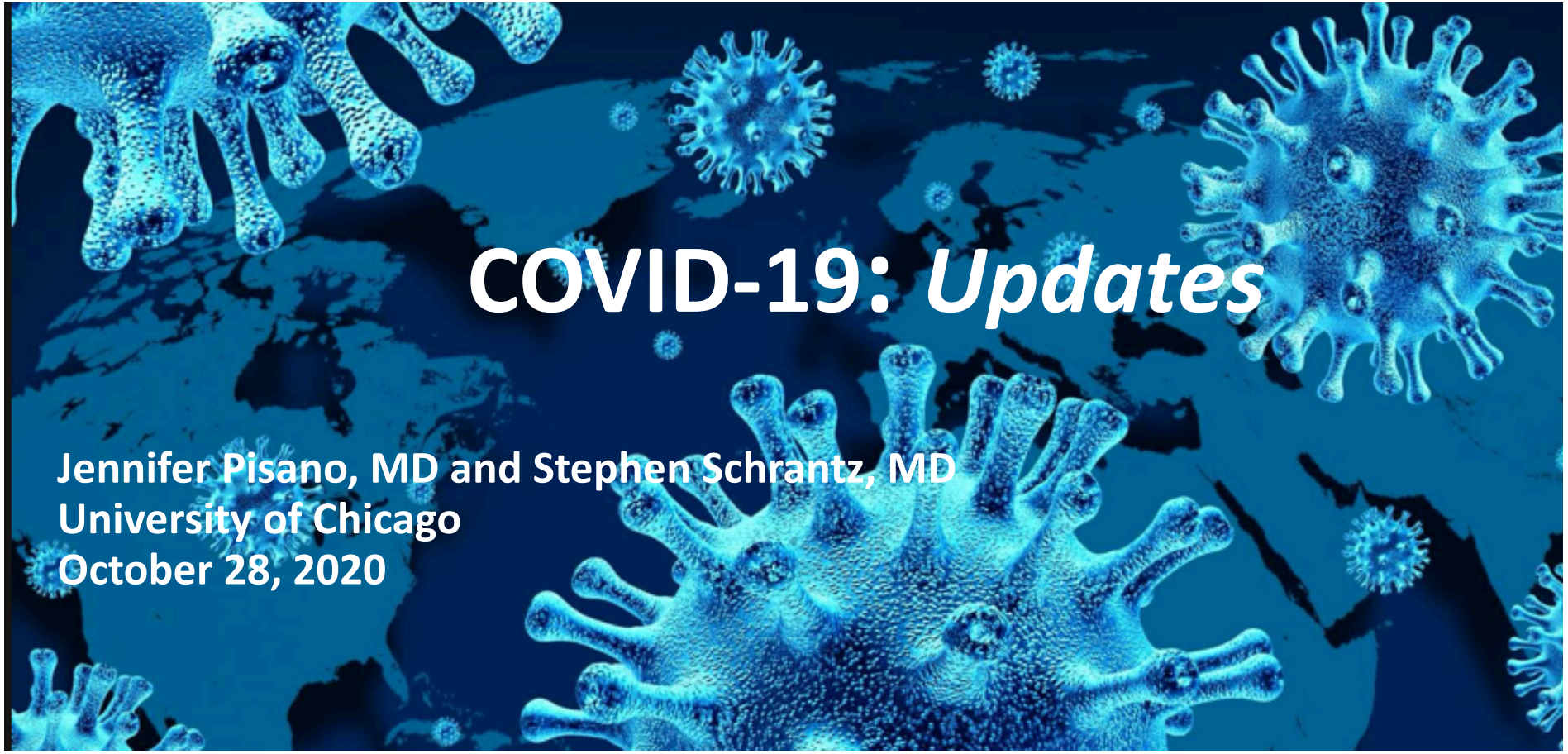


# COVID-19: *Updates*

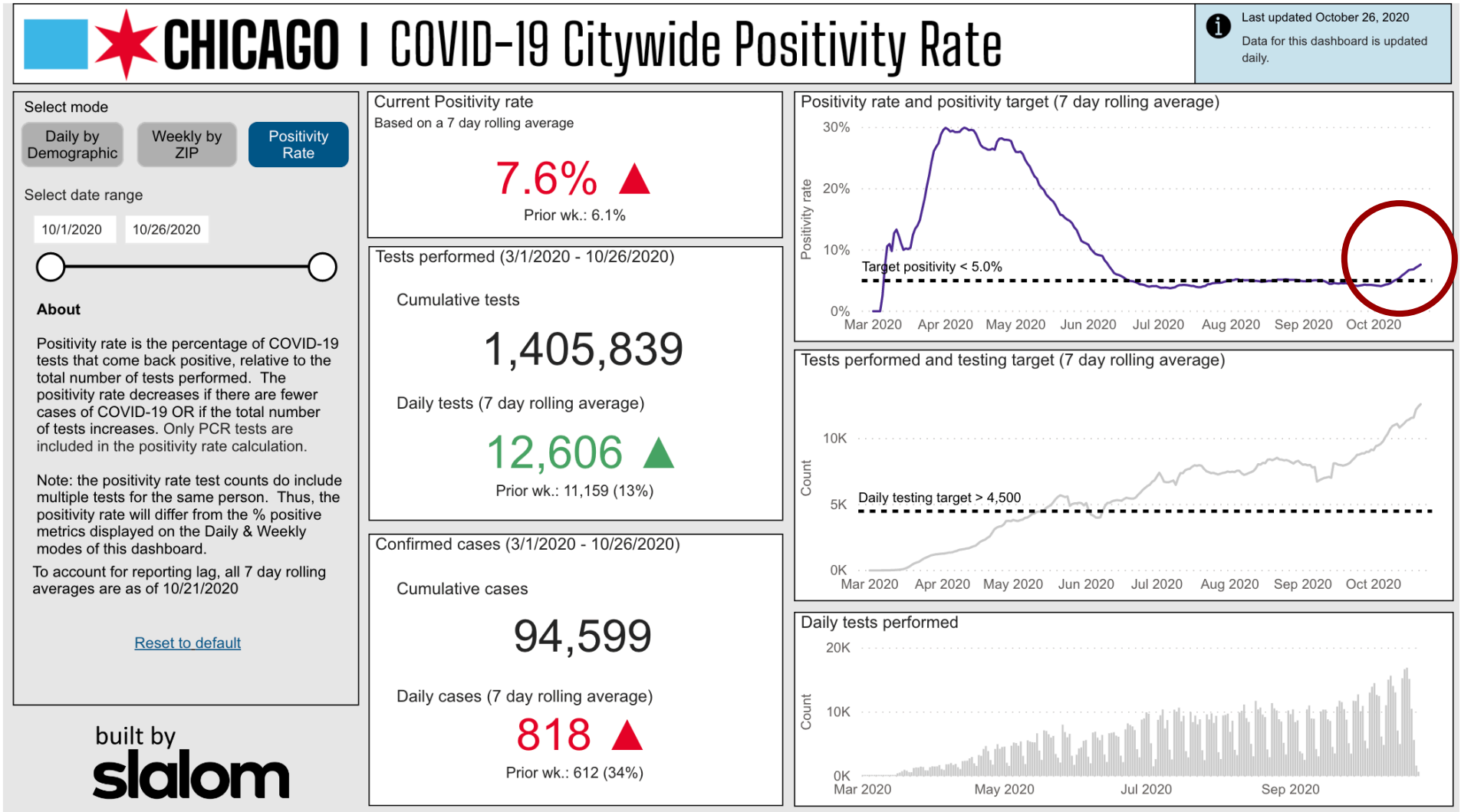
**Jennifer Pisano, MD and Stephen Schrantz, MD**
**University of Chicago**
**October 28, 2020**

ECHO CHICAGO

# Disclosures

- We have no relevant financial interests to disclose.

