Welcome to today's webinar:

Vaccine Current State & Addressing Hesitancy

Moderator:

***John Young**, M.D., MBA*

Panelists:

***Jason Braithwaite,** PharmD, MS, BCPS*

***Michelle Fiscus,** M.D., FAAP*

***Michael Nottidge,** M.D., MPH, FACEP*

***S. Shaefer Spires,** M.D.*

- Questions will be responded to at the end of the session. Please use the chat feature in your WebEx tool bar to send in your questions.
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- All information provided in this slide deck is up to date as of 2/22/2021. Please refer to source references for future updates to the information.

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February, 25, 2021

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COVID-19 | Vaccine Current State & Addressing Hesitancy

Welcome & Introductions

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Moderator

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Panelists

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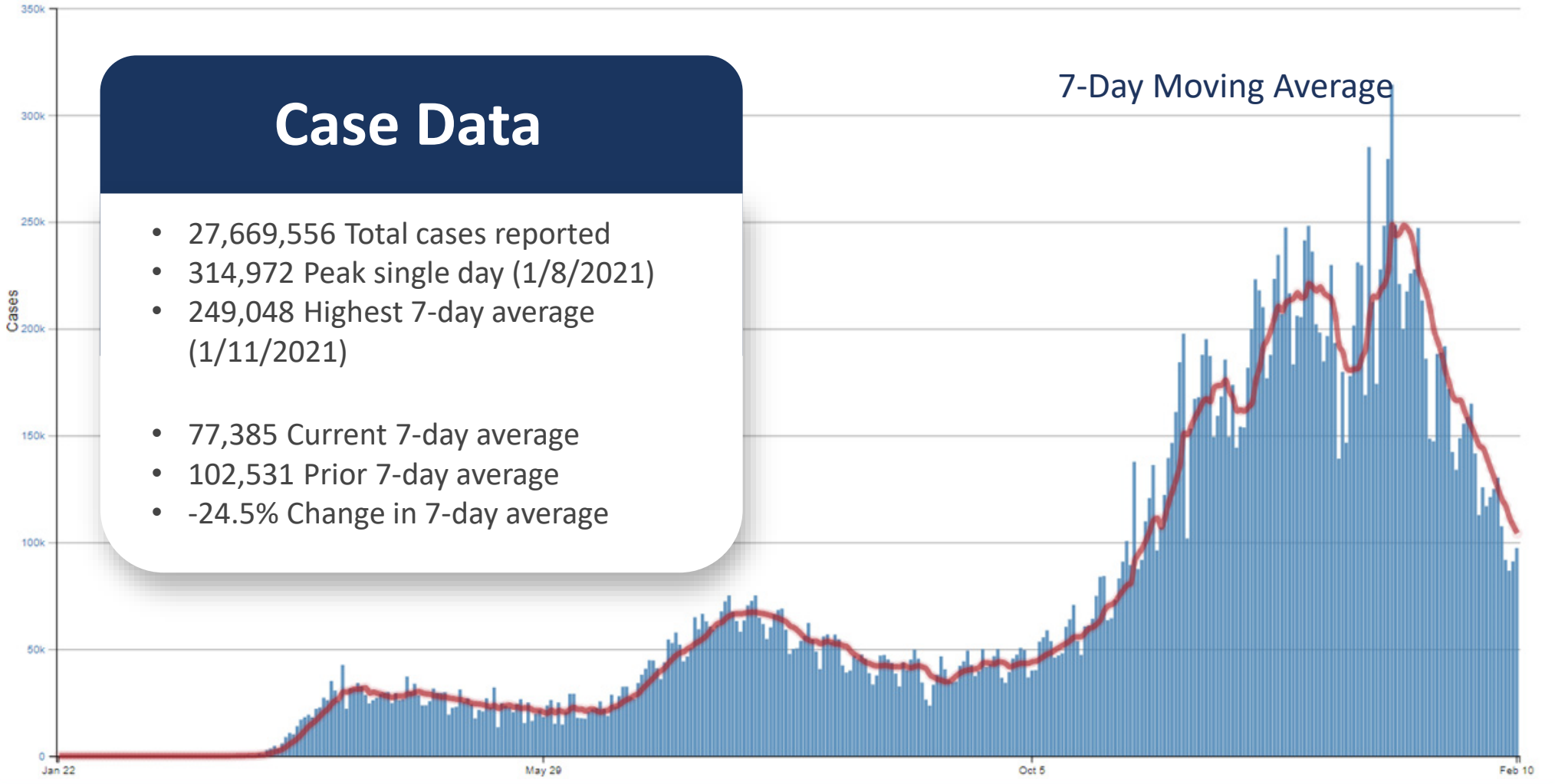
Daily Trends in U.S. COVID-19 Cases – Feb. 19, 2021

Case Data

- 27,669,556 Total cases reported
- 314,972 Peak single day (1/8/2021)
- 249,048 Highest 7-day average (1/11/2021)

- 77,385 Current 7-day average
- 102,531 Prior 7-day average
- -24.5% Change in 7-day average



