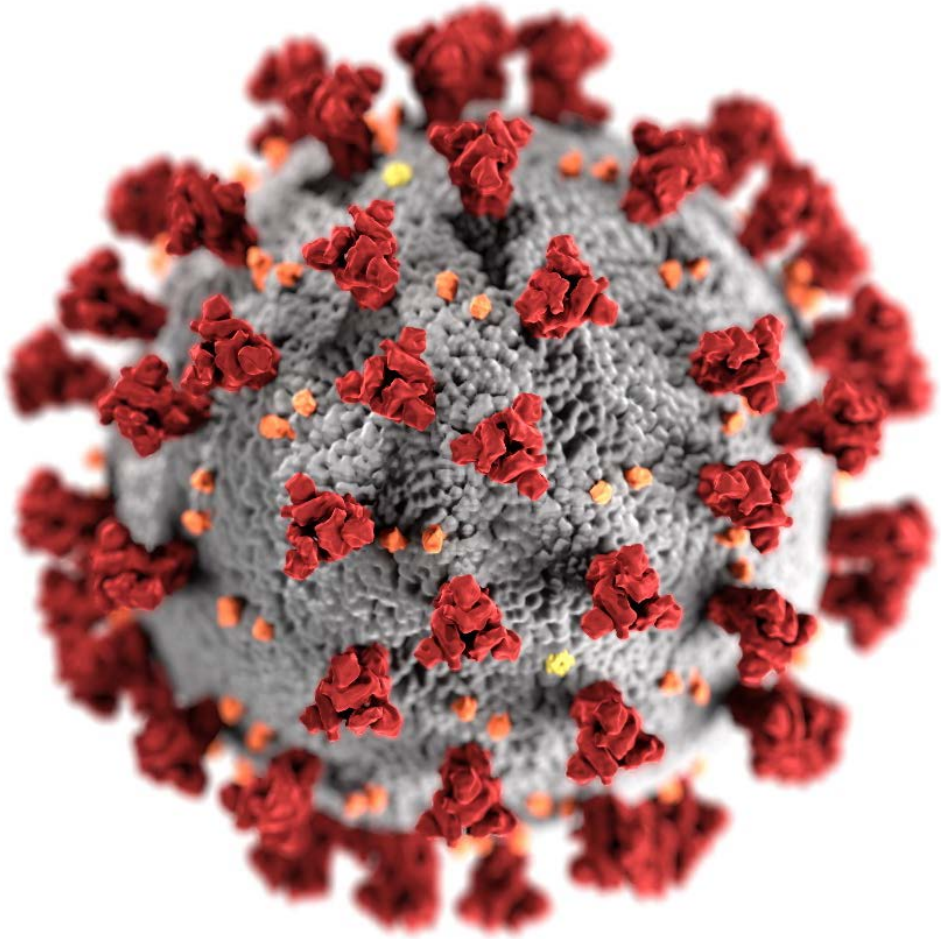
Updates to COVID-19 Immunity and Epidemiology to Inform Vaccine Policy



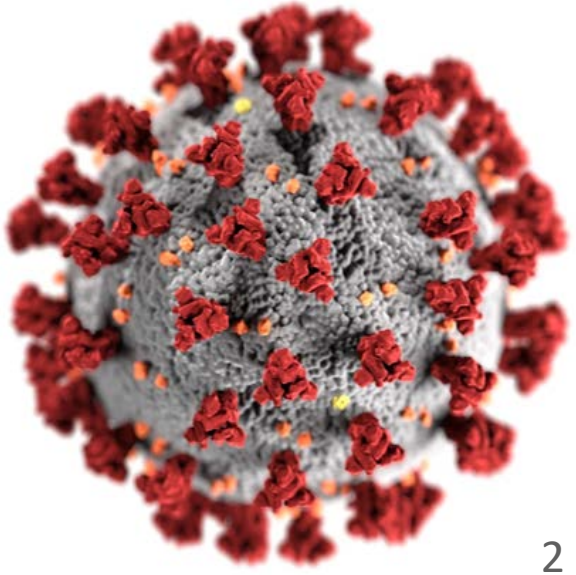
Megan Wallace, DrPH, MPH

ACIP Meeting
October 30, 2020

For more information: **www.cdc.gov/COVID19**

Outline

- Overview of U.S. COVID-19 epidemiology
- COVID-19 post-infection immunity
- COVID-19 reinfection
- Epidemiology of COVID-19 in pregnant women



