# The Daily COVID-19 Literature Surveillance Summary

## April 05, 2021

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# 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**

- Injection-site skin manifestations (COVID-arm) were found in some healthcare workers who took the Pfizer (BNT162b2) mRNA COVID-19 vaccine. Dermatologists from the Ramn y Cajal University Hospital in Madrid, Spain conducted a retrospective study to investigate the "Covid-arm" skin manifestations in response to the mRNA vaccine from Pfizer (BNT162b2). In 4775 subjects, 103 (2.1%) had delayed-injection-site reactions. Histological examination of one such lesion showed evidence of perivascular inflammation and vessel dilation. While pathophysiology is unknown, authors propose several mechanisms and suggest these side effects should not preclude vaccination with the BNT162b2 vaccine.

# TABLE OF CONTENTS

# QUANTIFYING SARS-COV-2 TRANSMISSION SUGGESTS EPIDEMIC CONTROL WITH DIGITAL CONTACT TRACING

Ferretti L, Wymant C, Kendall M, Zhao L, Nurtay A, Abeler-Dörner L, Parker M, Bonsall D, Fraser C.. Science. 2020 May 8;368(6491):eabb6936. doi: 10.1126/science.abb6936. Epub 2020 Mar 31.
Level of Evidence: 5 - Modeling

## BLUF

In May 2020, data scientists from the University of Oxford used a mathematical model to analyze SARS-CoV-2 transmission routes and determine the impact of different degrees of isolation and contact tracing to control the pandemic (Table 1). They found manual contact tracing was too slow for viral spread at the time, but app-based tracing that could memorize proximity contacts and notify individuals of positive cases could control the pandemic (Figures 3, 4). The authors suggest this method could prevent mass lockdowns via targeting only those at risk, but should be adopted democratically due to potential ethical concerns regarding privacy.

## ABSTRACT

The newly emergent human virus SARS-CoV-2 (severe acute respiratory syndrome-coronavirus 2) is resulting in high fatality rates and incapacitated health systems. Preventing further transmission is a priority. We analyzed key parameters of epidemic spread to estimate the contribution of different transmission routes and determine requirements for case isolation and contact tracing needed to stop the epidemic. Although SARS-CoV-2 is spreading too fast to be contained by manual contact tracing, it could be controlled if this process were faster, more efficient, and happened at scale. A contact-tracing app that builds a memory of proximity contacts and immediately notifies contacts of positive cases can achieve epidemic control if used by enough people. By targeting recommendations to only those at risk, epidemics could be contained without resorting to mass quarantines ("lockdowns") that are harmful to society. We discuss the ethical requirements for an intervention of this kind.

## FIGURES

**Table 1. Parameters of the infectiousness model.**

| Name | Symbol | Description | Central value | Uncertainty | Source |
|---|---|---|---|---|---|
| *Parameters directly calculated from data* | | | | | |
| Doubling time | $T_2$ | The time taken for the epidemic to double in size during the early uncontrolled phase of expansion | 5.0 days | 95% CI: 4.2–6.4 | (20) |
| Incubation period (two parameters) | $s(\tau)$ | Lognormal meanlog<br>Lognormal sdlog | 1.644<br>0.363 | 95% CI: 1.495–1.798<br>95% CI: 0.201–0.521 | (21) |
| Generation time (two parameters) | $w(\tau)$ | Weibull shape<br>Weibull scale | 2.826<br>5.665 | 95% CI: 1.75–4.7<br>95% CI: 4.7–6.9 | This paper |
| *Parameters with Bayesian priors informed by anecdotal reports or indirect evidence* | | | | | |
| Proportion asymptomatic | $P_a$ | The proportion of infected individuals who are asymptomatic | 0.4 | Prior = beta ($\alpha$ = 1.5, $\beta$ = 1.75)<br>Mode = 0.4<br>Mean = 0.46 | Media reports (Diamond Princess) |
| Relative infectiousness of asymptomatics | $x_a$ | The ratio of infectiousness of asymptomatic individuals to infectiousness of symptomatic individuals | 0.1 | Prior = beta ($\alpha$ = 1.5, $\beta$ = 5.5)<br>Mode = 0.1<br>Mean = 0.21 | Observation of few missing links in Singapore outbreak to date [suggestion from (19)] |
| Fraction of all transmission that is environmentally mediated | $R_E/R_0$ | Self-explanatory | 0.1 | Prior = beta ($\alpha$ = 1.5, $\beta$ = 5.5)<br>Mode = 0.1<br>Mean = 0.21 | Anecdotal observation that many infections can be traced to close contacts once detailed tracing is completed |
| Environmental infectiousness | $E(l)$ | Rate at which a contaminated environment infects new people after a time lag $l$ | 3 | Box function (0, $n$) days, prior for $n$ = gamma (shape = 4, rate = 1)<br>Mode = 3<br>Mean = 4 | (39); variety of values for many different surfaces |

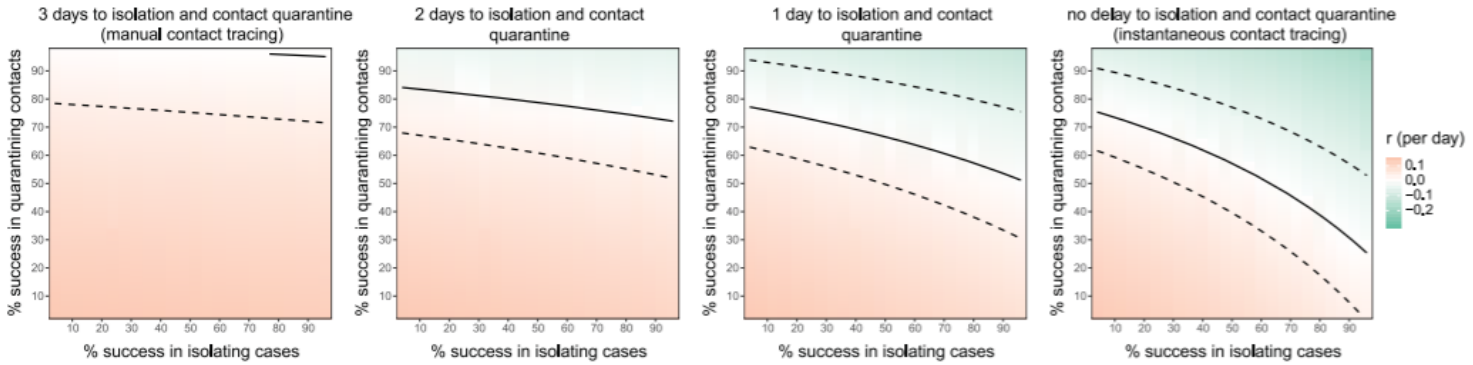



**Fig. 3. Quantifying intervention success.** Heat map plot shows the exponential growth rate of the epidemic *r* as a function of the success rate of instant isolation of symptomatic cases (*x* axis) and the success rate of instant contact tracing (*y* axis). Positive values of *r* (red) imply a growing epidemic; negative values of *r* (green) imply a declining epidemic, with greater negative values implying faster decline. The solid black line shows $r = 0$ (i.e., the threshold for epidemic control). The dashed lines show uncertainty in the threshold due to uncertainty in $R_0$ (see figs. S15 to S17). The different panels show variation in the delay associated with the intervention, from initiation of symptoms to case isolation and quarantine of contacts.

