SARS-CoV-2 Variants

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April 22, 2021

NBIMU Conference

Conflicts of Interest

I have received speaking honoraria from the following organizations:

- NBIMU
- NBMS

Variant of Interest

- A variant with specific genetic markers that have been associated with changes to receptor binding, reduced neutralization by antibodies generated against previous infection or vaccination, reduced efficacy of treatments, potential diagnostic impact, or predicted increase in transmissibility or disease severity.

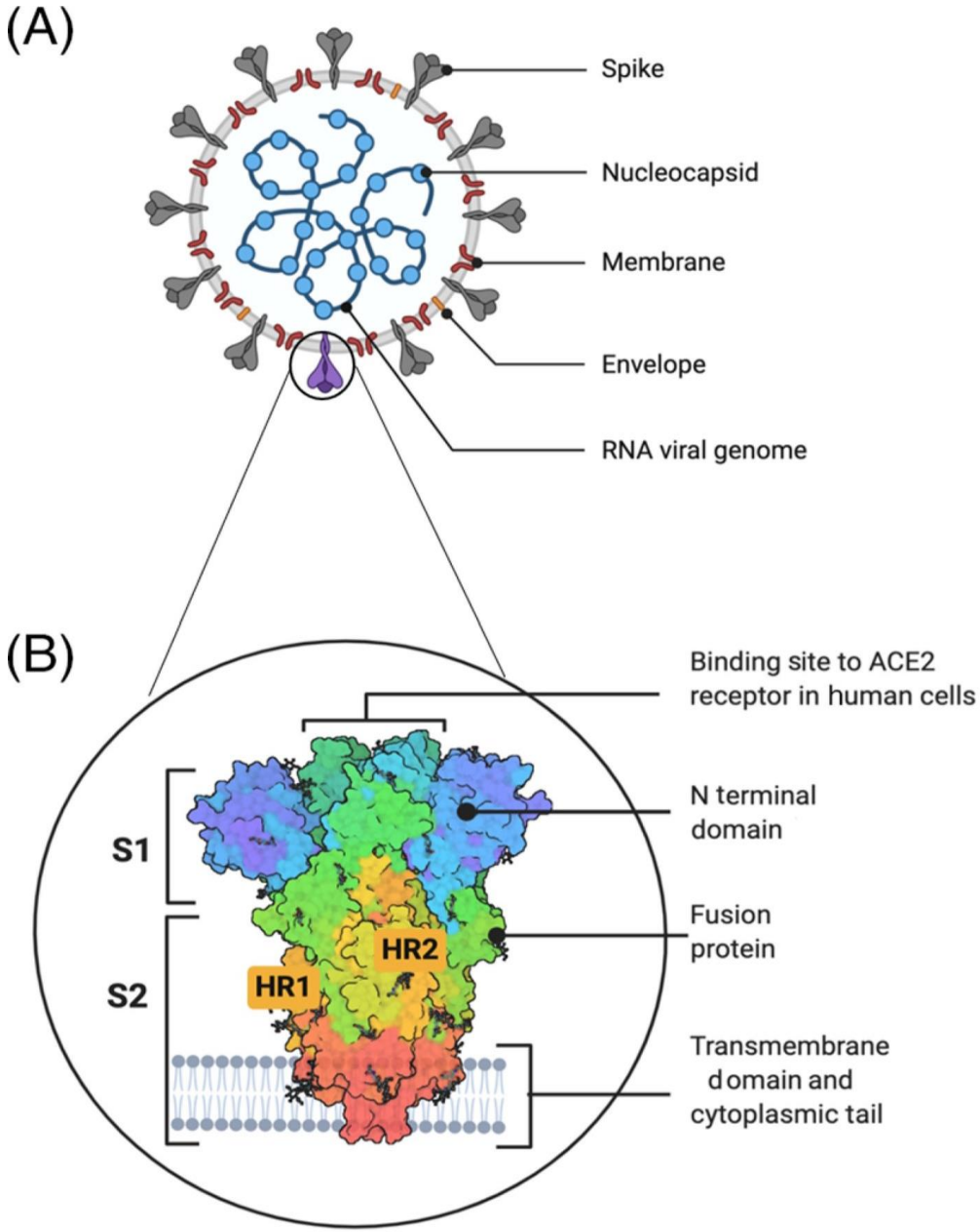
Variant of Concern

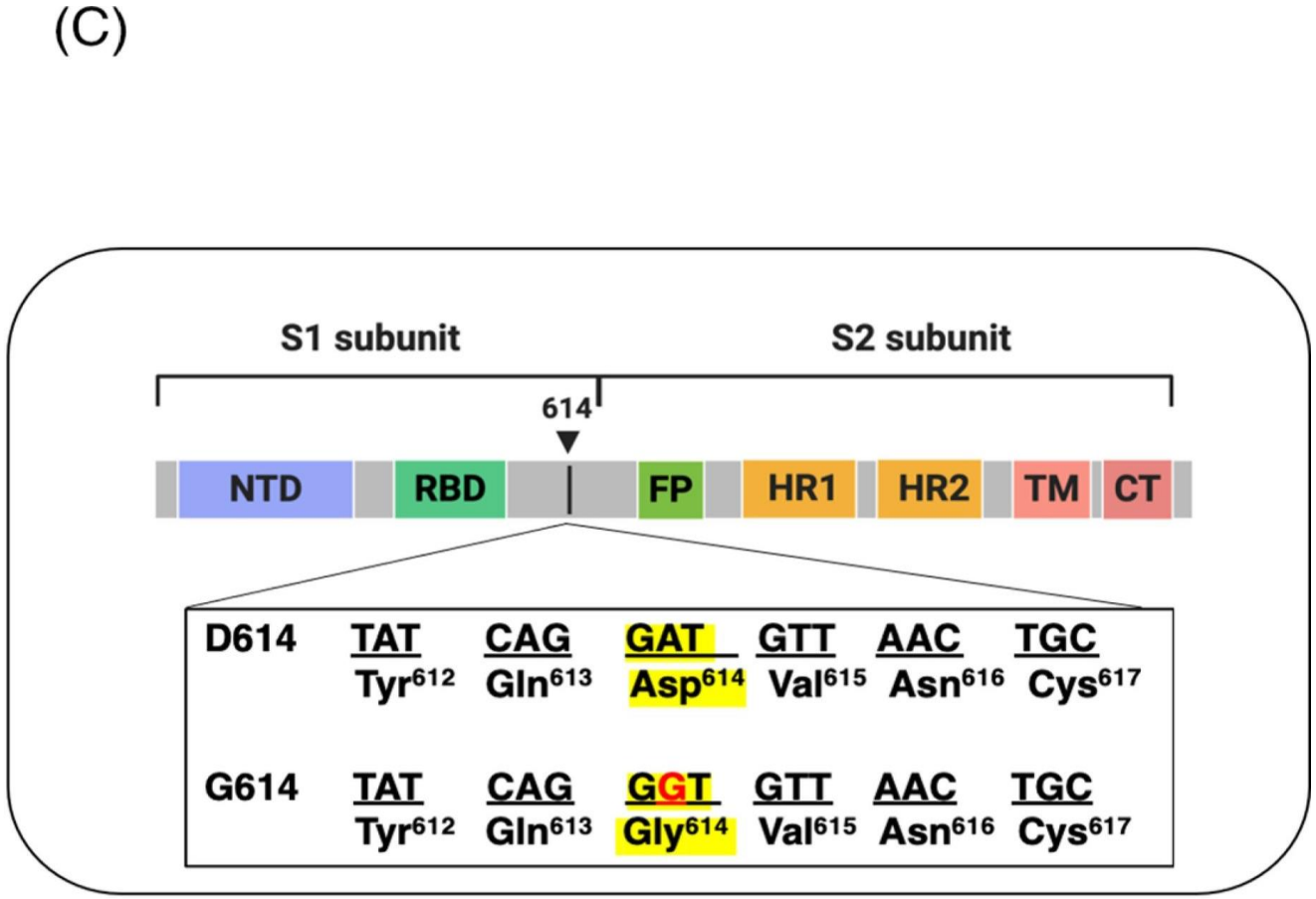
- A variant for which there is evidence of an increase in transmissibility, more severe disease (increased hospitalizations or deaths), significant reduction in neutralization by antibodies generated during previous infection or vaccination, reduced effectiveness of treatments or vaccines, or diagnostic detection failures.

