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1. **Coping with COVID-19 stressors: Adverse and protective factors responding to emotions in a Chinese sample**
Xu R., Zhang X., Liu D., Li Q., Wang Y., Jiao R., Gong X., Hou X., Xu T., Qing X., Song K., Kavcic V., Yan S., Gu R., Stratton T., Jiang Y.
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Abstract
Background: The potential roles of affective responses to environmental stressors in individuals' physical and mental health are complex and multi-faceted. This study, then, explores Chinese citizens' emotional responses to COVID-19-related stressors and influence factors which may boost or buffer such effects. Methods: From late March to early June (2020), a cross-sectional study was conducted using an anonymous online questionnaire included demographic characteristics, COVID-19-related stressors related to individuals' daily functioning, and the self-assessed impact of protective and adverse internal factors on emotions. Results: 1,662 questionnaires were received from residents in 32 Chinese provinces classified by prevalence level according to COVID-19 infections. Among the 17 positive and negative emotional responses, agglomerative hierarchical clustering revealed four subclassifications: (1) stress relations; (2) missing someone relations; (3) individual relations; and (4) social relations. Additionally, heightened regional prevalence levels positively corresponded to intensity of stress relations. Lowest intensity of social relations was found in the areas surrounding Wuhan and coastal areas. Specially, economic- and work-related stressors as well as negative self-perceptions (e.g., suppression, emotionally unstable, self-denial) implicated in negative emotions. While positive emotions were tied to demographic characteristics (e.g., high education, young age and male) and protective traits (e.g., creativity, sympathy, social responsibility), and inversely linked to relationships- and pandemic-related stressors, etc. Conclusion: Associations were clearly noted among Chinese residents' emotions to specific stressors during pandemic. Providing appropriate psychological resources/supports during future or extended public health crises may help offset the cognitive burden of individuals striving to regain an adequate level of normalcy and emotional well-being.

2. **SARS-CoV-2 genomic monitoring in the São Paulo State unveils new sublineages of the AY.43 strain**
Lima A.R.J., Ribeiro G., Viala V.L., de Lima L.P.O., Martins A.J., dos Santos Barros C.R., Marqueze E.C., de Souza Todao Bernardino J., Moretti D.B., Rodrigues E.S., Santos E.V., Brassaloti R.A., de Lello Rocha Campos Cassano R., Mariani P.D.S.C., Clemente L.G., Assato P.A., da Silva da Costa F.A., Poleti M.D., Lesbon J.C.C., Mattos E.C., Banho C.A., Sacchetto L., Moraes M.M., Palmieri M., da Silva F.E.V., Grotto R.M.T., Souza-Neto J.A., Giovanetti M., de Alcantara L.C.J., Nogueira M.L., Fukumasu H., Coutinho L.L., Kashima S., Neto R.M., Covas D.T., Slavov S.N., Elias M.C., Sampaio S.C.
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Abstract

Delta VOC is highly diverse and more than 120 sublineages have been identified in Pango lineages with the continuous description of emerging ones. Brazil is now one of the most vaccinated countries against SARS-CoV-2 in the world which can enhance the emergence of viral mutations related to improved viral fitness. In this study, we identified two novel sublineages of the AY.43 lineage which were classified as AY.43.1 and AY.43.2 as observed on the specific clustering on the obtained phylogenetic tree. The novel sublineages were defined by the following characteristic nonsynonymous mutations ORF1ab:A4133V and ORF3a:T14I for AY.43.1 and ORF1ab:G1155C for AY.43.2. The majority of the analyzed sequences of both lineages were Brazilian, which shows that probably these two emerging sublineages have Brazilian origin. It is still unknown how these two sublineages are disseminated in São Paulo State and Brazil and their potential impact on the ongoing vaccination process. However, the performed study reinforces the importance of the SARS-CoV-2 genome monitoring for timely identification of emerging SARS-CoV-2 variants which can impact the ongoing SARS-CoV-2 vaccination and public health policies.

3. **SARS-CoV-2 Delta variant saliva viral load is 15-fold higher than wild-type strains**
Imai K., Ikeno R., Tanaka H., Takada N.
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Abstract

The emergence of SARS-CoV-2 Delta variants has escalated COVID-19 cases globally due to their high transmissibility. Since saliva is crucial for SARS-CoV-2 transmission, we hypothesized that a higher viral load of Delta variants in saliva than their parental wild-type strains contributed to the high transmissibility in the first place. However, studies have not reported this particular comparison done with viral copy numbers. Twenty-two genetically confirmed -positive saliva samples for wild-type strain and 32 Delta variants were statistically compared for viral copy number per milliliter determined by real-time qPCR combined with synthesized viral RNA and Poisson's null distribution equation between the groups of wild and variant strains and between whole saliva and centrifugal supernatant in each group. We found that the copy number of the Delta variants was 15.1 times higher than wild-type strains of the whole saliva. In addition, the viral load of both strains in the whole saliva was higher than the pertinent supernatant, indicating that most viruses in the whole saliva are associated with host cells. Meanwhile, more than a million virions per milliliter of the viral load of the variants in the supernatants were 4.0 times higher but not significant than wild-type strains. Humanity must share our findings; the simple but concrete note that Delta variant viral load is abundant in the saliva is critical for preventing the spread of infection.

4. **Phase shift between age-specific COVID-19 incidence curves points to a potential epidemic driver function of kids and juveniles in Germany**
Diebner H.H.
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Abstract

Mutual phase shifts between three German COVID-19 incidence curves corresponding to the age classes of children, juveniles and adults, respectively, are calculated by means of delay-cross-correlations. At the country level, a phase shift of −5 weeks during the first half of the epidemic between the incidence curves corresponding to the juvenile age class and the curve corresponding to the adult class is observed. The children's incidence curve is shifted by −3 weeks with respect to the adults' curve. On the regional level of the 411 German districts (Landkreise) the distributions of observed time lags are inclined towards negative values. Regarding the incidence time series of the juvenile sub-population, 20% of the German districts exhibit negative phase shifts and only 3% show positive shifts versus the incidence curves of the adult sub-population. Similarly for the children with 6% positive shifts. Thus, children's and juveniles' epidemic activity is ahead of the adults' activity. The correlation coefficients of shifted curves are large (> 0.9 for juveniles versus adults on the country level) which indicates that aside from the phase shift the sub-populations follow a similar epidemic dynamics. Negative phase shifts of the children's incidence curves during the first and second epidemic waves are predictors for high incidences during the current fourth wave with respect to the corresponding districts.

5. **Use of heat-not-burn tobacco products, moderate alcohol drinking, and anti-SARS-CoV-2 IgG antibody titers after BNT162b2 vaccination among Japanese healthcare workers**
Yamamoto S., Tanaka A., Ohmagari N., Yamaguchi K., Ishitsuka K., Morisaki N., Kojima M., Nishikimi A., Tokuda H., Inoue M., Tanaka S., Umezawa J., Okubo R., Nishimura K., Konishi M., Miyo K., Mizoue T.
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Abstract

Background: The effect of heat-not-burn (HNB) tobacco product use and moderate alcohol drinking on immunogenicity to coronavirus disease (COVID-19) vaccines remain elusive. This study aimed to examine the association of tobacco product use and alcohol consumption with anti-SARS-CoV-2 spike IgG antibody titers after the BNT162b2 vaccine. Methods: Participants were 3,457 fully vaccinated healthcare workers in the 4 national centers for advanced medical and research in Japan. Smoking status and alcohol consumption were assessed via a questionnaire, and anti-SARS-CoV-2 spike IgG titers were measured by chemiluminescent enzyme immunoassay using serum collected on the median of 64 days after the second vaccination. Multilevel linear regression models were used to estimate the geometric mean titers (GMT) and the ratios of means (RoM) between groups. Results: Of vaccinated participants, 99.5% (3,440/3,457) were seropositive. Compared with never-smokers (GMT=119), IgG antibody titers were significantly lower among HNB tobacco users (including those who also smoked cigarettes) (GMT=105; RoM=0.88 [95%CI: 0.78-0.99]) and exclusive cigarettes smokers (GMT=96; RoM=0.81 [95%CI: 0.71-0.92]). Compared with non-drinkers of alcohol (GMT=123), alcohol drinkers consuming <1 go/day (GMT=114; RoM=0.93 [95%CI: 0.88-0.98]), 1-1.9 go/day (GMT=105; RoM=0.85 [95%CI: 0.79-0.93]), and ≥2 go/day (GMT=101; RoM=0.82 [95%CI: 0.72-0.94]) had significantly lower antibody titers (P for trend<0.01). Spline analysis showed a large reduction of antibody until around 1 go/day of alcohol consumption, and then they gradually decreased. Conclusions: Results suggest that in addition to conventional cigarette smoking and heavy alcohol drinking, use of HNB tobacco products and moderate alcohol drinking may be predictors of lower immunological response to COVID-19 vaccine.

6. **A case series of SARS-CoV-2 reinfections caused by the variant of concern Gamma in Brazil**

Naveca F.G., Nascimento V.A., Nascimento F., Ogrzewalska M., Pauvolid-Corrêa A., Araujo M.F., Arantes I., Rocha Batista É.L., Álvares Magalhães A.L., Vinhal F., Mattos T.P., Riediger I., do Carmo Debur M., Grinsztejn B., Veloso V.G., Brasil P., Rodrigues R.R., Rovaris D.B., Fernandes S.B., Fernandes C., Abdalla Santos J.H., Abdalla L.F., Costa-Filho R., Silva M., Souza V., Costa Á.A., Mejía M., Brandão M.J., Gonçalves L.F., Silva G.A., de Jesus M.S., Pessoa K., de Lima Guerra Corado A., Gomes Duarte D.C., Machado A.B., de Azevedo Zukeram K., Valente N., Lopes R.S., Pereira E.C., Appolinario L.R., Rocha A.S., Lopez Tort L.F., Sekizuka T., Itokawa K., Hashino M., Kuroda M., Wallau G.L., Delatorre E., Gräf T., Siqueira M.M., Bello G., Resende P.C.

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Abstract

The rapid spread of the SARS-CoV-2 Variant of Concern (VOC) Gamma during late 2020 and early 2021 in Brazilian settings with high seroprevalence raised some concern about the potential role of reinfections in driving the epidemic. Very few cases of reinfection associated with the VOC Gamma, however, have been reported. Here we describe 25 cases of SARSCoV-2 reinfection confirmed by real-time RT-PCR twice within months apart in Brazil. SARS-CoV-2 genomic analysis confirmed that individuals were primo-infected between March and December 2020 with distinct viral lineages, including B.1.1, B.1.1.28, B.1.1.33, B.1.195 and P.2, and then reinfected with the VOC Gamma between 3 to 12 months after primo-infection. The overall mean cycle threshold (Ct) value of the first (25.7) and second (24.5) episodes were roughly similar for the whole group and 14 individuals displayed mean Ct values < 25.0 at reinfection. Sera of 14 patients tested by plaque reduction neutralization test after reinfection displayed detectable neutralizing antibodies against Gamma and other SARS-CoV-2 variants (B.1.33, B.1.1.28 and Delta). All individuals have milder or no symptoms after reinfection and none required hospitalization. The present study demonstrates that the VOC Gamma was associated with reinfections during the second Brazilian epidemic wave in 2021 and raised concern about the potential infectiousness of reinfected subjects. Although individuals here analyzed failed to mount a long-term sterilizing immunity, they developed a high anti-Gamma neutralizing antibody response after reinfection that may provide some protection against severe disease.

7. **Unequal impact of the Covid-19 pandemic on excess deaths, life expectancy, and premature mortality across Spanish regions in 2020 and 2021**

Islam N., García López F.J., Jdanov D.A., Royo-Bordonada M.Á., Khunti K., Lewington S., Lacey B., White M., Morris E.J.A., Zunzunegui M.V.

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Abstract

Spain is one of the most heavily affected countries by the Covid-19 pandemic. In this study, we estimated the regional

inequalities in excess deaths and premature mortality in Spain. Between January 2020 and June 2021, an estimated 89,200 (men: 48,000; women: 41,200) excess deaths occurred in the 17 Spanish regions with a substantial variability (highest in Madrid: 22,000, lowest in Canary Islands: -210). Highest reductions in life expectancy at birth (e_0) in 2020 were observed in Madrid (men: -3.48 years, women: -2.15), Castile La Mancha (men: -2.67, women: -2.30), and Castile and León (men: -2.00, women: -1.32). In the first six months of 2021, the highest reduction in e_0 was observed in Valencian Community (men: -2.04, women: -1.63), Madrid (men: - 2.37), and Andalusia (men: -1.75; women: -1.43). In some Spanish regions, life expectancy at age 65 during the Covid-19 pandemic in 2020 was comparable to that observed as far back as 20 years ago.

8. **Transient adverse events after REGN-CoV2 administration for mild COVID-19 patients and their potential predictive factors: A single center analysis**

Kano G., Taniguchi K., Oue Y.

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Abstract

Background REGN-COV2, a monoclonal antibody cocktail drug against the SARS-COV-2 virus, has proven to be effective in preventing the development of severe COVID-19 and is increasingly being administered in outpatient and home settings. Adverse events such as fever and decreased oxygen saturation may occur after administration of REGN-COV2, and although these symptoms are generally mild and transient, predicting the occurrence of these adverse events is useful in developing a monitoring plan for patients. Methods We performed a retrospective analysis of 76 patients who received REGN-CoV2 between August and September 2021. We collected information on fever, decreased oxygen saturation requiring oxygen supplementation, and other adverse events from medical records. Patients were divided into two subgroups: those who presented with fever or oxygen desaturation and those who did not, and underlying medical conditions and laboratory data were compared between each group. The parameters that exhibited significant differences were further tested using Fisher's exact test to evaluate whether appropriate thresholds could be set to distinguish the incidence group from the non-incidence group. Findings Of the 76 patients, 47 had fever of 38.5°C or higher within 24 hours after administration, and 27 of these patients had a body temperature of 37.5°C or lower before administration. Oxygen was required in 17 cases, 7 of which required oxygen more than 24 hours after administration of REGN-COV2, and additional treatment such as dexamethasone was given as the disease progressed to moderate. Among the parameters analyzed, lymphocyte count and IFNλ3 showed significant differences between the fever and non-fever groups. This was also the case in the comparison excluding patients who had fever before administration. There was also a significant difference in ferritin and CRP between the oxygen required and non-required groups. In addition to IFNλ3, ferritin, and CRP, there was a significant difference in LDH between the group that required additional treatment and the group that did not. When lymphocytes count <950/μL was used to predict fever, the sensitivity and specificity were 55% and 79%, respectively, with odds ratio 4.746 (95% CI: 1.666 to 14.12, p=0.004) in contingency table analysis. Similarly, when IFNλ3 >5.0 was used as the cutoff, sensitivity 72%, specificity 76%, odds ratio 8.220 (2.857 to 22.22; p<0.0001). Interpretations Transient fever and decreased oxygen saturation are common adverse events after REGN-CoV2 administration, and their occurrence correlated with the severity factor of COVID-19 itself. Evaluation of these items at the time of administration is useful not only for predicting the severity of COVID-19 but also for the development of adverse events in patients receiving REGN-CoV2.

9. **Prioritizing interventions for preventing COVID-19 outbreaks in military basic training**

España G., Perkins T.A., Pollett S., Smith M.E., Moore S.M., Kwon P.O., Hall T.L., Beagle M.H., Murray C.K., Hakre S., Peel S., Modjarrad K., Scott P.T.

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Abstract

Like other congregate living settings, military basic training has been subject to outbreaks of COVID-19. We sought to identify improved strategies for preventing outbreaks in this setting using an agent-based model of a hypothetical cohort of trainees on a U.S. Army post. Our analysis revealed unique aspects of basic training that require customized approaches to outbreak prevention, which draws attention to the possibility that customized approaches may be necessary in other settings, too. In particular, we showed that introductions by trainers and support staff may be a major vulnerability, given that those individuals remain at risk of community exposure throughout the training period. We also found that increased testing of trainees upon arrival could actually increase the risk of outbreaks, given the potential for false-positive test results to lead to susceptible individuals becoming infected in group isolation and seeding outbreaks in training units upon release. Until an effective transmission-blocking vaccine is adopted at high coverage by individuals involved with basic training, need will persist for non-pharmaceutical interventions to prevent outbreaks in military basic training. Ongoing uncertainties about virus variants and breakthrough infections necessitate continued vigilance in this setting, even as vaccination coverage increases.

10. **Impact of the COVID-19 pandemic on the malaria burden in northern Ghana: Analysis of routine surveillance data**
Heuschen A.-K., Abdul-Mumin A., Adokiya M.N., Lu G., Jahn A., Razum O., Winkler V., Müller O.
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Abstract

Introduction: The COVID-19 pandemic and its collateral damage severely impact health systems globally and risk to worsen the malaria situation in endemic countries. Malaria is a leading cause of morbidity and mortality in Ghana. This study aims to analyze routine surveillance data to assess possible effects on the malaria burden in the first year of the COVID-19 pandemic in the Northern Region of Ghana. Methods: Monthly routine data from the District Health Information Management System II (DHIMS2) of the Northern Region of Ghana were analyzed. Overall outpatient department visits and malaria incidence rates from the years 2015 to 2019 were compared to the corresponding data of the year 2020. Results: Compared to the corresponding periods of the years 2015 to 2019, overall visits and malaria incidence in pediatric and adult outpatient departments in northern Ghana decreased in March and April 2020, when major movement and social restrictions were implemented in response to the pandemic. Incidence slightly rebounded afterwards in 2020 but stayed below the average of the previous years. Data from inpatient departments showed a similar but more pronounced trend when compared to outpatient departments. In pregnant women, however, malaria incidence in outpatient departments increased after the first COVID-19 wave. Discussion: The findings from this study show that the COVID-19 pandemic affects the malaria burden in health facilities of Ghana, with declines in in- and outpatient rates. Pregnant women may experience reduced access to intermittent preventive malaria treatment and insecticide treated nets, resulting in subsequent higher malaria morbidity. Further data from other African countries, particularly on community-based studies, are needed to fully determine the impact of the pandemic on the malaria situation.

11. **Modelling the effect of the interaction between vaccination and non-pharmaceutical measures on COVID-19 incidence**
Canga A., Bidegain G.
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Abstract

Since December 2019, the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread rapidly from Wuhan (China) across the globe, affecting more than 200 countries by mid-2021, with over 190 M reported cases and around 4 M fatalities. During the first year of the pandemic, affected countries implemented a variety of non-pharmaceutical interventions to control virus transmission. In December 2020, countries started administering several authorised vaccines under a limited supply scenario. In this context, a SEIR-type continuous-time deterministic disease model was developed to explore the effect of vaccination in terms of vaccination rate and efficacy, together with varying non-pharmaceutical protection measures, on disease incidence in the initial phase of vaccination. For this, the model incorporates (i) a protection measure including low (self-protection), medium (mobility limitation), high (closure of indoor facilities) and very high (lockdown) protection levels, (ii) quarantine for confirmed cases, and (iii) vaccination rate and efficacy of four type of vaccines (Pfizer, Modema, Astra Zeneca or Janssen). The model was verified and evaluated using the response timeline and vaccination strategies and rates in the Basque Country (N. Spain). Once the model performance was validated, different initial phase (when 30% of the population is vaccinated) vaccination scenarios were simulated, including (i) a realistic vaccine limited supply scenario, and (ii) four potential full vaccine supply scenarios where a unique vaccine type is administered. The Pfizer scenario resulted in the lowest prevalence of infection and cumulative mortality, particularly for low- and medium-level protection rates. However, regardless of the administered vaccine, a high-level protection scenario is the most effective to control the virus transmission and disease mortality in the studied initial phase of vaccination. The model here, which is based on this example, could be easily applied to other regions or countries, modifying the strategies implemented and initial conditions.

12. **Deficits in planned hospital care for vulnerable adolescents in England during the COVID-19 pandemic: Analysis of linked administrative data**
Grath-Lone L.M., Etoori D., Gilbert R., Harron K., Woodman J., Blackburn R.
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Abstract

Planned hospital care (outpatient attendances and planned hospital admissions) was disrupted during the pandemic, but we lack evidence on which groups of young people were most impacted. We aimed to describe differences in planned care for vulnerable adolescents receiving children's social care (CSC) services or special educational needs (SEN) support during the pandemic, relative to their peers. Using the ECHILD Database (linked de-identified administrative health, education and social care records for all children in England), we examined changes in planned hospital care from 23 March to 31 December 2020 for secondary school pupils in Years 7 to 11 (N=3,030,235). There were large deficits in planned care for adolescents overall, which disproportionately affected the 21% receiving SEN support or CSC services who bore 25% of the outpatient attendance deficit and 37% of the planned admissions deficit. These findings indicate a need for targeted 'catch-up' funding and resources, particularly for vulnerable groups.

13. **Analytical sensitivity and effectiveness of different SARS-CoV-2 testing options**
Lelie N., Koppelman M., van Drimmelen H., Bruisten S.
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Abstract

We prepared severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) working standards and reference panels from a pool of swab fluid samples before and after inactivation by beta-propiolactone and quantified viral load in nucleic acid amplification technology (NAT) detectable RNA copies/mL using limiting dilution analysis. The following 50% lower limits of detection (LOD) were estimated by probit analysis as compared to detection limits of rapid antigen tests on 1.5 fold dilutions of the native material: Roche cobas PCR 1.8 (1.0-3.3), Hologic Aptima TMA 6.6 (4.4-9.9), DRW SAMBA 15 (7-30), Molgen LAMP 23 (13-42), Fluorecare antigen 50,000, Abbott Panbio antigen 75,000 and Roche antigen 100,000 copies/mL. One 50% Tissue Culture Infectious Dose ($TCID_{50}$)/mL of culture fluid was estimated to be equivalent to approximately 1000 RNA copies/mL (2700-4300 International Units) in our working standard. When assuming this level as start of contagiousness in a log-linear ramp up viremia model with 10-fold rise of viral load per day for the B.1 (Wuhan) type we estimated relative time points of first detectability of early infection by the different SARS-CoV-2 assays from the LODs mentioned above. The four NAT assays would be able to detect early viremia 40-66 hours earlier than the 1000 copies/mL infectivity threshold, whereas the three antigen tests would become positive 41-48 hours later. Our modeling of analytical sensitivity data was found to be compatible with clinical sensitivity data of rapid antigen tests and confirms that NAT assays are more reliable than antigen assays for identifying early infected asymptomatic individuals who are potentially infectious.

14. **Emergence and spread of the SARS-CoV-2 Variant of Concern delta across different Brazilian regions**
Arantes I., Naveca F.G., Gräf T., Miyajima F., Faoro H., Wallau G.L., Delatorre E., Appolinario L.R., Pereira E.C., Venas T.M.M., Rocha A.S., Lopes R.S., Siqueira M.M., Bello G., Resende P.C.
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Abstract

The SARS-CoV-2 Variant of Concern (VOC) Delta was first detected in India in October 2020. The first imported cases of the Delta variant in Brazil were identified in April 2021 in the Southern region, followed by more cases in different country regions during the following months. By early September 2021, Delta was already the dominant variant in the Southeastern (87%), Southern (73%), and Northeastern (52%) Brazilian regions. This work aimed to understand the spatiotemporal dissemination dynamics of Delta in Brazil. To this end, we employed a combination of Maximum Likelihood (ML) and Bayesian methods to reconstruct the evolutionary relationship of 2,264 of VOC Delta complete genomes (482 from this study) recovered across 21 out of 27 Brazilian federal units. Our phylogeographic analyses identified three major transmission clusters of Delta in Brazil. The clade BR-I (n = 1,560) arose in Rio de Janeiro in late April 2021 and was the major cluster behind the dissemination of the VOC Delta in the Southeastern, Northeastern, Northern, and Central-Western regions. The clade BR-II (n = 207) arose in the Paraná state in late April 2021 and aggregated the largest fraction of sampled genomes from the Southern region. Lastly, the clade BR-III emerged in the São Paulo state in early June 2021 and remained mostly restricted to this state. In the rapid turnover of viral variants characteristic of the SARS-CoV-2 pandemic, Brazilian regions seem to occupy different stages of an increasing prevalence of the VOC Delta in their epidemic profiles. This process demands continuous genomic and epidemiological surveillance toward identifying and mitigating new introductions, limiting their dissemination, and preventing the establishment of more significant outbreaks in a population already heavily affected by the COVID-19 pandemic.

15. **Modelling the interplay of SARS-CoV-2 variants in the United Kingdom**
Barreiro N.L., Govezensky T., Ventura C.I., Núñez M., Bolcatto P.G., Barrio R.A.
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Abstract

Most COVID-19 vaccines have proved to be effective to combat the pandemic and to prevent severe disease but their distribution proceeds in a context of global vaccine shortage Their uneven distribution favors the appearance of new variants of concern, as the highly transmissible Delta variant, affecting especially non-vaccinated people. We consider that devising reliable models to analyse the spread of the different variants is crucial. These models should include the effects of vaccination as well as non-pharmaceutical measures used to contain the pandemic by modifying social behaviour. In this work, we present a stochastic geographical model that fulfills these requirements. It consists of an extended compartmental model that includes various strains and vaccination strategies, allowing to study the emergence and dynamics of the new COVID-19 variants. The models conveniently separates the parameters related to the disease from the ones related to social behavior and mobility restrictions. The geographical spread of the virus is modeled taking into account the actual population distribution in any given country of interest. Here we choose the UK as model system, taking advantage of the reliable available data, in order to fit the recurrence of the currently prevalent variants. Our computer simulations allow to describe some global features observed in the daily number of cases, as the appearance of periodic waves and the features that determine the prevalence of certain variants. They also provide useful predictions aiming to help planning future vaccination boosters. We stress that the model could be applied to any other country of interest.

16. **Community healthcare workers' experiences during and after COVID-19 lockdown: A qualitative study from Aotearoa New Zealand**

Holroyd E., Long N.J., Appleton N.S., Davies S.G., Deckert A., Fehoko E., Laws M., Martin-Anatias N., Simpson N., Sterling R., Trnka S., Tunufa'i L.