# Local Epidemiology

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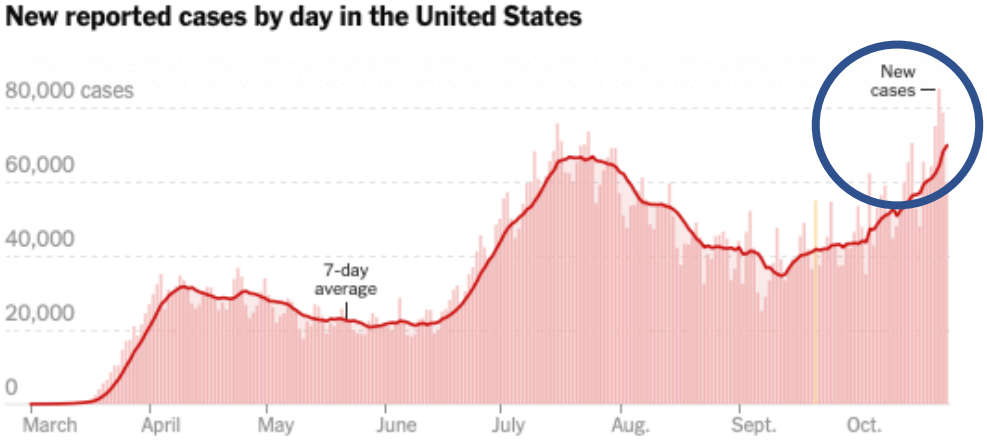
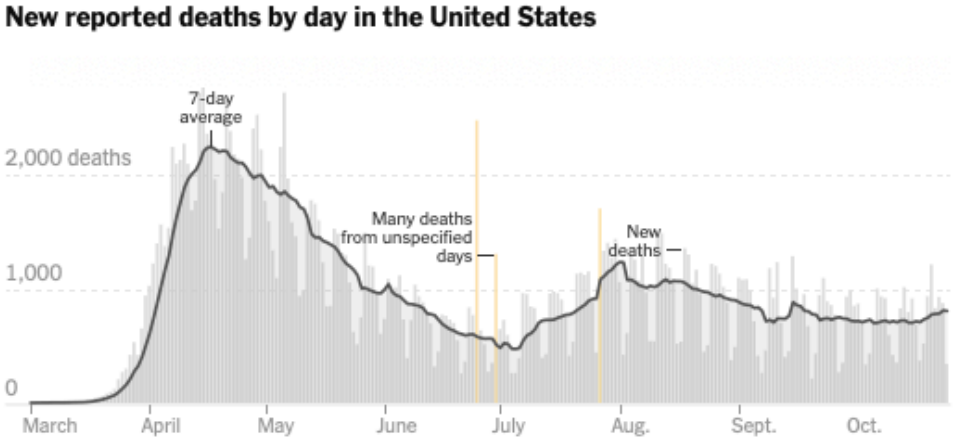
https://www.chicago.gov/city/en/sites/covid-19/home/covid-dashboard.html

# And Elsewhere…


https://www.nytimes.com/interactive/2020/us/coronavirus-us-cases.html

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CORONAVIRUS ILLINOIS

# New Chicago COVID-19 restrictions on bars, restaurants include indoor dining ban; Mayor Lightfoot pushes back against Governor Pritzker

## Indoor dining banned in Chicago and all bars & restaurants must close by 11 p.m. starting Friday

**New COVID-19 mitigations for Chicago and suburban Cook County**

**Bars:**

-No indoor service
-All outside bar service closes at 11:00 p.m.
-All bar patrons should be seated at tables outside
-No ordering, seating, or congregating at bar (bar stools should be removed)
-Tables should be 6 feet apart
-No standing or congregating indoors or outdoors while waiting for a table or exiting
-No dancing or standing indoors
-Reservations required for each party

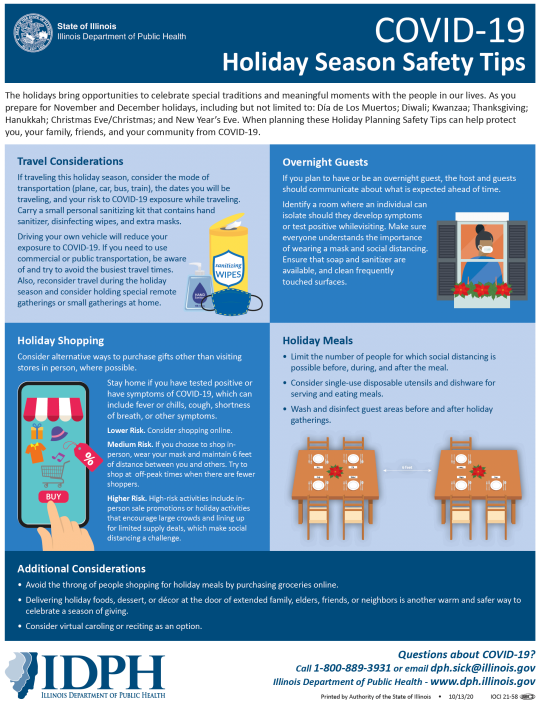
-No seating of multiple parties at one table

**Restaurants**

-No indoor dining or bar service
-All outdoor dining closes at 11:00 p.m.
-Outside dining tables should be 6 feet apart
-No standing or congregating indoors or outdoors while waiting for a table or exiting
-Reservations required for each party
-No seating of multiple parties at one table

**Meetings, Social Events, Gatherings**

-Limit to lesser of 25 guests or 25 percent of overall room capacity
-No party buses
-Gaming and Casinos close at 11:00 p.m., are limited to 25 percent capacity, and follow mitigations for bars and restaurants, if applicable



State of Illinois
Illinois Department of Public Health

COVID-19
Holiday Season Safety Tips

The holidays bring opportunities to celebrate special traditions and meaningful moments with the people in our lives. As you prepare for November and December holidays, including but not limited to: Dia de Los Muertos; Diwali; Kwanzaa; Thanksgiving; Hanukkah; Christmas Eve/Christmas; and New Year's Eve. When planning these Holiday Planning Safety Tips can help protect you, your family, friends, and your community from COVID-19.

**Travel Considerations**

If traveling this holiday season, consider the mode of transportation (plane, car, bus, train), the dates you will be traveling, and your risk to COVID-19 exposure while traveling. Carry a small personal sanitizing kit that contains hand sanitizer, disinfecting wipes, and extra masks.

Driving your own vehicle will reduce your exposure to COVID-19. If you need to use commercial or public transportation, be aware of and try to avoid the busiest travel times. Also, reconsider travel during the holiday season and consider holding special remote gatherings or small gatherings at home.

**Overnight Guests**

If you plan to have or be an overnight guest, the host and guests should communicate about what is expected ahead of time.

Identify a room where an individual can isolate should they develop symptoms or test positive while visiting. Make sure everyone understands the importance of wearing a mask and social distancing. Ensure that soap and sanitizer are available, and clean frequently touched surfaces.

**Holiday Shopping**

Consider alternative ways to purchase gifts other than visiting stores in person, where possible.