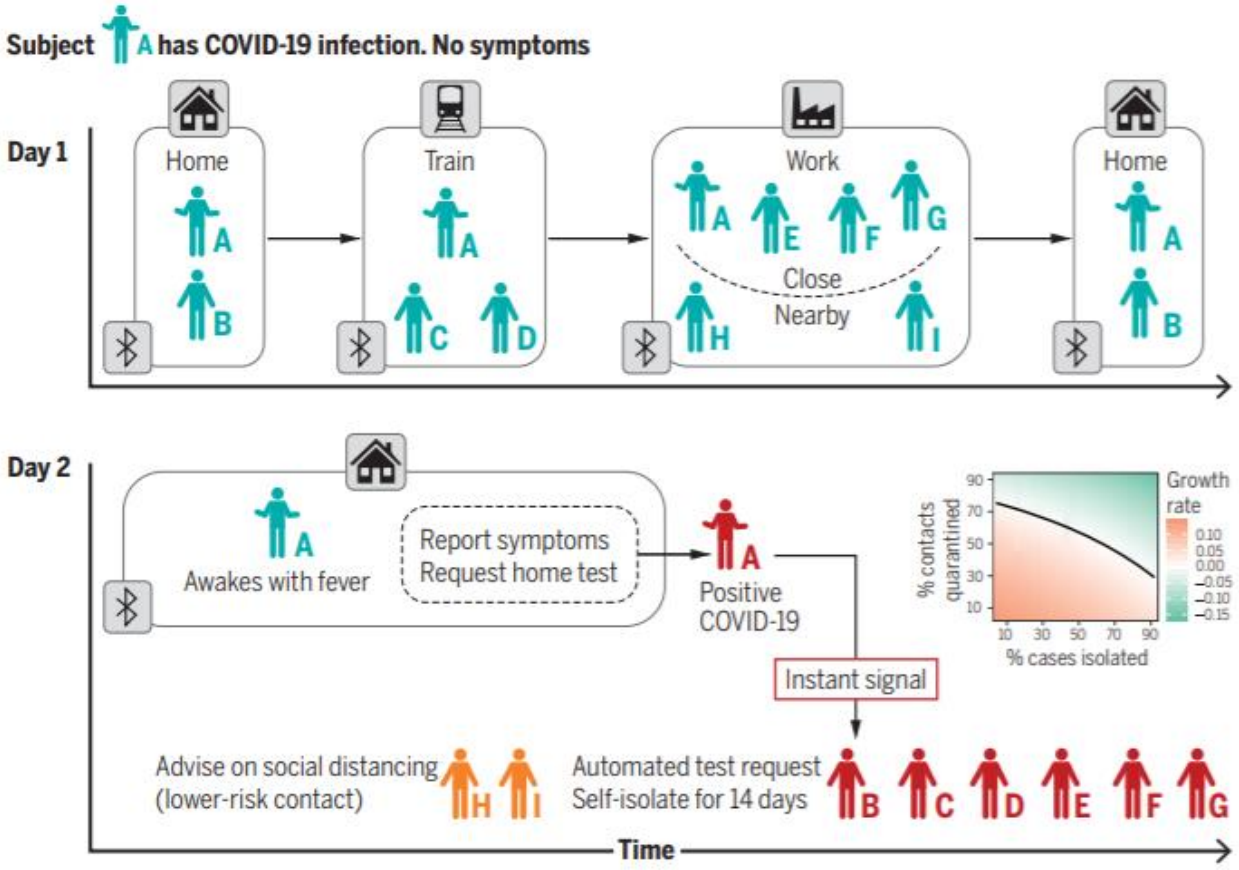



**Fig. 4. A schematic of app-based COVID-19 contact tracing.** Contacts of individual A (and all individuals using the app) are traced using low-energy Bluetooth connections with other app users. Individual A requests a SARS-CoV-2 test (using the app) and that person's positive test result triggers an instant notification to individuals who have been in close contact. The app advises isolation for the case (individual A) and quarantine of the individual's contacts.

# FUNCTIONAL ANALYSIS OF SARS-COV-2 PROTEINS IN DROSOPHILA IDENTIFIES ORF6-INDUCED PATHOGENIC EFFECTS WITH SELINEXOR AS AN EFFECTIVE TREATMENT

Zhu JY, Lee JG, van de Leemput J, Lee H, Han Z.. Cell Biosci. 2021 Mar 25;11(1):59. doi: 10.1186/s13578-021-00567-8.
Level of Evidence: 5 - Modeling

## BLUF

Endocrinologists and developmental biologists from the University of Maryland generated transgenic Drosophilia lines for individual SARS-CoV-2 genes using a Gal4-UAS system and studied their pathogenicity. They found that ubiquitous expression of Drosophila genes Orf6, Nsp6 or Orf7a led to many defects (e.g., reduced mitochondria, viability, and climbing ability), and that Selinexor (see summary) decreased lethality and locomotion defects (Figure 2, Figure 4, Figure 6). The authors suggest Drosophila are useful models for studying SARS-CoV2 gene expression and that Orf6 is a highly pathogenic protein.

## SUMMARY

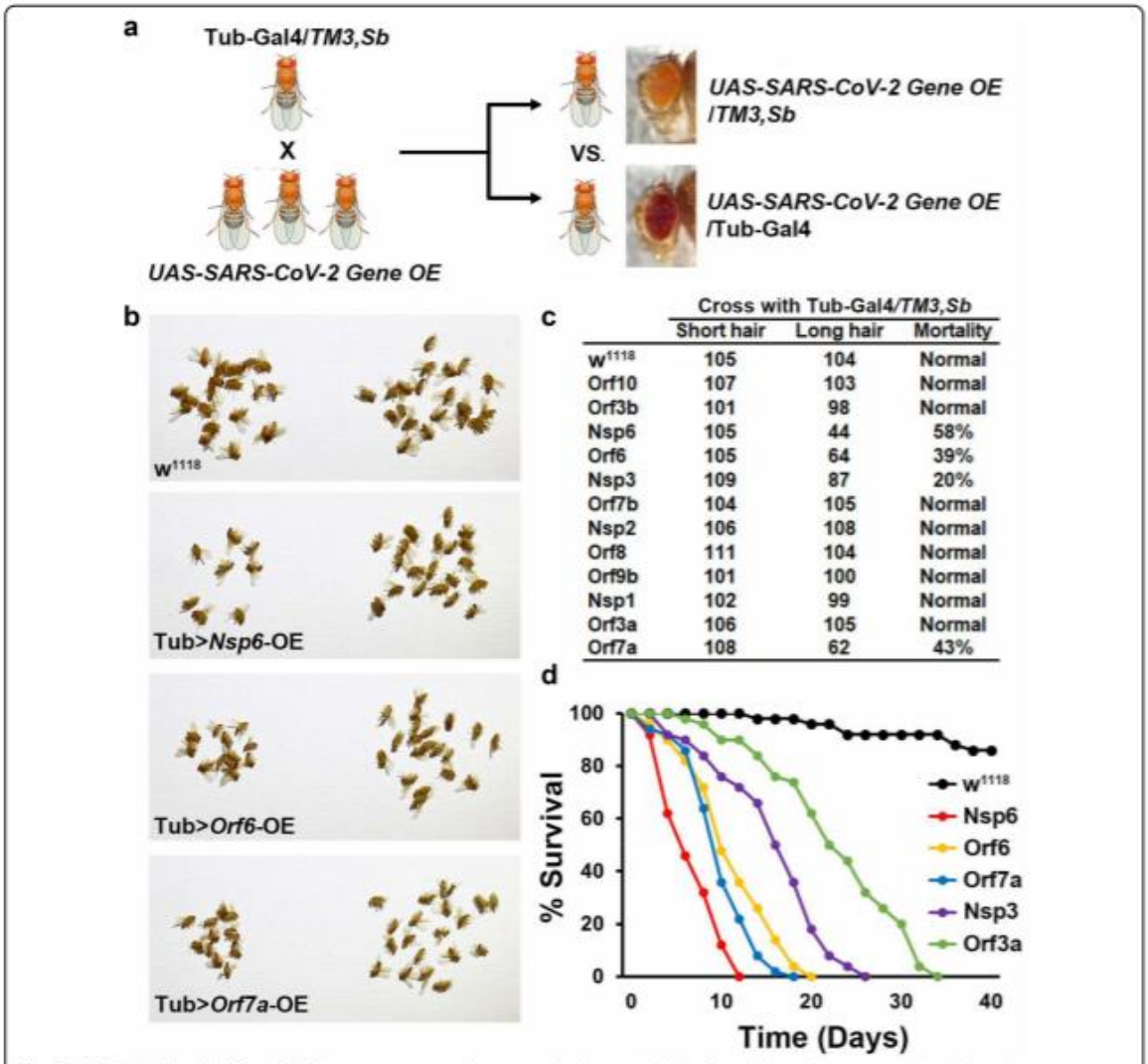
Bioinformatic analysis demonstrated that SARS-CoV-2 virus-host interactions involve human proteins that are conserved in Drosophila.

