What are the Prenatal Implications of Congenital Cytomegalovirus for the Provider and Patient?

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Objectives

1

Understand the current role for testing the pregnant mother for cytomegalovirus (CMV).

2

Appreciate the recommended evaluation for the pregnant mother suspected to have CMV infection.

3

Entertain future directions to enhance the evaluation and treatment of the pregnant mother with CMV infection.

Clinical Case

Autumn:

- 32 years old at 15 weeks' gestation.
- She works in a daycare center and reports a possible recent CMV exposure 1 week ago.
- No fever, muscle aches.
- + Fatigue, occasional nausea

Evaluation:
Ultrasound: normal growth, no abnormalities

Bloodwork:
CMV IgG positive
CMV IgM positive

CMV IgG Avidity: Intermediate

Option: amniocentesis for CMV PCR
Wait 6-8 weeks

Diagnosis and evaluation in pregnancy

- Ultrasound
- Maternal antibodies
  - difficult to interpret
- Amniotic fluid CMV PCR
  - Confirms fetal infection, not long-term impact
- No validated tools to:
  - Predict cCMV
  - Predict impact of cCMV
  - Treat CMV before birth

TABLE
Ultrasound abnormalities from cases of confirmed congenital cytomegalovirus infection[12,20]

Ultrasound finding	Frequency, %
Cerebral calcifications	0.6–17.4
Microcephaly	14.5
Echogenic bowel	4.5–13
Fetal growth restriction	1.9–13
Subependymal cysts	11.6
Cerebral ventriculomegaly	4.5–11.6
Ascites	8.7
Pericardial effusion	7.2
Hyperechogenic kidneys	4.3
Hepatomegaly	4.3
Placentomegaly or placental calcifications	4.3
Hepatic calcifications	1.4
Hydrops	0.6

SMFM. Congenital CMV diagnosis and antenatal management. Am J Obstet Gynecol 2016.

ORIGINAL ARTICLE

A Trial of Hyperimmune Globulin to Prevent Congenital Cytomegalovirus Infection

Brenna L. Hughes, M.D., Rebecca G. Clifton, Ph.D., Dwight J. Rouse, M.D., George R. Saade, M.D., Mara J. Dinsmoor, M.D., M.P.H., Uma M. Reddy, M.D., Robert Pass, M.D., Donna Allard, R.N., Gail Mallett, R.N., Lida M. Fette, M.S., Cynthia Gyamfi-Bannerman, M.D., Michael W. Varner, M.D., et al., for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network*

- Randomized controlled trial (2021)
  - Hyperimmune globulin (concentrated anti-CMV antibodies) vs placebo
  - 17 U.S. centers (university, community, military) from 2012-2018
  - Primary outcome: cCMV or death

