Vaccines and Related Biological Products Advisory Committee February 26, 2021 Meeting Presentation

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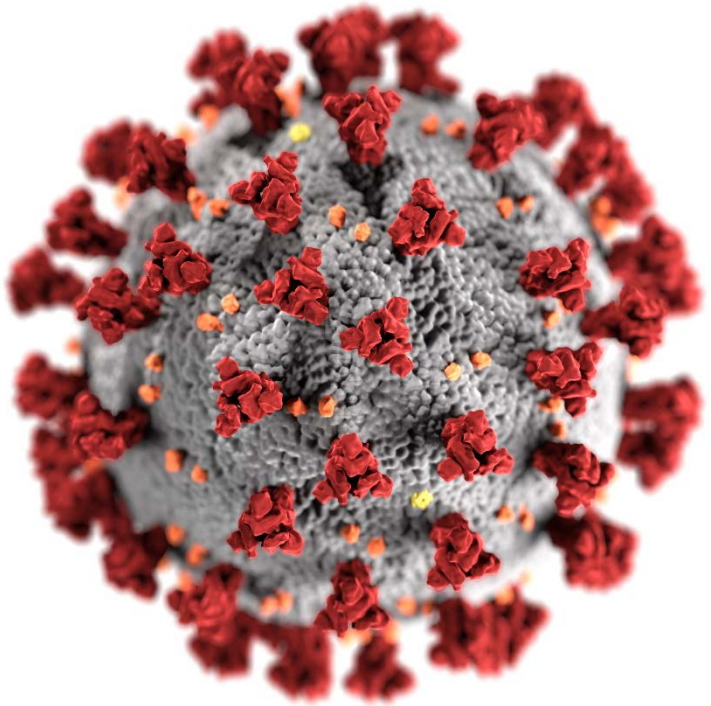
Epidemiology of SARS-CoV-2 variants

Adam MacNeil, PhD, MPH

Epidemiology Taskforce, COVID-19 response

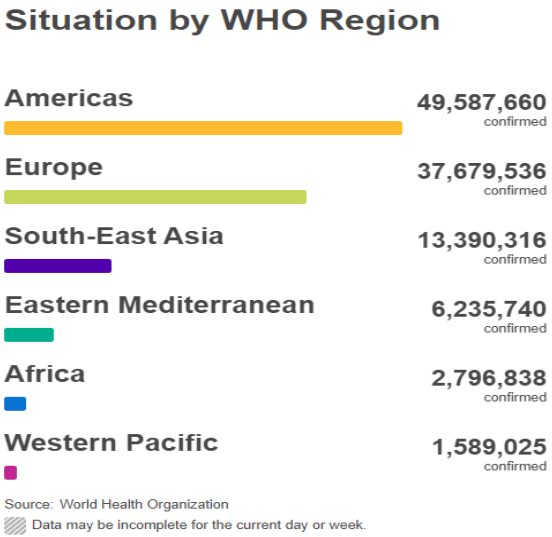


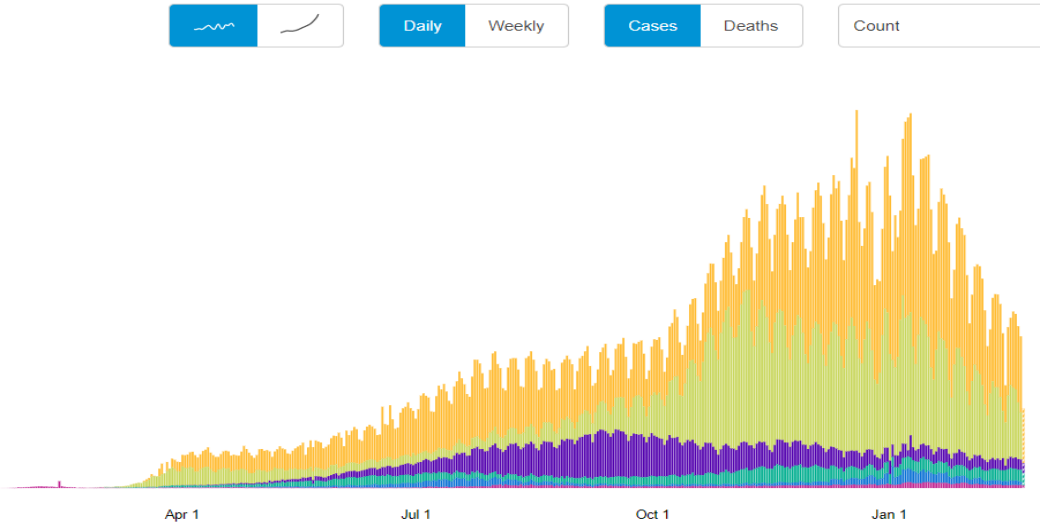
February 26, 2021

cdc.gov/coronavirus

Global burden of SARS-CoV-2

- 111,279,680 confirmed cases
- 2,466,639 deaths





https://covid19.who.int/ ; accessed 02/23/2021

Criteria for defining variants (including variant of interest and variant of concern)

- Various organizations developing definitions, including WHO
- United States government definition being reviewed as part of interagency activities
- Key criteria
  - Evidence of immune escape (vaccine or natural infection)
  - Convergent evolution
  - Impact on diagnostics
  - Impact on therapeutics
  - Evidence of increased transmissibility
  - Evidence of increased disease severity

Current Variants of Concern

Variant designation	First identification		Characteristic mutations (protein: mutation)
	Location	Date	
B.1.1.7 (20I/501Y.V1)	United Kingdom	Sep 2020	ORF1ab: T1001I, A1708D, I2230T, del3675–3677 SGF
			S: del69–70 HV, del144 Y, N501Y, A570D, D614G, P681H, T761I, S982A, D1118H
			ORF8: Q27stop, R52I, Y73C
			N: D3L, S235F
B.1.351 (20H/501Y.V2)	South Africa	Oct 2020	ORF1ab: K1655N
			E: P71L
			N: T205I
			S:K417N, E484K, N501Y, D614G, A701V
P.1 (20J/501Y.V3)	Brazil and Japan	Jan 2021	ORF1ab: F681L, I760T, S1188L, K1795Q, del3675–3677 SGF, E5662D
			S: L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G, H655Y, T1027I
			ORF3a: C174G
			ORF8: E92K
			ORF9: Q77E
			ORF14: V49L
			N: P80R

Galloway SE, Paul P, MacCannell DR, et al. Emergence of SARS-CoV-2 B.1.1.7 Lineage — United States, December 29, 2020–January 12, 2021. MMWR Morb Mortal Wkly Rep 2021;70:95–99. DOI: http://dx.doi.org/10.15585/mmwr.mm7003e2external icon

Current Variants of Concern

Variant designation	First identification		Characteristic mutations (protein: mutation)
	Location	Date	
B.1.1.7 (20I/501Y.V1)	United Kingdom	Sep 2020	ORF1ab: T1001I, A1708D, I2230T, del3675–3677 SGF
			S: del69–70 HV, del144 Y, N501Y, A570D, D614G, P681H, T761I, S982A, D1118H
			ORF8: Q27stop, R52I, Y73C
			N: D3L, S235F
B.1.351 (20H/501Y.V2)	South Africa	Oct 2020	ORF1ab: K1655N
			E: P71L
			N: T205I
			S:K417N, E484K, N501Y, D614G, A701V
P.1 (20J/501Y.V3)	Brazil and Japan	Jan 2021	ORF1ab: F681L, I760T, S1188L, K1795Q, del3675–3677 SGF, E5662D
			S: L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G, H655Y, T1027I
			174G
			2K
			7E
			49L
			N: P80R

- Convergent evolution
- E484K potential reduced neutralization

Galloway SE, Paul P, MacCannell DR, et al. Emergence of SARS-CoV-2 B.1.1.7 Lineage — United States, December 29, 2020–January 12, 2021. MMWR Morb Mortal Wkly Rep 2021;70:95–99. DOI: http://dx.doi.org/10.15585/mmwr.mm7003e2external icon