Selinexor inhibits XPO1 (Orf6 was found to interact with XPO1).

## ABSTRACT

BACKGROUND: SARS-CoV-2 causes COVID-19 with a widely diverse disease profile that affects many different tissues. The mechanisms underlying its pathogenicity in host organisms remain unclear. Animal models for studying the pathogenicity of SARS-CoV-2 proteins are lacking. METHODS: Using bioinformatic analysis, we found that 90% of the virus-host interactions involve human proteins conserved in Drosophila. Therefore, we generated a series of transgenic fly lines for individual SARS-CoV-2 genes, and used the Gal4-UAS system to express these viral genes in Drosophila to study their pathogenicity. RESULTS: We found that the ubiquitous expression of Orf6, Nsp6 or Orf7a in Drosophila led to reduced viability and tissue defects, including reduced trachea branching as well as muscle deficits resulting in a "held-up" wing phenotype and poor climbing ability. Furthermore, muscles in these flies showed dramatically reduced mitochondria. Since Orf6 was found to interact with nucleopore proteins XPO1, we tested Selinexor, a drug that inhibits XPO1, and found that it could attenuate the Orf6-induced lethality and tissue-specific phenotypes observed in flies. CONCLUSIONS: Our study established Drosophila as a model for studying the function of SARS-CoV2 genes, identified Orf6 as a highly pathogenic protein in various tissues, and demonstrated the potential of Selinexor for inhibiting Orf6 toxicity using an in vivo animal model system.

## FIGURES




| | Cross with Tub-Gal4/*TM3,Sb* | | |
|---|---|---|---|
| | Short hair | Long hair | Mortality |
| $w^{1118}$ | 105 | 104 | Normal |
| Orf10 | 107 | 103 | Normal |
| Orf3b | 101 | 98 | Normal |
| Nsp6 | 105 | 44 | 58% |
| Orf6 | 105 | 64 | 39% |
| Nsp3 | 109 | 87 | 20% |
| Orf7b | 104 | 105 | Normal |
| Nsp2 | 106 | 108 | Normal |
| Orf8 | 111 | 104 | Normal |
| Orf9b | 101 | 100 | Normal |
| Nsp1 | 102 | 99 | Normal |
| Orf3a | 106 | 105 | Normal |
| Orf7a | 108 | 62 | 43% |

**Fig. 2** SARS-CoV-2 Nsp6, Orf6 and Orf7a transgene expression causes developmental lethality. **a** Schematic representation of genetic screen to identify individual SARS-CoV-2 genes with pathogenic effect. **b** Images of adult progeny emerging from pupa stage from cross in **a**, distinguished by carrying the balancer (*TM3, Sb*; orange eyes and short hair on back; no viral transgene expression) or with expression of the SARS-CoV-2 gene driven by the ubiquitous Tubulin (Tub) enhancer (red eyes and long hair). $w^{1118}$ is a wild type control. **c** Quantification of mortality rate prior to eclosion for the individually expressed SARS-CoV-2 genes from the cross in **a**. Mortality calculated as: (long hair − short hair) / short hair × 100. **d** Graph displaying lifespan data for adult flies carrying SARS-CoV-2 Nsp6, Orf6, Orf7a, Nsp3 or Orf3a transgenes. $w^{1118}$ is a wild type control. N = 100 flies per group. Abbreviations: E, envelope protein; M, membrane protein; N, nucleocapsid protein; Nsp, non-structural protein; OE, overexpression; Orf, accessory protein; S, spike protein; Sb, stubble TM3, chromosome 3

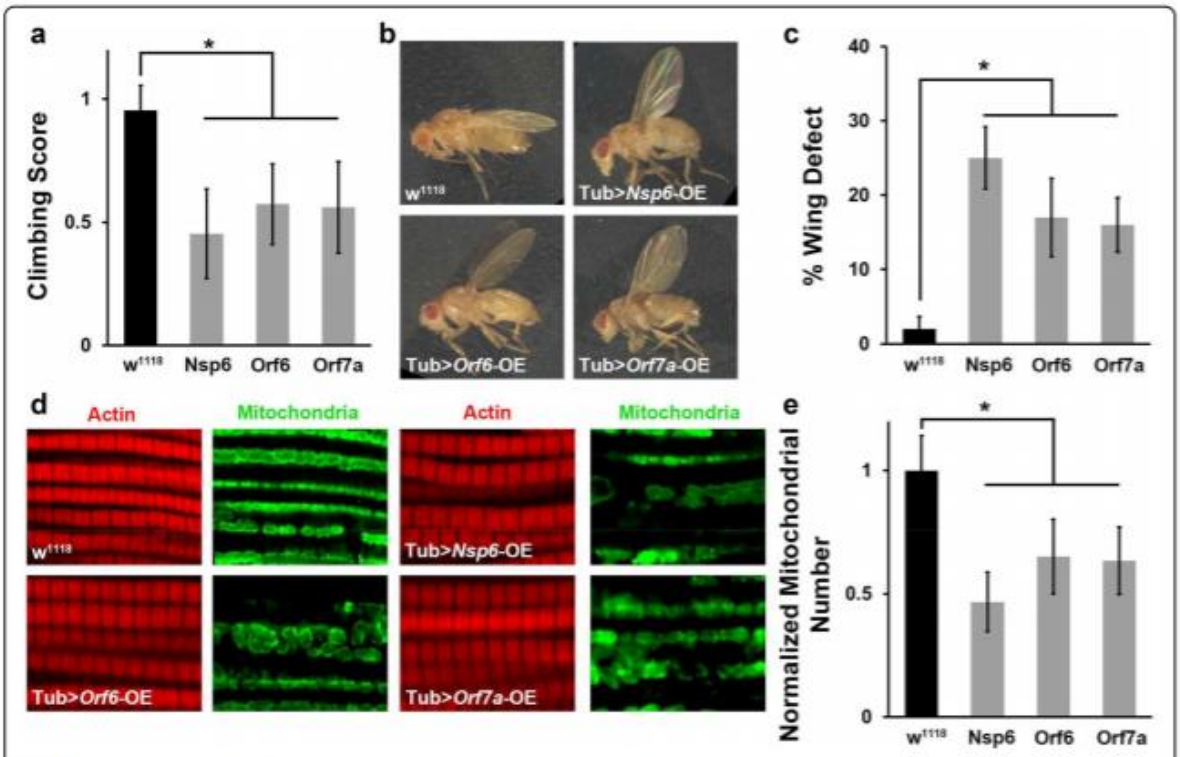



**Fig. 4** SARS-CoV-2 Nsp6, Orf6 and Orf7a transgene expression in *Drosophila* results in locomotion defect and reduced mitochondria. **a** Quantification of climbing ability in SARS-CoV-2 Nsp6, Orf6 and Orf7a transgenic flies. N = 30 flies per group. **b** Representative images of typical (wild type, $w^{1118}$) and "held-up" wing phenotype in SARS-CoV-2 Nsp6, Orf6 and Orf7a expression flies. **c** Quantification of flies with "held-up" wing phenotype (i.e. % Wing Defect). Four replicates, each replicate N = 50 flies per group. **d** Representative images of indirect flight muscle (labeled with Phalloidin, red) and mitochondria (labeled with ATPSA, green) morphology in SARS-CoV-2 Nsp6, Orf6 and Orf7a flies. **e** Quantification of the number of mitochondria in the fly indirect flight muscle of both wings, normalized based on wild type ($w^{1118}$) counts. N = 10 flies per group. The results are presented as mean ± SD. Statistical significance (*) is defined as $P < 0.05$

