RSV: should I take the shot in pregnancy or give my baby the monoclonal antibodies?

Elizabeth Mumper

MD, IFMCP, FMAPS

Respiratory Syncytial Virus

- By age two, 97% of babies have been infected with RSV
- Infants present with rapid breathing, copious nasal secretions, and cough
- Most babies recover in about a week; some will develop a chronic cough
- Occasionally babies get a severe infection, especially in their first three to six months

    Paul Thomas: no RSV deaths in 40-year career

    Liz Mumper: no RSV deaths in 42-year career

The vast majority of babies survive RSV

LOTS OF OUTPATIENT MANAGEMENT

- According to the CDC about 17 babies die from RSV each year in the US
- Based on twelve years of death certificate data reviewed by CDC (2005-2016)

INTERACTIVE DASHBOARD:

CAN FOLLOW BY AGE

RESEARCH ARTICLE

Health Science Reports Open Access WILEY

Respiratory syncytial virus-associated deaths in the United States according to death certificate data, 2005 to 2016

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Abstract

Background and Aims: In the United States, respiratory infections due to respiratory

RSV infant mortality

17 deaths per year

3,664,292 babies born in US in 2021

- RSV hospitalizations
- Between 58,000 and 80,000 in US per year

Respiratory Syncytial Virus Hospitalization Surveillance Network (RSV-NET)| CDC

Older children and adults experience RSV as a URI = "cold"

COPIOUS NASAL SECRETIONS

ONE OF MANY URI VIRUSES

If we could make a vaccine for every strain of upper respiratory infections, should we?

Meryl Nass, MD, compiled a list of new and "exciting" therapies for RSV in the wake of the COVID crisis

Suddenly a multitude of RSV products have sprouted

An *old* monoclonal antibody given monthly to high risk, chronically ill babies (palivizumab by Medimmune)

A new monoclonal antibody to be given to all babies up to 8 months of age [redacted] (nirsevimab=Beyfortus by Sanofi)

A vaccine for pregnant women intended to protect their newborns is pending FDA approval (the expert advisors approved it in May, then did FDA get cold feet?) Pfizer

Two vaccines for elders to protect (briefly) against RSV-licensed in May (Arexvy by GSK and Abrysvo by Pfizer)

Another vaccine for elders awaiting licensure for RSV (mRNA 1345 by Moderna)

Goal to give new monoclonal antibody to ALL babies
Called an immunization but is NOT a vaccine

- Nirsevimab = Beyfortus by Sanofi
- Price:

  $395/dose to CDC $495/dose to insurers

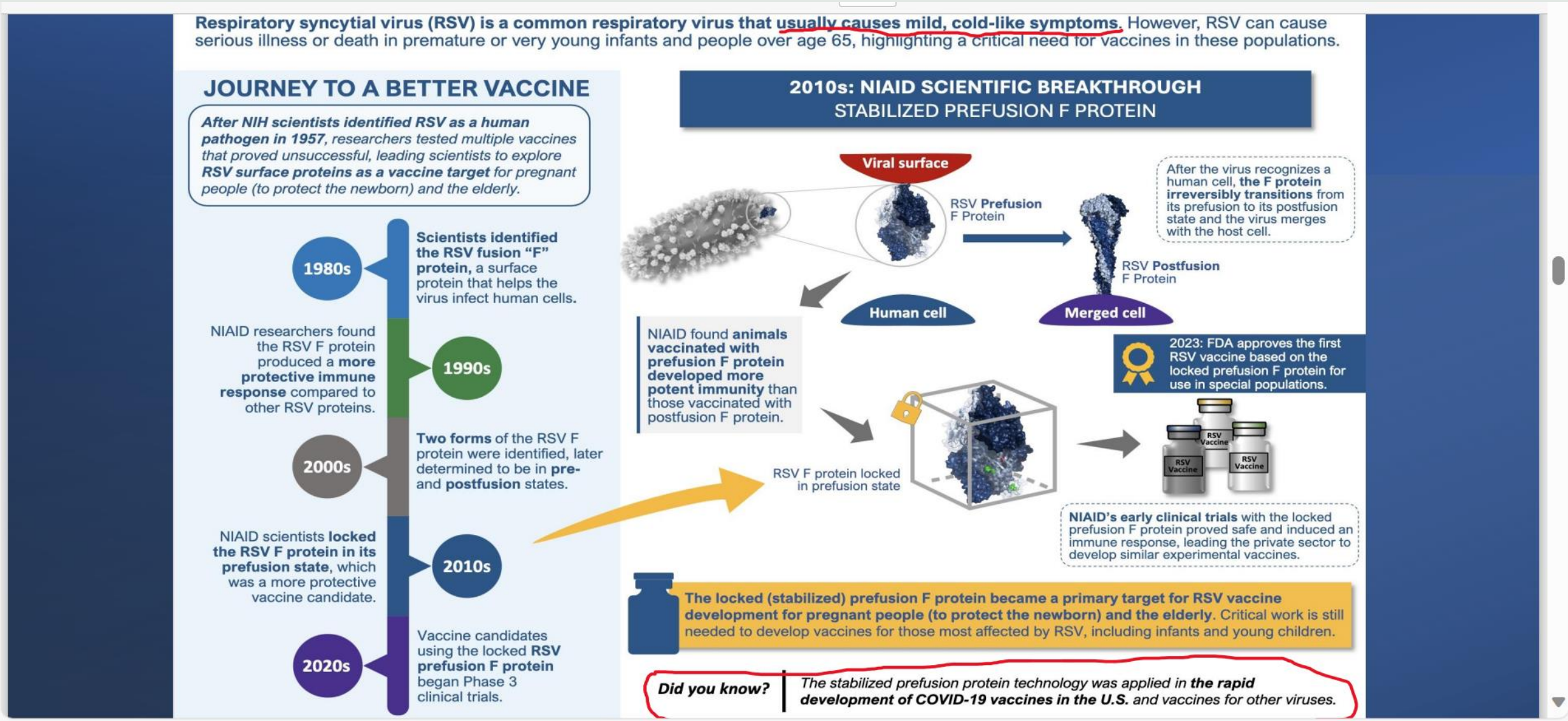
- No good evidence it saves lives
- Only side effects reported: rashes and anaphylaxis