Current Variants of Concern

Variant designation	First identification: Location	First identification: Date	Characteristic mutations (protein: mutation)
B.1.1.7 (20I/501Y.V1)	United Kingdom	Sep 2020	ORF1ab: T1001I, A1708D, I2230T, del3675–3677 SGF
			S: del69–70 HV, del144 Y, N501Y, A570D, D614G, P681H, T761I, S982A, D1118H
			[illegible]
			[illegible]
			[illegible]
			[illegible]
			[illegible]
			[illegible]614G, A701V
			[illegible]88L, K1795Q, del3675–3677 SGF, E5662D
			S: L18F, T20N, P26S, D138Y, R190S, K417T, E484K, N501Y, D614G, H655Y, T1027I
			ORF3a: C174G
			ORF8: E92K
			ORF9: Q77E
			ORF14: V49L
			N: P80R

- Deletion impacts S gene target on multiple diagnostic PCR assays
- Results in ‘S gene target failure’ (SGTF)
- Effective tool in screening for B.1.1.7

Galloway SE, Paul P, MacCannell DR, et al. Emergence of SARS-CoV-2 B.1.1.7 Lineage — United States, December 29, 2020–January 12, 2021. MMWR Morb Mortal Wkly Rep 2021;70:95–99. DOI: http://dx.doi.org/10.15585/mmwr.mm7003e2external icon

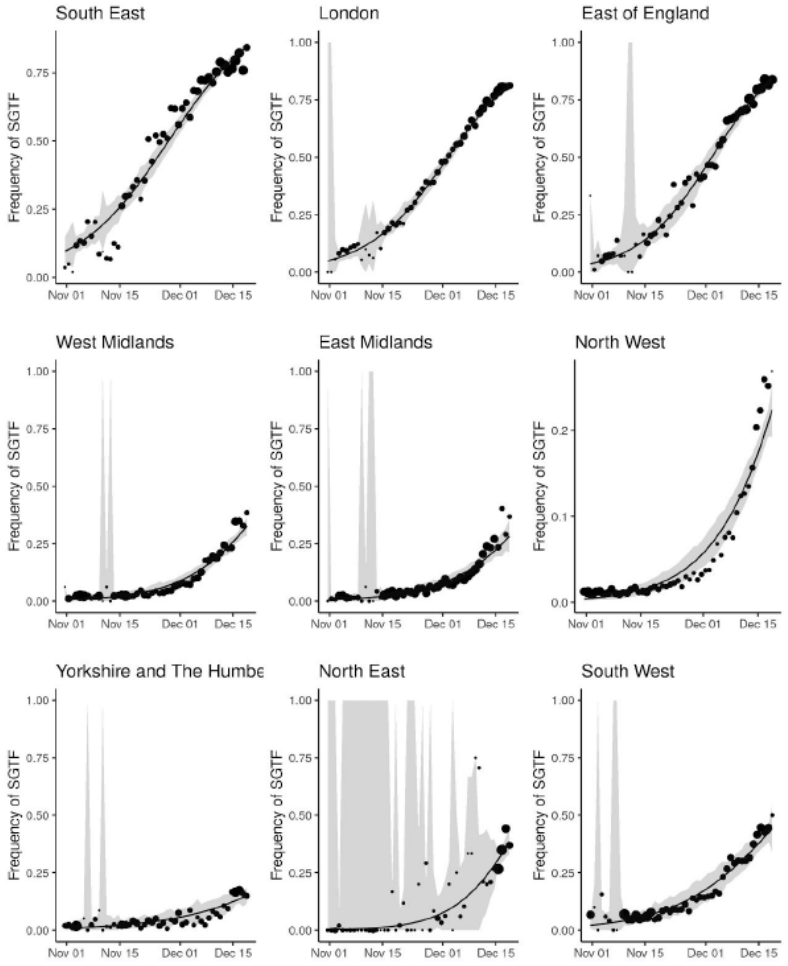
Global distribution of B.1.1.7

Country	Total Count	Count in previous 4 weeks	% of total B.1.1.7 in previous 4 weeks from 02/23/2021
United Kingdom	83,007	25,935	93.6
Denmark	2,614	1,149	37.3
USA	1,171	425	4.5
Belgium	1,032	359	36.3
France	1,006	334	53.4
Netherlands	941	378	28.5
Spain	925	192	35.6
Switzerland	713	389	27.7
Italy	658	357	72.7
Ireland	513	130	57.5

https://www.gisaid.org/hcov19-variants/; accessed 02/23/2021

B.1.1.7 United Kingdom

- Detected in England November 2020, likely emerged in September 2020 in SE England
- SGTF allowed monitoring approach for variant
- Rapid expansion throughout UK
- Reproductive number (R_t) estimated approximately 1.5 times higher transmissibility of B.1.1.7 in comparison to previous dominant virus



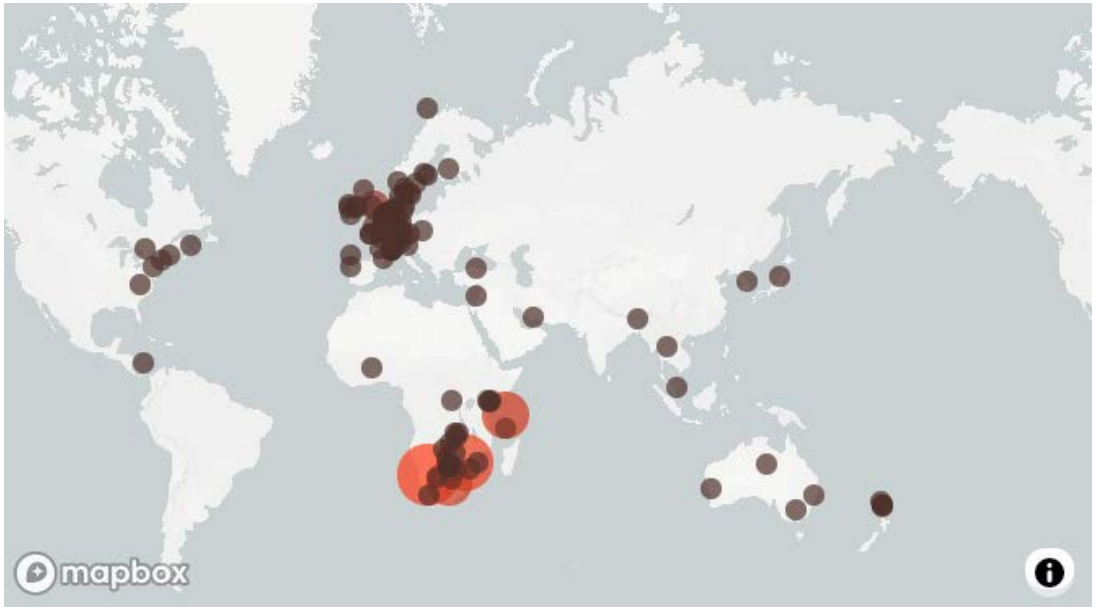
https://www.medrxiv.org/content/10.1101/2020.12.30.20249034v2

B.1.1.7 impact on outcomes

- Primarily unpublished data reviewed by the New and Emerging Viruses Threats Advisory Group (NERVTAG) on February 11, 2021
  - Composite conclusions from 22 analyses
  - Data using combination of B.1.1.7 variant of concern (VOC) and SGTF marker
- "There is evidence from analysis of multiple different datasets that infection with VOC B.1.1.7 is associated with an increased risk of hospitalization and death compared to infection with non-VOC viruses"
  - Results varied; some outcomes statistically significant
  - Ratios for hospitalization and death up to 1.7 times higher for variant
- "absolute risk of death per infection remains low"

https://www.gov.uk/government/publications/nervtag -update-note-on-b117-severity-11-february-2021