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Abstract

Shortly after the COVID-19 pandemic reached Aotearoa New Zealand, a stringent lockdown lasting seven weeks was introduced to manage community spread of the virus. This paper reports the findings of a qualitative study examining how lockdown policies impacted upon the lives of those caring for community-based patients. The study involved nationwide surveys and ethnographic interviews with 15 registered nurses (RN) employed in community settings, two community midwives, and five personal care assistants (PCAs). During the strict lockdown levels 4 and 3, RNs and PCAs in the community showed considerable courage in answering their "call to duty" by taking on heightened care responsibilities and going "the extra mile" to help others. They faced significant risks to personal and professional relationships when they were required to take on additional and complex responsibilities for community-based patients. Despite, and sometimes due to the hypervigilant monitoring of their personal protective equipment (PPE), the need to safeguard family and community members generated considerable stress and anxiety. Many also faced personal isolation and loneliness as a result of lockdown restrictions. Although 'care' and 'kindness' became social expectations throughout Aotearoa New Zealand during the lockdown, RNs and PCAs who were already doing care work in patient homes had to do more. This article makes five core service delivery and policy recommendations for supporting community-based nurses and PCAs in respiratory disease pandemics: acknowledging the crucial role played by community-based carers and the associated stress and anxiety endured, through championing respect and compassion; demystifying the "heroism" or "self-sacrifice" projected onto care workers to facilitate boundary setting; the timely provision of adequate protective equipment; improving remuneration with adequate provision for time off; and regular counselling, peer support groups, and education on work-life balance delivered by support workers in recognition of stressors arising from these complex and isolated working conditions.

17. **A fourth dose of the mRNA-1273 SARS-CoV-2 vaccine improves serum neutralization against the delta variant in kidney transplant recipients**

Benotmane I., Bruel T., Planas D., Fafi-Kremer S., Schwartz O., Caillard S.

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Abstract

In immunocompetent subjects, the effectiveness of SARS-CoV-2 vaccines against the delta variant appears three- to five-fold lower than that observed against the alpha variant. Additionally, three doses of SARS-CoV-2 mRNA-based vaccines might be unable to elicit a sufficient immune response against any variant in immunocompromised kidney transplant recipients. This study describes the kinetics of the neutralizing antibody (NAbs) response against the delta strain before and after a fourth dose of a

mRNA vaccine in 67 kidney transplant recipients who had experienced a weak antibody response after three doses. While only 16% of patients harbored NAbs against the delta strain prior to the fourth injection - this percentage raised to 66% afterwards. We also found that, after the fourth dose, the NAbs titer increased significantly (p=0.0001) from <7.5 (IQR: <7.5−15.1) to 47.1 (IQR <7.5−284.2). Collectively, our data indicate that a fourth dose of the mRNA-1273 vaccine in kidney transplant recipients with a weak antibody response after three previous doses improves serum neutralization against the delta variant. Research has suggested that even three doses of SARS-CoV-2 mRNA-based vaccines might be unable to elicit a sufficient immune response in immunocompromised kidney transplant recipients.[1-3] As a result, in June 2021 the French health authorities allowed offering a fourth vaccine dose to weak responder solid organ transplant recipients.While the antibody response mounted by the Pfizer and AstraZeneca vaccines in immunocompetent subjects seems sufficient to neutralize the currently dominant SARS-CoV-2 strain (delta variant)[4] the effectiveness appears three- to five-fold lower than that observed against the alpha variant.[5,6] In addition, standard vaccination schemes are beset by low immunogenicity in immunocompromised subjects - who remain prone to develop severe COVID-19.[4] The purpose of this study is to describe the kinetics of the neutralizing antibody response against the delta strain before and after a fourth dose of the mRNA-1273 (Moderna) vaccine in kidney transplant recipients who had experienced a weak antibody response after three previous doses. We also assessed the correlation between this neutralizing activity and levels of IgG against the receptor binding domain (RBD) of the spike (S) protein.

18. **Synthesis of high-resolution research-quality MRI data from clinical MRI data in patients with COVID-19**
Cali R.J., Freeman H.J., Billot B., Barra M.E., Fischer D., Sanders W.R., Huang S.Y., Conklin J., Fischl B., Iglesias J.E., Edlow B.L.
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Abstract

Pathophysiological mechanisms of neurological disorders in patients with coronavirus disease 2019 (COVID-19) are poorly understood, partly because of a lack of high-resolution neuroimaging data. We applied SynthSR, a convolutional neural network that synthesizes high-resolution isotropic research-quality data from thick-slice clinical MRI data, to a cohort of 11 patients with severe COVID-19. SynthSR successfully synthesized T1-weighted MPRAGE data at 1 mm spatial resolution for all 11 patients, each of whom had at least one brain lesion. Correlations between volumetric measures derived from synthesized and acquired MPRAGE data were strong for the cortical grey matter, subcortical grey matter, brainstem, hippocampus, and hemispheric white matter (r=0.84 to 0.96, p≤0.001), but absent for the cerebellar white matter and corpus callosum (r=0.04 to 0.17, p>0.61). SynthSR creates an opportunity to quantitatively study clinical MRI scans and elucidate the pathophysiology of neurological disorders in patients with COVID-19, including those with focal lesions.

19. **SARS-CoV-2 vaccination predicts COVID-19 progression and outcomes in hospitalized patients**
Padovani A., Cristillo V., Tomasoni D., Gipponi S., Pilotto A.
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Abstract

Background SARS-CoV-2 vaccination might impact on clinical progression of cases with breakthrough COVID-19 disease. Objective to evaluate the impact of SARS-CoV-2 vaccination on disease progression in COVID-19 hospitalized patient Methods and Findings Two-hundred eighty-four consecutive COVID-19 hospitalized patients, including 50 vaccinated cases entered the study. Compared to unvaccinated cases, vaccinated patients were older, exhibited more comorbidities and did not differ for COVID-19 severity at admission. During hospitalisation, unvaccinated patients showed worse disease progression, including higher need of oxygen and higher risk of death compared to vaccinated patients (OR 3.3; 1.05-10.7 95% CI in the whole cohort and OR 54.8; 3.5-852 in the ventilated cases). Discussion These findings argue for an important reduction in severity among vaccine breakthrough infection compared to unvaccinated cases in COVID-19 disease.

20. **Pandemic inequity in a megacity: A multilevel analysis of individual, community and health care vulnerability risks for COVID-19 mortality in Jakarta, Indonesia**
Surendra H., Salama N., Lestari K.D., Adrian V., Widyastuti , Oktavia D., Lina R.N., Djaafara B.A., Fadilah I., Sagara R., Ekawati L.L., Nurhasim A., Ahmad R.A., Kekalih A., Syam A.F., Shankar A.H., Thwaites G., Baird J.K., Hamers R.L., Elyazar I.R.F.
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Abstract

Background The 33 recognized megacities comprise approximately 7% of the global population, yet account for 20% COVID-19 deaths. The specific inequities and other factors within megacities that affect vulnerability to COVID-19 mortality remain poorly defined. We assessed individual, community-level and health care factors associated with COVID-19related mortality in a megacity of Jakarta, Indonesia, during two epidemic waves spanning March 2, 2020, to August 31, 2021. Methods This retrospective cohort included all residents of Jakarta, Indonesia, with PCR-confirmed COVID-19. We extracted demographic, clinical, outcome (recovered or died), vaccine coverage data, and disease prevalence from Jakarta Health Office surveillance records, and collected sub-district level socio-demographics data from various official sources. We used multi-level logistic regression to examine individual, community and sub-district-level health care factors and their associations with COVID-19-mortality. Findings Of 705,503 cases with a definitive outcome by August 31, 2021, 694,706 (98·5%) recovered and 10,797 (1·5%) died. The median age was 36 years (IQR 24-50), 13·2% (93,459) were <18 years, and 51·6% were female. The sub-district level accounted for 1·5% of variance in mortality (p<0.0001). Individual-level factors associated with death were older age, male sex, comorbidities, and, during the first wave, age <5 years (adjusted odds ratio (aOR) 1·56, 95%CI 1·04-2·35; reference: age 20-29 years). Community-level factors associated with death were poverty (aOR for the poorer quarter 1·35, 95%CI 1·17-1·55; reference: wealthiest quarter), high population density (aOR for the highest density 1·34, 95%CI 1·14-2·58; reference: the lowest), low vaccine coverage (aOR for the lowest coverage 1·25, 95%CI 1·13-1·38; reference: the highest). Interpretation In addition to individual risk factors, living in areas with high poverty and density, and low health care performance further increase the vulnerability of communities to COVID-19-associated death in urban low-resource settings.

21. **SARS-CoV-2 convalescent sera binding and neutralizing antibody concentrations compared with COVID-19 vaccine efficacy estimates against symptomatic infection**
Schuh A.J., Satheshkumar P.S., Dietz S., Bull-Otterson L., Charles M., Edens C., Jones J.M., Bajema K.L., Clarke K.E.N., McDonald L.C., Patel S., Cuffe K., Thornburg N.J., Schiffer J., Chun K., Bastidas M., Fernando M., Petropoulos C.J., Wrin T., Cai S., Adcock D., Sesok-Pizzini D., Letovsky S., Fry A.M., Hall A.J., Gundlapalli A.V.
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Abstract

Previous vaccine efficacy (VE) studies have estimated neutralizing and binding antibody concentrations that correlate with protection from symptomatic infection; how these estimates compare to those generated in response to SARS-CoV-2 infection is unclear. Here, we assessed quantitative neutralizing and binding antibody concentrations using standardized SARS-CoV-2 assays on 3,067 serum specimens collected during July 27, 2020-August 27, 2020 from COVID-19 unvaccinated persons with detectable anti-SARS-CoV-2 antibodies using qualitative antibody assays. Quantitative neutralizing and binding antibody concentrations were strongly positively correlated (r=0.76, p<0.0001) and were noted to be several fold lower in the unvaccinated study population as compared to published data on concentrations noted 28 days post-vaccination. In this convenience sample, ~88% of neutralizing and ~63-86% of binding antibody concentrations met or exceeded concentrations associated with 70% COVID-19 VE against symptomatic infection from published VE studies; ~30% of neutralizing and 1-14% of binding antibody concentrations met or exceeded concentrations associated with 90% COVID-19 VE. These data support observations of infection-induced immunity and current recommendations for vaccination post infection to maximize protection against symptomatic COVID-19.

22. **Anatomy of the first six months of COVID-19 vaccination campaign in Italy**
Gozzi N., Chinazzi M., Davis J.T., Mu K., Piontti A.P.Y., Ajelli M., Perra N., Vespignani A.
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Abstract

We analyze the effectiveness of the first six months of vaccination campaign against SARS-CoV-2 in Italy by using a computational epidemic model which takes into account demographic, mobility, vaccines, as well as estimates of the introduction and spreading of the more transmissible Alpha variant. We consider six sub-national regions and study the effect of vaccines in terms of number of averted deaths, infections, and reduction in the Infection Fatality Rate (IFR) with respect to counterfactual scenarios with the actual non-pharmaceuticals interventions but no vaccine administration. Furthermore, we compare the effectiveness in counterfactual scenarios with different vaccines allocation strategies and vaccination rates. Our results show that, as of 2021/07/05, vaccines averted 29, 350 (IQR: [16, 454 − 42, 826]) deaths and 4, 256, 332 (IQR: [1, 675, 564 − 6, 980, 070]) infections and a new pandemic wave in the country. During the same period, they achieved a −22.2% (IQR: [−31.4%; −13.9%]) reduction in the IFR. We show that a campaign that would have strictly prioritized age groups at higher risk of dying

from COVID-19, besides frontline workers, would have implied additional benefits both in terms of avoided fatalities and reduction in the IFR. Strategies targeting the most active age groups would have prevented a higher number of infections but would have been associated with more deaths. Finally, we study the effects of different vaccination intake scenarios by rescaling the number of available doses in the time period under study to those administered in other countries of reference. The modeling framework can be applied to other countries to provide a mechanistic characterization of vaccination campaigns worldwide.

23. **Durability of SARS-CoV-2 antibodies from natural infection in children and adolescents**
Messiah S.E., Brito F., Kohl H.W., DeSantis S., Valerio-Shewmaker M., Ross J., Swartz M.D., Yaseen A., Kelder S.H., Zhang S., Omega-Njemnobi O.S., Gonzalez M.O., Wu L., Boerwinkle E., Lakey D., Shuford J.A., Pont S.J.
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Abstract

Background. Recent data suggest the SARS-CoV-2 Delta (B.1.617.2) variant is more transmissible among children compared to the Alpha (B.1.1.7) variant. The true incidence and longitudinal presence of antibody response to SARS-CoV-2 infection is not known, however. We provided estimates of antibody response using Texas Coronavirus Antibody REsponse Survey (Texas CARES) data, a prospective population-based seroprevalence project designed to assess antibody status over time among the general population throughout the state. Methods. In October 2020 Texas CARES began enrolling adults (aged 20-80 years) and children (aged 5-19 years). Participants were offered a series of three SARS-CoV-2 antibody tests over 6-8 months, or every 2-3 months that includes the immunoassay for detection of antibodies to the SARS-CoV-2 nucleocapsid protein (Roche N-test). Descriptive characteristics and COVID-19 infection-related symptom status was determined by questionnaire at the time of enrollment and prior to each successive blood draw. This analysis included participants ages 5-to-19 years old who have completed all three antibody assessments. Results. From our sample (n=159; mean age 12.5 years, SD 3.6), 96% of those with evidence of nucleocapsid antibodies at baseline assessment continued to have antibodies > six months later (mean 7.0 months, SD 0.97). There was no difference in the presence of antibodies by symptom status (asymptotic versus symptomatic) or severity (mild-moderate versus severe), sex, age group, or body mass index group (underweight, healthy weight, overweight, obesity) over the three antibody measurement timepoints. Conclusions. These results suggest that infection-induced antibodies persist and thus may provide some protection against future infection for at least half a year. 57.9% of the sample were negative for infection-induced antibodies at their third measurement point, suggesting a significant proportion of children have still not acquired natural infection.

24. **Behaviour, booster vaccines and waning vaccine protection: Modelling the medium-term dynamics of SARS-CoV-2 transmission in England**
Barnard R.C., Davies N.G., Jit M., Edmunds W.J.
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Abstract

England has experienced a heavy burden of COVID-19, with high infection levels observed throughout the summer months of 2021. Alongside the emergence of evidence suggesting that COVID-19 vaccine protection wanes over time, booster vaccinations began for individuals aged 50 and above in September 2021. Using a model fitted to 18 months of epidemiological data, we project potential dynamics of SARS-CoV-2 transmission in England to September 2022. We consider key uncertainties including behavioural change, waning vaccine protection, strategies for vaccination, and the reintroduction of public health and social measures. We project the current wave of transmission will peak in Autumn 2021, with low levels of transmission in early 2022. The extent to which SARS-CoV-2 transmission resurges in 2022 depends largely on assumptions around waning vaccine protection and booster vaccinations. Widespread booster vaccinations or the reimposition of mild public health and social measures such as work-from-home policies could largely mitigate the wave of COVID-19 transmission projected to occur in England in Spring/Summer 2022.

25. **Sustained negative mental health outcomes among healthcare workers over the first year of the COVID-19 pandemic: A prospective cohort study**
Mediavilla R., Fernández-Jiménez E., Martinez-Morata I., Jaramillo F., Andreo-Jover J., Morán-Sánchez I., Mascayano F., Moreno-Küstner B., Minué S., Ayuso-Mateos J.L., Bryant R.A., Bravo-Ortiz M.-F., Martínez-Alés G., Ortiz-Calvo E., González-Gómez E., Muñoz-Sanjose A., Rivera-Izquierdo M., García Román C., Guzmán-Parra J., Lorenzo Herrero P., Cañada E., Venzalá M.B., Sánchez A., Valmisa E., Macheño J.J., Ferreira M.C., Lopez Tovar I., Navarro M.P.C., Ros A.I., Sánchez Martínez D.A., Madrigal P., Guardiola J.A., Serrano S., Bethencourt M.K., López Romero P.A., Estrella E., Morata M.M., Ferreira M.C., Martínez D.S., Egea Á.
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Abstract

Objective: To characterize the evolution of healthcare workers' mental health status over the 1-year period following the initial COVID-19 pandemic outbreak and to examine baseline characteristics associated with resolution or persistence of mental health problems over time. Methods: We conducted an 8-month follow-up cohort study. Eligible participants were healthcare workers working in Spain. Baseline data were collected during the initial pandemic outbreak. Survey-based self-reported measures included COVID-19-related exposures, sociodemographic characteristics, and three mental health outcomes (psychological distress, depression symptoms, and posttraumatic stress disorder symptoms). We examined three longitudinal trajectories in mental health outcomes between baseline and follow-up assessments (namely asymptomatic/stable, recovering, and persistently symptomatic/worsening). Results: We recruited 1,807 participants. Between baseline and follow-up assessments, the proportion of respondents screening positive for psychological distress and probable depression decreased, respectively, from 74% to 56% and from 28% to 21%. Two-thirds remained asymptomatic/stable in terms of depression symptoms and 56% remained symptomatic or worsened over time in terms of psychological distress. Conclusions: Poor mental health outcomes among healthcare workers persisted over time. Occupational programs and mental health strategies should be put in place.

26. **Modeling on wastewater treatment process in Saudi Arabia: A perspective of Covid-19**

Ahmadini A., Msmali A., Mutum Z., Raghav Y.S.

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Abstract

The novel coronavirus diseases (COVID-19) has resulted in an ongoing pandemic affecting the health system and devastating impact on global economy. The virus has been found in human feces, in sewage and in wastewater treatment plants. We highlight the transmission behavior, occurrence, and persistence of coronavirus in sewage and wastewater treatment plants. Our approach is to follow in the process of identifying a coronavirus hotspot through existing wastewater plants in major cities of Saudi Arabia. The mathematical distributions including log-normal distribution, Gaussian model and susceptible-exposed-infection-recovered- (SEIR) model are adopted to predict the coronavirus load in wastewater plants. This paper highlights not only the potential virus removal techniques from wastewater treatment plants but also to facilitate tracing of SARS-CoV-2 virus in human through wastewater treatment plants.

27. **Determining international spread of novel B.1.1.523 SARS-CoV-2 lineage**

Zemaitis L., Alzbutas G., Gecys D., Komissarov A., Pautienius A., Ugenskiene R., Sukys M., Lesauskaite V.

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Abstract

Here we report the emergence of variant lineage B.1.1.523 that contains a set of mutations including 156_158del, E484K and S494P in Spike protein. E484K and S494P are known to significantly reduce SARS-CoV-2 neutralization by convalescent and vaccinee sera and are considered as mutations of concern. Lineage B.1.1.523 has presumably originated in Russian Federation and spread across European countries with the peak of transmission in April - May 2021. The B.1.1.523 lineage has now been reported from 27 countries.

28. **Neutralization of SARS-CoV-2 variants by rVSV-ΔG-spike-elicited human sera**

Yahalom-Ronen Y., Erez N., Fisher M., Tamir H., Politi B., Achdout H., Melamed S., Glinert I., Weiss S., Cohen-Gihon I., Israeli O., Izak M., Mandelboim M., Caraco Y., Madar-Balakirski N., Mechaly A., Shinar E., Cohen D., Beth-Din A., Zvi A., Marcus H., Israely T., Paran N.

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Abstract

BriLife® (rVSV-ΔG-spike) is a SARS-CoV-2 vaccine candidate based on vesicular stomatitis virus (VSV) platform. We show that sera from BriLife® vaccinees maintain neutralization capacity against alpha, beta, gamma and delta SARS-CoV-2 variants. BriLife® spontaneously-acquired spike mutations, corresponding with key SARS-CoV-2 variants' mutations, may contribute to its efficacy against SARS-CoV-2 variants.

29. **Investigating SARS-CoV-2 breakthrough infections per variant and vaccine type**

Dingemans J., van der Veer B.M.J.W., Gorgels K.M.F., Hackert V., Hensels A.Y.J., den Heijer C.D.J., Hoebe C.J.P.A., Savelkoul P.H.M., van Alphen L.B.

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Abstract

Breakthrough SARS-CoV-2 infections have been reported in fully vaccinated individuals, in spite of the high efficacy of the currently available vaccines, proven in trials and real-world studies. Several variants of concern (VOC) have been proffered to be associated with breakthrough infections following immunization. In this study, we investigated 378 breakthrough infections recorded between January and July 2021 and compared the distribution of SARS-CoV-2 genotypes identified in 225 fully vaccinated individuals to the frequency of circulating community lineages in the region of South Limburg (The Netherlands) in a week-by-week comparison. Although the proportion of breakthrough infections was relatively low and stable when the Alpha variant was predominant, the rapid emergence of the Delta variant lead to a strong increase in breakthrough infections, with a higher relative proportion of individuals vaccinated with Oxford-AstraZeneca or J&J/Janssen being infected compared to those immunized with mRNA-based vaccines. A significant difference in median age was observed when comparing fully vaccinated individuals with severe symptoms (83 years) to asymptomatic cases (46.5 years) or individuals with mild-to-moderate symptoms (42 years). There was no association between SARS-CoV-2 genotype or vaccine type and disease symptoms. Interestingly, symptomatic individuals harbored significantly higher SARS-CoV-2 loads than asymptomatic vaccinated individuals and breakthrough infections caused by the Delta variant are associated with increased viral loads compared to those caused by the Alpha variant. Altogether, these results indicate that the emergence of the Delta variant might have lowered the efficiency of particular vaccine types to prevent SARS-CoV-2 infections and that, although rare, the elderly are particularly at risk of becoming severely infected as the consequence of a breakthrough infection.

30. **In vitro, classical complement activation differs by disease severity and between SARS-CoV-2 antigens**

Lamerton R.E., Marcial-Juarez E., Faustini S.E., Perez-Toledo M., Goodall M., Jossi S.E., Newby M.L., Chapple I., Dietrich T., Veenith T., Shields A.M., Harper L., Henderson I.R., Rayes J., Wraith D.C., Watson S.P., Crispin M., Drayson M.T., Richter A.G., Cunningham A.F.

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Abstract

Antibodies specific for the spike glycoprotein (S) and nucleocapsid (N) SARS-CoV-2 proteins are typically present during severe COVID-19, and induced to S after vaccination. The binding of viral antigens by antibody can initiate the classical complement pathway. Since complement could play pathological or protective roles at distinct times during SARS-CoV-2 infection we determined levels of antibody-dependent complement activation along the complement cascade. Here, we used an ELISA assay to assess complement protein binding (C1q) and the deposition of C4b, C3b, and C5b to S and N antigens in the presence of anti-SARS-CoV-2 antibodies from different test groups: non-infected, single and double vaccinees, non-hospitalised convalescent (NHC) COVID-19 patients and convalescent hospitalised (ITU-CONV) COVID-19 patients. C1q binding correlates strongly with antibody responses, especially IgG1 levels. However, detection of downstream complement components, C4b, C3b and C5b shows some variability associated with the antigen and subjects studied. In the ITU-CONV, detection of C3b-C5b to S was observed consistently, but this was not the case in the NHC group. This is in contrast to responses to N, where median levels of complement deposition did not differ between the NHC and ITU-CONV groups. Moreover, for S but not N, downstream complement components were only detected in sera with higher IgG1 levels. Therefore, the classical pathway is activated by antibodies to multiple SARS-CoV-2 antigens, but the downstream effects of this activation may differ depending on the specific antigen targeted and the disease status of the subject.

31. **Uptake of Covid-19 preventive measures among 10 immigrant ethnic groups in Norway**

Gele A., Sheikh N.S., Kour P., Qureshi S.A.

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Abstract

Background: A pessimistic view of the impact of Covid-19 on immigrants has generated an interest in exploring the role of socio-economic and cultural factors on excess infection, hospitalization and death among immigrants. Nowhere in the world is such interest more palpable than in Western countries, including Norway. An expanding amount of literature has demonstrated that preexisting socio-economic inequalities have affected Covid-19 control programs through a disruption of immigrants' uptake to preventive measures. Nonetheless, until very recently, no qualitative research has been conducted to address the impact of socioeconomic and socio-cultural factors on immigrants' uptake on preventive measures of Covid-19 in Norway. Methods: An interview-based qualitative study consisting of 88 participants (49 women and 39 men) from 10 immigrant ethnic groups were carried out. Participants were recruited through purposive sampling and snowballing. In-depth interviews were held through telephone or online for those who have experience in the use of zoom or teams. Data were analyzed using thematic analysis Results: We found that participants' attitudes toward the pandemic in general, and more specifically their adherence to preventive measures, have increased over time. However, the number of barriers that hinder immigrants from adhering to preventive measures were identified and classified more broadly into three main subthemes: 1) socio-economic barriers; 2) socio-cultural barriers, and 3) other barriers. Socio-economic barriers include overcrowded households, working in first-line jobs, education and language. Socio-cultural barriers include collectivist culture, religious fatalism and risk perception toward the pandemic. Conclusion: To reduce the health inequality that arises from overcrowded housing, there is a need for a long-term strategy to help improve the housing situation of low-income immigrant families that live in overcrowded households. In addition, increasing health literacy and more generally, the integration of immigrants, may also reduce the effect of socio-cultural factors on an immigrant's uptake of preventive measures.

32. **Final sizes and durations of new COVID-19 pandemic waves in Ukraine and around the world predicted by generalized SIR model**

Nesteruk I.

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Abstract

New waves of the COVID-19 pandemic in Ukraine, which began in the summer of 2021, and after holidays in the middle of October 2021, were characterized by almost exponential growth of smoothed daily numbers of new cases. This is a matter of great concern and the need to immediately predict the epidemic dynamics in order to assess the possible maximum values of new cases, the risk of infection and the number of deaths. The generalized SIR-model and corresponding parameter identification procedure was used to simulate and predict the dynamics of two new epidemic waves in Ukraine and one in the whole world. Results of calculations show that new cases in Ukraine will not stop to appear before November 2022. If the global situation with vaccination, testing and treatment will not change, the pandemic could continue for another ten years.

33. **SARS-CoV-2 genome-based severity predictions correspond to lower qPCR values and higher viral load**

Skarzynski M., McAuley E.M., Maier E.J., Fries A.C., Voss J.D., Chapleau R.R.