Contraindication = anaphylaxis (newborn history)

Monoclonal antibodies in babies

- Never given as mass preventative intervention before
- Already have RSV strains that are resistant to the antibodies
- Ads from CDC promoting monoclonal antibodies on day of birth started August 3, 2023

https://www.niaid.nih.gov/disease-conditions/respiratory-syncytial-virus-rsv



RSV vaccines: A new gold rush?

NIAID employees who developed the product eligible for $150,000 per year in royalties on top of NIH salaries

- NIAID research center developed the antigen for RSV vaccines
- Licensed for commercial companies to use

The process for RSV vaccines

NIAID makes antigen

FDA approves

CDC markets to pregnant women

https://www.cell.com/action/showPdf?pii=S1931-3128%2822%2900572-8

Rethinking next-generation vaccines for coronaviruses, influenzaviruses, and other respiratory viruses

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"**Past unsuccessful attempts** to elicit solid protection against mucosal respiratory viruses and to control the deadly outbreaks and pandemics they cause **have been a scientific and public health failure** that must be urgently addressed. We are excited and invigorated that many investigators and collaborative groups are rethinking, from the ground up, all of our past assumptions and approaches to preventing important respiratory viral diseases and working to find bold new paths forward."

RSV vaccines in development for >50 years

2 infants died in small trials previously

https://www.bmj.com/content/381/bmj.p1021

- GSK and Pfizer's RSV vaccines nearly identical.
- Prefusion-stabilized antigen RSV vaccine (not based on mRNA technology)
- **Both vaccines, when given to pregnant mothers, cause an increase in premature births and infant deaths.**
- NIAID developed the technology.

Glaxo-Smith-Kline withdrew application for approval

- 3496 babies in trial
- 238 born preterm = 6.8%

  4.9% preterm infants in placebo group
- 13 deaths in vaccine group (due to prematurity complications)

  3 deaths in placebo group

  increased risk of death: >4 to 1

Pfizer trial RSV vaccine in pregnancy – ultimately approved

- Deaths in placebo versus vaccine group not reported (said small numbers)
- Rate of prematurity

    3 of 116 in placebo group = 2.6%

    6 of 114 in vaccine group = 5.3%

Recommended at 32-36 weeks of pregnancy

Hospitalization with respiratory syncytial virus

$300 million per year in US

~70,000 babies per year in US

- Pfizer vaccine claims to prevent 57% of severe illness and hospitalization
- “no safety concerns”

Fun with math: create 9,893 premies for every RSV death saved?