Global distribution of B.1.351

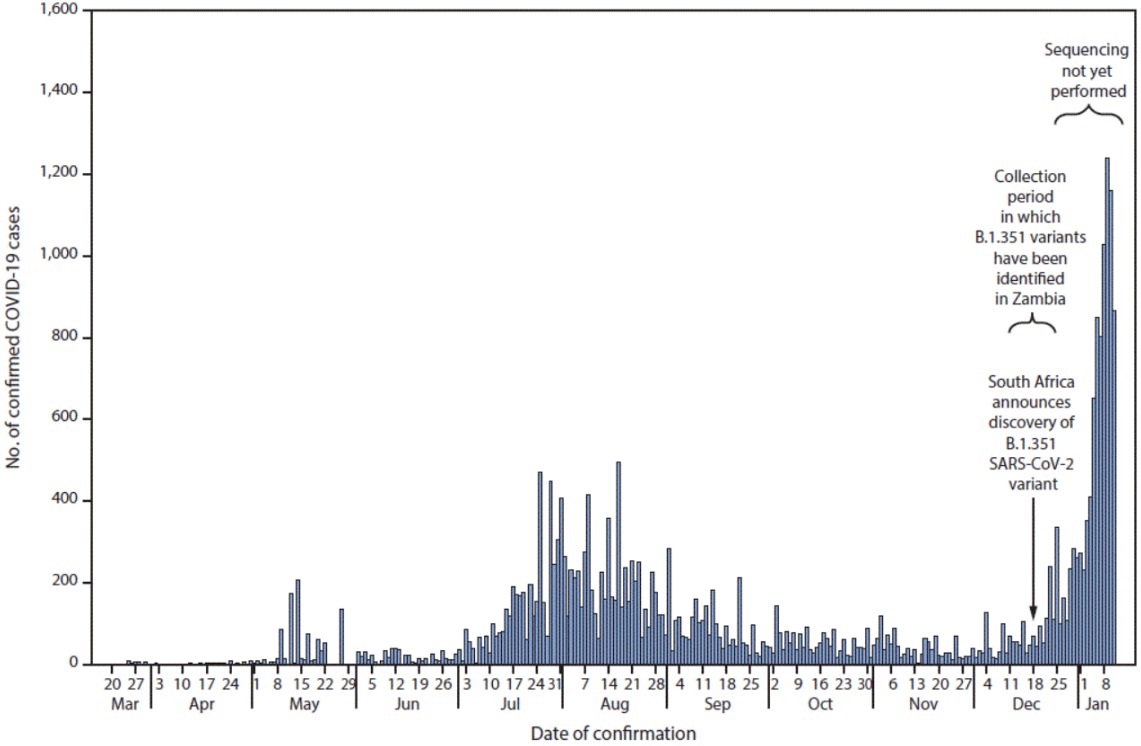


Country	Total Count	Count in previous 4 weeks	% of total B.1351 in previous 4 weeks from 02/23/2021
South Africa	958	30	96.8
Mayotte	304	168	76.7
United Kingdom	169	36	0.1
Belgium	89	32	3.2
Netherlands	67	29	2.2
France	65	31	5
Switzerland	52	30	2.1
Mozambique	41	0	0
Botswana	40	0	0
Zambia	31	0	0

https://www.gisaid.org/hcov19-variants/; accessed 02/23/2021

B.1.351 Zambia

- 16-fold increase in confirmed COVID-19 cases in approximately 1 month (December 2020–January 2021)
- 22/23 samples sequenced from December 16–23 were B.1.351
- Previously, zero of 245 were from B.1.351 lineage



Mwenda M, Saasa N, Sinyange N, et al. Detection of B.1.351 SARS-CoV-2 Variant Strain — Zambia, December 2020. MMWR Morb Mortal Wkly Rep. ePub: 17 February 2021. DOI: http://dx.doi.org/10.15585/mmwr.mm7008e2external icon

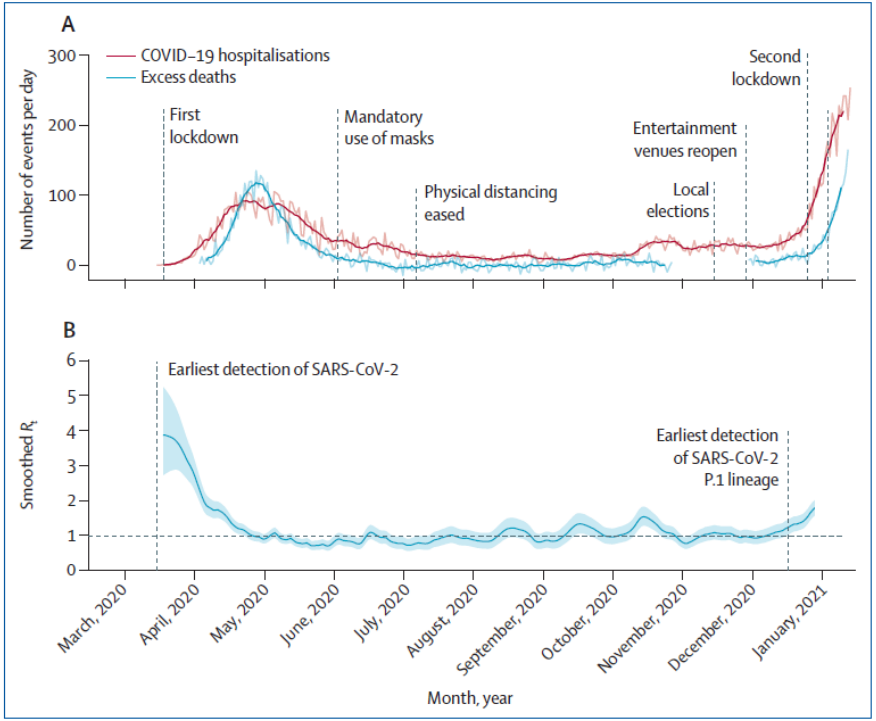
Global distribution of P.1

Country	Total Count	Count in previous 4 weeks	% of total P.1 in previous 4 weeks from 02/23/2021
Brazil	143	12	50
Italy	12	6	1.2
Switzerland	12	12	0.9
Colombia	10	2	50
Japan	10	2	6.2
USA	9	0	0
United Arab Emirates	9	0	0
Singapore	9	4	4.3
Belgium	7	7	0.7
France	6	2	0.3

https://www.gisaid.org/hcov19-variants/; accessed 02/23/2020

P.1 variant, Manaus, Brazil

- Widespread outbreak in 2020
  - Large peak in excess mortality in May 2020
  - Blood donor serology estimated 76% seroprevalence in October 2020
- Second large peak in hospitalizations and excess mortality started in January 2021
- P.1 variant detected January 12, 2021
- Suggestive of potential antigenic escape

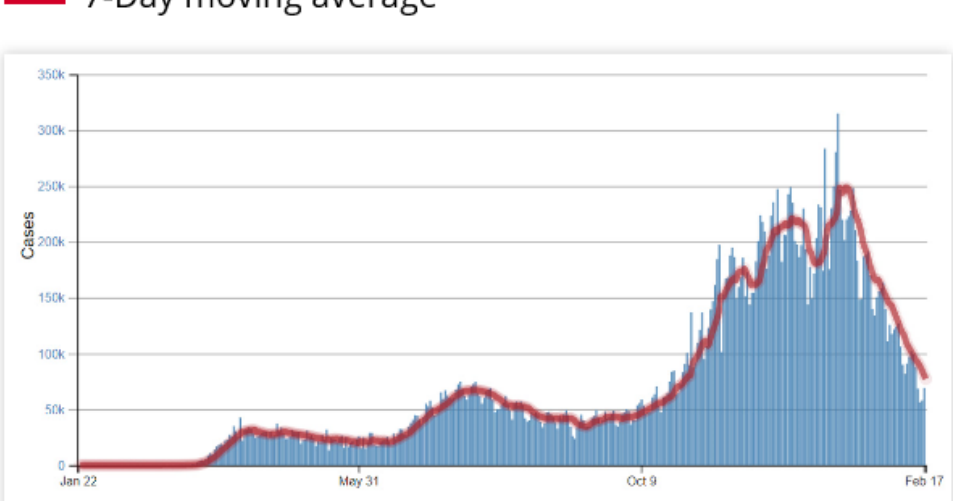


Sabino EC et al. Lancet 2021: 397(10275): 452-455

SARS-CoV-2 in the United States

69,165 New Cases Reported	77,385 Current 7-Day Average
27,669,556 Total Cases Reported	102,531 Prior 7-Day Average
314,972 Peak*	-24.5% Change in 7-Day Average