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Abstract

The 2019 coronavirus disease (COVID-19) pandemic has demonstrated the importance of predicting, identifying, and tracking mutations throughout a pandemic event. As the COVID-19 global pandemic surpassed one year, several variants had emerged resulting in increased severity and transmissibility. In order to reduce the impact on human life, it is critical to rapidly identify which genetic variants result in increased virulence or transmission. To address the former, we evaluated if a genome-based predictive algorithm designed to predict clinical severity could predict polymerase chain reaction (PCR) results, as a surrogate for viral load and severity. Using a previously published algorithm, we compared the viral genome-based severity predictions to clinically-derived PCR-based viral load of 716 viral genomes. For those samples predicted to be “severe” (predicted severity score > 0.5), we observed an average cycle threshold (Ct) of 18.3, whereas those in in the “mild” category (severity prediction < 0.5) had an average Ct of 20.4 (P = 0.0017). We found a non-trivial correlation between predicted severity probability and cycle threshold (r = -0.199). Additionally, when divided into quartiles by prediction severity probability, the most probable quartile (≥75% probability) had a Ct of 16.6 (n=10) as compared to those least probable to be severe (<25%) of 21.4 (n=350) (P = 0.0045). Taken together, our results suggest that the severity predicted by a genome-based algorithm can be related to the

metrics from the clinical diagnostic test, and that relative severity may be inferred from diagnostic values.

34. **Favipiravir for treatment of outpatients with asymptomatic or uncomplicated COVID-19: A double-blind randomized, placebo-controlled, phase 2 trial**

Holubar M., Subramanian A., Purington N., Hedlin H., Bunning B., Walter K.S., Bonilla H., Boumis A., Chen M., Clinton K., Dewhurst L., Epstein C., Jagannathan P., Kaszynski R.H., Panu L., Parsonnet J., Ponder E.L., Quintero O., Sefton E., Singh U., Soberanis L., Truong H., Andrews J.R., Desai M., Khosla C., Maldonado Y.

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Abstract

Background: Favipiravir is an oral, RNA-dependent RNA polymerase inhibitor with in vitro activity against SARS-CoV2. Despite limited data, favipiravir is administered to patients with COVID-19 in several countries. Methods: We conducted a phase 2 double-blind randomized controlled outpatient trial of favipiravir in asymptomatic or mildly symptomatic adults with a positive SARS-CoV2 RT-PCR within 72 hours of enrollment. Participants were randomized 1:1 to receive placebo or favipiravir (1800 mg BID Day 1, 800mg BID Days 2-10). The primary outcome was SARS-CoV-2 shedding cessation in a modified intention-to-treat (mITT) cohort of participants with positive enrollment RT-PCRs. Using SARS-CoV-2 deep sequencing, we assessed favipiravir's impact on mutagenesis. Results: From July 8, 2020 - March 23, 2021, we randomized 149 participants with 116 included in the mITT cohort. The participants' mean age was 43 years (SD 12.5) and 57 (49%) were women. We found no difference in time to shedding cessation by treatment arm overall (HR 0.76 favoring placebo, 95% confidence interval [CI] 0.48 - 1.20) or in sub-group analyses (age, sex, high-risk comorbidities, seropositivity or symptom duration at enrollment). We observed no difference in time to symptom resolution (initial: HR 0.84, 95% CI 0.54 - 1.29; sustained: HR 0.87, 95% CI 0.52 - 1.45). We detected no difference in accumulation of transition mutations in the viral genome during treatment. Conclusions: Our data do not support favipiravir use at commonly used doses in outpatients with uncomplicated COVID-19. Further research is needed to ascertain if higher doses of favipiravir are effective and safe for patients with COVID-19.

35. **Serological responses to COVID-19 booster vaccine in England**

Ireland G., Whitaker H., Ladhani S.N., Baawuah F., Subbarao V., Linley E., Warrener L., O'Brien M., Whillock C., Moss P., Ramsay M.E., Amirthalingam G., Brown K.E.

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Abstract

Introduction: There are limited data on immune responses after COVID-19 vaccine boosters in individuals receiving primary immunisation with BNT162b2 (Pfizer-BioNTech) or AZD1222 (AstraZeneca). Methods: A prospective, cohort study to assess SARS-CoV-2 antibody responses before and after booster vaccination with BNT162b2 in adults receiving either (i) two BNT162b2 doses <30 days apart (BNT162b2-control), (ii) two BNT162b2 doses ≥30 days apart (BNT162b2-extended) or (iii) two AZD1222 doses ≥30 days apart (AZD1222-extended) in London, England. SARS-CoV-2 spike protein antibody geometric mean titres (GMTs) before and 2-4 weeks after booster were compared. Results: Of 750 participants, 626 provided serum samples for up to 38 weeks after their second vaccine dose. Antibody GMTs peaked at 2-4 weeks after the second dose, before declining by 68% at 36-38 weeks after dose 2 for BNT162b2-control participants, 85% at 24-29 weeks for BNT162b2-extended participants and 78% at 24-29 weeks for AZD1222-extended participants. Antibody GMTs was highest in BNT162b2-extended participants (942 [95%CI, 797-1113]) than AZD1222-extended (183 [124-268]) participants at 24-29 weeks or BNT162b2-control participants at 36-38 weeks (208; 95%CI, 150-289). At 2-4 weeks after booster, GMTs were significantly higher than after primary vaccination in all three groups: 18,104 (95%CI, 13,911-23,560; n=47) in BNT162b2-control (76.3-fold), 13,980 (11,902-16,421; n=118) in BNT162b2-extended (15.9-fold) and 10,799 (8,510-13,704; n=43) in AZD1222-extended (57.2-fold) participants. BNT162b2-control participants (median:262 days) had a longer interval between primary and booster doses than BNT162b2-extended or AZD1222-extended (both median:186 days) participants. Conclusions: We observed rapid serological responses to boosting with BNT162b2, irrespective of vaccine type or schedule used for primary immunisation, with higher post-booster responses with longer interval between primary immunisation and boosting. Boosters will not only provide additional protection for those at highest risk of severe COVID-19 but also prevent infection and, therefore, interrupt transmission, thereby reducing infections rates in the population. Ongoing surveillance will be important for monitoring the duration of protection after the booster.

36. **Germany's low SARS-CoV-2 seroprevalence confirms effective containment in 2020: Results of the nationwide RKI-SOEP study**

Neuhauser H., Rosario A.S., Butschalowsky H., Haller S., Hoebel J., Michel J., Nitsche A., Poethko-Müller C., Prütz F., Schlaud M., Steinhauer H.W., Wilking H., Wieler L.H., Schaade L., Liebig S., Gößwald A., Grabka M.M., Zinn S., Ziese T.

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Abstract

Pre-vaccine SARS-CoV-2 seroprevalence data from Germany are scarce outside hotspots, and socioeconomic disparities remained largely unexplored. The nationwide RKI-SOEP study with 15,122 adult participants investigated seroprevalence and testing in a supplementary wave of the SocioEconomic-Panel conducted predominantly in October-November 2020. Self-collected oral-nasal swabs were PCR-positive in 0.4% and Euroimmun anti-SARS-CoV-2-S1-IgG ELISA from dry capillary blood in 1.3% (95% CI 0.9-1.7%, population-weighted, corrected for sensitivity=0.811, specificity=0.997). Seroprevalence was 1.7% (95% CI 1.2-2.3%) when additionally adjusting for antibody decay. Overall infection prevalence including self-reports was 2.1%. We estimate 45% (95% CI 21-60%) undetected cases and analyses suggest lower detection in socioeconomically deprived districts. Prior SARS-CoV-2 testing was reported by 18% from the lower educational group compared to 25% and 26% from the medium and high educational group (p<0.0001). Symptom-triggered test frequency was similar across educational groups. However, routine testing was more common in low-educated adults, whereas travel-related testing and testing after contact with an infected person was more common in highly educated groups. In conclusion, pre-vaccine SARS-CoV-2-seroprevalence in Germany was very low. Notified cases appear to capture more than half of infections but may underestimate infections in lower socioeconomic groups. These data confirm the successful containment strategy of Germany until winter 2020.

37. **Human phospho-signaling networks of SARS-CoV-2 infection are rewired by population genetic variants**
Pellegrina D., Bahcheli A.T., Krassowski M., Reimand J.
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Abstract

SARS-CoV-2 infection hijacks signaling pathways and induces protein-protein interactions between human and viral proteins. Human genetic variation may impact SARS-CoV-2 infection and COVID-19 pathology; however, the role of genetic variation in these signaling networks remains uncharacterized. We studied human single nucleotide variants (SNVs) affecting phosphorylation sites modulated by SARS-CoV-2 infection, using machine learning to identify amino acid changes altering kinase-bound sequence motifs. We found 2033 infrequent phosphorylation-associated SNVs (pSNVs) that are enriched in sequence motif alterations, potentially reflecting the evolution of signaling networks regulating host defenses. Proteins with pSNVs are involved in viral life cycle processes and host responses, including regulators of RNA splicing and interferon response, as well as glucose homeostasis pathways with potential associations with COVID-19 co-morbidities. Certain pSNVs disrupt CDK and MAPK substrate motifs and replace these with motifs recognized by Tank Binding Kinase 1 (TBK1) involved in innate immune responses, indicating consistent rewiring of infection signaling networks. Our analysis highlights potential genetic factors contributing to the variation of SARS-CoV-2 infection and COVID-19 and suggests leads for mechanistic and translational studies.

38. **In vitro nasal tissue model for the validation of nasopharyngeal and mid-turbinate swabs for SARS-CoV-2 testing**
Hartigan D.R., Adelfio M., Shutt M.E., Jones S.M., Patel S., Marchand J.T., McGuinness P.D., Buchholz B.O., Ghezzi C.E.
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Abstract

Large-scale population testing is a key tool to mitigate the spread of respiratory pathogens, as in the current COVID-19 pandemic, where swabs are used to collect samples in the upper airways (e.g. nasopharyngeal and mid-turbinate nasal cavities) for diagnostics. However, the high volume of supplies required to achieve large-scale population testing has posed unprecedented challenges for swab manufacturing and distribution, resulting in a global shortage that has heavily impacted testing capacity world-wide and prompted the development of new swabs suitable for large-scale production. Newly designed swabs require rigorous pre-clinical and clinical validation studies that are costly and time consuming (i.e. months to years long); reducing the risks associated with swab validation is therefore paramount for their rapid deployment. To address these shortages, we developed a 3D-printed tissue model that mimics the nasopharyngeal and mid-turbinate nasal cavities, and we validated its use as a new tool to rapidly test swab performance. In addition to the nasal architecture, the tissue model mimics the soft nasal tissue with a silk-based sponge lining, and the physiological nasal fluid with asymptomatic and symptomatic viscosities of synthetic mucus. We performed several assays comparing standard flocked and injection-molded swabs. We quantified the swab pick-up and release, and determined the effect of viral load and mucus viscosity on swab efficacy by spiking

the synthetic mucus with heat-inactivated SARS-CoV-2 virus. By molecular assays, we found that injected molded swabs performed similarly or superiorly in comparison to standard flocked swabs and we underscored a viscosity-dependent difference in cycle threshold values between the asymptomatic and symptomatic mucus for both swabs. To conclude, we developed an in vitro nasal tissue model, that corroborated previous swab performance data from clinical studies, with the potential of providing researchers with a clinically relevant, reproducible, safe, and cost-effective validation tool for the rapid development of newly designed swabs.

39. **Development and performance verification of colloidal gold labeled SARS-CoV-2 antigen detection method for routine popular screening of COVID-19 with clinical samples in Poland and China**
Guo C., Yao L., Chen F., Zhang C., Chen W.
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Abstract

In this research, we have constructed and optimized the colloidal gold labeled lateral flow strip (LFS) for rapid detection of antigen of SARS-CoV-2 and rapid screening of COVID-19. Based on the constructed and optimized colloidal gold lateral flow strip, the parameters of the LFS have been well evaluated with the clinical samples in the professional labs. The screening performance have also been evaluated from the aspects including the CT values, age distribution and onset of symptoms. Finally, based on the detection results of 420 clinical samples, the LFS can achieve the screening of COVID-19 with the positive percentage agreement (PPA, sensitivity), negative percent agreement (NPA, specificity), the positive predictive value (PPV) and the negative predictive value (NPV) of 96.8%, 100%, 100% and 96.6%, respectively, indicating the powerful potential for practical screening applications in pandemic control. Of great significance, this developed SARS-CoV-2 antigen detection method has also been successfully utilized for screening of delta-variant of SARS-CoV-2.

40. **Simulating the impact of vaccination rates on the initial stages of a COVID-19 outbreak in New Zealand (Aotearoa) with a stochastic model**
Watson L.M.
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Abstract

Aim: The August 2021 COVID-19 outbreak in Auckland has caused the New Zealand government to transition from an elimination strategy to suppression, which relies heavily on high vaccination rates in the population. As restrictions are eased and as COVID-19 leaks through the Auckland boundary, there is a need to understand how different levels of vaccination will impact the initial stages of COVID-19 outbreaks that are seeded around the country. Method: A stochastic branching process model is used to simulate the initial spread of a COVID-19 outbreak for different vaccination rates. Results: High vaccination rates are effective at minimizing the number of infections and hospitalizations. Increasing vaccination rates from 20% (approximate value at the start of the August 2021 outbreak) to 80% (approximate proposed target) of the total population can reduce the median number of infections that occur within the first four weeks of an outbreak from 1011 to 14 (25^{th} and 75^{th} quantiles of 545-1602 and 2-32 for V=20% and V=80%, respectively). As the vaccination rate increases, the number of breakthrough infections (infections in fully vaccinated individuals) and hospitalizations of vaccinated individuals increases. Unvaccinated individuals, however, are 3.3x more likely to be infected with COVID-19 and 25x more likely to be hospitalized. Conclusion: This work demonstrates the importance of vaccination in protecting individuals from COVID-19, preventing high caseloads, and minimizing the number of hospitalizations and hence limiting the pressure on the healthcare system.

41. **Establishing and characterising large COVID-19 cohorts after mapping the information system for research in primary care in Catalonia to the OMOP common data model**
Burn E., Fernández-Bertolín S., Voss E.A., Blacketer C., Aragón M., Recalde M., Roel E., Pistillo A., Raventós B., Reyes C., van Sandijk S., Halvorsen L., Rijnbeek P.R., Duarte-Salles T.
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Abstract

Background Few datasets have been established that capture the full breadth of COVID-19 patient interactions with a health system. Our first objective was to create a COVID-19 dataset that linked primary care data to COVID-19 testing, hospitalisation, and mortality data at a patient level. Our second objective was to provide a descriptive analysis of COVID-19 outcomes among the general population and describe the characteristics of the affected individuals. Methods We mapped patient-level data from Catalonia, Spain, to the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM). More than 3,000 data quality checks were performed to assess the readiness of the database for research. Subsequently, to summarise the COVID-19 population captured, we established a general population cohort as of the 1st March 2020 and identified outpatient COVID-19 diagnoses or positive test results for SARS-CoV-2, hospitalisations with COVID-19, and COVID-19 deaths during follow-up, which went up until 30th June 2021. Findings Mapping data to the OMOP CDM was performed and high data quality was observed. The mapped database was used to identify a total of 5,870,274 individuals, who were included in the general population cohort as of 1st March 2020. Over follow up, 604,472 had either an outpatient COVID-19 diagnosis or positive test result, 58,991 had a hospitalisation with COVID-19, 5,642 had an ICU admission with COVID-19, and 11,233 had a COVID-19 death. People who were hospitalised or died were more commonly older, male, and with more comorbidities. Those admitted to ICU with COVID-19 were generally younger and more often male than those hospitalised in general and those who died. Interpretation We have established a comprehensive dataset that captures COVID-19 diagnoses, test results, hospitalisations, and deaths in Catalonia, Spain. Extensive data checks have shown the data to be fit for use. From this dataset, a general population cohort of 5.9 million individuals was identified and their COVID-19 outcomes over time were described.

42. **A population framework for predicting the proportion of people infected by the far-field airborne transmission of SARS-CoV-2 indoors**

Iddon C., Jones B., Sharpe P., Cevik M., Fitzgerald S.

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Abstract

The number of occupants in a space influences the risk of far-field airborne transmission of the SARS-CoV-2 virus because the likelihood of having infectious and susceptible people both scale with the number of occupants. Mass-balance and dose-response models determine far-field transmission risks for an individual person and a population of people after sub-dividing a large reference space into 10 identical comparator spaces. For a single infected person when the per capita ventilation rate is preserved, the dose received by an individual person in the comparator space is 10-times higher because the equivalent ventilation rate per infected person is lower. However, accounting for population dispersion, such as the community infection rate, the probability of an infected person being present and uncertainty in their viral load, shows the probability of transmission increases with occupancy. Also, far-field transmission is likely to be a rare event that requires a set of Goldilocks conditions that are just right, when mitigation measures have limited effect. Therefore, resilient buildings should deliver the equivalent ventilation rate required by standards and increase the space volume per person, but also require reductions in the viral loads and the infection rate of the wider population.

43. **Efficacy and safety of a novel antiviral preparation in ICU-admitted patients with COVID-19: A phase III randomized controlled trial**

Faramarzi H., Sahebkar A., Hosseinpour A., Khaloo V., Chamanpara P., Heydari M.R., Najafi S., Khankahdany F.F., Movahedpour A.

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Abstract

Introduction Despite an increasing number of studies, there is as yet no efficient antiviral treatment developed for the disease. In this clinical trial, we examined the efficacy of a novel herbal antiviral preparation comprising Zataria multiflora Boiss, Glycyrrhiza glabra, Cinnamomum Vermont, Allium sativuml, and Syzygium aromaticum in critically ill patients with COVID-19 patients. Methods A total number of 120 ICU-admitted patients requiring pulmonary support with a diagnosis of COVID-19 pneumonia were recruited to the trial. Participants were equally randomized to receive either the novel antiviral preparation sublingually, for up to two consecutive weeks or till discharge, or normal saline as the matching placebo. Clinical and laboratory parameters as well as survival rates were compared between the two groups at the study end. Results The cumulative incidence of death throughout the study period was 8.33% in the medication group and 60% in the placebo group (risk ratio: 0.14; 95% confidence interval [CI], 0.05 to 0.32; P<0.001). Survival rates were significantly higher in the treatment group. Additionally, on day 7, several laboratory factors including white blood cells (WBCs) count, C-reactive protein (CRP), and SpO2 were improved in patients treated with the novel antiviral preparation compared with the placebo group. Conclusion The novel antiviral preparation tested in this trial significantly improved the survival rate and reduced mortality in critically ill patients with COVID-19. Thus, this preparation might be suggested as a potentially promising COVID-19 treatment.

44. **Pausing methotrexate improves immunogenicity of COVID-19 vaccination in patients with rheumatic diseases**
Arumahandi de Silva A.N., Frommert L.M., Albach F.N., Klotsche J., Scholz V., Jeworowski L.M., Schwarz T., ten Hagen A., Zernicke J., Corman V.M., Drosten C., Burmester G.R., Biesen R.
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Abstract

Objective: To study the effect of methotrexate (MTX) and its discontinuation on the humoral immune response after COVID-19 vaccination in patients with autoimmune rheumatic diseases (AIRD). Methods: Neutralising SARS-CoV-2 antibodies were measured after second vaccination in 64 rheumatic patients on methotrexate therapy, 31 of whom temporarily paused medication without a fixed regimen. The control group consisted of 21 AIRD patients without immunosuppressive medication. Results: MTX patients showed a significantly lower median antibody response compared to AIRD patients without immunosuppressive therapy (p< 0.001). Young age (<60 years) and MTX-hold after vaccination were found to be the main factors influencing antibody response after vaccination, while BMI or MTX dose demonstrated no effect. For patients taking MTX, age correlated negatively with immune response (r=-0.49; p<0.001) and all patients with antibody levels (14 %) below the cut-off were older than 60 years. Patients who held MTX during at least one vaccination showed significantly higher median neutralising antibody levels after second vaccination, compared to patients who continued MTX therapy during both vaccinations (68.82 %, 92.73 %, p=<0.001). This effect was particularly pronounced in patients older than 60 years (p=0.0016). The impact of the time period after vaccination was greater than of the time before vaccination with the critical cut-off being 10 days. Conclusion: MTX reduces the immunogenicity of SARS-CoV-2 vaccination in an age-dependent manner. Our data further suggest that holding MTX for at least 10 days after vaccination significantly improves the antibody response in patients over 60 years of age.

45. **Space-time classification index for assessing COVID-19 hotspots**
Haynes D., Tiwari C.
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Abstract

Objectives: To develop new methods to address problems associated with use of traditional measures of disease surveillance, including prevalence and positivity rates. Methods: We use data from the public New York Times Github repository to develop a space-time classification index of COVID-19 hotspots. The Local Indicator of Spatial Association (LISA) statistic is applied to identify daily clusters of COVID-19 cases, from July 4th to July 19th. Results: The classification index is a spatial and temporal assessment tool that seeks to incorporate temporal trends of the clusters that are “high-high” and “high-low”. Two classifications support the index: severity and temporal duration. We define severity as the number of times a county is statistically significant and temporal duration captures the number of consecutive days a county is a hotspot. Conclusions: The space-time classification index provides a statistically robust measure of the spatial patterns of COVID-19 hotspots. Spatial information is not captured through measures like the positivity rate, which merely divides the number of cases by tests conducted. The index proposed in this paper can guide intervention efforts by classifying counties with six-levels of importance.

46. **COVID-19 vaccination and menstrual cycle changes: A United Kingdom (UK) retrospective case-control study**
Alvergne A., Kountourides G., Austin Argentieri M., Agyen L., Rogers N., Knight D., Sharp G.C., Maybin J.A., Olszewska Z.
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Abstract

Background. There has been increasing public concern that COVID-19 vaccines cause menstrual cycle disturbances, yet there is currently limited data to evaluate the impact of vaccination on menstrual health. Our objectives were (1) to evaluate the prevalence of menstrual changes following vaccination against COVID-19, (2) to test potential risk factors for any such changes, and (3) to identify patterns of symptoms in participants' written accounts. Methods. We performed a secondary analysis of a retrospective online survey titled “The Covid-19 Pandemic and Women's Reproductive Health”, conducted in March 2021 in the UK before widespread media attention regarding potential impacts of SARS-CoV-2 vaccination on menstruation. Participants were recruited via a Facebook ad campaign in the UK and eligibility criteria for survey completion were age greater than 18 years, having ever menstruated and currently living in the UK. In total, 26,710 people gave consent and completed the survey.

For this analysis we selected 4,989 participants who were pre-menopausal and vaccinated. These participants were aged 28 to 43, predominantly from England (81%), of white background (95%) and not using hormonal contraception (58%). Findings. Among pre-menopausal vaccinated individuals (n=4,989), 80% did not report any menstrual cycle changes up to 4 months after their first COVID-19 vaccine injection. Current use of combined oral contraceptives was associated with lower odds of reporting any changes by 48% (OR = 0.52, 95CI = [0.34 to 0.78], P<0.001). Odds of reporting any menstrual changes were increased by 44% for current smokers (OR = 1.16, 95CI = [1.06 to 1.26], P<0.01) and by more than 50% for individuals with a positive COVID status [Long Covid (OR = 1.61, 95CI = [1.28 to 2.02], P<0.001), acute COVID (OR = 1.54, 95CI = [1.27 to 1.86], P<0.001)]. The effects remain after adjusting for self-reported magnitude of menstrual cycle changes over the year preceding the survey. Written accounts report diverse symptoms; the most common words include “cramps”, “late”, “early”, “spotting”, “heavy” and “irregular”, with a low level of clustering among them. Conclusions. Following vaccination for COVID-19, menstrual disturbance occurred in 20% of individuals in a UK sample. Out of 33 variables investigated, smoking and a previous history of SARS-CoV-2 infection were found to be risk factors while using oestradiol-containing contraceptives was found to be a protective factor. Diverse experiences were reported, from menstrual bleeding cessation to heavy menstrual bleeding.

47. **Clinical outcome of neurological patients with COVID-19: The impact of healthcare organization improvement between waves**

Cristillo V., Pilotto A., Benussi A., Libri I., Giunta M., Morotti A., Gipponi S., Locatelli M., Piccinelli S.C., Mazzoleni V., di Cola F.S., Masciocchi S., Pezzini D., Scalvini A., Premi E., Cottini E., Gamba M., Magoni M., Fontanella M.M., Padovani A.
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Abstract

Objective: The aim of this study is to evaluate the differences of clinical presentations and the impact of healthcare organization on outcomes of neurological COVID-19 patients admitted during the first and second pandemic waves. Methods: In this single center cohort study, we included all patients with SARS-CoV-2 infection admitted to a NeuroCOVID Unit. Demographic, clinical and laboratory data were compared between patients admitted during the first and second waves of COVID-19 pandemic. Results: 223 patients were included, of whom 112 and 111 hospitalized during the first and second pandemic waves, respectively. Patients admitted during the second wave were younger and exhibited pulmonary COVID-19 severity, resulting in less oxygen support (n=41, 36.9% vs n=79, 70.5%, p<0.001) and lower mortality rates (14.4% vs 31.3%, p=0.004). The different healthcare strategies and early steroid treatment emerged as significant predictors of mortality independently from age, premorbid conditions and COVID-19 severity in cox regression analyses. Conclusions: Differences in healthcare strategies during the second phase of COVID-19 pandemic probably explain the differences in clinical outcomes independently of disease severity, underlying the importance of standardized early management of neurological patients with SARS-CoV-2 infection.