Stay home if you have tested positive or have symptoms of COVID-19, which can include fever or chills, cough, shortness of breath, or other symptoms.

**Lower Risk.** Consider shopping online.

**Medium Risk.** If you choose to shop in-person, wear your mask and maintain 6 feet of distance between you and others. Try to shop at off-peak times when there are fewer shoppers.

**Higher Risk.** High-risk activities include in-person sale promotions or holiday activities that encourage large crowds and lining up for limited supply deals, which make social distancing a challenge.

**Holiday Meals**

- Limit the number of people for which social distancing is possible before, during, and after the meal.
- Consider single-use disposable utensils and dishware for serving and eating meals.
- Wash and disinfect guest areas before and after holiday gatherings.

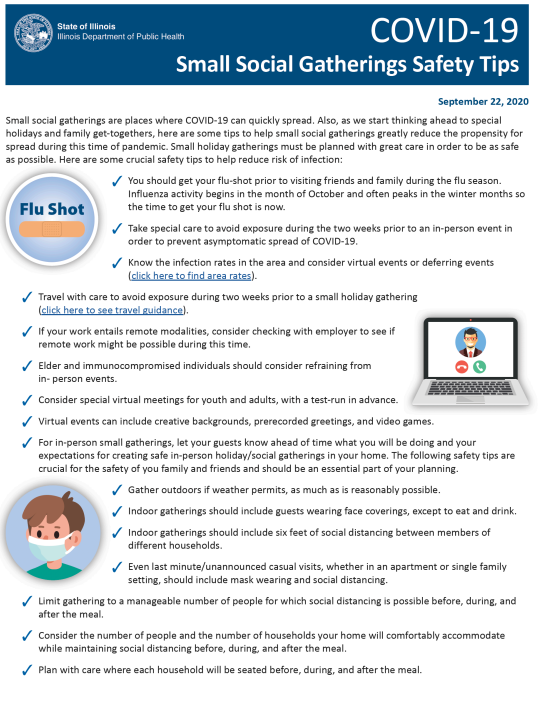
**Additional Considerations**

- Avoid the throng of people shopping for holiday meals by purchasing groceries online.
- Delivering holiday foods, dessert, or décor at the door of extended family, elders, friends, or neighbors is another warm and safer way to celebrate a season of giving.
- Consider virtual caroling or reciting as an option.

IDPH
Illinois Department of Public Health

*Questions about COVID-19?*
*Call 1-800-889-3931 or email dph.sick@illinois.gov*
*Illinois Department of Public Health - www.dph.illinois.gov*

Printed by Authority of the State of Illinois • 10/13/20 IOCI 21-58



State of Illinois
Illinois Department of Public Health

COVID-19
Small Social Gatherings Safety Tips

**September 22, 2020**

Small social gatherings are places where COVID-19 can quickly spread. Also, as we start thinking ahead to special holidays and family get-togethers, here are some tips to help small social gatherings greatly reduce the propensity for spread during this time of pandemic. Small holiday gatherings must be planned with great care in order to be as safe as possible. Here are some crucial safety tips to help reduce risk of infection:

Flu Shot

- ✓ You should get your flu-shot prior to visiting friends and family during the flu season. Influenza activity begins in the month of October and often peaks in the winter months so the time to get your flu shot is now.
- ✓ Take special care to avoid exposure during the two weeks prior to an in-person event in order to prevent asymptomatic spread of COVID-19.
- ✓ Know the infection rates in the area and consider virtual events or deferring events (click here to find area rates).
- ✓ Travel with care to avoid exposure during two weeks prior to a small holiday gathering (click here to see travel guidance).
- ✓ If your work entails remote modalities, consider checking with employer to see if remote work might be possible during this time.
- ✓ Elder and immunocompromised individuals should consider refraining from in- person events.
- ✓ Consider special virtual meetings for youth and adults, with a test-run in advance.
- ✓ Virtual events can include creative backgrounds, prerecorded greetings, and video games.
- ✓ For in-person small gatherings, let your guests know ahead of time what you will be doing and your expectations for creating safe in-person holiday/social gatherings in your home. The following safety tips are crucial for the safety of you family and friends and should be an essential part of your planning.
- ✓ Gather outdoors if weather permits, as much as is reasonably possible.
- ✓ Indoor gatherings should include guests wearing face coverings, except to eat and drink.
- ✓ Indoor gatherings should include six feet of social distancing between members of different households.
- ✓ Even last minute/unannounced casual visits, whether in an apartment or single family setting, should include mask wearing and social distancing.
- ✓ Limit gathering to a manageable number of people for which social distancing is possible before, during, and after the meal.
- ✓ Consider the number of people and the number of households your home will comfortably accommodate while maintaining social distancing before, during, and after the meal.
- ✓ Plan with care where each household will be seated before, during, and after the meal.

https://abc7chicago.com/health/new-chicago-covid-19-restrictions-take-effect-friday-/7414934/

https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/personal-social-activities.html

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RESTORE ILLINOIS

## Winter Updates to All Sports Policy

| HIGHER RISK | MODERATE RISK | LOWER RISK |
|---|---|---|
| • Basketball<br>• Boxing<br>• Football<br>• Hockey<br>• Lacrosse<br>• Martial Arts<br>• Rugby<br>• Ultimate Frisbee<br>• Wrestling | • Fencing<br>• Flag Football or 7v7 Football<br>• Paintball<br>• Racquetball<br>• Soccer<br>• Volleyball<br>• Water Polo<br>• Wheelchair Basketball | • Archery<br>• Badminton<br>• Baseball<br>• Bass Fishing<br>• Bowling<br>• Competitive Cheer<br>• Competitive Dance<br>• Climbing<br>• Crew<br>• Cross Country<br>• Cycling<br>• Disc Golf<br>• Golf<br>• Gymnastics<br>• Horseback Riding<br>• Ice Skating<br>• Ropes Courses<br>• Sailing, Canoeing, Kayaking<br>• Sideline Spirit<br>• Skateboarding<br>• Softball<br>• Skiing<br>• Swimming/Diving<br>• Tennis<br>• Track and Field<br>• Weight Lifting |

Below are the **Type of Play Levels:**

Updated Tues, Oct 27, 2020

| | |
|---|---|
| **Level 1** | No-contact practices, and trainings only |
| **Level 2** | Intra-team scrimmages allowed, with parental consent for minors; no competitive play |
| **Level 3** | Intra-conference or Intra-EMS-region[1] or intra-league play/meets only; state- or league-championship game/meet allowed for low-risk sports only |
| **Level 4** | Tournaments, out-of-conference/league play, out-of-state play allowed; championship games allowed |

**Current Conditions Allow for the Following Types of Play per Sport Risk Level:**

- Lower-risk sports can currently play at Levels 1, 2, and 3
- Medium-risk sports can currently play at Level 1 and 2
- Higher-risk sports can currently play at Level 1

- Updated guidance moves basketball from medium to high risk
- Cheer and dance are categorized as lower risk if masking and distancing are enforced
- Low risk sports of swimming, diving, gymnastics, bowling are permitted to play during the winter
- Make temperature checks available
- Monitor for symptoms
- Masks should be worn by everyone in attendance