Variant of High Consequence

- A variant of high consequence has clear evidence that prevention measures or medical countermeasures (MCMs) have significantly reduced effectiveness relative to previously circulating variants.

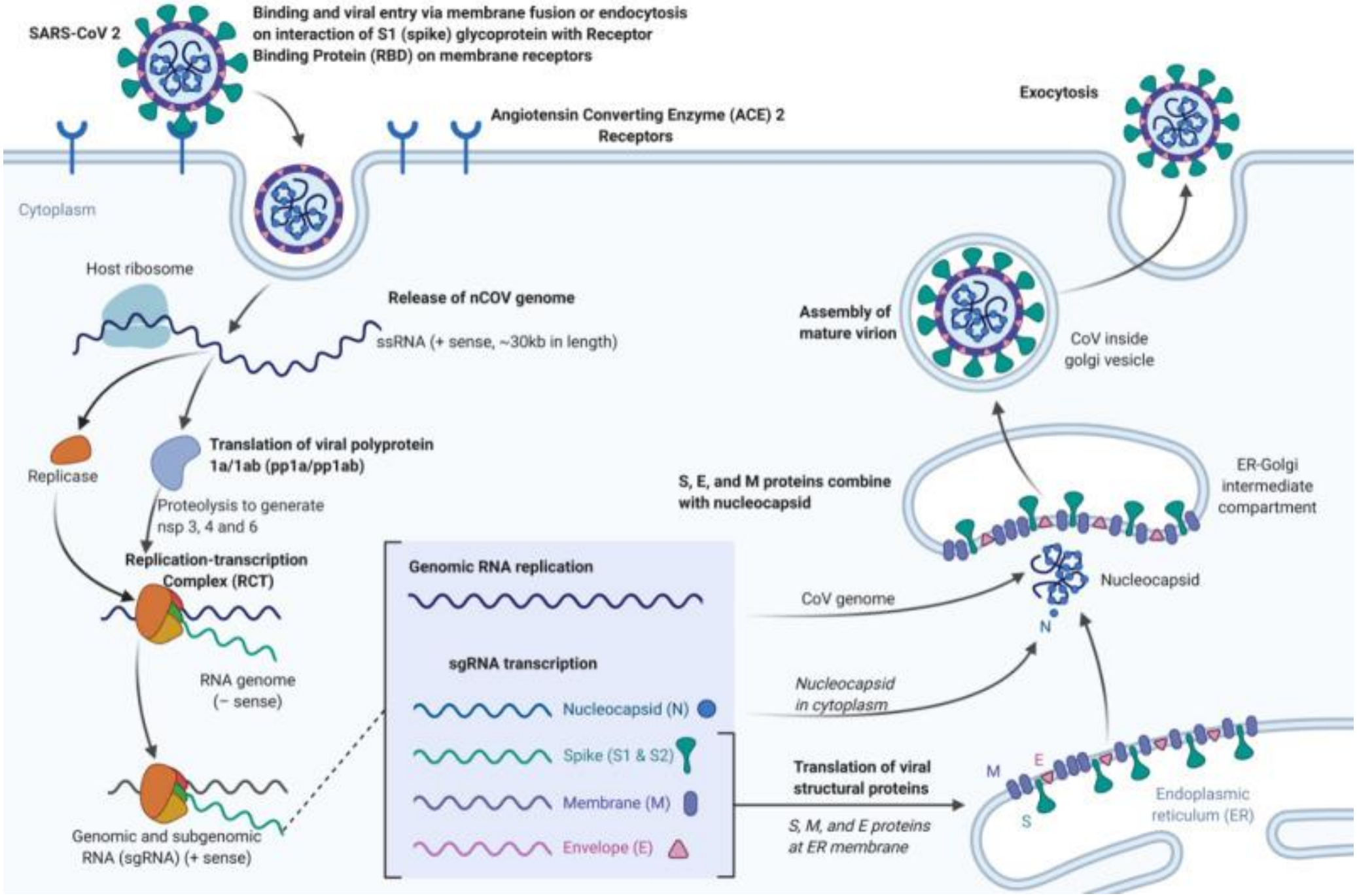
CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION





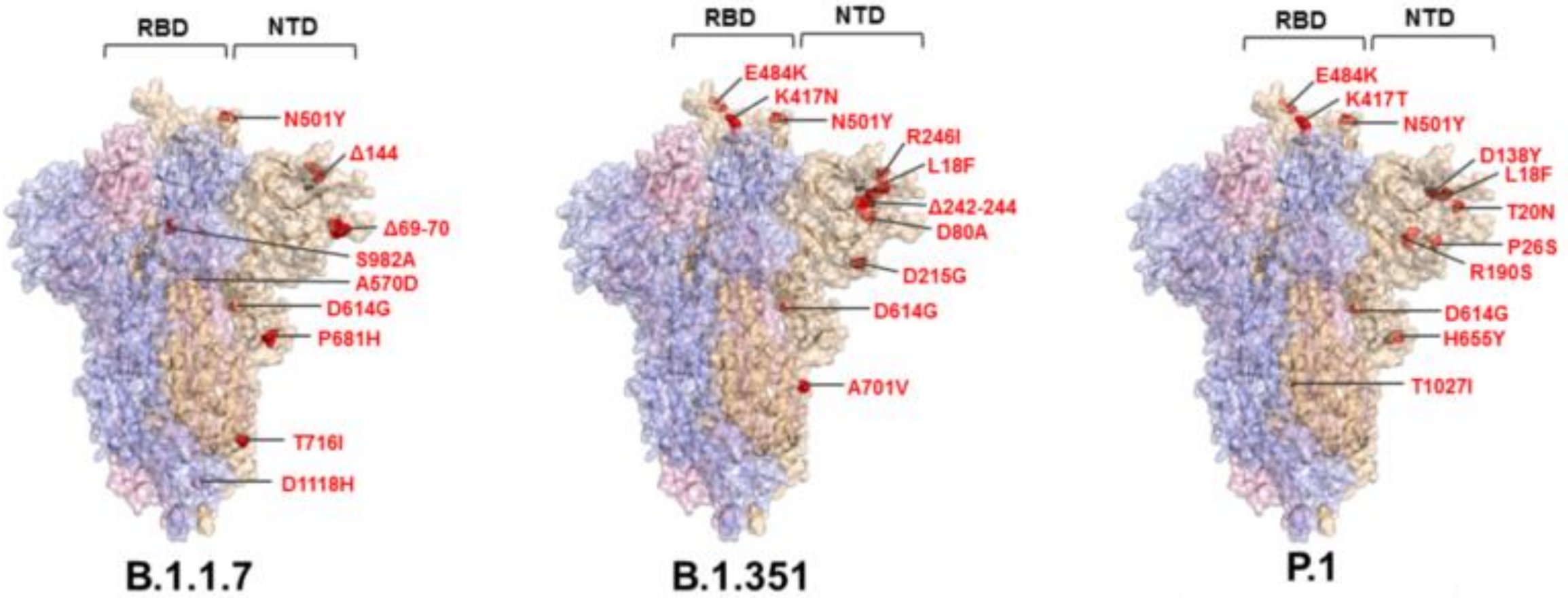
Trends in Genetics

Trends in Genetics 2021 37299-302DOI: (10.1016/j.tig.2020.12.004)