48. **COVID-19 health care behaviour in the Gambia: A cross-sectional survey of 205 adults who went through mandatory institutional quarantine**

Johm P., Nkereuwem O., Manjang A.-M., Ceesay O., Leigh L., Ceesay A., Bittaye 5.1.2e **A., Manjang B., Sambou S., Sanneh S., Saidy L., Saidy B., Kampmann B.**
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Abstract

Background: To control the spread of the novel Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome novel Coronavirus-2 (SARS-CoV-2), countries around the world subsequently implemented several public health measures, including the adoption of mandatory institutional quarantine for close contacts. This study explored the experiences of individuals who underwent institutional quarantine in The Gambia to inform government measures to increase its effectiveness and reduce its associated negative impacts. Methods: Questionnaires were administered via mobile phone call with data collectors calling and directly recording participant responses on a tablet in an electronic online form developed in REDCap (Research Electronic Data Capture). The questionnaire contained questions on COVID-19 related knowledge, health care behaviour, attitudes, perceptions and stigma. Data were analysed using STATA v.13 (Stata Corp, College Station, TX, USA). Results: In total, 205 adults who observed the mandatory institutional quarantine were interviewed. There was varied knowledge of COVID-19 causes, spread, symptoms, diagnosis, treatment, and severity. Participants believed the purpose of quarantine was monitoring for signs and symptoms of coronavirus disease, testing for SARS-CoV-2, separation from the community, and protection from coronavirus disease. While a majority reported positive experiences while in quarantine, some expressed prominent dissatisfaction related to the essential services and quality of care provided. Different forms of stigma were also experienced before, during and after the quarantine experience. Conclusion: This study provides important information on quarantine experiences in The Gambia during the global COVID-19 pandemic. The Ministry of Health in The Gambia and other countries could improve the experience of quarantined individuals by consistently providing psychosocial support, compensation for loss of earnings, and timely provision of SARS-CoV-2 test results. Furthermore, stigma experiences and practices should be addressed during and after individuals stay in quarantine via the provision of psychosocial support.

49. **Persistent autoimmune activation and proinflammatory state in post-COVID syndrome**
Acosta-Ampudia Y., Monsalve D.M., Rojas M., Rodríguez Y., Zapata E., Ramírez-Santana C., Anaya J.-M.
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Abstract

Background The immunopathological pathways enabling post-COVID syndrome (PCS) development are not entirely known. We underwent a longitudinal analysis of patients with COVID-19 who developed PCS aiming to evaluate the autoimmune and immunological status associated with this condition. Methods Thirty-three patients were included for longitudinal clinical and autoantibody analyses of whom 12 patients were assessed for cytokines and lymphocyte populations. Patients were followed during 7-11 months after acute COVID-19. Autoimmune profile and immunological status were evaluated mainly by enzyme-linked-immunosorbent assays and flow cytometry. Results Latent autoimmunity and overt autoimmunity persisted over time. A proinflammatory state was observed in patients with PCS characterized by upregulated IFN-α, TNF-α, G-CSF, IL-17A, IL-6, IL-1β, and IL-13, whereas IP-10 was decreased. In addition, PCS was characterized by increased levels of Th9, CD8+ effector T cells, naive B cells, and CD4+ effector memory T cells. Total levels of IgG S1-SARS-CoV-2 antibodies remained elevated over time. Discussion The clinical manifestations of PCS are associated with the persistence of a proinflammatory, and effector phenotype induced by SARS-CoV-2 infection. This long-term persistent immune activation may contribute to the development of latent and overt autoimmunity. Results suggest the need to evaluate the role of immunomodulation in the treatment of PCS.

50. **Healthcare workers' SARS-CoV-2 infection rates during the second wave of the pandemic: Prospective cohort study**
Würtz A.M., Kinnerup M.B., Pugdahl K., Schlünssen V., Vestergaard J.M., Nielsen K., Cramer C., Bonde J.P., Biering K., Carstensen O., Hansen K.K., Dalbøge A., Flachs E.M., Hansen M.L., Thulstrup A.M., Würtz E.T., Kjærsgaard M., Christensen M.W., Kolstad H.A.
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Abstract

Objectives: To assess if healthcare workers during the second wave of the COVID-19 pandemic had increased SARS-CoV-2 infection rates following close contact with patients, co-workers and persons outside work with COVID-19. Design: Prospective cohort study. Setting: Public hospital employees in Denmark. Participants: 5985 healthcare workers (88.6% women) who daily on a smartphone reported COVID-19 contact. Main outcome measures: SARS-CoV-2 infection rates defined by the first positive polymerase chain reaction (PCR) test recorded in a register with complete test coverage. Results: 159 positive and 35 996 negative PCR tests for SARS-CoV-2 were recorded during 514 165 person-days of follow-up November 25, 2020 - April 30, 2021. The SARS-CoV-2 infection rate for healthcare workers who during the previous 3-7 days had close contact with COVID-19 patients was 153.7 per 100 000 person-days (0.15% per day) corresponding with an incidence rate ratio of 3.17 (40 cases, 95% CI 2.15 to 4.66) when compared with no close contact with COVID-19 patients. SARS-CoV-2 incidence rate ratios following close contact with co-workers and persons outside work with COVID-19 were 2.54 (10 cases, 95% CI 1.30 to 4.96) and 17.79 (35 cases, 95% CI 12.05 to 26.28). These estimates were mutually adjusted and further adjusted for age, sex, month and number of previous PCR tests. Conclusions: Despite strong focus on preventive actions during the second wave of the pandemic, healthcare workers were still at increased risk of SARS-CoV-2 infection when in close contact with patients with COVID-19. The numbers affected were comparable to the numbers affected following COVID-19 contact outside work. Close contact with co-workers was also a risk factor. This stresses the need for increased focus on preventive actions to secure healthcare workers' health during ongoing and future waves of SARSCoV-2 and other infections.

51. **How many relevant SARS-CoV-2 variants might we expect in the future?**
Littera R., Melis M.
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Abstract

Objectives: The emergence of new SARS-CoV-2 variants is a major challenge in the management of Covid-19 pandemic. A crucial issue is to quantify the number of variants which may represent a potential risk for public health in the future. Methods:

We fitted the data on the most relevant SARS-CoV-2 variants recorded by the World Health Organization (WHO). The function exploited for the fit is related to the total number of infected subjects in the world since the start of the epidemic. Results: We found that the number of relevant SARS-CoV-2 variants up to November 2021 was about 44. Moreover, the number of new relevant variants per ten million cases turned out to be 1.64 in November 2021, slightly decreased in comparison to the value of 2.29 in March 2020. Conclusions: Our simple mathematical model can evaluate the number of relevant SARS-CoV-2 variants as the cumulative number of cases increase worldwide and may represent a useful tool in planning strategies to effectively contrast the pandemic.

52. **Krebs von den Lungen 6 levels in COVID-19 ICU patients are associated with mortality**
Scarpati G., Baldassarre D., Lacava G., Oliva F., Pascale G., Boffardi M., Pagliano P., Calabrese V., Tripepi G.L., Piazza O.
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Abstract

Rationale Krebs von den Lungen 6 (KL-6) is a high molecular weight mucin-like glycoprotein produced by type II pneumocytes and bronchial epithelial cells. Elevated circulating levels of KL-6 may denote disorder of the alveolar epithelial lining. Objective Aim of this study was to verify if KL-6 values may help to risk stratify and triage severe COVID-19 patients. Methods We performed a retrospective prognostic study on 110 COVID-19 ICU patients, evaluating the predictive role of KL-6 for mortality. Measurements and Main Results The study sample was divided in two groups related according to the median KL-6 value [Group A (KL-6 lower than the log-transformed median (6.73)) and Group B (KL-6 higher than the log-transformed median)]. In both linear and logistic multivariate analyses, ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (P/F) was significantly and inversely related to KL-6. Death rate was higher in group B than in group A (80.3 versus 45.9%) ($p<0.001$). Accordingly, the Cox regression analysis showed a significant prognostic role of KL-6 on mortality in the whole sample as well as in the subgroup with SOFA lower than its median value. Conclusions At ICU admission, KL-6 serum level was significantly lower in the survivors group. Our findings shown that, in severe COVID19 patients, elevated KL-6 was strongly associated with mortality in ICU.

53. **SeroTracker-ROB: Reproducible decision rules for risk of bias assessment of seroprevalence studies**
Bobrovitz N., Noël K., Li Z., Cao C., Deveaux G., Selemon A., Lane M.Y., Yan T., Arora R.
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Abstract

Background: Conducting risk of bias assessments for seroprevalence studies is a crucial component of infection surveillance but can be a time-consuming and subjective process. We aimed to develop and evaluate decision rules for transparent and reproducible risk of bias assessments of seroprevalence studies. Methods: We developed the SeroTracker-ROB decision rules, which generate risk of bias assessments for seroprevalence studies from an adapted version of the Joanna Briggs Institute Critical Appraisal Checklist for Prevalence Studies. The decision rules were developed using published guidance on risk of bias assessment for prevalence studies, and the consensus opinions of researchers that have critically appraised thousands of prevalence studies. The decision rules were evaluated against SeroTracker's living systematic review database of SARS-CoV-2 seroprevalence studies. We determined decision rule coverage by calculating the proportion of database studies for which SeroTracker-ROB yielded a risk of bias assessment, and reliability by calculating intraclass correlations between SeroTracker-RoB assessments and the consensus manual judgements of two independent reviewers. Results: The SeroTracker-ROB decision rules for risk of bias assessment classified 100% (n = 2,070) of prevalence studies in SeroTracker's database and showed good reliability compared to manual review (intraclass correlation 0.77, 95% CI 0.74 to 0.80). We developed a tool that implements these decision rules for use by other researchers. Conclusions: The SeroTracker-ROB decision rules enabled rapid, transparent, and reproducible risk of bias assessment of seroprevalence studies, and may serve to support infection surveillance.

54. **An integrative method for COVID-19 patients' classification from chest X-ray using deep learning network with image visibility graph as feature extractor**
Pal M., Tiwari Y., Vineeth Reddy T., Sai Ram Aditya P., Panigrahi P.K.
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Abstract

We propose a method by integrating image visibility graph and deep neural network (DL) for classifying COVID-19 patients from their chest X-ray images. The computed assortative coefficient from each image horizonal visibility graph (IHVG) is utilized as a physical parameter feature extractor to improve the accuracy of our image classifier based on Resnet34 convolutional neural network (CNN). We choose the most optimized recently used CNN deep learning model, Resnet34 for training the pre-processed chest X-ray images of COVID-19 and healthy individuals. Independently, the preprocessed X-ray images are passed through a 2D Haar wavelet filter that decomposes the image up to 3 labels and returns the approximation coefficients of the image which is used to obtain the horizontal visibility graph for each X-ray image of both healthy and COVID-19 cases. The corresponding assortative coefficients are computed for each IHVG and was subsequently used in random forest classifier whose output is integrated with Resnet34 output in a multi-layer perceptron to obtain the final improved prediction accuracy. We employed a multilayer perceptron to integrate the feature predictor from image visibility graph with Resnet34 to obtain the final image classification result for our proposed method. Our analysis employed much larger chest X-ray image dataset compared to previous used work. It is demonstrated that compared to Resnet34 alone our integrative method shows negligible false negative conditions along with improved accuracy in the classification of COVID-19 patients. Use of visibility graph in this model enhances its ability to extract various qualitative and quantitative complex network features for each image. Enables the possibility of building disease network model from COVID-19 images which is mostly unexplored. Our proposed method is found to be very effective and accurate in disease classification from images and is computationally faster as compared to the use of multimode CNN deep learning models, reported in recent research works.

55. **Role of body mass and physical activity in autonomic function modulation on post-COVID-19 condition: An observational subanalysis of fit-covid study**

Freire A.P.C.F., de Lira F.S., von Ah Morano A.E., Pereira T., Silva M.-J.C., Caseiro A., Christofaro D.G.D., Marchioto O., Dorneles G.P., Pinho R.A., de Alencar Silva B.S.

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Abstract

The harmful effects of coronavirus disease 2019 (COVID-19) can reach the autonomic nervous system (ANS) and endothelial function. Therefore, the detrimental multiorgan effects of COVID-19 could be induced by deregulations in ANS that may persist after the acute SARS-CoV-2 infection. Additionally, investigating the differences in ANS response in overweight/obese, and physically inactive participants who had COVID-19 compared to those who did not have the disease is necessary. The aim of the study was to analyze the autonomic function of young adults after mild-to-moderate infection with COVID-19 and to assess whether body mass index (BMI) and levels of physical activity modulates autonomic function in participants with and without COVID-19. Patients previously infected with COVID-19 and healthy controls were recruited for this cross-sectional observational study. A general anamnesis was taken and BMI and physical activity levels were assessed. The ANS was evaluated through heart rate variability. A total of 57 subjects were evaluated. Sympathetic nervous system activity in post-COVID-19 group was increased (stress index; p=0.0273). They also presented lower values of parasympathetic activity (p<0.05). Overweight/obese subjects in the post-COVID-19 group presented significantly lower parasympathetic activity and reduced global variability compared to non-obese in control group (p<0.05). Physically inactive subjects in post-COVID-19 group presented significantly higher sympathetic activity than active subjects in control group. Parasympathetic activity was significantly increased in physically active subjects in control group compared to the physically inactive post-COVID-19 group (p<0.05). COVID-19 promotes changes in the ANS of young adults, and these changes are modulated by Overweight/obesity and physical activity levels.

56. **Serum SARS-CoV-2 antigens for the determination of COVID-19 severity**

Favresse J., Bayart J.-L., David C., Gillot C., Wieërs G., Roussel G., Sondag G., Elsen M., Eucher C., Dogné J.-M., Douxfils J.

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Abstract

The diagnostic of SARS-CoV-2 infection relies on reverse transcriptase polymerase chain reactions (RT-PCR) performed on nasopharyngeal (NP) swabs. Nevertheless, false negative results can be obtained with inadequate sampling procedures making the use of other matrices of interest. This study aims at evaluating the kinetic of serum N antigen in severe and non-severe patients and compare the clinical performance of serum antigenic assays with NP RT-PCR. Ninety patients were included and monitored for several days. Disease severity was determined according to the WHO clinical progression scale. The serum N

antigen was measured with a chemiluminescent assay (CLIA) and the Single Molecular Array (Simoa). Thresholds for severity were determined. In severe patients, the peak antigen response was observed 7 days after the onset of symptoms followed by a decline. No peak response was observed in non-severe patients. Severity threshold for the Simoa and the CLIA provided positive likelihood ratio of 30.0 and 10.9 for the timeframe between day 2 and day 14, respectively. Compared to NP RT-PCR, antigenic assays were able to discriminate the severity of the disease (p = 0.0174, 0.0310 and p = 0.1551 with the Simoa, the CLIA and the NP RT-PCR, respectively). Sensitive N antigen detection in serum thus provides a valuable new marker for COVID-19 diagnosis and evaluation of disease severity. When assessed during the first 2 weeks since the onset of symptoms, it may help in identifying patients at risk of developing severe COVID-19 to optimize better intensive care utilization.

57. **Healthcare workers benefit from second dose of COVID-19 mRNA vaccine: Effects of partial and full vaccination on sick leave duration and symptoms**
Strum E., Casagrande Y., Newton K., Unger J.B.
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Abstract

Importance: In addition to morbidity and mortality of individuals, COVID-19 can affect staffing among organizations. It is important to determine whether vaccination can mitigate this burden. Objective: This study examined the association between COVID-19 vaccination status and time until return to work among 952 healthcare workers (HCW) who tested positive for COVID-19. Design: Data were collected prospectively between December 2020 and July 2021. HCW who tested positive for COVID-19 completed an initial interview and were followed until they returned to work. Setting: An academic campus in Southern California consisting of two large hospitals and multiple outpatient clinics and other facilities. Participants: Clinical and nonclinical HCW who tested positive for COVID-19 during the study period (N=952, mean age=39.2 years, 69% female, 45% Hispanic, 14% white, 14% Asian/Pacific Islander, 5% African American, and 21% other race/ethnicity). Exposure: COVID-19 vaccination status (unvaccinated, partially vaccinated, or fully vaccinated) Main Outcome Measures: Days until return to work, presenting symptom Results: Return-to-work time for fully vaccinated HCWs (mean=10.9 days) was significantly shorter than that of partially vaccinated HCWs (15.5 days), which in turn was significantly shorter than that of unvaccinated HCWs (18.0 days). Fully vaccinated HCWs also showed milder symptom profiles compared to partially vaccinated and unvaccinated HCWs. Conclusions and Relevance: COVID-19 vaccination has the potential to prevent long absences from work and the adverse financial, staffing, and managerial consequences of these long absences.

58. **Enoxaparin for thromboprophylaxis in hospitalized COVID-19 patients: Comparison of 40 mg o.d. vs 40 mg b.i.d. The X-COVID19 randomized clinical trial**
Morici N., Podda G., Birocchi S., Bonacchini L., Merli M., Trezzi M., Massaini G., Agostinis M., Carioti G., Serino F.S., Gazzaniga G., Barberis D., Antolini L., Valsecchi M.G., Cattaneo M.
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Abstract

It is uncertain whether higher doses of anticoagulants than recommended for thromboprophylaxis are necessary in COVID-19 patients hospitalized in general wards. This is a multicentre, open-label, randomized trial performed in 9 Italian centres, comparing 40 mg b.i.d. vs 40 mg o.d. enoxaparin in COVID-19 patients, between April 30, 2020 and April 25, 2021. Primary efficacy outcome was in-hospital incidence of venous thromboembolism (VTE): asymptomatic or symptomatic proximal deep vein thrombosis (DVT) diagnosed by serial compression ultrasonography (CUS), and/or symptomatic pulmonary embolism (PE) diagnosed by computed tomography angiography (CTA). Secondary endpoints included each individual component of the primary efficacy outcome and a composite of death, VTE, mechanical ventilation, stroke, myocardial infarction, admission to ICU. Safety outcomes included major bleeding. The study was interrupted prematurely due to slow recruitment. We included 183 (96%) of the 189 enrolled patients in the primary analysis (91 in b.i.d., 92 in o.d.). Primary efficacy outcome occurred in 6 patients (6·5%, 0 DVT, 6 PE) in the o.d. group and 0 in the b.id. group (ARR 6·5, 95% CI, 1·5-11·6). Absence of concomitant DVT and imaging characteristics suggest that most pulmonary artery occlusions were actually caused by local thrombi rather than PE. Statistically non-significant differences in secondary and safety endpoints were observed, with two major bleeding events in each arm. In conclusion, no DVT developed in COVID-19 patients hospitalized in general wards, independently of enoxaparin dosing used for thromboprophylaxis. Pulmonary artery occlusions developed only in the o.d. group. Our trial is underpowered and with few events.

59. **Causal inference and COVID-19 nursing home patients: Identifying factors that reduced mortality risk**
Ahmed A., Goldberg R., Swiader J., Wintrob Z.A.P., Yilmaz M.
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Abstract

Less than 1% of the US population lives in long-term care facilities, yet this subset of the population accounts for 22% of total COVID-19 related deaths. Because of a lack of experimental evidence to treat COVID-19, analysis of real-world data to identify causal relationships between treatments/policies to mortality and morbidity among high-risk individuals is critical. We applied causal inference (CI) analysis to longitudinal patient-level health data of 4,091 long-term care high-risk patients with COVID-19 to determine if any actions or therapies delivered from January to August of 2020 reduced COVID-19 patient mortality rates during this period. Causal inference findings determined that certain supportive care interventions caused reduced mortality rates for nursing home residents regardless of severity of disease (as measured by oxygen saturation level, presence of pneumonia and organ failure), comorbidities or social determinants of health such as race, age, and weight. While we do not address the biological mechanisms associated with specific medical interventions and their impact on mortality, this analysis suggests methods to validate and optimize treatment protocols using domain knowledge and causal inference analysis of real-world data across patient populations and care settings.

60. **Failure of concentric regulatory zones to halt the spread of COVID-19 in South Brooklyn, New York: October-November 2020**

Harris J.E.

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Abstract

We relied on reports of confirmed case incidence and test positivity, along with data on the movements of devices with location-tracking software, to evaluate a novel scheme of three concentric regulatory zones introduced by then New York Governor Cuomo to address an outbreak of COVID-19 in South Brooklyn in the fall of 2020. The regulatory scheme imposed differential controls on access to eating places, schools, houses of worship, large gatherings and other businesses within the three zones, but without restrictions on mobility. Within the central red zone, COVID-19 incidence temporarily declined from 131.2 per 100,000 population during the week ending October 3 to 62.5 per 100,000 by the week ending October 31, but then rebounded to 153.6 per 100,000 by the week ending November 28. Within the intermediate orange and peripheral yellow zones combined, incidence steadily rose from 28.8 per 100,000 during the week ending October 3 to 109.9 per 100,000 by the week ending November 28. Data on device visits to pairs of eating establishments straddling the red-orange boundary confirmed compliance with access controls. More general analysis of device movements showed stable patterns of mobility between and beyond zones unaffected by the Governor's orders. A geospatial regression model of COVID-19 incidence in relation to device movements across zip code tabulation areas identified a cluster of five high-mobility ZCTAs with estimated reproduction number 1.91 (95% confidence interval, 1.27-2.55). In the highly populous area of South Brooklyn, controls on access alone, without restrictions on mobility, were inadequate to halt an advancing COVID-19 outbreak.

61. **Very high relative seroprevalence of anti-SARS-CoV-2 antibodies among communities in Bangui, Central African Republic**

Alexandre M., Christian M., Martial Y.B., Henri D.S.-C., de Dieu L.J., Joella N., Gomelle C.-R.C.S., Modeste B., Darnycka B.M.R., Baptiste R.J., Patrice K.N., Gérard G., Guy V., Marie-Astrid V., Emmanuel N.

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Abstract

Background: Large-scale population-based seroprevalence studies of SARS-CoV-2 are essential to characterize the cumulative incidence of SARS-CoV-2 infection and to extrapolate the prevalence of presumptive immunity at the population level. Objective: The objective of our survey was to estimate the cumulative population immunity for COVID-19 and to identify individual characteristics associated with a positive serostatus. Method: This was a clustered cross-sectional study conducted from July 12 to August 20, 2021, in households in the city of Bangui, the capital of the Central African Republic. Information regarding demographic characteristics (age, gender, and place of residence), comorbidities (chronic diseases) was collected. A venous blood sample was obtained for each participant to determine the level of total anti-SARS-CoV-2 antibodies using a WANTAI SARS-CoV-2 Ab ELISA kit. Results: All up, 799 participants were surveyed. The average age was 27 years, and 45·8% of the respondents were male (sex ratio: 0.8). The overall proportion of respondents with a positive serostatus was 74·1%. Participants over 20 years of age were twice as likely to have a positive serostatus, with an OR of 2.· ·2 (95% CI: [1·6, 3·1]). Interpretation:

The results of this survey revealed a high cumulative level of immunity in Bangui, thus indicating a significant degree of spread of SARS-CoV-2 in the population. The public health implications of this high level of immunity to SARS-CoV-2, particularly on its variants burden, remain to be determined.

62. **Baseline hypocapnia is associated with intubation in COVID-19 diagnosed patients**
Gounidis A., Evangeliou A.P., Kloura C., Manganari E., Parisi C., Kourtidis M., Kotronis G., Apostolopoulou M., Apostolidou-Kiouti F.
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Abstract

Introduction Hypocapnia may be one of the several factors predefining the need for intubation of patients needing hospitalization for COVID-19 pneumonia. Methods A retrospective evaluation of patient files hospitalized for COVID-19 pneumonia from October 2020 until January 2021. Univariate and multivariate regression was used, as well as a multinomial regression to account for multiple endpoints (discharge, intubation, death). Results Hypocapnia was strongly associated with intubation (OR: 0.86, 95% CI: 0.76, 0.97). Additionally, last pCO2 (OR: 1.08, 95% CI: 1.01, 1.16), baseline FiO2 (OR: 1.05, 95% CI: 1.03, 1.07) as well as last FiO2 (OR: 1.21, 95% CI: 1.11, 1.46), total severity score on admission (OR: 1.18, 95% CI: 1.03, 1.37) and last pO2 (OR: 0.89, 95% CI: 0.85, 0.92) were found to have a significant impact on intubation. Incorporation of deceased patients withheld the negative association with pCO2 levels (OR: 0.88, 95% CI: 0.78, 0.98). Conclusion The dissociation between respiratory failure and a clinically comfortable patient is partly due to decreased carbon dioxide levels and clinicians should bare it in mind when handling patients with COVID-19 pneumonia. Hypocapnia seems to be a determinant factor of intubation in patients with COVID-19 pneumonia in this study.

63. **Longitudinal SARS-CoV-2 RNA wastewater monitoring across a range of scales correlates with total and regional COVID-19 burden in a well-defined urban population**
Acosta N., Bautista M.A., Waddell B.J., McCalder J., Beaudet A.B., Man L., Pradhan P., Sedaghat N., Papparis C., Bacanu A., Hollman J., Krusina A., Southern D., Williamson T., Li C., Bhatnagar S., Murphy S., Chen J., Kuzma D., Meddings J., Hu J., Cabaj J.L., Conly J.M., Ruecker N.J., Achari G., Ryan M.C., Frankowski K., Hubert C.R.J., Parkins M.D.
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Abstract

Wastewater-based epidemiology (WBE) is an emerging surveillance tool that has been used to monitor the ongoing COVID-19 pandemic by tracking SARS-CoV-2 RNA shed into wastewater. WBE was performed to monitor the occurrence and spread of SARS-CoV-2 from three wastewater treatment plants (WWTP) and six neighborhoods in the city of Calgary, Canada (population 1.3 million). A total of 222 WWTP and 192 neighborhood samples were collected from June 2020 to May 2021, encompassing the end of the first-wave (June 2020), the second-wave (November end to December, 2020) and the third-wave of the COVID-19 pandemic (mid-April to May, 2021). Flow-weighted 24-hour composite samples were processed to extract RNA that was then analyzed for two SARS-CoV-2-specific regions of the nucleocapsid gene, N1 and N2, using reverse transcription-quantitative polymerase chain reaction (RT-qPCR). Using this approach SARS-CoV-2 RNA was detected in 98.06 % (406/414) of wastewater samples. SARS-CoV-2 RNA abundance was compared to clinically diagnosed COVID-19 cases organized by the three-digit postal code of affected individuals' primary residences, enabling correlation analysis at neighborhood, WWTP and city-wide scales. Strong correlations were observed between N1 & N2 gene signals in wastewater and new daily cases for WWTPs and neighborhoods. Similarly, when flow rates at Calgary's three WWTPs were used to normalize observed concentrations of SARS-CoV-2 RNA and combine them into a city-wide signal, this was strongly correlated with regionally diagnosed COVID-19 cases and clinical test percent positivity rate. Linked census data demonstrated disproportionate SARS-CoV-2 in wastewater from areas of the city with lower socioeconomic status and more racialized communities. WBE across a range of urban scales was demonstrated to be an effective mechanism of COVID-19 surveillance.

