New Research
*note, PREPRINTS have not undergone formal peer review

COVID-19 related publications by Providence caregivers – see Digital Commons

Clinical Syndrome

   https://bmjopen.bmj.com/content/12/4/e057863
   PA before COVID-19 infection was associated with a reduced risk of moderate illness severity and a reduced risk of experiencing fatigue, dry cough and chest pain, suggesting that engaging in PA may be an effective approach to minimise the severity of COVID-19.

Diagnostics & Screening

   https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2791915
   The results of this cohort study of home antigen tests suggest that sensitivity for SARS-CoV-2 was moderate compared with RT-PCR and high compared with viral culture. The results also suggest that symptomatic individuals with an initial negative home antigen test result for SARS-CoV-2 infection should test again 1 to 2 days later because test sensitivity peaked several days after illness onset and improved with repeated testing.

Epidemiology & Public Health

   https://www.nature.com/articles/s41598-022-10344-3
   This retrospective study analyzed data from 6906 hospitalized adults with COVID-19 from a community health system across five states in the western United States. Risk models were developed to predict mechanical ventilation illness or death across one to 56 days of hospitalization, using clinical data available within the first hour after either admission with COVID-19 or a first positive SARS-CoV-2 test.
For the seven-day interval, models for age ≥ 18 and < 50 years reached AUROC 0.81 (95% CI 0.71-0.91) and models for age ≥ 50 years reached AUROC 0.82 (95% CI 0.77-0.86). Models revealed differences in the statistical significance and relative predictive value of risk factors between older and younger patients including age, BMI, vital signs, and laboratory results. In addition, for hospitalized patients, sex and chronic comorbidities had lower predictive value than vital signs and laboratory results.


Racial and ethnic-related health disparities in the United States have been intensified by the greater burden of Coronavirus Disease 2019 (COVID-19) in racial and ethnic minority populations. Compared to non-Hispanic White individuals, non-Hispanic Black and Hispanic/Latinx individuals infected by COVID-19 are at greater risk for hospitalization, intensive care unit admission, and death. There are several factors that may contribute to disparities in COVID-19-related severity and outcomes in these minority populations, including the greater burden of cardiovascular and metabolic diseases as discussed in our companion review article. Social determinants of health are a critical, yet often overlooked, contributor to racial and ethnic-related health disparities in non-Hispanic Black and Hispanic/Latinx individuals relative to non-Hispanic White individuals. Thus, the purpose of this review is to focus on the essential role of social factors in contributing to health disparities in chronic diseases and COVID-19 outcomes in minority populations. Herein, we begin by focusing on structural racism as a social determinant of health at the societal level that contributes to health disparities through downstream social level (e.g., occupation and residential conditions) and individual level health behaviors (e.g., nutrition, physical activity, and sleep). Lastly, we conclude with a discussion of practical applications and recommendations for future research and public health efforts that seek to reduce health disparities and overall disease burden.


Data collected from an online survey, administered in Arkansas between July and August 2020 (n = 1205). Wearing a face mask was the most commonly reported behavior (97.4%), followed by handwashing (97.2%). Protective behaviors increased with higher levels of fear, more stressors, and age. Female and Black respondents reported engaging in more protective behaviors than males or other races/ethnicities. In future pandemic planning, there will be a need to create messaging and interventions to increase health protective behaviors directed at young adults, men, and those with lower education levels. Providers will need to address fears related to COVID-19 and help their patients to manage those fears and anxieties.

*Healthcare Delivery & Healthcare Workers*

The National Emerging Special Pathogens Training and Education Center (NETEC) was established in 2015 to improve the capabilities of healthcare facilities to provide safe and effective care to patients with Ebola and other special pathogens in the United States. Through NETEC, a collaborative network of 10 Regional Emerging Special Pathogen Treatment Centers (RESPTCs) undertook readiness activities that included potential respiratory pathogens. These preparations, which took place before the COVID-19 pandemic, established a foundation of readiness that enabled RESPTCs to play a pivotal role in the US COVID-19 pandemic response. As initial COVID-19 cases were detected in the United States, RESPTCs provided essential isolation capacity, supplies, and subject matter expertise that allowed for additional time for healthcare systems to prepare. Through the Special Pathogen Research Network, RESPTCs rapidly enrolled patients into early clinical trials. During periods of high community transmission, RESPTCs provided educational, clinical, and logistical support to a wide range of healthcare and nonhealthcare settings. In this article, we describe how NETEC and the RESPTC network leveraged this foundation of special pathogen readiness to strengthen the national healthcare system’s response to the COVID-19 pandemic. NETEC and the RESPTC network have proven to be an effective model that can support the national response to future emerging special pathogens.