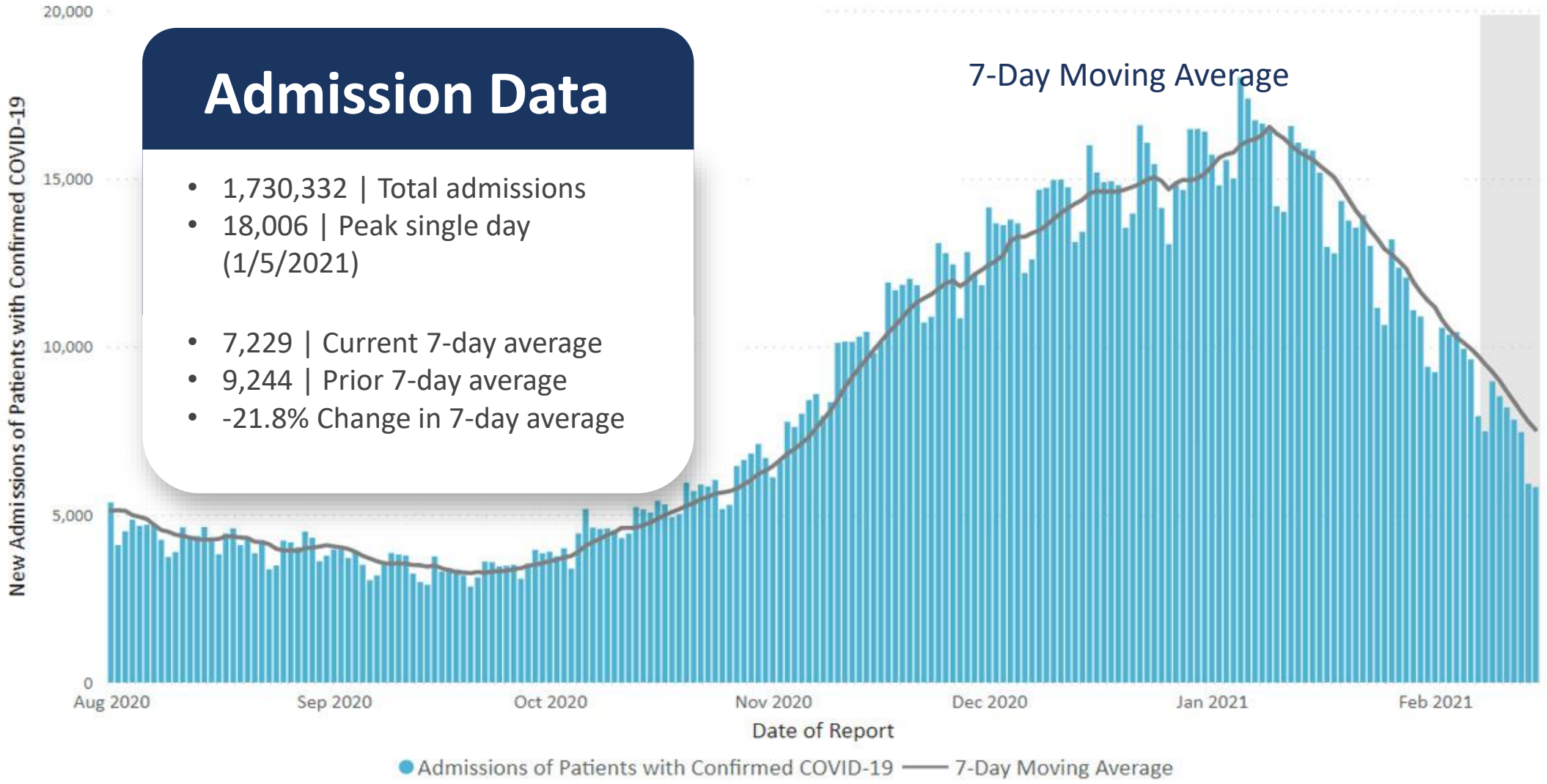
https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html

Daily Trends in U.S. COVID-19 New Hospital Admissions – Feb. 19, 2021

Admission Data

- 1,730,332 | Total admissions
- 18,006 | Peak single day (1/5/2021)

- 7,229 | Current 7-day average
- 9,244 | Prior 7-day average
- -21.8% Change in 7-day average