64. **Modelling optimal vaccination strategies against Covid-19 in a context of Gamma variant predominance in Brazil**
Ferreira L.S., de Almeida G.B., Borges M.E., Simon L.M., Poloni S., Bagattini Â.M., da Rosa M.Q.M., Filho J.A.F.D., de Souza Kuchenbecker R., Camey S.A., Kraenkel R.A., Coutinho R.M., Toscano C.M.
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Abstract

Brazil experienced moments of collapse in its health system throughout 2021, driven by a timid initial vaccination strategy against Covid-19, combined with the emergence of variants of interest (VOC). Mathematical modelling has been used to subsidize decision-makers in public health planning. Considering the vaccine products available, effectiveness estimates, the emergence of Gamma as the predominant VOC circulating in 2021, and national estimated doses available for the next several months, we developed a Markov-chain mathematical modelling approach to evaluate optimal strategies for Covid-19 vaccination in Brazil in terms of Covid deaths averted. Our main findings are that in order to reach higher vaccination impact in Brazil, Covid-19 immunization strategies should include recovering vaccination coverage rates in high-risk groups reaching higher coverage; expanding vaccination to younger age groups should be considered only after ensuring at least 80% coverage in older age groups; reducing the interval between doses of AZD1222 from 12 to 8 weeks. We also demonstrate that the latter is only feasible if accompanied by an increase in vaccine supply of at least 50% in the next six month period.

65. **Emergence and widespread circulation of a recombinant SARS-CoV-2 lineage in North America**

Gutierrez B., Castelán Sánchez H.G., da Silva Candido D., Jackson B., Fleishon S., Ruis C., Delaye L., Rambaut A., Pybus O.G., Escalera-Zamudio M.

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Abstract

Genetic recombination is an important driving force of coronavirus evolution. While some degree of virus recombination has been reported during the COVID-19 pandemic, previously detected recombinant lineages of SARS-CoV-2 have shown limited circulation and been observed only in restricted areas. Prompted by reports of unusual genetic similarities among several Pango lineages detected mainly in North and Central America, we present a detailed phylogenetic analysis of four SARS-CoV-2 lineages (B.1.627, B.1.628, B.1.631 and B.1.634) in order to investigate the possibility of virus recombination among them. Two of these lineages, B.1.628 and B.1.631, are split into two distinct clusters (here named major and minor). Our phylogenetic and recombination analyses of these lineages find well-supported phylogenetic differences between the Orf1ab region and the rest of the genome (S protein and remaining reading frames). The lineages also contain several deletions in the NSP6, Orf3a and S proteins that can augment reconstruction of reliable evolutionary histories. By reconciling the deletions and phylogenetic data, we conclude that the B.1.628 major cluster originated from a recombination event between a B.1.631 major virus and a lineage B.1.634 virus. This scenario inferred from genetic data is supported by the spatial and temporal distribution of the three lineages, which all co-circulated in the USA and Mexico during 2021, suggesting this region is where the recombination event took place. We therefore support the designation of the B.1.628 major cluster as recombinant lineage XB in the Pango nomenclature. The widespread circulation of lineage XB across multiple countries over a longer timespan than the previously designated recombinant XA lineage raises important questions regarding the role and potential effects of recombination on the evolution of SARS-CoV-2 during the ongoing COVID-19 pandemic.

66. **Myocarditis and pericarditis following COVID-19 vaccination: Rapid systematic review of incidence, risk factors, and clinical course**

Pillay J., Bialy L., Gaudet L., Wingert A., Mackie A.S., Paterson D.I., Hartling L.

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Abstract

Objectives: Myocarditis and pericarditis are adverse events of special interest after vaccination with mRNA vaccines. This rapid systematic review examined incidence rates of myocarditis and pericarditis after COVID-19 vaccination, and the presentation and clinical course of cases. Design: Rapid systematic review Data sources: Medline, Embase and the Cochrane Library were searched from October 2020 to October 6, 2021; reference lists and grey literature (to Oct 21, 2021). Review methods: Randomized controlled trials (RCTs) and large population-based/multisite observational studies and surveillance data reporting on myocarditis or pericarditis in people of any age after receiving any COVID-19 vaccine; systematic reviews of case series. A single reviewer completed screening and another verified 50% of exclusions, using a machine-learning program to prioritize records. A second reviewer verified all exclusions at full text, data extractions, and (for incidence) risk of bias assessments using Cochrane Risk of Bias 2.0 and Joanna Briggs Institute tools. Certainty of evidence ratings for incidence were based on team consensus using GRADE. Patient partners provided key messages from their interpretations of the findings. Results: 3457 titles/abstracts and 159 full texts were screened. For incidence rates we included 7 RCTs (n=3732 to 44,325) and 22 large observational studies/data sources using passive (n=10) and active (n=12) surveillance; for case presentation, we included 11 case series published as articles and three based on publicly available websites (n=12,636 cases). Mainly due to imprecision,

the RCTs provided very low certainty evidence for incidence of myocarditis or pericarditis. From observational data, the incidence of myocarditis following mRNA vaccines is low but probably highest in males 12-17 years (55 [7-day risk] to 134 [30-day risk] cases per million; specific to Pfizer) and 18-29 years (40 [7-day risk] to 99 [21-30 day risk]) cases per million) (Moderate certainty evidence). Incidence is lower (<20 per million) or little-to-none in older ages and across all ages of females (Low certainty). Evidence for pericarditis was of very low certainty. Among adult males under 40 years, Moderna compared with Pfizer vaccine may be associated with a small increase (<20 per million) in risk for myocarditis or (one of) myocarditis or pericarditis following vaccination (Low certainty); the evidence for youth under 18 years was very uncertain. No study examined differences in incidence based on pre-existing condition(s) or risk factors apart from age and sex. The majority of myocarditis cases involved males (often >90%) in their 20s, with a short symptom onset of 2 to 4 days after a second dose (71-100%). The majority of cases presented with chest pain/pressure and troponin elevation; a minority (<30%) had left ventricular dysfunction. Most were hospitalized (≥84%), without stays in intensive care units, for a short duration (2-4 d) and treated with anti-inflammatory and/or other supportive therapies. Almost all reports of death are from unverified cases and of unclear cause. Most cases of pericarditis were unconfirmed; for this outcome there appears to be more variation in age, sex, onset timing and rate of hospitalization. Conclusions:Incidence of myocarditis following mRNA vaccines is low but probably highest in males 12-29 years old. Existing evidence does not strongly support preference of one mRNA vaccine, even in young males. Continued active surveillance of myocarditis incidence out to 30 days from dosing is recommended with respect to i) new populations (i.e., children <12y), ii) third and subsequent doses, and iii) affected individuals receiving subsequent mRNA vaccine doses. Future research is needed to examine other risk factors and long-term effects.

67. **Race-specific, U.S. state-specific COVID-19 vaccination rates adjusted for age**
Wrigley-Field E., Berry K.M., Persad G.
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Abstract

We provide the first age-standardized race/ethnicity-specific, state-specific vaccination rates for the United States, encompassing all states reporting race/ethnicity-specific vaccinations. The data reflect vaccinations through mid-October 2021. We use indirect age standardization to compare racial/ethnic state vaccination rates to national age-specific vaccination patterns. Results show that white and Black state median vaccination rates are, respectively, 89% and 76% of what would be predicted based on age; Hispanic and Native rates are almost identical to what would be predicted; and Asian-American/Pacific Islander rates are 110% of what would be predicted. We also find that racial/ethnic group vaccination rates are associated with state politics, as proxied by 2020 Trump vote share: for each percentage point increase in 2020 Trump vote share, vaccination rates decline by 1.08 percent of what would be predicted based on age. This decline is sharpest for Native American populations, although Native vaccinations are reported for relatively few states.

68. **SARS-CoV2 serology assays: Utility and limits of different antigen based tests through the evaluation and the comparison of four commercial tests**
Gdoura M., Halouani H., Mrad M., Donia S., Chamsa W., Mabrouk M., Salem K.B., Hogga N., Triki H.
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Abstract

Introduction: SARS-CoV2 serology testing is multipurpose provided to choose an efficient test. We evaluated and compared 4 different commercial serology tests, three of them had the Food and Drug Administration (FDA) approval. Our goal was to provide new data to help to guide the interpretation and the choice of the serological tests. Methods: Four commercial tests were evaluated: Cobas®Roche®(total anti-N antibodies), VIDAS®Biomerieux®(IgM and IgG anti-RBD antibodies), Mindray®(IgM and IgG anti-N and anti-RBD antibodies) and Access®Beckman Coulter®(IgG anti-RBD antibodies). Were tested: a positive panel (n=72 sera) obtained from COVID-19 confirmed patients and a negative panel (n=119) of pre-pandemic sera. Were determined the analytical performances and was drawn the ROC curve to assess the manufacturer's threshold. Results: A large range of variability between the tests was found. Mindray®IgG and Cobas® tests showed the best overall sensitivity 79,2%CI95%[67,9-87,8]. Cobas® showed the best sensitivity after D14; 85,4%CI95%[72,2-93,9]. The best specificity was noted for Cobas®, VIDAS®IgG and Access® IgG(100%CI95%[96,9-100]). Access® had the lower sensitivity even after D14 (55,5% CI95%[43,4-67,3]). VIDAS®IgM and Mindray®IgM tests showed the lowest specificity and sensitivity rates. Overall, only 43 out of 72 sera gave concordant results (59,7%). Retained cut-offs for a significantly better sensitivity and accuracy, without altering significantly the specificity, were: 0,87 for Vidas®IgM($p=0,01$), 0,55 for Vidas®IgG($p=0,05$) and 0,14 for Access®($p<10^{-4}$). Conclusion: Although FDA approved, each laboratory should realize its own evaluation for commercial tests. Tests variability may raise some concerns that seroprevalence studies may vary significantly based on the used serology test.

69. **Patient experience with healthcare: Feedback for a 'post COVID-19 clinic' at a tertiary care center in rural area**
Garg A., Subramain M., Barlow P.B., Garvin L., Hoth K.F., Dukes K., Hoffman R.M., Comellas A.P.
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Abstract

Purpose: Post-acute sequelae of SARS-CoV-2 (PASC) is a complex condition with multisystem involvement. We assessed patients' perspectives and experience with a PASC clinic established at University of Iowa in June 2020. Methods: We conducted a mixed-method survey in June 2021 to ask PASC clinic patients about 1) PASC symptoms and their impact on physical and mental health, and cognition using the PROMIS Global Health and Cognitive Function abilities items, and 2) satisfaction with clinic services and referrals, barriers to care, and recommended support resources. Findings: Ninety-seven patients (97/277, 35% response rate) completed the survey. Most were women (67%, n=65/97), Caucasian (93%, n=90/97) and received outpatient care during acute COVID-19 illness (79%). Fifty percent reported wait time of 1-3 months and 40% traveled >1 hour for appointment. The most common symptoms >3 months from initial infection were fatigue (77%), "brain fog" (73%), exercise intolerance (73%), anxiety (63%), sleep difficulties (56%) and depression (44%). Qualitative analysis of open-ended answers added valuable context to quantitative results. A minority of patients reported significantly reduced functioning (≥1.5 SD below mean) of their physical health (22.5%), mental health (15.9%) and cognitive abilities (17.6%). Satisfaction with clinical services was high though participants identified barriers to care including scheduling delays and financial concerns. Respondents suggested potential strategies for optimizing recovery including continuity of care, a co-located multispecialty clinic and being provided with timely information from emerging research. Conclusion: Our study reports high PASC symptom burden, its impact on health and patient experience with healthcare. It is important that primary healthcare professionals listen to patients with empathy and support them during recovery. Healthcare systems and policymakers should focus on accessible, comprehensive, and patient-centered integrated care.

70. **Immunogenicity of heterologous prime/boost inactivated and mRNA COVID-19 vaccine**
Wanlapakorn N., Yorsaeng R., Phowatthanasathian H., Suntronwong N., Kanokudom S., Sudhinaraset N., Poovorawan Y.
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Abstract

Introduction: In August 2021, Thailand imported the BNT162b2 mRNA COVID-19 vaccine. The prioritised group to receive the BNT162b2 vaccine were health professionals. The BNT162b2 vaccine scheduled for healthcare workers were two-dose regimen administered three weeks apart, the third dose booster in two-dose inactivated CoronaVac vaccine recipients or as a second dose in health professionals who had received the CoronaVac or adenoviral-vectored (ChAdOx1-S) vaccine as the first dose regardless of the interval between the first and second dose. Methods: This study aims to evaluate the immunogenicity of the heterologous prime boost CoronaVac followed by BNT162b2 in health professionals. Results: The CoronaVac/BNT162b2 vaccine recipients elicited higher neutralizing activity against the original Wuhan and all variants of concern than in the recipients of the two-dose CoronaVac. Conclusions: The heterologous CoronaVac/BNT162b2 could be used as an alternative regimen in countries experiencing the vaccine shortages and in individuals experiencing the adverse events following CoronaVac.

71. **Strategy for a rapid screening and surveillance of SARS-CoV-2 variants by real time RT-PCR: A key tool that allowed control and delay in Delta spread in Cordoba, Argentina**
Castro G.M., Sicilia P., Bolzon M.L., López L., Barbás M.G., Pisano M.B., Ré V.E.
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Abstract

Background: SARS-CoV-2 variants of concern (VOC) and interest (VOI) present mutations in reference to the original virus, being more transmissible. We implemented a rapid strategy for the screening of SARS-CoV-2 VOC/VOIs using real time RT-PCR and performed monitoring and surveillance of the variants in our region. Methods: consecutive real-time RT-PCRs for detection of the relevant mutations/deletions present in the Spike protein in VOC/VOIs (TaqMan™ SARS-CoV-2 Mutation Panel, Applied Biosystems) were implemented. An algorithm was established and 3941 SARS-CoV-2 RNA samples (Cts<30) obtained from oropharyngeal swabs from infected individuals in Córdoba, Argentina, between January and October 2021, were analyzed.

Results: the strategy of choice included a first screening of 3 mutations (N501Y, E484K, L452R) followed by the detection of other mutations/deletions based on the results. The analyses of the samples showed introductions of VOCs Alpha and Gamma in February and March 2021, respectively. Since then, Alpha presented a low to moderate circulation (1.7% of the SARS-CoV-2 currently detected). Gamma showed an exponential increase, with a peak of detection in July (72%), until reaching a current frequency of 41.1%. VOC Delta was first detected in July in travellers and currently represents 35% of detections in the community. VOI Lambda presented a gradual increase, showing a current frequency of 29%. Conclusions: we report a useful tool for VOC/VOI detection, innovative for Argentina, capable to quickly and cost-effectively monitor currently recognized variants. It was key in the early detection of Delta, being able to implement measures to delay its dissemination.

72. **A SARS-CoV-2 delta variant containing mutation in the probe binding region used for qRT-PCR test in Japan exhibited atypical PCR amplification and might induce false negative result**
Rajib S.A., Ogi Y., Hossain Md.B., Ikeda T., Tanaka E., Kawaguchi T., Satou Y.
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Abstract

A recent pandemic of SARS-CoV-2 infection has caused severe health problems and substantially restricted social and economic activities. To cope with such an outbreak, the identification of infected individuals with high accuracy is vital. qRT-PCR plays a key role in the diagnosis of SARS-CoV-2 infection. The N protein-coding region is widely analyzed in qRT-PCR for the diagnosis of SARS-CoV-2 infection in Japan. We recently encountered two cases of SARS-CoV-2-positive specimens showing atypical amplification curves in the qRT-PCR. We performed whole-genome sequencing and found that the virus was a Delta-type variant of SARS-CoV-2 with a single nucleotide mutation in the probe-binding site. To evaluate the extent of spread of the variant in the area, we performed whole viral genome sequencing of samples collected from 61 patients infected with SARS-CoV-2 during the same time and in the same area. There were no other cases with the same mutation, indicating that the variant had not spread in the area. Furthermore, we performed phylogenetic analysis with various SARS-CoV-2 sequences deposited in the public database. Hundreds of variants were reported globally, and one in Japan were found to contain the same mutation. Phylogenetic analysis showed that the variant was very close to other Delta variants endemic in Japan but quite far from the variants containing the same mutation reported from outside Japan, suggesting that the variant would have been sporadically generated in some domestic areas. These findings propose two key points: i) mutations in the region used for SARS-CoV-2 qRT-PCR can cause abnormal amplification curves; therefore, the qRT-PCR result should not just be judged in an automated manner, but also manually checked by the examiner to prevent false-negative results, and ii) various mutations can be generated sporadically and unpredictably; therefore, efficient and robust screening systems are needed to promptly monitor the emergence of de novo variants.

73. **A prospective study of asymptomatic SARS-CoV-2 infection among individuals involved in academic research under limited operations during the COVID-19 pandemic**
Pettifor A., DiPrete B.L., Shook-Sa B.E., Premkumar L., Kuczynski K., Dittmer D., Aiello A., Wallet S., Maile R., Tan J., Jadi R., Pluta L., de Silva A.M., Weber D.J., Kim M., Seña A.C., Jones C.D.
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Abstract

Background: Early in the pandemic, transmission risk from asymptomatic infection was unclear making it imperative to monitor infection in workplace settings. Further, data on SARS-CoV-2 seroprevalence within university populations has been limited. Methods: We performed a longitudinal study of University research employees on campus July-December 2020. We conducted questionnaires on COVID-19 risk factors, RT-PCR testing, and SARS-CoV-2 serology using an in-house spike RBD assay, laboratory-based Spike NTD assay, and standard nucleocapsid platform assay. We estimated prevalence and cumulative incidence of seroconversion with 95% confidence intervals using the inverse of the Kaplan-Meier estimator. Results: 910 individuals were included in this analysis. At baseline, 6.2% (95% CI 4.29-8.19) were seropositive using the spike RBD assay; four (0.4%) were seropositive using the nucleocapsid assay, and 44 (4.8%) using the Spike NTD assay. Cumulative incidence was 3.61% (95% CI: 2.04-5.16). Six asymptomatic individuals had positive RT-PCR results. Conclusions: Prevalence and incidence of SARS-CoV-2 infections was low; however differences in target antigens of serological tests provided different estimates. Future research on appropriate methods of serological testing in unvaccinated and vaccinated populations is needed. Frequent RT-PCR testing of asymptomatic individuals is required to detect acute infections, and repeated serosurveys are beneficial for monitoring subclinical infection.

74. **Encounters after appointments cancelled due to COVID-19 in the veterans affairs health care system**
Tran L.D., Rose L., Urech T., Vashi A.

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Abstract

This statistical brief examines subsequent encounters after a cancellation due to COVID-19 in the Veterans Affairs System. We find that he vast majority of VA patients that had appointments cancelled in mid-March to mid-April of 2020 had another encounter within 180 days. The most common next encounter was a virtual visit with a VA provider on the same day of the original appointment. We also find that patients that saw a provider through VA community care had a lower median time to next encounter.

75. **Impact of dexamethasone on persistent symptoms of COVID-19: An observational study**

Milne A., Maskell S., Sharp C., Hamilton F.W., Arnold D.T.

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Abstract

Introduction Dexamethasone has been shown to reduce mortality for patients hospitalised with acute COVID-19 pneumonia. However, a significant proportion of patients suffer persistent symptoms following COVID-19 and little is known about the longer-term impact of this intervention on symptom burden. Methods Patients initially hospitalised with COVID-19 were prospectively recruited to an observational study (April-August 2020) with follow-up at 8 months (Dec 2020-April 2021) post-admission. A review of ongoing symptoms using a standardised systems-based proforma was performed alongside health-related quality of life assessment. In the UK, patients with COVID-19 (requiring oxygen) only received dexamethasone following the pre-print of the RECOVERY trial (June 2020), or as part of randomisation to that trial, allowing for a comparison between patients treated and not treated with dexamethasone. Results Between April to August 2020, 198 patients were recruited to this observational study. 87 required oxygen and were followed up at 8-months, so were eligible for this analysis. Of these 39 received an inpatient course of dexamethasone (cases) and 48 did not (controls). The groups were well matched at baseline in terms of age, comorbidity and frailty score. Over two-thirds of patients reported at least 1 ongoing symptom at 8-month follow-up. Patients in the dexamethasone group reported fewer symptoms (n=73, 1.9 per patient) than the non-dexamethasone group (n=152, 3.2 per patient) (p = 0.01). Conclusions In conclusion, in this case-control observational study, patients who received oral dexamethasone for hospitalised COVID-19 were less likely to experience persistent symptoms at 8-month follow-up. These are reassuring results for physicians administering dexamethasone to this patient group.

76. **Modeling COVID-19 care capacity in a major health system**

Erlendsdottir M., Eshghi S., Crawford F.

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Abstract

Hospital resources, especially critical care beds and ventilators, have been strained by additional demand throughout the COVID-19 pandemic. Rationing of scarce critical care resources may occur when available resource limits are exceeded. However, the dynamic nature of the COVID-19 pandemic and variability in projections of the future burden of COVID-19 infection pose challenges for optimizing resource allocation to critical care units in hospitals. Connecticut experienced a spike in the number of COVID-19 cases between March and June 2020. Uncertainty about future incidence made it difficult to predict the magnitude and duration of the increased COVID-19 burden on the healthcare system. In this paper, we describe a model of COVID-19 hospital capacity and occupancy that generates estimates of the resources necessary to accommodate COVID-19 patients under infection scenarios of varying severity. We present the model structure and dynamics, procedure for parameter estimation, and publicly available web application where we implemented the tool. We then describe calibration using data from over 3,000 COVID-19 patients seen at the Yale-New Haven Health System between March and July 2020. We conclude with recommendations for modeling tools to inform decision-making using incomplete information during future crises.

77. **HLA-A*03:01 is associated with increased risk of fever, chills, and more severe reaction to Pfizer-BioNTech COVID-19 vaccination**

Bolze A., Neveux I., Schiabor Barrett K.M., White S., Isaksson M., Dabe S., Lee W., Grzymski J.J., Washington N.L.,

Cirulli E.T.
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Abstract

COVID-19 vaccines are safe and highly effective, but some individuals experience unpleasant reactions to vaccination. As the majority of adults in the US have received a COVID-19 vaccine this year, there is an unprecedented opportunity to study the genetics of reactions to vaccination via surveys of individuals who are already part of genetic research studies. Here, we have queried 17,440 participants in the Helix DNA Discovery Project and Healthy Nevada Project about their reactions to COVID-19 vaccination. Our GWAS identifies an association between severe difficulties with daily routine after vaccination and HLA-A*03:01. This association was statistically significant only for those who received the Pfizer-BioNTech vaccine (BNT162b2; p=4.70E-11), but showed a trending association in those who received the Moderna vaccine (mRNA-1273; p=0.005) despite similar sample sizes for study. In Pfizer-BioNTech recipients, HLA-A*03:01 was associated with a two-fold increase in risk of severe vaccine reactions. The effect was consistent across ages, sexes, and whether the person had previously had a COVID-19 infection. The reactions experienced by HLA-A*03:01 carriers were driven by associations with chills, fever, fatigue, and in general feeling unwell.

78. **COVID-19 management in social care in England: A systematic review of changing policies and newspaper reported staff perspectives**
Bertini L., Bogen-Johnston L., Middleton J., Wood W., Sadhwani S., Forder J., Roland D., Sharp R., Drury J., Cassell J.A.
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Abstract

Adult social care has been a major focus of public attention and infection control guidance during the COVID-19 pandemic, with a high mortality both for carers and those receiving care. To protect themselves and others from infection, staff in residential and domiciliary care settings had to quickly adapt to infection control measures that heavily impacted on their working and every-day life, whilst navigating new responsibilities, uncertainties and anxieties. We sought to explore the production and reception of guidance and look at ways these can be adapted to improve the working life of care staff in domiciliary and residential care whilst reducing the risk of SARS-CoV-2 transmission amid this pandemic and of future emerging infections. We conducted two complementary and integrated systematic reviews of published documents in the pre-vaccination era: (1) National guidance for social care (conducted between 29 July to 28 October 2020), and (2) Newspaper coverage of infection control issues in social care (conducted between 27th July to 10th September 2020). Three higher order common themes emerged in the integrated systematic review of guidance documents and newspaper articles: a) Testing, b) Personal Protective Equipment, c) Employment. The reviews revealed a sharp disjunction between the content of infection control guidance and its usability and applicability in social care settings. We suggest that infection control guidance needs to be better adapted to social care settings and informed by the sector. The practicalities of care work and care settings need to be at the core of the process for guidance to be relevant and effective. Modes and timings of communications also need to be optimised.

79. **Durability of anti-Spike antibodies in the infant after maternal COVID-19 vaccination**
Shook L.L., Atyeo C.G., Yonker L.M., Fasano A., Gray K.J., Alter G., Edlow A.G.
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Abstract

COVID-19 vaccination in pregnancy generates functional anti-Spike IgG antibodies that are known to cross the placenta. However, the durability of vaccine-induced maternal anti-S IgG in infant circulation, and how it compares to durability of antibody from maternal natural infection, is unknown. We quantified anti-S IgG in 92 2-month and 6-month-old infants whose mothers were vaccinated in pregnancy, and in 12 6-month-old infants after maternal natural infection with SARS-CoV-2. In the vaccinated group, 94% (58/62) of infants had detectable anti-S IgG at 2 months, and 60% (18/30) had detectable antibody at 6 months. In contrast, 8% (1/12) of infants born to women infected with SARS-CoV-2 in pregnancy had detectable anti-S IgG at the 6-month timepoint. Vaccination resulted in significantly higher maternal and cord titers at delivery and significantly greater antibody persistence in infants at 6 months, compared to natural infection.