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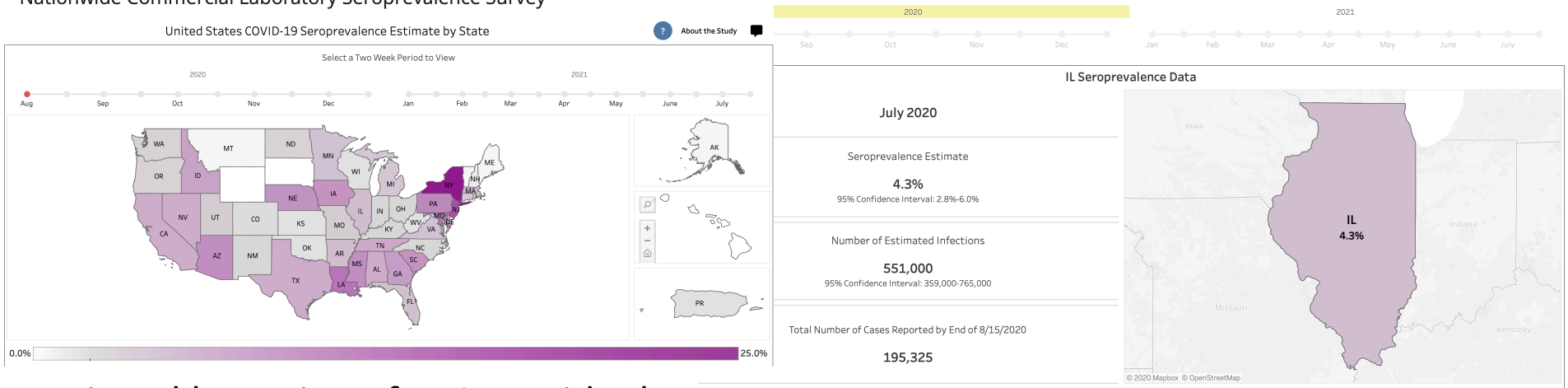
https://dceocovid19resources.com/assets/Restore-Illinois/businessguidelines4/youthsports.pdf

## Nationwide Commercial Laboratory Seroprevalence Survey




- Biweekly testing of ~50K residual commercial lab specimens for SARS-CoV-2 antibodies
- Seroprevalence ranges 0.4 -> 23%
- Areas of highest seroprevalence, rates were highest in children and young adults

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https://covid.cdc.gov/covid-data-tracker/#national-lab

# Is exposure risk cumulative?

**Close Contact**

Someone who was within 6 feet of an infected person for a cumulative total of 15 minutes or more over a 24-hour period* starting from 2 days before illness onset (or, for asymptomatic patients, 2 days prior to test specimen collection) until the time the patient is isolated.

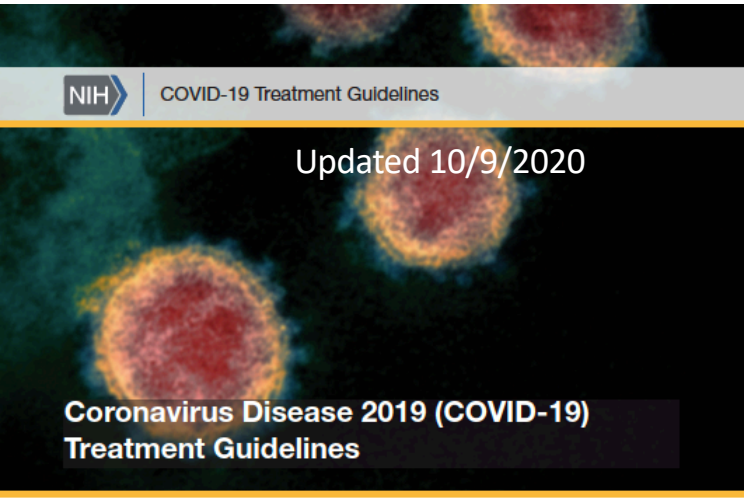
** Individual exposures added together over a 24-hour period (e.g., three 5-minute exposures for a total of 15 minutes). Data are limited, making it difficult to precisely define "close contact;" however, 15 cumulative minutes of exposure at a distance of 6 feet or less can be used as an operational definition for contact investigation. Factors to consider when defining close contact include proximity (closer distance likely increases exposure risk), the duration of exposure (longer exposure time likely increases exposure risk), whether the infected individual has symptoms (the period around onset of symptoms is associated with the highest levels of viral shedding), if the infected person was likely to generate respiratory aerosols (e.g., was coughing, singing, shouting), and other environmental factors (crowding, adequacy of ventilation, whether exposure was indoors or outdoors). Because the general public has not received training on proper selection and use of respiratory PPE, such as an N95, the determination of close contact should generally be made irrespective of whether the contact was wearing respiratory PPE. At this time, differential determination of close contact for those using fabric face coverings is not recommended.*

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Early Release / Vol. 69
October 21, 2020

## COVID-19 in a Correctional Facility Employee Following Multiple Brief Exposures to Persons with COVID-19 — Vermont, July–August 2020

Julia C. Pringle, PhD[1,2]; Jillian Leikauskas, MPH[2]; Sue Ransom-Kelley[3]; Benjamin Webster[3]; Samuel Santos[3]; Heidi Fox, MSN[3]; Shannon Marcoux[3]; Patsy Kelso, PhD[2]; Natalie Kwit, DVM[2]

For COVID-19, a close contact is anyone who was within 6 feet of an infected person for a total of 15 minutes or more. An infected person can spread COVID-19 starting from 48 hours (or 2 days) before the person has any symptoms or tests positive for COVID-19.




### Serologic Testing and Immunity to SARS-CoV-2 Infection

The Panel **recommends against** the use of serologic testing to determine whether a person is immune to SARS-CoV-2 infection (**AIII**). If serologic tests are performed and antibody is detected, results should be interpreted with caution for the following reasons:

- It is currently unknown how long antibodies persist following infection, *and*
- It is currently unknown whether the presence of antibody confers protective immunity against future infection.

In communities where the prevalence of SARS-CoV-2 infection is low, the proportion of positive tests that are false positives may be quite high. In these situations, confirmatory testing using a second independent antibody assay, ideally one that uses a different antigenic target (e.g., the nucleocapsid phosphoprotein if the first assay targeted the spike glycoprotein), can substantially improve the probability that persons with a positive test result are antibody positive.

Assuming the test is reliable, serologic tests to identify recent or prior SARS-CoV-2 infection may be used to:

- Determine who may be eligible to donate blood to manufacture convalescent plasma.
- Measure the immune response in SARS-CoV-2 vaccine studies.
- Estimate the proportion of the population exposed to SARS-CoV-2.

Lastly, serologic tests **should not be used** to:

- Make decisions about the grouping of persons residing in or being admitted to congregate settings (e.g., schools, dormitories, correctional facilities), *or*
- Determine whether persons should return to the workplace.

### Rationale

AIIRs lower the risk of cross-contamination among rooms and lower the risk of infection for staff and patients outside the room when aerosol-generating procedures are performed. AIIRs were effective in preventing virus spread during the SARS epidemic.[2] If an AIIR is not available, a high-efficiency particulate air (HEPA) filter should be used, especially for patients on high-flow nasal cannula or noninvasive ventilation. HEPA filters reduce virus transmission in simulations.[5]

### Recommendations

- For health care workers who are providing usual care for non-ventilated patients with COVID-19, the Panel recommends using an N95 respirator (or equivalent or higher-level respirator) or a surgical mask, in addition to other PPE (i.e., gloves, gown, and eye protection such as a face shield or safety goggles) (**AII**).
- For health care workers who are performing non-aerosol-generating procedures on patients with COVID-19 who are on closed-circuit mechanical ventilation, the Panel recommends using an N95 respirator (or equivalent or higher-level respirator), in addition to other PPE (i.e., gloves, gown, and eye protection such as a face shield or safety goggles) because ventilator circuits may become disrupted unexpectedly (**BIII**).

