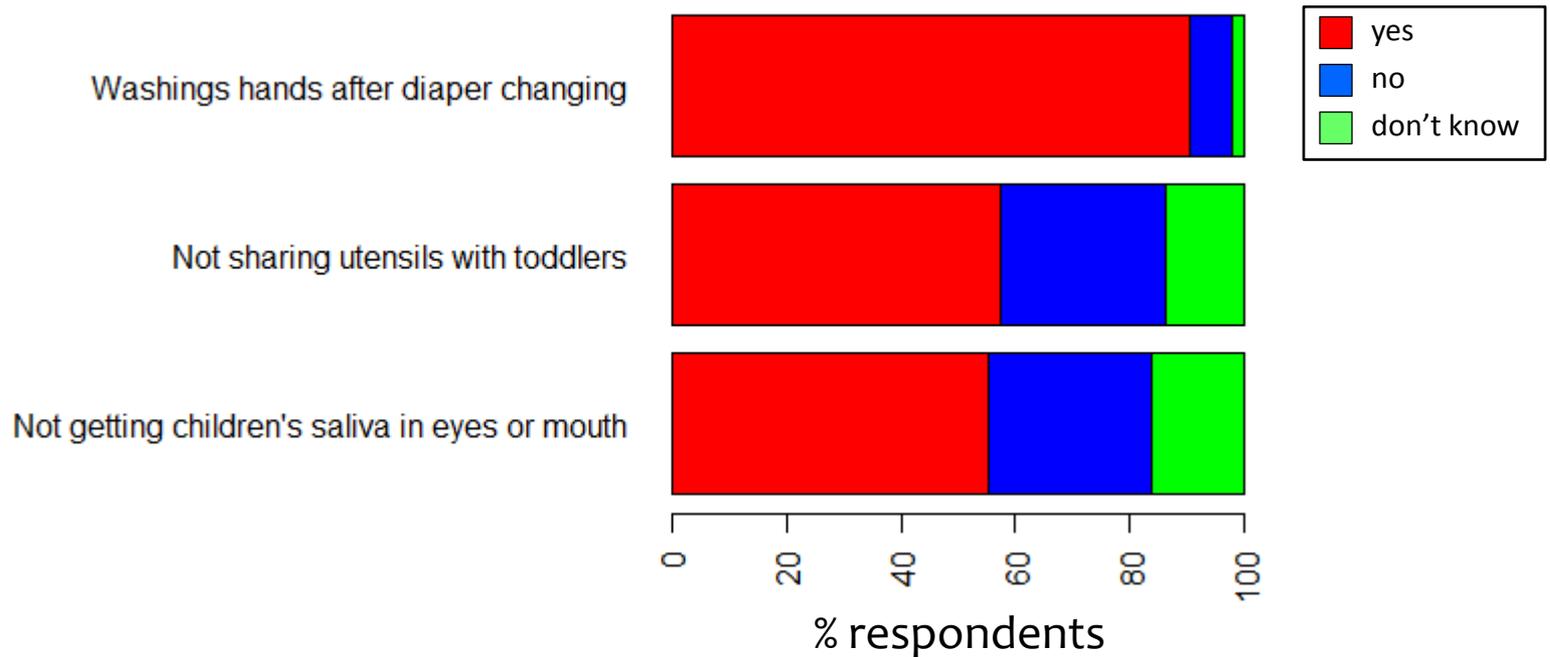


... so why the awareness gap?

cCMV awareness gap (OB/GYNs)

- Knowledge and Practices of OB/GYNs Regarding CMV Infection during Pregnancy (CDC 2008)