80. **Experiences of staff providing specialist palliative care during COVID-19: A multiple qualitative case study**
Bradshaw A., Dunleavy L., Garner I., Preston N., Bajwah S., Cripps R., Fraser L.K., Maddocks M., Hocaoglu M., Murtagh F.E.M., Oluyase A.O., Sleeman K.E., Higginson I.J., Walshe C.
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Abstract

Objectives: To explore the experiences of, and impact on, staff working in palliative care during the COVID-19 pandemic. Design: Qualitative multiple case study using semi-structured interviews between November 2020 and April 2021 as part of the CovPall study. Data were analysed using thematic framework analysis. Setting: Organisations providing specialist palliative services in any setting. Participants: Staff working in specialist palliative care, purposefully sampled by the criteria of role, care setting and COVID-19 experience. Main outcome measures: Experiences of working in palliative care during the COVID-19 pandemic. Results: Five cases and 24 participants were recruited (n=12 nurses, 4 clinical managers, 4 doctors, 2 senior managers, 1 healthcare assistant, 1 allied healthcare professional). Central themes demonstrate how infection control constraints prohibited and diluted participants' ability to provide care that reflected their core values, resulting in experiences of moral distress. Despite organisational, team, and individual support strategies, continually managing these constraints led to a 'crescendo effect' in which the impacts of moral distress accumulated over time, sometimes leading to burnout. Solidarity with colleagues and making a valued contribution provided 'moral comfort' for some. Conclusions: This study provides a unique insight into why and how healthcare staff have experienced moral distress during the pandemic, and how organisations have responded. Despite their experience of dealing with death and dying, the mental health and well-being of palliative care staff was affected by the pandemic. Organisational, structural, and policy changes are urgently required to mitigate and manage these impacts.

81. **Immunoglobulin G1 Fc glycosylation as an early hallmark of severe COVID-19**
Pongracz T., Nouta J., Wang W., van Meijgaarden K.E., Linty F., Vidarsson G., Joosten S.A., Ottenhoff T.H.M., Hokke C.H., de Vries J.J.C., Arbous S.M., Roukens A.H.E., Wuhrer M., van den Berg B.M., Cannegieter S., Cobbaert C.M., van der Does A., van Dongen J.J.M., Eikenboom H.C.J., Feltkamp M.C.M., Geluk A., Goeman J.J., Giera M., 5.1.2e ., Heemskerk M.H.M., Hiemstra P.S., Janse J.J., Jochems S.P., Kikkert M., Lamont L., Manniën J., del Prado M.R., Queralt Rosinach N., 5.1.2e ., Roos M., Smits H.H., Snijder E.J., Staal F.J.T., Trouw L.A., Tsonaka R., Verhoeven 1 ., 5.1.2e L.G., de Vries J.J.C., van Westerloo D.J., Wigbers J., van der Wijk H.J., van Wissen R.C., Yazdanbakhsh M., Zlei M., Baysan M., de Boer M.G.J., van der Bom A.G., Dekkers O.M., Eikenboom A.M., ter Haar S.B., Heerdink L., van Heurn L.J., de Jonge I., Lijfering W., Meier R., Oud J.A., Rosendaal F., Toppenberg A.G.L., Uzorka J., van IJlzinga Veenstra A.A., Wigbers J., Wubbolts J.M.
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Abstract

Background Immunoglobulin G1 (IgG1) effector functions are impacted by the structure of fragment crystallizable (Fc) tail-linked N-glycans. Low fucosylation levels on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike protein specific (anti-S) IgG1 has been described as a hallmark of severe coronavirus disease 2019 (COVID-19) and may lead to activation of macrophages via immune complexes thereby promoting inflammatory responses, altogether suggesting involvement of IgG1 Fc glycosylation modulated immune mechanisms in COVID-19. Methods In this prospective, observational single center cohort study, IgG1 Fc glycosylation was analyzed by liquid chromatography - mass spectrometry following affinity capturing from serial plasma samples of 159 SARS-CoV-2 infected patients. Findings At baseline close to disease onset, anti-S IgG1 glycosylation was highly skewed when compared to total plasma IgG1. A rapid, general reduction in glycosylation skewing was observed during the disease course. Low anti-S IgG1 galactosylation and sialylation as well as high bisection were early hallmarks of disease severity, whilst high galactosylation and sialylation and low bisection were found in patients with low disease severity. In line with these observations, anti-S IgG1 glycosylation correlated with various inflammatory markers. Interpretation Association of low galactosylation, sialylation as well as high bisection with disease severity suggests that Fc-glycan modulated interactions contribute to disease mechanism. Further studies are needed to understand how anti-S IgG1 glycosylation may contributes to disease mechanism and to evaluate its biomarker potential.

82. **Evaluation of a novel direct capture method for virus concentration n wastewater from COVID-19 infectious ward and correlation analysis with the number of inpatients**
Inaba M., Nakao R., Imamura F., Nakashima Y., Miyazono S., Akamatsu Y.
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Abstract

The global outbreak of the SARS-CoV-2 pandemic has increased the focus of Wastewater-based epidemiology (WBE) studies as a tool for understanding the epidemic and risk management. A highly sensitive and rapid method for the virus concentration from wastewater is needed to obtain the accurate information for early detection of SARS-CoV-2 outbreak and epidemic. In this study, we evaluated the efficiency of the direct capture method provided from Promega, based on column adsorption using the wastewater from actual infectious diseases ward. The efficiency of the nucleic acid extraction-purification process was also evaluated by Maxwell® RSC instrument (fully automated extraction) and QIAamp Viral RNA mini kit (manual extraction). The obtained SARS-CoV-2 data from wastewater were analyzed with the number of inpatients which is the consideration of the severity and the days of onset. The combination of direct capture and Maxwell's method (DC-MW) was suggested to be a highly sensitive and simple method with better concentration efficiency and quantification than other methods. Moreover, the inpatient conditions (severity and days of after onset) should be considered to accurately understand the actual status of the correlation between the number of inpatients and SARS-CoV-2 concentration in wastewater. The highly sensitive method of DC-MW was suggested to assess more actual situation of SARS-CoV-2 shedding into the wastewater.

83. **Transmission potential of vaccinated and unvaccinated persons infected with the SARS-CoV-2 Delta variant in a federal prison, July—August 2021**

Salvatore P.P., Lee C.C., Sleweon S., McCormick D.W., Nicolae L., Knipe K., Dixon T., Banta R., Ogle I., Young C., Dusseau C., Salmonson S., Ogden C., Godwin E., Ballom T., Ross T., Wynn N.T., David E., Bessey T.K., Kim G., Suppiah S., Tamin A., Harcourt J.L., Sheth M., Lowe L., Browne H., Tate J.E., Kirking H.L., Hagan L.M.

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Abstract

Background The extent to which vaccinated persons who become infected with SARS-CoV-2 contribute to transmission is unclear. During a SARS-CoV-2 Delta variant outbreak among incarcerated persons with high vaccination rates in a federal prison, we assessed markers of viral shedding in vaccinated and unvaccinated persons. Methods Consenting incarcerated persons with confirmed SARS-CoV-2 infection provided mid-turbinate nasal specimens daily for 10 consecutive days and reported symptom data via questionnaire. Real-time reverse transcription-polymerase chain reaction (RT-PCR), viral whole genome sequencing, and viral culture was performed on these nasal specimens. Duration of RT-PCR positivity and viral culture positivity was assessed using survival analysis. Results A total of 978 specimens were provided by 95 participants, of whom 78 (82%) were fully vaccinated and 17 (18%) were not fully vaccinated. No significant differences were detected in duration of RT-PCR positivity among fully vaccinated participants (median: 13 days) versus those not fully vaccinated (median: 13 days; p=0.50), or in duration of culture positivity (medians: 5 days and 5 days; p=0.29). Among fully vaccinated participants, overall duration of culture positivity was shorter among Moderna vaccine recipients versus Pfizer (p=0.048) or Janssen (p=0.003) vaccine recipients. Conclusions As this field continues to develop, clinicians and public health practitioners should consider vaccinated persons who become infected with SARS-CoV-2 to be no less infectious than unvaccinated persons. These findings are critically important, especially in congregate settings where viral transmission can lead to large outbreaks.

84. **The unmitigated profile of COVID-19 infectiousness**

Sender R., Bar-On Y.M., Park S.W., Noor E., Dushoff J., Milo R.

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Abstract

Quantifying the temporal dynamics of infectiousness of individuals infected with SARS-CoV-2 is crucial for understanding the spread of the COVID-19 pandemic and for analyzing the effectiveness of different mitigation strategies. Many studies have tried to use data from the onset of symptoms of infector-infectee pairs to estimate the infectiousness profile of SARS-CoV-2. However, both statistical and epidemiological biases in the data could lead to an underestimation of the duration of infectiousness. We correct for these biases by curating data from the initial outbreak of the pandemic in China (when mitigation steps were still minimal), and find that the infectiousness profile is wider than previously thought. For example, our estimate for the proportion of transmissions occurring 14 days or more after infection is an order of magnitude higher - namely 19% (95% CI 10%-25%). The inferred generation interval distribution is sensitive to the definition of the period of unmitigated transmission, but estimates that rely on later periods are less reliable due to intervention effects. Nonetheless, the results are robust to other factors such as the model, the assumed growth rate and possible bias of the dataset. Knowing the unmitigated infectiousness profile of infected individuals affects estimates of the effectiveness of self-isolation and quarantine of contacts. The framework presented here can help design better quarantine policies in early stages of future epidemics using data from the initial stages of

transmission.

85. **Humoral immune response after COVID-19 infection or BNT162b2 vaccine among older adults: Evolution over time and protective thresholds**
Meyer M., Constancias F., Worth C., Meyer A., Muller M., Boussuge A., Kaltenbach G., Schmitt E., Chayer S., Velay A., Vogel T., Fafi-Kremer S., Karcher P.
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Abstract

INTRODUCTION The objectives of this study were to assess the dynamics of the SARS-CoV-2 anti-RBD IgG response over time among older people after COVID-19 infection or vaccination and its comparison with speculative levels of protection assumed by current data. METHODS From November 2020 to October 2021, we included geriatric patients with serological test results for COVID-19. We considered antibody titre thresholds thought to be high enough to protect against SARS-CoV-2 infection: 141 BAU/ml for protection/vaccine efficacy > 89.3%. Three cohorts are presented. A vaccine group (n=34) that received two BNT162b2/Comirnaty injections 21 days apart, a group of natural COVID-19 infection (n=32) and a third group who contracted COVID-19 less than 15 days after the first BNT162b2/Comirnaty injection (n=17). RESULTS 83 patients were included, the median age was 87 (81-91) years. In the vaccine group at 1 month since the first vaccination, the median BAU/ml with IQR was 620 (217-1874) with 87% of patients above the threshold of 141 BAU/ml. Seven months after the first vaccination the BAU/ml was 30 (19-58) with 9.5% of patients above the threshold of 141 BAU/ml. In the natural COVID-19 infection group, at 1 month since the date of first symptom onset, the median BAU/ml was 798 (325-1320) with 86.7% of patients above the threshold of 141 BAU/ml and fell to 88 (37-385) with 42.9% of patients above the threshold of 141 BAU/ml at 2 months. The natural infection group was vaccinated three months after the infection. Five months after the end of the vaccination cycle the BAU/ml was 2048 (471-4386) with 83.3% of patients above the threshold of 141 BAU/ml. DISCUSSION On the humoral level, this supports the clinical results describing the decrease in vaccine protection over time.

86. **Anti-SARS-CoV-2 antibodies seroprevalence among patients submitted to treatment for tuberculosis in Rio de Janeiro, Brazil: A cross-sectional study**
Gomes K.M., Leite S.P., Moutinho M.H.V., de Souza T.A., de Cássia Batista R., de Oliveira L.C.M., Redner P., Ramos J.P., da Rocha F.M.G., de Oliveira G.P., Teva A., do Couto Mottad F., de Siqueira M.A.M.T., Duarte R.S., Bastos F.I.P.M., de Sousa Viana P.V.
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Abstract

Due to tuberculosis (TB) patients' pulmonary damages, some authors believe that a SARS-CoV-2 coinfection may result in unfavorable outcomes. A cross-sectional anti-SARS-CoV-2 antibodies seroprevalence study was conducted at a TB treatment tertiary referral unit in Rio de Janeiro, Brazil, to estimate the proportion (in %) of TB patients exposed to the new coronavirus and their main outcomes. Of 83 patients undergoing TB treatment, 26.5% have already been infected by the new coronavirus. Most patients were. asymptomatic (69%) or had mild COVID-19 cases (31%). Only one patient required hospitalization. Among the symptoms and signs presented, the most frequently reported were: fever, headache, and myalgia. People with less education and less purchasing power seemed to had been more exposed to SARS-CoV-2.

87. **Effects of trust, risk perception, and health behavior on COVID-19 disease burden: Evidence from a multi-state US survey**
Ridenhour B.J., Sarathchandra D., Seamon E., Brown H., Leung F.-Y., Johnson-Leon M., Megheib M., Miller C.R., Johnson-Leung J.
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Abstract

Early public health strategies to prevent the spread of COVID-19 in the United States relied on non-pharmaceutical interventions (NPIs) as vaccines and therapeutic treatments were not yet available. Implementation of NPIs, primarily social distancing and

mask wearing, varied widely between communities within the US due to variable government mandates, as well as differences in attitudes and opinions. To understand the interplay of trust, risk perception, behavioral intention, and disease burden, we developed a survey instrument to study attitudes concerning COVID-19 and pandemic behavioral change in three states: Idaho, Texas, and Vermont. We designed our survey (n = 1034) to detect whether these relationships were significantly different in rural populations. The best fitting structural equation models show that trust indirectly affects protective pandemic behaviors via health and economic risk perception. We explore two different variations of this social cognitive model: the first assumes behavioral intention affects future disease burden while the second assumes that observed disease burden affects behavioral intention. In our models we include several exogenous variables to control for demographic and geographic effects. Notably, political ideology is the only exogenous variable which significantly affects all aspects of the social cognitive model (trust, risk perception, and behavioral intention). While there is a direct negative effect associated with rurality on disease burden, likely due to the protective effect of low population density in the early pandemic waves, we found a marginally significant, positive, indirect effect of rurality on disease burden via decreased trust (p = 0.095). This trust deficit creates additional vulnerabilities to COVID-19 in rural communities which also have reduced healthcare capacity. Increasing trust by methods such as in-group messaging could potentially remove some of the disparities inferred by our models and increase NPI effectiveness.

88. **Epithelial RIG-I inflammasome activation suppresses antiviral immunity and promotes inflammatory responses in virus-induced asthma exacerbations and COVID-19**

Radzikowska U., Eljaszewicz A., Tan G., Stocker N., Heider A., Westermann P., Steiner S., Dreher A., Wawrzyniak P., Rückert B., Rodriguez-Coira J., Zhakparov D., Huang M., Jakiela B., Sanak M., Moniuszko M., O'Mahony L., Kebadze T., Jackson D.J., Edwards M.R., Thiel V., Johnston S.L., Akdis C.A., Sokolowska M.

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Abstract

Rhinoviruses (RV) and inhaled allergens, such as house dust mite (HDM) are the major agents responsible for asthma onset, its life-threatening exacerbations and progression to severe disease. The role of severe acute respiratory syndrome coronavirus (SARS-CoV-2) in exacerbations of asthma or the influence of preexisting viral or allergic airway inflammation on the development of coronavirus disease 2019 (COVID-19) is largely unknown. To address this, we compared molecular mechanisms of HDM, RV and SARS-CoV-2 interactions in experimental RV infection in patients with asthma and healthy individuals. RV infection was sensed via retinoic acid-inducible gene I (RIG-I) helicase, but not via NLR family pyrin domain containing 3 (NLRP3), which led to subsequent apoptosis-associated speck like protein containing a caspase recruitment domain (ASC) recruitment, oligomerization and RIG-I inflammasome activation. This phenomenon was augmented in bronchial epithelium in patients with asthma, especially upon pre-exposure to HDM, which itself induced a priming step, pro-IL-1b release and early inhibition of RIG-I/TANK binding kinase 1/IkB kinase e /type I/III interferons (RIG-I/TBK1/IKKe/IFN-I/III) responses. Excessive activation of RIG-I inflammasomes was partially responsible for the alteration and persistence of type I/III IFN responses, prolonged viral clearance and unresolved inflammation in asthma. RV/HDM-induced sustained IFN I/III responses initially restricted SARS-CoV-2 replication in epithelium of patients with asthma, but even this limited infection with SARS-CoV-2 augmented RIG-I inflammasome activation. Timely inhibition of the epithelial RIG-I inflammasome and reduction of IL-1b signaling may lead to more efficient viral clearance and lower the burden of RV and SARS-CoV-2 infection.

89. **Attenuation of antibody titres during 3-6 months after the second dose of the BNT162b2 vaccine depends on sex, with age and smoking as risk factors for lower antibody titres at 6 months**

Nomura Y., Sawahata M., Nakamura Y., Koike R., Katsube O., Hagiwara K., Niho S., Masuda N., Tanaka T., Sugiyama K.

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Abstract

Objective: We aimed to determine antibody titres at 6 months and their rate of change during 3-6 months after the second dose of the BNT162b2 coronavirus disease 2019 (COVID-19) mRNA vaccine (Pfizer/BioNTech) and to explore clinical variables associated with titres in Japan. Methods: We enrolled 365 healthcare workers (250 women, 115 men) whose 3-month antibody titres were analyzed in our previous study and whose blood samples were collected 183 ± 15 days after the second dose. Participant characteristics collected previously were used. The relationships of these factors with antibody titres at 6 months and rates of change in antibody titres during 3-6 months were analyzed. Results: Median age was 44 years. Median antibody titre at 6 months was 539 U/mL. Older participants had significantly lower antibody titres (20s, 752 U/mL; 60s-70s, 365 U/mL). In age-adjusted analysis, smoking was the only factor associated with lower antibody titres. Median rate of change in antibody titres during 3-6 months was −29.4%. The only factor significantly associated with the rate of change in Ab titres was not age or smoking, but sex (women, −31.6%; men, −25.1%). Conclusion: The most important factors associated with lower antibody titres at 6 months were age and smoking, as at 3 months, probably reflecting their effect on peak antibody titres. However, antibody titres significantly attenuated during 3-6 months in women alone, which reduced the sex difference in antibody titres seen during the first 3 months. Antibody titres may be affected by different factors at different time points.

90. **A booster dose of an inactivated vaccine increases neutralizing antibodies and T cell responses against SARS-CoV-2**

Schultz B.M., Melo-González F., Duarte L.F., Gálvez N.M.S., Pacheco G.A., Soto J.A., Berríos-Rojas R.V., González L.A., Moreno-Tapia D., Rivera-Pérez D., Hoppe-Elsholz G., Iturriaga C., Ríos M., Vallejos O.P., Urzua M., Vázquez Y., Navarrete M.S., Rojas Á., Weiskopf D., Sette A., Zeng G., Meng W., González-Aramundiz J.V., González P.A., Abarca K., Kalergis A.M., Bueno S.M.

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Abstract

Numerous vaccines have been generated to decrease the morbidity and mortality of COVID-19. CoronaVac® is an inactivated SARS-CoV-2 vaccine approved by the World Health Organization (WHO) to prevent COVID-19 that has safety and immunogenicity profiles described in different clinical trials. We previously reported an increase in levels of neutralizing antibodies two- and four-weeks after administering two doses of CoronaVac® in a two-week interval (0-14 day) vaccination schedule, as compared to pre-immune sera in adults in the Chilean population that are participating in a phase 3 clinical trial. Here we report the levels of antibodies directed against the Receptor Binding Domain of the SARS-CoV-2 spike protein comparing their neutralizing capacities and the cellular response at five months after the second dose and four weeks after a booster (third) dose in volunteers immunized with two doses of CoronaVac® in a four-week interval (0-28 day) vaccination schedule. We observed a decrease in the levels of anti-SARS-CoV-2 antibodies with neutralizing capacities five months after the second dose (GMU 39.0 95% confidence interval (CI)□(32.4-47.0), which increased up to 12 times at four weeks after the booster dose (GMU 499.4, 95% CI=370.6-673.0). Equivalent results were observed in adults aged 18-59 years old and individuals ≥60 years old. In the case of cellular response, we observed that activation of specific $CD4^+$ T cell increases in time and reaches its maximum at four weeks after the booster dose in both groups. Our results support the notion that a booster dose of the SARS-CoV-2 inactivated vaccine increases the levels of neutralizing antibodies and the specific cellular response in adults of both groups, which is likely to boost the protective capacity of these vaccines against COVID-19.

91. **Impact of SARS-CoV-2 vaccines on Covid-19 incidence and mortality in the United States**

Fang F., 5.1.2e **J.D., Zhang Z.-F., Brewer T.F.**

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Abstract

Background: Despite safe and effective vaccines to prevent Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) infections and disease, a substantial minority of the US remains resistant to getting vaccinated. It is imperative to know if expanding vaccination rates could reduce community-wide Coronavirus 2019 (COVID-19) disease, not just among those vaccinated. Methods: Negative binomial models were used to estimate associations between U.S. county-level vaccination rates and county-wide COVID-19 incidence and mortality between April 23rd and September 30th, 2021. A two-week lag and a four-week lag were introduced to assess vaccination rate impact on incidence and mortality, respectively. Stratified analyses were performed for county vaccination rates >40%, and before and after Delta became the dominant variant. Findings: Among 3,070 counties, each percentage increase in population vaccination rates reduced county-wide COVID-19 incidence by 0·9% (relative risk (RR) 0. 9910 (95% CI: 0·9869, 0·9952)) and mortality by 1·9% (RR 0·9807 (95% CI: 0·9745, 0·9823)). Among counties with vaccination coverage >40%, each percentage increase in vaccination rates reduced COVID-19 disease by 1·5%, RR 0·9850 (95% CI: 0·9793, 0·9952) and mortality by 2·7% (RR 0·9727 (95% CI: 0·9632, 0·9823)). These associations were not observed among counties with <40% vaccination rates. Increasing vaccination rates from 40% to 80% would have reduced COVID-19 cases by 45·4% (RR 0·5458 (95% CI: 0·4335, 0·6873)) and deaths by 67·0% (RR 0·3305 (95% CI: 0·2230, 0·4898)). An estimated 5,989,952 COVID-19 cases could have been prevented and 127,596 lives saved had US population vaccination rates increased from 40% to 80%. Interpretations: Increasing U.S. SARS-CoV-2 vaccination rates results in population-wide reductions in COVID-19 incidence and mortality. Furthermore, increasing vaccination rates above 40% has protective effects among non-vaccinated persons. Given ongoing vaccine hesitancy in the U.S., increasing vaccination rates could better protect the entire community and potentially reach herd immunity.

92. **Unraveling the spatiotemporal spread of COVID-19 in Brazil through spatial network connectivity**

Barrozo L.V., Small C.

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Abstract

Background: Describing and understanding the process of diffusion can allow local managers better plan emergence scenarios. Thus, the main aim of this study was to describe and unveil the spatiotemporal patterns of diffusion of the COVID-19 in Brazil from February 2020 until April 2021. Methods: This is a retrospective purely observational ecologic study including all notified cases and deaths. We used satellite-derived night light imagery and spatiotemporal Empirical Orthogonal Function analysis to quantify the spatial network structure of lighted development and the spatiotemporal transmission of the pathogen through the network. Results: The more populous state capitals within the largest network components presented higher frequency of deaths and earlier onset compared to the increasing numbers of smaller, less populous municipalities trending toward lower frequency of deaths and later onset. By week 48 2020, the full network was almost completely affected. Cases and deaths showed a distinct second wave of wider geographic expansion beginning in early November 2020. Conclusions: The spatiotemporal diffusion in Brazil was characterized by an intertwined process of overseas relocation, hierarchical network transmission and contagious effects. A rapid response as the immediate control of all ports, airports and borders combined with mandatory quarantine are critical to retard disease diffusion.

93. **The direct and indirect effects of a global pandemic on US fishers and seafood workers**

White E., Levine J., Moeser A., Sorensen J.

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Abstract

The United States' seafood industry experienced major shifts in consumer demand and COVID-19 social-distancing restrictions starting in March 2020, when the early stages of the pandemic were unfolding. However, the specific effects on workers across seafood value chains are less well known. According to the US Centers for Disease Control and Protection (CDC), fishers and seafood workers face an increased risk of workplace exposure to COVID-19 given the close proximity to others in processing facilities and on fishing vessels, long work hours, and communal housing, living, and transportation arrangements associated with seasonal employment. To explore this hypothesis, and given a lack of data on the sector, we reviewed news articles, scientific articles, and white papers to identify the various effects of COVID-19 on US seafood workers and to track COVID-19 cases and outbreaks. Here, we show that most COVID-19 cases among seafood workers were reported during the summer of 2020 and during the beginning of 2021 with outbreaks primarily occurring in seafood processing. COVID-19 cases were documented throughout coastal areas, with Alaska experiencing the largest number of cases and outbreaks. Based on news reports, seafood workers were about twice as likely to contract COVID-19 as workers in other parts of the overall US food system. By examining news articles and scientific literature, we also documented several indirect effects of the pandemic. Social-distancing restrictions limited crew size and number of workers on processing lines, resulting in longer work hours and more physical and mental taxation. Economic consequences of the pandemic were reportedly a primary concern for fishers and aquaculture businesses, including changes in markets, supply, and demand, in addition to revenue loss, price fluctuations, supply chain issues, and labor shortages. Fewer outlets interviewed workers in seafood processing; however, concerns about workplace safety, contracting COVID-19, access to medical services, vaccination, and paid sick leave were all noted. We also highlight several inequities in COVID-19 responses within the seafood sector, both along racial and gender lines. Peer-reviewed studies and news coverage all point to diverse direct and indirect effects of the COVID-19 pandemic on workers across seafood value chains. The summary of these effects can serve as a foundation for future work on infection control and occupational outreach to workers in the seafood sector.

94. **Estimating COVID-19-induced excess mortality in Lombardy**

Maruotti A., Jona-Lasinio G., Divino F., Lovison G., Ciccozzi M., Farcomeni A.

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Abstract

We compare the expected all-cause mortality with the observed one for different age classes during the pandemic in Lombardy, which was the epicenter of the epidemic in Italy and still is the region most affected by the pandemic. A generalized linear mixed model is introduced to model weekly mortality from 2011 to 2019, taking into account seasonal patterns and year-specific trends. Based on the 2019 year-specific conditional best linear unbiased predictions, a significant excess of mortality is estimated in 2020, leading to approximately 35000 more deaths than expected, mainly arising during the first wave. In 2021, instead, the excess mortality is not significantly different from zero, for the 85+ and 15-64 age classes, and significant reductions with respect to the 2020 estimated excess mortality are estimated for other age classes.