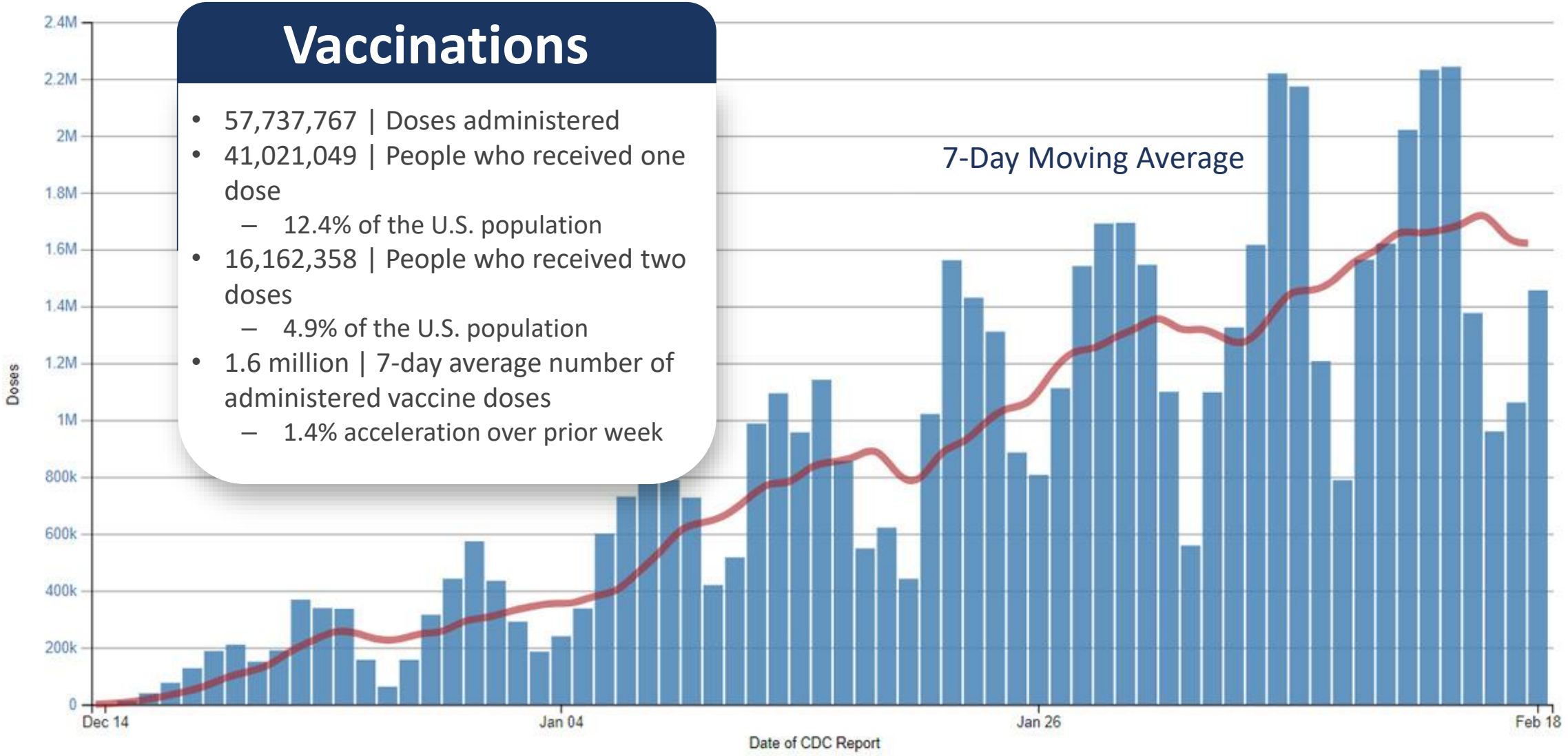


https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html

Daily Change in Number of U.S. COVID-19 Vaccinations – Feb. 19, 2021

Vaccinations

- 57,737,767 | Doses administered
- 41,021,049 | People who received one dose
  - 12.4% of the U.S. population
- 16,162,358 | People who received two doses
  - 4.9% of the U.S. population
- 1.6 million | 7-day average number of administered vaccine doses
  - 1.4% acceleration over prior week



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

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U.S. COVID-19 Vaccines With EUA Approval

	BNT162b2	mRNA-1273
Manufacturer	Pfizer & BioNTech	Moderna
EUA Approval	Yes	Yes
Platform	mRNA	mRNA
Phase 3 Study Population	• 43,538 participants enrolled • Age 12–85 years	• 30,000 participants enrolled • Age ≥18 years
Dosing	2 doses, 21 days apart 30 mcg/0.3 mL IM	2 doses, 28 days apart 100 mcg/0.5 mL IM
How Supplied	Solution for dilution in 6-dose vial	Solution in 10-dose vial
Storage & Stability	• 6 months in ultra-low temp freezer at -60 C to -80°C • 15 days in thermal shipper at -60°C to -80°C • 14 days in standard freezer -25°C to -15°C (Pending FDA approval) • 5 days in fridge at 2°C to 8°C • After dilution, 6 hours at room temperature	• 6 months in freezer at -20°C • 30 days in fridge at 2°C to 8°C • 12 hours at room temperature • Once entered, 6 hours at room temperature

https://clinicaltrials.gov
https://www.cdc.gov/vaccines/acip/meetings/slides-2021-1-27-21.html

COVID-19 Vaccine Candidates

Earliest Candidates in Phase 3 in the U.S. (without EUA)

	Ad26.COV2.S	AZD1222	NVX-CoV2373
Manufacturer	Janssen	AstraZeneca & University of Oxford	Novavax
Platform	Non-Replicating Viral Vector	Non-Replicating Viral Vector	Protein Subunit
Phase 3 Study Population	• ~43,000 participants • Age ≥18 years	• ~30,000 participants planned • Age ≥18 years	• ~30,000 participants planned • Age ≥18 years
Dosing	5×10^{10} vp/0.5 mL IM, 1 dose	5×10^{10} vp/0.5 mL IM, 2 doses, 28 days apart	5 µg + 50 µg adjuvant/0.5 mL IM, 2 doses, 21 days apart
How Supplied	Solution in 5-dose vial	Solution in 10-dose vial	Solution in 10-dose vial
Storage & Stability	• 3 months at 2–8°C • Once entered, 6 hours at 2-8°C	• 6 months at 2-8°C • Once entered, 48 hours at 2–8°C or 6 hours at 20–25°C	• 2–8°C
Timeline	Feb 4 – filed for EUA Feb 26 – VRBPAC meeting	April 2021	U.S. & Mexico phase 3 enrollment expected to complete in mid-Feb.
U.S. Dose Commitments	100 million ± 200 million	300 million	100 million
Medicare Reimbursement	$28.39	1st dose: $16.94 2nd dose: $28.39	TBD
Efficacy	U.S.: 72% Central & South America: 66% South Africa: 57%	UK: 74% Brazil: 64%	UK: 89% South Africa: 50%

Janssen Phase 3 Interim Analysis

ENSEMBLE 1 Trial

Baseline Characteristic	N=43,783
Age ≥60 years	34%
Male	55%
Race	
White/Caucasian	59%
Black/African American	19%
Native American	9%
Asian	3%
Ethnicity	
Hispanic and/or Latinx	45%
Country	
U.S.	44%
Central & South America	41%
South Africa	15%
Comorbidities	
Obesity	28.5%
Type 2 diabetes	7.3%
Hypertension	10.3%
HIV	2.8%

Outcome (starting 28 days post-vaccination)	Vaccine Efficacy
Moderate to severe COVD-19	66%
U.S.	72%
Central & South America	66%
South Africa	57%
Severe COVID-19	85%

- "Complete protection against COVID-related hospitalization and death, 28 days post-vaccination"
- No reported cases of COVID-19 requiring medical intervention among vaccine participants, 28 days post-vaccination
- In South Africa, 95% of COVID-19 cases were due to a SARS-CoV-2 variant from the B.1.351 lineage
- Fever: 9%; Grade 3 fever: 0.2%
- Serious adverse events were higher in placebo participants vs. vaccine participants
- No anaphylaxis observed

https://www.jnj.com/johnson-johnson-announces-single-shot-janssen-covid-19-vaccine-candidate-met-primary-endpoints-in-interim-analysis-of-its-phase-3-ensemble-trial