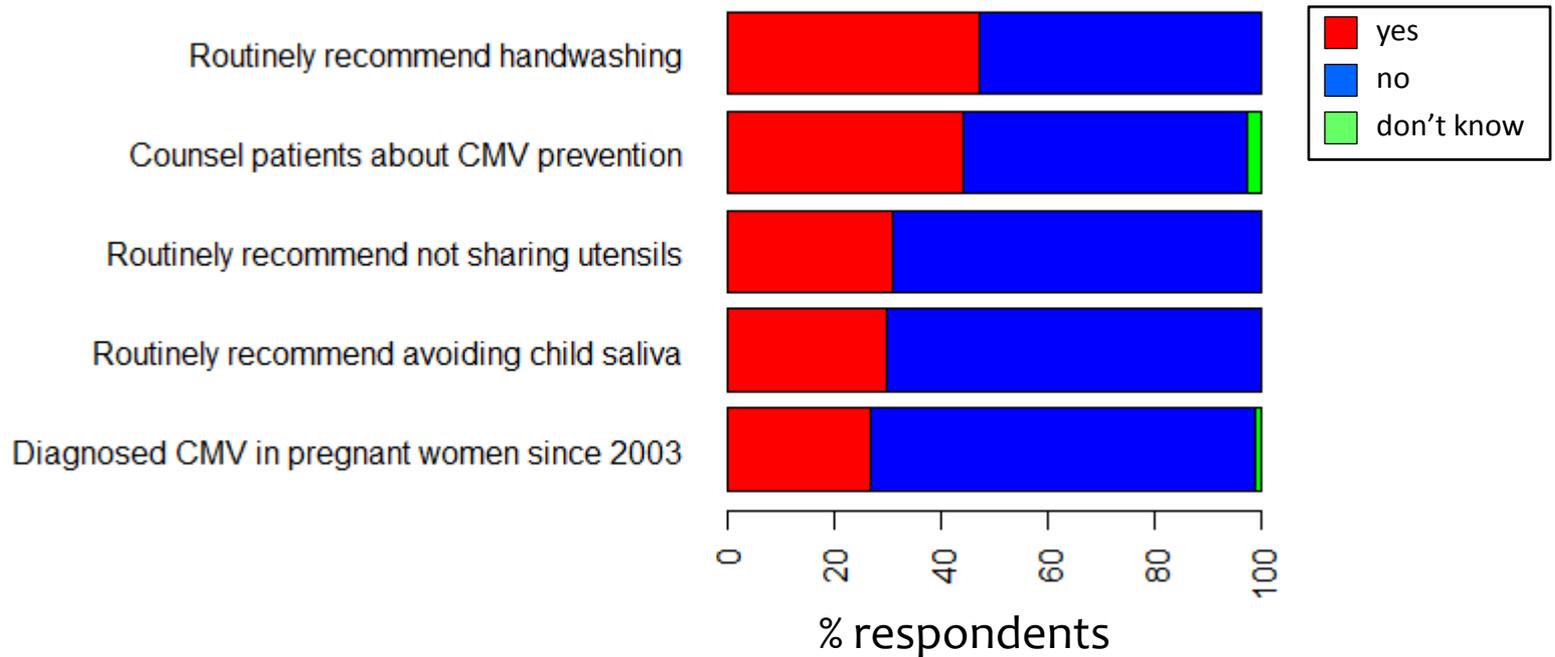
Self-reported* familiarity with actions that can reduce cCMV transmission