Overview of U.S. COVID-19 Epidemiology

United States COVID-19 Cases by County

January 22 to October 29, 2020

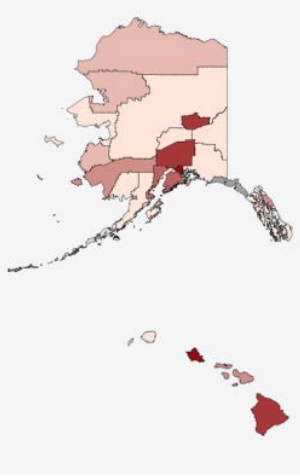
USA

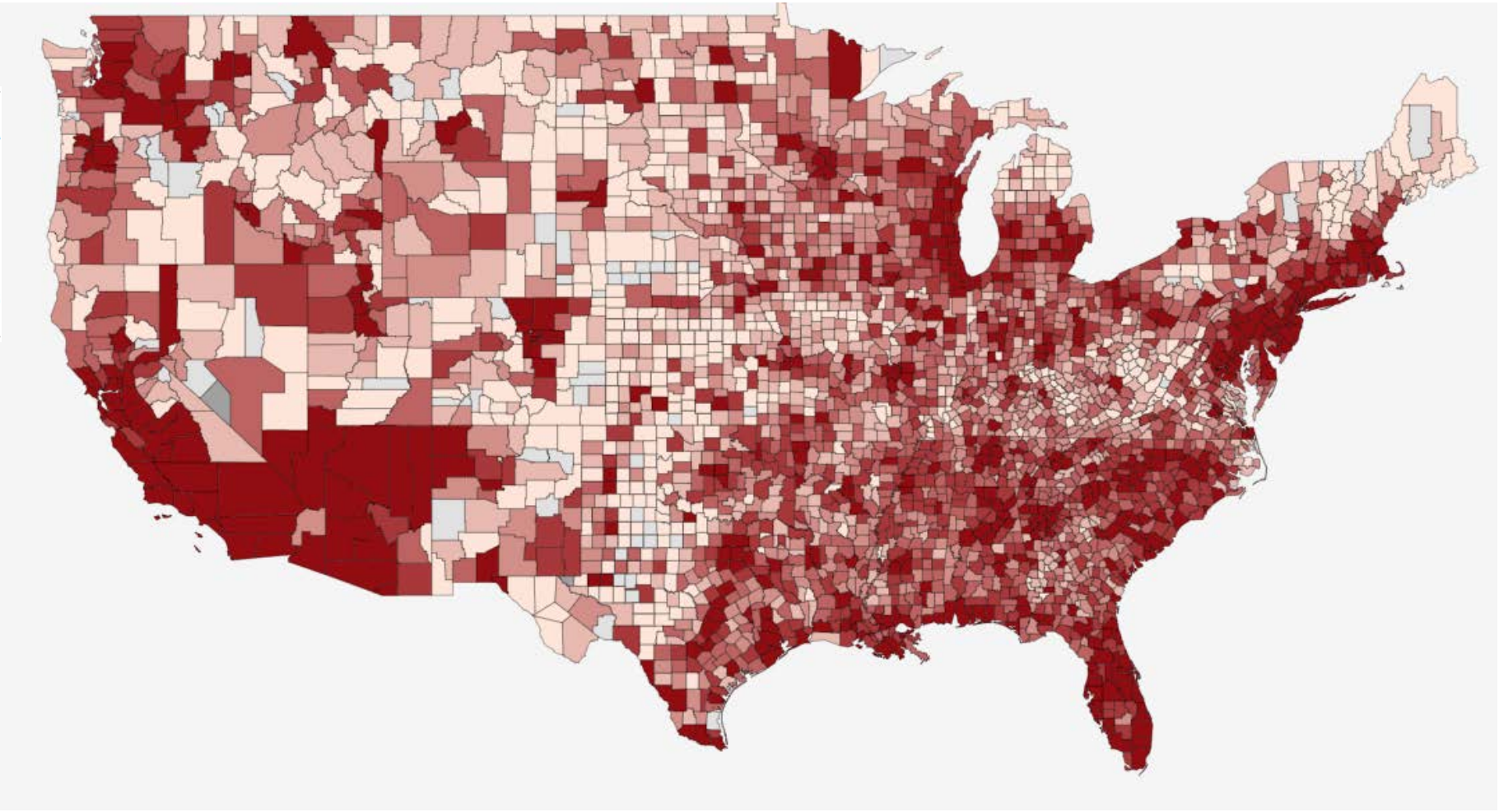
8,834,393

TOTAL CASES

+81,599 New Cases

CDC | Updated: Oct 29 2020 12:47PM

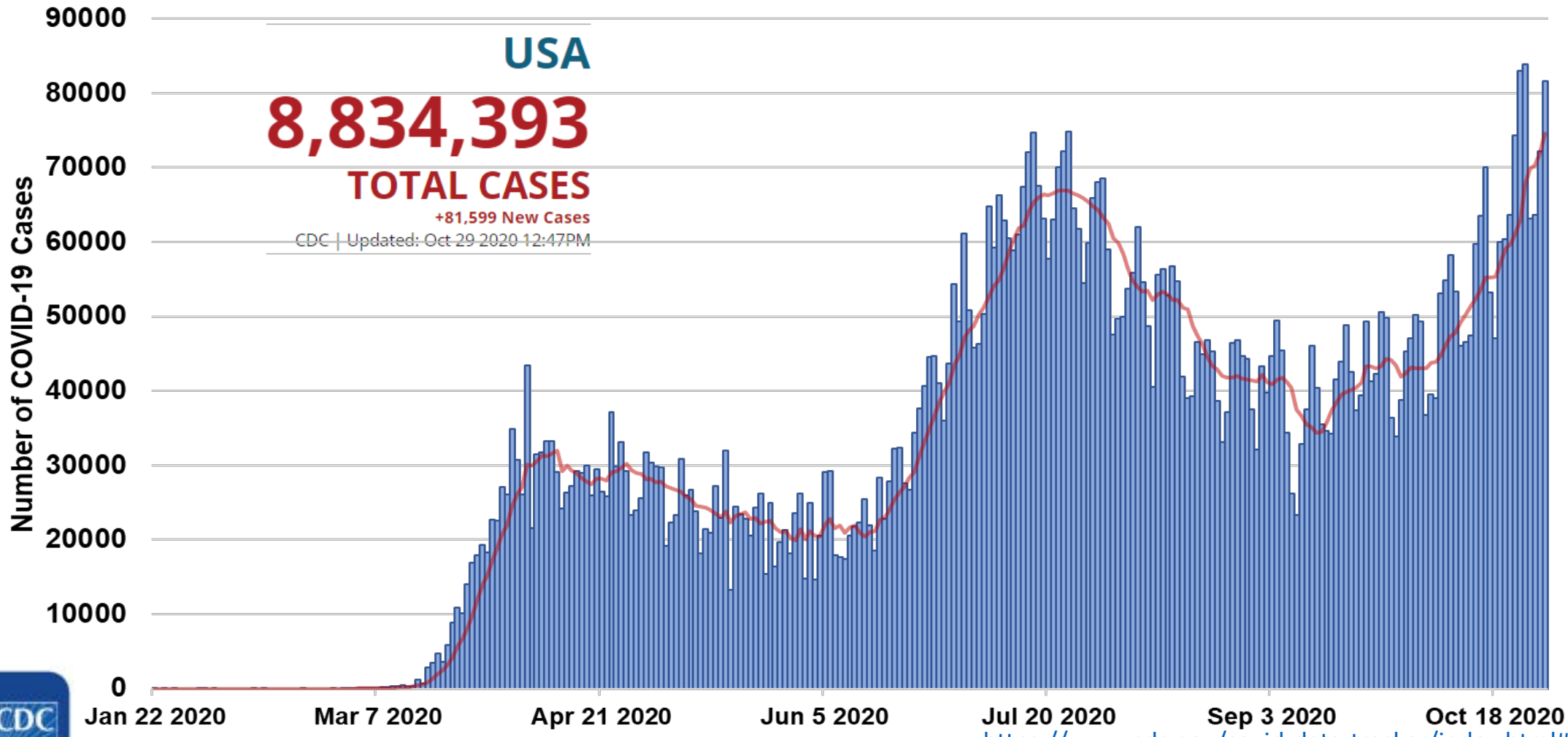




https://www.cdc.gov/covid-data-tracker/index.html

Trends in Number of COVID-19 Cases in the US

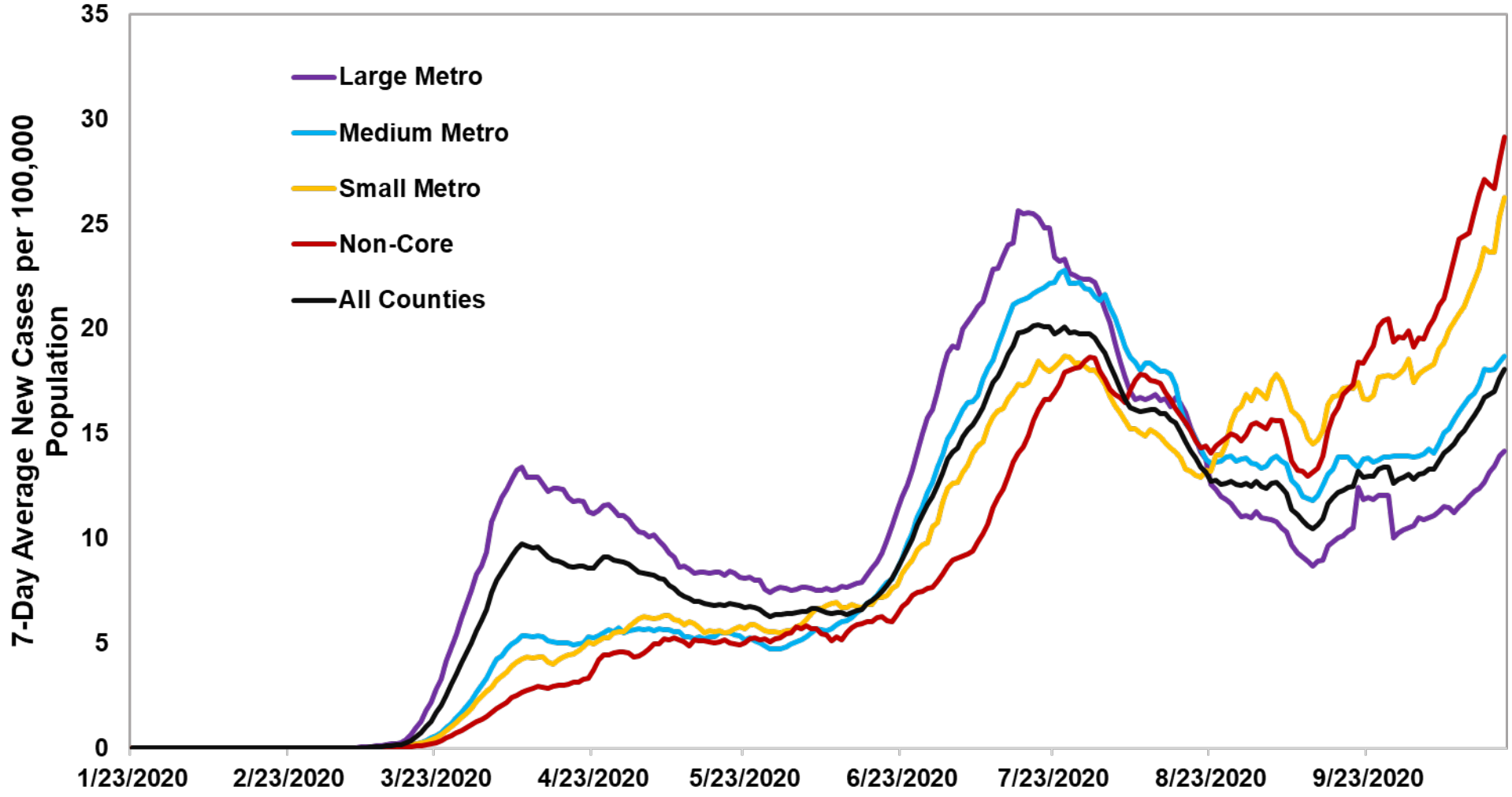
January 22 to October 29, 2020



https://www.cdc.gov/covid-data-tracker/index.html#trends

Trends in COVID-19 Case Rate by Urban/Rural Classification

January 22 to October 20, 2020

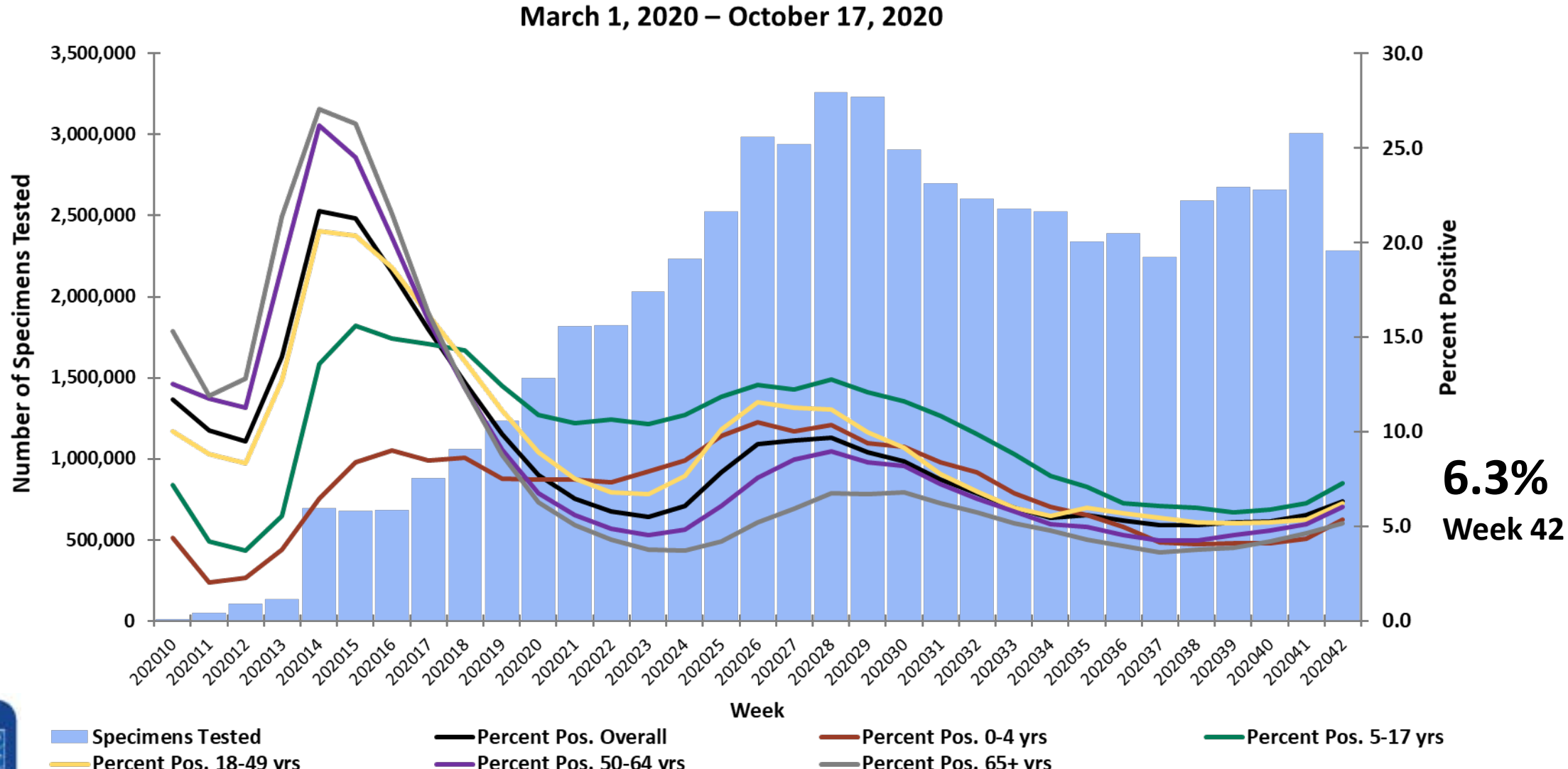


*Non-core counties are nonmetropolitan counties that are not in a micropolitan statistical area and may be thought of as the most rural areas. .

https://www.cdc.gov/covid-data-tracker/index.html#trends

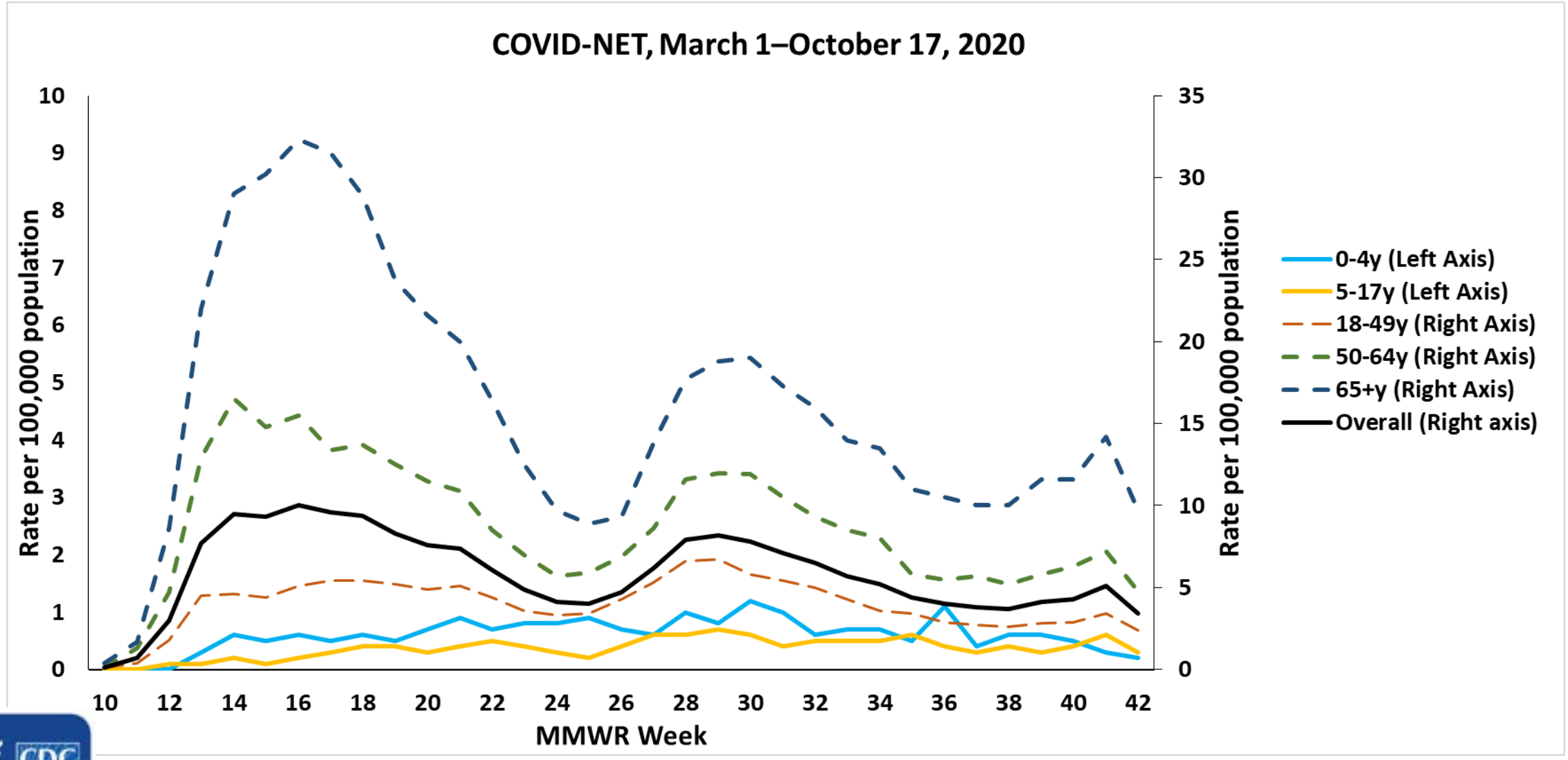
Number of Specimens Tested and Percent Positive for SARS-CoV-2:

Combined Laboratories Reporting to CDC



https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html

Weekly COVID-19-associated Hospitalization Rates by Age Group



https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html

United States COVID-19 Deaths by County

January 22 to October 29, 2020

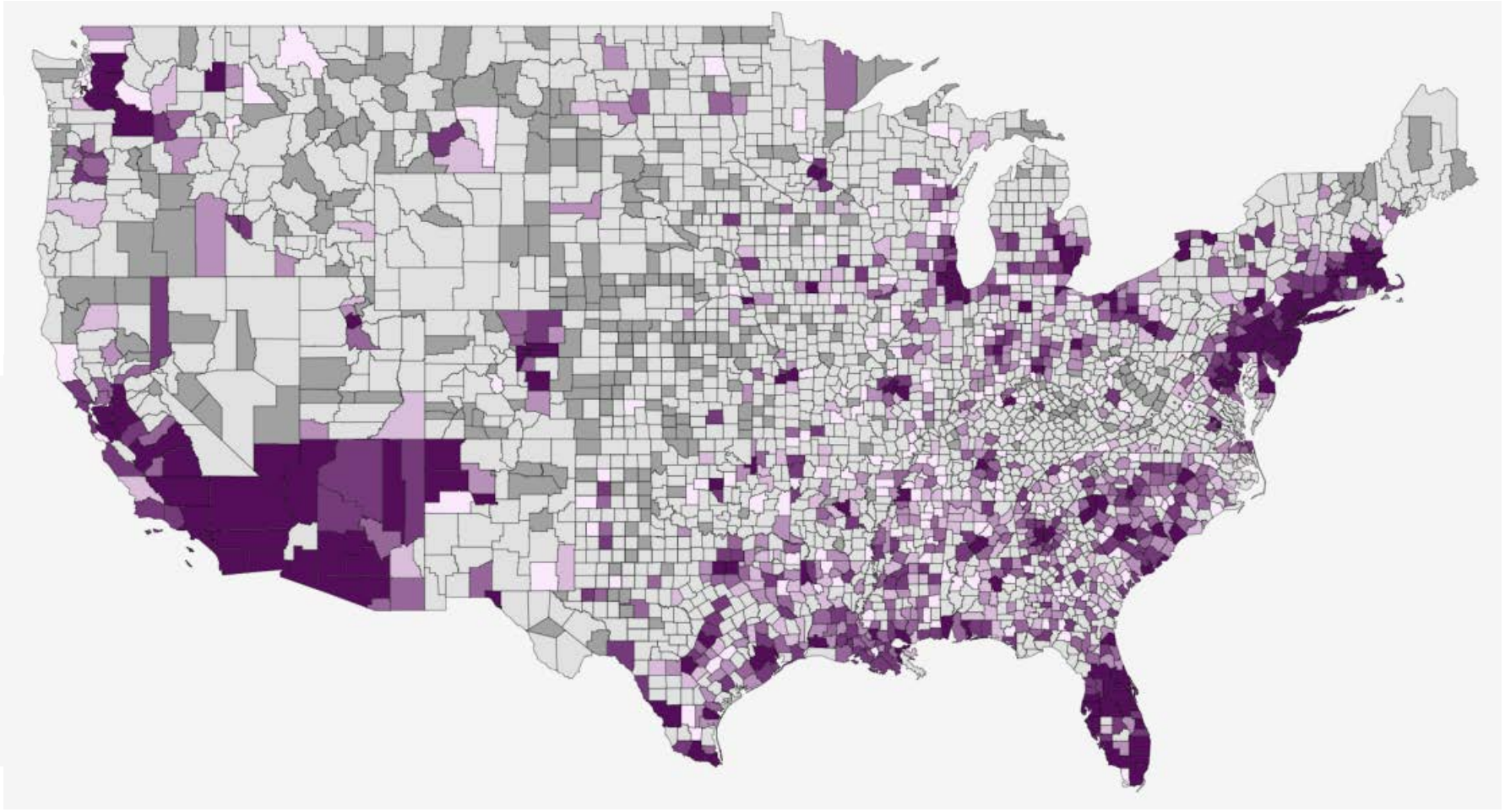
USA

227,045

TOTAL DEATHS

+1,060 New Deaths

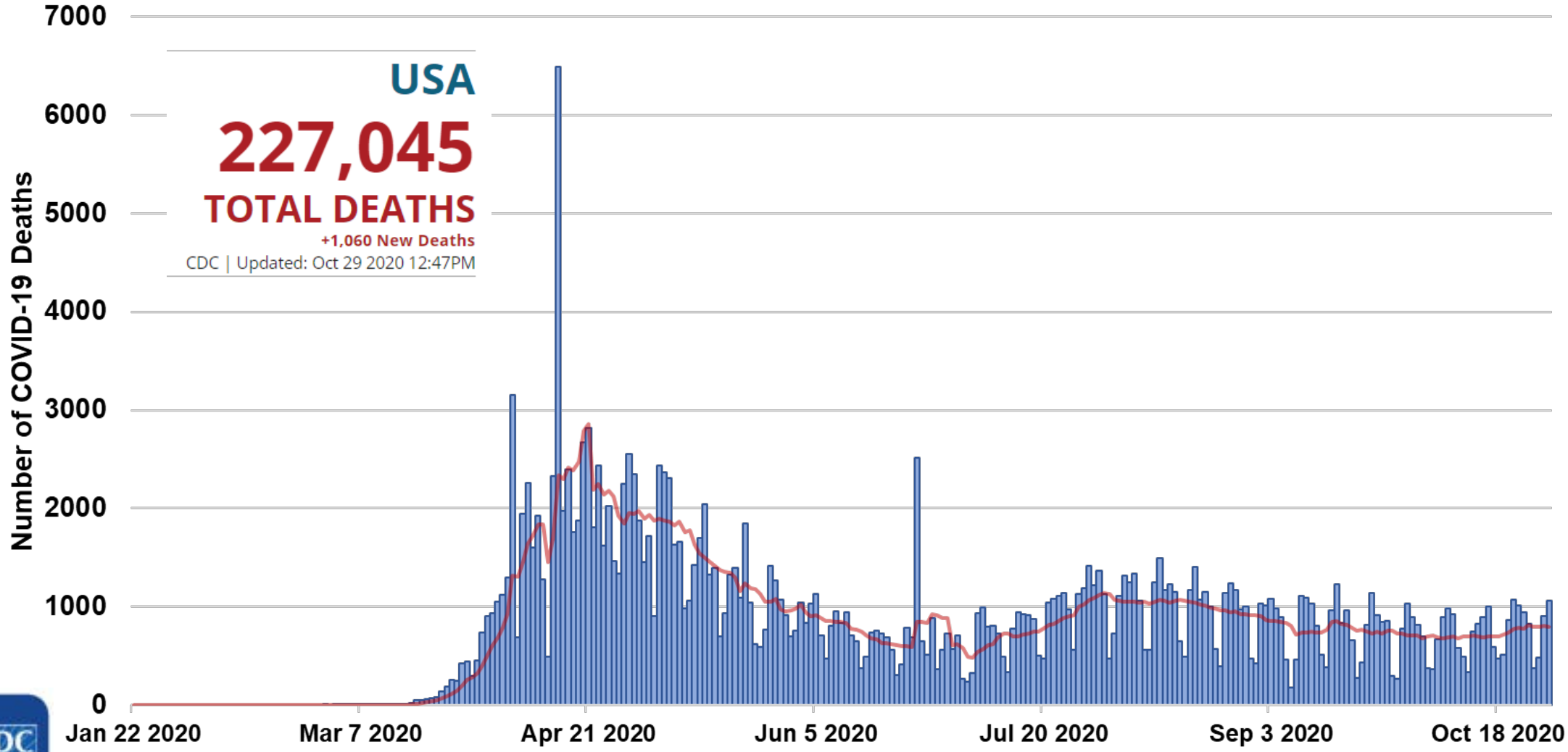
CDC | Updated: Oct 29 2020 12:47PM



https://www.cdc.gov/covid-data-tracker/index.html

Trends in Number of COVID-19 Deaths in the US

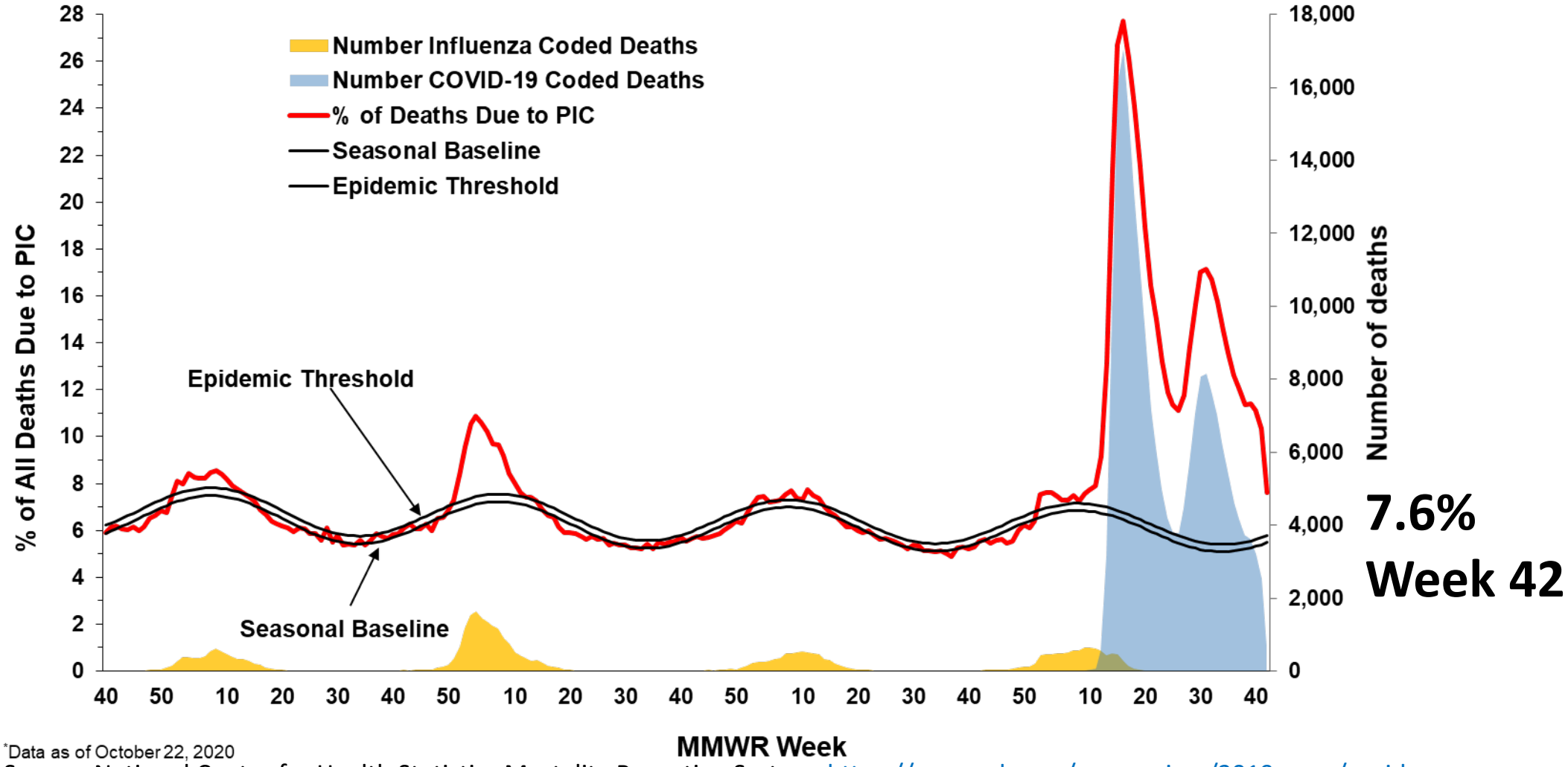
January 22 to October 29, 2020



https://www.cdc.gov/covid-data-tracker/index.html#trends

Trends in Pneumonia, Influenza and COVID-19 Mortality

Data through the week ending October 17, 2020



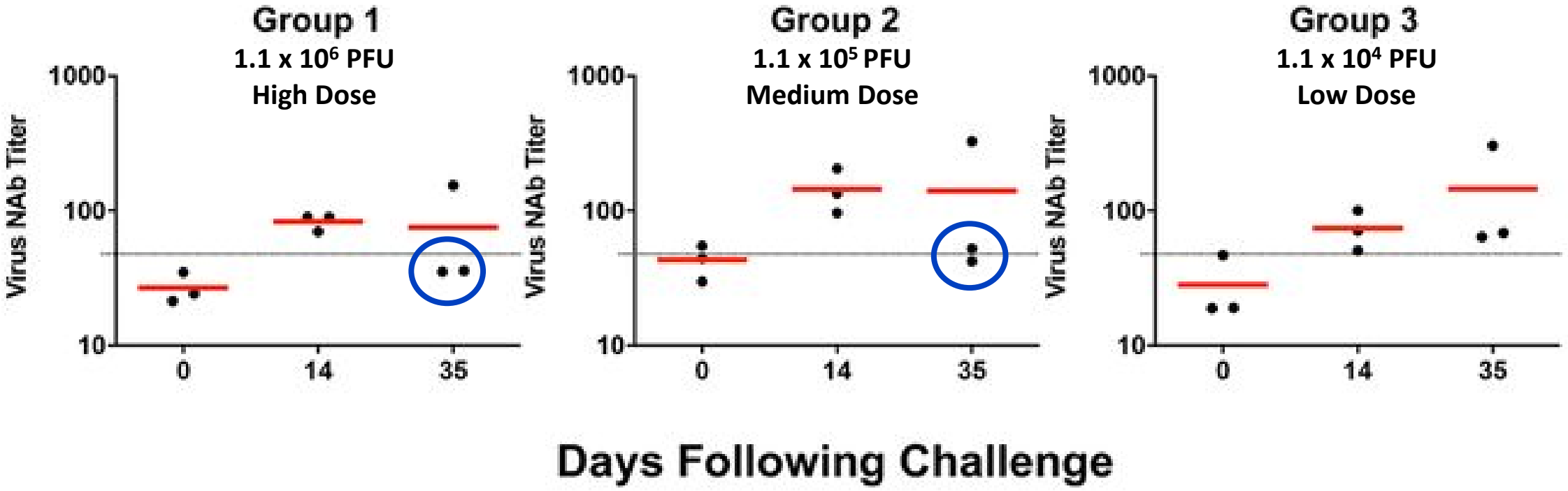
*Data as of October 22, 2020

Source: National Center for Health Statistics Mortality Reporting System: https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html

COVID-19 Post-infection Immunity

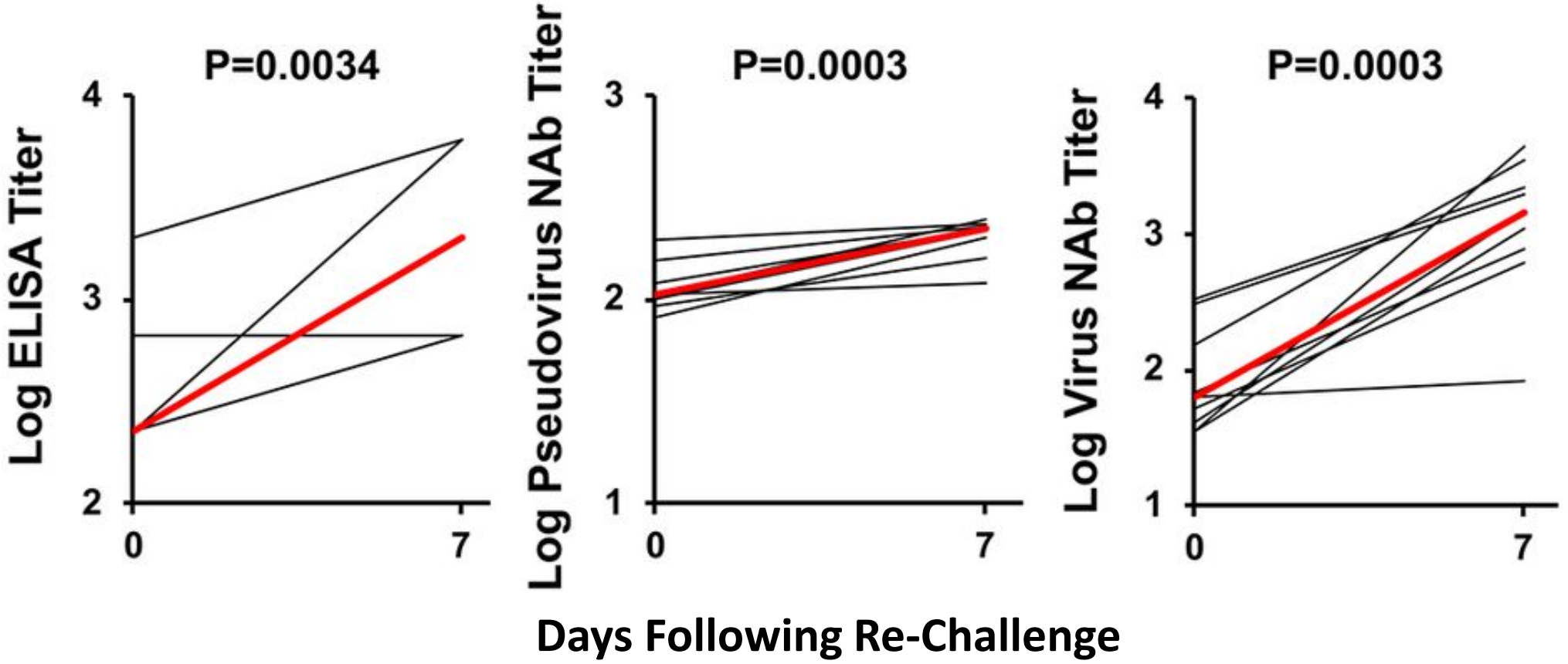
What happens to anti-SARS-CoV-2 antibodies after infection?

Rhesus macaques challenged with SARS-CoV-2 developed binding and neutralizing antibody responses.



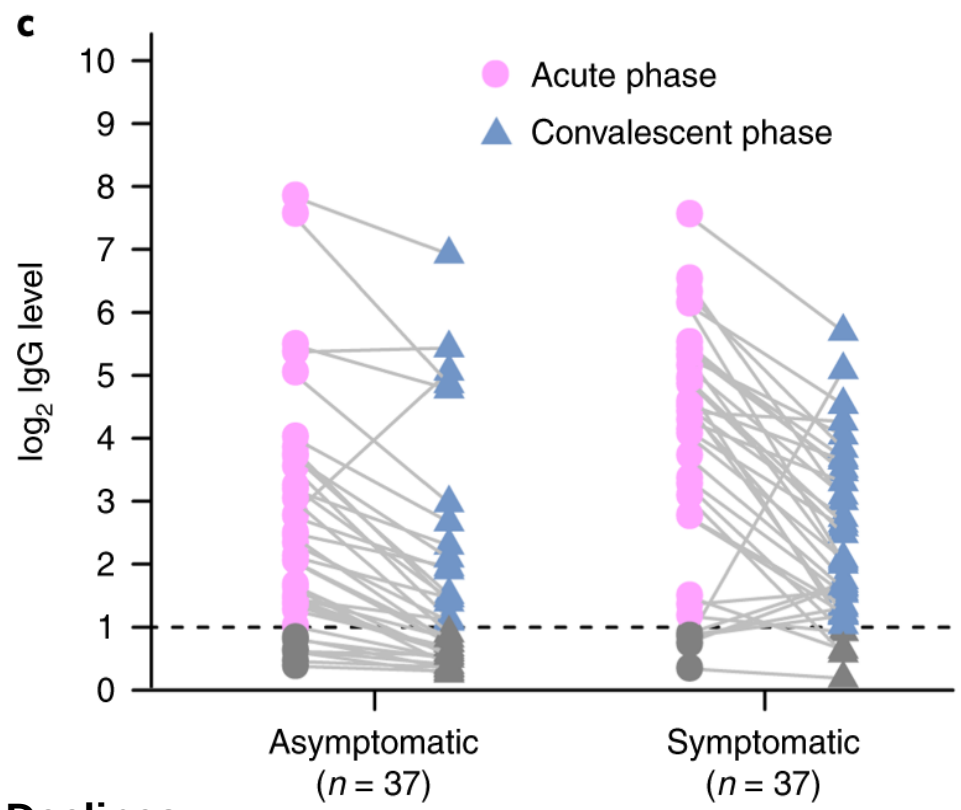
Chandrashekar et al, Science. 20 May 2020

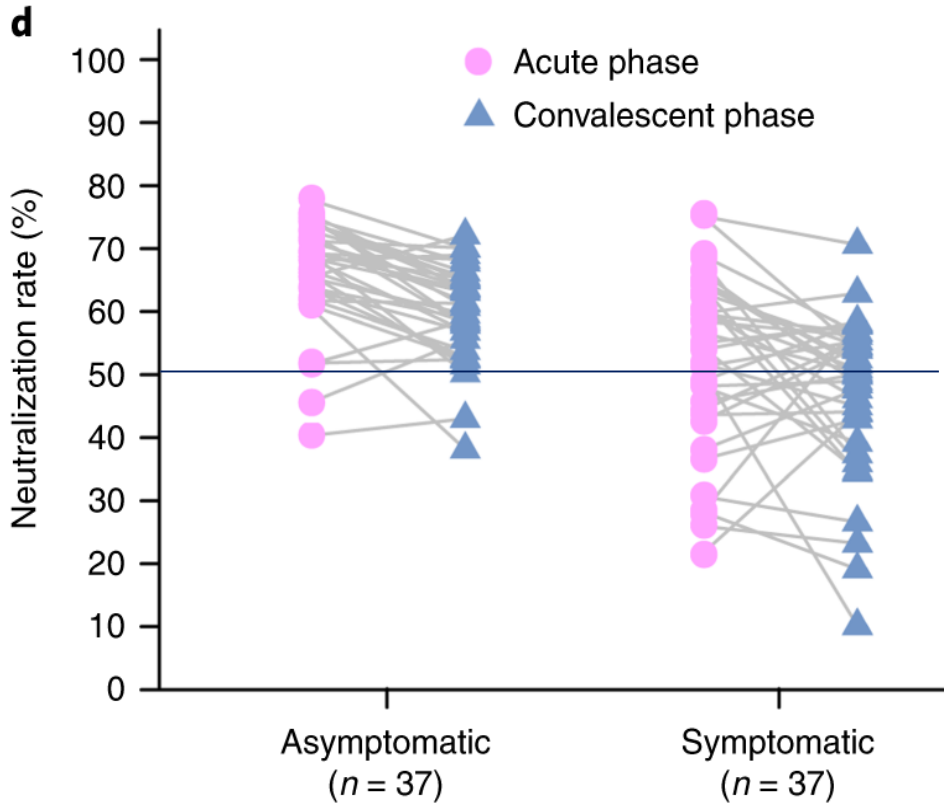
Re-challenge of rhesus macaques boosted SARS-CoV-2 antibody responses.