95. **Continued effectiveness of COVID-19 vaccination among urban healthcare workers during delta variant predominance**

Lan F.-Y., Sidossis A., Iliaki E., Buley J., Nathan N., Bruno-Murtha L.A., Kales S.N.

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Abstract

Background: Data on COVID-19 vaccine effectiveness (VE) among healthcare workers (HCWs) during periods of delta variant predominance are limited. Methods: We followed a population of urban Massachusetts HCWs (45% non-White) subject to epidemiologic surveillance. We accounted for covariates such as demographics and community background infection incidence, as well as information bias regarding COVID-19 diagnosis and vaccination status. Results and Discussion: During the study period (December 16, 2020 to September 30, 2021), 4615 HCWs contributed to a total of 1,152,486 person-days at risk (excluding 309 HCWs with prior infection) and had a COVID-19 incidence rate of 5.2/10,000 (114 infections out of 219,842 person-days) for unvaccinated person-days and 0.6/10,000 (49 infections out of 830,084 person-days) for fully vaccinated person-days, resulting in an adjusted VE of 82.3% (95% CI: 75.1-87.4%). For the secondary analysis limited to the period of delta variant predominance in Massachusetts (i.e., July 1 to September 30, 2021), we observed an adjusted VE of 76.5% (95% CI: 40.9-90.6%). Independently, we found no re-infection among those with prior COVID-19, contributing to 74,557 re-infection-free person-days, adding to the evidence base for the robustness of naturally acquired immunity. Background Data on COVID-19 vaccine effectiveness (VE) among healthcare workers (HCWs) during periods of delta variant predominance are limited. Literature accounting for other potential determinants of infection rates is even more scarce. Objective To investigate the continued effectiveness of COVID-19 vaccination during the Delta variant predominance in a diverse and urban healthcare setting.

96. **Presence of SARS-CoV-2 in food surfaces and public space surfaces in 3 districts of Lima, Peru**

Alvis-Chirinos K., Angulo-Bazán Y., Escalante-Maldonado O., Fuentes D., Rodriguez M.G.P., Gonzales-Achuy E., Mormontoy H., Hinojosa P., Huamán-Espino L., Aparco J.P.

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Abstract

Objective: The goal of this study is to determine the presence of SARS-CoV-2 in food surfaces and public space surfaces in 3 districts of Lima, Peru. Material and methods: Cross-sectional descriptive study, carried out in the districts of San Juan de Lurigancho, San Martin de Porres and Villa el Salvador. Surfaces that were exposed to the greatest user manipulation were selected, samples were swabbed for 4 weeks and transported to the laboratory to determine the presence of the virus. Results: 1095 inert surface samples and 960 food surface samples were evaluated for the identification of SARS-CoV-2 by the RT-PCR molecular test, whereby only one sample from an ATM (Automated Teller Machine) was positive. Conclusions: Most of the inert and food surfaces evaluated did not show the presence of SARS-CoV-2 during the time of sample collection. Despite the negative results, the frequency of disinfection measures should be maintained and increased, especially on inert high-contact surfaces, and hygiene measures on food should be continue.

97. **Repeat subcutaneous administration of REGEN-COV® in adults is well-tolerated and prevents the occurrence of COVID-19**

Isa F., Forleo-Neto E., Meyer J., Zheng W., Rasmussen S., Armas D., Oshita M., Brinson C., Folkerth S., Faria L., Heirman I., Sarkar N., Musser B.J., Bansal S., O'Brien M.P., Turner K.C., Ganguly S., Mahmood A., Dupljak A., Hooper A.T., Hamilton J.D., Kim Y., Kowal B., Soo Y., Geba G.P., Lipsich L., Braunstein N., Yancopoulos G.D., Weinreich D.M., Herman G.A.

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Abstract

Background: Data show that a single dose of casirivimab and imdevimab (REGEN-COV®) is effective in treating hospitalized individuals and outpatients with COVID-19 and in post-exposure prophylaxis. We present results from a phase 1, double-blind, placebo-controlled trial evaluating the safety, tolerability, and efficacy of repeat monthly doses of subcutaneous (SC) REGEN-COV in uninfected adult volunteers who were healthy or had chronic stable medical conditions. Methods: Subjects were

randomized (3:1) to SC REGEN-COV 1200 mg or placebo dosed every 4 weeks for up to 6 doses. The primary and secondary endpoints evaluated the safety, pharmacokinetics, and immunogenicity of multiple-dose administration of REGEN-COV. Efficacy was evaluated by the incidence of COVID-19 or SARS-CoV-2 seroconversion. Results: In total, 969 subjects were treated. Repeat monthly dosing of SC REGEN-COV led to a 92.4% relative risk reduction in clinically-defined COVID-19 compared to placebo (3/729 [0.4%] vs 13/240 [5.4%]; odds ratio: 0.07 [95% CI, 0.01–0.27]), and a 100% reduction in laboratory-confirmed COVID-19 (0/729 vs 10/240 [4.2%]; odds ratio 0.00). Development of anti-drug antibodies was low (<5% subjects). No grade ≥3 injection-site reactions (ISRs) or hypersensitivity reactions were reported. A slightly higher percentage of subjects reported TEAEs with REGEN-COV (54.9%) than placebo (48.3%), due to ISRs (all grade 1-2). Serious adverse events were rare and occurred at similar percentages in the REGEN-COV and placebo groups. No deaths were reported in the 6-month treatment period. Conclusions: Repeated monthly administration of 1200 mg SC REGEN-COV was well-tolerated with low immunogenicity, and showed a substantial risk reduction in COVID-19 occurrence.

98. **Positive end expiratory pressure in invasive and non-invasive ventilation of COVID-19 acute respiratory distress syndrome: Computational modeling illuminates the data**
Weaver L., Bates D.G., Camporota L.
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Abstract

Positive end expiratory pressure (PEEP) is routinely used as part of lung protective ventilation strategies in the treatment of acute respiratory distress syndrome (ARDS). In the case of ARDS arising due to COVID-19 (CARDS), there is some debate as to whether the atypical pathophysiological characteristics of the disease which lead to hypoxaemia could warrant a modified approach to ventilator management, particularly with regards to PEEP settings. Here we review the available evidence for the existence of a unique underlying lung pathophysiology in CARDS, and for the suitability of standard approaches to setting PEEP, in both the invasive and non-invasive ventilation settings. We show how detailed computational models informed by this evidence can shed light on the available data, and help to interpret recent results in the literature.

99. **COVID-19 vaccination, risk-compensatory behaviours, and contacts in the UK**
Buckell J., Jones J., Matthews P.C., Diamond S.I., Rourke E., Studley R., Cook D., Walker A.S., Pouwels K.B.
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Abstract

The physiological effects of vaccination against SARS-CoV-2 (COVID-19) are well documented, yet the behavioural effects are largely unknown. Risk compensation suggests that gains in personal safety, as a result of vaccination, are offset by increases in risky behaviour, such as socialising, commuting and working outside the home. This is potentially problematic because transmission of SARS-CoV-2 is driven by contacts, which could be amplified by vaccine-related risk compensation behaviours. Here, we show that behaviours were overall unrelated to personal vaccination, but - adjusting for variation in mitigation policies - were responsive to the level of vaccination in the wider population: individuals in the UK were risk compensating when rates of vaccination were rising. This effect was observed across four nations of the UK, each of which varied policies autonomously.

100. **Association of COVID-19 employment disruption with mental and social wellbeing: Evidence from nine UK longitudinal studies**
Wels J., Booth C., Wielgoszewska B., Green M.J., Di Gessa G., Huggins C.F., Griffith G.J., Kwong A.S.F., Bowyer R.C.E., Maddock J., Patalay P., Silverwood R.J., Fitzsimons E., Shaw R.J., Thompson E., Steptoe A., Hughes A., Chaturvedi N., Steves C.J., Katikireddi S.V., Ploubidis G.B.
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Abstract

Background: The COVID-19 pandemic has led to major economic disruptions. In March 2020, the UK implemented the Coronavirus Job Retention Scheme - known as furlough - to minimize the impact of job losses. We investigate associations between change in employment status and mental and social wellbeing during the early stages of the pandemic. Methods: Data

from 25,670 respondents, aged 16 to 66, from nine UK longitudinal studies were analysed. Changes in employment (including being furloughed) were defined by comparing employment status pre-pandemic and during the first lockdown. Mental and social wellbeing outcomes included psychological distress, life satisfaction, self-rated health, social contact, and loneliness. Study-specific modified Poisson regression estimates, adjusting for socio-demographic characteristics and pre-pandemic outcome measures, were pooled using meta-analysis. Results: Compared to those who remained working, furloughed workers were at greater risk of psychological distress (adjusted risk ratio, ARR=1.12; 95% CI: 0.97, 1.29), low life satisfaction (ARR=1.14; 95% CI: 1.07, 1.22), loneliness (ARR=1.12; 95% CI: 1.01, 1.23), and fair/poor self-rated health (ARR=1.26; 95% CI: 1.05, 1.50), but risk ratios appear less pronounced compared to those no longer employed (e.g., psychological distress, ARR=1.39; 95% CI: 1.21, 1.59) or stable unemployed (e.g., psychological distress, ARR=1.33; 95% CI: 1.09, 1.62). Conclusions: During the early stages of the pandemic those furloughed had increased risk for poor mental and social wellbeing. However, their excess risk was lower in magnitude than those who became or remained unemployed, suggesting that furlough partly mitigated poorer outcomes.

101. **Assessment of breakthrough infections among post-vaccinated healthcare workers in a Tertiary Dental Hospital in New Delhi, India**

Maurya D., Kaur A., Faraz F., Tandon S., Rana A., Grover S.
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Abstract

Background: COVID-19 vaccination in India has been rolled out on a national level, with healthcare workers (HCWs) becoming the first recipient of both Covishield and Covaxin. However, concerns over efficacy of vaccines have been much debated. This study highlights COVID-19 infections among vaccinated HCWs in a teaching dental hospital in Delhi, India. Methodology: This cross-sectional survey was conducted using a pretested, validated, self-instituted questionnaire assessing COVID-19 like symptoms and/or confirmed infections among partially or fully vaccinated HCWs (all faculty, staff and students) of the institute from 16th January to 31st July 2021. The number of infections was also matched with hospital records. Results: Out of 397 HCWs, 386 (97.2%) were vaccinated and 355 (89.4%) had received both doses. COVID-19 like symptoms appeared in 21 HCWs (5.4%) post any dose of vaccine. Symptomatic breakthrough infections >14 days after second dose occurred was seen in 16 HCWs (4.5%). Except one (required hospitalization), all other cases had mild infection. No significant difference was observed between Covishield and Covaxin. Most common symptom was fever and body ache. Conclusion: The study identifies the possibility of breakthrough infections among vaccinated HCWs, and ensures the impact of vaccination in limiting disease severity. The findings suggest that COVID-19 preventive measures should be continued even among vaccinated individuals.

102. **Inhaled prostacyclin improves oxygenation in patients with COVID-19-induced acute respiratory distress syndrome**

Haeberle H.A., Calov S., Martus P., Higuita L.M.S., Koeppen M., Goll A., Zarbock A., Meersch M., Weiss R., Mehrländer M., Marx G., Putensen C., Nieswandt B., Mirakaj V., Rosenberger P.
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Abstract

Background. Acute Respiratory Distress Syndrome (ARDS) results in significant hypoxia, and ARDS is the central pathology of COVID-19. Inhaled prostacyclin has been proposed as a therapy for ARDS, but data regarding its role in this syndrome are unavailable. Therefore, we investigated whether inhaled prostacyclin would affect the oxygenation and survival of patients suffering from ARDS. Methods. We performed a prospective randomized controlled single-blind multicenter trial across Germany. The trial was conducted from March 2019 with final follow-up on 12th of August 2021. Patients with moderate to severe ARDS were included and randomized to receive either inhaled prostacyclin (3 times/day for 5 days) or sodium chloride. The primary outcome was the oxygenation index in the intervention and control groups on Day 5 of therapy. Secondary outcomes were mortality, secondary organ failure, disease severity and adverse events. Findings. Of 707 patients approached 150 patients were randomized to receive inhaled prostacyclin (n=73) or sodium chloride (n=77). Data from 144 patients were analyzed. The baseline oxygenation index did not differ between groups. The primary analysis of the study was negative, and prostacyclin improved oxygenation by 20 mmHg more than NaCl (p=0·17). Oxygenation was significantly improved in patients with ARDS who were COVID-19-positive (34 mmHg, p=0·04). Mortality did not differ between groups. Secondary organ failure and adverse events were similar in the intervention and control groups. Interpretation. Although the primary result of our study was negative, our data suggest that inhaled prostacyclin might be a more beneficial treatment than standard care for patients with ARDS.

103. **Global prevalence of post-acute sequelae of COVID-19 (PASC) or long COVID: A meta-analysis and systematic**

review

Chen C., Haupert S.R., Zimmermann L., Shi X., Fritsche L.G., Mukherjee B.
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Abstract

Importance As SARS-CoV-2 pervades worldwide, considerable focus has been placed on the longer lasting health effects of the virus on the human host and on the anticipated healthcare needs. Objective The primary aim of this study is to examine the prevalence of post-acute sequelae of COVID-19 (PASC), commonly known as long COVID, across the world and to assess geographic heterogeneities through a systematic review and meta-analysis. A second aim is to provide prevalence estimates for individual symptoms that have been commonly reported as PASC, based on the existing literature. Data Sources PubMed, Embase, and iSearch for preprints from medRxiv, bioRxiv, SSRN, and others, were searched on July 5, 2021 with verification extending to August 12, 2021. Study Selection Studies written in English that consider PASC (indexed as ailments persisting at least 28 days after diagnosis or recovery for SARS-CoV-2 infection) and that examine corresponding prevalence, risk factors, duration, or associated symptoms were included. A total of 40 studies were included with 9 from North America, 1 from South America, 17 from Europe, 11 from Asia, and 2 from other regions. Data Extraction and Synthesis Data extraction was performed and separately cross-validated on the following data elements: title, journal, authors, date of publication, outcomes, and characteristics related to the study sample and study design. Using a random effects framework for meta-analysis with DerSimonian-Laird pooled inverse-variance weighted estimator, we provide an interval estimate of PASC prevalence, globally, and across regions. This meta-analysis considers variation in PASC prevalence by hospitalization status during the acute phase of infection, duration of symptoms, and specific symptom categories. Main Outcomes and Measures Prevalence of PASC worldwide and stratified by regions. Results Global estimated pooled PASC prevalence derived from the estimates presented in 29 studies was 0.43 (95% confidence interval [CI]: 0.35, 0.63), with a higher pooled PASC prevalence estimate of 0.57 (95% CI: 0.45, 0.68), among those hospitalized during the acute phase of infection. Females were estimated to have higher pooled PASC prevalence than males (0.49 [95% CI: 0.35, 0.63] versus 0.37 [95% CI: 0.24, 0.51], respectively). Regional pooled PASC prevalence estimates in descending order were 0.49 (95% CI: 0.21, 0.42) for Asia, 0.44 (95% CI: 0.30, 0.59) for Europe, and 0.30 (95% CI: 0.32, 0.66) for North America. Global pooled PASC prevalence for 30, 60, 90, and 120 days after index test positive date were estimated to be 0.36 (95% CI: 0.25, 0.48), 0.24 (95% CI: 0.13, 0.39), 0.29 (95% CI: 0.12, 0.57) and 0.51 (95% CI: 0.42, 0.59), respectively. Among commonly reported PASC symptoms, fatigue and dyspnea were reported most frequently, with a prevalence of 0.23 (95% CI: 0.13, 0.38) and 0.13 (95% CI: 0.09, 0.19), respectively. Conclusions and Relevance The findings of this meta-analysis suggest that, worldwide, PASC comprises a significant fraction (0.43 [95% CI: 0.35, 0.63]) of COVID-19 tested positive cases and more than half of hospitalized COVID-19 cases, based on available literature as of August 12, 2021. Geographic differences appear to exist, as lowest to highest PASC prevalence is observed for North America (0.30 [95% CI: 0.32, 0.66]) to Asia (0.49 [95% CI: 0.21, 0.42]). The case-mix across studies, in terms of COVID-19 severity during the acute phase of infection and variation in the clinical definition of PASC, may explain some of these differences. Nonetheless, the health effects of COVID-19 appear to be prolonged and can exert marked stress on the healthcare system, with 237M reported COVID-19 cases worldwide as of October 12, 2021.

104. **High COVID-19 vaccine coverage allows for a re-opening of European universities**
Lasser J., Hell T., Garcia D.
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Abstract

Returning universities to full on-campus operations while the COVID-19 pandemic is ongoing has been a controversial discussion in many countries. The risk of large outbreaks in dense course settings is contrasted by the benefits of in-person teaching. Transmission risk depends on a range of parameters, such as vaccination coverage, number of contacts and adoption of non-pharmaceutical intervention measures (NPIs). Due to the generalised academic freedom in Europe, many universities are asked to autonomously decide on and implement intervention measures and regulate on-campus operations. In the context of rapidly changing vaccination coverage and parameters of the virus, universities often lack the scientific facts to base these decisions on. To address this problem, we analyse a calibrated, data-driven simulation of transmission dynamics of 10755 students and 974 faculty in a medium-sized university. We use a co-location network reconstructed from student enrolment data and calibrate transmission risk based on outbreak size distributions in other Austrian education institutions. We focus on actionable interventions that are part of the already existing decision-making process of universities to provide guidance for concrete policy decisions. Here we show that with the vaccination coverage of about 80% recently reported for students in Austria, universities can be safely reopened if they either mandate masks or reduce lecture hall occupancy to 50%. Our results indicate that relaxing NPIs within an organisation based on the vaccination coverage of its sub-population can be a way towards limited normalcy, even if nation wide vaccination coverage is not sufficient to prevent large outbreaks yet.

105.

associated with post-acute sequelae of COVID-19 in a digital research cohort

Schultheiß C., Willscher E., Paschold L., Gottschick C., Klee B., Henkes S.-S., Bosurgi L., Dutzmann J., Sedding D., Frese T., Girndt M., Höll J.I., Gekle M., Mikolajczyk R., Binder M.

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Abstract

Post-acute sequelae of COVID-19 (PASC) emerge as a global problem with unknown molecular drivers. In a digital epidemiology approach, we rapidly recruited 8,077 individuals out of 129,733 households in Halle (Saale) to the cohort study for digital health research in Germany (DigiHero). These responded to a basic questionnaire followed by a PASC-focused survey and blood sampling in case of prior positive SARS-CoV-2 testing in their household. The presented analysis is based on the first 318 DigiHero participants, the majority thereof after mild infections. PASC were reported in 67.8% of cases, consisted predominantly in fatigue, dyspnea and concentration deficit, persisted in 60% over the follow-up period of on average eight months and their resolution was unaffected by post-infection vaccination. PASC was not associated with post-COVID-19 autoantibodies, but with elevated levels of IL-1ß, IL-6 and TNF-α. Blood profiling and single-cell data from validation cohorts with early infection suggested the induction of these cytokines in COVID-19 lung pro-inflammatory macrophages creating a self-sustaining feedback loop. Our data indicate a long-lasting cytokine triad - potentially underlying PASC symptoms - to be driven by macrophage primed during infection. We demonstrate how the combination of digital epidemiology with selective biobanking can rapidly generate hints towards disease mechanisms.

106. **Seroprevalence in Tamil Nadu through India's two COVID waves: Evidence on antibody decline following infection and vaccination**

Selvavinayagam T.S., Somasundaram A., Selvam J.M., Ramachandran S., Sampath P., Vijayalakshmi V., Kumar A.B.C., Subramaniam S., Raju S., Avudaiselvi R., Prakash V., Yogananth N., Subramanian G., Roshini A., Dhiliban D.N., Imad S., Tandel V., Parasa R., Sachdeva S., Malani A.

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Abstract

Three rounds of population-representative serological studies through India's two COVID waves (round 1, 19 October-30 November 2020; round 2, 7-30 April 2021; and round 3, 28 June-7 July7, 2021) were conducted at the district-level in Tamil Nadu state (population 72 million). State-level seroprevalence in rounds 1, 2 and 3 were 31.5%, 22.9%, and 67.1%. Estimated seroprevalence implies that at least 22.6 and 48.1 million persons were infected by the 30 November 2020 and 7 July 2021. There was substantial variation across districts in the state in each round. Seroprevalence ranged from 11.1 to 49.8% (round 1), 7.9 to 50.3% (round 2), and 37.8 to 84% (round 3). Seroprevalence in urban areas was higher than in rural areas (35.7 v. 25.7% in round 1, 74.8% v. 64.1% in round 3). Females had similar seroprevalence to males (30.8 v. 30.2% in round 1, 67.5 v. 65.5% in round 3). While working age populations (age 40-49: 31.6%) had significantly higher seroprevalence than the youth (age 18-29: 30.4%) or elderly (age 70+: 26.5%) in round 1, only the gap between working age (age 40-49: 66.7%) and elderly (age 70+: 59.6%) remained significant in round 3. Seroprevalence was greater among those who were vaccinated for COVID (25.7% v. 20.9% in round 2, 80.0% v. 62.3% in round 3). While the decline in seroprevalence from round 1 to 2 suggests antibody decline after natural infection, we do not find significant decline in antibodies among those receiving at least 1 dose of vaccine between rounds 2 and 3.

107. **Curating, collecting, and cataloguing global COVID-19 datasets for the aim of predicting personalized risk**

Khatami S.G., Russo M.F., Domingo-Fernández D., Zaliani A., Mubeen S., Gadiya Y., Sargsyan A., Karki R., Gebel S., Ruppa Surulinathan R.K., Lage-Rupprecht V., Archipovas S., Mingrone G., 5.1.2e ., Claussen C., Hofmann-Apitius M., Kodamullil A.T.

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Abstract

The COVID-19 data catalogue is a repository that provides a landscape view of COVID-19 studies and datasets as a putative source to enable researchers to develop personalized COVID-19 predictive risk models. The COVID-19 data catalogue currently contains over 400 studies and their relevant information collected from a wide range of global sources such as global initiatives,

clinical trial repositories, publications and data repositories. Further, the curated content stored in this data catalogue is complemented by a web application, providing visualizations of these studies, including their references, relevant information such as measured variables, and the geographical locations of where these studies were performed. This resource is one of the first to capture, organize and store studies, datasets and metadata in the area of COVID-19 in a comprehensive repository. We are convinced that our work will facilitate future research and development of personalized predictive risk models of COVID-19.

108. **The challenge of SARS-CoV-2 environmental monitoring in schools using floors and portable HEPA filtration units: Fresh or relic RNA?**
Zuniga-Montanez R., Coil D.A., Eisen J.A., Pechacek R., Guerrero R.G., Kim M., Shapiro K., Bischel H.N.
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Abstract

Testing surfaces in school classrooms for the presence of SARS-CoV-2, the virus that causes COVID-19, can provide public-health information that complements clinical testing. We monitored the presence of SARS-CoV-2 RNA in five schools (96 classrooms) in Davis, California (USA) by collecting weekly surface-swab samples from classroom floors and/or portable high-efficiency particulate air (HEPA) units. Twenty-two surfaces tested positive, with qPCR cycle threshold (Ct) values ranging from 36.07–38.01. Intermittent repeated positives in a single room were observed for both floor and HEPA filter samples for up to 52 days, even following regular cleaning and HEPA filter replacement after a positive result. We compared the two environmental sampling strategies by testing one floor and two HEPA filter samples in 57 classrooms at Schools D and E. HEPA filter sampling yielded 3.02% and 0.41% positivity rates per filter sample collected for Schools D and E, respectively, while floor sampling yielded 0.48% and 0% positivity rates. Our results indicate that HEPA filter swabs are more sensitive than floor swabs at detecting SARS-CoV-2 RNA in interior spaces. During the study, all schools were offered weekly free COVID-19 clinical testing. On-site clinical testing was offered in Schools D and E, and upticks in testing participation were observed following a confirmed positive environmental sample. However, no confirmed COVID-19 cases were identified among students associated with classrooms yielding positive environmental samples. The positive samples detected in this study appeared to reflect relic viral RNA from individuals infected before the monitoring program started and/or RNA transported into classrooms via fomites. The high-Ct positive results from environmental swabs further suggest the absence of active infections. Additional research is needed to differentiate between fresh and relic SARS-CoV-2 RNA in environmental samples and to determine what types of results should trigger interventions.

109. **Controlling SARS-CoV-2 in schools using repetitive testing strategies**
Torneri A., 5.1.2e L., Colizza V., Kremer C., Meuris C., Darcis G., Hens N., Libin P.
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Abstract

SARS-CoV-2 remains a worldwide emergency. While vaccines have been approved and are widely administered, these are only available to adults and adolescents in Europe. Therefore, in order to mitigate the spread of more transmissible SARS-CoV-2 variants among children, the use of non-pharmaceutical interventions is still warranted. We investigate the impact of different testing strategies on the SARS-CoV-2 infection dynamics in a primary school environment, using an individual-based modelling approach. Specifically, we consider three testing strategies: 1) symptomatic isolation, where we test symptomatic individuals and isolate them when they test positive, 2) reactive screening, where a class is screened once one symptomatic individual was identified, and 3) repetitive screening, where the school in its entirety is screened on regular time intervals. Through this analysis, we demonstrate that repetitive testing strategies can significantly reduce the attack rate in schools, contrary to a reactive screening approach. Furthermore, we investigate the impact of these testing strategies on the average number of school days lost per child.