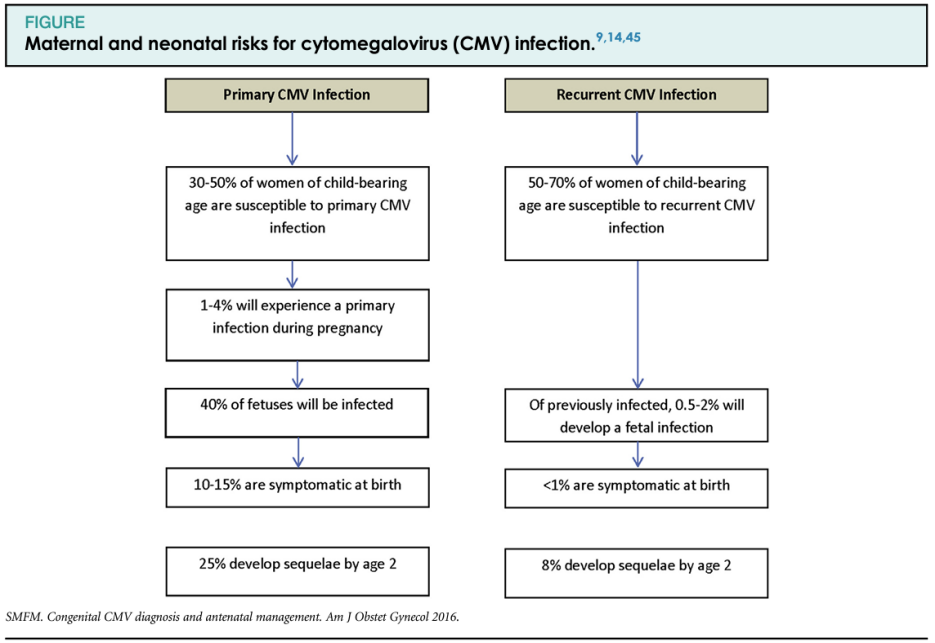
Results

- Treatment did not improve any measured outcome
- Tested 206,082 participants for primary CMV before 24 weeks
  - 713 (0.3%) tested positive for primary CMV
    - *12 (1.7%) had findings on ultrasound*
  - 399 were randomized

Clinical case:

Autumn:

Probability her fetus/child is impacted:



30-50% risk of susceptibility to primary CMV

→ *40% risk of fetal infection*

→ *25% risk of **any** clinical findings by age 2*

→ *total risk: 3-5%*

→*If we knew she were susceptible: 10%*

→*If we knew she is immune: <1%*

Diagnosis in Pregnancy: Summary

1. Available tests leave lots of uncertainty and are *slow*

2. When would I test for CMV during pregnancy?
   a) Specific ultrasound findings (brain/liver calcifications)
   b) Maternal exposure/request after discussion of pros/cons
   c) No proven prenatal treatments

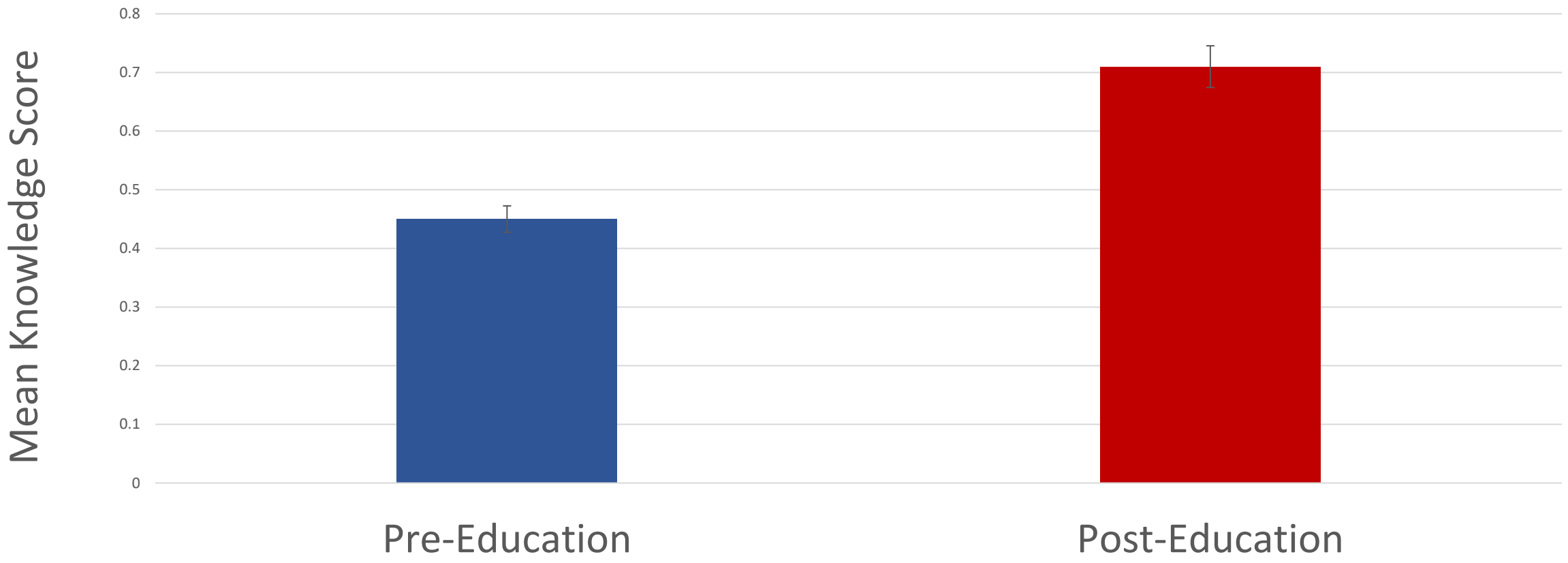
3. Does knowing pre-pregnancy status help?
   a) Not sure!
   b) Prevention guidelines apply to everyone