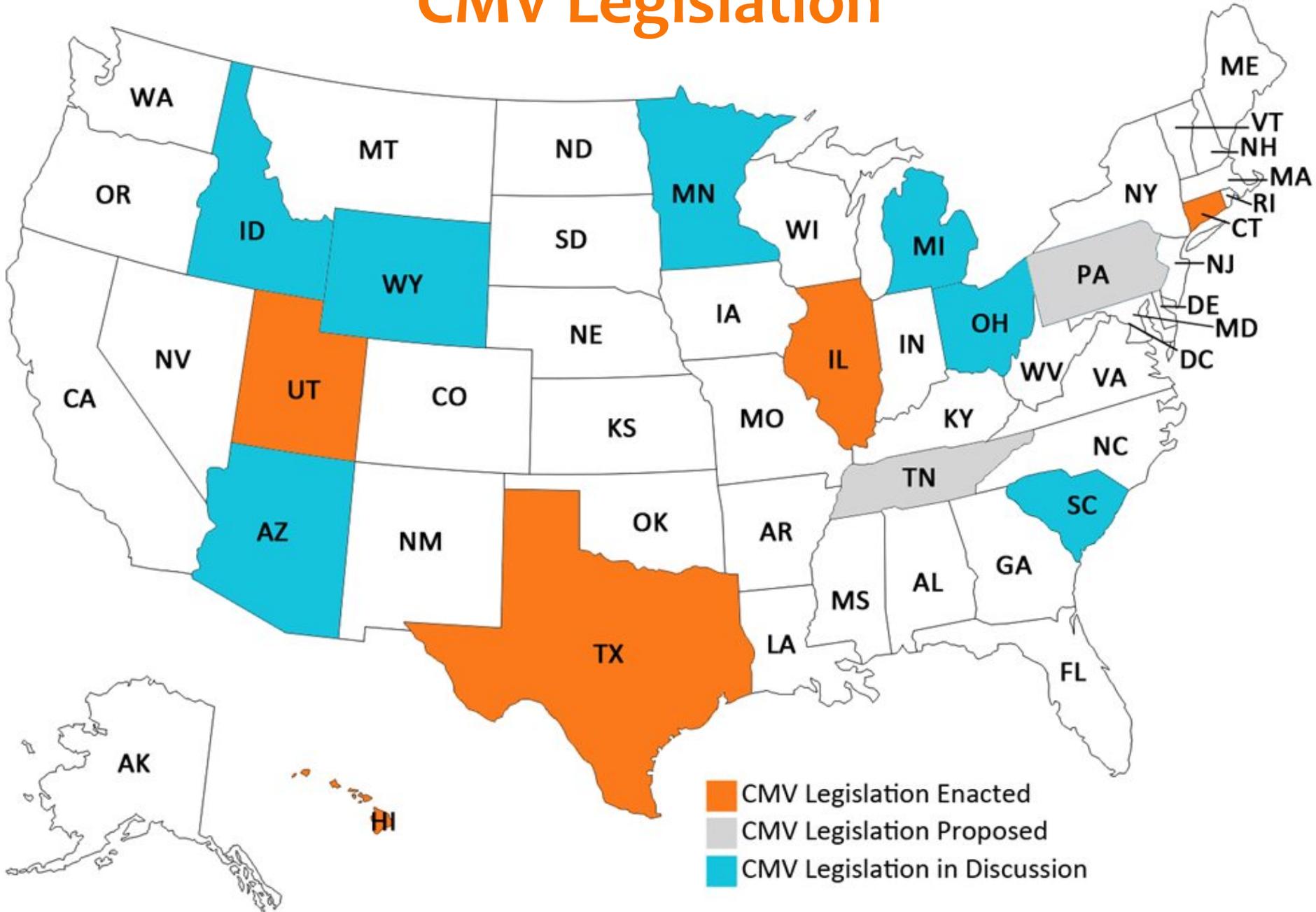
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