COVID-19: Update
More Than Ever A Moving Target

Boca Grande Health Clinic Foundation
November 4, 2020

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Johns Hopkins Univ. Coronavirus Resource Center

EPIDEMIOLOGY, TRANSMISSION & TRAVEL

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Global COVID-19 (11/19/2020)

https://gisanddata.maps.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6

COVID CASES/100,000 – 7d average

Reported cases per 100,000 residents by county since last week

JHU/ Wash Post 11/19/20

4
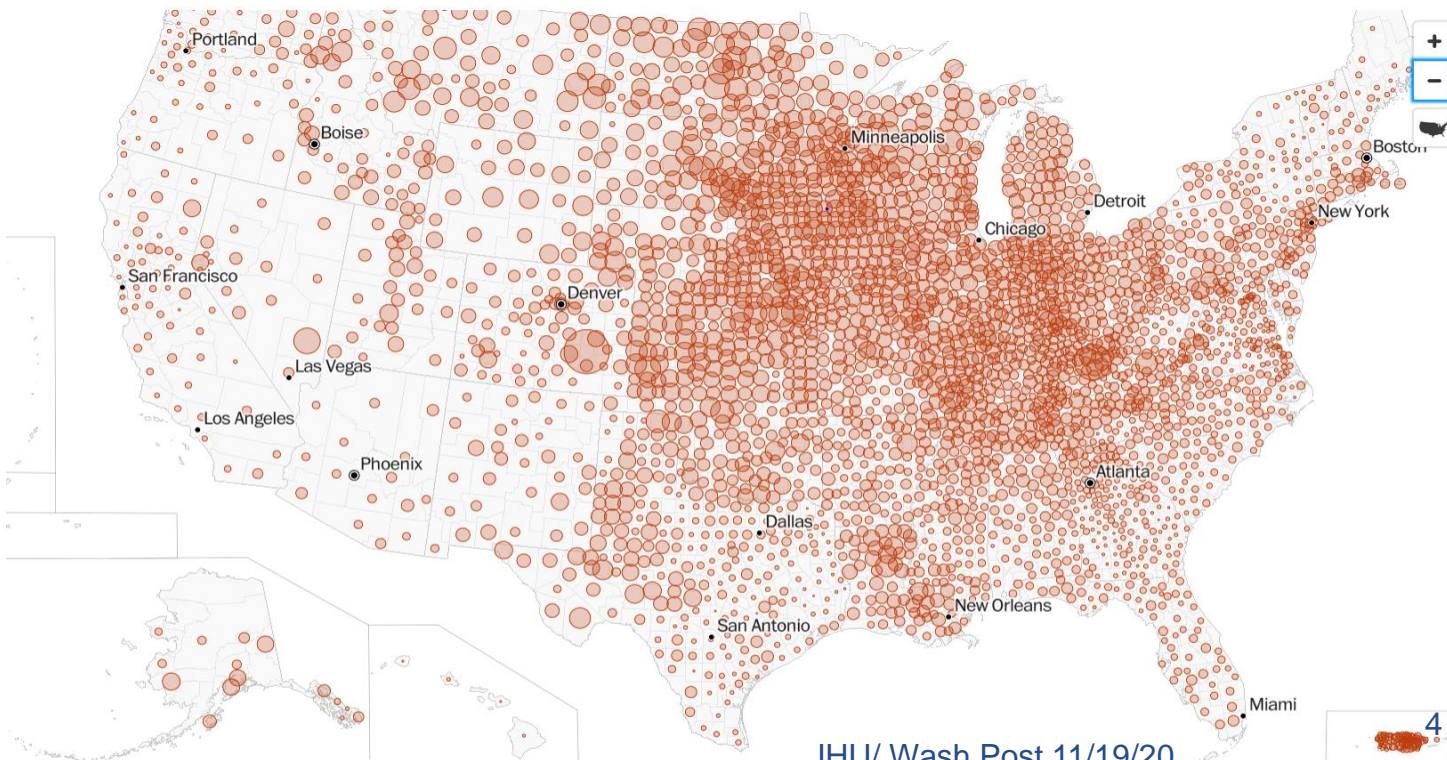
NYC Mortality March – August 2020 [Drop from 25.6% → 7.6%]
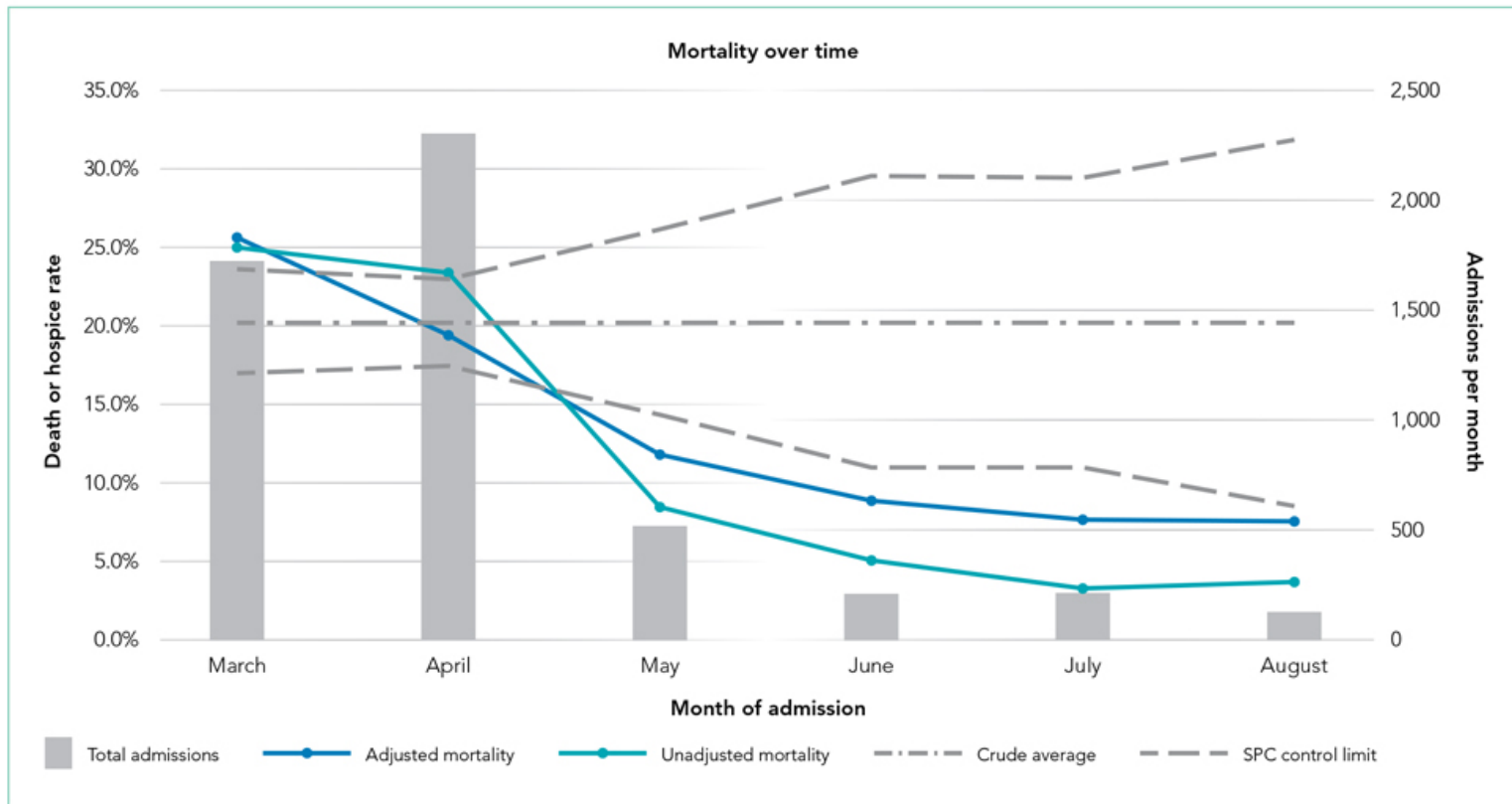
FIG. Adjusted and Unadjusted Mortality or Hospice Rate, by Month of Admission.