Daily Trends in COVID-19 Cases in the United States Reported to CDC



https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html; accessed 02/23/2021

Genomic epidemiology: key objectives and approaches

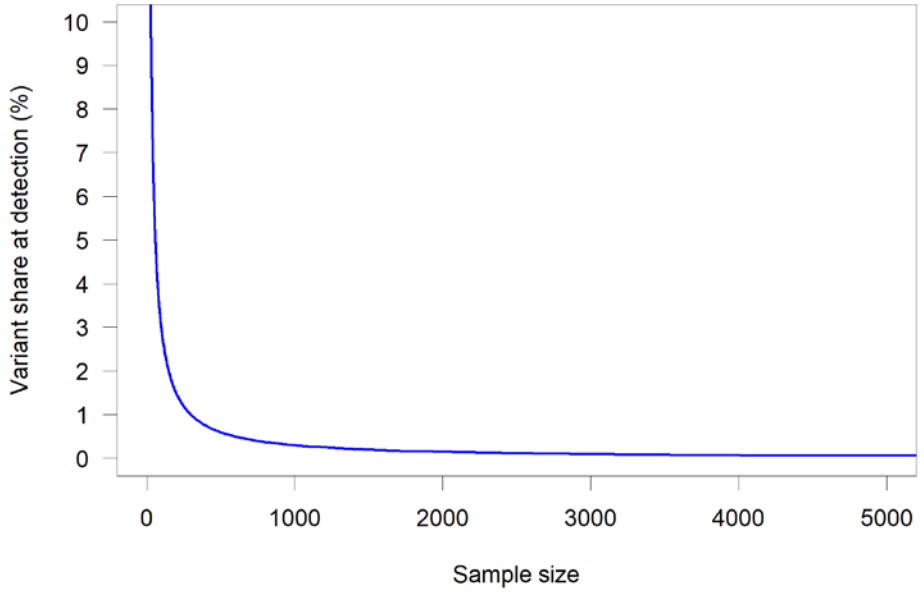
- Situational awareness / surveillance
  - Understand prevalence, spread of variants
  - Use for public health decisions
  - Requires widespread sampling, dependent on overall burden of infection
- Novel variant detection
  - Identify the presence of novel variant for further investigation
  - Relatively fixed sample size
- Focused studies
  - Characterize viral transmission, clinical outcomes, vaccine effectiveness, etc.
  - Extensive sampling and sequencing in targeted population

Challenges in genomic epidemiology of SARS-CoV-2

- Relatively small proportion of viruses sequenced
- Time lag between sample collection and sequence result
  - Sequencing is not a rapid diagnostic test
  - Limited clinical utility currently
  - May not inform immediate public health action (for instance, contact tracing)
- Not yet demonstrated effective as containment strategy
  - Broad global spread of SARS-CoV-2 variants
- Sequencing has limitations in predicting epidemiologic outcomes
  - Need for supporting virologic and immunologic studies
  - Clinical and epidemiologic evidence take time

Novel variant detection: estimating sampling sizes

- Adapted from Influenza Virologic Surveillance Right Size Roadmap
- Disease-agnostic sample size calculation
- Various factors, including sampling strategy, variant prevalence, turnaround time affect actual numbers
- To have 95% chance of identifying a variant that occurs in 1 out of 1000 cases (0.1% prevalence), need ~3,000 sequences per week

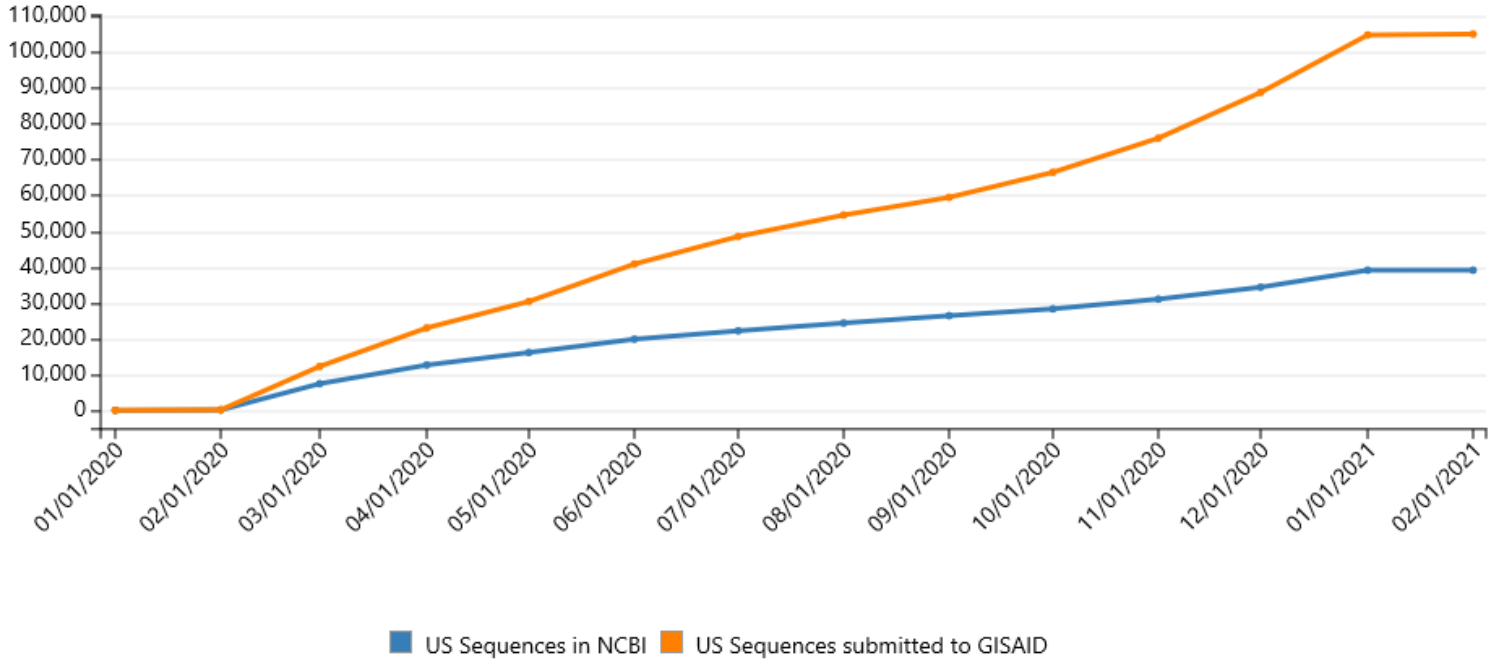


https://www.aphl.org/programs/infectious_disease/influenza/Influenza-Virologic-Surveillance-Right-Size-Roadmap/Pages/Influenza-Sample-Size-Calculators.aspx

CDC approaches to genomic surveillance and epidemiology

- National SARS-CoV-2 Strain Surveillance (NS3)
  - Approximately 3,000 random specimens/month regularly submitted from health departments and public health agencies across United States
  - Additional priority specimens (variants, vaccine breakthroughs)
- Partnership with commercial diagnostic laboratories
  - Scaling to 6000+ sequences/week
- Focused epidemiologic studies
- Contracts and partnerships with state and local health departments and universities
- The SPHERES consortium
  - Consortium of >160 partners
  - https://www.cdc.gov/coronavirus/2019-ncov/covid-data/spheres.html

US Sequences Available in Public Repositories



https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-surveillance/genomic-surveillance-dashboard.html

Nation Center for Biotechnology Information (NCBI); Global Initiative on Sharing Avian Influenza Data (GISAID)

Focused epidemiologic studies

- Adapting preexisting protocols and study platforms to address key epidemiologic and clinical questions on variants
- Dependent on variant prevalence (actively planning for B.1.1.7 projections)
- Conducting surveillance for and investigation of vaccine breakthroughs

Symptoms and Transmission of SARS-CoV-2 Among Children — Utah and Wisconsin, March–May 2020