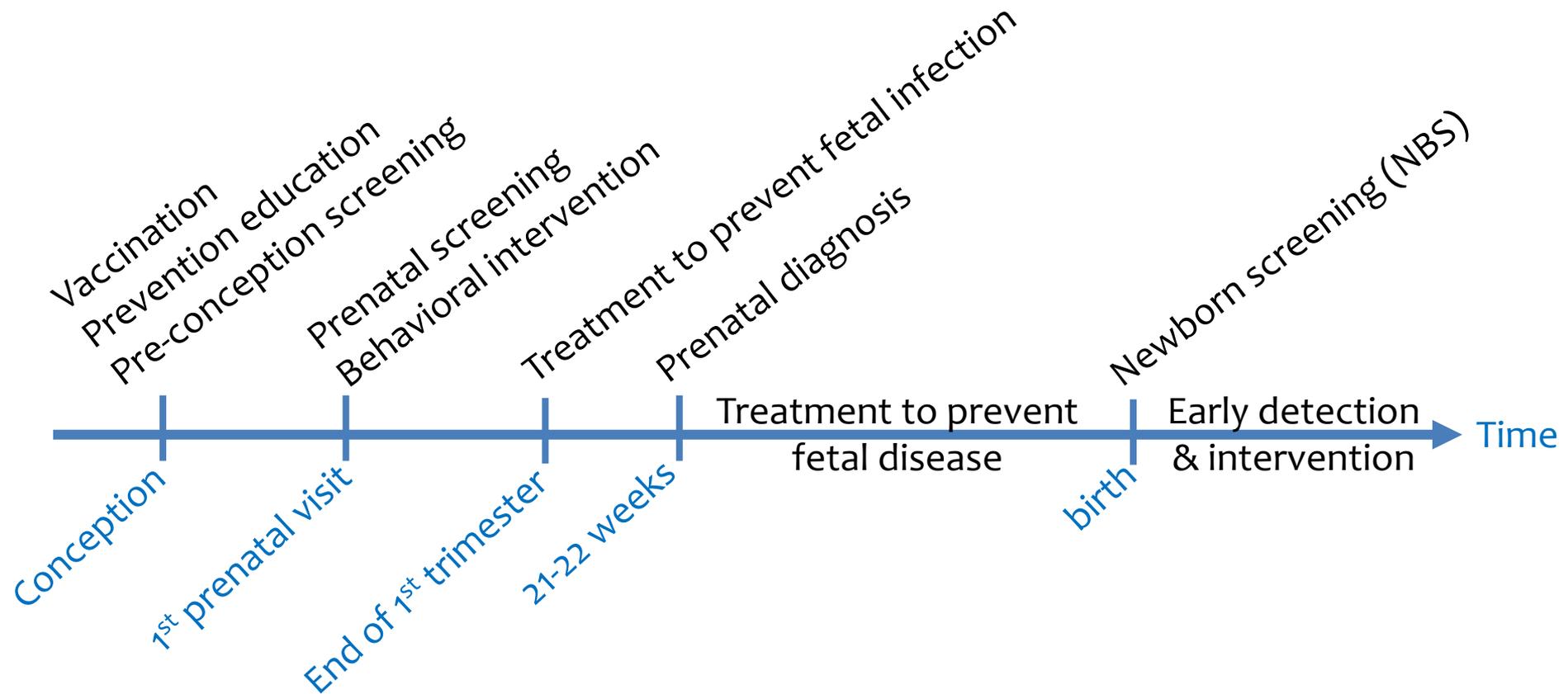
Self-reported* practices related to cCMV diagnosis and prevention