SARS-CoV 2
Binding and viral entry via membrane fusion or endocytosis on interaction of S1 (spike) glycoprotein with Receptor Binding Protein (RBD) on membrane receptors
Angiotensin Converting Enzyme (ACE) 2 Receptors
Exocytosis
Cytoplasm
Host ribosome
Release of nCOV genome
ssRNA (+ sense, ~30kb in length)
Assembly of mature virion
CoV inside golgi vesicle
Replicase
Translation of viral polyprotein 1a/1ab (pp1a/pp1ab)
Proteolysis to generate nsp 3, 4 and 6
S, E, and M proteins combine with nucleocapsid
ER-Golgi intermediate compartment
Replication-transcription Complex (RCT)
Genomic RNA replication
CoV genome
Nucleocapsid
N
sgRNA transcription
Nucleocapsid in cytoplasm
RNA genome (– sense)
Nucleocapsid (N)
Spike (S1 & S2)
Membrane (M)
Envelope (E)
Translation of viral structural proteins
S, M, and E proteins at ER membrane
M
E
S
Endoplasmic reticulum (ER)
Genomic and subgenomic RNA (sgRNA) (+ sense)

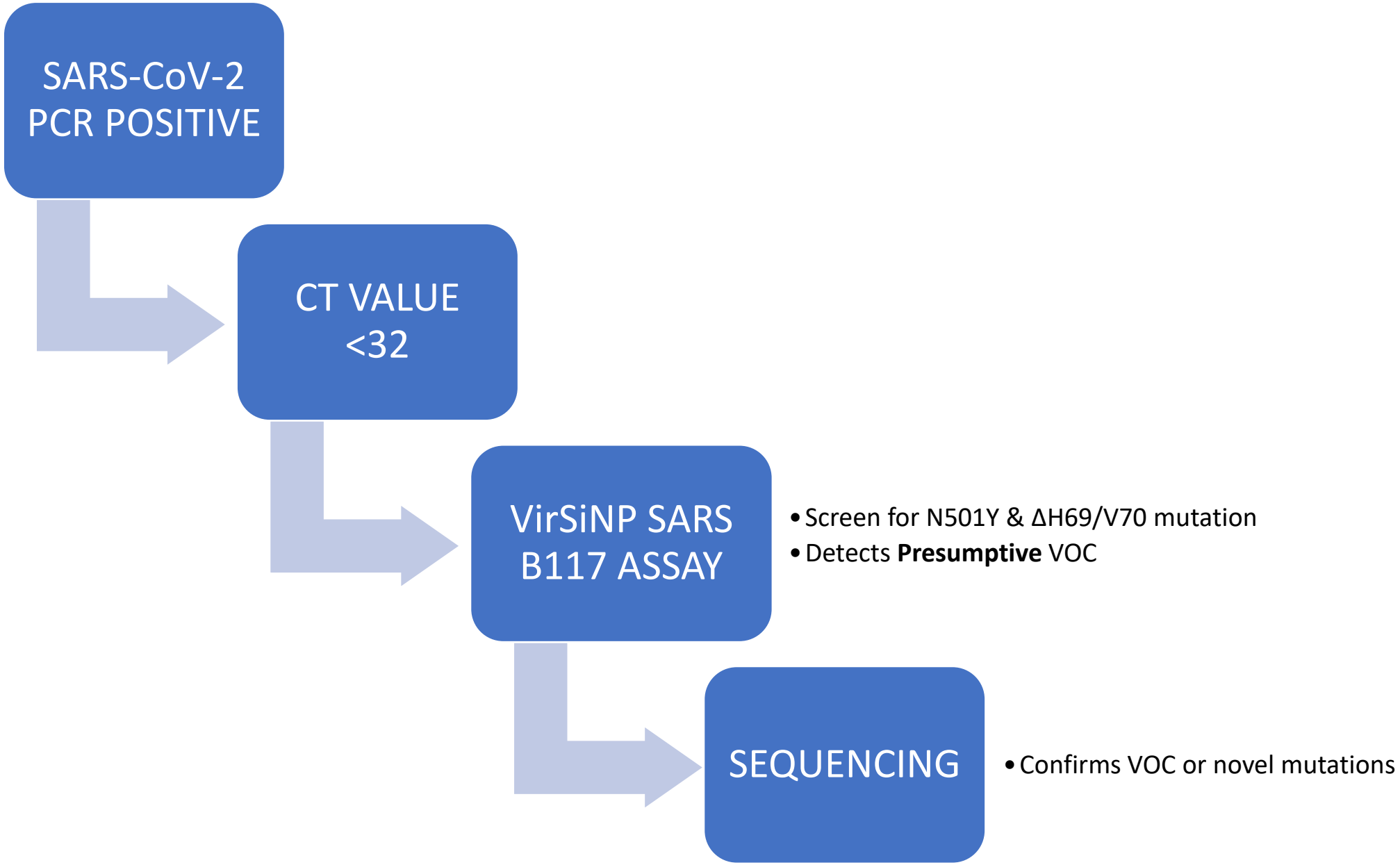
3D models of B.1.1.7, B.1.351 and P.1 strains