AstraZeneca – UK, Brazil & South Africa Exploratory Analysis

Timing of Booster Dose

Outcome (starting 14 days post-2nd dose)	AZD1222, n/N	Control, n/N	Vaccine Efficacy (95% CI)
Symptomatic COVID-19	84/8597 (1.0%)	248/8580 (2.9%)	**66.7% (57.4, 74.0)**
SD/SD	74/7201 (1.0%)	197/7178 (2.7%)	**63.1% (51.8, 71.7)**
<6 weeks	35/3900 (0.9%)	76/3860 (2.0%)	**54.9% (32.7, 69.7)**
6-8 weeks	20/1103 (1.8%)	44/1004 (4.4%)	**59.9% (32.1, 76.4)**
9-11 weeks	11/905 (1.2%)	32/957 (3.3%)	**63.7% (28.0, 81.7)**
≥12 weeks	8/1293 (0.6%)	45/1356 (3.3%)	**82.4% (62.7, 91.7)**
LD/SD	10/1396 (0.7%)	51/1402 (3.6%)	**80.7% (62.1, 90.2)**
<6 weeks	0/15 (0.0%)	0/15 (0.0%)	NR
6-8 weeks	0/12 (0.0%)	0/14 (0.0%)	NR
9-11 weeks	3/624 (0.5%)	20/636 (3.1%)	NR (84.7% calculated)
≥12 weeks	7/745 (0.9%)	31/737 (4.2%)	NR (77.7% calculated)

LD/SD = low 1st dose/standard 2nd dose; SD/SD = standard 1st dose/standard 2nd dose

SD/SD efficacy was lower than LD/SD efficacy (63.1% vs 80.7%)

31% of SD/SD participants had 1st & 2nd doses ≥9 weeks apart
&
98% of LD/SD participants had 1st & 2nd doses ≥9 weeks apart

Efficacy increased with longer intervals between 1st & 2nd doses

↓

Suggests higher efficacy with LD/SD was because of longer dosing interval, not lower 1st dose

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3777268

Variant Update

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SARS-CoV-2 Variants

Variant	Emerged	Date	Reported in U.S.	Spike Changes	Benefit to the Virus
B.1.1.7 (201/501Y.V1, VOC 202012/)	United Kingdom	9/2020	12/2020	8 changes in N501Y	Increased transmissibility, but early reports no impact on vaccine efficacy.
B.1.351 (20H/501Y.V2)	South Africa	10/2020	1/2021	10 changes N501Y, E484K, K417T/N	No evidence to suggest impact on disease severity. One of the spike mutations may affect neutralization by some polyclonal & monoclonal antibodies.
P.1	Brazil	12/2020	1/2021	12 changes N501Y, E484K, K417T/N	Increased transmissibility & impact on antigenic profile, which may affect ability of antibodies previously generated through infection or vaccination to recognize and neutralize the virus.

Resource: Centers for Disease Control and Prevention. Emerging SARS-CoV-2 Variants. Available at: https://www.cdc.gov/coronavirus/2019-ncov/more/science-and-research/scientific-brief-emerging-variants.html Accessed: 2.13.2020

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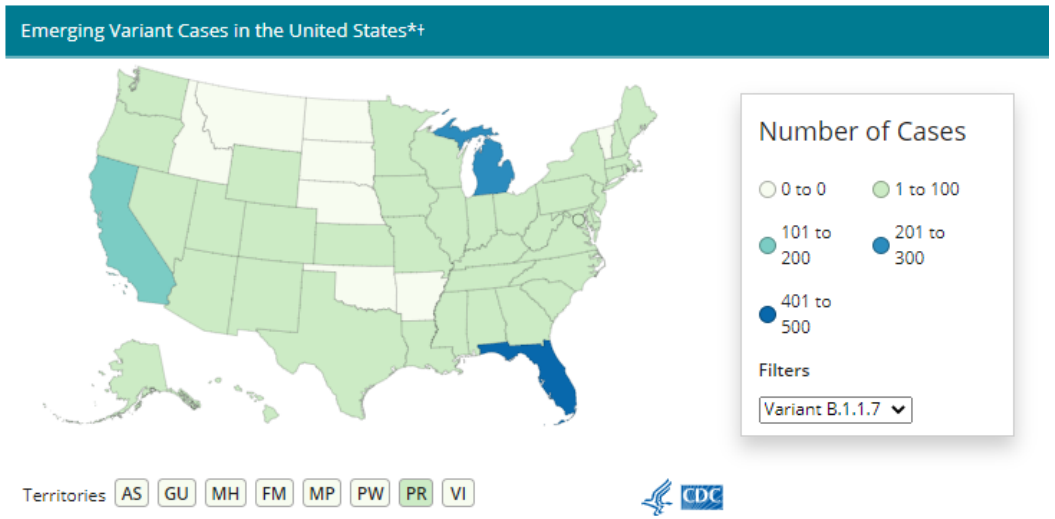
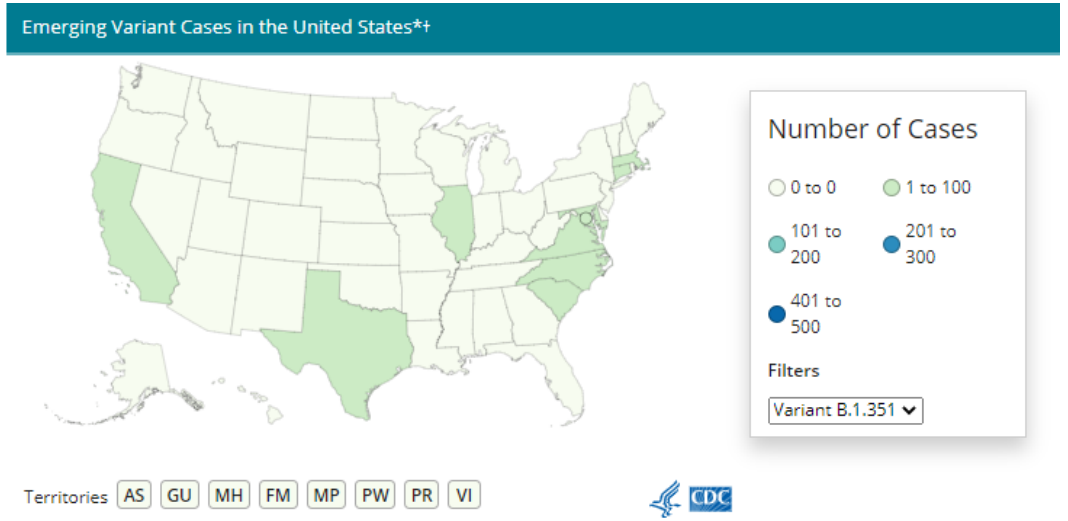
Emerging Variant Cases in the United States – Feb. 21, 2021

