NURSE PRACTITIONER
2021 Virtual CE Summit

Evolving Recommendations Regarding COVID-19: What You Need to Know

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This CE activity for AANP credit is jointly provided by Global Education Group and Integrity Continuing Education.

Learning Objectives

- Explain the impact of COVID-19 on healthcare providers and health system infrastructures
- Discuss the epidemiology, clinical features, differential diagnosis, and treatment of COVID-19
- Review emerging vaccines and treatment options for patients with COVID-19

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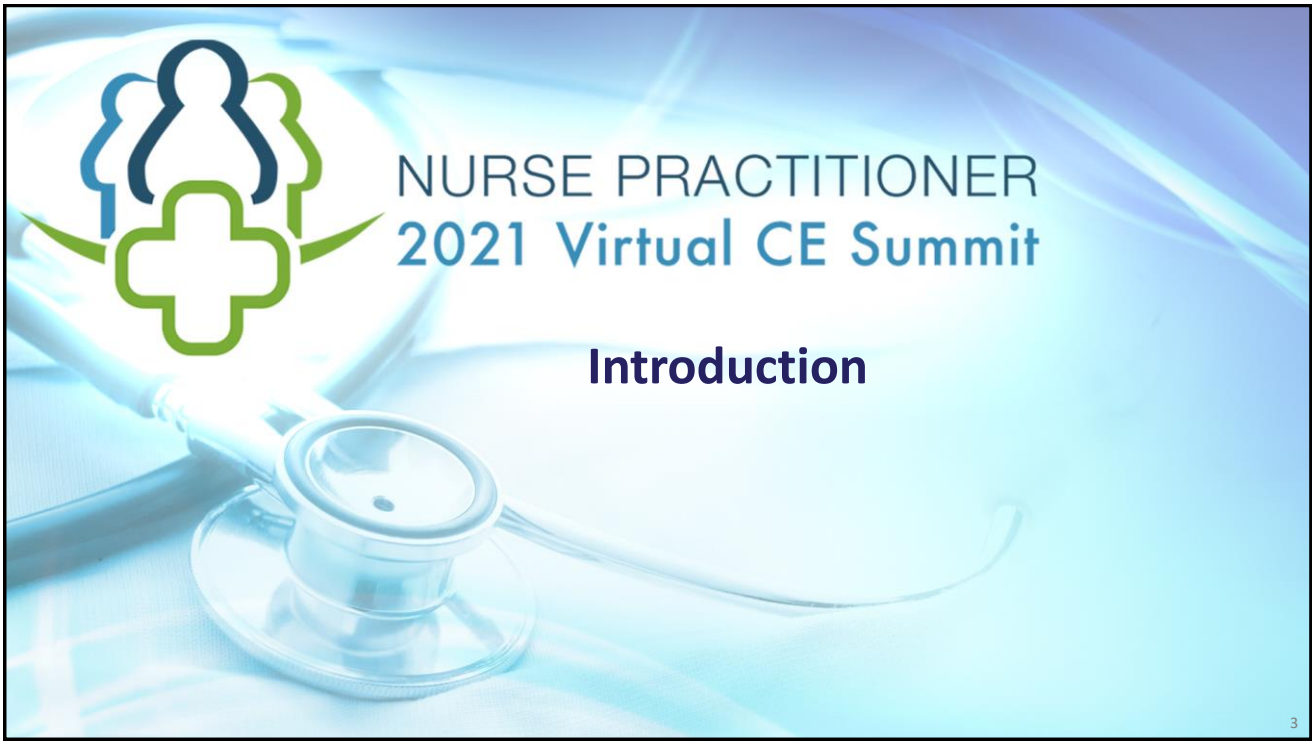

Audience Polling Question

What is your agreement with the following statement?

My healthcare system was sufficiently prepared to respond to the COVID-19 pandemic.