Why declining mortality? Likely many factors

COVID-NET | A Weekly Summary of U.S. COVID-19 Hospitalization Data

COVID-19 Laboratory-Confirmed Hospitalizations
Preliminary data as of Oct 24, 2020

Covid-19-associated Hospitalizations By Age

Age	0-4 yr	5-17 yr	18-49 yr	50-64 yr	65+ yr	Total
2020	391	647	19480	18424	26201	65143

The Coronavirus Disease 2019 (COVID-19)-Associated Hospitalization Surveillance Network (COVID-NET) hospitalization data are preliminary and subject to change as more data become available. In particular, case counts and rates for recent hospital admissions are subject to lag. As data are received each week, prior case counts and rates are updated accordingly.

CDC data

Why declining mortality? Likely many factors

- Shift to more young infected
- Mask wear and social distancing = exposure to lower viral loads
- Less chaos, more experience
  - Patients presenting earlier
  - Proning
  - Ventilator management
- Treatments
 - Remdesivir
  - Dexamethasone

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Most infectious

Meyerowitz EA et al. *Ann Intern Med*. 2020;M20-5008: online ahead of print.
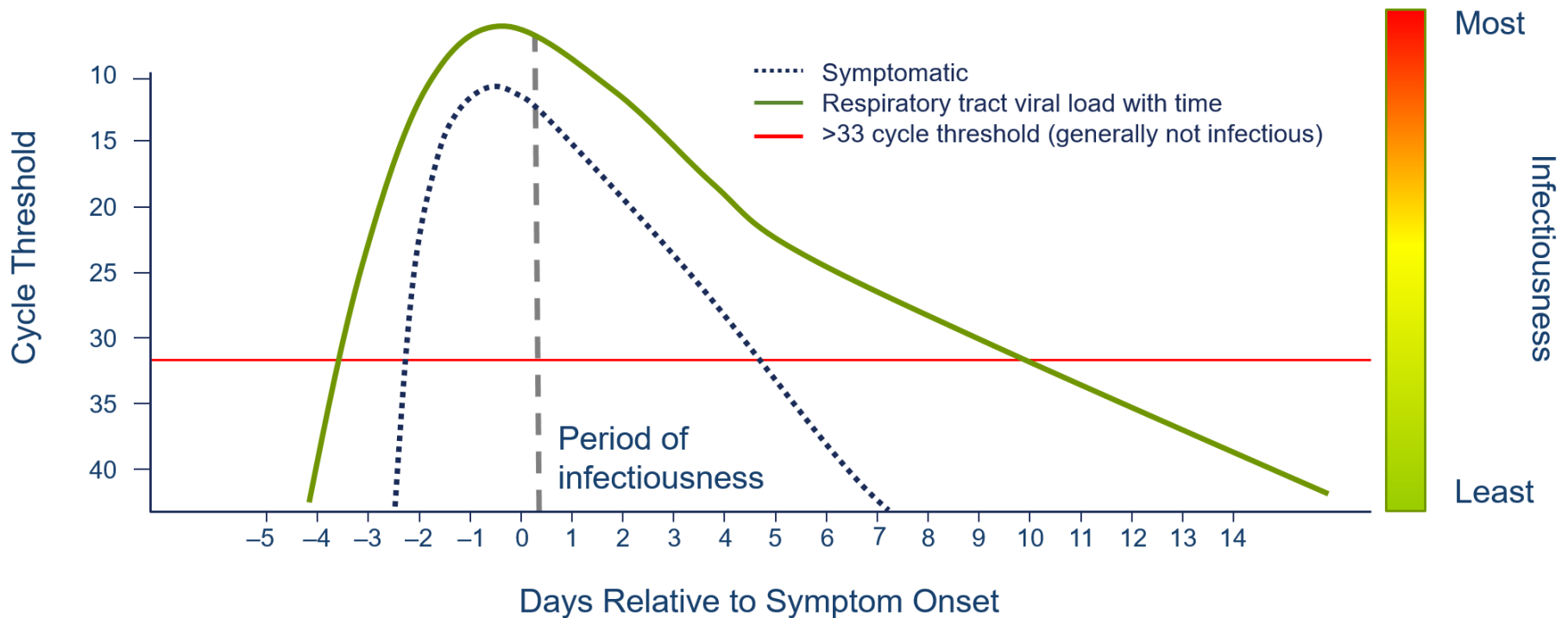
Where are most infections acquired?