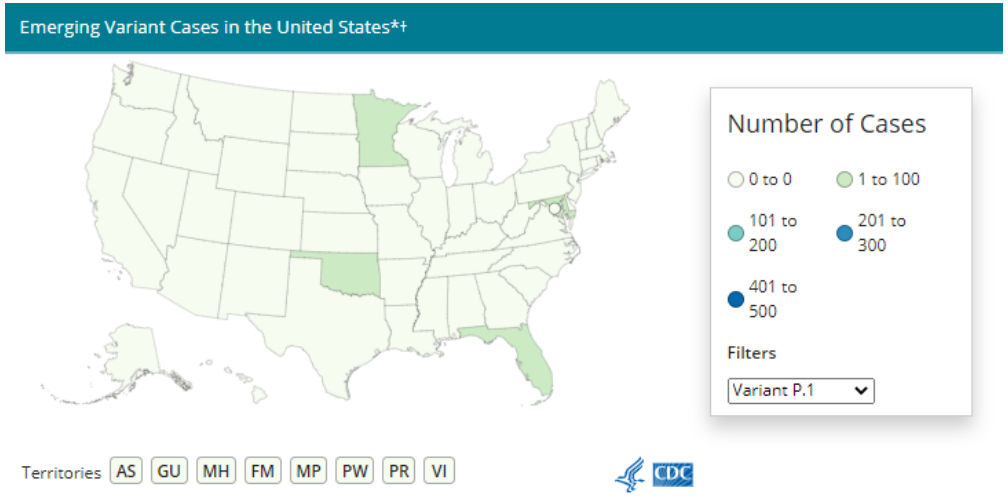
United Kingdom-Variant B.1.1.7



South Africa Variant B.1.351



Brazil Variant P.1



https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant-cases.html

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AstraZeneca Exploratory Analyses

Efficacy Against Variant Strains

B.1.1.7 Variant in UK Phase 2/3 Study

Outcome (starting 15 days post-2nd dose)	AZD1222 (n=4236)	Control (n=4270)	Vaccine Efficacy (95% CI)
Symptomatic COVID-19	52 (1.2%)	198 (4.6%)	**74.2% (65.0, 81.0)**
B.1.1.7	7 (0.2%)	27 (0.6%)	**74.6% (41.6, 88.9)**
Other variants	12 (0.3%)	74 (1.7%)	**84.1% (70.7, 91.4)**
No sequence result	5 (0.1%)	20 (0.5%)	**75.4% (34.3, 90.8)**
Not sequenced	28 (0.7%)	77 (1.8%)	**64.3% (44.9, 76.8)**
Asymptomatic COVID-19	96 (2.3%)	112 (2.6%)	15.7% (-10.7, 35.8)
B.1.1.7	6 (0.1%)	8 (0.2%)	26.5% (-112.0, 74.5)
Other variants	6 (0.1%)	24 (0.6%)	**75.4% (39.9, 89.9)**
No sequence result	21 (0.5%)	16 (0.4%)	-28.7% (-146.6, 32.8)
Not sequenced	63 (1.5%)	64 (1.5%)	3.1% (-37.3, 31.6)

https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3779160

B.1.351 Variant in South Africa Phase 1/2 Study

- "…a two-dose regimen of the ChAdOx1 nCoV-19 vaccine provides **minimal protection against mild-moderate COVID-19 infection from the B.1.351 coronavirus variant** first identified in South Africa"
- "Protection against **moderate-severe disease, hospitalisation or death could not be assessed** in this study as the target population were at such low risk."

https://www.ox.ac.uk/news/2021-02-07-chadox1-ncov-19-provides-minimal-protection-against-mild-moderate-covid-19-infection