Red lines reflect mean responses. P values reflect two-sided Mann-Whitney tests.
Chandrashekar et al, Science. 20 May 2020

In humans with SARS-CoV-2 infection, serum antibodies decline between acute phase and 2 months post discharge.



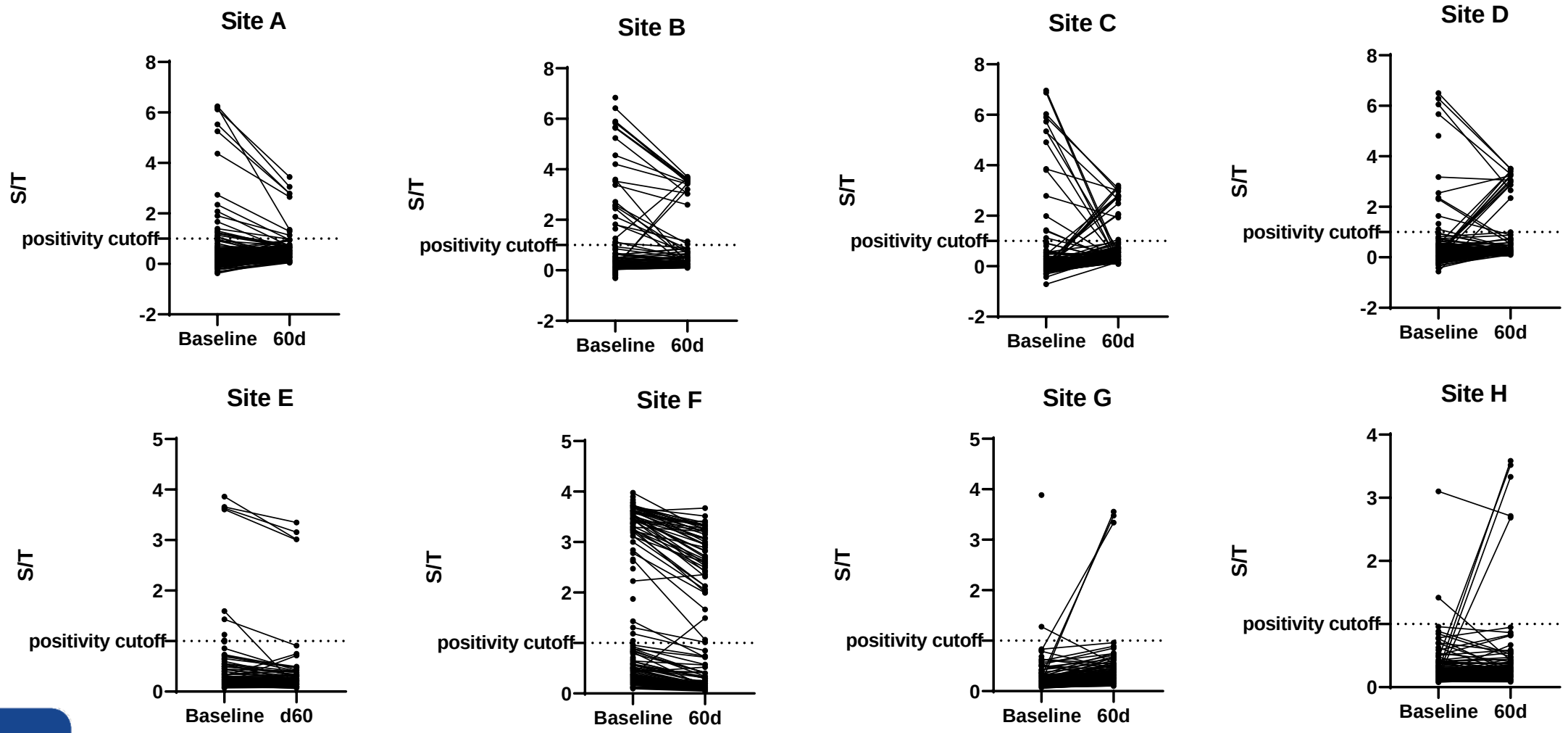


Declines seen in:

93% **97%** **81%** **62%**

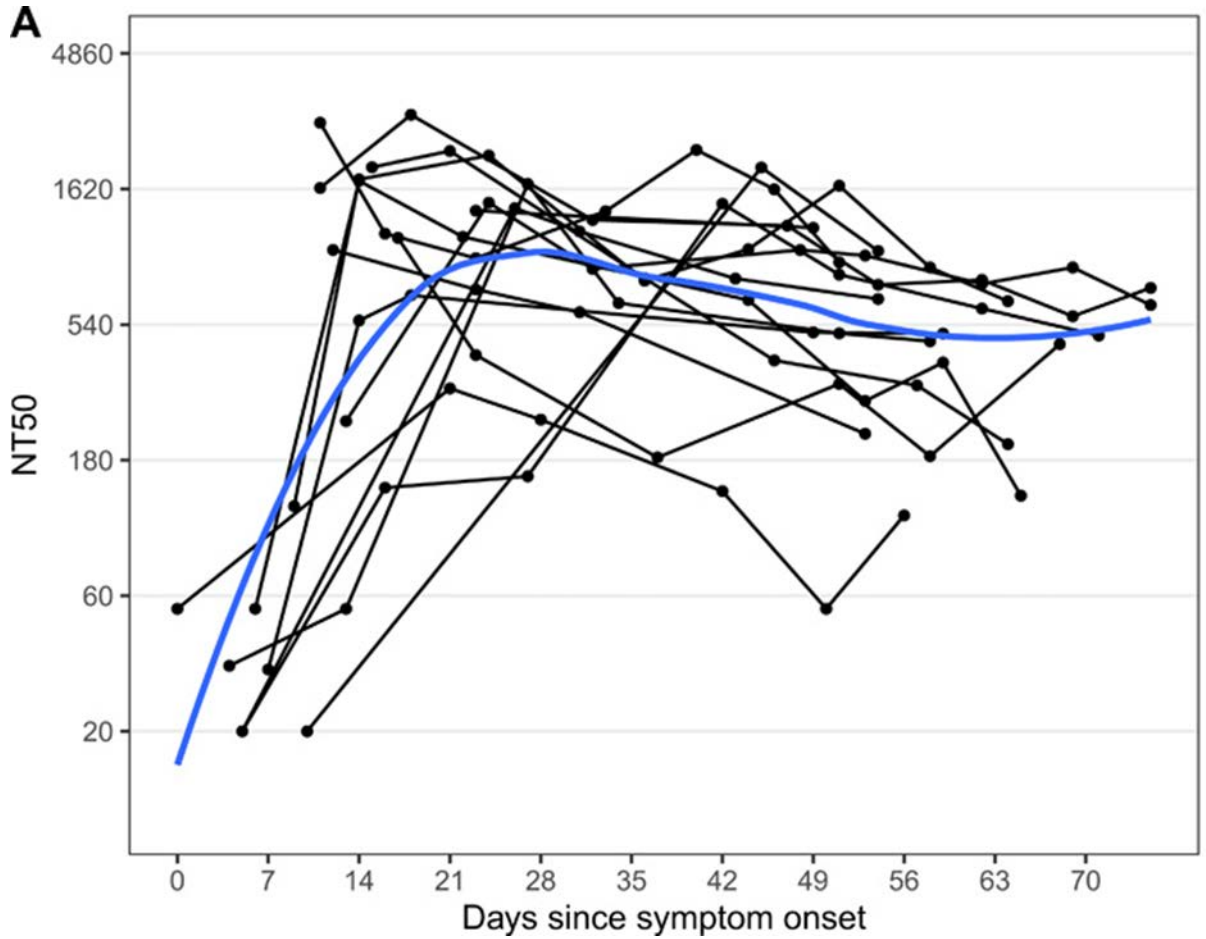
Long et al. Nature Medicine. 18 JUN 2020

In healthcare workers with a history of mild SARS-CoV-2 infection, serum antibodies waned 2 months post-infection.



Manish Patel, Wesley Self, Melissa Coughlin, CDC MPIR lab, IVY investigators, manuscript in preparation

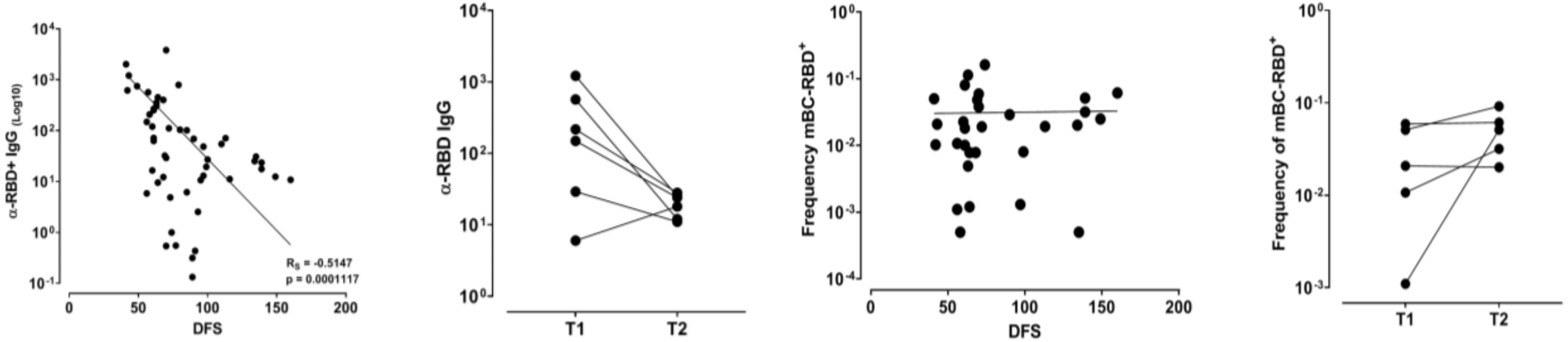
Among hospitalized persons with SARS-CoV-2 neutralizing antibody titers demonstrated little to no decrease over 75 days since symptom onset.



Data from 88 samples from 15 individuals collected between 0- and 75-days post-symptoms. Each point represents a measurement of 50% neutralizing titer (NT50). Lines connect measurements from the same individual and a loess smooth function is shown in blue.
Iyer *et al.* Science immunology. October 8, 2020.

Do persons infected with SARS-CoV-2 mount cellular immune responses?

In symptomatic COVID-19 patients, SARS-CoV-2 memory B cells did not wane at the same rate as serum antibodies.

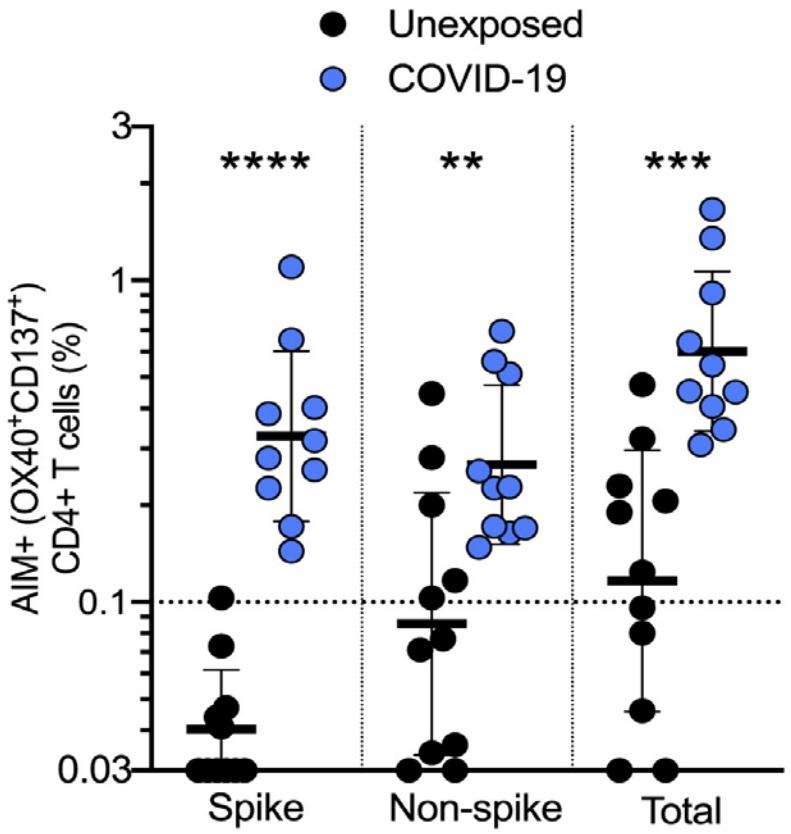


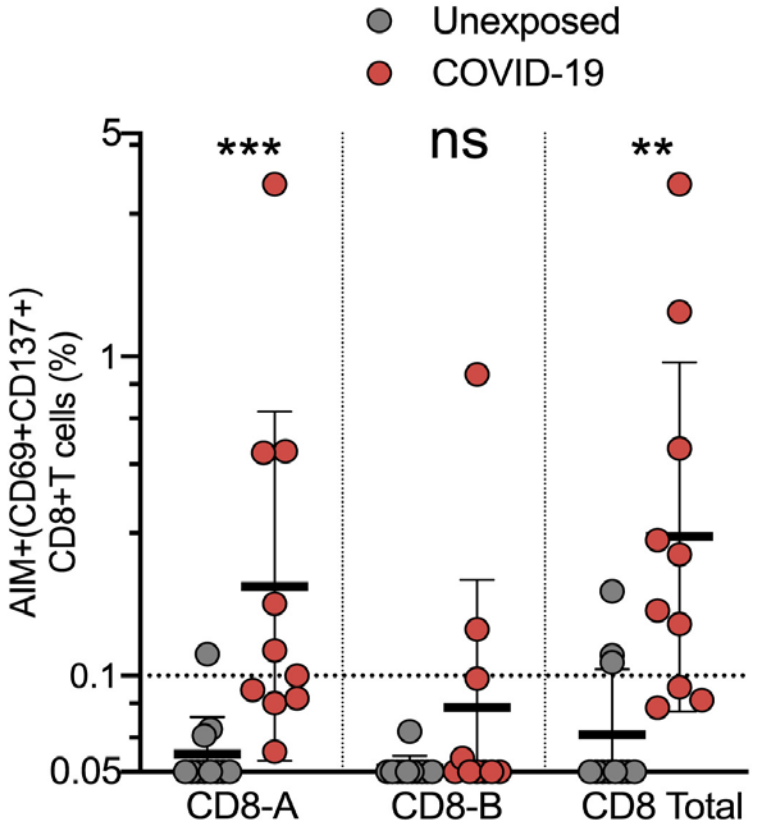
Serum antibodies

Memory B cells

*DAF: Days following onset of symptoms
Vaisman-Mentesh et al. MedRxiv.