SARS-CoV-2 spread across spatial scales

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is mostly transmitted within households and household-like settings. A decreasing proportion of transmission events take place at increasing spatial scales, but these events become more critical for sustaining the pandemic.

★ Superspreading events

Households and congregate living

Communities

Interregional

Proportion of transmission events
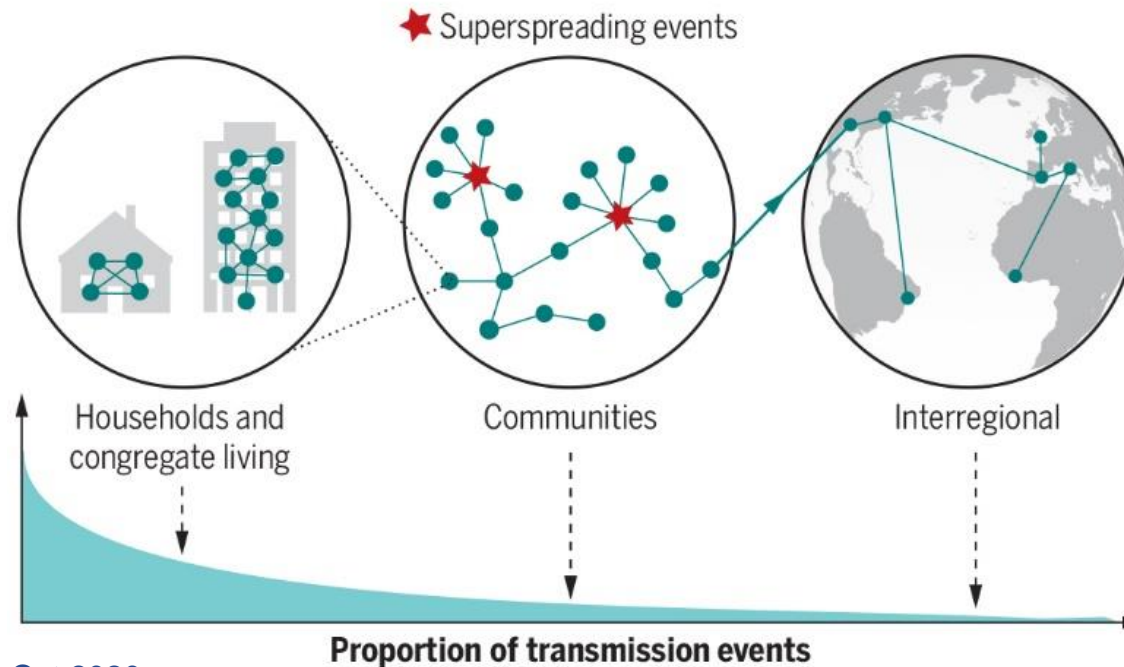
Risks at Home

- **Meta-analysis of 40 studies**
  - Secondary attack rate 18.8% (95% CI, 15.4% to 22.2%)
    - Higher for spouse/partner
    - Lower for other household members
    - Variable, depending on environmental factors
- **Rates only lower if mask wearing and social distancing in household**
  - Strongly suggested for high-risk people

Youth Is Wasted on the Young (?)
--George Bernard Shaw

FIGURE. Cumulative number of confirmed COVID-19 cases, by age group (N = 757) — Winnebago County, Wisconsin, March 1–July 18, 2020

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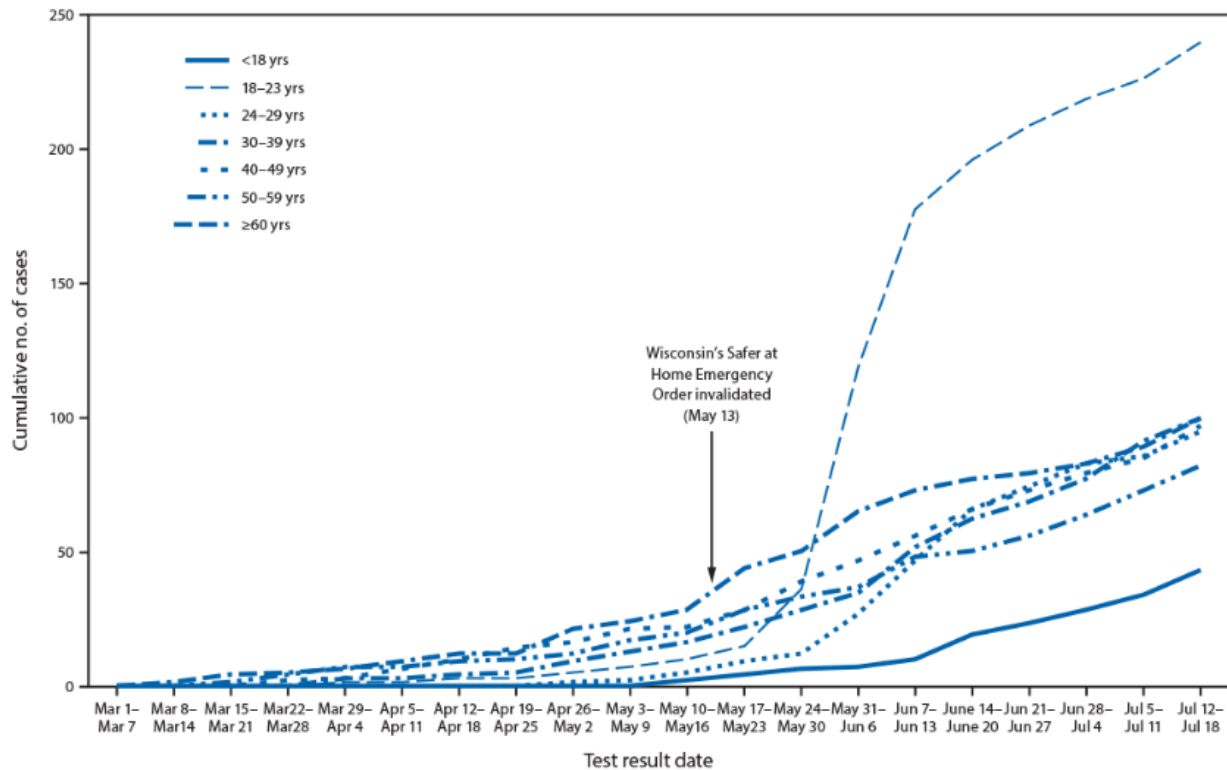
Top risks: Age and Gender

RISK WITH AGE
A person's age is the strongest predictor of their risk of dying of COVID-19. The risk increases from the age of 50.

