The Daily COVID-19 Literature Surveillance Summary

April 16, 2021

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COVID-19 Daily Literature Surveillance

COVID19LST

Bringing you real time, distilled information for guiding best practices during the COVID-19 pandemic

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".
Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

** OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson*

EXECUTIVE SUMMARY

Transmission & Prevention

- Single-dose BNT162b2 offer significant short-term protection against SARS-CoV-2. Infectious disease experts from Cambridge University evaluated the effectiveness of a single-dose BNT162b2 vaccine in a cross-sectional analysis of SARS-CoV-2 positivity in 8819 healthcare workers (HCW) over two weeks in January 2021. They found asymptomatic infections were four times lower in vaccinated HCWs compared to non-vaccinated HCWs 12 or more days after the first vaccine dose (4/1,989 positive tests [0.2%, Wilson's interval 0.1-0.5%] vs 26/3,252 [0.8%, Wilson's interval 0.6-1.2%], p=0.004). Authors suggest single-dosage vaccinations of BNT162b2 do offer significant short-term protection against SARS-CoV-2 transmission.

- How will antigenic changes viral variations affect antibody-mediated immunity? Immunologists and virologists from the National Institute of Allergy and Infectious Diseases discuss the emergence of a new California variant of SARS-CoV-2 described in a JAMA article by Zhang, et al and explore its potential clinical consequences. Based on data from Zhang, et al and other studies of SARS-CoV-2 variants, the authors observe that viral variation can result in antigenic changes that alter antibody-mediated immunity, as seen in a South African strain partially to fully resistant to neutralization by some monoclonal antibodies in vitro. The authors suggest that even though current data shows that current vaccines effectively reduce overall mortality in the setting of antigenic variation, more research into viral transmissibility is needed in order to determine whether changes in vaccine composition are necessary to limit evasion of vaccine-induced immunity.

- S-gene target failures (SGTF) mutations confer higher transmissibility in the SARS-CoV-2 lineage B.1.1.7. Epidemiologists from the MRC Centre for Global Infectious Disease Analysis at Imperial College London conducted a community-based, whole genome analysis of a random sample of SARS-CoV-2 sequences collected from community-based diagnostic testing in England between October 1, 2020 and January 16, 2021. They found the new variant of concern (VOC) SARS-COV-2 lineage B.1.1.7 expanded rapidly and possessed an advantageous S-gene target failures (SGTF) mutation that appeared to confer higher transmissibility. Authors emphasize the importance of genomic surveillance and its potentially valuable insights into new VOC that may impact transmissibility and disease outcomes.

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TRANSMISSION & PREVENTION

SINGLE-DOSE BNT162B2 VACCINE PROTECTS AGAINST ASYMPTOMATIC SARS-COV-2 INFECTION

Jones NK, Rivett L, Seaman S, Samworth RJ, Warne B, Workman C, Ferris M, Wright J, Quinnell N, Shaw A; Cambridge COVID-19 Collaboration, Goodfellow IG, Lehner PJ, Howes R, Wright G, Matheson NJ, Weekes MP.. Elife. 2021 Apr 8;10:e68808. doi: 10.7554/eLife.68808. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Infectious disease experts from Cambridge University evaluated the effectiveness of a single-dose BNT162b2 vaccine in a cross-sectional analysis of SARS-CoV-2 positivity in 8819 healthcare workers (HCW) over two weeks in January 2021. They found asymptomatic infections were four times lower in vaccinated HCWs compared to non-vaccinated HCWs 12 or more days after the first vaccine dose (4/1,989 positive tests [0.2%, Wilson's interval 0.1-0.5%] vs 26/3,252 [0.8%, Wilson's interval 0.6-1.2%], p=0.004)(Table 1, Figure 1). Authors suggest single-dosage vaccinations of BNT162b2 do offer significant short-term protection against SARS-CoV-2 transmission.