Recovered COVID-19 patients have SARS-CoV-2 – specific CD4+ T cells and CD8+ T cells.





Grifoni et al. Cell. 181: 1489-1501

Conclusions

- Repeat exposure to SARS-CoV-2 may cause boosting of immune response.
- Several studies have observed waning of serum antibodies in COVID-19 patients after a few months. The implications for protection are unknown.
- Neutralizing antibody titers demonstrated little or no decrease at 75 days post-symptom onset.
- SARS-CoV-2 specific cellular B and T cell responses detected in COVID-19 patients. Memory B cells did not wane as fast as serum antibody titers.

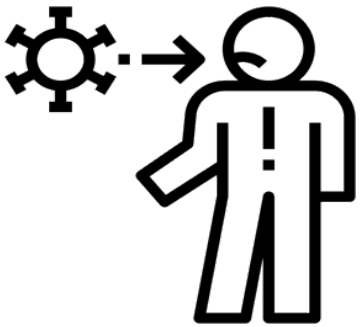
COVID-19 Reinfection

COVID-19 Reinfection

- Infection with SARS-CoV-2 following recovery from previous documented SARS-CoV-2 infection.

- Reinfections occur with other human coronaviruses and become more common over time.
  - Likely as a function of both waning immunity and increased exposure.

Reinfection with HCoV-229E in human experiment

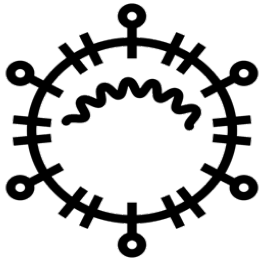


15 volunteers inoculated with HCoV-229E

1-10 days

10 had subsequent live viral shedding, of which 8 had clinical colds.

1 year

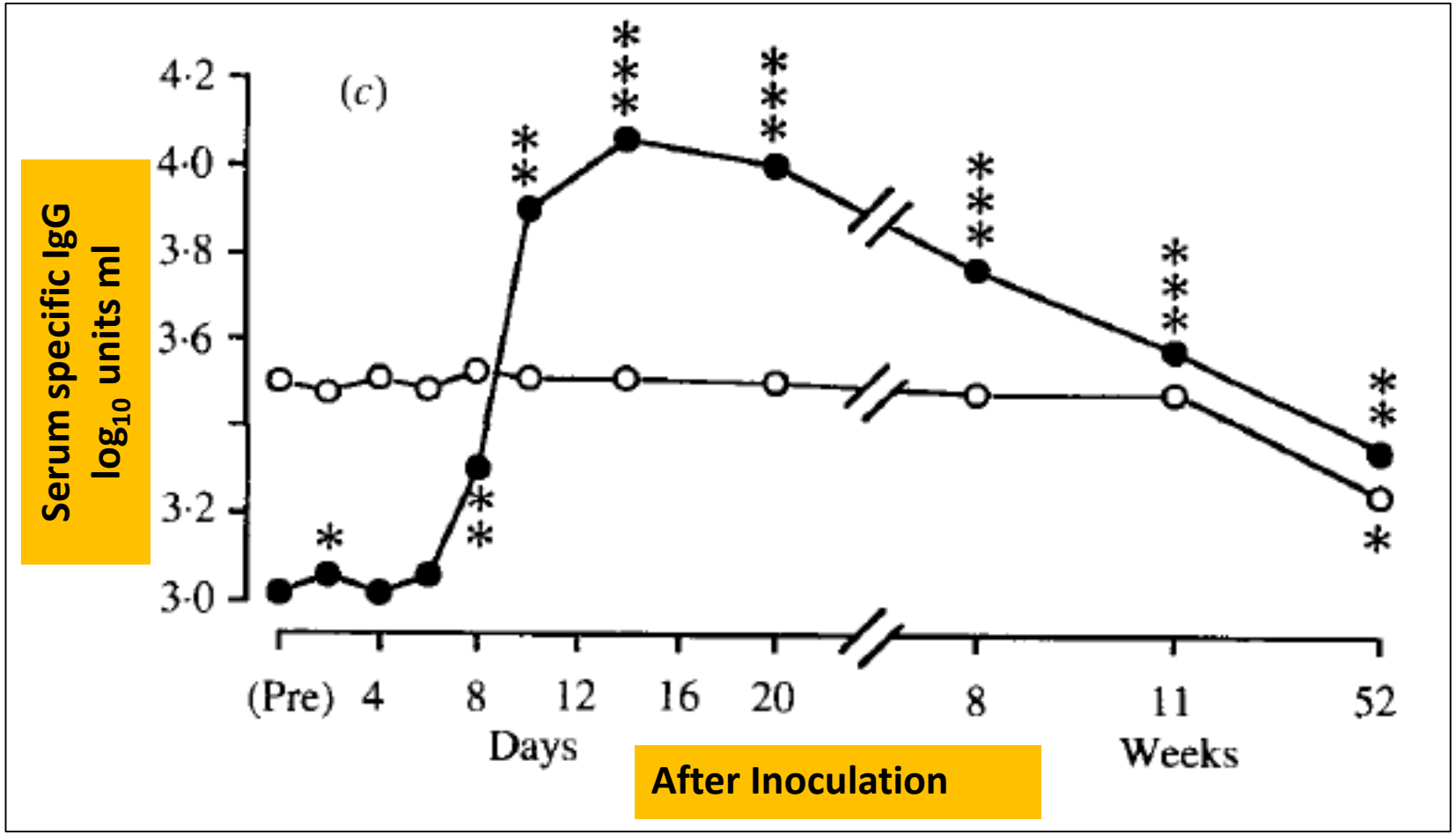


6 of 9 previously infected volunteers were re-infected on repeat challenge. All asymptomatic

Callow KA, Parry HF, Sergeant M, Tyrrell DA. The time course of the immune response to experimental coronavirus infection of man. Epidemiology & Infection. 1990 Oct;105(2):435-46

Reinfection with HCoV-229E in human experiment

Changes in IgG 1 year after HCoV-229E inoculation



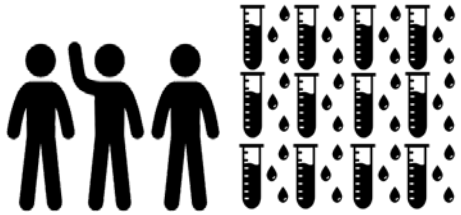
● Infected Volunteers
○ Uninfected Volunteers

Significance of difference from pre-inoculation values:
***P<0.05**
****P <0.01**
*****P<0.001**

In this experimental model, reinfection with live viral shedding occurred for most subjects 1 year after initial inoculation. Reinfection occurred in spite of raised antibody titers.

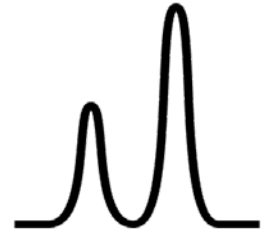
Callow KA, Parry HF, Sergeant M, Tyrrell DA. The time course of the immune response to experimental coronavirus infection of man. Epidemiology & Infection. 1990 Oct;105(2):435-46

Reinfection with seasonal coronaviruses – 10 volunteers, 35 years of observation



10 adult male volunteers had blood drawn every 3-6 months for > 10 years between 1985 –2020.

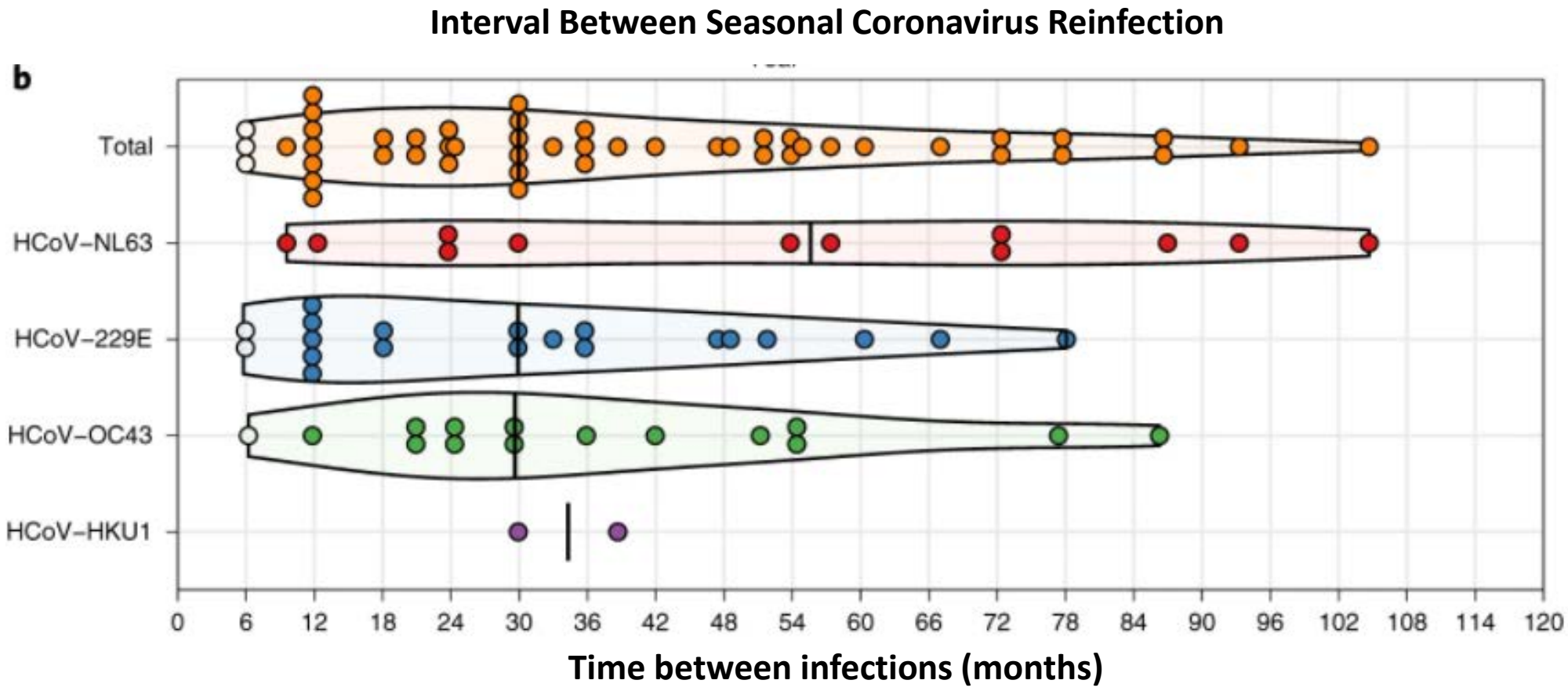
Antibodies against each of the 4 seasonal coronaviruses were measured.



≥ 1.4 fold change in antibody optical density was considered an infection event.

Edridge, A.W.D., Kaczorowska, J., Hoste, A.C.R. et al. Seasonal coronavirus protective immunity is short-lasting. Nat Med (2020). https://doi.org/10.1038/s41591-020-1083-1

Reinfection with seasonal coronaviruses – 10 volunteers, 35 years of observation



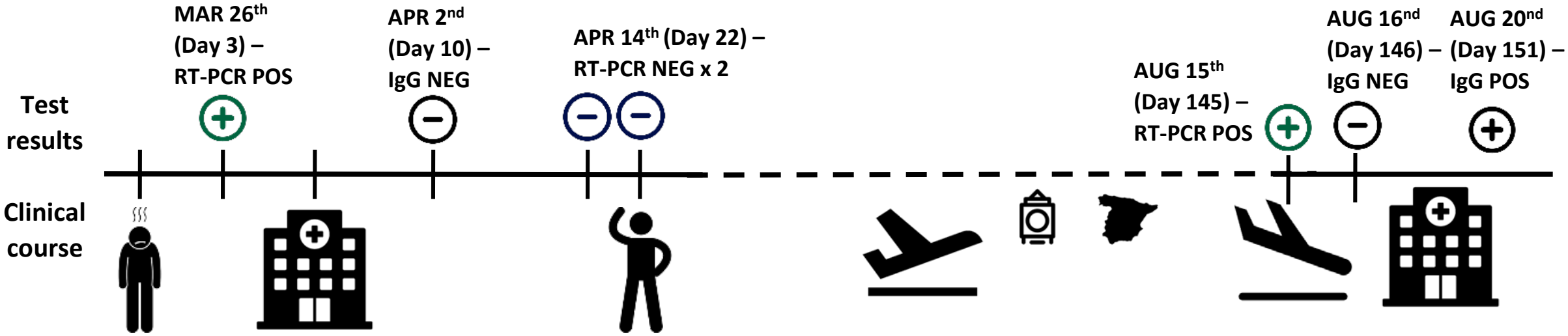
White dots: reinfections without an intermediate decrease in antibody levels;
Black vertical lines: median reinfection times

Edridge, A.W.D., Kaczorowska, J., Hoste, A.C.R. et al. Seasonal coronavirus protective immunity is short-lasting. Nat Med (2020). https://doi.org/10.1038/s41591-020-1083-1

Based on the current evidence for SARS-CoV-2, reinfections are likely uncommon within 3 months.

Hong Kong Case of Reinfection

33-year-old with no pre-existing conditions



MAR 23rd – developed productive cough, sore throat, fever, headache

MAR 29th (Day 6) – hospitalized (per policy), but with improving symptoms.

APR 14th (Day 22) – discharged from hospital

AUG – vacation to London and Spain.

AUG 15th (Day 145) – Returned to Hong Kong, underwent entry screening; asymptomatic. Hospitalized again (per policy), chest imaging negative; CRP elevated at 8.6 mg/L.