Vaccine Confidence

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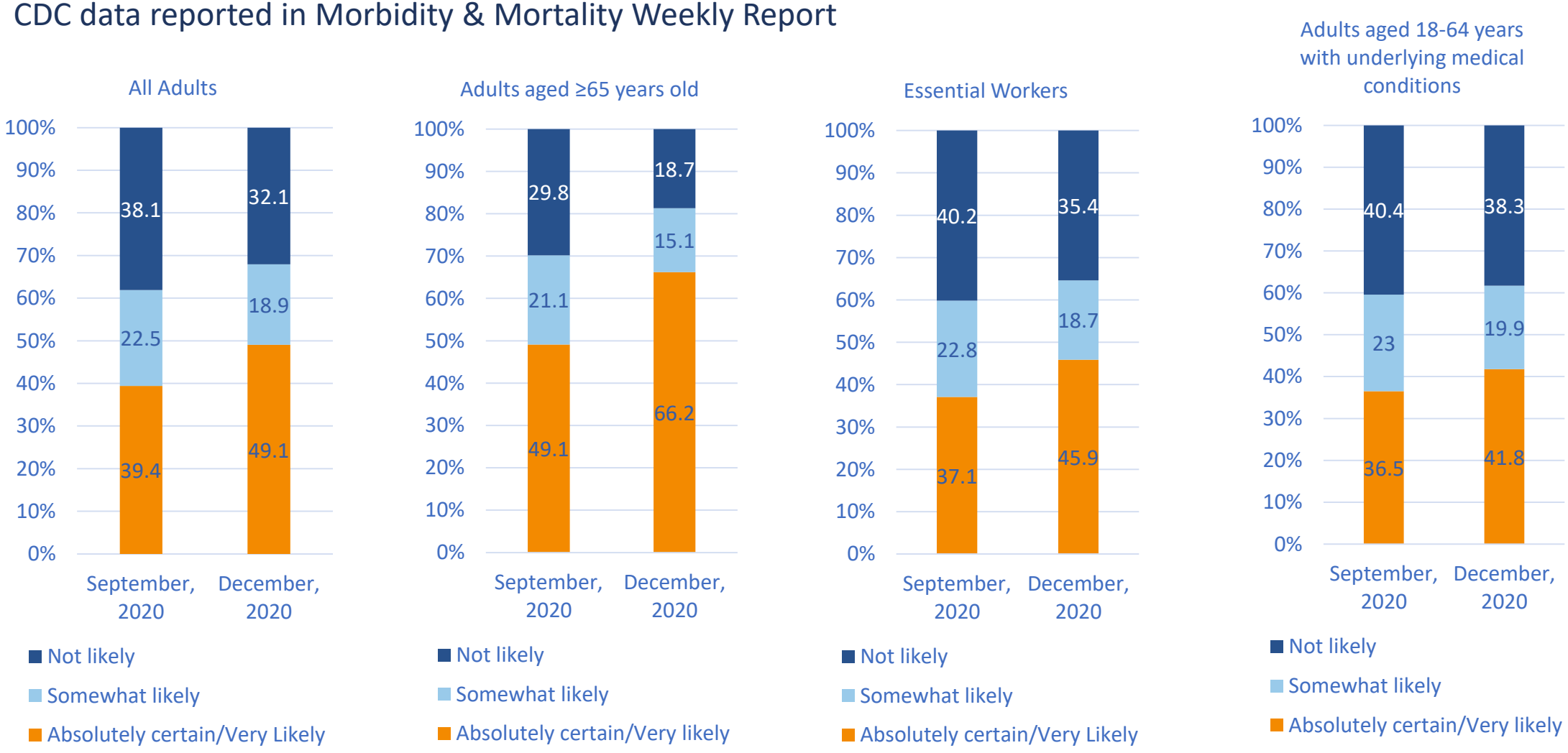
Intent to receive COVID-19 Vaccine – CDC

CDC data reported in Morbidity & Mortality Weekly Report



Nguyen KH, Srivastav A, Razzaghi H, et al. COVID-19 Vaccination Intent, Perceptions, and Reasons for Not Vaccinating Among Groups Prioritized for Early Vaccination — United States, September and December 2020. MMWR Morb Mortal Wkly Rep 2021;70:217–222. DOI: http://dx.doi.org/10.15585/mmwr.mm7006e3external icon.

Further Detail Regarding Hesitancy

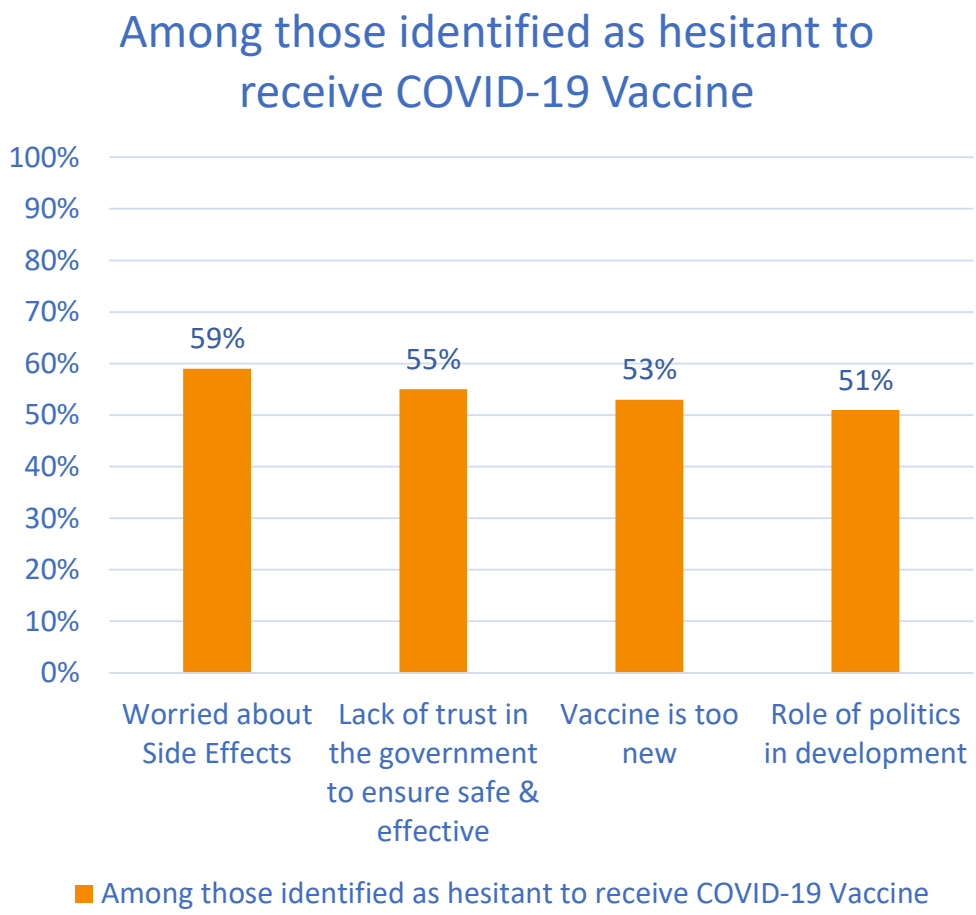
CDC Morbidity & Mortality Weekly Report

Additional Data September to December, 2020

- Intent **not** to receive COVID 19 Vaccine
  - Males dropped from 33.8% to 27.8%
  - Female dropped from 42.1% to 36.0%
  - Employed dropped from 38.6% to 32.3%
  - Not employed/Not in workforce dropped 36.6% to 31.5%
- Concern about COVID-19 illness for self
  - Very/Somewhat concerned 27.6%-18.8%
  - Slightly/Not concerned 50.1%-51.3%
- Concern about side effects of vaccine for self
  - Very/Somewhat concerned 43.7%-40.5%
  - Slightly/Not concerned 28.9%-21.5%
- While the data is improving, we have a long way to go