ABSTRACT

The BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech) is being utilised internationally for mass COVID-19 vaccination. Evidence of single-dose protection against symptomatic disease has encouraged some countries to opt for delayed booster doses of BNT162b2, but the effect of this strategy on rates of asymptomatic SARS-CoV-2 infection remains unknown. We previously demonstrated frequent pauci- and asymptomatic SARS-CoV-2 infection amongst healthcare workers (HCWs) during the UK's first wave of the COVID-19 pandemic, using a comprehensive PCR-based HCW screening programme (Rivett et al., 2020; Jones et al., 2020). Here, we evaluate the effect of first-dose BNT162b2 vaccination on test positivity rates, and find a four-fold reduction in asymptomatic infection amongst HCWs >=12 days post-vaccination. These data provide real-world evidence of short-term protection against asymptomatic SARS-CoV-2 infection following a single dose of BNT162b2 vaccine, suggesting that mass first-dose vaccination will reduce SARS-CoV-2 transmission, as well as the burden of COVID-19 disease.

FIGURES

	Unvaccinated			<12 days since vaccination			≥12 days since vaccination		
Week start	Total tests	Positive tests	%	Total tests	Positive tests	%	Total tests	Positive tests	%
28/12/2020	2097	16	0.8%	8	0	0.0%	6	0	0.0%
04/01/2021	4762	43	0.9%	93	0	0.0%	22	0	0.0%
11/01/2021	3273	27	0.8%	978	6	0.6%	30	0	0.0%
18/01/2021	2183	17	0.8%	1716	8	0.5%	483	1	0.2%
25/01/2021	1069	9	0.8%	1819	5	0.3%	1506	3	0.2%
01/02/2021	699	1	0.1%	758	1	0.1%	2825	1	0.0%

Table 1: Weekly numbers and proportions of positive SARS-CoV-2 test results spanning six weeks around the main study period (indicated in grey)

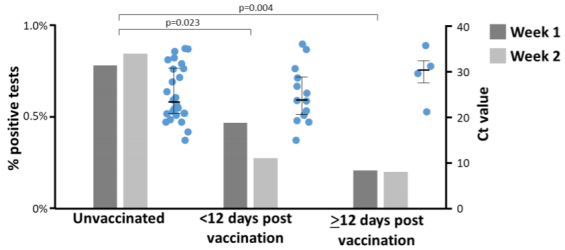

Figure 1: Proportion of positive screening tests for SARS-CoV-2 amongst HCWs from the CUHNHFT asymptomatic screening programme (grey bars; week 1, 18/01/2021-24/01/2021; week 2, 25/01/2021-31/01/2021) and Ct values of positive tests (CT<36; blue dots; both weeks). RT-PCR targeting the SARS-CoV-2 ORF1ab genes was conducted at the Cambridge COVID-19 Testing Centre (part of the UK Lighthouse Labs Network). For proportions of positive screening tests, p values for pair-wise comparisons of unvaccinated HCWs with HCWs <12 days or ≥12 days post-vaccination are shown (Fisher's exact test; both weeks). For Ct values, medians ± interquartile ranges are shown.

SARS-COV-2 VIRAL VARIANTS-TACKLING A MOVING TARGET

Mascola JR, Graham BS, Fauci AS.. JAMA. 2021 Apr 6;325(13):1261-1262. doi: 10.1001/jama.2021.2088.
Level of Evidence: 5 - Expert Opinion

BLUF

Immunologists and virologists from the National Institute of Allergy and Infectious Diseases discuss the emergence of a new California variant of SARS-CoV-2 described in a JAMA article by Zhang, et al and explore its potential clinical consequences. Based on data from Zhang, et al and other studies of SARS-CoV-2 variants, the authors observe that viral variation can result in antigenic changes that alter antibody-mediated immunity, as seen in a South African strain partially to fully resistant to neutralization by some monoclonal antibodies in vitro. The authors suggest that even though current data shows that current vaccines effectively reduce overall mortality in the setting of antigenic variation, more research into viral transmissibility is needed in order to determine whether changes in vaccine composition are necessary to limit evasion of vaccine-induced immunity.