Geneva
Age
≥65 — 5.6 Infection fatality ratio (%)
50–64 — 0.14
20–49 — 0.01
10–19 — 0
5–9 — 0

England
≥75 — 11.6
65–74 — 3.1
45–64 — 0.5
15–44 — 0.03

Spain
≥80 — 7.2
70–79 — 3.4
60–69 — 1
50–59 — 0.3
40–49 — 0.07
30–39 — 0.03
20–29 — 0.01
10–19 — 0
0–9 — 0
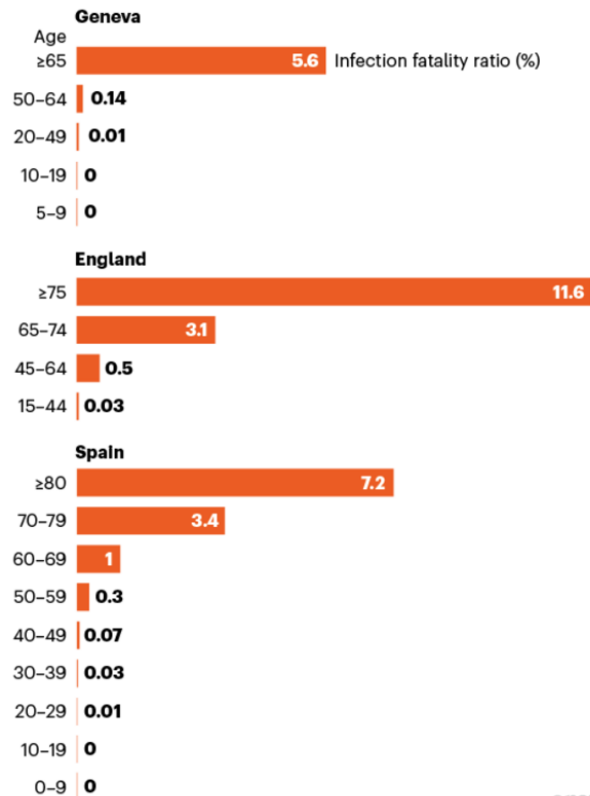
VULNERABLE MEN
A study in Spain found that men are at higher risk of dying from COVID-19 than are women.

■ Women   ■ Men

Age: ≥80, 70–79, 60–69, 50–59, 40–49, 30–39, 20–29, 10–19, 0–9
Infection fatality ratio (%)

©nature

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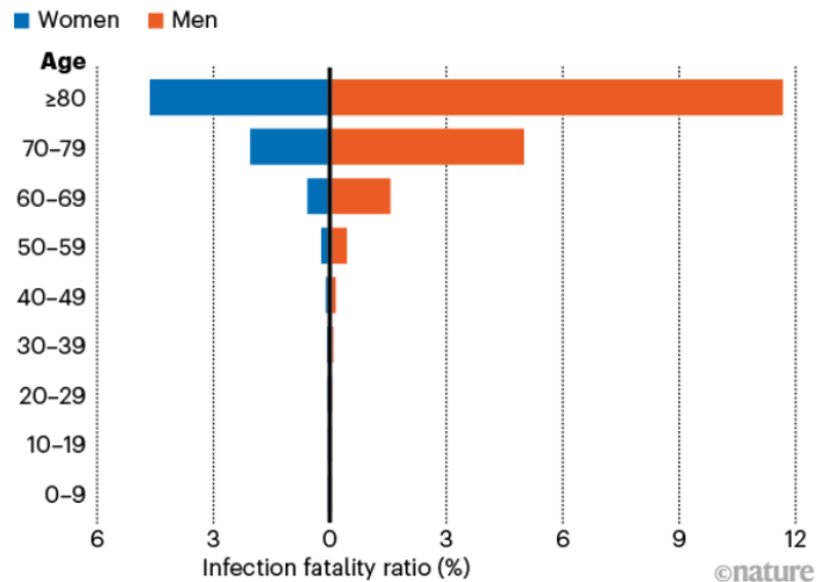
Risk for Hospitalization among People with Chronic Conditions

- Having more than 1 of these chronic conditions is related to even worse outcomes
- Notably, many of these conditions cluster together
- Obesity is a strong correlate of the vascular and lung diseases associated with severe COVID-19

RISK FOR HOSPITALIZATION IF YOU HAVE ANY OF THESE CONDITIONS AND GET COVID-19 COMPARED TO PEOPLE WITHOUT THE CONDITION(S).