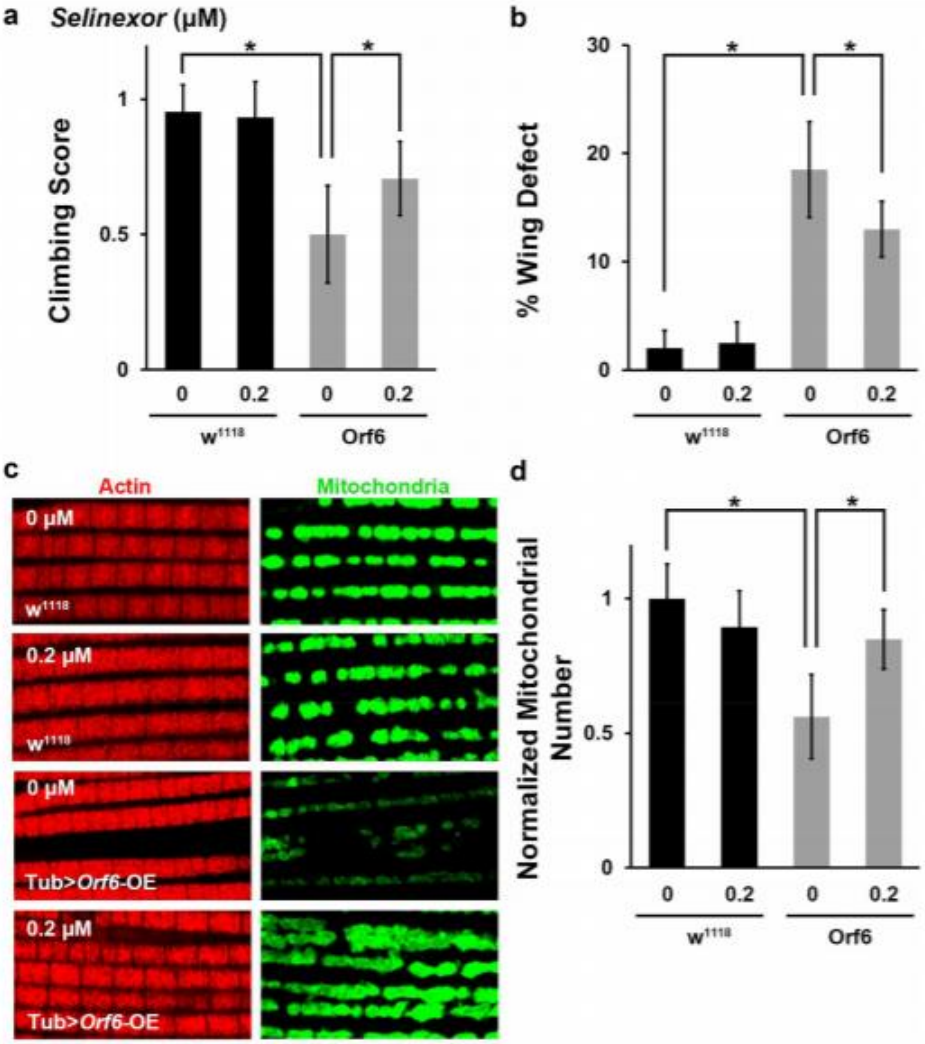



**Fig. 6** Selinexor attenuates locomotion defect and reduced mitochondria caused by SARS-CoV-2 Orf6 transgene expression in flies. Comparative assays of phenotypes in wild type ($w^{1118}$) and SARS-CoV-2 Orf6 transgenic [overexpression (OE) driven by ubiquitous enhancer Tubulin (Tub)] flies following treatment with Selinexor (0.2 μM). **a** Quantification of climbing ability. N = 30 flies per group. **b** Quantification of flies with "held-up" wing phenotype (i.e. % Wing Defect). Four replicates, each replicate N = 50 flies per group. **c** Representative images of indirect flight muscle (labeled with Phalloidin, red) and mitochondria (labeled with ATPSA, green) morphology. **d** Quantification of the number of mitochondria in the fly indirect flight muscle, normalized based on wild type ($w^{1118}$) counts. N = 10 flies per group. Results are presented as mean ± SD. Statistical significance (*) is defined as $P < 0.05$

# SKIN MANIFESTATIONS OF THE BNT162B2 MRNA COVID-19 VACCINE IN HEALTHCARE WORKERS. "COVID-ARM": A CLINICAL AND HISTOLOGICAL CHARACTERIZATION

Fernandez-Nieto D, Hammerle J, Fernandez-Escribano M, Moreno-Del Real CM, Garcia-Abellas P, Carretero-Barrio I, Solano-Solares E, de-la-Hoz-Caballer B, Jimenez-Cauhe J, Ortega-Quijano D, Fernandez-Guarino M.. J Eur Acad Dermatol Venereol. 2021 Mar 30. doi: 10.1111/jdv.17250. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

## BLUF

Dermatologists from the Ramn y Cajal University Hospital in Madrid, Spain conducted a retrospective study to investigate the "Covid-arm" skin manifestations in response to the mRNA vaccine from Pfizer (BNT162b2). In 4775 subjects (Table 1), 103 (2.1%) had delayed-injection-site reactions (Figure 1). Histological examination of one such lesion showed evidence of perivascular inflammation and vessel dilation (Figures 2, 3). While pathophysiology is unknown, authors propose several mechanisms and suggest these side effects should not preclude vaccination with the BNT162b2 vaccine.

## ABSTRACT

The coronavirus disease 2019 (COVID-19) has been associated to a wide clinical spectrum of skin manifestations, including chilblain-like, urticarial, vesicular, maculopapular, livedoid and vasculitic lesions, among others1,2 . However, the exact pathophysiology for the appearance of skin lesions is still unknown. Several hypotheses have been suggested, including viral hypersensitivity reactions, overexpression of type I interferons, COVID-19 induced coagulopathy, thrombotic microangiopathy and direct viral damage3-6 .

## FIGURES

| Characteristics | |
|---|---|
| Number of subjects | 103 |
| Age, mean, years (range) | 40.4 (20-64) |
| Sex, male (%) | 12 (11.7%) |
| Sex, female (%) | 91 (88.3%) |
| After 1st dose | 49 (47.6%) |
| After 2nd dose | 54 (52.4%) |
| Itch (%) | 70 (68.0%) |
| Duration <8h (%) | 23 (22.3%) |
| Duration 8-24h (%) | 28 (27.1%) |
| Duration 24-72h (%) | 38 (36.9%) |
| Duration >72h (%) | 14 (13.6%) |

Table 1
Characteristics and demographic data of the subjects with delayed injection-site reaction obtained from the registry of the BNT162b2 mRNA Covid-19 Vaccine