DEVELOPMENTS IN TRANSMISSION & PREVENTION

ASSESSING TRANSMISSIBILITY OF SARS-COV-2 LINEAGE B.1.1.7 IN ENGLAND

Volz E, Mishra S, Chand M, Barrett JC, Johnson R, Geidelberg L, Hinsley WR, Laydon DJ, Dabrera G, O'Toole Á, Amato R, Ragonnet-Cronin M, Harrison I, Jackson B, Ariani CV, Boyd O, Loman NJ, McCrone JT, Gonçalves S, Jorgensen D, Myers R, Hill V, Jackson DK, Gaythorpe K, Groves N, Sillitoe J, Kwiatkowski DP; COVID-19 Genomics UK (COG-UK) consortium, Flaxman S, Ratmann O, Bhatt S, Hopkins S, Gandy A, Rambaut A, Ferguson NM.. Nature. 2021 Mar 25. doi: 10.1038/s41586-021-03470-x. Online ahead of print.
Level of Evidence: 1 - Local and current random sample surveys (or censuses)

BLUF

Epidemiologists from the MRC Centre for Global Infectious Disease Analysis at Imperial College London conducted a community-based, whole genome analysis of a random sample of SARS-CoV-2 sequences collected from community-based diagnostic testing in England between October 1, 2020 and January 16, 2021. They found the new variant of concern (VOC) SARS-COV-2 lineage B.1.1.7 expanded rapidly (Figure 1) and possessed an advantageous S-gene target failures (SGTF) mutation that appeared to confer higher transmissibility (Figure 2). Authors emphasize the importance of genomic surveillance and its potentially valuable insights into new VOC that may impact transmissibility and disease outcomes.

ABSTRACT

The SARS-CoV-2 lineage B.1.1.7, designated a Variant of Concern 202012/01 (VOC) by Public Health England1, originated in the UK in late Summer to early Autumn 20202. Whole genome SARS-CoV-2 sequence data collected from community-based diagnostic testing shows an unprecedentedly rapid expansion of the B.1.1.7 lineage during Autumn 2020, suggesting a selective advantage. We find that changes in VOC frequency inferred from genetic data correspond closely to changes inferred by S-gene target failures (SGTF) in community-based diagnostic PCR testing. Analysis of trends in SGTF and non-SGTF case numbers in local areas across England shows that the VOC has higher transmissibility than non-VOC lineages, even if the VOC has a different latent period or generation time. The SGTF data indicate a transient shift in the age composition of reported cases, with a larger share of under 20 year olds among reported VOC than non-VOC cases. Time-varying reproduction numbers for the VOC and cocirculating lineages were estimated using SGTF and genomic data. The best supported models did not indicate a substantial difference in VOC transmissibility among different age groups. There is a consensus among all analyses that the VOC has a substantial transmission advantage with a 50% to 100% higher reproduction number.

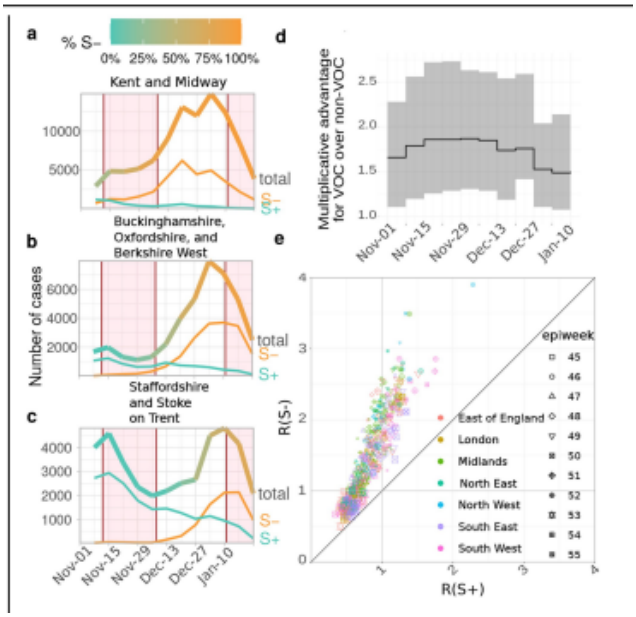

Figure 2. Trends of diagnosed cases and SGTF over time and between regions and reproduction numbers of the VOC inferred from SGTF. A-C. The number of diagnosed cases over time for three English STP regions which represent a wide spectrum of outcomes in terms of time of VOC introduction into the region. Each line segment is shaded with the frequency of SGTF in each week. Vertical shaded regions represent the time of the second and third UK lockdowns. D. The estimated multiplicative transmission advantage of the VOC over time. E. The reproduction number of S-gene negative cases versus the reproduction number of S-gene positive cases over time and between STP regions.