CMV Legislation

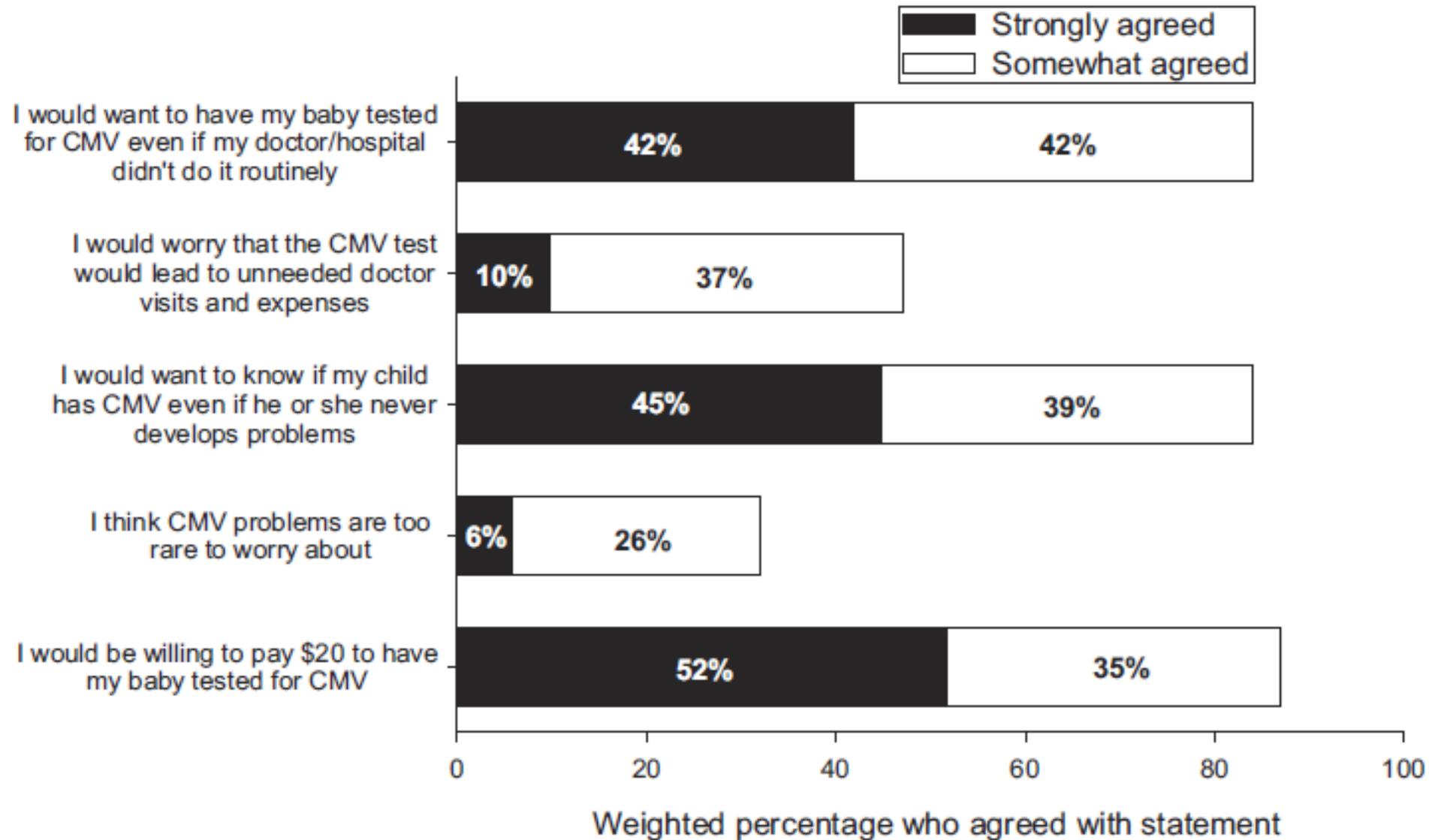


Potential Clinical and Public Health Interventions for cCMV



Currently, none of these interventions are routine in the US

Weighted responses to statements about newborn screening for CMV (Din, 2011)



Take Home Points

- **cCMV is RIPE for public health intervention!**
- cCMV transmission is **preventable** through behavioral interventions. It is spread primarily through contact with saliva and urine. Standard precautions virtually eliminates risk of transmission
- **disparities** indicate that interventions, such as vaccines or education campaigns, may need to be tailored to meet the needs of different ethnic and age groups, and women
- CMV is less easily transmitted than some other infections, such as rubella, but likely more easily transmitted than Zika
- relatively low force of infection means that modestly effective vaccines and rates of vaccination could significantly reduce CMV transmission
- **public health awareness strategies are effective in reducing risk of CMV transmission among at-risk groups**

Summary

1965: Rubella (German measles) makes the cover of Life Magazine to warn pregnant women about the damage that could occur to their unborn babies if the virus is contracted during their pregnancy. An estimated 20,000 babies/year would be affected by CRS. There was a massive media awareness campaign, culminating in the development of a vaccine a few years later.



2016: Cytomegalovirus (CMV) remains unknown to the majority of women of child-bearing age. An estimated 40,000 babies/year are affected by cCMV in the USA alone.

Women should be informed of practices that can reduce their risk of CMV infection during pregnancy.



Thank you

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kmuldo@midwestern.edu