Asthma
1.5x

Hypertension
3x

Obesity (BMI ≥ 30)
3x

Diabetes
3x

Chronic Kidney Disease
4x

Severe Obesity (BMI ≥ 40)
4.5x

2 Conditions*
4.5x

3 or More Conditions*
5x
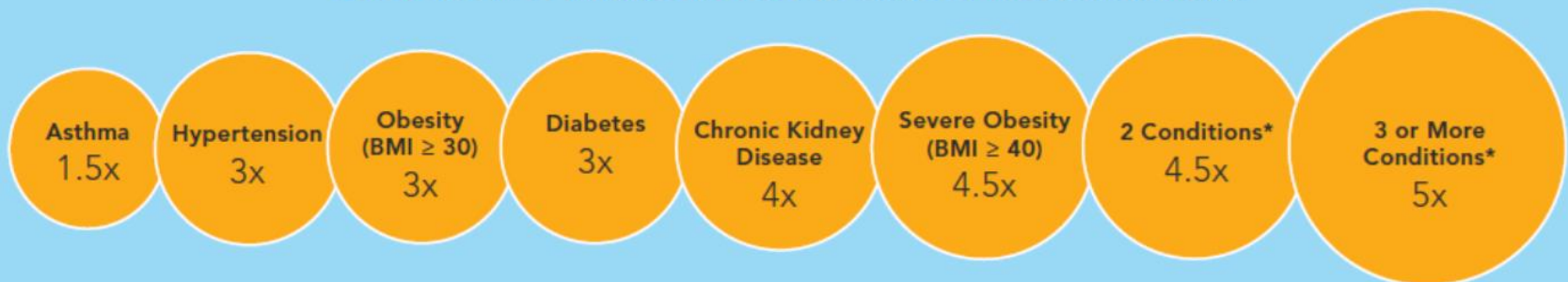
*Conditions include asthma, obesity, diabetes, chronic kidney disease, severe obesity, coronary artery disease, history of stroke and COPD.

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Long haulers—growing issue?

POST-COVID-19

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Social Media Patient-led Research: "Long Haul" COVID-19

Slack

BODY POLITIC

- 640 responses
- 72% US, 76% White, 4% hosp.
- 58% pre-existing conditions

Persistence of Symptoms

Number of Participants who had Reached Week x (1-8) In the Survey

https://www.wearebodypolitic.com/covid19   Data Published May 11, 2020

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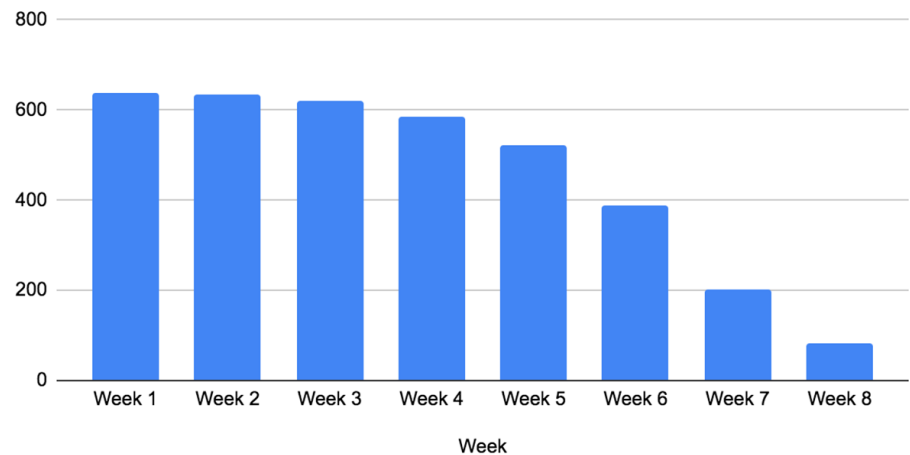
Long-Term Care Cases Make Up A Smaller Share of Cases Now Than Earlier In The Pandemic

Long-Term Care Coronavirus Cases as a Share of Total Coronavirus Cases

Data points by date:
- 4/19/2020: 14%
- 4/26/2020: 17%
- 5/3/2020: 18%
- 5/10/2020: 18%
- 5/17/2020: 17%
- 5/24/2020: 17%
- 5/31/2020: 17%
- 6/7/2020: 16%
- 6/14/2020: 16%
- 6/21/2020: 15%
- 6/28/2020: 14%
- 7/5/2020: 13%
- 7/12/2020: 12%
- 7/19/2020: 11%
- 7/26/2020: 11%
- 8/2/2020: 10%
- 8/9/2020: 10%
- 8/16/2020: 10%
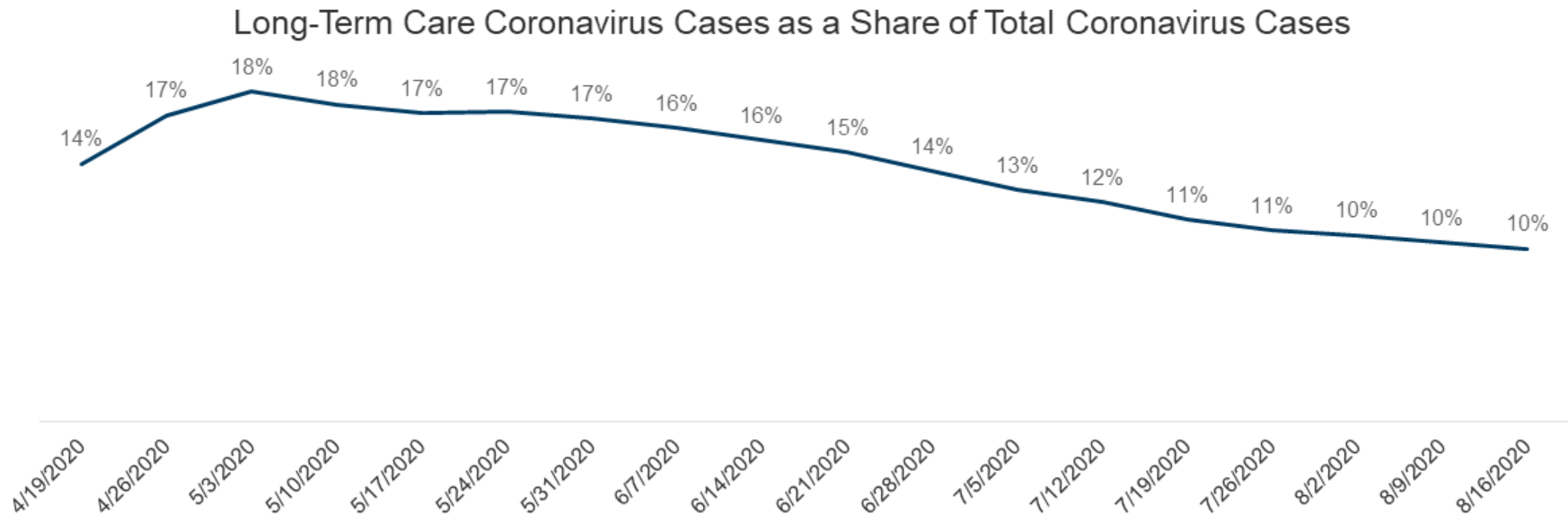
NOTES: Denominator is based on number of states reporting each week. The number of states included in each week's calculation of share of cases varies from 24-35 states. Data is available for <10 states prior to April 19th, so a national share of cases was not calculated for those weeks.
SOURCE: KFF analysis of available state reports, press releases, official state data from news reports, & The COVID Tracking Project.