A. Strongly agree
B. Agree
C. Neutral
D. Disagree
E. Strongly disagree

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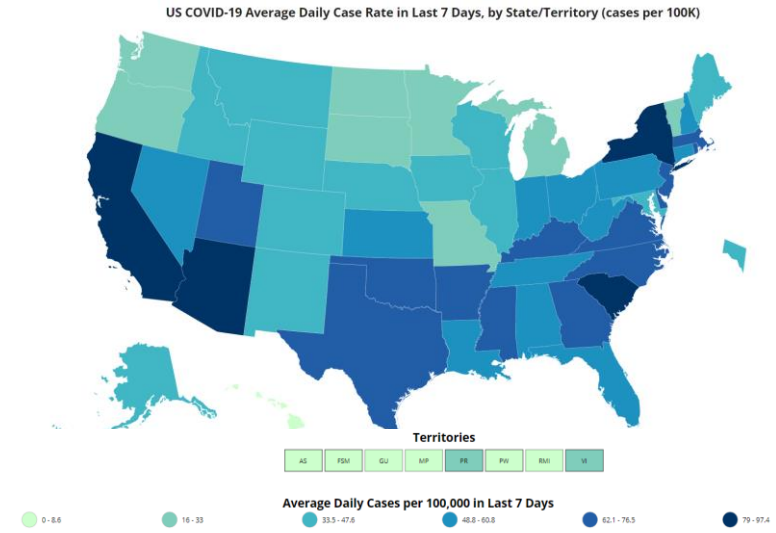
Current COVID-19 Cases and Deaths



TOTAL CASES

27,417,468

+88,193 New Cases

AVERAGE DAILY CASES PER 100K IN LAST 7 DAYS

28.3

TOTAL DEATHS

482,536

+3,317 New Deaths

Centers for Disease Control. United States COVID-19 cases and deaths by state. https://covid.cdc.gov/covid-data-tracker/#cases_casesper100klast7days

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Discussion

- What are some of the biggest impacts your practice has experienced as a result of COVID-19?
- What has been done to address these changes?
  - What was addressed correctly?
  - What was addressed poorly?

Stress during an outbreak can include:

- Fear and worry about your own health and health of loved ones
- Changes in sleep or eating patterns
- Difficulty sleeping or concentrating
- Worsening of chronic health problems
- Worsening of mental health conditions
- Increased use of alcohol, tobacco, or other drugs

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Audience Polling Question

According to past surveys of health care workers, a good number of them believe that ***medical and nursing staff have a duty to deliver care to sick people even if it exposes them to personal danger***

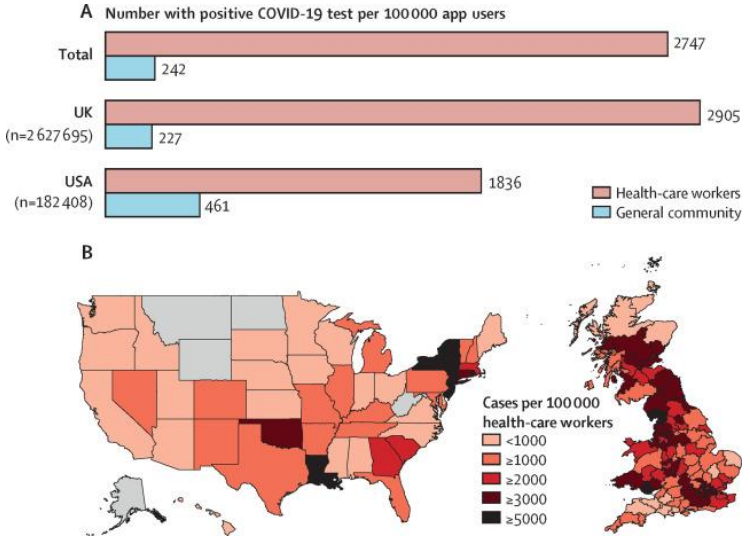
What is your agreement with the above statement?

A. Strongly agree
B. Agree
C. Neutral
D. Disagree
E. Strongly disagree

Fear on the Front Lines

General practitioners account for 1/3rd of COVID-19 mortality among healthcare workers

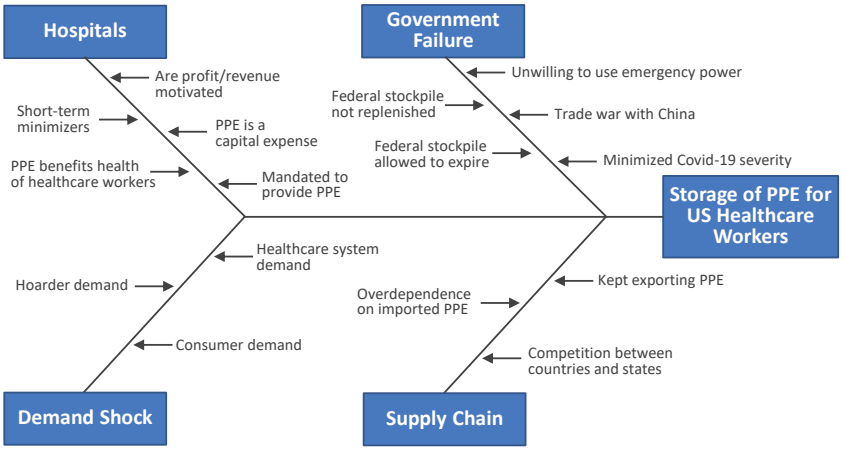
Mental health outcomes reported by HCPs on the frontlines of COVID-19:



Shortage of PPE for US Healthcare Workers

How has PPE shortage affected your practice since the pandemic began?

Factors Contributing to PPE Shortage[1]



PPE, personal protective equipment.

Cohen J, van der Meulaen Rodgers Y. *Prev Med.* 2020;141:106263.

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Discussion: Past, Present, and Future of Healthcare

- **COVID-19's long-term threat**
  - Have we passed the worst?
  - When will non-COVID patient volumes return?
- **Infection prevention**
  - How will regulatory bodies heighten infection prevention protocols, equipment inventory, and data collection?
- **Revenue loss**
  - How will the healthcare provider organization landscape evolve as so many struggle to stay afloat financially?
- **Virtual care**
  - Can virtual care improve chronic disease management, discharge management, readmissions, and reduce visits to emergency departments and urgent cares?

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Audience Polling Question

What is your agreement with the following statement?

I am confident in my ability to diagnose and manage the treatment of a patient with COVID-19.

A. Strongly agree
B. Agree
C. Neutral
D. Disagree
E. Strongly disagree

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COVID-19 Clinical Presentation & Screening

- Estimated incubation period up to 14 days from exposure
- Spectrum of illness ranges from asymptomatic to severe pneumonia with acute respiratory distress and death
- Screening patients before they enter a facility:
  - Reduces exposures for other patients and healthcare personnel
  - Helps prevent the spread of disease within the facility
  - Helps ensure personal protective equipment (PPE) is used effectively

The COVID-19 Treatment Guidelines Panel regularly updates the recommendations in these guidelines as new information on the management of COVID-19 becomes available. The most recent version of the guidelines can be found on the COVID-19 Treatment Guidelines website (https://www.covid19treatmentguidelines.nih.gov/).

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Diagnosing COVID-19: NAATs vs Antigen Tests

	Nucleic Acid Amplification Tests (NAAT)	Antigen Tests
Intended use	Detect current infection	Detect current infection
Analyte Detected	Viral Ribonucleic Acid (RNA)	Viral antigens
Specimen Type(s)	Nasal, nasopharyngeal, sputum, saliva	Nasal, nasopharyngeal
Sensitivity	Varies by test, but generally high	Moderate
Specificity	High	High
Text Complexity	Varies by test	Relatively easy to use
Authorized for Use at the Point-of-Care	Most are not, some are	Most are, some are not
Turnaround Time	Ranges from 15 minutes to >2 days	Ranges from 15 minutes to >2 days
Cost/Test	Moderate (~$100/test)	Low ($5 - $50/test)

Centers for Disease Control. Interim guidance for antigen testing for SARS-CoV-2. Updated Dec 16, 2020. https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html

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Ambulatory Care of Mild to Moderate Disease

IDSA Guidelines

Bamlanivimab or casirivimab/imdevimab: suggest against routine use
In ambulatory patients with COVID-19 or in patients with mild-moderate COVID admitted to the hospital for management of conditions other than COVID-19 who are at increased risk, is a reasonable treatment option if, after informed decision-making, the patient puts a high value on the uncertain benefits and a low value on uncertain adverse events.

Ivermectin: suggests against use except in clinical trial

Baricitinib + remdesivir + corticosteroids: recommended only in context of a clinical trial

NIH Guidance

There are insufficient data to recommend either for or against any specific antiviral or antibody therapy.

SARS-CoV-2 neutralizing antibodies (bamlanivimab or casirivimab + imdevimab) are available through EUAs for outpatients who are at high risk of disease progression.

These EUAs do not authorize use in hospitalized patients.

Dexamethasone should not be used.

Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19. Available at: https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/. Accessed February 13, 2021.
https://www.covid19treatmentguidelines.nih.gov/therapeutic-management/

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Outpatient Use of Monoclonal Antibodies

- 2 anti-SARS-CoV-2 monoclonal antibodies available through EUA for outpatients at high risk for disease progression:
  - Bamlanivimab
  - Casirivimab + imdevimab
- Remdesivir remains only drug FDA-approved for COVID-19
- Modest reduction in viral load/viral replication
- Shown to reduce medically-attended visits
- Only for outpatient use – not for inpatients

EUA, emergency use authorization; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
National Institutes of Health. Therapeutic management of adults with COVID-19. Updated Feb 11, 2021. https://www.covid19treatmentguidelines.nih.gov/therapeutic-management/

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Care of Hospitalized Patients: IDSA Guidelines

Hospitalized: mild-to-moderate disease without need for supplemental oxygen	**Corticosteroids: suggest against use** **Tocilizumab: suggest against routine use** **Convalescent plasma: recommended only in the context of a clinical trial** **Remdesivir: suggest against routine use** **Famotidine: suggest against use except in a clinical trial**
Hospitalized: severe but noncritical disease (spO_2 <94% on room air)	**Corticosteroids: suggest use** If dexamethasone is unavailable, equivalent total daily doses of alternative glucocorticoids may be used **Tocilizumab: suggest against routine use** **Convalescent plasma: recommended only in the context of a clinical trial** **Remdesivir: suggest use** In patients on mechanical ventilation or ECMO, duration of treatment is 10 days. **Famotidine: suggest against use except in a clinical trial** **Bamlanivimab or casirivimab/imdevimab: recommended against use** **Baricitinib + remdesivir: suggest use** For hospitalized patients who cannot receive corticosteroids because of a contraindication. Baricitinib 4 mg daily dose for 14 days (or until hospital discharge). The benefits of baricitinib plus remdesivir for persons on mechanical ventilation are uncertain **Ivermectin: suggests against use except in clinical trial**
Hospitalized: critical disease	**Corticosteroids: recommend use** If dexamethasone is unavailable, equivalent total daily doses of alternative glucocorticoids may be used **Tocilizumab: suggest against routine use** **Convalescent plasma: recommended only in the context of a clinical trial** **Remdesivir: suggest use** Remdesivir appears to demonstrate the most benefit in those with severe COVID-19 on supplemental oxygen rather than in patients on mechanical ventilation or ECMO. **Famotidine: suggest against use except in a clinical trial**

Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19. Available at: https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/. Accessed February 13, 2021.

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Care of Hospitalized Patients: NIH Guidance

Hospitalized[a] but does not require supplemental oxygen	**Dexamethasone** should not be used **(AIIa)**. There are insufficient data to recommend either for or against the routine use of **remdesivir**. For patients at high risk of disease progression, the use of remdesivir may be appropriate.
Hospitalized[a] and requires supplemental oxygen (But does not required oxygen delivery through a high-flow device, noninvasive ventilation, invasive mechanical ventilation, or extracorporeal membrane oxygenation [ECMO])	Use one of the following options: • **Remdesivir** (eg, for patients who require minimal supplemental oxygen) **(BIIa)** • **Dexamethasone plus remdesivir** (e.g., for patients who require increasing amounts of supplemental oxygen) **(BIII)** • **Dexamethasone** (eg, when combination therapy with remdesivir cannot be used or is not available) **(BI)**
Hospitalized[a] and requires oxygen delivery through a high-flow device or noninvasive ventilation	Use one of the following options: • **Dexamethasone (AI)** • **Dexamethasone plus remdesivir (BIII)**
Hospitalized[a] and requires invasive mechanical ventilation or ECMO	**Dexamethasone (AI)**

Ratings of Recommendations: A = strong; B = moderate; C = optional; **Rating of Evidence:** I = one or more randomized trials without major limitations; IIa = other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = expert opinion.

https://www.covid19treatmentguidelines.nih.gov/therapeutic-management/

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Inpatient Treatment of COVID-19

- Monoclonal antibodies work for outpatients but are **not recommended** for inpatients
- Dexamethasone has been found to ***improve survival*** in hospitalized patients who require oxygen
  - Greatest effect seen in patients on mechanical ventilation

https://www.covid19treatmentguidelines.nih.gov/therapeutic-management/

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Discussion

- What clinical strategies are most useful in the treatment of COVID-19?
- What considerations and precautions must be taken in patients with comorbidities that predispose them to severe illness?