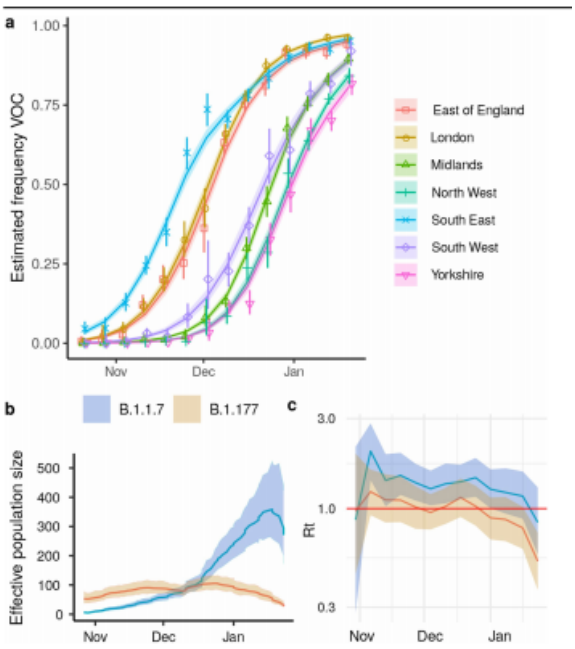

Figure 1. Expansion of lineage B.1.1.7 relative to co-circulating lineages in England. A. Estimated frequency of sampling the VOC (lines) over time in NHS regions. Shaded regions show a 95% credible region based on Bayesian regression. Points show empirical proportions of the VOC in each week with error bars showing 95% confidence interval based on binomial sampling error. B. Effective population size over time for lineage B.1.1.7 and estimates based on a matched sample of the most abundant co-circulating lineage, B.1.177. Shaded regions show a 95% bootstrap confidence interval. C. The effective reproduction number inferred from growth of effective population size.

STATIN THERAPY IS ASSOCIATED WITH LESS ICU ADMISSIONS IN COVID-19 PATIENTS. A PRELIMINARY ANALYSIS OF THE CURRENT OBSERVATIONS

Zuin M, Rigatelli G, Bilato C, Zuliani G, Roncon L.. Minerva Anestesiol. 2021 Mar 10. doi: 10.23736/S0375-9393.21.15600-7. Online ahead of print.

Level of Evidence: 1 - Systematic review of inception cohort studies

BLUF

Cardiologists from the University of Ferrera in Italy conducted a systematic review of 7 articles including 17,661 patients exploring the use of statins in COVID-19 before January 8, 2021(Figure 1A). They found patients already taking statins (n= 2,532) had a lower risk of ICU admission compared to non-statin users (OR: 0.84, 95% CI:0.72-0.99, p=0.004, I2: 39.2%, Figure 1B). While the findings suggest a potentially protective effect of statin therapy prior to admission, authors suggest that without understanding the pathophysiology behind this phenomena, further experimentation and investigation is necessary.

FIGURES

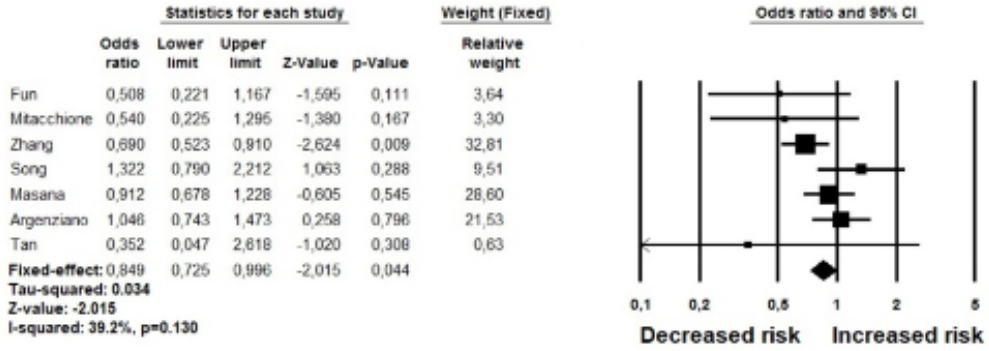

Figure 1. (A) Flow diagram of selected studies for the meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA). (B) Forest plot of studies investigating the risk of intensive care unit (ICU) admission in relation to statin treatment before hospitalization forCOVID-19.

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