Nguyen KH, Srivastav A, Razzaghi H, et al. COVID-19 Vaccination Intent, Perceptions, and Reasons for Not Vaccinating Among Groups Prioritized for Early Vaccination — United States, September and December 2020. MMWR Morb Mortal Wkly Rep 2021;70:217–222. DOI: http://dx.doi.org/10.15585/mmwr.mm7006e3external icon. Accessed2/15/2021

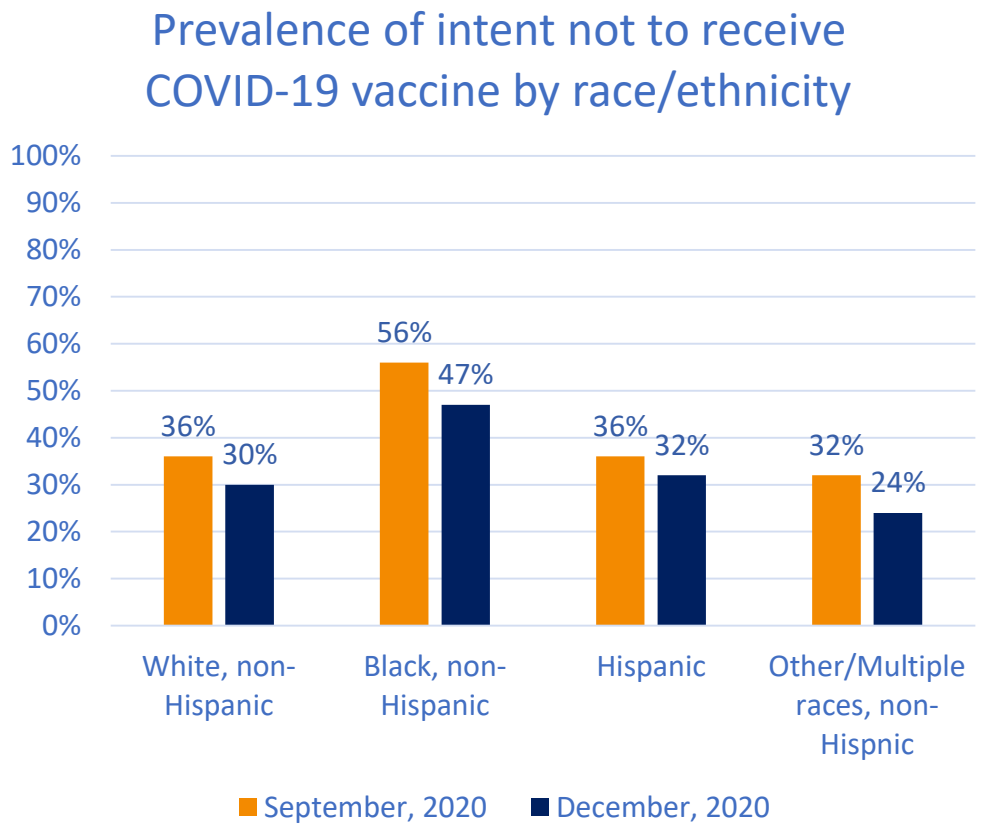
KFF COVID-19 Vaccine Monitor: December 2020



Hamel L, Kirzinger A, Munana C, Brodie M. KFF COVID-19 Vaccine Monitor: December 2020. Kaiser Family Foundation. *WordPress* Available at: https://www.kff.org/coronavirus-covid-19/report/kff-covid-19-vaccine-monitor-december-2020/ Accessed 1.14.2021.

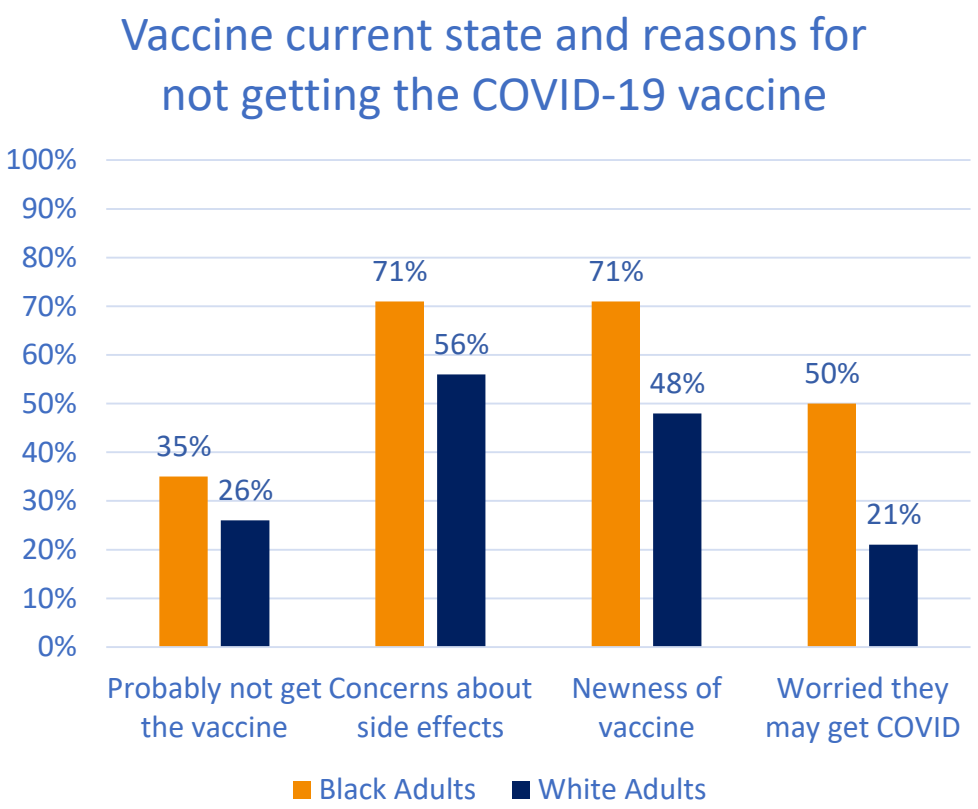
Race/Ethnicity Data

CDC: Morbidity & Mortality Weekly Report



Nguyen KH, Srivastav A, Razzaghi H, et al. COVID-19 Vaccination Intent, Perceptions, and Reasons for Not Vaccinating Among Groups Prioritized for Early Vaccination — United States, September and December 2020. MMWR Morb Mortal Wkly Rep 2021;70:217–222.
DOI: http://dx.doi.org/10.15585/mmwr.mm7006e3external icon.