### Rationale

There is evidence from viral diseases, including SARS, that both surgical masks and N95 masks reduce transmission of infection.[6] Current evidence suggests that surgical masks are probably not inferior to N95 respirators for preventing transmission of laboratory-confirmed, seasonal respiratory viral infections (e.g., influenza).[7,8] A recent systematic review and meta-analysis of randomized controlled trials that compared the protective effect of medical masks with N95 respirators demonstrated that the use of medical masks did not increase laboratory-confirmed viral (including coronavirus) respiratory infection or clinical respiratory illness.[9]

- Surgical mask or N95 **PLUS eye protection**/gowns/gloves for usual care PLUS eye protection for usual care
- N95 for usual care of patients on closed-circuit ventilators (PLUS gowns/gloves/eye protection (in case circuit is disrupted)

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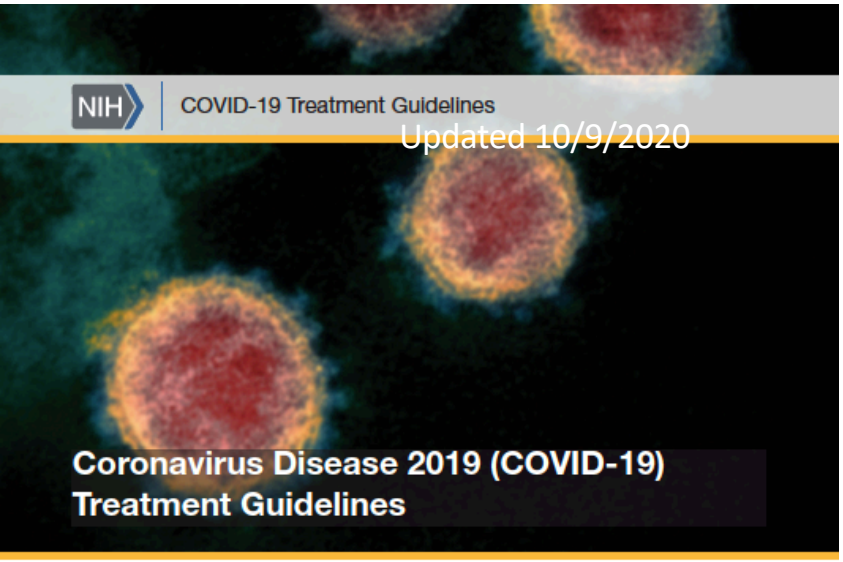



No rec for routine VTE prophylaxis for patients *being discharged* but may be beneficial in some high risk patient populations

***Patients with COVID-19 Who Are Discharged from the Hospital:***

- Routine post-discharge VTE prophylaxis is **not recommended** for patients with COVID-19 (AIII). However, the benefits of post-discharge prophylaxis for certain high-risk patients without COVID-19 led to the Food and Drug Administration approval of two regimens: rivaroxaban 10 mg daily for 31 to 39 days, and betrixaban 160 mg on Day 1, followed by betrixaban 80 mg once daily for 35 to 42 days.[16,17] Inclusion criteria for the trials that studied these regimens included:
  - Modified IMPROVE-VTE score ≥4; ***or***
  - Modified IMPROVE-VTE score ≥2 and D-dimer level >2 times the upper limit of normal;[16] ***or***
  - Age ≥75 years; ***or***
  - Age >60 years and D-dimer level >2 times the upper limit of normal; ***or***
  - Age 40 to 60 years, D-dimer level >2 times the upper limit of normal, and previous VTE event or cancer.[17]
- Any decision to use post-discharge VTE prophylaxis should consider the individual patient's risk factors, including reduced mobility, bleeding risks, and feasibility.

Figure 1. Recommendations for Pharmacologic Management of Patients with COVID-19 Based on Disease Severity

| DISEASE SEVERITY | PANEL'S RECOMMENDATIONS (Recommendations are listed in order of preference in each category below; however, all options are considered acceptable.) |
|---|---|
| Not Hospitalized or Hospitalized but Does Not Require Supplemental Oxygen | No specific antiviral or immunomodulatory therapy recommended<br>The Panel **recommends against** the use of **dexamethasone (AI)**<br>See the Remdesivir section for a discussion of the data on using this drug in hospitalized patients with moderate COVID-19.[a] |
| **Hospitalized and Requires Supplemental Oxygen** (but Does Not Require Oxygen Delivery Through a High-Flow Device, Noninvasive Ventilation, Invasive Mechanical Ventilation, or ECMO) | **Remdesivir** 200 mg IV for one day, followed by remdesivir 100 mg IV once daily for 4 days or until hospital discharge, whichever comes first **(AI)**[b,c,d]<br>*or*<br>**Remdesivir** (dose and duration as above) plus **dexamethasone**[e] 6 mg IV or PO for up to 10 days or until hospital discharge, whichever comes first **(BIII)**[f]<br>If **remdesivir** cannot be used, **dexamethasone**[e] may be used instead **(BIII)** |
| **Hospitalized and Requires Oxygen Delivery Through a High-Flow Device or Noninvasive Ventilation** | **Dexamethasone**[e] plus **remdesivir** at the doses and durations discussed above **(AIII)**[f]<br>*or*<br>**Dexamethasone**[e,g] at the dose and duration discussed above **(AI)** |
| **Hospitalized and Requires Invasive Mechanical Ventilation or ECMO** | **Dexamethasone**[e,g] at the dose and duration discussed above **(AI)**<br>*or*<br>**Dexamethasone**[e] plus **remdesivir** for patients who have recently been intubated at the doses and durations discussed above **(CIII)**[f] |

**Rating of Recommendations:** A = Strong; B = Moderate; C = Optional
**Rating of Evidence:** I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies; III = Expert opinion

[a] The Panel recognizes that there may be situations in which a clinician judges that remdesivir is an appropriate treatment for a hospitalized patient with moderate COVID-19 (e.g., a patient who is at a particularly high risk for clinical deterioration). However, the Panel finds the data insufficient to recommend either for or against using remdesivir as routine treatment for all hospitalized patients with moderate COVID-19.
[b] Treatment duration may be extended to up to 10 days if there is no substantial clinical improvement by Day 5.
[c] The Panel recognizes there is a theoretical rationale for initiating remdesivir plus dexamethasone in patients with rapidly progressing COVID-19.
[d] For patients who are receiving remdesivir but progress to requiring oxygen through a high-flow device, noninvasive ventilation, invasive mechanical ventilation, or ECMO, remdesivir should be continued until the treatment course is completed.
[e] If dexamethasone is not available, equivalent doses of other corticosteroids, such as prednisone, methylprednisolone, or hydrocortisone, may be used. See Corticosteroids for more information.
[f] The combination of dexamethasone and remdesivir has not been studied in clinical trials; see text for the rationale for using this combination.