Remdesivir for Patients Hospitalized With COVID-19…but Not Without Controversy

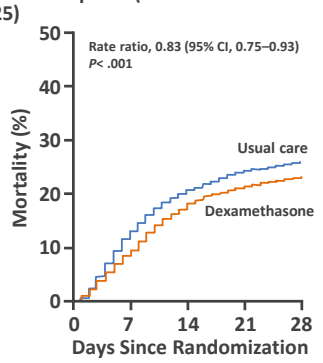
- ACCT-1 Trial of n = 1062 patients randomized to remdesivir or placebo[1]
  - Patients receiving remdesivir more likely to have clinical improvement at day 15
  - Estimates of mortality:
    - Day 15: 6.7% remdesivir; 11.9% placebo
    - Day 29: 11.4% remdesivir; 15.2% placebo
- Solidarity Trial: international randomized trial of ~12,000 patients launched by WHO investigating remdesivir, hydroxychloroquine, lopinavir/ritonavir, and interferon[2]
  - Interim results published October, 2020 found all therapies had little or no effect on mortality, initiation of ventilation, and duration of stay in hospitalized patients

1. Beigel JH, et al. *NEJM.* 2020;383:1813-1826. **2**. World Health Organization. "Solidarity" clinical trial for COVID-19 treatments. Accessed Feb 13, 2020. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments

Dexamethasone Reduced 28-day Mortality in Patients Hospitalized With COVID-19

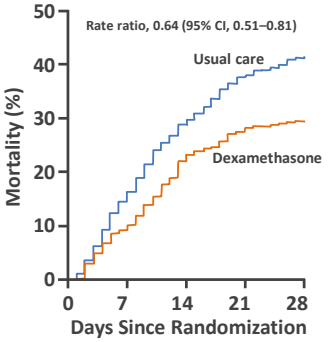
- N = 2104 patients assigned to dexamethasone vs n=4321 to usual care
- Dexamethasone resulted in lower 28-day mortality among those receiving either invasive mechanical ventilation or oxygen alone at randomization but not among those receiving no respiratory support

A All Participants (N = 6425)



No. at Risk					
Usual care	4321	3754	3427	3271	3205
Dexamethasone	2104	1903	1725	1659	1621

B Invasive Mechanical Ventilation (N = 1007)



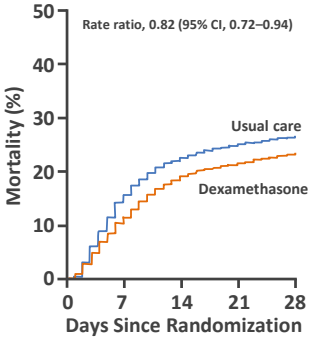
No. at Risk					
Usual care	683	572	481	424	400
Dexamethasone	324	290	248	232	228

RECOVERY Collaborative Group. *NEJM*. 2020. DOI: 10.1056/NEJMoa2021436.

Dexamethasone Reduced 28-day Mortality in Patients Hospitalized with COVID-19 *(cont.)*

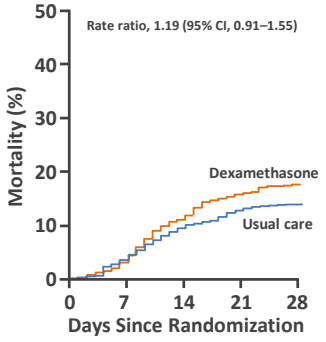
- N=2104 patients assigned to dexamethasone vs n=4321 to usual care
- Dexamethasone resulted in lower 28-day mortality among those receiving either invasive mechanical ventilation or oxygen alone at randomization but not among those receiving no respiratory support

C Oxygen Only (N=3883)



No. at Risk					
Usual care	2604	2195	2018	1950	1916
Dexamethasone	1279	1135	1036	1006	981

D No Oxygen Received (N=1535)



No. at Risk					
Usual care	1034	987	928	897	889
Dexamethasone	501	478	441	421	412

RECOVERY Collaborative Group. *NEJM*. 2020. DOI: 10.1056/NEJMoa2021436.