Prospective Study on Prenatal cCMV Education

Design:

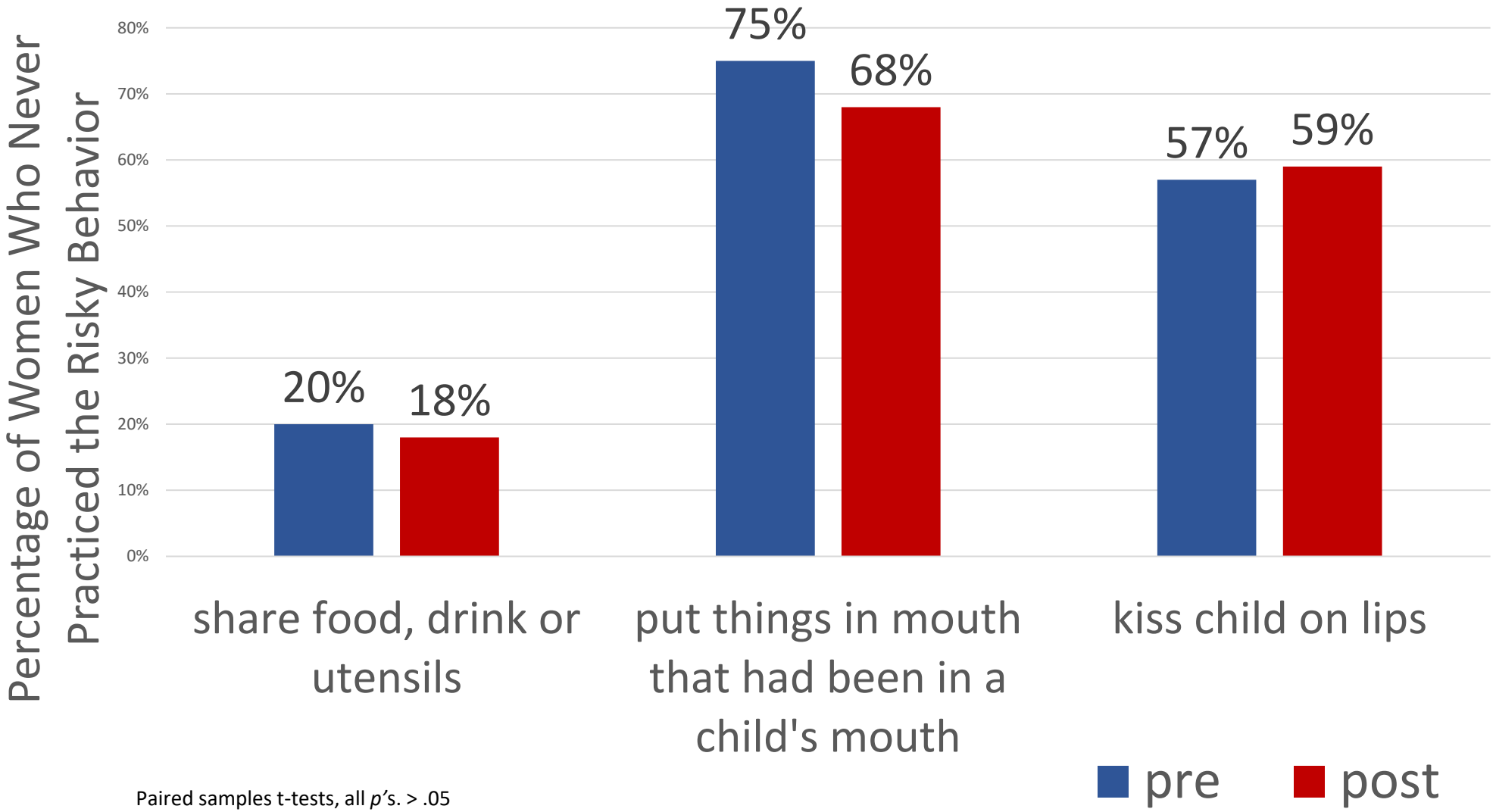
- 136 pregnant women received educational materials at first prenatal visit (8-10 weeks gestation)
- Randomized to Print or Video Materials
- Pre/Post Assessment of cCMV knowledge and behaviors