RBD: Receptor binding domain
NTD: N-terminal domain

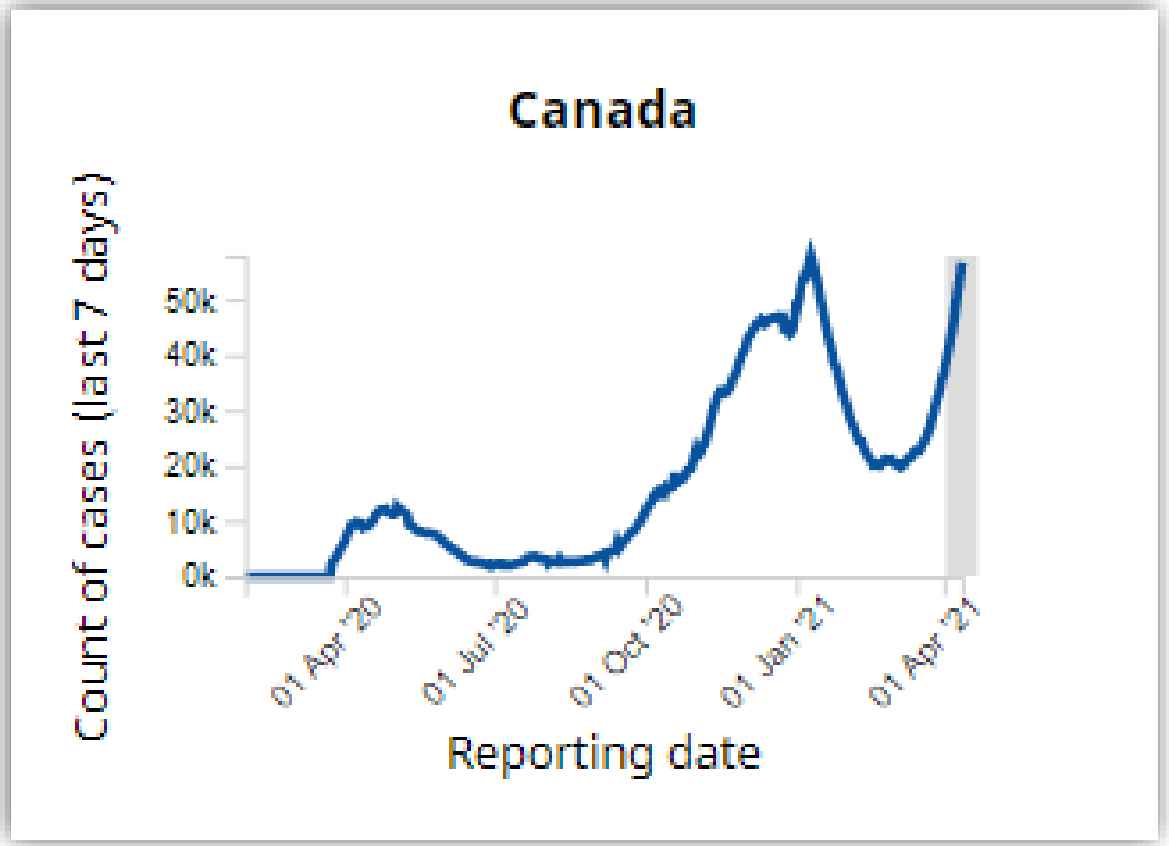


moderna

Detecting Variants of Concern (VOC) in New Brunswick

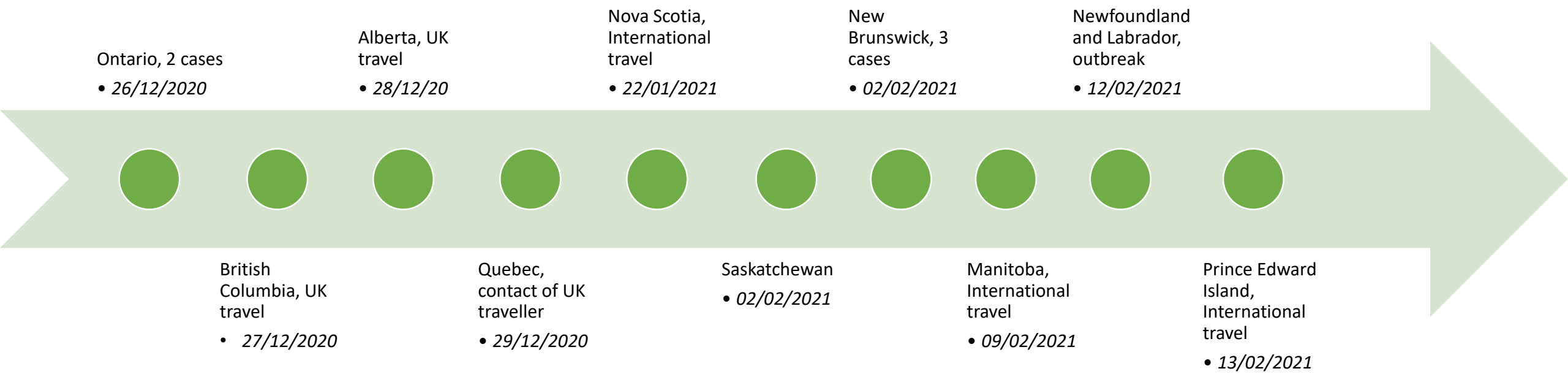


Variants of Concern are increasing worldwide and are driving to the 3rd wave of COVID-19 in Canada



- B.1.1.7 – UK Variant
- B.1.351 – South African Variant
- P.1 – Brazil Variant

B.1.1.7 UK Variant Arrival to Canada



Alberta reports Canada's 1st case of coronavirus variant found in South Africa

Province reports 1,183 new cases of COVID-19, 24 new deaths

CBC News · Posted: Jan 08, 2021 4:31 PM MT | Last Updated: January 8

By end of March cases of B.1.351 in BC, Saskatchewan, Manitoba, Ontario, Quebec, Nova Scotia, Newfoundland and Labrador

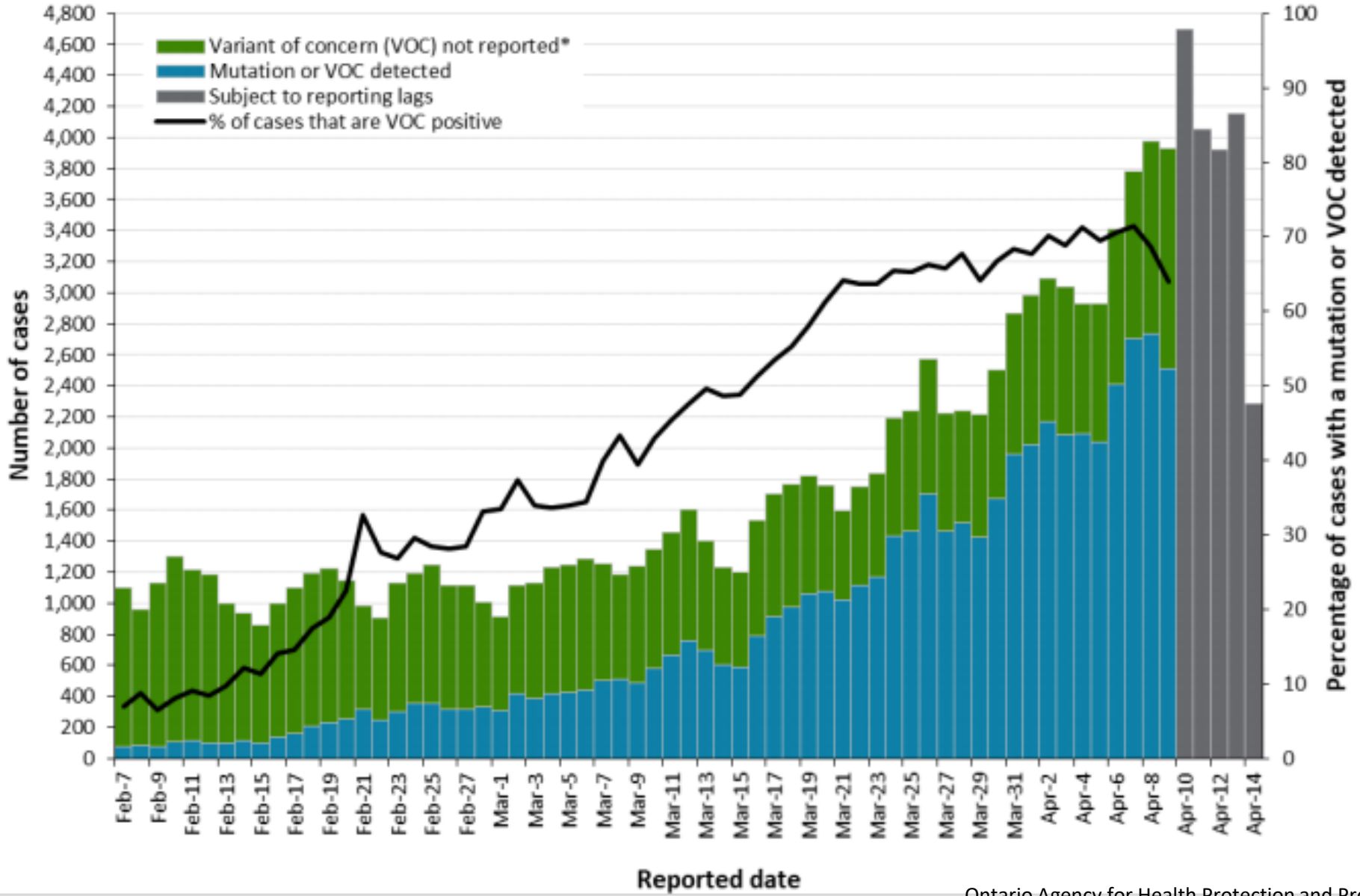
Two cases of COVID-19 variant first associated with South Africa confirmed in New Brunswick

KEVIN BISSETT
FREDERICTON
THE CANADIAN PRESS
PUBLISHED APRIL 12, 2021

P.1 Brazil Variant in Canada

Cumulative number of cases involving variants of concern (VOC) publicly reported, as of April 15, 2021 7:00 PM EST			
Location	**B.1.1.7 variant**	**B.1.351 variant**	**P.1 variant**
Canada	49,371	396	1,885
British Columbia	3,633	65	1,532
Alberta	13,770	29	153
Saskatchewan	1,426	9	0
Manitoba	567	20	1
Ontario	27,278	95	191
Quebec	2,287	163	7
Newfoundland and Labrador	178	1	0
New Brunswick	180	4	0
Nova Scotia	44	10	0
Prince Edward Island	6	0	0
Yukon	1	0	1
Northwest Territories	1	0	0
Nunavut	0	0	0

Figure 5. Number of confirmed COVID-19 cases and percent positive for mutations or VOCs: Ontario, February 7, 2021 to April 14, 2021



Ontario Agency for Health Protection and Promotion (Public Health Ontario).

Why the Concern?