NIH Recommendations on Emerging Therapies

Drug	NIH Panel Recommendation (January 2021)

Blood-Derived Products	• There are **insufficient data** for the Panel to recommend either for or against the use of the following blood-derived products for the treatment of COVID-19:
	  • COVID-19 convalescent plasma
	  • Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) immunoglobulins
	• The Panel **recommends against** the use of the following blood-derived products for the treatment of COVID-19, except in a clinical trial:
	  • Mesenchymal stem cells
	  • Non-SARS-CoV-2-specific intravenous immunoglobulin (IVIG). *This recommendation should not preclude the use of IVIG when it is otherwise indicated for the treatment of complications that arise during the course of COVID-19.*

Immunomodulators	• There are **insufficient data** for the Panel to recommend either for or against the use of the following immunomodulators for the treatment of COVID-19:
	  • Interleukin (IL)-1 inhibitors (e.g., anakinra).
	  • Interferon beta for the treatment of early (i.e., <7 days from symptom onset) mild and moderate COVID-19.
	• The Panel **recommends against** the use of the following immunomodulators for the treatment of COVID-19, except in a clinical trial:
	  • Anti-IL-6 receptor monoclonal antibodies (e.g., sarilumab, tocilizumab) or anti-IL-6 monoclonal antibody (siltuximab).
	  • Interferons (alfa or beta) for the treatment of severely or critically ill patients with COVID-19.
	  • Bruton's tyrosine kinase inhibitors (e.g., acalabrutinib, ibrutinib, zanubrutinib) and Janus kinase inhibitors (e.g., baricitinib, ruxolitinib, tofacitinib).

National Institutes of Health. Coronavirus disease 2019 (COVID-19) treatment guidelines. https://www.covid19treatmentguidelines.nih.gov/

Long-term Complications of COVID-19: Consequences 6-months After Discharge

- COVID-19, caused by SARS-CoV-2, can involve sequelae and other medical complications that last weeks to months after initial recovery, which has come to be called Long-COVID or COVID long-haulers
- Systematic review and meta-analysis of identified 55 long-term effects[1]
  - Most common were fatigue (58%), headache (44%), attention disorder (27%), hair loss (25%), dyspnea (24%)
- Ambidirectional cohort study of n = 1,733 patients in Wuhan, China[2]
  - At 6 months after acute infection, survivors were mainly troubled with fatigue or muscle weakness, sleep difficulties, and anxiety or depression
  - Patients who were more severely ill during their hospital stay had more severe impaired pulmonary diffusion capacities and abnormal chest imaging manifestations, and are the main target population for intervention of long-term recovery.

1. Lopez-Leon S, et al. *medRxiv*. 2021;2021.01.27.21250617. Preprint
2. Huang C, et al. *Lancet*. 2021;10270:220-232.

Audience Polling Question

Have you been vaccinated for SARS-CoV-2?

A. Yes
B. No

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Audience Polling Question

Which of the following statements most closely reflects your view of the two vaccines available for SARS-CoV-2?

A. They're great! I encourage most of my patients to get vaccinated once available.
B. They're a necessary step in fighting the pandemic, but I have my concerns.
C. I don't trust the safety/efficacy of them, but I received my vaccination/intend to be vaccinated and tell my patients they should, too.
D. I don't trust the safety/efficacy of them, and I do not intend to be vaccinated or recommend vaccination to my patients.

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Vaccines Currently Available or in Late-Stage Development

Vaccine	Pfizer	Moderna	Janssen	AstraZeneca-Oxford	Novavax
Type	mRNA	mRNA	Viral Vector DNA	Viral Vector DNA	Subunit Protein-Based
Doses	**2x doses** 21 days apart	**2x doses** 28 days apart	**1 dose**	**2x doses** ~4-12 weeks apart	**2x doses** 21 days apart
Storage	**Refrigeration** 2-8 °C ≤ 5 days **Ultra-Frozen** -80 to -60 °C ≤ 6 months	**Refrigeration** 2-8 °C ≤ 30 days **Frozen** -25 to -15 °C ≤ 6 months	**Refrigeration** 2-8 °C ≤ 3 months **Frozen** ≤ -20 °C ≤ 2 years	**Refrigeration** 2-8 °C ≤ 6 months	**Refrigeration** 2-8 °C no time limit given
Availability	Available via EUA for **Ages 16 and up** Dec 11th, 2020	Available via EUA for **Ages 18 and up** Dec 20th, 2020	EUA hearing Feb 26th, 2020	EUA filing ~Q1 2021	EUA filing ~Q1 2021