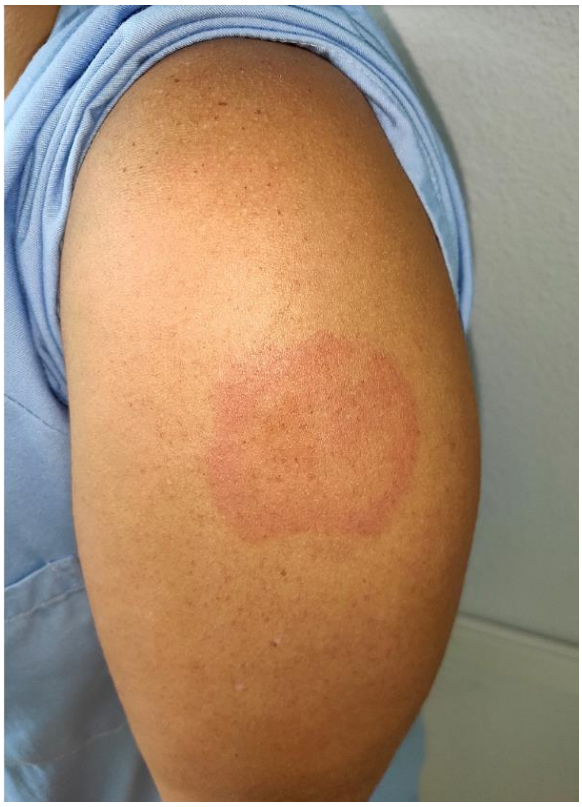
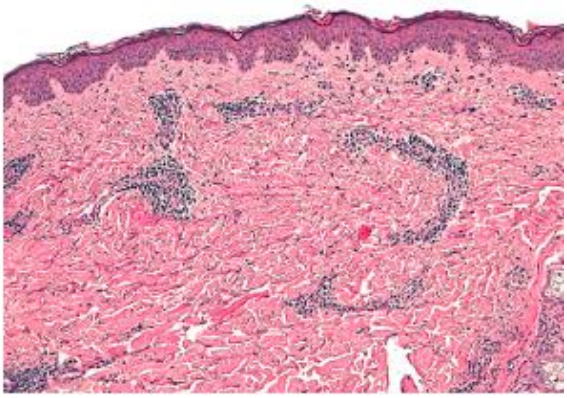


Figure 1. A 34-year-old female healthcare worker showing a slightly indurated erythematous targetoid patch at the injection site reaction of 6x4.5cm diameter, 8 days after the first dose of the BNT162b2 vaccine.



B) Histologic examination shows a superficial and deep perivascular lymphocytic infiltrate (H-E x100).

## HETEROLOGOUS PRIME-BOOST: BREAKING THE PROTECTIVE IMMUNE RESPONSE BOTTLENECK OF COVID-19 VACCINE CANDIDATES

He Q, Mao Q, An C, Zhang J, Gao F, Bian L, Li C, Liang Z, Xu M, Wang J.. Emerg Microbes Infect. 2021 Mar 11:1-22. doi: 10.1080/22221751.2021.1902245. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

### BLUF

Immunologists from the National Institute for Food and Drug control in China evaluated the effectiveness of a prime-boost strategy for several Chinese made COVID-19 vaccines using a mouse model. They found that priming with Ad5-vectored vaccines (rAd) followed by inactivated (INA), recombinant protein (rRBD), or mRNA vaccines significantly improved the immune response, specifically neutralizing antibodies and Th1 biased T-cell responses, compared with single-dose rAd COVID-19 vaccine immunization (Figures 1, 2, 3). While their experiments were limited to measuring immune responses and cannot

be directly translated to vaccine efficacy, authors suggest heterologous prime-boost using an adenovirus vector in combination with other vaccine types could be employed to improve vaccine efficacy.

## ABSTRACT

COVID-19 vaccines emerging from different platforms differ in efficacy, duration of protection, and side effects. To maximize the benefits of vaccination, we explored the utility of employing a heterologous prime-boost strategy in which different combinations of the four types of leading COVID-19 vaccine candidates that are undergoing clinical trials in China were tested in a mouse model. Our results showed that sequential immunization with adenovirus vectored vaccine followed by inactivated/recombinant subunit/mRNA vaccine administration specifically increased levels of neutralizing antibodies and promoted the modulation of antibody responses to predominantly neutralizing antibodies. Moreover, a heterologous prime-boost regimen with an adenovirus vector vaccine also improved Th1-biased T cell responses. Our results provide new ideas for the development and application of COVID-19 vaccines to control the SARS-CoV-2 pandemic.

## FIGURES

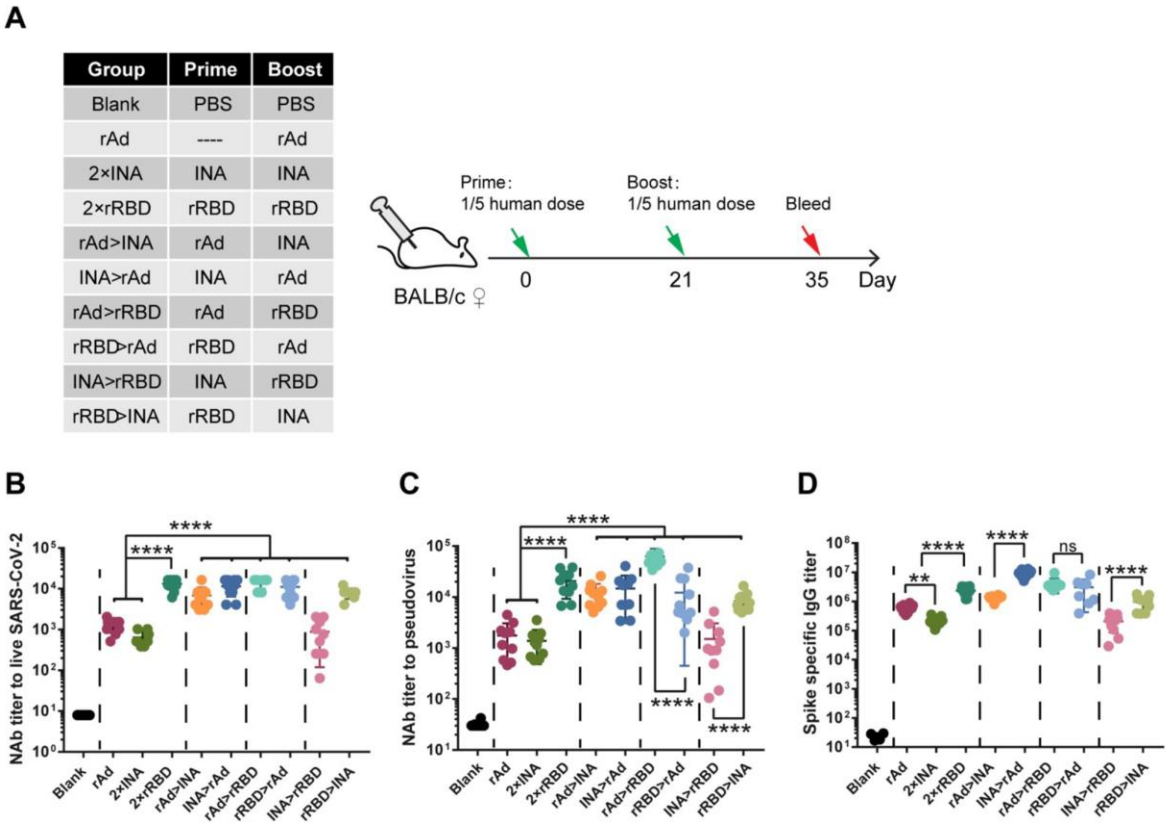



Figure 1. Comparison of humeral immune responses induced by COVID-19 vaccines of different technology platforms and heterologous prime-boost regimens. (A). Schematic representation of experimental protocols and immunization groups. Mice in 9 groups were immunized with different COVID-19 vaccines or vaccine combinations: rAd, 2 × INA, 2 × rRBD,, rAd > INA, INA > rAd, rAd > rRBD, rRBD > rAd, INA > rRBD, rRBD > INA. (rAd: recombinant Ad5 vectored vaccine, INA: inactivated vaccine, rRBD: recombinant RBD vaccine), Mice in a blank control group were sham-vaccinated with PBS. For rAd group, mice were immunized with one dose of rAd vaccine and blood samples were collected 14 days post - vaccination; for other groups, blood samples were only collected 14 days after the second vaccine dose (B,C). Serum Nab levels measured by live SARS-CoV-2 virus (B) and pseudovirus (C). NAb titres are expressed as 50% inhibitory dilution (EC50) of serum. D. Spike-specific binding IgG titres were measured by ELISA (n = 8–10 per group, one spot represents one sample). Bars represent means ± SD, **p < 0.01, ****p < 0.0001, ns: p > 0.05.