Who Has Persistent Symptoms after COVID-19

UK: after hospitalization

- 163 pts; 141 @ 28 days followup
- median age 60, 56% male

Persistent symptoms @ 8-12 wks by WHO criteria

- 16 (59%) mild (no O_2 req.)
- 49 (75%) mod. (O_2 req.)
- 16 (89%) severe (ICU, HF, or intubation)

Arnold D.
https://doi.org/10.1101/2020.08.12.20173526. posted 8/14/2020

Paris

- women (sex ratio 4:1)
- ~ 40 yrs old
- no relevant medical history
- few biological abnormalities
- Few +PRP; 50% Abs +

Davido B, Seang S, Tubiana R, de Truchis P. Post–COVID-19 chronic symptoms: a postinfectious entity? https://doi.org/10.1016/j.cmi.2020.07.028

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Confusing for many

TESTING

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Salivary-based testing: Is Drool Good?

- Emerging
- Likely less sensitive than nasopharyngeal swab
  - Detects only ~80-90%
- No tests widely available
- Decreases barrier to testing
  - Who is most contagious?

A woman spits into a tube so that her saliva can be tested for the presence of novel coronavirus. UNIVERSITY OF ILLINOIS, URBANA-CHAMPAIGN.

Antigen Testing

Antibody against antigen, linked to detector molecule ●

Antibody against antigen

Control antibody

● Antigen

Before Use   Sample Applied   + Result   − Result
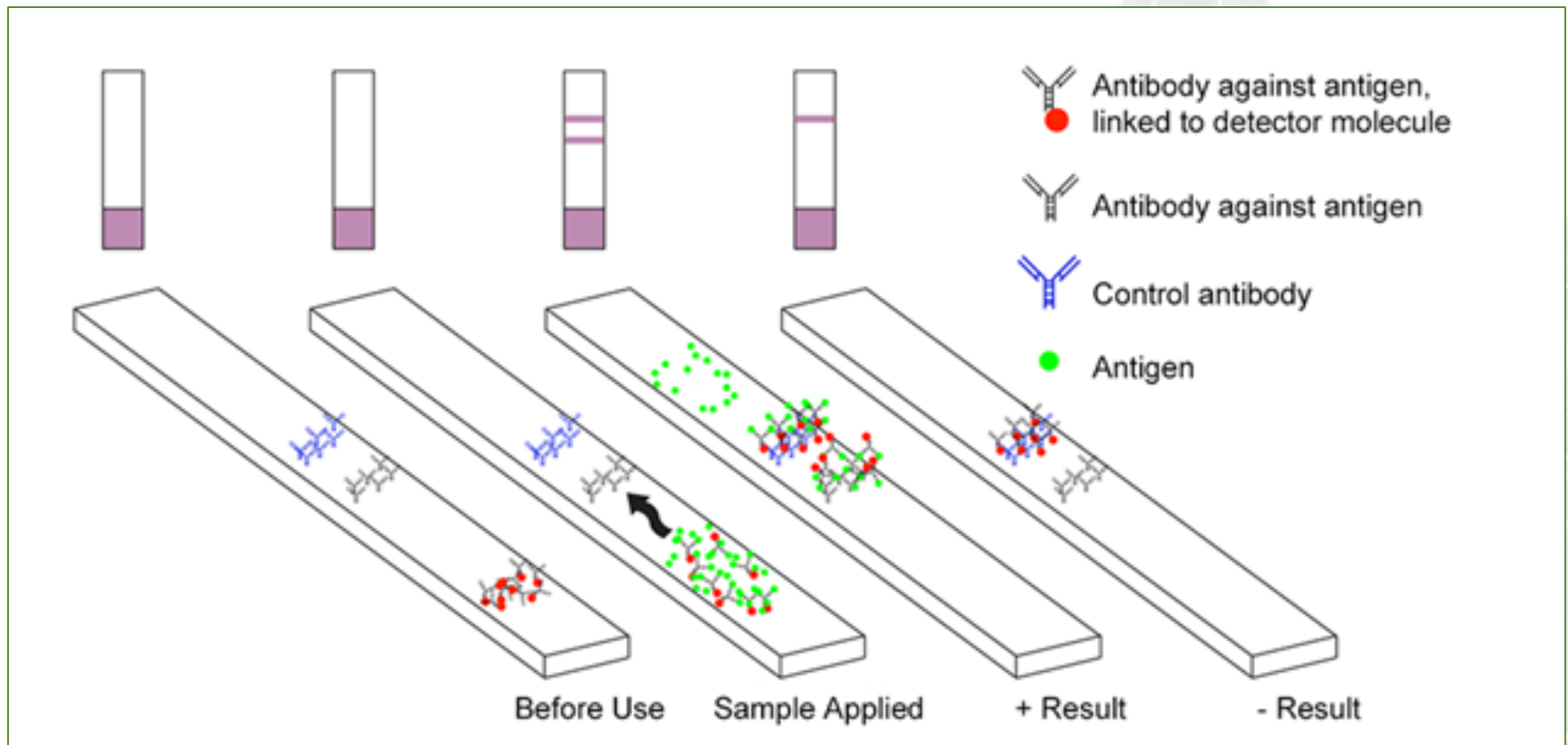
Adapted from Campbell IM. commons.wikimedia.org/wiki/File:Diagnostic_Medical_Dipstick.png. Accessed Oct 29, 2020.