To et al, Clinical Infectious Diseases, 25 August 2020, https://doi.org/10.1093/cid/ciaa1275

Review of 5 reports of suspected cases of SARS CoV-2 Reinfection

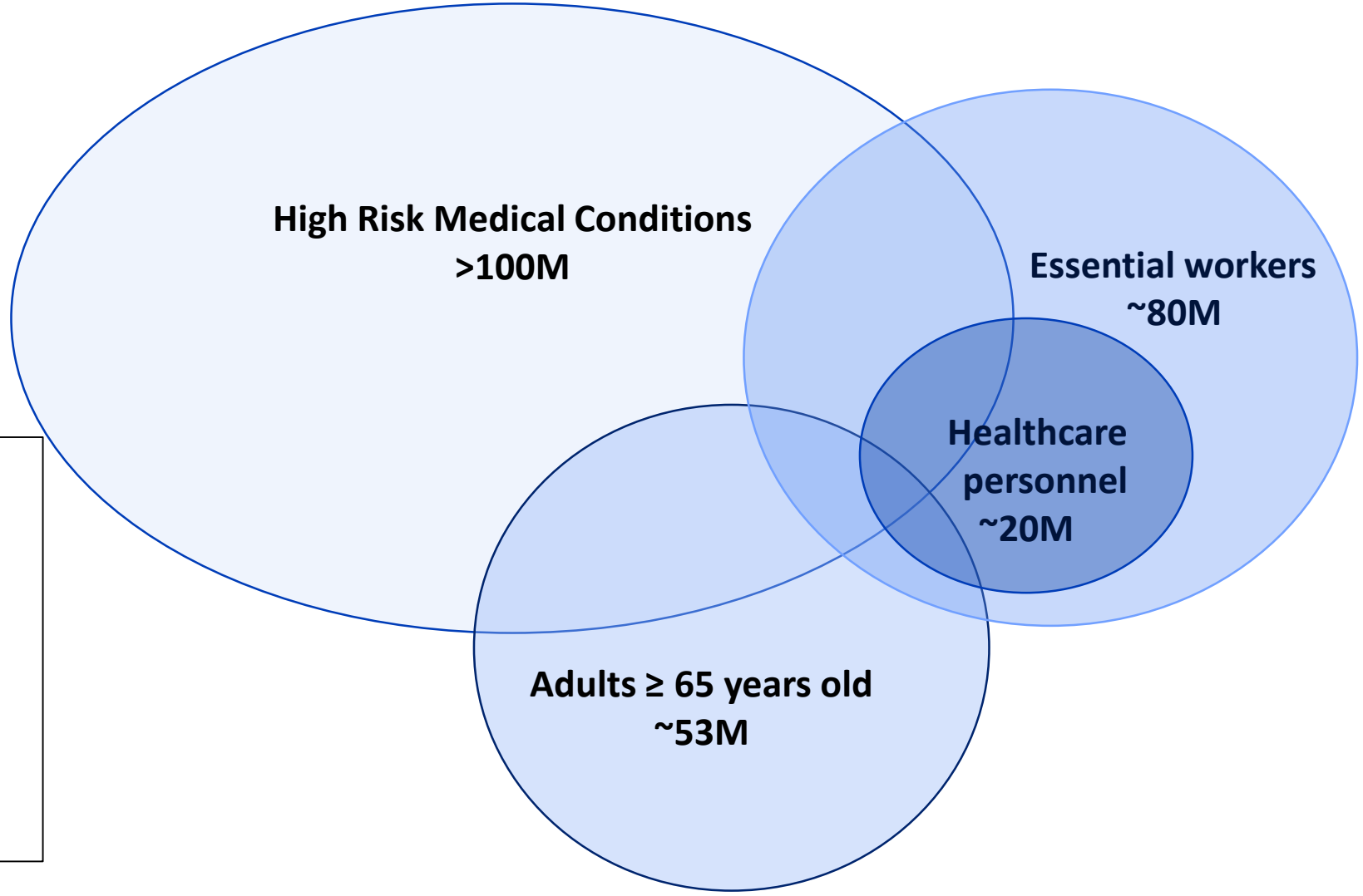
Report	Days from 1st course onset	Features of 2nd clinical course	Evidence for reinfection/Contribution to literature
To et al. – Healthy 33M from Hong Kong (Aug 25)	145 days	Asymptomatic	**Strongest evidence published case** – demonstrated evidence for acute, substantial infection (high viral load, serological conversion after) as well as substantial genome differences (23 nucleotides, different clades/lineages).
Van Eslande et al – 52F on inhaled corticosteroids from Belgium (Sep 05)	93 days	Symptomatic w/ similar but milder URI symptoms	**Intermediate evidence** - demonstrated RT-PCR positive (Ct value = 33 on reinfection) and genomic difference > expected molecular clock (11 nucleotides).
Tillet et al. – 25M from Reno, Nevada (Aug 31)	43 days	Atypical pneumonia w/ hypoxemia; 2nd course worse than 1st	**Lesser degree of evidence** – demonstrated distinct viral genomes from 2 episodes (7 nucleotides) but did not demonstrate significant viral burden (Ct =35).
Raddad. et al – migrant workers in Qatar (Aug 26)	Median of 65 days	Unknown clinical course, uses location of swab (health facility vs survey) as proxy	**First attempt at quantifying reinfection** – searched for repeat positive RT-PCR >45 days among 133K cases. 35 (0.03%) of which had Ct values <30 on the 2nd specimen
CDC Reinfection Investigation	Initial 3 months after primary infection	Recurrent COVID-19 like symptoms with positive SARS-CoV-2 RT-PCR, but no alternate etiology identified for their symptoms.	26 cases with specimens available for both illness episodes. All specimens from the second episode of infection had Ct values >30 and no replication-competent virus isolated.

Conclusions

- Reinfections occur with other human coronaviruses and become more common over time.
- Reinfection for SARS-CoV-2 is possible, but likely uncommon within 3 months.

Epidemiology of COVID-19 in Pregnant Women

Possible groups for Phase 1 vaccination



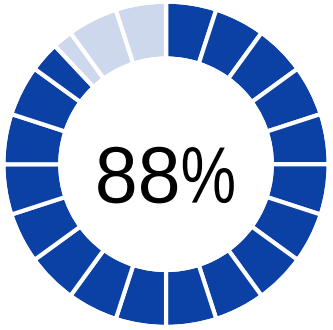
From prior ACIP Discussions:

Phase 1a:
-HCP

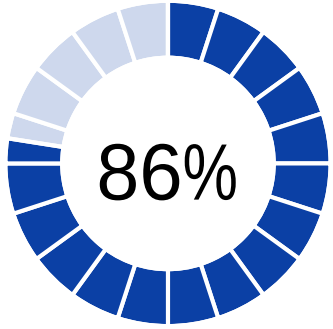
Phase 1b:
-Essential Workers
-High Risk Med Conditions
-Adults ≥ 65 years old

75% of the healthcare workforce are women.

Women are a majority among the largest healthcare personnel groups



Registered Nurses



Healthcare support workers: Nursing, psychiatric, and personal and home health aides

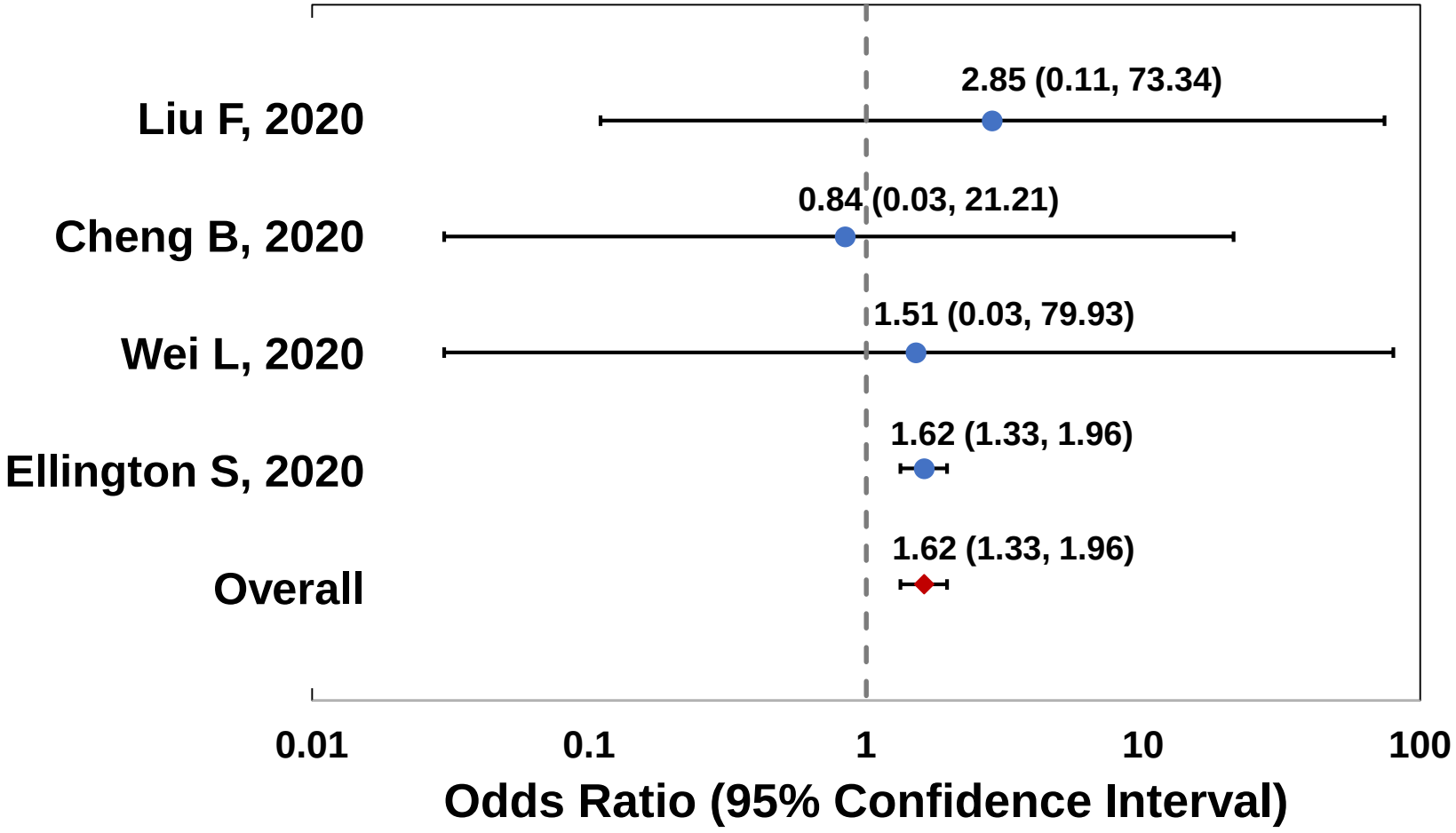
From 2019 Census Data

Around 330,000 healthcare personnel expected to be pregnant or recently postpartum

https://data.census.gov/cedsci/table?q=registered%20nurse&tid=ACSDT1Y2019.B24010&tp=false&hidePreview=true
https://www.cdc.gov/reproductivehealth/emergency/pdfs/pregnacyestimatobrochure508.pdf

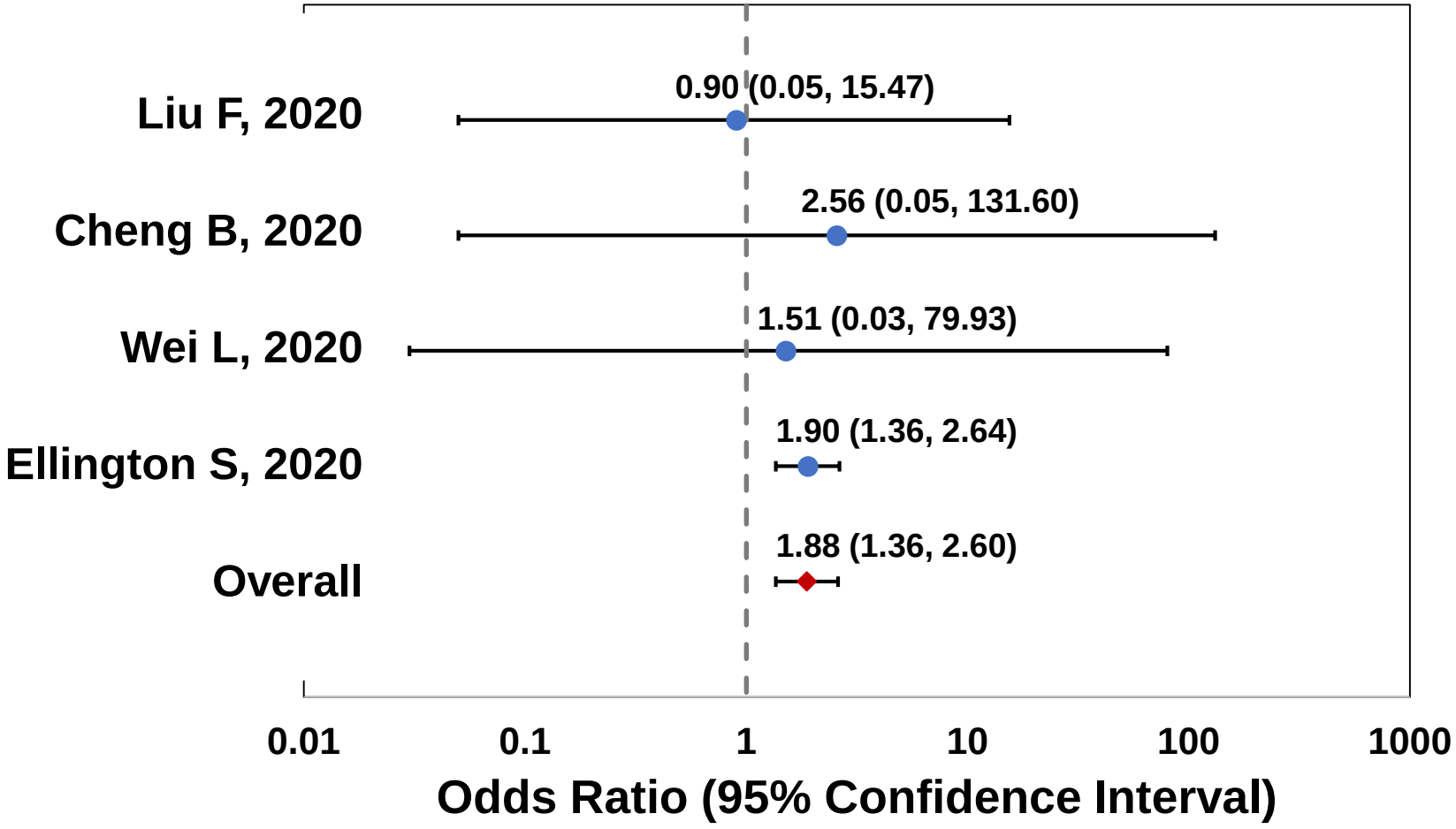
Risks of COVID-19 During Pregnancy

Pregnant women with COVID-19 have an increased odds of ICU admission compared with non-pregnant women of reproductive age.