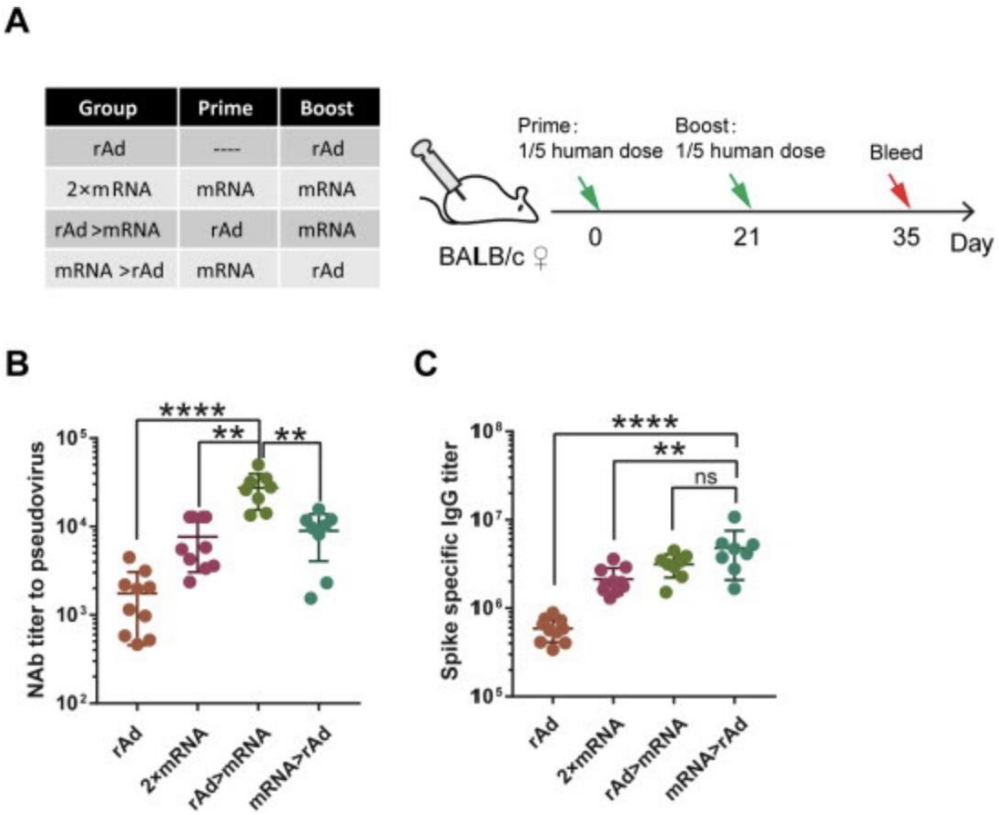



Figure 2. Humeral immune responses induced by heterologous prime-boost regimen of adenovirus vectored and mRNA-based COVID-19 vaccine. (A). Schematic representation of experimental protocol and immunization groups. Mice in 4 groups were immunized with adenovirus vectored vaccine or mRNA vaccine: rAd, 2 × mRNA, rAd>mRNA, mRNA>rAd. (rAd: recombinant Ad5 vectored vaccine, RNA: mRNAbased vaccine). For the rAd group, mice were immunized with one dose of rAd vaccine and blood samples were collected 14 days post-vaccination; for other groups, bloods were collected 14 days post the second vaccine dose. (B). NAbs of serum measured by live SARS-CoV-2 virus and expressed as 50% inhibitory dilution (EC50) of serum. (C). Spike-specific binding IgG titers were measured by ELISA (n = 8-10 per group, one spot represents one sample. Bars represent means ± SD, **p < 0.01, ****p < 0.0001, ns: p > 0.05.

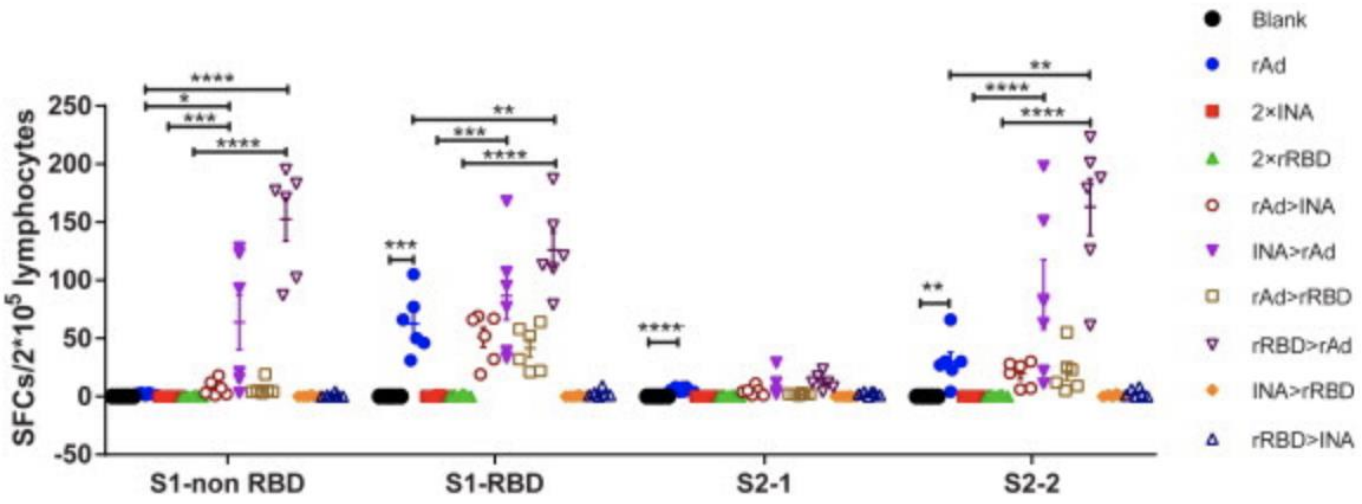



Figure 3. T cell responses to SARS-CoV-2 spike peptides measured by IFN-γ ELISPOT. 6 mice in Figure 1 were sacrificed and T cell response were measured. Isolated lymphocytes were stimulated with 4 peptide pools spanning spike respectively, and the IFN-γ secreting cells were quantified by ELISPOT assay. (n = 6 per group, one spot represents one sample). Bars represent means ± SEM, *p < 0.05, **p <0.01, ***p < 0.001, ****p < 0.0001.

## TRUST, EFFICACY AND ETHICACY WHEN TESTING PRISONERS FOR COVID-19

Lambert S, Wilkinson D.. Int J Prison Health. 2021 Mar 10;ahead-of-print(ahead-of-print). doi: 10.1108/IJPH-10-2020-0084.
Level of Evidence: 5 - Review / Literature Review

### BLUF

In this review, Faculty of Education and Children's Services and Social Science from the University of Chester in the UK, detail the challenges of COVID-19 testing in prison systems, including ethical issues such as assumed participation of consent, practicality issues such as test administration and technological barriers, and issues of social misconception regarding prison populations. COVID-19 outbreaks have been rampant in many prison systems (Table 1) given overcrowding, insufficient sanitation, poor ventilation, inadequate health care, and many prisoners with chronic underlying medical conditions. The authors suggest the complex issues and nuances within the prison system be carefully addressed to properly undergo mass testing and eventual vaccinations, to avoid unwarranted confusion and mistrust.