Rebecca L. Laws, PhD, MPH, Rebecca J. Chancey, MD, Elizabeth M. Rabold, MD, MPH, Victoria T. Chu, MD, MPH, Nathaniel M. Lewis, PhD, Mark Fajans, MPH, Hannah E. Reses, MPH, Lindsey M. Duca, PhD, Patrick Dawson, PhD, MPH, Erin E. Conners, PhD, MPH, Radhika Gharpure, DVM, MPH, Sherry Yin, MPH, Sean Buono, PhD, Mary Pomeroy, MSN, Anna R. Yousaf, MD, Daniel Owusu, PhD, Ashutosh Wadhwa, PhD, Eric Pevzner, PhD, MPH, Katherine A. Battey, BSN, MPH, Henry Njuguna, MD, Victoria L. Fields, DVM, MPH, Phillip Salvatore, PhD, SM, Michelle O'Hegarty, PhD, Jeni Vuong, MS, Christopher J. Gregory, MD, MPH, Michelle Banks, MS, Jared Rispens, MD, Elizabeth Dietrich, PhD, Perrine Marcenac, PhD, Almea Matanock, MD, MS, Ian Pray, PhD, MPH, Ryan Westergaard, MD, PhD, Trivikram Dasu, PhD, Sanjib Bhattacharyya, PhD, Ann Christiansen, MPH, Lindsey Page, MPH, Angela Dunn, MD, Robyn Atkinson-Dunn, PhD, Kim Christensen, BS, Tair Kiphibane, BSN, Sarah Willardson, MPH, Garrett Fox, MPH, Dongni Ye, PhD, Scott A. Nabity, MD, Alison Binder, MS, Brandi D. Freeman, PhD, Sandra Lester, PhD, Lisa Mills, PhD, Natalie Thornburg, PhD, Aron J. Hall, DVM, MSPH, Alicia M. Fry, MD, MPH, Jacqueline E. Tate, PhD, Cuc H. Tran, PhD, MPH, Hannah L. Kirking, MD

abstract

BACKGROUND AND OBJECTIVES: Limited data exist on severe acute respiratory syndrome coronavirus 2 in children. We described infection rates and symptom profiles among pediatric household contacts of individuals with coronavirus disease 2019.

METHODS: We enrolled individuals with coronavirus disease 2019 and their household contacts, assessed daily symptoms prospectively for 14 days, and obtained specimens for severe acute respiratory syndrome coronavirus 2 real-time reverse transcription polymerase chain reaction and serology testing. Among pediatric contacts (<18 years), we described transmission, assessed the risk factors for infection, and calculated symptom positive and negative predictive values. We compared secondary infection rates and symptoms between pediatric and adult contacts using generalized estimating equations.

RESULTS: Among 58 households, 188 contacts were enrolled (120 adults; 68 children). Secondary infection rates for adults (30%) and children (28%) were similar. Among households with potential for transmission from children, child-to-adult transmission may have occurred in 2 of 10 (20%), and child-to-child transmission may have occurred in 1 of 6 (17%). Pediatric case patients most commonly reported headache (79%), sore throat (68%), and rhinorrhea (68%); symptoms had low positive predictive values, except measured fever (100%; 95% confidence interval [CI]: 44% to 100%). Compared with symptomatic adults, children were less likely to report cough (odds ratio [OR]: 0.15; 95% CI: 0.04 to 0.57), loss of taste (OR: 0.21; 95% CI: 0.06 to 0.74), and loss of smell (OR: 0.29; 95% CI: 0.09 to 0.96) and more likely to report sore throat (OR: 3.4; 95% CI: 1.04 to 11.18).

CONCLUSIONS: Children and adults had similar secondary infection rates, but children generally had less frequent and severe symptoms. In two states early in the pandemic, we observed possible transmission from children in approximately one-fifth of households with potential to observe such transmission patterns.

Morbidity and Mortality Weekly Report

Telework Before Illness Onset Among Symptomatic Adults Aged ≥18 Years With and Without COVID-19 in 11 Outpatient Health Care Facilities — United States, July 2020

Kiva A. Fisher, PhD[1]; Samantha M. Olson, MPH[1]; Mark W. Tenforde, MD, PhD[1,2]; Leora R. Feldstein, PhD[1]; Christopher J. Lindsell, PhD[3,4]; Nathan I. Shapiro, MD[3,5]; D. Clark Files, MD[3,6]; Kevin W. Gibbs, MD[3,6]; Heidi L. Erickson, MD[3,7]; Matthew E. Prekker, MD[3,7]; Jay S. Steingrub, MD[3,8]; Matthew C. Exline, MD[3,9]; Daniel J. Henning, MD[3,10]; Jennifer G. Wilson, MD[3,11]; Samuel M. Brown, MD[3,12]; Ithan D. Peltan, MD[3,12]; Todd W. Rice, MD[3,4]; David N. Hager, MD, PhD[3,13]; Adit A. Ginde, MD[3,14]; H. Keipp Talbot, MD[3,4]; Jonathan D. Casey, MD[3,4]; Carlos G. Grijalva, MD[3,4]; Brendan Flannery, PhD[1]; Manish M. Patel, MD[1]; Wesley H. Self, MD[3,4]; IVY Network Investigators; CDC COVID-19 Response Team

Since March 2020, large-scale efforts to reduce transmission of SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19), have continued. Mitigation measures to reduce workplace exposures have included work site policies to support flexible work site options, including telework, whereby employees work remotely without commuting to a central place of work.* Opportunities to telework have varied across industries among U.S. jobs where telework options are feasible (*1*). However, little is known about the impact of telework on risk for SARS-CoV-2 infection. A case-control investigation was conducted to compare telework between eligible symptomatic persons who received positive SARS-CoV-2 reverse transcription–polymerase chain reaction (RT-PCR) test results (case-patients, 153) and symptomatic persons with negative test results (control-participants, 161). Eligible participants were identified in outpatient health care facilities during July 2020. Among employed participants who reported on their telework status during the 2 weeks preceding illness onset (248), the percentage who were able to telework on a full- or part-time basis was lower among case-patients (35%; 42 of 120) than among control-participants (53%; 68 of 128) (p<0.01). Case-patients were more likely than were control-participants to have reported going exclusively to an office or school setting (adjusted odds ratio [aOR] = 1.8; 95% confidence interval [CI] = 1.2–2.7) in the 2 weeks before illness onset. The association was also observed when further restricting to the 175 participants who reported working in a profession outside the critical infrastructure[†] (aOR = 2.1; 95% CI = 1.3–3.6). Providing the option to work

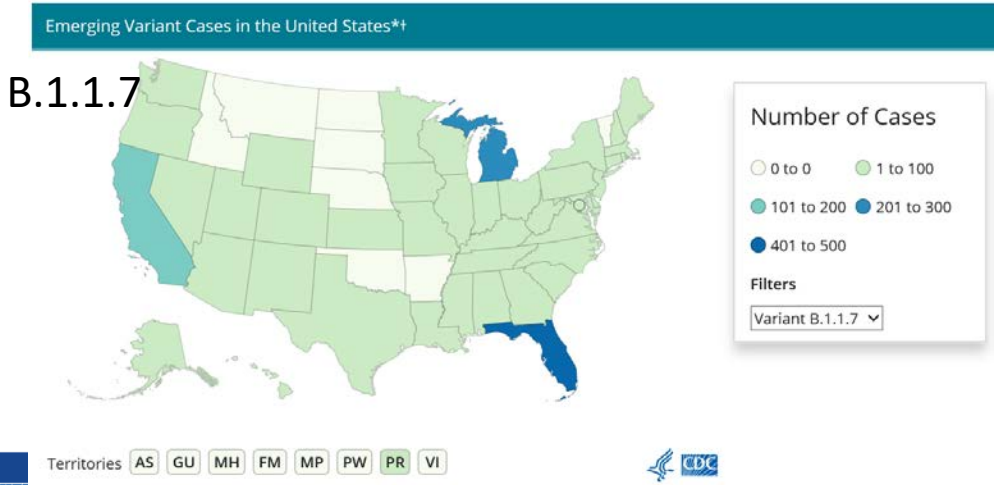
This multistate case-control study assessed possible exposures to COVID-19. Methods have been described elsewhere (*2*). In brief, the investigation included symptomatic adults aged ≥18 years who received their first SARS-CoV-2 test at one of 11 Influenza Vaccine Effectiveness in the Critically Ill (IVY) Network outpatient testing or health care centers[§] during July 1–29, 2020 (*3*). Laboratory-confirmed case-patients were randomly sampled. Two control-participants were matched based on age, sex, and study location to each case patient, resulting in 615 potential case-patients and 1,212 control-participants. Case-patients and control-participants were contacted 14–23 days after their SARS-CoV-2 test and interviewed to identify participants who were symptomatic and had not been previously tested for SARS-CoV-2. A total of 802 adults (295 case-patients and 507 control-participants) agreed to participate in structured interviews in English or five other languages[¶] administered by CDC personnel via telephone with data collected in REDCap software (version 10.3.8; REDCap Consortium) (*4*); 163 adults (9%) declined to participate.