The effect Variants of Concern have on:

1. Viral transmissibility
2. Disease severity
3. Vaccine effectiveness (i.e., escape from vaccine-induced immunity)
4. Reinfection rates (i.e., escape from natural immunity)

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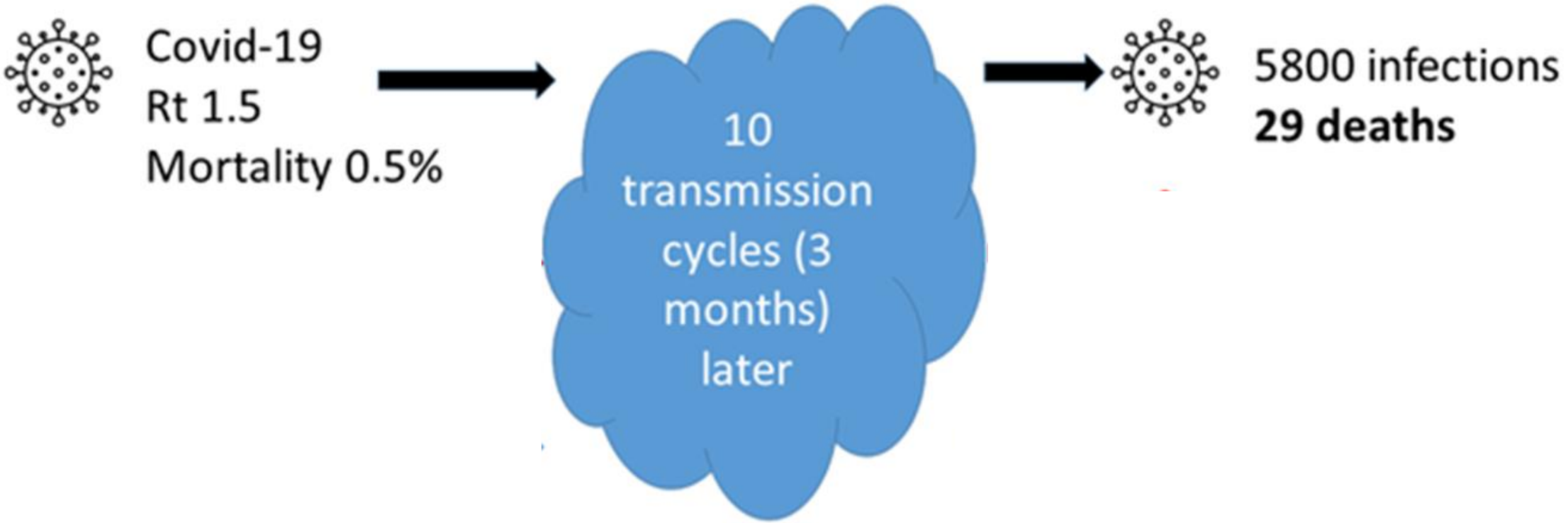
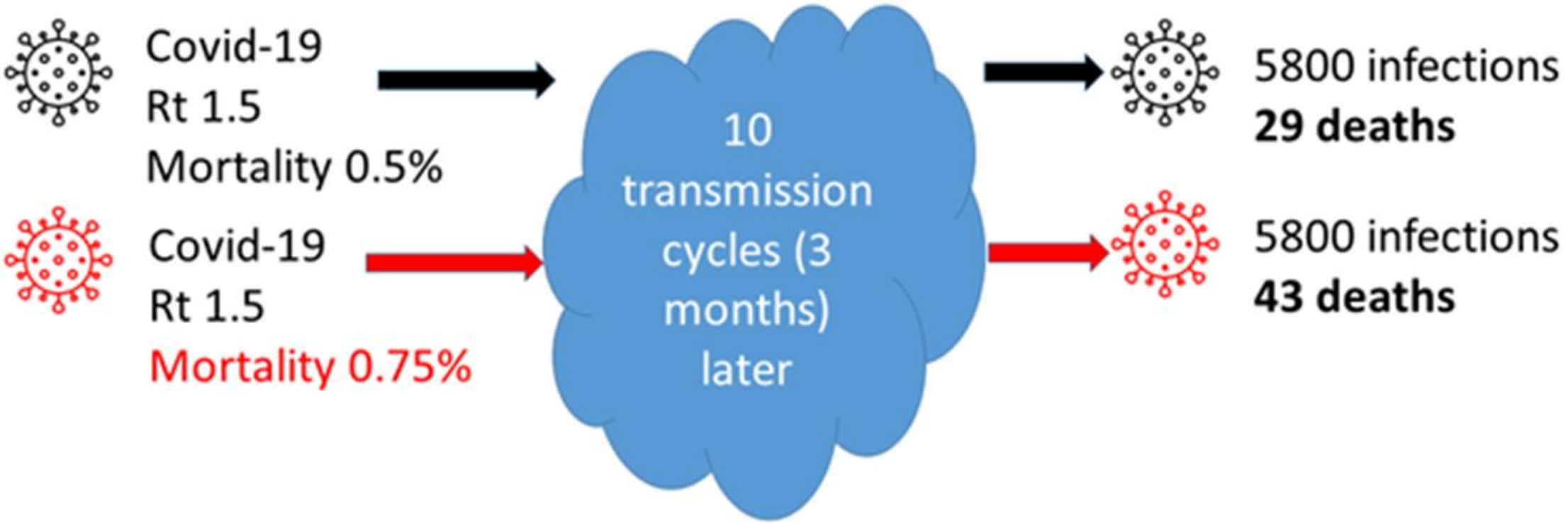
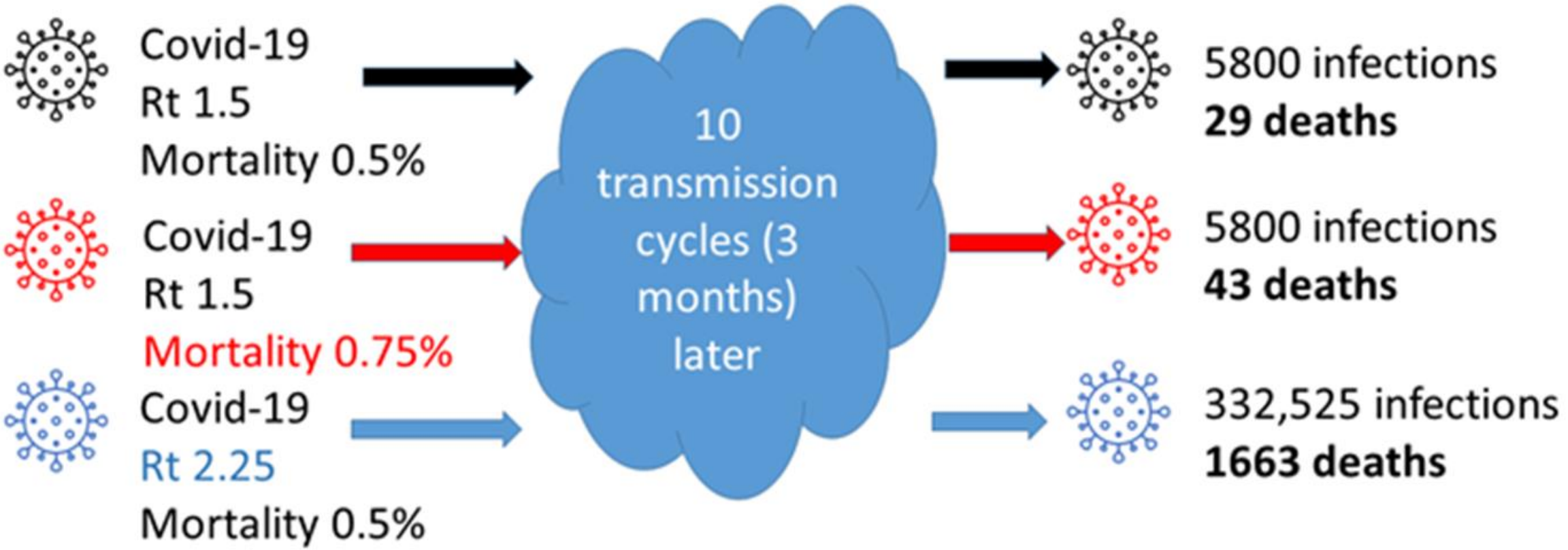

Covid-19
Rt 1.5
Mortality 0.5%
10 transmission cycles (3 months) later
5800 infections
29 deaths


Covid-19
Rt 1.5
Mortality 0.5%
Covid-19
Rt 1.5
Mortality 0.75%
10 transmission cycles (3 months) later
5800 infections
29 deaths
5800 infections
43 deaths


Covid-19
Rt 1.5
Mortality 0.5%
Covid-19
Rt 1.5
Mortality 0.75%
Covid-19
Rt 2.25
Mortality 0.5%
10 transmission cycles (3 months) later
5800 infections
29 deaths
5800 infections
43 deaths
332,525 infections
1663 deaths

Why the Concern?