KFF COVID-19 Vaccine Monitor



Hamel L, Kirzinger A, Munana C, Brodie M. KFF COVID-19 Vaccine Monitor: December 2020. Kaiser Family Foundation. *WordPress* Available at: https://www.kff.org/coronavirus-covid-19/report/kff-covid-19-vaccine-monitor-december-2020/ Accessed 1.14.2021.

Understanding Herd Immunity

Red = Contagious

Orange = Susceptible (no natural or vaccine-generated immunity)

Blue = Immunity (vaccine or natural)

- Once a high percentage of the community is immune to COVID-19 either due to vaccination or prior illness we can achieve herd immunity.
- We do not know what this number is for COVID-19, however it is being studied.

No immunity. Disease can spread easily from person to person.

People start to gain natural or vaccine-generated immunity. These people are protected for a period of time.

When enough people are immunized, the disease cannot easily spread to susceptible individuals.

CDC COVID-19 *Frequently asked questions about COVID-19 Vaccination.* Available at https://www.cdc.gov/coronavirus/2019-ncov/vaccines/faq.html Accessed 2.12.2021

Strategies for Building Confidence in the COVID-19 Vaccines

The National Academies of Sciences, Engineering & Medicine

Strategies for engaging communities to combat mistrust & build confidence

- Form partnerships with community organizations
- Engage with and center the voices and perspectives of trusted messengers who have roots in the community
- Engage across multiple, accessible channels
- Begin or continue working toward racial equity
- Allow and encourage public ownership of COVID-19 vaccination
- Measure and communicate inequities in vaccine distribution

Communication strategies for ensuring demand for & promoting acceptance of COVID-19 vaccines

- Meet people where they are, and don't try to persuade everyone
- Avoid repeating false claims
- Tailor messages to specific audiences
- Adapt messaging as circumstances change
- Respond to adverse events in a transparent, timely manner
- Identify trusted messengers to deliver messages
- Emphasize support for vaccination instead of focusing on naysayers
- Leverage trusted vaccine endorsers
- Pay attention to delivery details that also convey information

National Academies of Sciences, Engineering, and Medicine 2021. *Strategies for Building Confidence in the COVID-19 Vaccines*. Washington, DC: The National Academies Press. https://doi.org/10.17226/26068.

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Appendix

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Novavax UK Phase 3 Interim Analysis

Outcome (starting 7 days post-2nd dose)	NVX-CoV2373 (n=7,016)	Placebo (n=7,033)	Vaccine Efficacy (95% CI)
COVID-19	6	56	**89.3% (75.2, 95.4)**
Mild	1	15	Not reported
Moderate	5	40	Not reported
Severe	0	1	Not reported

Safety	NVX-CoV2373 (n=7,016)	Placebo (n=7,033)
Any severe treatment emergent AE	81 (1.1 %)	53 (0.7%)
Any serious treatment emergent AE	31 (0.4%)	30 (0.4%)
Any medically attended AE	202 (2.7%)	201 (2.8%)

- Preliminary PCR data show >50% of cases attributable to UK 501Y.V1 escape variant (aka B.1.1.7 variant)
- 62 total COVID-19 cases in interim analysis
- 100 total COVID-19 cases needed for final analysis

https://www.novavax.com/sites/default/files/2021-02/20210202-NYAS-Novavax-Final.pdf

SARS-CoV-2 Variants: Implications for Vaccination

Following vaccination, study participant sera (n=8-20) tested in neutralization assays:

- Pfizer BioNTech COVID-19 Vaccine:
  - Studies demonstrated equivalent neutralizing titers against a panel of 19 individual SARS-CoV-2 spike variants and N501Y (variant) compared to wildtype virus
  - Reductions to neutralizing titers have been noted against the B.1.1.7 variant (all mutations):
    - ✓ 1.3-fold average reduction
    - ✓ 3.9 –fold median reduction
  - One study showed modest reduction (<3-fold) for some with neutralization against certain SARS-CoV-2 spike mutations from B.1.351 and P.1 variants: E484K and K417N:E484K:N501Y
- Moderna COVID-19 Vaccine:
  - One study with modest reduction (<3-fold) for some with neutralization against certain SARS-CoV-2 spike mutations from B.1.351 and P.1 variants: E484K and K417N:E484K:N501Y
  - Another study with no significant impact on neutralizing titers against B.1.1.7 variant, but 6-fold reduction for B.1.351 variant
  - Working on new vaccine for B.1.351 variant

Presented at ACIP Meeting January, 2021

Sahin et al. medRxiv preprint (Dec 11, 2020a); doi: https://doi.org/10.1101/2020.12.09.20245175 Xie et al. bioRxiv preprint (Jan 07, 2021) ; doi: https://doi.org/10.1101/2021.01.07.425740 Muik et al. bioRxiv preprint (Jan 19, 2021); doi: https://doi.org/10.1101/2021.01.18.426984
Collier et al. medRxiv preprint (Jan 20, 2021); doi: https://doi.org/10.1101/2021.01.19.21249840
Wang et al. bioRxiv preprint (Jan 15, 2021) ; doi: https://doi.org/10.1101/2021.01.15.426911
Wu et al. BioRxiv preprint ((Jan 25, 2021); doi: https://doi.org/10.1101/2021.01.25.427948