Knowledge of cCMV Improved after the Education



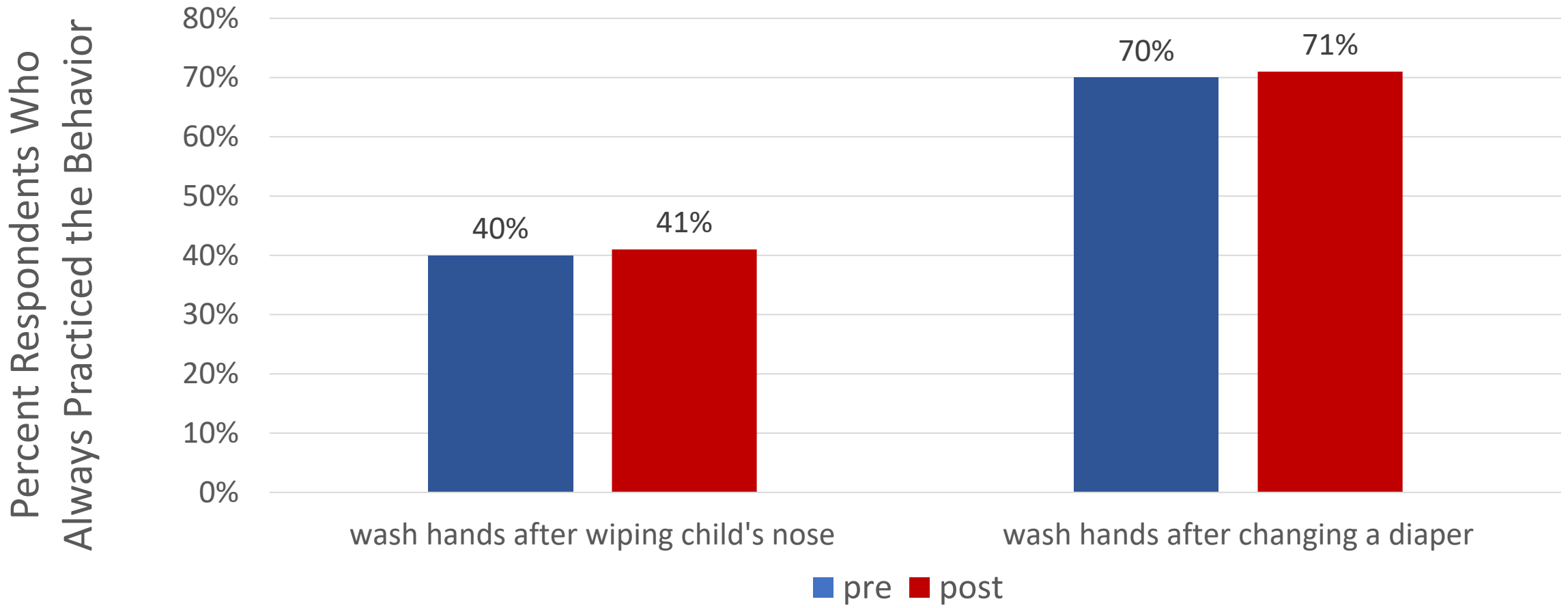
$t(105) = -7.69, p < .001$