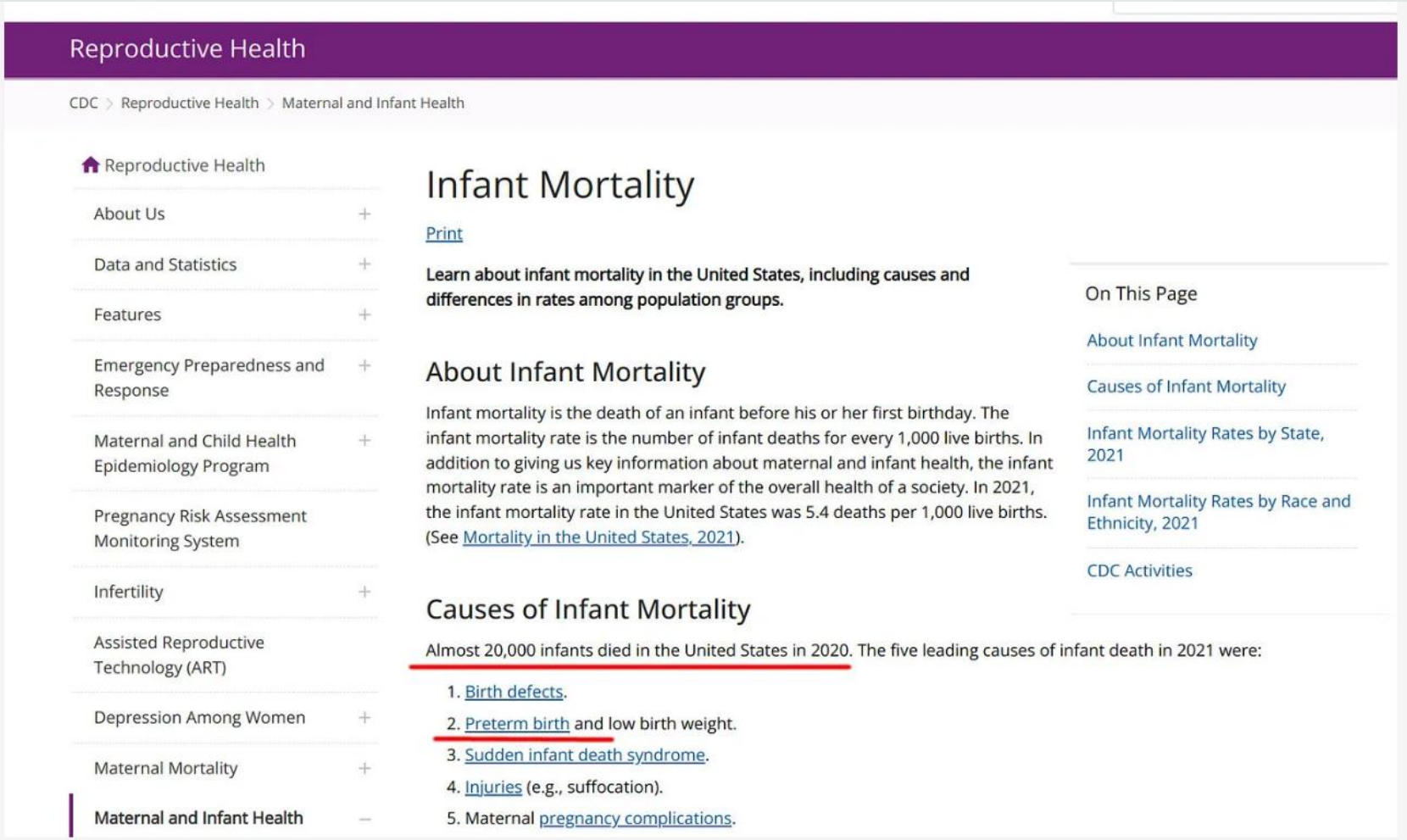
- If Pfizer vaccine increases preterm birth by 2%
- => 73,285 extra premies/year using the GSK rates
- If Pfizer vaccine increased preterm birth by 2.7%
- => 98,935 more premies/year using Pfizer rates

- If Pfizer vaccine prevents 57% of hospitalizations => 33,000 – 45,000 fewer
- If Pfizer vaccine prevents 57% of deaths=> prevent 10 deaths a year

    instead of 17 deaths would have 7 deaths

    we do not know their death data (or I cannot find it)

Pfizer's RSV Vaccine Math: Kill 4,000 Newborns to Save 300 from RSV (igor-chudov.com)



Reproductive Health

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Infant Mortality

Print

Learn about infant mortality in the United States, including causes and differences in rates among population groups.

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About Infant Mortality

Infant mortality is the death of an infant before his or her first birthday. The infant mortality rate is the number of infant deaths for every 1,000 live births. In addition to giving us key information about maternal and infant health, the infant mortality rate is an important marker of the overall health of a society. In 2021, the infant mortality rate in the United States was 5.4 deaths per 1,000 live births. (See Mortality in the United States, 2021).

Causes of Infant Mortality

Almost 20,000 infants died in the United States in 2020. The five leading causes of infant death in 2021 were:

1. Birth defects.
2. Preterm birth and low birth weight.
3. Sudden infant death syndrome.
4. Injuries (e.g., suffocation).
5. Maternal pregnancy complications.

https://www.cdc.gov/reproductivehealth/maternalinfanthealth/infantmortality.htm

Maternal RSV vaccine: Further analysis is urged on preterm births

BMJ 2023 ; 381 doi: https://doi.org/10.1136/bmj.p1021 (Published 10 May 2023)
Cite this as: *BMJ* 2023;381:p1021

Linked Editorial
Preventing respiratory syncytial virus bronchiolitis in infants

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Hristio Boytchev

Author affiliations

A "safety signal" in a similar respiratory syncytial virus (RSV) vaccine has led to trials being stopped and prompted calls for a cautious approach to using the vaccine in pregnant women, reports **Hristio Boytchev**

Experts have called for further analysis of trial data and post-approval monitoring of Pfizer's maternal RSV vaccine candidate after GSK's trials of a similar product were halted over a rise in preterm births and neonatal deaths.

Mumper recommendations

- These are new products with small trials and unknown data
- Just because something exists does not mean you have to use it
- We do not have favorable risk versus benefit data for the monoclonal antibodies or the RSV vaccine in pregnancy
- Pregnancy should be a time of careful interventions which have stood the test of time