https://www.ashp.org/-/media/assets/pharmacy-practice/resource-centers/Coronavirus/docs/Vaccine-candidate-tracking-table.ashx. Feb 8, 2021
https://www.idsociety.org/covid-19-real-time-learning-network/vaccines/Pfizer-BioNTech-COVID-19-Vaccine/. Feb 4, 2021.
https://www.idsociety.org/covid-19-real-time-learning-network/vaccines/moderna-covid-19-vaccine/. Feb 4, 2021.
https://www.idsociety.org/covid-19-real-time-learning-network/vaccines/vaccines/#Phase3. Feb 9, 2021.
https://www.biospace.com/article/comparing-covid-19-vaccines-pfizer-biontech-moderna-astrazeneca-oxford-j-and-j-russia-s-sputnik-v/

Vaccines Currently Available or in Late-Stage Development

Vaccine	Pfizer	Moderna	Janssen	AstraZeneca-Oxford	Novavax
Efficacy: Symptomatic COVID-19 (Primary Outcome), n	~44,000	~30,000	43,783	~30,000	~30,000
1st dose	52%	80%	66% (72% US trials)	76%	NR
2nd dose	95%	94%	Pending	66.7% 12-week vs 6-week intervals: 82.4% vs 54.9%	95.6% (original COVID-19); 89.3% (incl. variants)
Secondary Efficacy Outcomes					
Severe Disease	NR	100%	85%	NR	100%
Hospitalization/Death	100%	100%	100%	100%	NR
Efficacy Against Variants					
UK (B.1.1.7)	***Direct efficacy against variants unknown***		89%	75%	85.6%
South Africa (B.1.351)			57%	10%*	60% excl HIV; 49% incl HIV
Brazil (P.1)			66%	84%	NR

**Against mild to moderate infections only.*

https://www.ashp.org/-/media/assets/pharmacy-practice/resource-centers/Coronavirus/docs/Vaccine-candidate-tracking-table.ashx. Feb 8, 2021. https://www.idsociety.org/covid-19-real-time-learning-network/vaccines/Pfizer-BioNTech-COVID-19-Vaccine/. Feb 4, 2021. https://www.idsociety.org/covid-19-real-time-learning-network/vaccines/moderna-covid-19-vaccine/. Feb 4, 2021. https://www.idsociety.org/covid-19-real-time-learning-network/vaccines/vaccines/#Phase3. Feb 9, 2021. https://www.biospace.com/article/comparing-covid-19-vaccines-pfizer-biontech-moderna-astrazeneca-oxford-j-and-j-russia-s-sputnik-v/. Voysey M, et al. Lancet. Feb 1 2021. https://www.wsj.com/articles/astrazeneca-vaccine-effective-against-u-k-covid-19-variant-in-study-11612530912. Feb 5, 2021.

COVID-19 Vaccine Hesitancy

Patient Vaccine Hesitancy

- Only 60% of the general public said they would receive a COVID-19 vaccine (Data from October 2020 Harris poll)
- Factors weighing on acceptance
  - Are there side effects?
  - Does it work?
  - Is it safe?
  - How much does it cost?

Provider Vaccine Hesitancy

- American Nursing Foundation Survey (Oct 2020)
  - 63% were somewhat or very confident that the vaccine will be safe and effective
  - 34% would voluntarily receive COVID-19 vaccine
  - 57% are comfortable discussing COVID-19 vaccines with patients
- CDC web survey of healthcare providers (Sept-Oct 2020)
  - 63% said they would get a COVID-19 vaccine

https://www.cdc.gov/vaccines/covid-19/

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Audience Polling Question

Manage Vaccine Side Effects

- I feel comfortable recommending NSAIDs/APAP to manage side effects associated with COVID-19 vaccines.
  - True
  - False

APAP, automatic positive airway pressure; NSAIDs, nonsteroidal anti-inflammatory drugs.