**Key:** ECMO = extracorporeal membrane oxygenation; IV = intravenously; PO = orally

ECHO CHICAGO

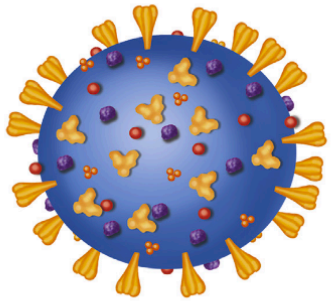
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 76, NO. 18, 2020

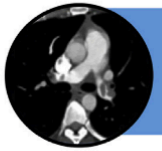

# Registry of Arterial and Venous Thromboembolic Complications in Patients With COVID-19

Gregory Piazza, MD, MS,[a] Umberto Campia, MD,[a] Shelley Hurwitz, PhD,[b] Julia E. Snyder, BS,[a] Samantha M. Rizzo, BA,[a] Mariana B. Pfeferman, BS,[a] Ruth B. Morrison, RN, BSN, CVN,[a] Orly Leiva, MD,[c] John Fanikos, RPh, MBA,[d] Victor Nauffal, MD,[a] Zaid Almarzooq, MD,[a] Samuel Z. Goldhaber, MD[a]

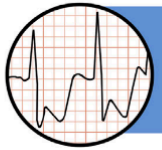
- Objective: Assess frequency of arterial and venous thromboembolic disease, risk factors, prevention and management patterns and outcomes in patients with COVID-19
- Retrospective cohort of 1,114 patients with COVID-19, analyzed by site of care (ICU, non-ICU in hospital, outpatient)
- 55% White, 22.3% Hispanic/Latinx, 14% Black
- HTN (35.8%), hyperlipidemia (28.6%), DM (18%)
- Prophylactic anticoagulation given in 89.4%

**CENTRAL ILLUSTRATION** Cardiovascular Complications in Patients With Coronavirus Disease-2019 at 30 Days From Diagnosis

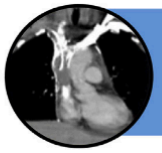


**Major Arterial or Venous Thromboembolism**
- ICU 35.3%
- Hospitalized non-ICU 2.6%



**Major Adverse Cardiovascular Events**
- ICU 45.9%
- Hospitalized non-ICU 6.1%



**Symptomatic Venous Thromboembolism**
- ICU 27%
- Hospitalized non-ICU 2.2%
- Despite 85%-90% thromboprophylaxis rate

**Piazza, G. et al. J Am Coll Cardiol. 2020;76(18):2060–72.**

Cardiovascular complications, including major arterial or venous thromboembolism, in 1,114 patients with coronavirus disease-2019 (COVID-19) at 30 days from diagnosis. Adjudicated major arterial (including myocardial infarction, stroke/transient ischemic attack, systemic embolism, and major adverse limb events) or venous thromboembolism, major adverse cardiovascular events, and symptomatic venous thromboembolism (VTE) (including catheter- and device-related deep vein thrombosis [DVT]) were frequent in patients with COVID-19 admitted to the intensive care unit (ICU) setting (n = 170). Among those admitted to the non-ICU setting (n = 229), the frequency of major arterial or venous thromboembolism, major adverse cardiovascular events, and symptomatic VTE was also elevated but lower than for those with critical illness. The increased frequency of thromboembolic complications occurred in the context of a relative high rate of thromboprophylaxis prescription. Outpatients (n = 715) were considered to be low risk for major arterial or venous thromboembolism, major adverse cardiovascular events, and symptomatic VTE.

((( ECHO )))
CHICAGO

JAMA Pediatrics | Original Investigation

# Outcomes of Neonates Born to Mothers With Severe Acute Respiratory Syndrome Coronavirus 2 Infection at a Large Medical Center in New York City

Dani Dumitriu, MD, PhD; Ukachi N. Emeruwa, MD, MPH; Erin Hanft, MD; Grace V. Liao, MD; Elizabeth Ludwig, MD; Lauren Walzer, DO; Brittany Arditi, MD, MSCR; Minna Saslaw, MD; Maria Andrikopoulou, MD, PhD; Tessa Scripps, MD; Caitlin Baptiste, MD; Adrita Khan, MD; Noelle Breslin, MD; David Rubenstein, MD; Lynn L. Simpson, MD; Margaret H. Kyle, BA; Alexander M. Friedman, MD, MPH; Daniel S. Hirsch, MD; Russell S. Miller, MD; Cristina R. Fernández, MD, MPH; Karin M. Fuchs, MD, MHA; M. Kathleen Kaown, MD; Melissa E. Glassman, MD, MPH, IBCLC; Ashley Stephens, MD; Archana Gupta, MD; Sally Sultan, MD; Caroline Sibblies, MD; Susan Whittier, PhD; Wanda Abreu, MD, IBCLC; Francis Akita, MD; Anna Penn, MD, PhD; Mary E. D'Alton, MD; Jordan S. Orange, MD, PhD; Dena Goffman, MD; Lisa Saiman, MD, MPH; Melissa S. Stockwell, MD, MPH; Cynthia Gyamfi-Bannerman, MD, MSc

- Objective: Describe outcomes of neonates born to mothers with perinatal SARS-CoV-2 infection and the IC practices associated with these outcomes
- Retrospective cohort analysis for 101 neonates born to 100 mothers positive for or with suspected SARS-CoV-2 infection 3/13-4/24/2020
- 82 infants in well-baby nurseries; **infants roomed in with moms and moms were required to wear masks**
- 19 infants in NICUs
- **Direct breast feeding after appropriate hygiene was encouraged**
- 141 tests obtained from 101 newborns on day 0-25 of life.
  - 2 newborns had indeterminate test results (low viral load?)
    - 1 never was retested but was well and other had negative results on retesting.
- Maternal severe/critical COVID-19 was associated with newborns born approximately 1 week earlier (37.9 v 39.1 weeks, p=.02 and at increased risk of requiring phototherapy (30 v 7%, p=.04) compared with asymptomatic/mild COVID-19
- **No clinical evidence of vertical transmission was identified in 101 newborns of mothers positive for or with suspected SARS-CoV-2 infection**

# Remdesivir (Veklury)– Now FDA Approved

- For use in adult and pediatric patients >12 years of age and weighing at least 40 kilograms (about 88 pounds) for the treatment of COVID-19 requiring hospitalization. Pediatric trials are ongoing.
- Remdesivir should only be administered in a hospital or in a healthcare setting capable of providing acute care comparable to inpatient hospital care.
- Remdesivir, which was originally developed as a treatment for Ebola and hepatitis C, interferes with the reproduction of viruses by jamming itself into new viral genes
- Studies have NOT found that remdesivir prevented deaths in patients with Covid-19.
- *Dr. Anthony Fauci, director of the National Institute of Allergy and Infectious Diseases, acknowledged in the spring that remdesivir was not a "knockout" drug.*

# Remdesivir Studies

| Study | Population | intervention | Outcome |
|---|---|---|---|
| Wang Y et al.<br>The Lancet, April 2020<br>Double blind, placebo-controlled, multi-center, RCT<br><br>*stopped early | N=237 hospitalized patients with SARS-CoV2 virus, with CXR changes and O2<94% RA | Remdesivir 10 days vs. placebo, 2:1 | • No associated difference in time to clinical improvement |
| Beigel JH et al.<br>ACTT-1, NEJM<br>May2020<br>Double blind, placebo-controlled, multi-center, RCT<br>*stopped early | N=1063 hospitalized patients with SARS-CoV2 virus and CXR changes and O2<94% RA | Remdesivir x 10 days vs. placebo | • Recovery time of patients receiving 10d of Rem vs. placebo was shorter (11 vs 15 days)<br>• No mortality difference bw drug (7.1%) and placebo (11.9%) |
| Goldman JD et al.<br>NEJM, May 2020<br>Randomized, open-label, phase 3 trial | N=397 hospitalized patients with SARS-CoV2, CXR changes and O2<94% RA | Remdesivir 5 vs. 10 days, 1:1<br><br>*10d group sicker at baseline | • Clinical status assessed day 14, assessed by a 7-point ordinal scale found no significant difference 5 v 10d<br>• Mortality lower 5d (8 v 11%) |
| Spinner, CD et al.<br>JAMA, August 2020<br>Randomized, open-label,multi-center phase 3 trial | N=584 hospitalized adults with moderate COVID-19 (pulmonary infiltrates **and RA O2%>94** | 10 days remdesivir vs. 5 days remdesivir vs. standard of care, 1:1:1<br><br>*Mean length of treatment 5d v 6 d (10-d arm) | • 5-day Rem group had statistically significantly higher odds of better clinical status (p=.02) vs. SOC on D11.<br>• No difference between 10-d and SOC groups (p=.18)<br>*difference of unclear clinical importance |