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1. Viral transmissibility
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4. Reinfection rates (i.e., escape from natural immunity)

SCIENCE TABLE
COVID-19 ADVISORY FOR ONTARIO

SCIENCE BRIEFS

COVID-19 Hospitalizations, ICU Admissions and Deaths Associated with the New Variants of Concern

Ashleigh R. Tuite, David N. Fisman, Ayodele Odutayo, Pavlos Bobos, Vanessa Allen, Isaac I. Bogoch, Adalsteinn D. Brown, Gerald A. Evans, Anna Greenberg, Jessica Hopkins, Antonina Maltsev, Douglas G. Manuel, Allison McGeer, Andrew M. Morris, Samira Mubareka, Laveena Munshi, V. Kumar Murty, Samir N. Patel, Fahad Razak, Robert J. Reid, Beate Sander, Michael Schull, Brian Schwartz, Arthur S. Slutsky, Nathan M. Stall, Peter Jüni on behalf of the Ontario COVID-19 Science Advisory Table

- Retrospective cohort study, Ontario
- Feb 7 – March 11, 2021
- 26,314 COVID+
  - 9,395 VOCs
- Adjusted for age, sex, comorbidities

	Adjusted odds ratio (95% CI)	
COVID-19 Hospitalizations	1.62 (1.41 to 1.87)	62%
COVID-19 ICU admissions	2.14 (1.52 to 3.02)	114%
COVID-19 Deaths	1.40 (1.01 to 1.94)	40%

Table 1. Risk of COVID-19 Hospitalization, Intensive Care Unit Admission and Death Associated with VOCs Compared to Early Variants in Ontario, Canada

Adjusted odds ratios and 95% confidence intervals for the risk of COVID-19 hospitalizations, intensive care unit admissions and deaths associated with new VOCs compared to early variants. VOC, variant of concern; CI, confidence interval; ICU, intensive care unit.

Tuite AR, Fisman DN, Odutayo A, et al. COVID-19 hospitalizations, ICU admissions and deaths associated with the new variants of concern. Science Briefs of the Ontario COVID19 Science Advisory Table. 2021;1(18). https://doi.org/10.47326/ocsat.2021.02.18.1.0

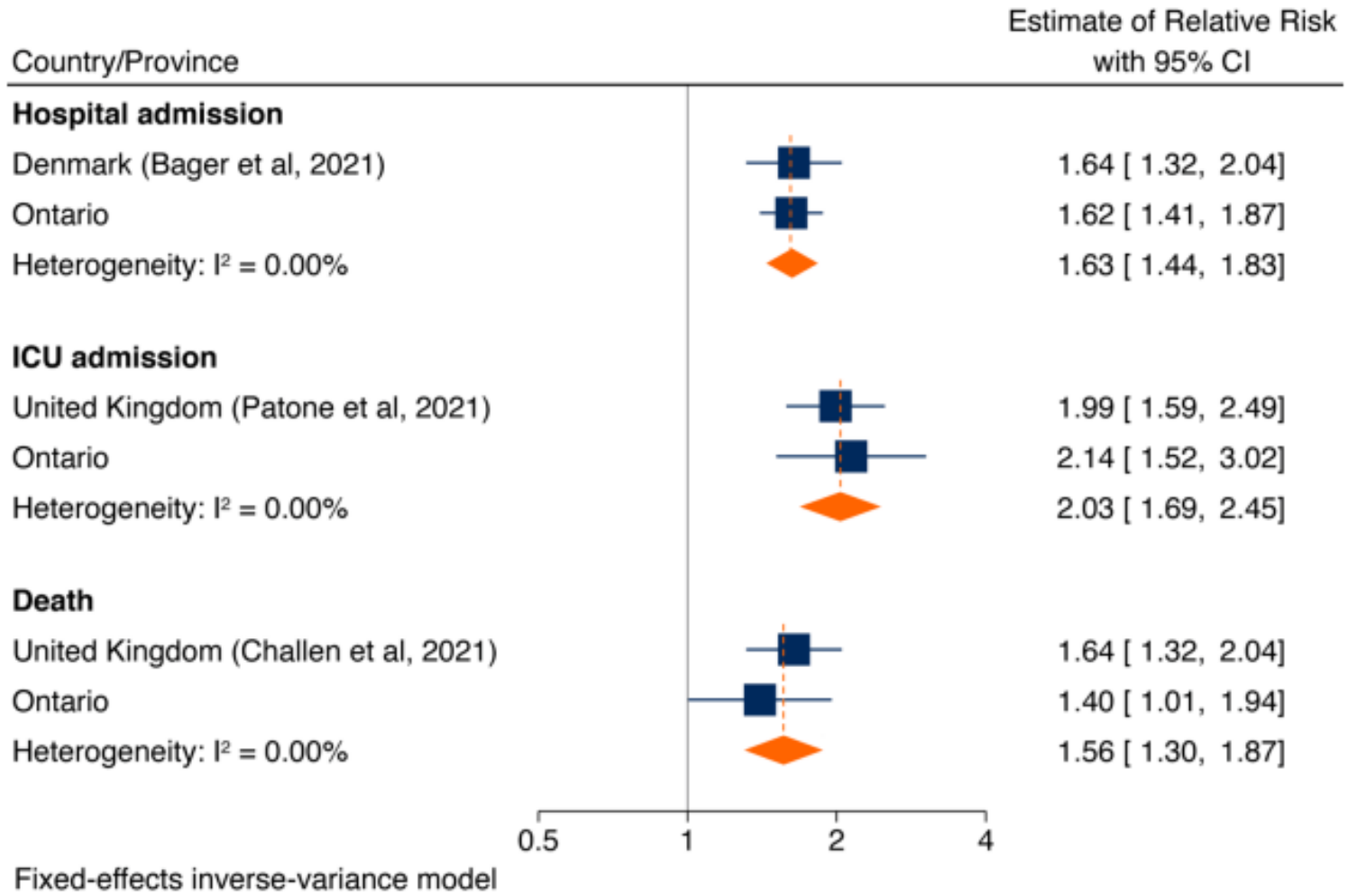

Figure 3. Meta-Analysis of the Risk of COVID-19 Hospitalization, Intensive Care Unit Admission and Death Associated with new VOCs Compared to Early Variants