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Discussion

- What are some communication strategies for discussing the vaccine with patients?
  - Why doesn't antigen testing work to confirm the vaccine's efficacy?
- What does the evidence say re: NSAIDs/APAP?
  - Before, during, and after vaccine

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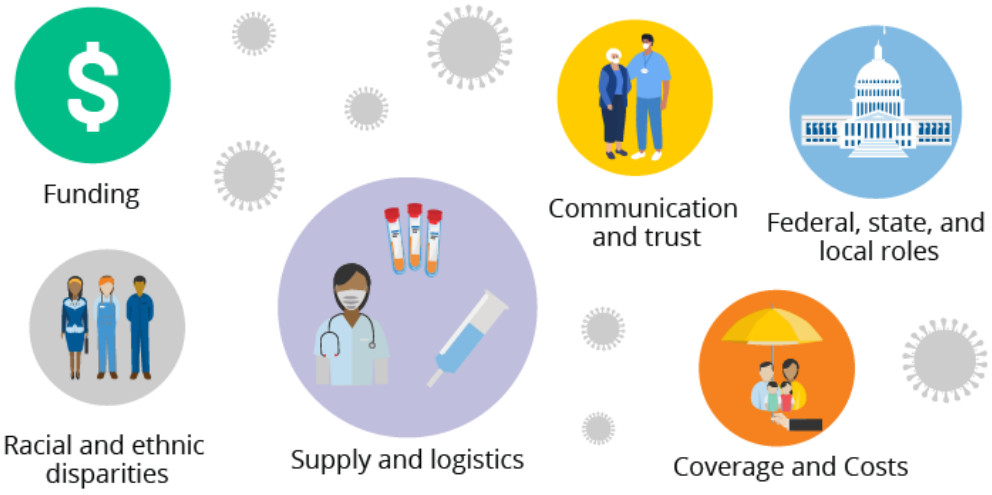
Vaccine Distribution Challenges



KFF. Distributing a COVID-19 vaccine across the US—a look at key issues. Oct 20, 2020. https://www.kff.org/report-section/distributing-a-covid-19-vaccine-across-the-u-s-a-look-at-key-issues-issue-brief/

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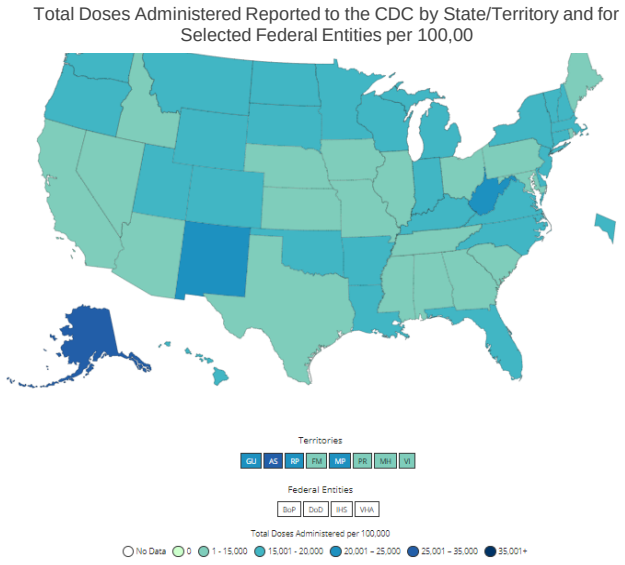
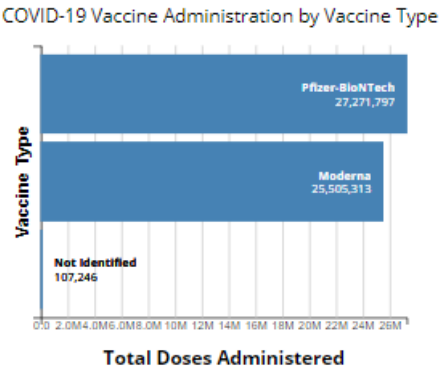
Current US Vaccination Statistics





COVID Data Tracker. Available at: covid.cdc.gov. Accessed February 13, 2021.

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Discussion

- How do HCPs best prepare to distribute COVID vaccines?
- What are pitfalls to avoid in distribution efforts?
- What is a realistic timeline to providing vaccine to anyone that wants one?

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Summary and Closing Thoughts

- COVID-19 caused an unprecedented shift in the US healthcare system and future developments in prevention and treatment are uncertain
- Presents as a spectrum of illnesses that range from asymptomatic to severe
- Effective testing mechanisms exist currently and may be helpful in reduction of transmission in addition to diagnosis and identification of asymptomatic individuals
- Available treatments for COVID-19 have specific strengths in outpatient and/or hospitalized patients
- Dexamethasone is the only treatment that has demonstrated mortality benefit and benefit is more pronounced in patients requiring supplemental oxygen or mechanical ventilation
- Two vaccines currently available and one more expected shortly
- Addressing vaccine hesitancy and supporting rollout efforts are critical needs towards future prevention

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