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Antigen Testing

Molecular vs Rapid Antigen Testing

- Antigen tests
  - For early diagnosis in *symptomatic* patients
  - *Not* for screening (clinical studies in progress)
  - Negative result should be followed up with a molecular assay

Factor	RT-PCR Tests	Antigen Tests
Intended use	Detect current infection	Detect current infection
Analyte detected	Viral RNA	Viral antigens
Specimen type(s)	Nasal swab, sputum, saliva	Nasal swab
Sensitivity	High	Moderate
Specificity	High	High
Test complexity	Varies	Relatively easy
Authorized for point of care	Most not	Yes
Turnaround time	15 min to >2 days	~15 min
Cost	Moderate	Low

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Vaccines and monoclonal antibodies

PREVENTION

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Bamlanivimab FDA EUA (11/10/20)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

SARS-CoV-2 Neutralizing Antibody LY-CoV555 in Outpatients with Covid-19

Peter Chen, M.D., Ajay Nirula, M.D., Ph.D., Barry Heller, M.D.,
Robert L. Gottlieb, M.D., Ph.D., Joseph Boscia, M.D., Jason Morris, M.D.,
Gregory Huhn, M.D., M.P.H.T.M., Jose Cardona, M.D., Bharat Mocherla, M.D.,
Valentina Stosor, M.D., Imad Shawa, M.D., Andrew C. Adams, Ph.D.,
Jacob Van Naarden, B.S., Kenneth L. Custer, Ph.D., Lei Shen, Ph.D.,
Michael Durante, M.S., Gerard Oakley, M.D., Andrew E. Schade, M.D., Ph.D.,
Janelle Sabo, Pharm.D., Dipak R. Patel, M.D., Ph.D., Paul Klekotka, M.D., Ph.D.,
and Daniel M. Skovronsky, M.D., Ph.D., for the BLAZE-1 Investigators*

BLAZE-1 RCT, interim analysis

Mild/moderate COVID-19

Single dose IV, 456 non-hospitalized patients

1° endpoint, change viral load d11

<u>NOT met</u>

Approval based on 2° endpoint:

Hospitalization or ED visit at d28

3% vs. 10% placebo

--Unclear how many ED vs. hospital

Role: (+) SARS-CoV-2, age ≥ 12, high risk for severe COVID-19

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REGN-COV2 monoclonal cocktail

- N = 799, placebo-controlled trial, outpatients mild/moderate COVID-19
- Reduced medical visits through d29
  - All: 58% reduction (2.8% v. 6.5%, p=0.024)
  - With 1 risk factor: 72% reduction (p = 0.0065)
- Most benefit in patients without SARS-CoV-2 antibodies present at time of administration
- Few adverse events

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# Approaches to **Viral Vaccine Development**

a. Live attenuated
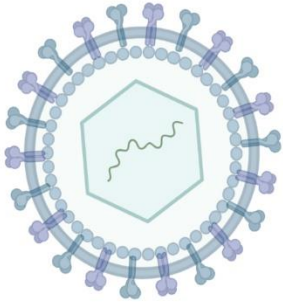
b. Whole inactivated
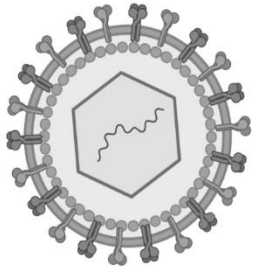
c. Split inactivated
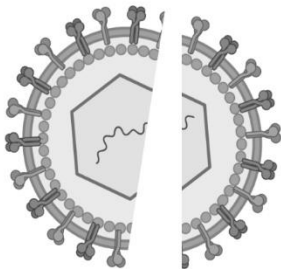
d. Synthetic peptides
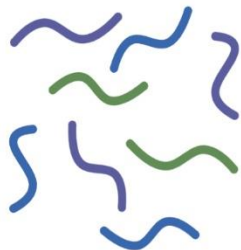
e. Virus-like particles

f. DNA or RNA

g. Recombinant subunits

VIRUS
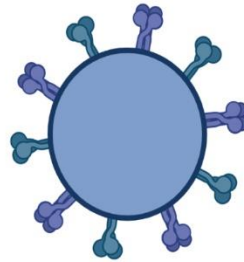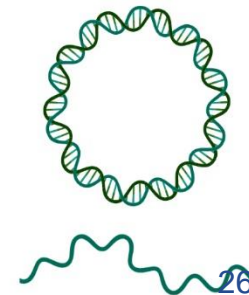
i. Recombinant viral vectors
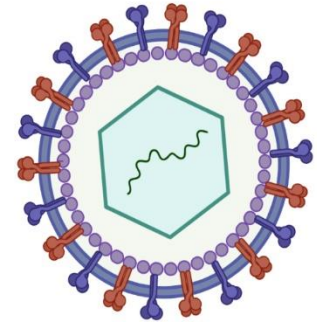
h. Recombinant bacterial vectors

26
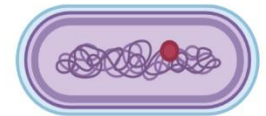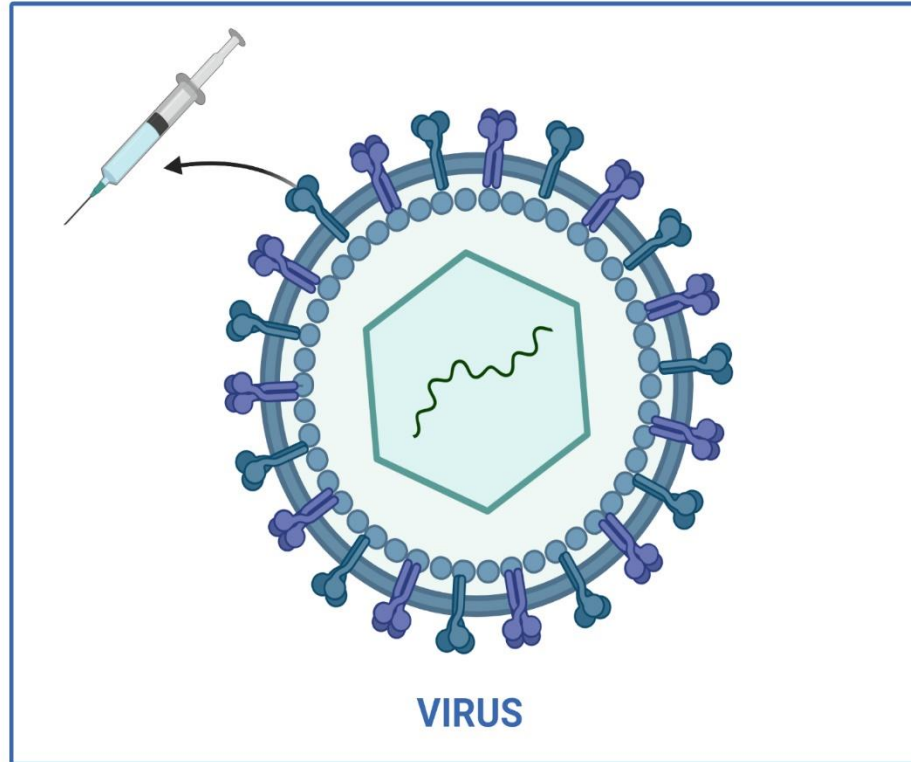
BioNTech/Pfizer mRNA COVID-19 Vaccine