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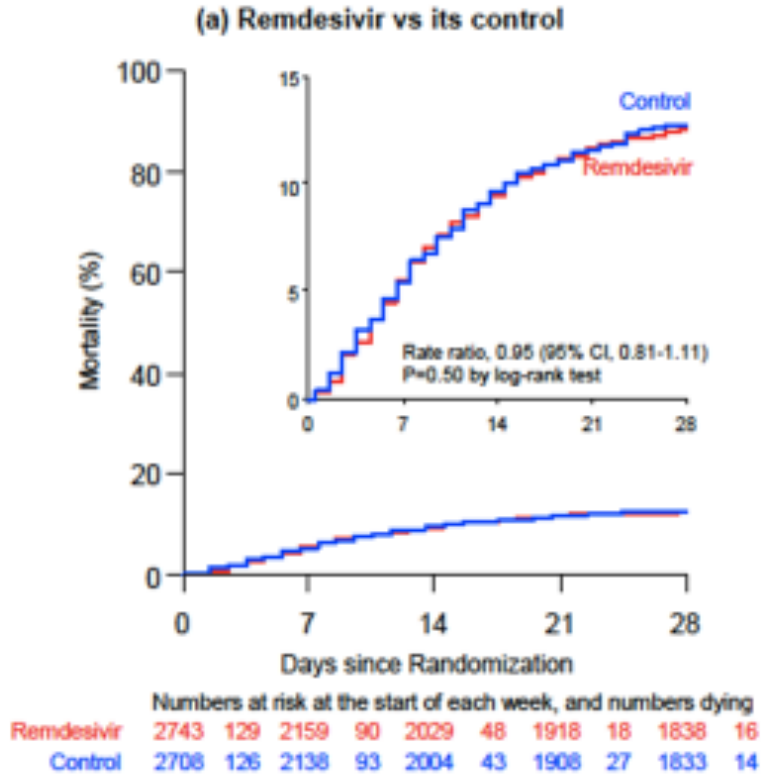
# SOLIDARITY: Repurposed antivirals vs standard of care for COVID-19

- Randomized, open-label study conducted in 11,266 hospitalized adults with COVID-19
- Study drugs: Remdesivir, hydroxychloroquine, lopinavir/ritonavir, and interferon-β1a
- Results: None of the interventions better than standard of care in reducing mortality or duration of hospitalization
- Study not yet peer-reviewed

https://www.medrxiv.org/content/10.1101/2020.10.15.20209817v1

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# WHO SOLIDARITY Trial – Solid?

- Study drugs were Remdesivir, Hydroxychloroquine, Lopinavir (fixed-dose combination with Ritonavir) and Interferon-β1a (mainly subcutaneous; initially with Lopinavir, later not). COVID-19 inpatients were randomized equally between whichever study drugs were locally available and open control (up to 5 options: 4 active and local standard-of-care). The intent-to-treat primary analyses are of in-hospital mortality in the 4 pairwise comparisons of each study drug vs its controls (concurrently allocated the same management without that drug, despite availability). Kaplan-Meier 28-day risks are unstratified; log-rank death rate ratios (RRs) are stratified for age and ventilation at entry.
- 405 hospitals in 30 countries 11,266 adults were randomized, with 2750 allocated Remdesivir, 954 Hydroxychloroquine, 1411 Lopinavir, 651 Interferon plus Lopinavir, 1412 only Interferon, and 4088 no study drug. Compliance was 94-96% midway through treatment, with 2-6% crossover.
- **Major critiques of this study** – lack of a consistent control arm and many in remdesivir arm were treated LATE in disease course
- *As for remdesivir, "I don't think this study is the nail in the coffin," said Dr. Taison Bell, a critical care physician at the University of Virginia. "But I do think it shows that we have to be selective about the patient population we use it in."*

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https://www.nytimes.com/2020/10/15/health/coronavirus-remdesivir-who.html
https://www.medrxiv.org/content/10.1101/2020.10.15.20209817v1.full.pdf

# Updates on COVID-19 Vaccines

- Both adenoviral vectored vaccine trials (AstraZeneca and Janssen) are back up and enrolling after SAEs halted enrollment and the DMSB's investigated concluding the vaccines are not implicated
- Moderna trial has met is 30,000 enrollee mark – did not meet its goal in African-Americans
- Pfizer is near its 44,000 and CEO has said it may be able to produce some results before Thanksgiving (same as Moderna)
- Pfizier's first analysis will come when there have been a total of only 32 cases of Covid-19 across the company's entire 42,000-volunteer study
  - NOT happened yet!
- It would be considered to be positive, Pfizer has said, if six or fewer of those 32 cases occurred in the group that received the vaccine, with the rest occurring in the group that received the placebo. The trial is expected to continue until 150 of the volunteers in the study have had Covid-19



https://www.statnews.com/2020/10/27/no-news-on-pfizers-covid-19-vaccine-is-good-news-and-bad-news/

# Importance of Asymptomatic Spread

- The likelihood that approximately 40% to 45% of those infected with SARS-CoV-2 will remain asymptomatic suggests that the virus might have greater potential than previously estimated to spread silently and deeply through human populations[1]
- Asymptomatic persons can transmit SARS-CoV-2 to others for an extended period, perhaps longer
- *Recent study in SNFs showed similar findings of asymptomatic and presymptomatic spread*[2]

**Table. Percentage of 5403 Cumulative SARS-CoV-2 Resident Cases Who Were Asymptomatic, Presymptomatic, or Symptomatic at Time of Initial Test in SNFs That Underwent at Least 1 Unit-Based or Facility-Wide Point Prevalence Survey as of July 15[a]**

| Variable | No. (%) | | | *P* value |
|---|---|---|---|---|
| | Skilled nursing facility testing type | | | |
| | 1 Or more unit-based point prevalence surveys (n = 9) | 1 Or more facility-wide point prevalence surveys (n = 173) | Total (n = 182) | |
| Asymptomatic | 145 (37.0) | 2049 (40.9) | 2194 (40.6) | .02 |
| Presymptomatic | 64 (16.3) | 969 (19.3) | 1033 (19.1) | |
| Symptomatic | 183 (46.7) | 1993 (39.8) | 2176 (40.3) | |
| Total cases | 392 (100.0) | 5011 (100.0) | 5403 (100.0) | |

[1] *Ann Intern Med.* 2020;173:362-367. doi:10.7326/M20-301
[2] JAMA Int Med doi:10.1001/jamainternmed.2020.5664