Oral Exposure Behaviors Were Relatively Common



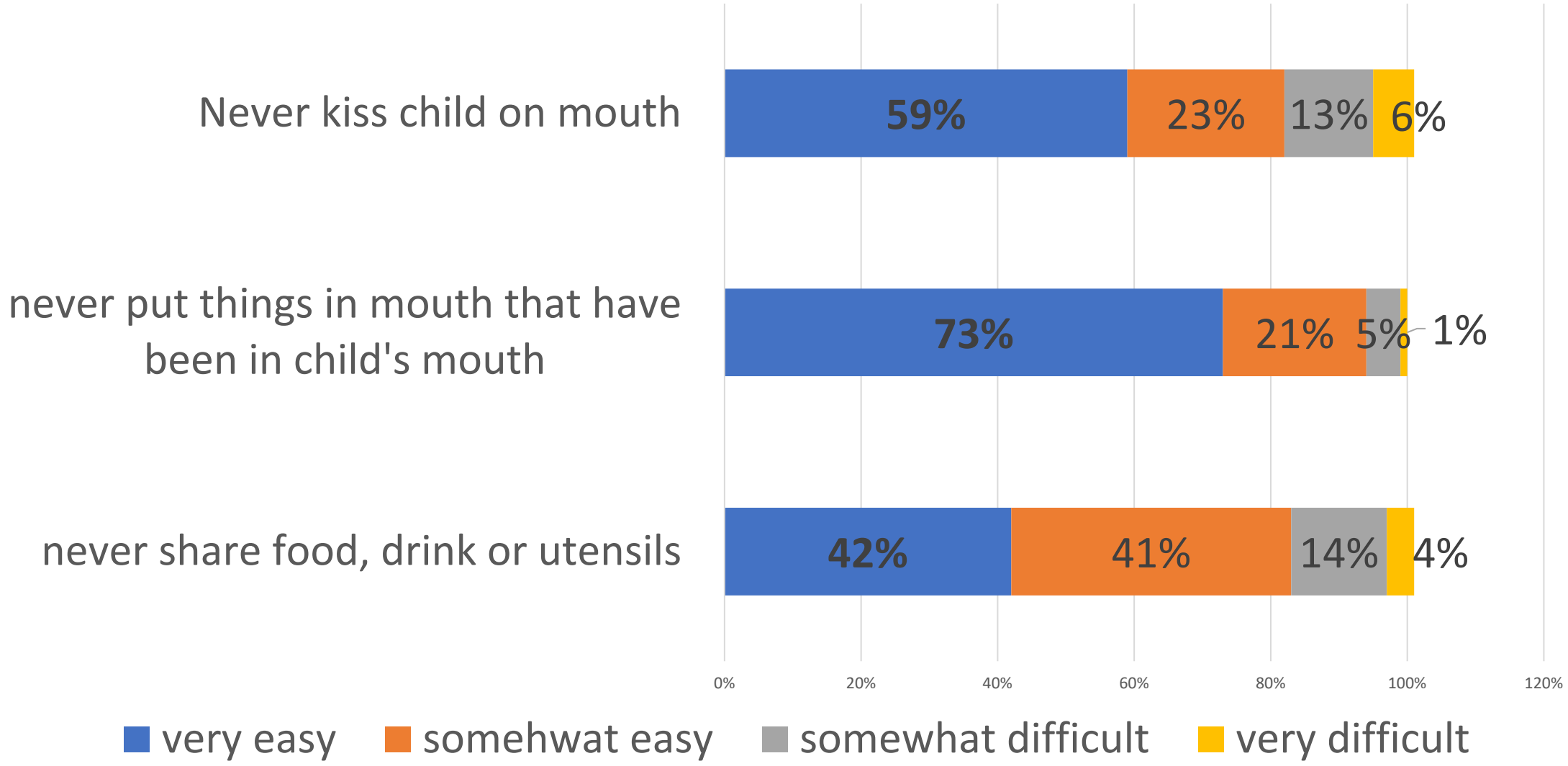
Paired samples t-tests, all *p*'s. > .05