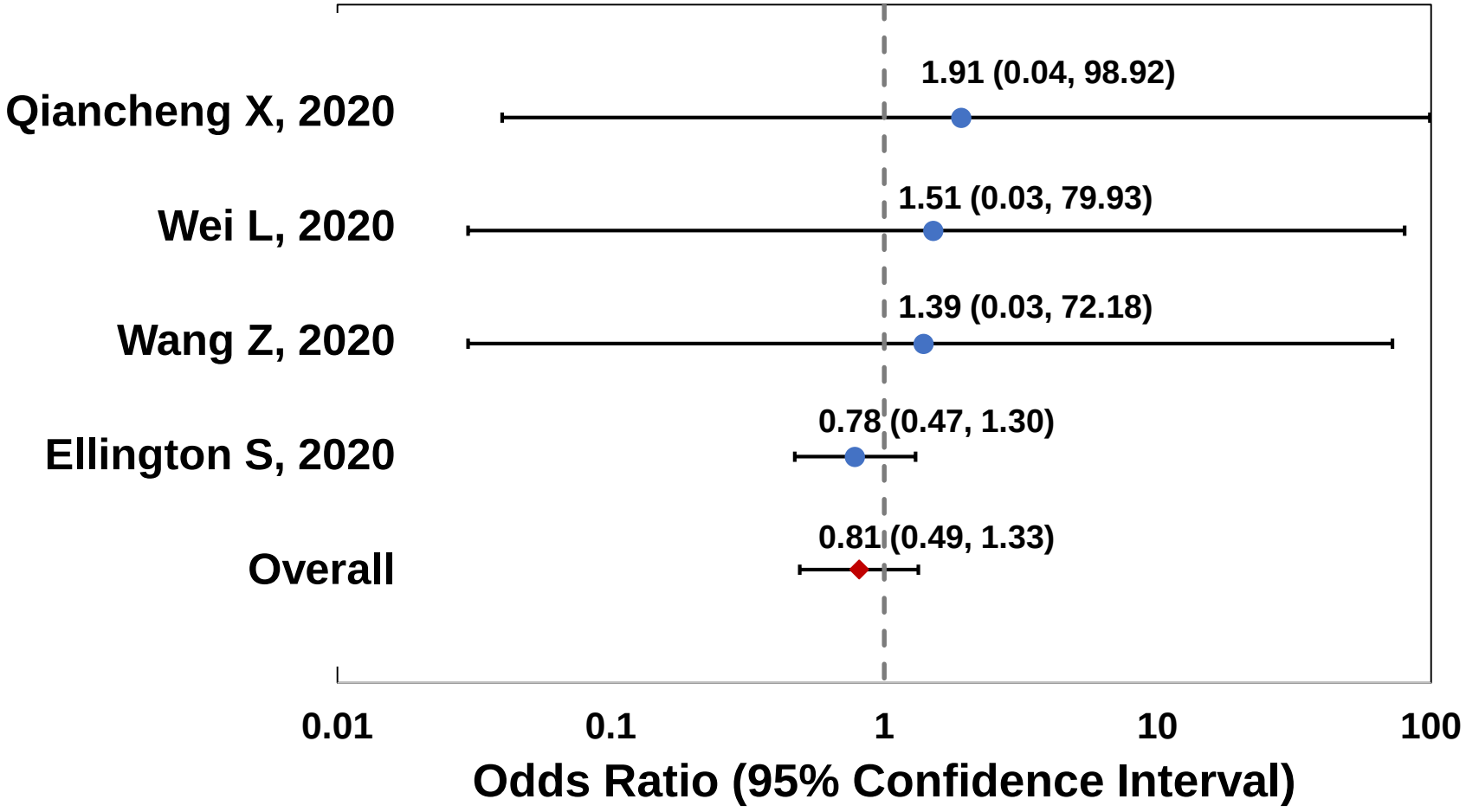
Adapted from: Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ. 2020;370:m3320. Published 2020 Sep 1. doi:10.1136/bmj.m3320

Pregnant women with COVID-19 have increased odds of invasive ventilation compared with non-pregnant women of reproductive age.



Adapted from: Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ. 2020;370:m3320. Published 2020 Sep 1. doi:10.1136/bmj.m3320

Pregnant women with COVID-19 have no increased odds of death compared with non-pregnant women of reproductive age.



Adapted from: Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ. 2020;370:m3320. Published 2020 Sep 1. doi:10.1136/bmj.m3320

Preliminary and unpublished U.S. data can add to the evidence base.

Centers for Disease Control and Prevention

MMWR

Update

Morbidity and Mortality Weekly Report

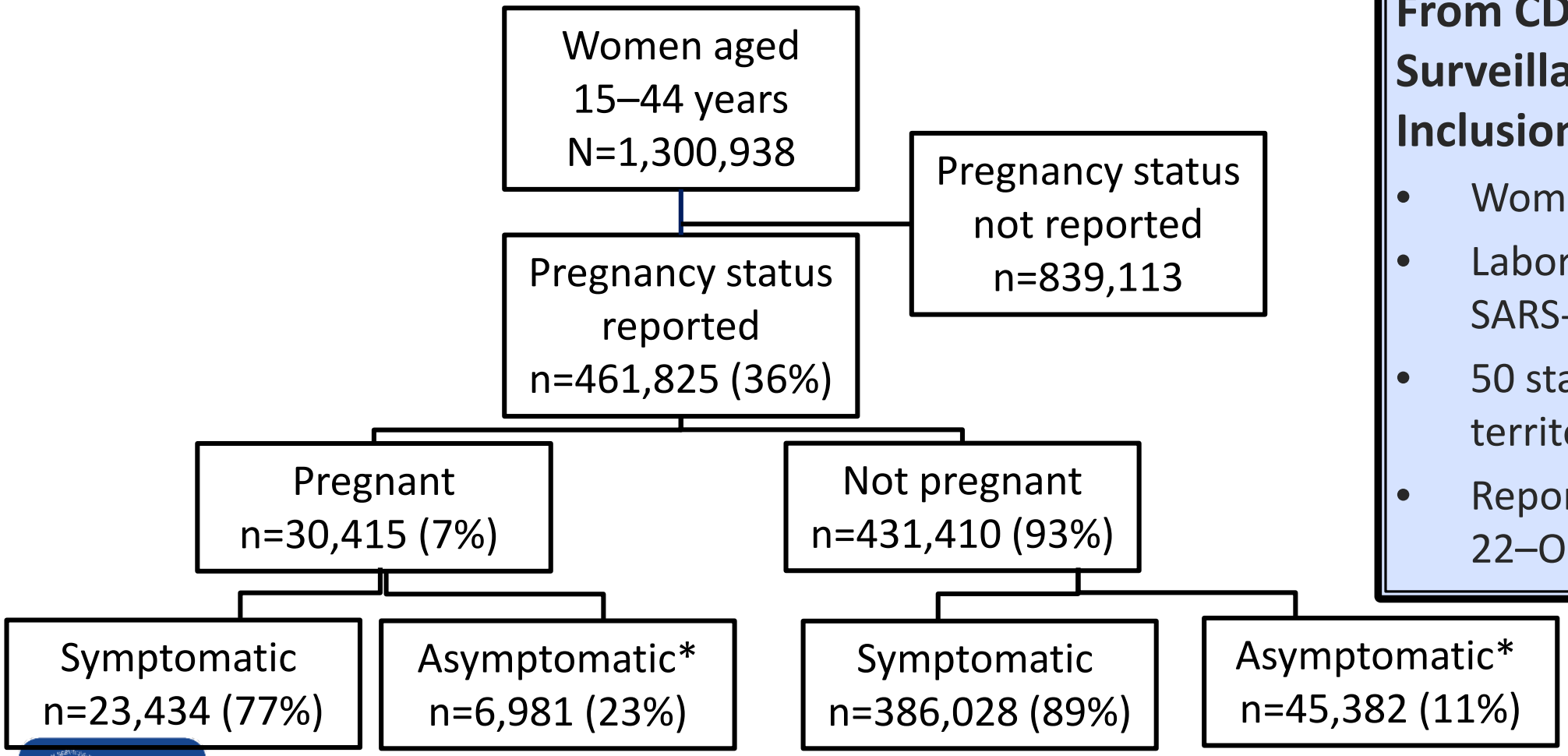
Weekly / Vol. 69 / No. 25

June 26, 2020

Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status — United States, January 22–June 7, 2020

Sascha Ellington, PhD[1]; Penelope Strid, MPH[1]; Van T. Tong, MPH[1]; Kate Woodworth, MD[1]; Romeo R. Galang, MD[1]; Laura D. Zambrano, PhD[1]; John Nahabedian, MS[1]; Kayla Anderson, PhD[1]; Suzanne M. Gilboa, PhD[1]

Women of Reproductive Age with COVID-19 by Pregnancy Status — January 22 – October 3, 2020



From CDC COVID-19 Case Surveillance Data Inclusion Criteria

- Women aged 15-44 years
- Laboratory-confirmed SARS-CoV-2 infection
- 50 states, NYC, DC, & territories
- Reported to CDC January 22–October 3, 2020

*Includes women reported as asymptomatic and those with unknown/missing symptom status

Preliminary Unpublished Data

Increased risk for ICU admission, mechanical ventilation and death during pregnancy

Outcomes of Interest	No. (%)*		Crude RR (95% CI)	aRR (95% CI)†	Previously Published¶ aRR (95% CI)†
	Pregnant women (N = 30,415)	Nonpregnant women (N = 431,410)			
ICU Admission	274 (0.9)	1,562 (0.4)	**2.5 (2.2-2.8)**	**2.5 (2.2-2.9)**	**1.5 (1.2-1.8)**
Mechanical Ventilation	88 (0.3)	447 (0.1)	**2.8 (2.2-3.5)**	**2.8 (2.2-3.5)**	**1.7 (1.2-2.4)**
ECMO¶	17 (0.1)	120 (<0.1)	**2.0 (1.2-3.3)**	**1.9 (1.1-3.2)**	--
Death	45 (0.2)	510 (0.1)	**1.3 (0.9-1.7)**	**1.5 (1.1-2.1)**	0.9 (0.5-1.5)

* Percentages calculated among total in pregnancy status group; those with missing data on outcomes were counted as not having the outcome

† Adjusted for age, race/ethnicity, and presence of underlying conditions. Nonpregnant women are the referent group.

§ Ellington S, Strid P, Tong VT, et al. Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status — United States, January 22–June 7, 2020. MMWR Morb Mortal Wkly Rep 2020;69:769–775. DOI: http://dx.doi.org/10.15585/mmwr.mm6925a1

¶ Extracorporeal membrane oxygenation

Preliminary Unpublished Data

Increased risk for ICU admission, mechanical ventilation and death during pregnancy

Outcomes of Interest	No. (%)*		Crude RR (95% CI)	aRR (95% CI)†	Previously Published¶ aRR (95% CI)†
	Pregnant women (N = 30,415)	Nonpregnant women (N = 431,410)			
ICU Admission	274 (0.9)	1,562 (0.4)	**2.5 (2.2-2.8)**	**2.5 (2.2-2.9)**	**1.5 (1.2-1.8)**
Mechanical Ventilation	88 (0.3)	447 (0.1)	**2.8 (2.2-3.5)**	**2.8 (2.2-3.5)**	**1.7 (1.2-2.4)**
ECMO¶	17 (0.1)	120 (<0.1)	**2.0 (1.2-3.3)**	**1.9 (1.1-3.2)**	--
Death	45 (0.2)	510 (0.1)	**1.3 (0.9-1.7)**	**1.5 (1.1-2.1)**	0.9 (0.5-1.5)

* Percentages calculated among total in pregnancy status group; those with missing data on outcomes were counted as not having the outcome

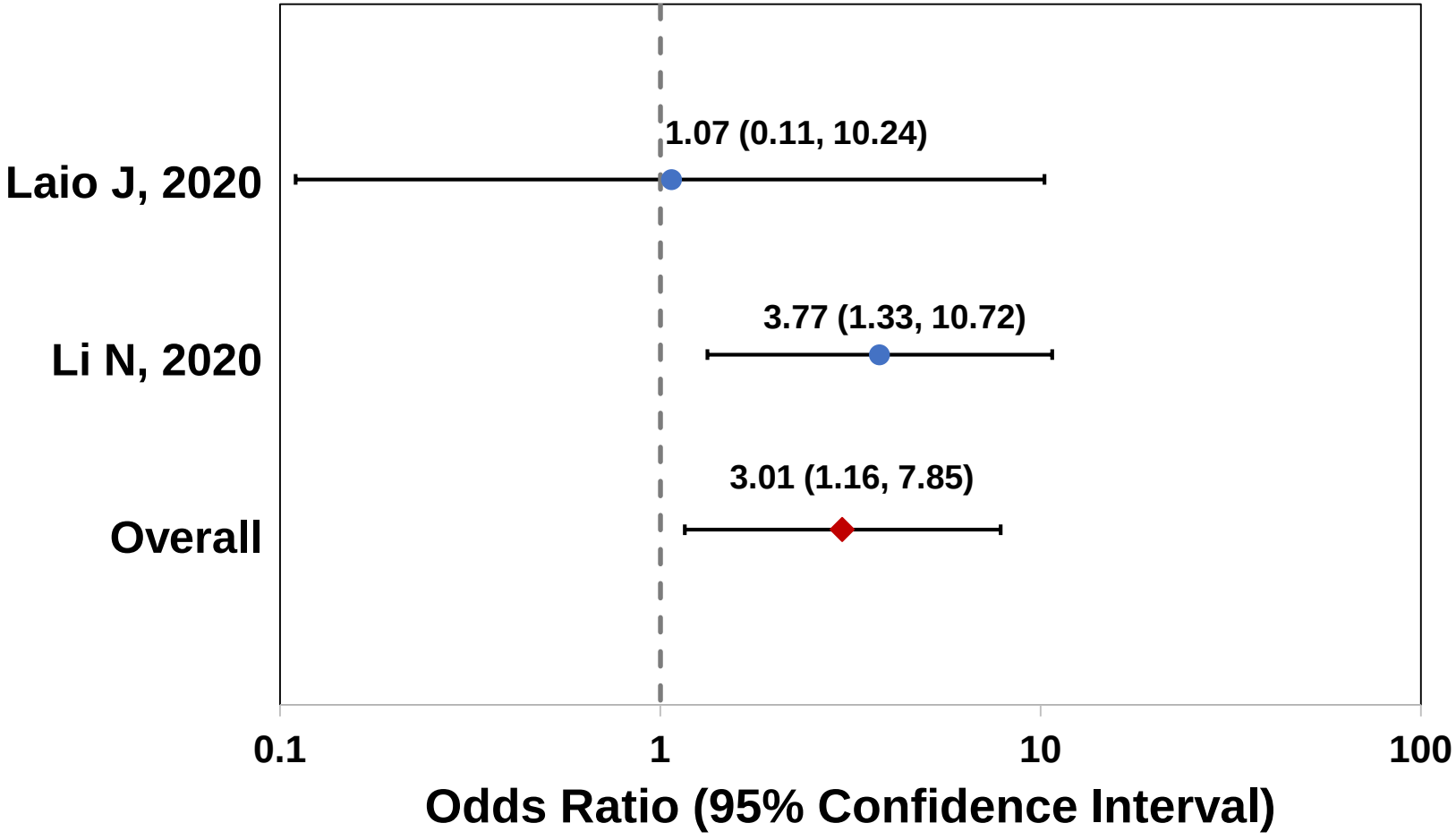
† Adjusted for age, race/ethnicity, and presence of underlying conditions. Nonpregnant women are the referent group.

§ Ellington S, Strid P, Tong VT, et al. Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status — United States, January 22–June 7, 2020. MMWR Morb Mortal Wkly Rep 2020;69:769–775. DOI: http://dx.doi.org/10.15585/mmwr.mm6925a1

¶ Extracorporeal membrane oxygenation

Preliminary Unpublished Data

Neonates of mothers with COVID-19 are at increased risk for preterm birth before 37 weeks compared to those without COVID-19.



Adapted from: Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ. 2020;370:m3320. Published 2020 Sep 1. doi:10.1136/bmj.m3320

COVID-19 and Breastfeeding

- Although samples of breast milk have tested positive by RT-PCR, current evidence indicates it is not likely a route of transmission.
- Rate of infection is no greater when a baby is breastfed or remains with the mother.
- Breast milk is the optimal source of nutrition for most infants, even those born to mothers with suspected or confirmed COVID-19.
  - Precautions to avoid spreading the virus to her infant should be taken.

Gro BR. Lancet. Detection of SARS-CoV-2 in human breastmilk
Chambers. JAMA. Evaluation for SARS-CoV-2 in Breast Milk From 18 Infected Women
Walker et al. Maternal transmission of SARS-COV-2 to the neonate, and possible routes for such transmission: a systematic review and critical analysis https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/pregnancy-breastfeeding.html

Conclusions

- We expect around 330,000 healthcare personnel to be pregnant or recently postpartum at the time a vaccine becomes available.
- Data demonstrate increased risks of severe maternal illness and preterm birth due to COVID-19.
- Although samples of breast milk have tested positive by RT-PCR, there is no evidence that this is an important risk for transmission, and breastfeeding is still recommended.