This study reports findings from a cross-sectional survey of NYC HCWs shortly after the initial 2020 infection surge. Over 800 hospital employees completed the survey that assessed professional quality of life indicators (compassion satisfaction [CS], burnout [BO], secondary traumatic stress [STS]), Coronavirus Anxiety (CS), Obsession with Coronavirus (OC), and PTSD symptoms. The survey also assessed pandemic-related work and life circumstances such as "do you have a family member or friend who tested positive for COVID". Relatively small percentages of HCWs endorsed probable Coronavirus Anxiety (6%), PTSD (13%), and Coronavirus Obsession (21%). We observed higher proportions of Burnout (29%), Moderate or High Secondary Traumatic Stress (45%), and High Compassion Satisfaction (52%). Adjusted regression models showed important implications for prior behavioral/emotional health concerns among HCWs, providing care for a patient that died from COVID-19, and other characteristics. This study supports prior studies documenting the mental health consequences for the healthcare workforce during the COVID-19 pandemic. This study builds on that base by including non-clinical staff in the sample and assessing pandemic life-stressors such as caring for sick family members.

In this UK qualitative study of clinicians using virtual ICU visiting, in the absence of in-person visiting, virtual visiting was perceived positively as an alternative that promoted family-centred care through virtual presence. We anticipate the perceived benefits of virtual visiting may extend to non-pandemic conditions through improved equity and timeliness of family access to the ICU by offering an alternative option alongside in-person visiting.

**Prognosis**


Clinicians may use the 4C Mortality Score in an urban, majority Black, U.S. inpatient population. The derivation and validation cohorts were treated in the pre-vaccine era so the 4C Score may over-predict mortality in current patient populations. With stubbornly high inpatient mortality rates, however, the 4C Score remains one of the best tools available to date to inform thoughtful triage and treatment allocation.

**Survivorship & Rehabilitation**


Our findings suggest that an online breathing and wellbeing programme can improve the mental component of HRQoL and elements of breathlessness in people with persisting symptoms after COVID-19. Mind-body and music-based approaches, including practical, enjoyable, symptom-management techniques might have a role supporting recovery.

FUNDING: Imperial College London.

**Therapeutics**


In COVID-19 critically ill patients receiving HFO or NIV, 28-day intubation rate was lower in patients who received Rem-Dexa and this finding corresponded to lower end-of-treatment clinical improvement. The individual contribution of either Remdesivir or Dexamethasone to the observed clinical effect should be further investigated.

ECMO was associated with a reduction in mortality in selected adults with covid-19 associated respiratory failure. Age, severity of hypoxaemia, and duration and intensity of mechanical ventilation were found to be modifiers of treatment effectiveness and should be considered when deciding to initiate ECMO in patients with covid-19.


In this paper we aim to investigate occurrence of bacteremia in a large real-life cohort of remdesivir-treated in comparison to matched control COVID-19 patients from our institution.


Remdesivir has no significant effect on patients with COVID-19 who are already being ventilated. Among other hospitalised patients, it has a small effect against death or progression to ventilation (or both).

**Transmission / Infection Control**


3,005 (2.6%) hospital workers acquired COVID-19. Almost half of all hospital workers with confirmed COVID-19 were likely index cases in their own households. When the index case in a family was an HCW, the secondary attack rate was 24.8%. At least 17.8% of all confirmed COVID-19 cases among hospital workers were acquired in the household. Our results suggest not only that many HCWs are infected with SARS-CoV-2 in their households but also that infected HCWs constitute a serious infection risk to members of the HCW's household.


Transmission of infectious SARS-CoV-2 via fomites is possible upon extensive moistening, but unlikely to occur in real-life scenarios and from droplet-contaminated fomites.

The safety of the NVX-CoV2373 vaccine in people living with HIV-1 was similar to that in HIV-negative participants. However, people living with HIV-1 not previously exposed to SARS-CoV-2 had attenuated humoral immune responses to NVX-CoV2373 compared with their HIV-negative vaccine counterparts, but not so if they were baseline SARS-CoV-2-positive.