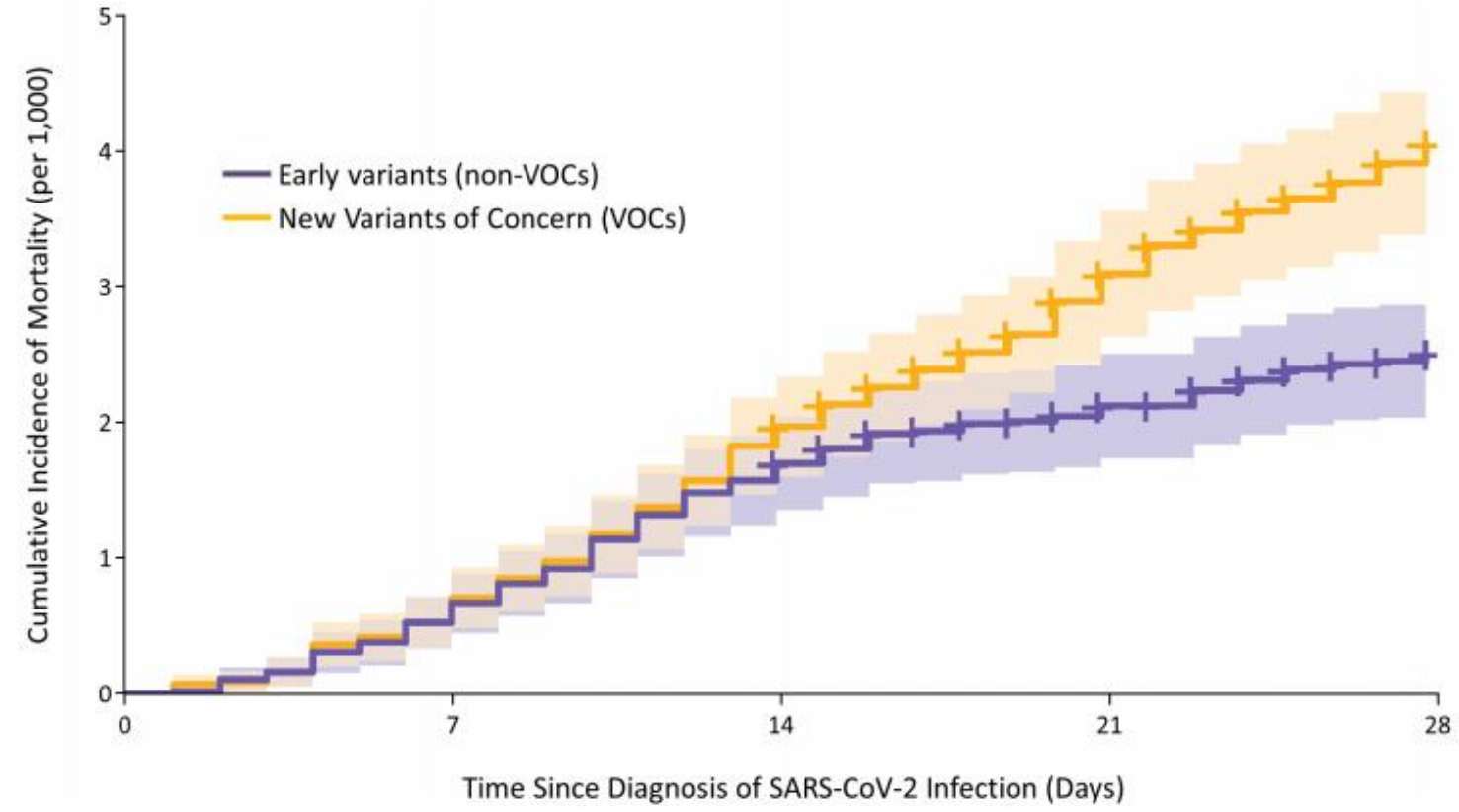

Figure 4. Time to Death Following SARS-CoV-2 Infection with New VOCs Compared with Early Variants

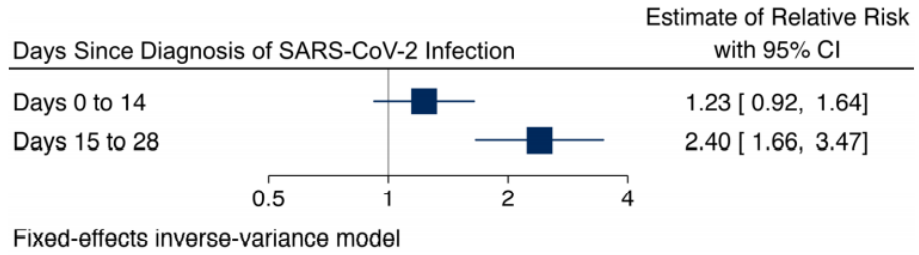

Figure 5. Risk of COVID-19 Death Associated with new VOCs Compared with Early Variants by Time Since Diagnosis of SARS-CoV-2 Infection

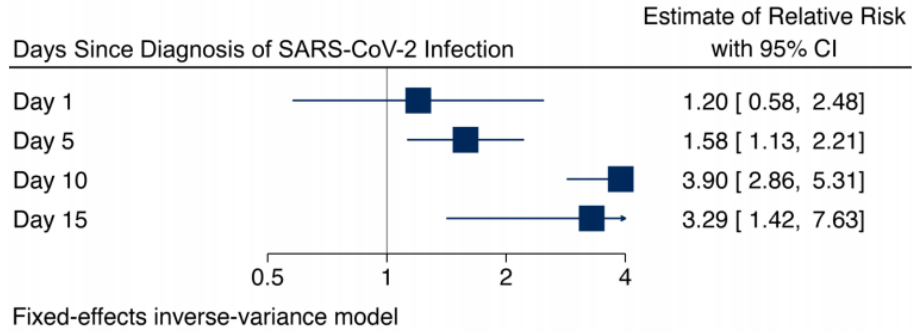

Figure 6. Risk of COVID-19 ICU Admission Associated with New VOCs Compared with Early Variants by Time Since Diagnosis of SARS-CoV-2 Infection

Why the Concern?

The effect Variants of Concern have on:

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3. **Vaccine effectiveness (i.e., escape from vaccine-induced immunity)**
4. Reinfection rates (i.e., escape from natural immunity)

Summary Results on SARS-CoV-2 Vaccine Trial Efficacy and Viral Neutralization of the B.1.1.7, P.1, and 501Y.V2 Variants, as Compared with Preexisting Variants.*

Table 1. Summary Results on SARS-CoV-2 Vaccine Trial Efficacy and Viral Neutralization of the B.1.1.7, P.1, and 501Y.V2 Variants, as Compared with Preexisting Variants.*

Vaccine (Company)	Preexisting Variants			Neutralization by Pseudovirion or Live Viral Plaque Assay			Efficacy in Settings with 501Y.V2 Variant
	Sample Size	Efficacy in Preventing Clinical Covid-19	Efficacy in Preventing Severe Covid-19	B.1.1.7 Variant	P.1 Variant	501Y.V2 Variant	
	no.	*% (no. of events with vaccine vs. placebo)*					%
Ad26.COV2.S (Johnson & Johnson)	43,783	66 (NA)	85 (NA)	NA	NA	NA	57†, 85‡
BNT162b2 (Pfizer)	34,922	95 (8 vs. 162)	90 (1 vs. 9)	Decrease by 2×	Decrease by 6.7×	Decrease by ≤6.5×	NA
mRNA-1273 (Moderna)	28,207	94 (11 vs. 185)	100 (0 vs. 30)	Decrease by 1.8×	Decrease by 4.5×	Decrease by ≤8.6×	NA
Sputnik V (Gamaleya)	19,866	92 (16 vs. 62)	100 (0 vs. 20)	NA	NA	NA	NA
AZD1222 (AstraZeneca)	17,177	67 (84 vs. 248)	100 (0 vs. 3)	NA	NA	Decrease by ≤86× to complete immune escape	22§
NVX-CoV2373 (Novavax)	15,000	89 (6 vs. 56)	100 (0 vs. 1)	Decrease by 1.8×	NA	NA	49§
CoronaVac (Sinovac)¶							
Brazil	12,396	51 (NA)	100 (NA)	NA	NA	NA	NA
Turkey	7,371	91 (3 vs. 26)	NA	NA	NA	NA	NA
BBIBP-CorV (Sinopharm)	NA	79 (NA)	NA	NA	NA	Decrease by 1.6×	NA

* Data were available up to March 18, 2021. The definitions of mild, moderate, and severe coronavirus disease 2019 (Covid-19) vary across the vaccine trials. A list of references associated with these vaccines is provided in the Supplementary Appendix, available with the full text of this letter at NEJM.org. NA denotes not available, and SARS-CoV-2 severe acute respiratory syndrome coronavirus 2.
† Shown is the efficacy of the vaccine, as compared with placebo, against moderate-to-severe Covid-19.
‡ Shown is efficacy of the vaccine, as compared with placebo, against severe Covid-19 and hospitalization.
§ Shown is efficacy of the vaccine, as compared with placebo, against symptomatic Covid-19.
¶ Data are shown separately for the trial sites in Brazil and Turkey.