Among these 802 adults contacted, 470 (59%) were ineligible (i.e., were not symptomatic or had a previous SARS-CoV-2 test), and 18 (2%) were excluded because of nonresponse to the telework and work-from-home question. The final analytic sample (314) included 153 (49%) case-patients and 161 (51%) control-participants. An unmatched analysis was performed because of the strict inclusion criteria that resulted in many participants being ineligible for the investigation. This activity was reviewed by CDC and participating sites and conducted consistent with applicable federal law and CDC policy.**

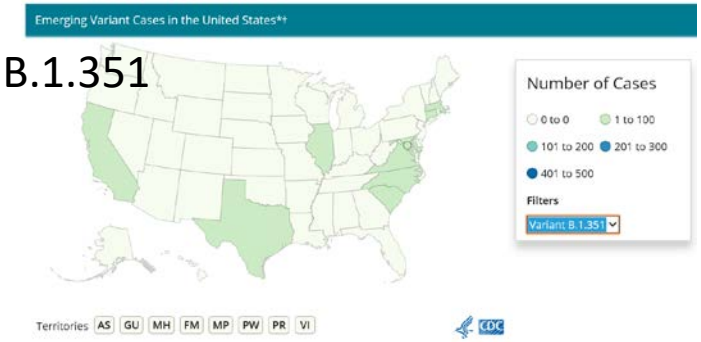
SARS-CoV-2 Variant cases detected in the US

Variant	Reported Cases in US	Number of States Reporting
B.1.1.7	1661	44
B.1.351	22	10
P.1	5	4

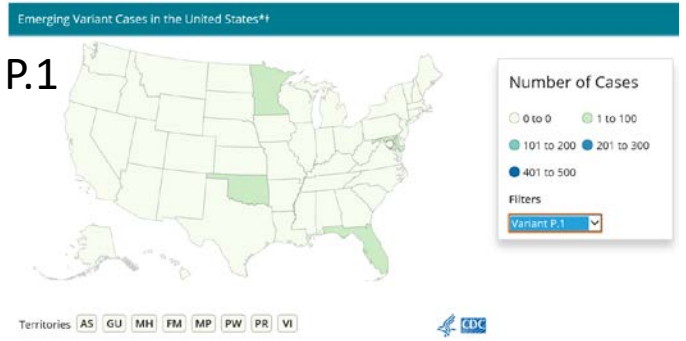
B.1.1.7



B.1.351

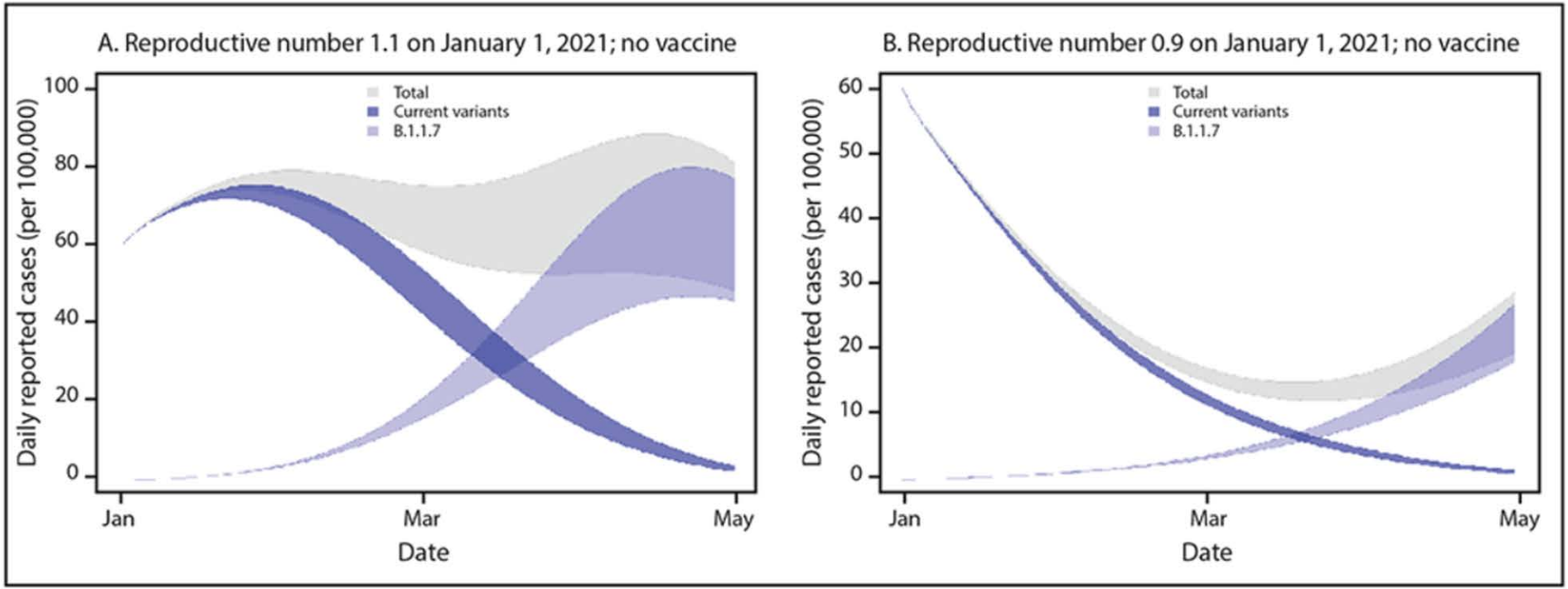


P.1



https://www.cdc.gov/coronavirus/2019-ncov/transmission/variant-cases.html; data as of 02/23/2021

Projecting spread of B.1.1.7 in the United States, assuming R_t 1.5 times greater (no vaccine)



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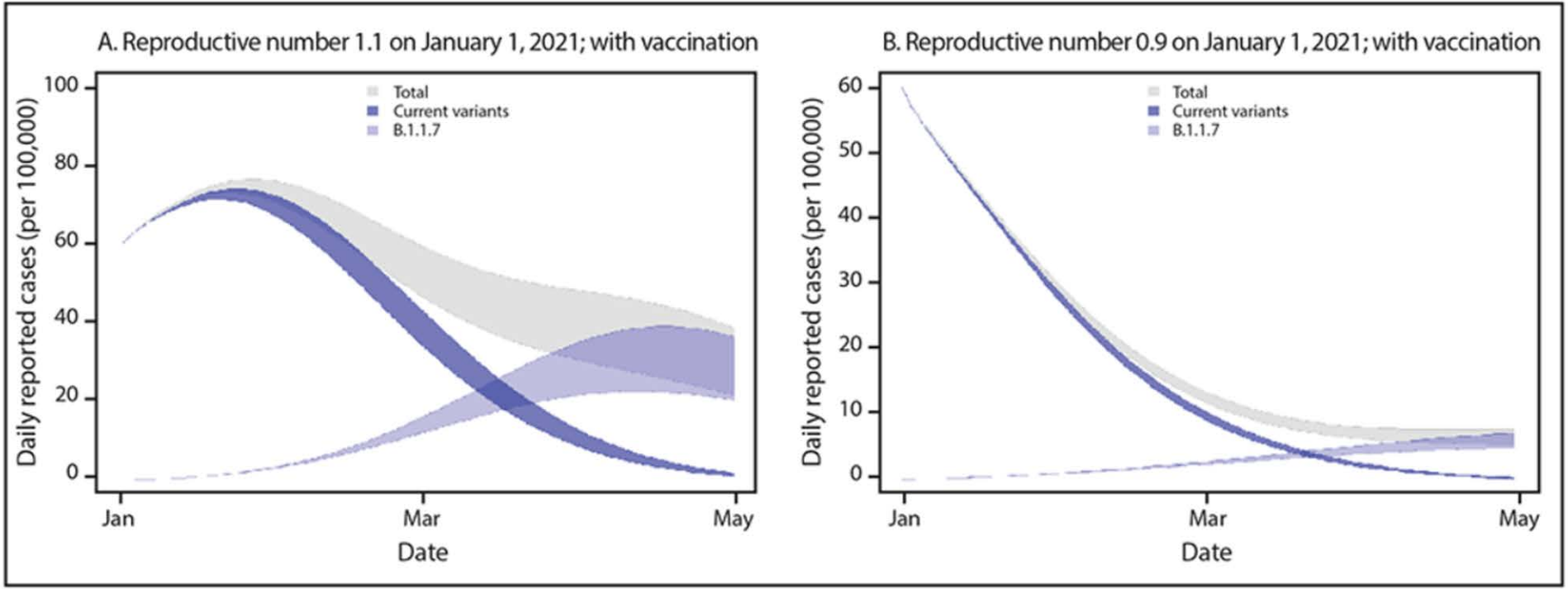
Projecting spread of B.1.1.7 in the United States, assuming R_t 1.5 times greater (vaccine)