Hygiene Behavior Did Not Change after Intervention

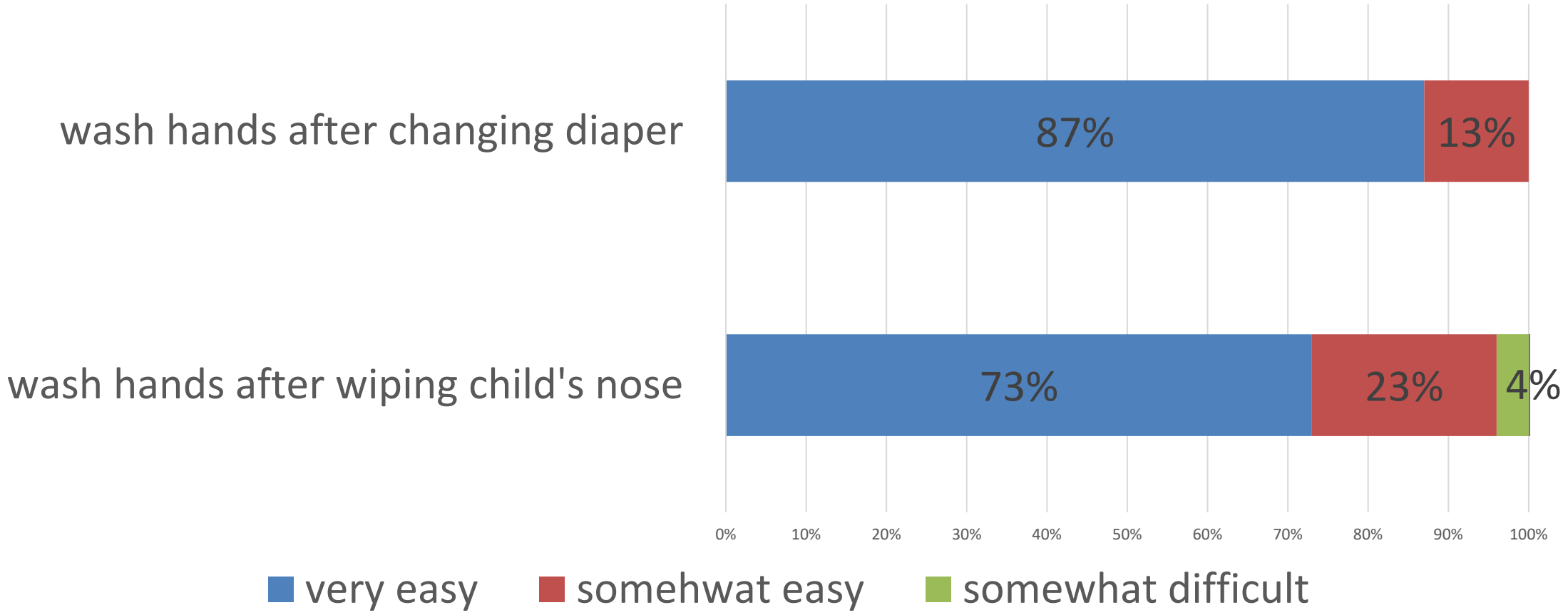


Paired samples t-tests, all *p*'s. > .05

Ease of Avoiding Oral Exposures



Ease of Implementing Hygiene Behaviors



Prenatal Education in Practice

Feasible to provide education in prenatal setting

Improves cCMV knowledge

Current education was limited in changing behavior

Discussion of Challenges

- Education needed around many congenital conditions
- Difficulty implementing some of these behaviors
- Fatigue around what can go wrong