### ABSTRACT

PURPOSE: The outbreak of the severe acute respiratory syndrome coronavirus 2 virus and subsequent COVID-19 illness has had a major impact on all levels of society internationally. The extent of the impact of COVID-19 on prison staff and prisoners in England and Wales is unknown. Testing for COVID-19 both asymptomatic and symptomatic, as well as for antibodies, to date, has been minimal. The purpose of this paper is to explore the widespread testing of COVID-19 in prisons poses philosophical and ethical questions around trust, efficacy and ethicacy. DESIGN/METHODOLOGY/APPROACH: This paper is both descriptive, providing an overview of the widespread testing of COVID-19 in prisoners in England and Wales, and conceptual in that it discusses and argues the issues associated with large-scale testing. This paper provides a discussion, using comparative studies, of the issues associated with large-scale testing of prisoners across the prison estate in England and Wales (120 prisons). The issues identified in this paper are contextualised through the lens of COVID-19, but they are equally transferrable to epidemiological studies of any pandemic. Given the prevalence of COVID-19 globally and the lack of information about its spread in prisons, at the time of writing this paper, there is a programme of asymptomatic testing of prisoners. However, there remains a paucity of data on the spread of COVID-19 in prisons because of the progress with the ongoing testing programme. FINDINGS: The authors argue that the widespread testing of prisoners requires careful consideration of the details regarding who is included in testing, how consent is gained and how tests are administered. This paper outlines and argues the importance of considering the complex nuance of power relationships within the prison system, among prisoner officers, medical staff and prisoners and the detrimental consequences. PRACTICAL IMPLICATIONS: The widespread testing of COVID-19 presents ethical and practical challenges. Careful planning is required when considering the ethics of who should be included in COVID-19 testing, how consent will be gained, who and how tests will be administered and very practical challenges around the recording and assigning of COVID-19 test kits inside the prison. The current system for the general population requires scanning of barcodes and registration using a mobile number; these facilities are not permitted inside a prison. ORIGINALITY/VALUE: This paper looks at the issues associated with mass testing of prisoners for COVID-19. According to the authors' knowledge, there has not been any research that looks at the issues of testing either in the UK or internationally. The literature available details countries' responses to the pandemic rather and scientific papers on the development of vaccines. Therefore, this paper is an original review of some of the practicalities that need to be addressed to ensure that testing can be as successful as possible.

### FIGURES

**Table 1** Comparison of four different initiatives compiling data on COVID-19 confirmed cases and deaths among prisoners and staff in correctional facilities across the USA; Franco-Paredes *et al.* (2020)

| *Data source* | *COVID-19 cases among jail–prison residents* | *COVID-19 cases among staff* | *COVID-19 deaths among residents* | *COVID-19 death among staff in jail/prisons* |
|---|---|---|---|---|
| UCLA Law COVID-19 behind bars | 38,616 | 10,182 | 470 | 42 |
| COVID-19 prisons data | 29,519 | 7,402 | 392 | 20 |
| CDC data | 4,893 | 2,778 | 88 | 15 |
| The Marshall Project | 29,251 | 7,435 | 415 | 33 |

Table 1. Comparison of four different initiatives compiling data on COVID-19 confirmed cases and deaths among prisoners and staff in correctional facilities across the USA.

# NEPHROLOGY

## PRIORITIZING PERITONEAL CATHETER PLACEMENT DURING THE COVID-19 PANDEMIC: A PERSPECTIVE OF THE AMERICAN SOCIETY OF NEPHROLOGY COVID-19 HOME DIALYSIS SUBCOMMITTEE

Oliver MJ, Crabtree JH.. Clin J Am Soc Nephrol. 2021 Mar 12:CJN.19141220. doi: 10.2215/CJN.19141220. Online ahead of print.
Level of Evidence: 5 - Expert Opinion

### BLUF

Nephrologists from the University of Toronto and University of California Los Angeles who work closely with the dialysis industry argue that the risk of COVID-19 infection is higher with in-center hemodialysis than home peritoneal dialysis (PD). They suggest taking advantage of a variety of catheter insertion methods, placing PD catheters at higher kidney function, and expanding patient education to increase PD use (Figure 1).

### FIGURES

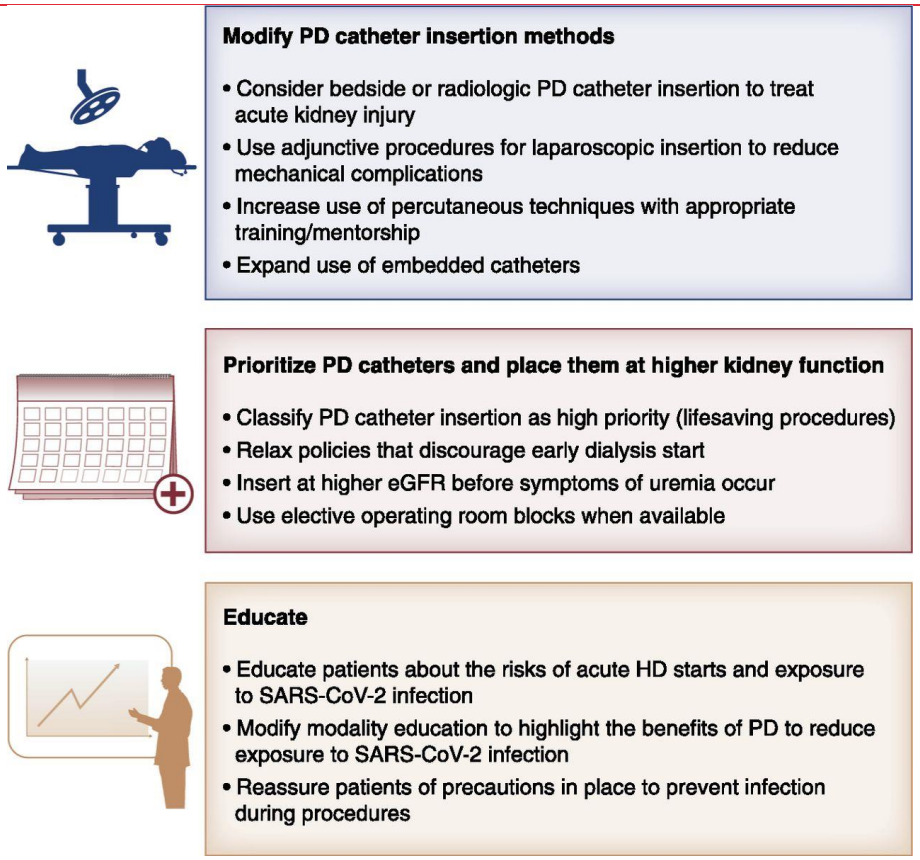



Figure 1: Strategies to facilitate peritoneal dialysis (PD) catheter insertion and facilitate PD during the coronavirus disease 2019 pandemic. HD, hemodialysis; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

## CHANGES IN SOURCE CONTRIBUTIONS TO PARTICLE NUMBER CONCENTRATIONS AFTER THE COVID-19 OUTBREAK: INSIGHTS FROM A DISPERSION NORMALIZED PMF

Dai Q, Ding J, Song C, Liu B, Bi X, Wu J, Zhang Y, Feng Y, Hopke PK.. Sci Total Environ. 2021 Mar 10;759:143548. doi: 10.1016/j.scitotenv.2020.143548. Epub 2020 Nov 6.
Level of Evidence: 5 - Modeling

### BLUF

Experts in environmental protection from Nankai University in China found a dispersion normalized positive matrix factorization (PMF) model considering eight environmental variables (Figure 5) improves the accuracy of source apportionment results on particle number concentration (PNC) datasets. They apply this model to a PNC dataset from the beginning of lockdowns in Tianjin, China (Graphical Abstract) and suggest changes in particle emissions, including decreases in traffic related emissions, reflect the secondary effect of community measures to reduce the spread of COVID-19.