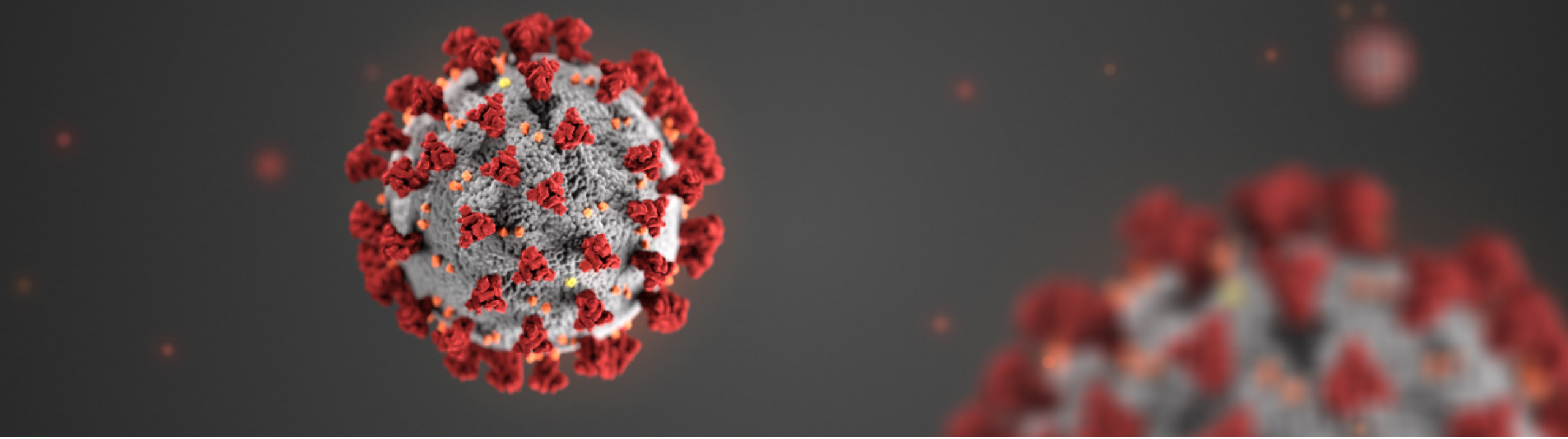
Summary

Summary

- **Overall**: As of October 29, over 8.8 million cases of COVID-19 diagnosed and over 227,000 COVID-19-associated deaths reported in the United States.
- **Post-infection Immunity**: Data on post-infection immunity are limited but suggests that antibodies wane over time. SARS-CoV-2 cellular immunity has been detected in COVID-19 patients.
- **Reinfection:** Data are limited but suggests that reinfection is unlikely within 3 months of infection.
- **Pregnancy:** Data demonstrate increased risks of severe maternal illness and preterm birth.

Acknowledgments

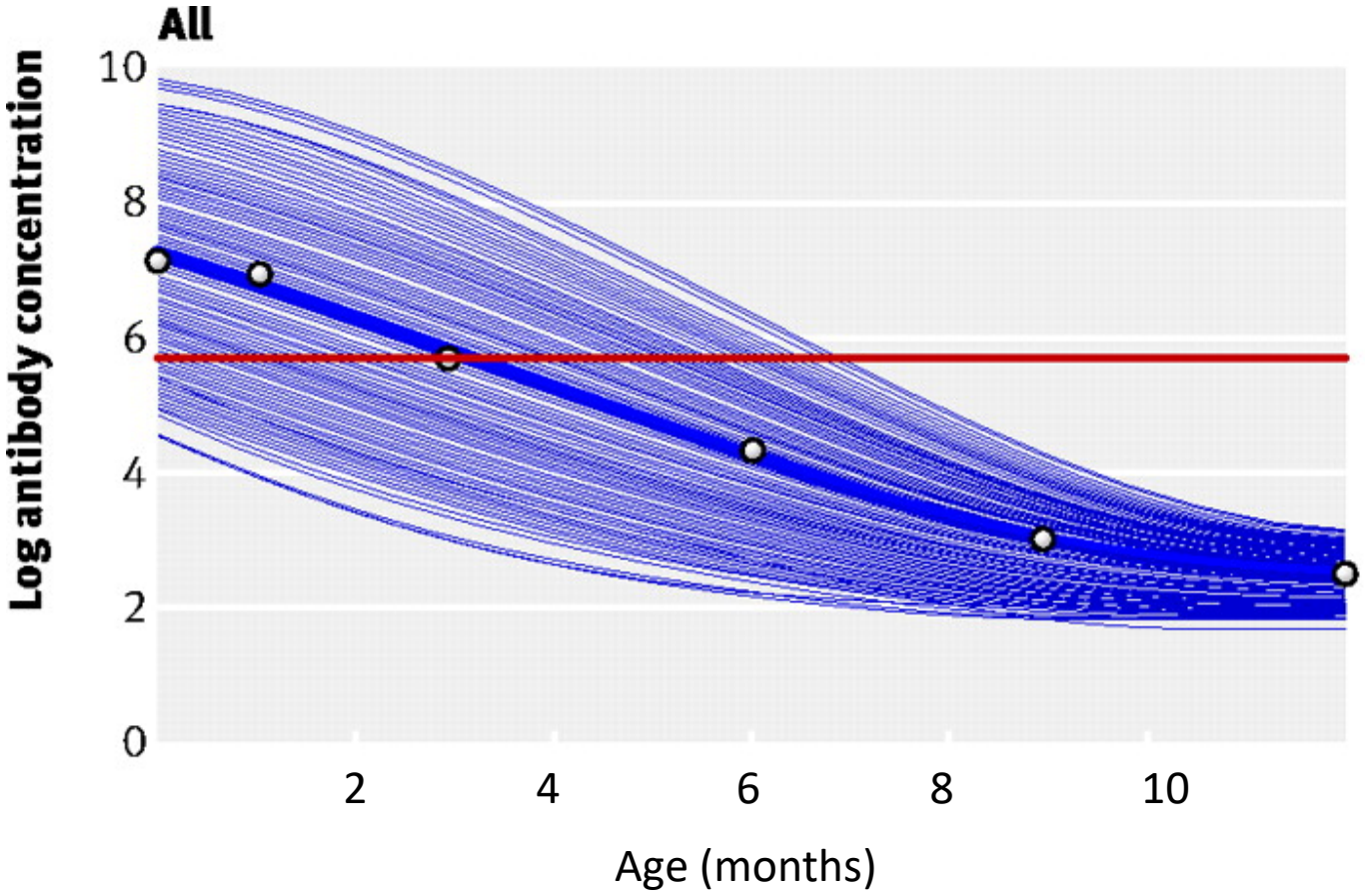
- COVID-19 post-infection immunity
  - Natalie Thornburg
  - Manish Patel
  - CDC MPIR lab
  - Wes Self and IVY investigators
- COVID-19 reinfection
  - Deblina Datta
  - James Lee
- Epidemiology of COVID-19 in pregnant women
  - AAP
  - ACOG
  - CDC PILOT
  - CDC Vaccine TF Leadership
  - CDC COVID-19 Response Leadership
  - NIH



For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Waning of passively transferred measles antibodies in infants occurs at approximately same rate, but time to seronegativity dependent upon initial titer.



Leuridan et al, BMJ 340:c1626

Increased Risk for ICU admission, Mechanical Ventilation and Death for **Symptomatic** Pregnant Women Compared to **Symptomatic** Nonpregnant Women of Reproductive Age

Outcomes of Interest	No. (%)*		Crude RR (95% CI)	aRR (95% CI) †
	Symptomatic Pregnant women with COVID-19 (N = 23,434)	Symptomatic Nonpregnant women with COVID-19 (N = 386,028)		
ICU Admission	245 (1.1)	1,492 (0.4)	**2.7 (2.4-3.1)**	**3.0 (2.6-3.4)**
Mechanical Ventilation	67 (0.3)	412 (0.1)	**2.7 (2.1-3.5)**	**2.9 (2.2-3.8)**
ECMO§	17 (0.1)	120 (<0.1)	**2.3 (1.4-3.9)**	**2.4 (1.5-4.0)**
Death	34 (0.2)	447 (0.1)	**1.3 (0.9-1.8)**	**1.7 (1.2-2.4)**

* Percentages calculated among total in pregnancy status group; those with missing data on outcomes were counted as not having the outcome

† Adjusted for age, race/ethnicity, and presence of underlying conditions. Nonpregnant women are the referent group.

§ Extracorporeal membrane oxygenation

Preliminary Unpublished Data

Strengths and Limitations of the Case Surveillance Data

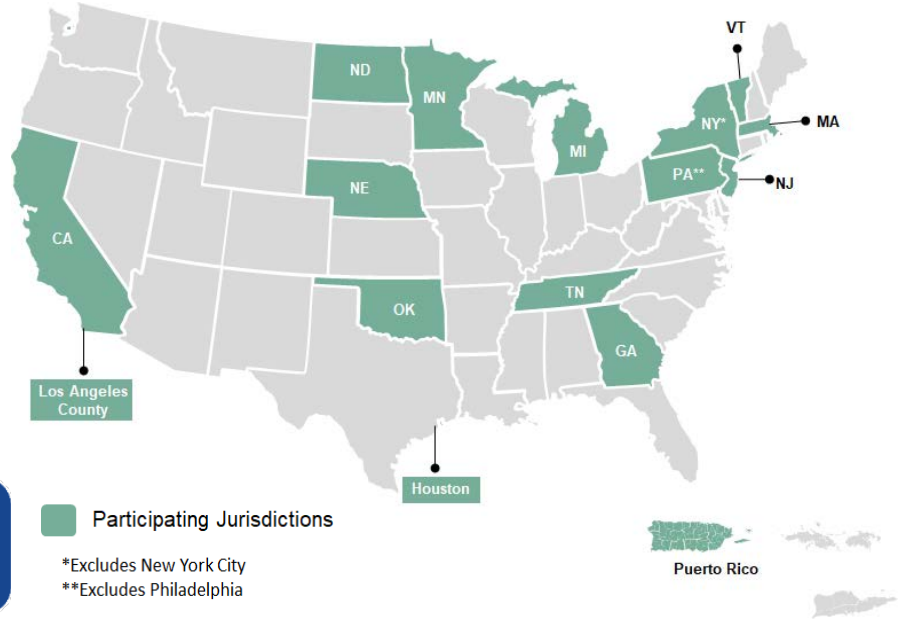
- **Strengths**
  - Population-level data
  - Large sample size with power to study rare outcomes like maternal deaths
- **Limitations**
  - Large proportion of cases with missing data
  - Representativeness of data and generalizability of findings
  - Inability to distinguish between hospitalization for COVID-19 from hospitalization for non-COVID-19 reasons
  - Incomplete ascertainment of outcomes
  - Does not capture data on pregnancy/birth outcomes and trimester of infection

Surveillance for Emerging Threats to Mothers and Babies Network (SET-NET) — Adaptation for COVID-19

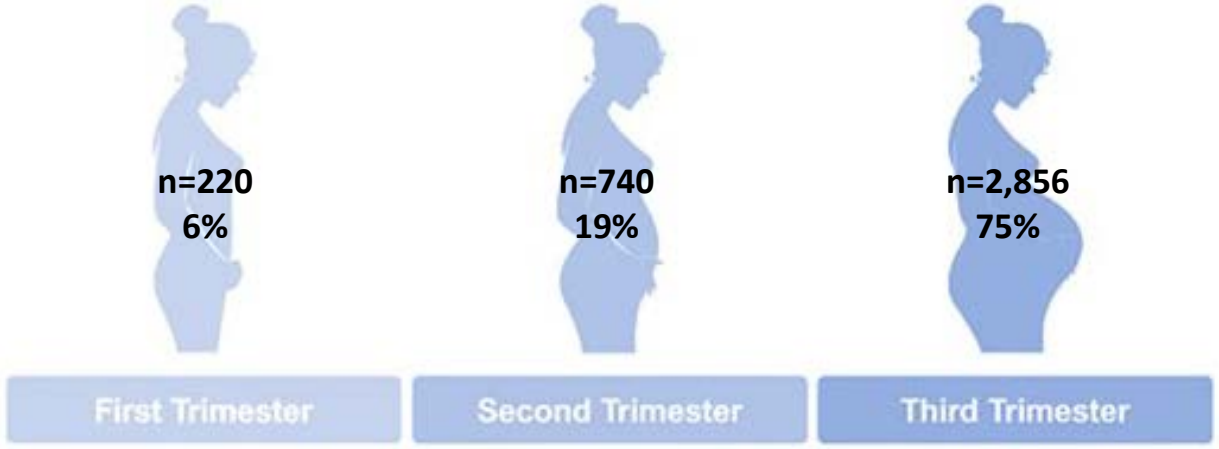
Inclusion Criteria

- Women with laboratory confirmed SARS-CoV-2 infection (PCR+) at any point during pregnancy, up to and including the day of delivery

Jurisdictions Reporting Birth and Infant Outcome Data, October 14, 2020 — 5,047 Pregnant Women with SARS-CoV-2 Infection



Pregnant Women with SARS-CoV-2 Infection by Trimester of Infection* — SET-NET, 16 Jurisdictions, March 29–October 14, 2020



*Excludes 1231 pregnant women with missing data on trimester of infection

Preliminary Unpublished Data

Birth and Infant Outcomes Among Pregnant Women with Laboratory-Confirmed SARS-CoV-2 Infection — SET-NET, 16 Jurisdictions, March 29–October 14, 2020

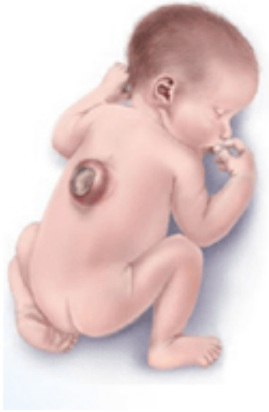
- N=4242 women with SARS-CoV-2 infection in pregnancy as of October 22
  - 9% asymptomatic, 52% symptomatic, 39% missing symptom status

- Of 3912 live births with reported gestational age, 12.9% (n=506) were preterm (<37 weeks)
  - 9.1% (n=357) Late preterm (34 to <37 weeks)
  - 1.3% (n=50) Moderate preterm (32 to <34 weeks)
  - 1.8% (n=69) Very preterm (28 to <32 weeks)
  - 0.8% (n=30) Extremely preterm

Preliminary Unpublished Data

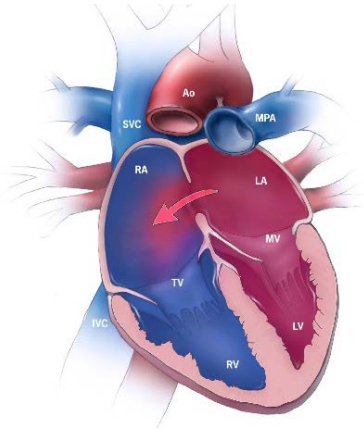
Fever During Pregnancy

- Studies have shown possible associations between maternal fever during early pregnancy and certain birth defects, including:



Neural tube defects

Orofacial clefts



Heart defects

Drier et al. Systematic review and meta-analyses: fever in pregnancy and health impacts in the offspring. Pediatrics. 2014 Mar;133(3):e674-88 https://pubmed.ncbi.nlm.nih.gov/24567014/
Kerr SM, Parker SE, Mitchell AA, Tinker SC, Werler MM. Periconceptional maternal fever, folic acid intake, and the risk for neural tube defects. Annals of Epidemiology. 2017 Dec;27(12):777-782.e1. https://pubmed.ncbi.nlm.nih.gov/29133009/