Recently a novel complication of SARS-CoV-2 targeted adenovirus vaccines has emerged: immune thrombocytopenia (ITP), either isolated, or accompanied by thrombosis (then termed VITT). This complication is characterized by low platelet counts, and in the case of VITT also by platelet-activating platelet factor 4 (PF4) antibodies reminiscent of heparin-induced thrombocytopenia leading to a prothrombotic state with clot formation at unusual anatomic sites. Here, we detected anti-platelet antibodies targeting platelet glycoprotein receptors in 30% of patients with proven VITT (n=27), as well as 42% of patients with isolated thrombocytopenia after ChAdOx1 nCov-19 vaccination (n=26), indicating broad antiplatelet autoimmunity in these clinical entities. We employ in vitro and in vivo models to characterize possible mechanisms of these platelet-targeted autoimmune responses leading to thrombocytopenia. We show that intravenous but not intramuscular injection of ChAdOx1 nCov-19 triggers platelet-adenovirus aggregate formation and platelet activation. After intravenous injection, these aggregates are phagocytosed by macrophages in the spleen and platelet remnants are found in the marginal zone and follicles. This is followed by a pronounced B-cell response with the emergence of circulating antibodies binding to platelets. Our work contributes to the understanding of platelet associated complications after ChAdOx1 nCov-19 administration and highlights accidental intravenous injection as a potential mechanism of platelet targeted autoimmunity. Hence, preventing intravenous injection when administering adenovirus-based vaccines could be a potential measure against platelet associated pathologies following the vaccination.


COVID-19 vaccine-induced AIH is an uncommon association with just 32 documented cases in the literature. Clinicians should be vigilant for AIH in patients who present with liver injury following vaccination. These new findings should under not deter individuals from getting vaccinated, as the
benefits of vaccination far outweigh the risks. Fortunately, COVID-19 vaccine-induced AIH appears amendable to corticosteroid therapy and appears to have a favorable outcome.


In this retrospective cohort study using deidentified administrative claims for Medicare Advantage and commercially insured individuals in a research database we examine over 3.5 million fully vaccinated individuals, including 8,848 individuals with SARS-CoV-2 infection, with a follow-up period between 14 and 151 days after their second dose. Our primary outcome was the rate of Covid-19 infection occurring at 30, 60, and 90 days at least 14 days after the second dose of either the mRNA-1273 vaccine or the BNT162b2 vaccine. We show that immunization with mRNA-1273, compared to BNT162b2, provides slightly more protection against SARS-CoV-2 infection that reaches statistical significance at 90 days with a number needed to vaccinate of >290. There are no differences in vaccine effectiveness for protection against hospitalization, ICU admission, or death/hospice transfer.


Using a unique dataset from Israel National Emergency Medical Services (EMS) from 2019 to 2021, the study aims to evaluate the association between the volume of cardiac arrest and acute coronary syndrome EMS calls in the 16-39-year-old population with potential factors including COVID-19 infection and vaccination rates. An increase of over 25% was detected in both call types during January-May 2021, compared with the years 2019-2020. Using Negative Binomial regression models, the weekly emergency call counts were significantly associated with the rates of 1st and 2nd vaccine doses administered to this age group but were not with COVID-19 infection rates. While not establishing causal relationships, the findings raise concerns regarding vaccine-induced undetected severe cardiovascular side-effects and underscore the already established causal relationship between vaccines and myocarditis, a frequent cause of unexpected cardiac arrest in young individuals. Surveillance of potential vaccine side-effects and COVID-19 outcomes should incorporate EMS and other health data to identify public health trends, and promptly investigate potential underlying causes.


Interim results provide continued evidence for protection of 2 doses of mRNA-1273 against SARS-CoV-2 infection over 8 months post-vaccination and during the Delta period, and against COVID-19 hospitalization and hospital death.

The CoVLP+AS03 vaccine was effective in preventing Covid-19 caused by a spectrum of variants, with efficacy ranging from 69.5% against symptomatic infection to 78.8% against moderate-to-severe disease. (Funded by Medicago; ClinicalTrials.gov number, NCT04636697.).


In a large cohort of adults, the ZF2001 vaccine was shown to be safe and effective against symptomatic and severe-to-critical Covid-19 for at least 6 months after full vaccination.


IMID-patients had an attenuated response to standard vaccination as compared to healthy controls. A third vaccine dose was safe and resulted in serological response in most patients. These data facilitate identification of patient groups at risk of attenuated vaccine response, and support administering a third vaccine dose to poorly-responding IMID-patients.