BioNTech (BNT162: a1, b1, b2, c2)

Delivery vehicle:
Lipid nanoparticle

5' G — P P P | Spike/RBD | AAA- 3'
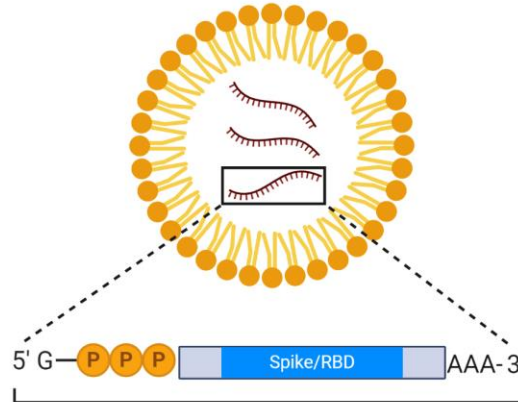
Nucleoside modified RNA (modRNA)
Uridine containing mRNA (uRNA)
Self-amplifying mRNA (saRNA)

Platform: Four individual LNP-encapsulated mRNA vaccines (2 modRNA, 1uRNA, 1 saRNA) encoding Spike protein or Receptor Binding Domain (RBD).

Press release data:
Final Phase 2/3
164 cases (11/18/20)
- 95% effective
- Age > 65 yrs
  - 94%
- Also reduction
Severe COVID-19

Initial safety data
(full safety data
→ 6 mos)

BioRender

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The COVID-19 Vaccine Race

- ➢ **300 candidate vaccines**
- ➢ **61 in human trials**

Coronavirus Vaccine Tracker

By Jonathan Corum, Sui-Lee Wee and Carl Zimmer   Updated November 18, 2020

PHASE 1	PHASE 2	PHASE 3	LIMITED	APPROVED
38	17	12	6	0
Vaccines testing safety and dosage	Vaccines in expanded safety trials	Vaccines in large-scale efficacy tests	Vaccines approved for early or limited use	Vaccines approved for full use
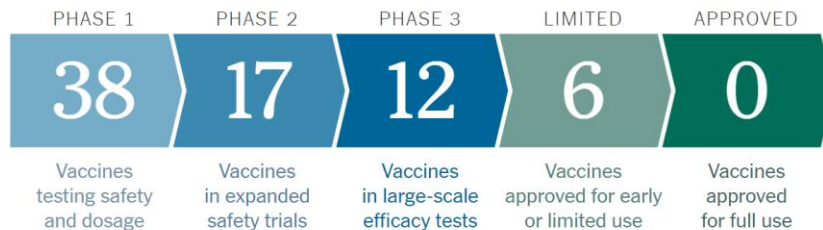
All two injections except:
JNJ & CanSinoBio (single injections)

Vaccines in Phase 3 trials

- • **Moderna (mRNA)**
- • **BioNTech/Pfizer (mRNA)**
- • CanSinoBio* (Ad5)
- • **Gamaleya* (Ad5/Ad26)**
- • Oxford/AstraZeneca (ChAdOx1)
- • Sinovac* (inactivated)
- • Wuhan Inst/Sinopharm (inactivated)
- • Sinopharm* (inactivated)
- • Murdoch (BCG vaccine)
- • JNJ (Ad26)
- • Bharat (inactivated)

NYT 11/18/20   *approved for early use in some countries   28

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Vaccine Distribution
CDC Interim Playbook: First Phase

Assumes limited initial supply

- Healthcare personnel who have the potential for direct or indirect exposure to patients or infectious materials)

- Non-healthcare essential workers

- Adults with high-risk medical conditions who possess risk factors for severe COVID-19 illness

- People 65 years of age and older (including those living in long-term care facilities

States create distribution plan

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Next Phases

Phase 1

Phase 1a "Jumpstart Phase"
- High-risk health workers
- First responders

Phase 1b
- People of all ages with comorbid and underlying conditions that put them at *significantly* higher risk
- Older adults living in congregate or overcrowded settings

Phase 2

- K-12 teachers and school staff and child care workers
- Critical workers in high-risk settings—workers who are in industries essential to the functioning of society and at substantially higher risk of exposure
- People of all ages with comorbid and underlying conditions that put them at *moderately* higher risk
- People in homeless shelters or group homes for individuals with disabilities, including serious mental illness, developmental and intellectual disabilities, and physical disabilities or in recovery, and staff who work in such settings
- People in prisons, jails, detention centers, and similar facilities, and staff who work in such settings
- All older adults not included in Phase 1

Phase 3

- Young adults
- Children
- Workers in industries and occupations important to the functioning of society and at increased risk of exposure not included in Phase 1 or 2

Phase 4

- Everyone residing in the United States who did not have access to the vaccine in previous phases

Equity is a crosscutting consideration: In each population group, vaccine access should be prioritized for geographic areas identified through CDC's Social Vulnerability Index or another more specific index.

FIGURE: A Phased Approach to Vaccine Allocation for COVID-19

NATIONAL ACADEMY of MEDICINE

The National Academies of SCIENCES ENGINEERING MEDICINE

QUESTIONS?

November 23, 2020