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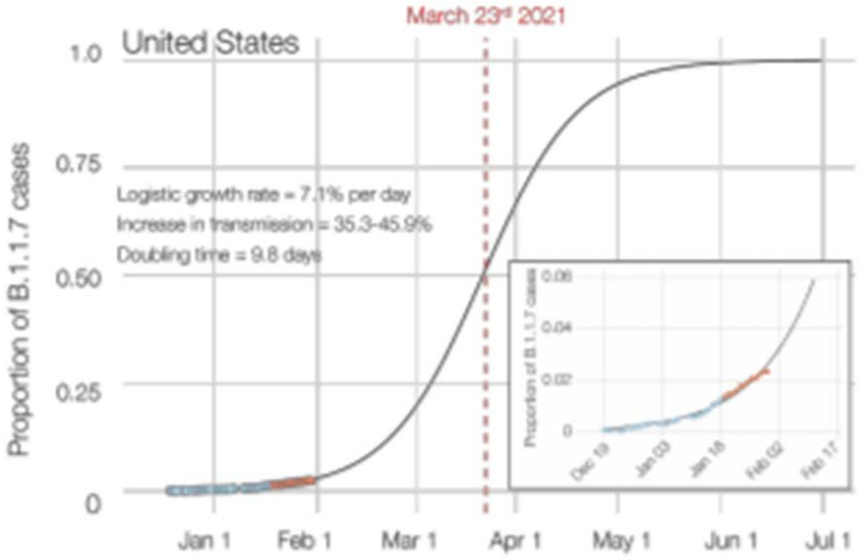
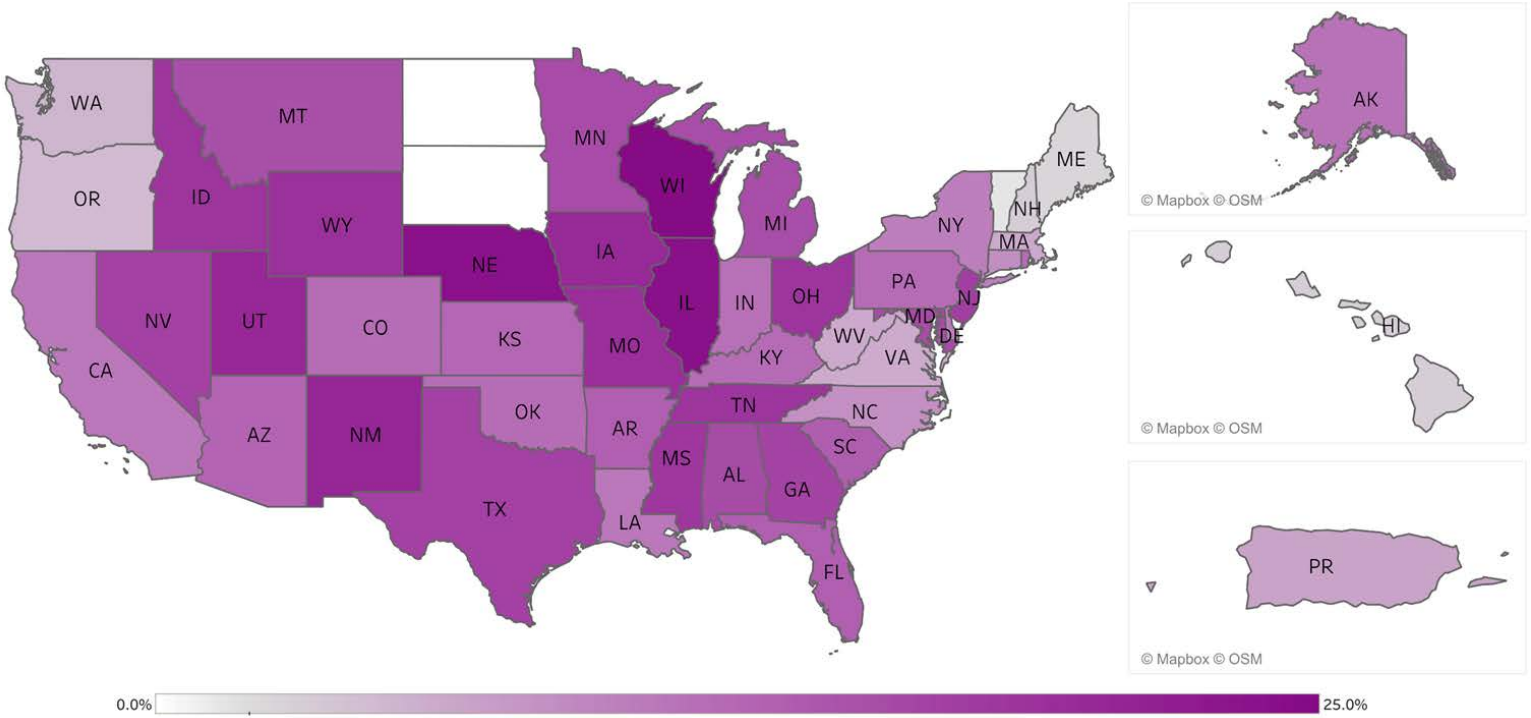
B.1.1.7 trajectory in the United States

- Likely arrived in the United States in November 2020
- Multiple introductions
- First identified January 2021
- Geographically widespread (confirmed in 44 states)
- Current prevalence estimated 1-2%
- Commercial diagnostic data suggest early phase logistic expansion



https://www.medrxiv.org/content/10.1101/2021.02.06.21251159v1.full.pdf

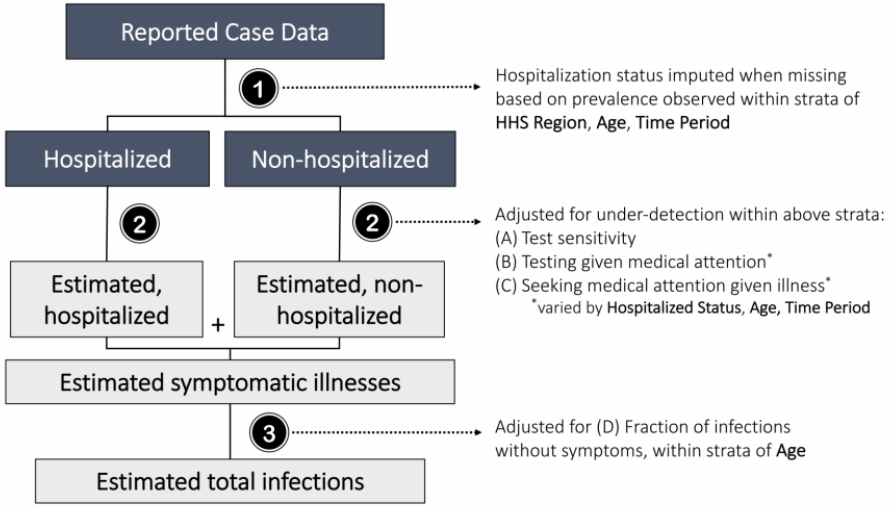
Seroprevalence (overall) among commercial diagnostic specimens from December, 2020, United States