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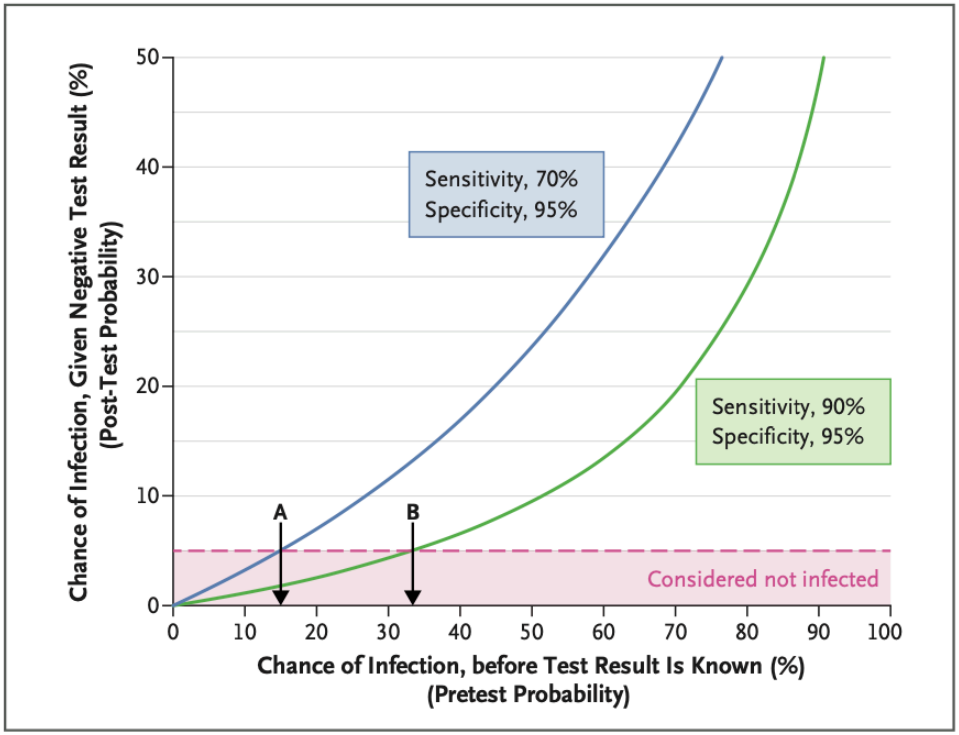
# Accurate tests?

- Designing a reference standard for measuring the sensitivity in asymptomatic people is an unsolved problem
- Simply following people for the subsequent development of symptoms may be inadequate, since they may remain asymptomatic yet be infectious
- Graph highlights need to reduce pretest probability (masks, social distancing)




**Chance of SARS-CoV-2 Infection, Given a Negative Test Result, According to Pretest Probability.**

n engl j med 383;6 nejm.org August 6, 2020

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# False Positives!

- **Individual perspective**
  - For swab tests taken for screening purposes before elective procedures or surgeries: unnecessary treatment cancellation or postponement
  - For swab tests taken for screening purposes during urgent hospital admissions: potential exposure to infection following a wrong pathway in hospital settings as an in-patient
  - Financial losses related to self-isolation, income losses, and cancelled travel, among other factors
  - Psychological damage due to misdiagnosis or fear of infecting others, isolation, or stigmatization
- **Global perspective**
  - Misspent funding (often originating from taxpayers) and human resources for test and trace
  - Unnecessary testing
  - Funding replacements in the workplace
  - Various business losses
  - Overestimating COVID-19 incidence and the extent of asymptomatic infection
  - Misleading diagnostic performance, potentially leading to mistaken purchasing or investment decisions if a new test shows high performance by identification of negative reference samples as positive (ie, is it a false positive or does the test show higher sensitivity than the other comparator tests used to establish the negativity of the test sample?)
  - Misdirection of policies regarding lockdowns and school closures
  - Increased depression and domestic violence (eg, due to lockdown, isolation, and loss of earnings after a positive test).



***Lancet Respir Med* 2020** September 29, 2020 https://doi.org/10.1016/ S2213-2600(20)30453-7

# False Negatives!

- Diagnostic testing will help in safely opening the country, but only if the tests are highly sensitive and validated under realistic conditions against a clinically meaningful reference standard.
- FDA should ensure that manufacturers provide details of tests' clinical sensitivity and specificity at the time of market authorization; tests without such information will have less relevance to patient care.
- Measuring test sensitivity in asymptomatic people is an urgent priority. It will also be important to develop methods (e.g., prediction rules) for estimating the pretest probability of infection (for asymptomatic and symptomatic people) to allow calculation of post-test probabilities after positive or negative results
- Negative results even on a highly sensitive test cannot rule out infection if the pretest probability is high, so clinicians should not trust unexpected negative results (i.e., assume a negative result is a "false negative" in a person with typical symptoms and known exposure). It's possible that performing several simultaneous or repeated tests could overcome an individual test's limited sensitivty; however, such strategies need validation.
- Thresholds for ruling out infection need to be developed for a variety of clinical situations. Since defining these thresholds is a value judgement



n engl j med 383;6 nejm.org August 6, 2020

# More testing in some settings is useful

- Serial antigen testing of asymptomatic persons within a closed congregate setting, such as a long-term care facility or a correctional facility, has been suggested by the CDC as a potential strategy to rapidly identify cases of SARS-CoV-2 infection to prevent further transmission in the facility
- CDC cites modeling evidence shows that outbreak control depends largely on the frequency of testing and the speed of reporting and is only marginally improved by high test sensitivity

**When testing asymptomatic persons without a known exposure**

It is important to emphasize that negative test results only indicate that the test did not detect the virus at the time the test was taken. With widespread community transmission, any person who interacts with other people runs a daily risk of acquiring COVID-19. This daily risk increases in crowded places, in confined spaces (especially indoors), with close contact, and when protective actions, such as maintaining physical distancing, correctly using face coverings when around others, frequent hand hygiene, and other job-specific protective measures, are not followed.

A false negative result can happen when an infected individual is still incubating the infection (i.e., that the test was taken too early in the course of the infection) and/or that the test simply failed to detect the SARS-CoV-2 virus.

A negative test does NOT mean the person can safely ignore physical distancing and mask requirements. Refer the patient to Information about Testing.

https://doi.org/10.1101/2020.06.22.20136309
http://publichealth.lacounty.gov/acd/ncorona2019/testing/

# Employees: Exposure risk & required quarantines

| Exposed individual's PPE | COVID+ individual's PPE | Situation (<6 feet for >15 minutes) | Risk | Quarantine |
|---|---|---|---|---|
| Mask | Mask | Any situation except aerosol-generating procedure (AGP) | Low | No |
| Mask and eye protection | None | Any situation except AGP | Low | No |
| N95* and eye protection | None or Mask | Any situation, including AGPs | Low | No |
| Mask | None | Any situation | Med/High | Yes |
| None | Mask | Any situation | Med/High | Yes |
| None | None | Any situation | Med/High | Yes |
| Mask and eye protection | None | AGP | Med/High | Yes |

Quarantine for exposed HCW: Isolate at home for 14 days. Asymptomatic HCW who do NOT care for patients with stem cell transplants or new solid organ transplants can be tested for COVID-19 on Day 5-7 after exposure and return to work on Day 8 if test is negative. See page 7 for travel-related exposure quarantine rules.

# Quarantine is the SAFER option!

- The Pandemic continues to spread and is not going away!
- ASYMPTOMATIC SPREAD!
- Tests are not accurate enough to be trusted

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