SS Abdool Karim, T de Oliveira. N Engl J Med 2021. DOI: 10.1056/NEJMc2100362

The NEW ENGLAND JOURNAL of MEDICINE

Why the Concern?

The effect Variants of Concern have on:

1. Viral transmissibility
2. Disease severity
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4. **Reinfection rates (i.e., escape from natural immunity)**

Variant	AKA	First Described	Increased Transmissibility?	Increased Severity?	Vaccine Efficacy?	Evade Natural Immunity?
B.1.1.7	501Y.V1	United Kingdom, Dec 2020	Yes (43-82%)[1]	Yes (~60% ↑ risk of death)[3,4]	Modest ↓ in neutralization, no impact on efficacy	
B.1.351	501Y.V2	South Africa, Dec 2020	Yes (50%)[2]	Possibly	↓ efficacy, (AZ ↓↓), E484K mutation	Yes[6]
P.1	501Y.V3 / B.1.1.28.1	Brazil, Jan 2021	Yes (1.4-2.2X)[5]		↓ in neutralization, E484K mutation, possible ↓ efficacy	Yes[5]
B.1.427/ B.1.429*		USA, California July 2020	Yes (~20%)[7]		Modest ↓ in neutralization[8]	
B.1.525*		Nigeria, Dec 2020				
B.1.526*		USA, New York Nov 2020			?, E484K mutation	

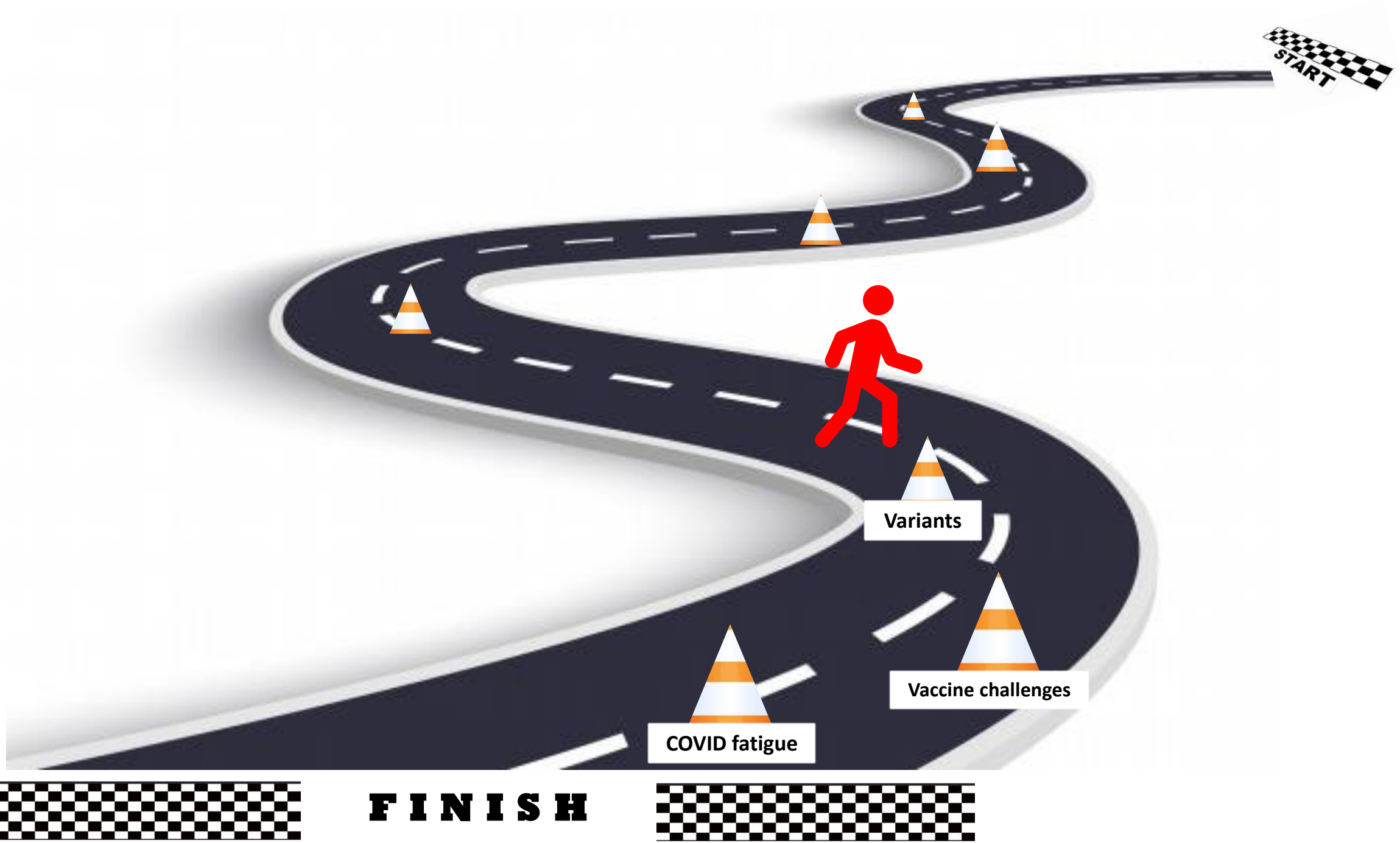
*Variant Under Investigation

1 Davies et al., Science, 2021
2 SABC, 2021
3 Davies et al, Nature, 2021
4 Challen et al, BMJ, 2021
5 Faria et al, 2021
6 Novavax, 2021
7 Deng et al, 2021
8 Shen et al, NEJM, 2021

Controlling the spread of Variants of Concern

- All public health measures to reduce transmission of SARS-CoV-2 continue and are effective but require more rigorous application due to increased transmission risk:
  - lower threshold isolating contacts as high risk of exposure
  - contacts of contacts isolation
  - enhanced asymptomatic testing
  - manage symptomatic contacts as probable cases while awaiting results

- Current COVID-19 Infection Prevention and Control practices remain
  - No changes to PPE practices related to the emergence of these VOC


START
Variants
Vaccine challenges
COVID fatigue
FINISH

Take Home Points

Variants of concern (VOC) are more transmissible and more severe than previously circulating variants.

PCR-based tests used in New Brunswick for COVID-19 detect the 3 most common VOC and can continue to be used for diagnosis.

Based on current evidence available vaccines protect against VOC, with some notable exceptions (ex: AZD1222 and B.1.351 variant).

Public health measures and infection control practices are effective to prevent the spread of variants of concern.

References:

Challen R et al. (2021). Risk of mortality in patients infected with SARS-CoV-2 variant of concern 202012/1: matched cohort study. *BMJ (Clincal Research Ed.)*, 372, n579. https://doi.org/10.1136/bmj.n579.

Davies N, Abbott S, Barnard RC, et al.(2021) Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England. *Science* 10.1126/science.abg3055.

Davies N, et al. (2021) Incrased moratality in community-tested cases of SARS-CoV-2 lineage B.1.1.7. *Nature*, 1-5. https://doi.org/10.1038/s41586-021-03426-1.

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Shen et al, (2021) Neutralization of SARS-CoV-2 Variants B.1.429 and B.1.1351. *NEJM* DOI: 10.1056/NEJMc2103740.

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Ontario Agency for Health Protection and Promotion (Public Health Ontario). Epidemiologic summary: COVID-19 in Ontario – January 15, 2020 to April 14, 2021. Toronto, ON: Queen's Printer for Ontario; 2021.