### ABSTRACT

Factor analysis models use the covariance of measured variables to identify and apportion sources. These models, particularly positive matrix factorization (PMF), have been extensively used for analyzing particle number concentrations (PNCs) datasets. However, the variation of observed PNCs and particle size distribution are driven by both the source emission rates and atmospheric dispersion as well as chemical and physical transformation processes. This variation in the observation data caused by meteorologically induced dilution reduces the ability to obtain accurate source apportionment results. To reduce the influence of dilution on quantitative source estimates, a methodology for improving the accuracy of source apportionment results by incorporating a measure of dispersion, the ventilation coefficient, into the PMF analysis (called dispersion normalized PMF, DN-PMF) was applied to a PNC dataset measured from a field campaign that includes the Spring Festival event and the start of the COVID-19 lockdown in Tianjin, China. The data also included gaseous pollutants and hourly PM2.5 compositional data. Eight factors were resolved and interpreted as municipal incinerator, traffic nucleation, secondary inorganic aerosol (SIA), traffic emissions, photonucleation, coal combustion, residential heating and festival emissions. The DN-PMF enhanced the diel patterns of photonucleation and the two traffic factors by enlarging the differences between daytime peak values and nighttime concentrations. The municipal incinerator plant, traffic emissions, and coal combustion have cleaner and more clearly defined directionalities after dispersion normalization. Thus, dispersion normalized PMF is capable of enhancing the source emission patterns. After the COVID-19 lockdown began, PNC of traffic nucleation and traffic emissions decreased by 41% and 44%, respectively, while photonucleation produced more particles likely due to the reduction in the condensation sink. The significant changes in source emissions indicate a substantially reduced traffic volume after the implement of lockdown measures.

### FIGURES

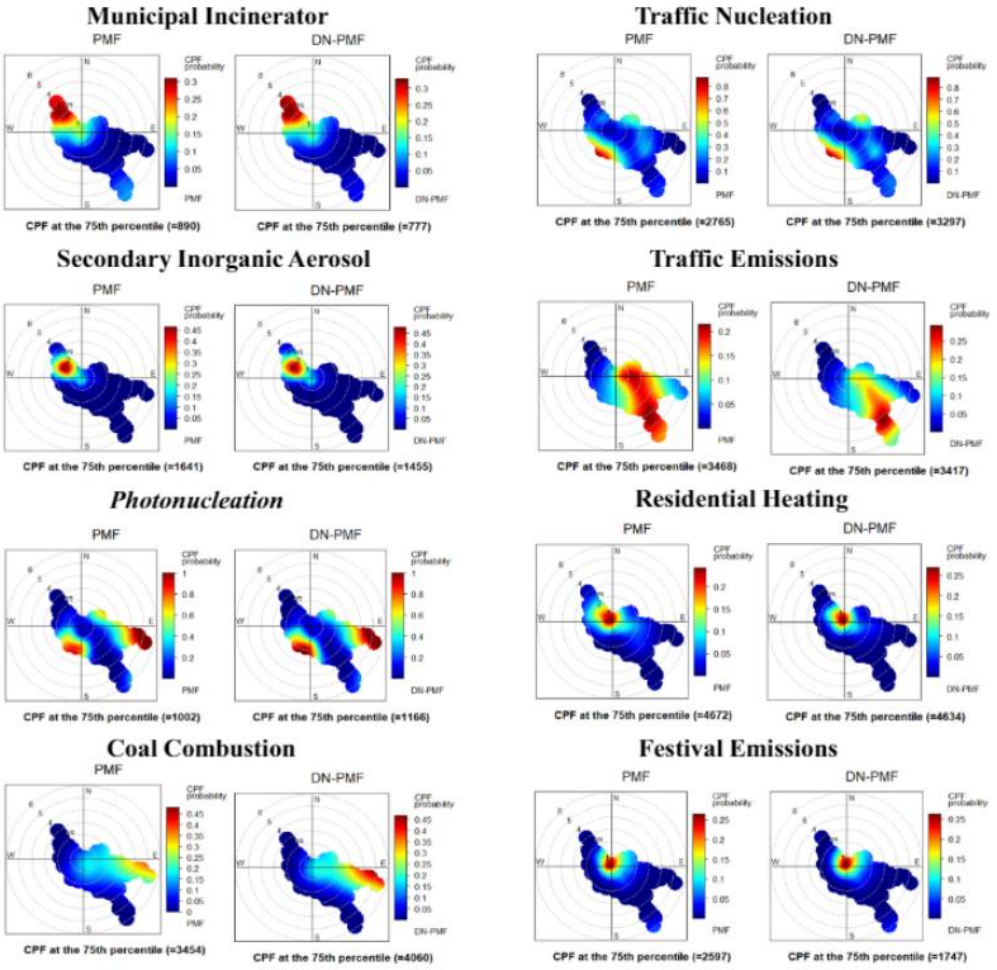
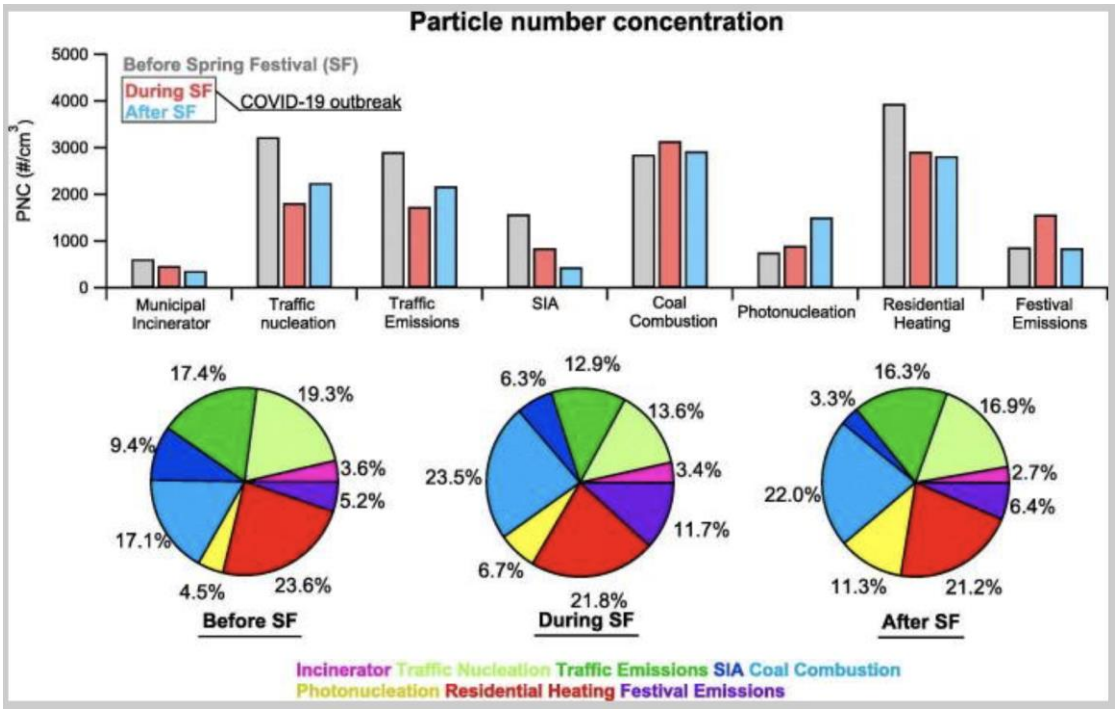



Fig. 5. CBPF plots for the eight factors resolved from PMF and DN-PMF.

Figure 5. CBPF plots for the eight factors resolved from PMF and DN-PMF



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## CONTRIBUTORS

Hamza Sultan
Leah Merker
Michael Wang
Nicolas Longobardi
Veronica Graham

## EDITORS

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