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

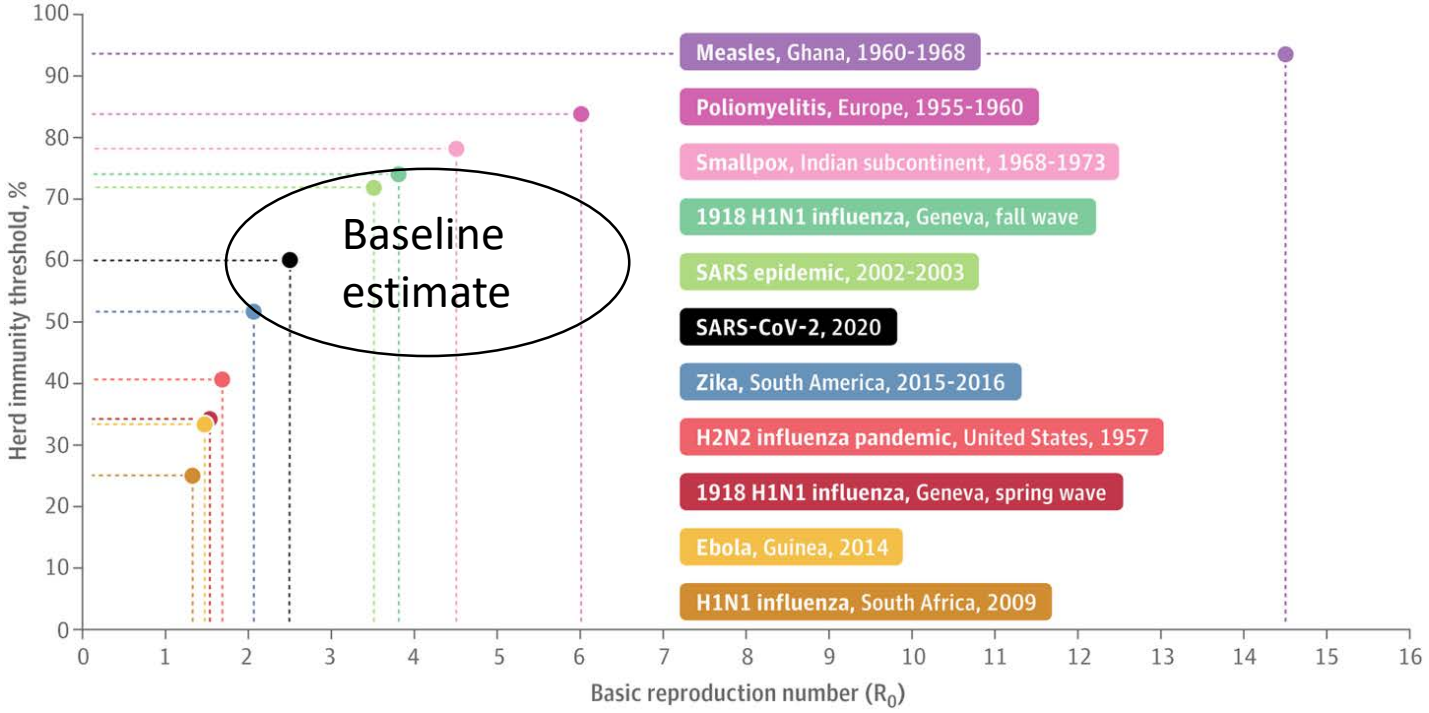
Estimated disease burden in the United States, February-December 2020

- Probabilistic multiplier model to account for under-detection and under-reporting of infections
- **83.1 million** estimated total infections
- **70.4 million** estimated symptomatic illnesses
- **4.1 million** estimated hospitalizations



Primary reference: Reese H et al. Clin Infect Dis. 2020 Nov 25 : ciaa1780.
https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/burden.html#anchor_1607017301754

Herd immunity and SARS-CoV-2



Omer SB, Yildirim I, and Forman HP. JAMA. 2020;324(20):2095. doi:10.1001/jama.2020.20892

Potential implications of variants on viral transmission and population immunity

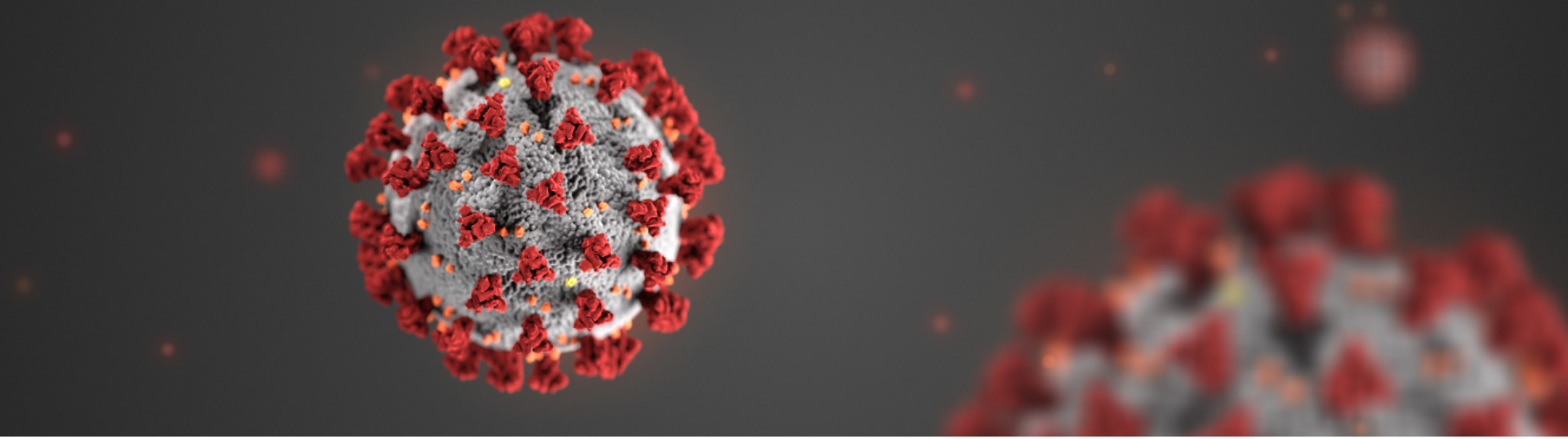
- Currently majority of the US population is not immune to SARS-CoV-2 infection, variants may increase this proportion
- Waning immunity has potential to continue to contribute to pool of individuals susceptible to infection or disease
- Increased transmissibility of a variant virus would require higher proportions to establish herd immunity
- Decreased effectiveness of vaccine to protect against infection may result in prolonged or continuous transmission of SARS-CoV-2

Key public health messages

- Current mitigation strategies work
  - Masking, social distancing, handwashing, quarantine, public health policies
- Variants demonstrate the need to further push these measures
  - Current epidemiologic data moving in the right (downward) direction
  - Potential of increased transmissibility means adherence to mitigation measures needs to be higher in order to maintain downward trend in cases
- Importance of vaccination and monitoring impact
  - General protection for the population against SARS-CoV-2
  - Impact of variants on VE still being characterized, even with decreased effectiveness, may still provide partial protection
  - Need robust epidemiology and virologic surveillance system to determine if vaccine updates needed

Conclusions

- 3 variants of concern currently identified
  - As SARS-CoV-2 evolves, additional variants likely to emerge
  - Importance of genomic surveillance
- Data suggest variants may have increased transmissibility, increased severity, immune evasion
- Epidemiology indicates broad global spread of variants
  - Containment thus far unsuccessful
- Importance of mitigation measures
  - Well-fitting mask, hand hygiene, social distancing, and avoiding crowded or poorly ventilated indoor spaces
  - Vaccination



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

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