Here we show in health care workers (n = 328) that two doses of BNT162b2, mRNA-1273, or a combination of ChAdOx1 adenovirus vector and mRNA vaccines administrated with a long 12-week dose interval induce equally high levels of anti-SARS-CoV-2 spike antibodies and neutralizing antibodies against D614 and Delta variant. By contrast, two doses of BNT162b2 with a short 3-week interval induce 2-3-fold lower titers of neutralizing antibodies than those from the 12-week interval, yet a third BNT162b2 or mRNA-1273 booster dose increases the antibody levels 4-fold compared to the levels after the second dose, as well as induces neutralizing antibody against Omicron BA.1 variant. Our data thus indicates that a third COVID-19 mRNA vaccine may induce cross-protective neutralizing antibodies against multiple variants.

27. Effectiveness of a COVID-19 Additional Primary or Booster Vaccine Dose in Preventing SARS-CoV-2 Infection Among Nursing Home Residents During Widespread Circulation of the Omicron Variant - United States, February 14-March 27, 2022. Prasad N et al. *MMWR Morb Mortal Wkly Rep*. 2022 May 6;71(18):633-637. doi: 10.15585/mmwr.mm7118a4. [https://www.cdc.gov/mmwr/volumes/71/wr/mm7118a4.htm?s_cid=mm7118a4_w](https://www.cdc.gov/mmwr/volumes/71/wr/mm7118a4.htm?s_cid=mm7118a4_w)

These findings indicate that among nursing home residents, COVID-19 additional primary or booster doses provide greater protection against Omicron variant infection than does primary series vaccination alone. All immunocompromised nursing home residents should receive an additional primary dose, and all nursing home residents should receive a booster dose, when eligible, to protect against COVID-19. Efforts to keep nursing home residents up to date with vaccination should be implemented in conjunction with other COVID-19 prevention strategies, including testing and vaccination of nursing home staff members and visitors.
While the RVE of SARS-CoV-2 mRNA booster vaccine dose in preventing infection against the Omicron variant is low, the RVE is substantial in preventing hospitalization and high in preventing the most severe/critical disease.

Real-world analysis of the incidence of SARS-CoV-2 infection post vaccination is important in determining the comparative effectiveness of the available vaccines. In this retrospective cohort study using deidentified administrative claims for Medicare Advantage and commercially insured individuals in a research database we examine over 3.5 million fully vaccinated individuals, including 8,848 individuals with SARS-CoV-2 infection, with a follow-up period between 14 and 151 days after their second dose. Our primary outcome was the rate of Covid-19 infection occurring at 30, 60, and 90 days at least 14 days after the second dose of either the mRNA-1273 vaccine or the BNT162b2 vaccine. Sub-analyses included the incidence of hospitalization, ICU admission, and death/hospice transfer. Separate analysis was conducted for individuals above and below age 65 and those without a prior diagnosis of Covid-19. We show that immunization with mRNA-1273, compared to BNT162b2, provides slightly more protection against SARS-CoV-2 infection that reaches statistical significance at 90 days with a number needed to vaccinate of >290. There are no differences in vaccine effectiveness for protection against hospitalization, ICU admission, or death/hospice transfer (aOR 1.23, 95% CI (0.67, 2.25)).

**Women & Children**

Among children hospitalized for COVID-19, thromboprophylaxis with twice-daily enoxaparin appears safe and warrants further investigation to assess efficacy.

In this exploratory surveillance study conducted in Canada from March 2020 to October 2021, SARS-CoV-2 infection during pregnancy was significantly associated with increased risk of adverse maternal outcomes and preterm birth.

We performed a retrospective cohort study of 59,335 ED visits prior to the pandemic and 51,990 ED visits during the pandemic in an ED with an automated sepsis alert based on systemic inflammatory response syndrome criteria. The proportion of ED visits triggering a sepsis alert was 7.0% (n=4,180) prior to and 6.1% (n=3,199) during the pandemic. The number of sepsis alerts triggered per diagnosed case of hypotensive septic shock was 24 in both time periods. There was no difference in the sensitivity (74.1% vs. 72.5%), specificity (93.2% vs. 94.0%), positive predictive value (4.1% vs. 4.1%), or negative predictive value (99.9% vs. 99.9%) of the sepsis alerts between these time periods. The alerts had a lower sensitivity (60% vs. 73.3%) and specificity (87.3% vs. 94.2%) for COVID-19 positive vs. negative patients. The sepsis alert algorithm evaluated in this study did not result in excess notifications and maintained adequate performance during the COVID-19 pandemic in the pediatric ED setting.

FDA / CDC / NIH / WHO Updates

Coronavirus (COVID-19) Update: FDA Limits Use of Janssen COVID-19 Vaccine to Certain Individuals | FDA

Commentary


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