110. **Pulmonary thromboembolism in COVID-19 patients on CT pulmonary angiography - A single-centre retrospective cohort study in the United Arab Emirates**
Gaba W.H., Saeed G.A., Al Kareem Adi A., Al Marshoodi R., Al Mazrouei S., Shah A.R.
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Abstract

Purpose. Our aim is to identify the prevalence and distribution of pulmonary thromboembolism in COVID-19 infected patients in our hospital. Materials and Methods. Data of all patients with COVID-19 infection either on RT-PCR testing or non-contrast high resolution CT(HRCT) who had CT pulmonary angiography (CTPA) from April to June 2020 were included. 133 patients were initially included in the study, 7 were excluded according to exclusion criteria, leaving a total number of 126 patients. Results. Twenty (15.8%) patients had evidence of pulmonary embolism (PE) on CTPA with mean age of 50 years (range 31-85) of which 95% were males. The mean D-dimer was 5.61mcg/mL among the PE-negative and 14.49 mcg/mL in the PE-positive groups respectively. Among the patients with evidence of pulmonary embolism on CTP, almost half required admission to intensive care unit in comparison to only one-fifth with negative CTPA. One-fourth died among the PE positive group with only 5% died among the PE negative group. There was a 33% reduction in the development of PE in the COVID-19 patients who had received low molecular weight heparin (LMWH) prior to their CTPA study versus those who had not. Conclusion. D-dimer correlates well with the incidence of pulmonary embolism among COVID-19 patients. Our data suggest that majority of our patients, developed pulmonary embolisms within 5 days into their hospital stay, accounting to almost two thirds of all positive cases diagnosed by CTPA. Those with PE among COVID-19 patients have high chances of ICU admission and mortality. Use of thromboprophylaxis early on might reduce the incidence of PE.

111. **Early and rapid identification of COVID-19 patients with neutralizing type I-interferon auto-antibodies by an easily implementable algorithm**

Akbil B., Meyer T., Stubbemann P., Thibeault C., Staudacher O., Niemeyer D., 5.1.2e., Mühlemann B., Doehn J., Tabeling C., Nusshag C., Hirzel C., Sanchez D.S., Nieters A., Lother A., Duerschmied D., Schallner N., Lieberum J.N., August D., Rieg S., Falcone V., Hengel H., Kölsch U., Unterwalder N., Hübner R.-H., Jones T.C., Suttorp N., Drosten C., Warnatz K., Spinetti T., Schefold J.C., Dörner T., Sander L., Corman V.M., Merle U., Kurth F., von Bernuth H., Meisel C., Goffinet C.

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Abstract

Purpose Six-19% of critically ill COVID-19 patients display circulating auto-antibodies against type I interferons (IFN-AABs). Here, we establish a clinically applicable strategy for early identification of IFN-AAB-positive patients for potential subsequent clinical interventions. Methods We analysed sera of 430 COVID-19 patients with severe and critical disease from four hospitals for presence of IFN-AABs by ELISA. Binding specificity and neutralizing activity were evaluated via competition assay and virus-infection-based neutralization assay. We defined clinical parameters associated with IFN-AAB positivity. In a subgroup of critically ill patients, we analyzed effects of therapeutic plasma exchange (TPE) on the levels of IFN-AABs, SARS-CoV-2 antibodies and clinical outcome. Results The prevalence of neutralizing AABs to IFN-α and IFN-ω in COVID-19 patients was 4.2% (18/430), while being undetectable in an uninfected control cohort. Neutralizing IFN-AABs were detectable exclusively in critically affected, predominantly male (83%) patients (7.6% IFN-α and 4.6% IFN-ω in 207 patients with critical COVID-19). IFN-AABs were present early post-symptom onset and at the peak of disease. Fever and oxygen requirement at hospital admission co-presented with neutralizing IFN-AAB positivity. IFN-AABs were associated with higher mortality (92.3% versus 19.1 % in patients without IFN-AABs). TPE reduced levels of IFN-AABs in three of five patients and may increase survival of IFN-AAB-positive patients compared to those not undergoing TPE. Conclusion IFN-AABs may serve as early biomarker for development of severe COVID-19. We propose to implement routine screening of hospitalized COVID-19 patients according to our algorithm for rapid identification of patients with IFN-AABs who most likely benefit from specific therapies.

112. **Individual factors influencing public's perceptions about the importance of COVID-19 immunity certificates: A cross-sectional online questionnaire survey in the UK**

Niculaescu C.-E., Sassoon I.K., Landa-Avila I.C., Colak O., Jun G.T., Balatsoukas P.

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Abstract

Objectives: To assess what were the main individual factors influencing people's perception of the importance of using COVID-19 immunity certificates. Design: Cross-sectional online survey. Setting: Nationally representative survey in the UK, conducted on the 3rd of August 2021. Participants: Responses from 534 participants, aged 18 and older, residents of the UK. Interventions: This was a cross-sectional survey and each participant replied to the same set of questions. Primary outcome measure and independent variables: The primary outcome measure (dependent variable) was the participants' perceived importance of using immunity certificates, computed as an index of six items. The following individual drivers were used as the independent variables: a) personal beliefs about COVID-19 (using constructs adapted from the Health Belief Model), b) personal views on vaccination, c) willingness to share immunity status with service providers, and d) variables related to respondents' lifestyle and socio-demographic characteristics. Results: Perceived importance of immunity certificates was higher among respondents who

felt that contracting COVID-19 would have a severe negative impact on their health (β=0.2564, p=0.0000) and felt safer if vaccinated (β =0.1552, p=0.0000). The prospect of future economic recovery positively influenced perceived importance of immunity certificates. Respondents who were employed or self-employed (β=-0.2412, p=0.0010), or experienced an increase in income after the COVID-19 pandemic (β=-0.1287, p=0.0020) perceived less important the use of immunity certificates compared to those who were unemployed or had retired or those who had experienced reduction in their income during the pandemic. Conclusions: The findings of our survey suggest that more vulnerable members in our society (unemployed or retired and those believing that COVID-19 would have a severe impact on their health) and people who experienced a reduction in income during the pandemic perceived the severity of not using immunity certificates in their daily life as higher.

113. **Using the Health Belief Model to design a questionnaire aimed at measuring people's perceptions regarding COVID-19 immunity certificates**
Niculaescu C.-E., Sassoon I.K., Landa-Avila I.C., Colak O., Jun G.T., Balatsoukas P.
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Abstract

The present short communication paper describes the methodological approach of applying the Health Belief Model to the use COVID-19 immunity certificates in the UK. We designed an online survey including an adaptation of the following Health Belief Model constructs: perceived COVID-19 susceptibility, perceived COVID-19 severity, perceived benefits of using immunity certificates, perceived barriers from using immunity certificates, perceived severity of not using immunity certificates, and perceived vaccination views. The online cross-sectional survey conducted on the 3rd of August 2021 gathered responses from 534 participants aged 18 and older, representative of the UK population in terms of gender, age, and ethnicity.

114. **Should we mitigate or suppress the next pandemic? Time-horizons and costs shape optimal social distancing strategies**
Nowak S., de Lima P.N., Vardavas R.
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Abstract

The COVID-19 pandemic has called for swift action from local governments, which have instated Nonpharmaceutical Interventions (NPIs) to curb the spread of SARSCov-2. The quick and decisive decision to save lives through blunt instruments has raised questions about the conditions under which decision-makers should employ mitigation or suppression strategies to tackle the COVID-19 pandemic. More broadly, there are still debates over which set of strategies should be adopted to control different pandemics, and the lessons learned for SARS-Cov-2 may not apply to a new pathogen. While curbing SARS-Cov-2 required blunt instruments, it is unclear whether a less-transmissible and less-deadly emerging pathogen would justify the same response. This paper illuminates this question using a parsimonious transmission model by formulating the social distancing lives vs. livelihoods dilemma as a boundary value problem. In this setup, society balances the costs and benefits of social distancing contingent on the costs of reducing transmission relative to the burden imposed by the disease. To the best of our knowledge, our approach is distinct in the sense that strategies emerge from the problem structure rather than being imposed a priori. We find that the relative time-horizon of the pandemic (i.e., the time it takes to develop effective vaccines and treatments) and the relative cost of social distancing influence the choice of the optimal policy. Unsurprisingly, we find that the appropriate policy response depends on these two factors. We discuss the conditions under which each policy archetype (suppression vs. mitigation) appears to be the most appropriate.

115. **Higher vaccination rate predicts reduction in SARS-CoV-2 transmission across the United States**
Au J.
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Abstract

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) began proliferating widely throughout the world in late 2019/early 2020, creating a global pandemic and health crisis. Although vaccines became available to the public approximately

one year after the onset of the pandemic, there still remains much hesitancy surrounding vaccination even two years into the pandemic. One key concern comes from reports of breakthrough infections among the vaccinated that show comparable levels of peak viral load as the unvaccinated, calling into question the ability of vaccines to slow or prevent transmission. Therefore young, healthy individuals who are at low risk of serious complications themselves have little incentive to receive a vaccine that they are not convinced will protect others around them. To address this important concern, this article analyzes COVID-19 incidence in the United States as a function of each state's vaccination rate. Results show that states with higher percentages of fully vaccinated individuals report fewer new cases among the remaining unvaccinated population. These data add to accumulating evidence that COVID-19 vaccinations can indeed slow the spread of SARS-CoV-2, and are an important tool in society's arsenal to put this pandemic behind us.

116. **SARS-CoV-2 mortality surveillance among community deaths brought to university teaching hospital mortuary in Lusaka, Zambia, 2020**

Hamukale A., Hines J.Z., Sinyange N., Fwoloshi S., Malambo W., Sivile S., Chanda S., Mucheleng'anga L.A., Kayeyi N., Himwaze C.M., Shibemba A., Leigh T., Mazaba M.L., Kapata N., Zulu P., Zyambo K., Mupeta F., Agolory S., Mulenga L.B., Malama K., Kapina M.

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Abstract

Introduction: During March-December 2020, Zambia recorded 20,725 confirmed COVID-19 cases, with the first wave peaking between July and August. Of the 388 COVID-19-related deaths occurring nationwide, most occurred in the community. We report findings from COVID-19 mortality surveillance among community deaths brought to the University Teaching Hospital (UTH) mortuary in Lusaka. Methods: In Zambia, when a person dies in the community, and is brought into a health facility mortuary, they are recorded as 'brought in dead' (BID). The UTH mortuary accepts persons BID for Lusaka District, the most populated district in Zambia. We analyzed data for persons BID at UTH during 2020. We analyzed two data sources: weekly SARS-CoV-2 test results for persons BID and monthly all-cause mortality numbers among persons BID. For all-cause mortality among persons BID, monthly deaths during 2020 that were above the upper bound of the 95% confidence interval for the historic mean (2017-2019) were considered significant. Spearman's rank test was used to correlate the overall percent positivity in Zambia with all-cause mortality and SARS-CoV-2 testing among persons BID at UTH mortuary. Results: During 2020, 7,756 persons were BID at UTH (monthly range 556-810). SARS-CoV-2 testing began in April 2020, and through December 3,131 (51.9%) of 6,022 persons BID were tested. Of these, 212 (6.8%) were SARS-CoV-2 positive with weekly percent test positivity ranging from 0-32%, with the highest positivity occurring during July 2020. There were 1,139 excess persons BID from all causes at UTH mortuary in 2020 compared to the 2017-2019 mean. The monthly number of persons BID from all causes was above the upper bound of the 95% confidence interval during June-September and December. Conclusion: Increases in all-cause mortality and SARS-CoV-2 test positivity among persons BID at UTH mortuary corresponded with the first peak of the COVID-19 epidemic in June and August 2020, indicating possible increased mortality related to the COVID-19 epidemic in Zambia. Combining all-cause mortality and SARS-CoV-2 testing for persons BID provides useful information about the severity of the epidemic in Lusaka and should be implemented throughout Zambia.

117. **Comparative analysis of antibody production by mRNA 1273, AZD 1222 and BBIBP-CorV on elderly people suffering from different co-morbidity in Bangladesh**

Hoque A., Rahman M.M., Parvez S., Imam H., Nahar N., Chowdhury F.U.H.

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Abstract

Background: As the pandemic spread so quickly all over the world, the scientist did not get the right time to cover all age group populations for a vaccine trial. The elderly population is usually vulnerable for COVID-19 which was proven by different research work and focus was to save this group of people was the prime concern for every country of the world. Though vaccines that got emergency use authorization have proven their efficacy which one is better for elderly people suffering from different co-morbid conditions is still not established. In this study, we want to evaluate the antibody production by mRNA 1273, AZD 1222, and BBIBP-CorV in elderly people with different comorbidity. Method: We include 40 people in each group who have at least one comorbid condition and the total sample size was 120. The sample was taken from them before vaccination and 14 days after the second dose. Adverse event following immunization was recorded if any. Antibody measurement was done by ELISA method by using DiaSino SARS-CoV-2 S1 RBD IgG Quant. Result: Among 120 participants with an equal number of participants in each of the vaccine groups all of them were aged between 60-72 years, of whom 65% were males and 35 % were females. Anti S1 RBD IgG was detected among all the participants from each vaccine group after 14 days of taking their 2nd dose. A non-parametric multiple comparison test (Kruskal-Wallis test) of Anti S1 RBD IgG levels among three vaccine groups revealed significant differences (P-value <0.05) between groups. The IgG level was almost twice in the mRNA-1273 group (mean 577.1± 44.33 AU/ml) compared to AZD1222(mean 308.5 ±37.91 AU/ml) and BBIBP-CorV group. Conclusion: From this

small sample size, we predicate that mRNA 1273 produce much higher anti-S1 RBD IgG than the other two vaccines. Every vaccine is safe and effective whose is approved by WHO. Calculative use of the vaccine may produce an outcome for the future as we are still way behind in the proper amount of vaccine production.

118. **Effectiveness of BNT162b2 (Comirnaty, Pfizer-BioNTech) COVID-19 booster vaccine against COVID-19 related symptoms in England: Test negative case-control study**

Andrews N., Stowe J., Kirsebom F., Gower C., Ramsay M., Lopez J.B.

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Abstract

Background In September 2021, the UK Government introduced a booster programme targeting individuals over 50 and those in a clinical risk group. Individuals were offered either a full dose of the BNT162b2 (Comirnaty, Pfizer-BioNTech) vaccine or a half dose of the mRNA-1273 (Spikevax, Moderna) vaccine, irrespective of the vaccine received as the primary course Methods We used a test-negative case-control design to estimate the Vaccine Effectiveness (VE) of the booster dose BNT162b2 (Comirnaty, Pfizer-BioNTech) in those aged over 50 against symptomatic disease in post booster time intervals compared to individuals at least 140 days post a second dose with no booster dose recorded. In a secondary analysis, we also compared to unvaccinated individuals and to the 2 to 6 day period after a booster dose was received. Analyses were stratified by which primary doses had been received and any mixed primary courses were excluded. Results The relative VE estimate in the 14 days after the BNT162b2 (Comirnaty, Pfizer-BioNTech) booster dose, compared to individuals that received a two-dose primary course, was 87.4 (95% confidence interval 84.9-89.4) in those individuals who received two doses ChAdOx1-S (Vaxzevria, AstraZeneca) as a primary course and 84.4 (95% confidence interval 82.8-85.8) in those individuals who received two doses of BNT162b2 (Comimaty, Pfizer-BioNTech) as a primary course. Using the 2-6 day period post the booster dose as the baseline gave similar results. The absolute VE from 14 days after the booster, using the unvaccinated baseline, was 93.1(95% confidence interval 91.7-94.3) in those with ChAdOx1-S (Vaxzevria, AstraZeneca) as their primary course and 94.0 (93.4-94.6) for BNT162b2 (Comimaty, Pfizer-BioNTech) as their primary course. Conclusions Our study provides real world evidence of significant increased protection from the booster vaccine dose against symptomatic disease in those aged over 50 year of age irrespective of which primary course was received.

119. **Case series of thrombosis with thrombocytopenia syndrome following COVID-19 vaccination—United States, December 2020–August 2021**

See I., Lale A., Marquez P., Streiff M.B., Wheeler A.P., Tepper N.K., Woo E.J., Broder K.R., Edwards K.M., Gallego R., Geller A.I., Jackson K.A., Sharma S., Talaat K.R., Walter E.B., Akpan I.J., Ortel T.L., Walker S.C., Yui J.C., Shimabukuro T.T., Mba-Jonas A., Su J.R., Shay D.K.

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Abstract

Background: Thrombosis with thrombocytopenia syndrome (TTS) is a potentially life-threatening condition associated with adenoviral-vectored COVID-19 vaccination. TTS presents similarly to autoimmune heparin-induced thrombocytopenia. Twelve cases of cerebral venous sinus thrombosis following Janssen/Johnson & Johnson (Ad26.COV2.S) COVID-19 vaccination have been described. Objective: Describe surveillance data and reporting rates of TTS cases following COVID-19 vaccination. Design: Case series. Setting: United States Patients: Case-patients reported to the Vaccine Adverse Event Reporting System (VAERS) receiving COVID-19 vaccine from December 14, 2020 through August 31, 2021, with thrombocytopenia and thrombosis (excluding isolated ischemic stroke or myocardial infarction). If thrombosis was only in an extremity vein or pulmonary embolism, a positive enzyme-linked immunosorbent assay for anti-platelet factor 4 antibody was required. Measurements: Reporting rates (cases/million vaccine doses) and descriptive epidemiology. Results: 52 TTS cases were confirmed following Ad26.COV2.S (n=50) or mRNA-based COVID-19 (n=2) vaccination. TTS reporting rates were 3.55 per million (Ad26.COV2.S) and 0.0057 per million (mRNA-based COVID-19 vaccines). Median age of patients with TTS following Ad26.COV2.S vaccination was 43.5 years (range: 18–70); 70% were female. Both TTS cases following mRNA-based COVID-19 vaccination occurred in males aged >50 years. All cases following Ad26.COV2.S vaccination involved hospitalization including 32 (64%) with intensive care unit admission. Outcomes of hospitalizations following Ad26.COV2.S vaccination included death (12%), discharge to post-acute care (16%), and discharge home (72%). Limitations: Under-reporting and incomplete case follow-up. Conclusion: TTS is a rare but serious adverse event associated with Ad26.COV2.S vaccination. The different demographic characteristics of the two cases reported after mRNA-based COVID-19 vaccines and the much lower reporting rate suggest that these cases represent a background rate.

120. **Using high-resolution contact networks to evaluate SARS-CoV-2 transmission and control in large-scale multi-**

day events

Pung R., Firth J.A., Spurgin L.G., Lee V.J., Kucharski A.J.
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Abstract

The emergence of the highly transmissible SARS-CoV-2 Delta variant has created a need to reassess the risk posed by increasing social contacts as countries resume pre-pandemic activities, particularly in the context of resuming large-scale events over multiple days. To examine how social contacts formed in different activity settings influences interventions required to control outbreaks, we combined high-resolution data on contacts among passengers and crew on cruise ships with network transmission models. We found passengers had a median of 20 (IQR 10–36) unique close contacts per day, and over 60% of their contact episodes were made in dining or sports areas where mask wearing is typically limited. In simulated outbreaks, we found that vaccination coverage and rapid antigen tests had a larger effect than mask mandates alone, indicating the importance of combined interventions against Delta to reduce event risk in the vaccine era.

121. **Aortic stenosis post-COVID-19: A mathematical model on waiting lists and mortality**

Stickels C.P., Nadarajah R., Gale C.P., Jiang H., Sharkey K.J., Gibbison B., Holliman N., Lombardo S., Schewe L., Sommacal M., Sun L., Weir-McCall J., Cheema K., Rudd J.H.F., Mamas M.A., Erhun F.
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Abstract

Objectives: To provide estimates for how different treatment pathways for the management of severe aortic stenosis (AS) may affect NHS England waiting list duration and associated mortality. Design: We constructed a mathematical model of the excess waiting list and found the closed-form analytic solution to that model. From published data, we calculated estimates for how the following strategies may affect the time to clear the backlog of patients waiting for treatment and the associated waiting list mortality. Interventions: 1) increasing the capacity for the treatment of severe AS, 2) converting proportions of cases from surgery to transcatheter aortic valve implantation, and 3) a combination of these two. Results: In a capacitated system, clearing the backlog by returning to pre-COVID-19 capacity is not possible. A conversion rate of 50% would clear the backlog within 666 (95% CI, 533–848) days with 1419 (95% CI, 597–2189) deaths whilst waiting during this time. A 20% capacity increase would require 535 (95% CI, 434–666) days, with an associated mortality of 1172 (95% CI, 466–1859). A combination of converting 40% cases and increasing capacity by 20% would clear the backlog within a year (343 (95% CI, 281–410) days) with 784 (95% CI, 292–1324) deaths whilst awaiting treatment. Conclusion: A strategy change to the management of severe AS is required to reduce the NHS backlog and waiting list deaths during the post-COVID-19 'recovery' period. However, plausible adaptations will still incur a substantial wait and many hundreds dying without treatment.

122. **Revisiting the estimation of Covid-19 prevalence: Implications for rapid testing**

Zhou L., Díaz-Pachón D.A., Rao J.S.
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Abstract

Surveillance studies for Covid-19 prevalence estimation are subject to sampling bias due to oversampling of symptomatic individuals and error-prone tests, particularly rapid antigen tests which are known to have high false negative rates for asymptomatic individuals. This results in naïve estimators which can be very far from the truth.In this work, we present a method that removes these two sources of error directly. Moreover, our procedure can be easily extended to the stratified error situation in which a test has very different error rate profiles for symptomatic and asymptomatic individuals as is the case for rapid antigen testing. The result is an easily understandable four-step algorithm that produces much more reliable prevalence estimates as demonstrated on data from the Israeli Ministry of Health. Thus it may re-open the debate about whether we are under-valuing rapid testing as a surveillance tool and may have policy implications in Third-World countries or disadvantaged communities where access to PCR testing may be less accessible.

AI/ML models to aid in the diagnosis of COVID-19 illness from forced cough vocalizations: Results and

123. **challenges of a systematic review of the relevant literature**
Kelley K., Sakara A.A., Kelley M., Kelley S.C., McLenaghan P., Aldir R., Cox M., Donaldson N., Stogsdill A., Kotchou S., Sula G., Ramirez M.A.
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Abstract

From a comprehensive and systematic search of the relevant literature on signal data signature (SDS)-based artificial intelligence/machine learning (AI/ML) systems designed to aid in the diagnosis of COVID-19 illness, we aimed to reproduce the reported systems and to derive a performance goal for comparison to our own medical device with the same intended use. These objectives were in line with a pathway to regulatory approval of such devices, as well as to acceptance of this unfamiliar technology by disaster/pandemic decision makers and clinicians. To our surprise, none of the peer-reviewed articles or pre-print server records contained details sufficient to meet the planned objectives. Information amassed from the full review of more than 60 publications, however, did underscore discrete impediments to bringing AI/ML diagnostic solutions to the bedside during a pandemic. These challenges then were explored by the authors via a gap analysis and specific remedies were proposed for bringing AI/ML technologies in closer alignment with the needs of a Total Product Life Cycle (TPLC) regulatory approach.

124. **Rationale and design of the health professional students at the University of Illinois Chicago (HOLISTIC) Cohort Study**
Dommaraju S.R., Rivera S.G., Rocha E.G., Bicknell S., Loizzo D., Mohammad A., Rajan P., Seballos A., Datta A., Ahmed R., Krishnan J.A., Keehn M.
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Abstract

Objectives: The objectives of the HOLISTIC Cohort Study are to establish a 3-year prospective cohort study that characterizes the health of students within and across health professionals' education programs during the coronavirus disease 2019 (COVID-19) pandemic, implement an interprofessional student research team, and inform initiatives to improve student health. This report describes the rationale and design of the HOLISTIC Cohort Study, including recruitment strategy, survey development, data management, and descriptive statistics of the first wave of study participants. Methods: An interprofessional student research team was formed to continuously inform study design. The first wave of recruitment was conducted from April 14, 2021 to May 5, 2021 across seven health science colleges (applied health, dentistry, medicine, nursing, pharmacy, public health, social work) at the University of Illinois Chicago in Chicago, IL. Eligible students were sent an invitation via email to complete an online survey after providing electronic informed consent. The online survey was based on the U.S. Centers for Disease Control and Prevention's Behavioral Risk Factor Surveillance System 2019 survey and the 2014 World Health Organization Report of the Strategic Advisory Group of Experts Working Group Questionnaire. Two additional recruitment waves are planned in the Spring 2022 and Spring 2023; follow-up of participants previously enrolled will occur during these second and third recruitment waves. Results: Of 5,118 students invited to participate in the first wave, 553 (10.8%) completed the survey and includes participants from all seven health science colleges. The average age of participants is 27.3 years, 435 (78.8%) identify as female, and 137 (24.8%) identify as an underrepresented minority. Overall, 465 (84.6%) participants reported being currently employed for wages. Just over half (51%) reported no days with poor physical health within a month but only 11.2% reported no days with poor mental health within a month. Nearly one in ten (9.4%) reported having ever had a positive test for COVID-19. Conclusion: The HOLISTIC Cohort Study of health professional students across seven health science colleges has completed the first of three waves of enrollment during the COVID-19 pandemic. Based on the first wave of study participants, increased attention to supporting the mental and physical health of health professional students is needed.

125. **Maternal immune response and placental antibody transfer after COVID-19 vaccination across trimester and platforms**
Atyeo C.G., Shook L.L., Brigida S., De Guzman R.M., Demidkin S., Muir C., Akinwunmi B., Baez A.M., McSweeney E., Burns M., Nayak R., Kumar M.K., Patel C.D., Fialkowski A., Cvrk D., Goldfarb I.T., Yonker L.M., Fasano A., Elovitz M.A., Gray K.J., Alter G., Edlow A.G.
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Abstract

The availability of three COVID-19 vaccines in the United States provides an unprecedented opportunity to examine how vaccine platforms and timing of vaccination in pregnancy impact maternal and neonatal immunity. Here, we characterized the antibody profile after Ad26.COV2.S, mRNA-1273 or BNT162b2 vaccination in 158 pregnant individuals, and evaluated transplacental antibody transfer by profiling maternal and umbilical cord blood in 175 maternal-neonatal dyads. These analyses revealed lower vaccine-induced functions and Fc-receptor binding after Ad26.COV2.S compared to mRNA vaccination, and subtle advantages in titer and function with mRNA-1273 versus BN162b2. mRNA vaccinees had higher titers and functions against SARS-CoV-2 variants of concern. First and third trimester vaccination resulted in enhanced maternal immune responses relative to second trimester. Higher cord:maternal transfer ratios following first and second trimester vaccination reflect placental compensation for waning maternal titers. These results support vaccination early in pregnancy to maximize maternal protection throughout gestation, without compromising neonatal antibody protection.

126. **Machine learning based prediction of COVID-19 mortality suggests repositioning of anticancer drug for treating severe cases**

Linden T., Hanses F., Domingo-Fernández D., DeLong L.N., Kodamullil A.T., Schneider J., Vehreschild M.J.G.T., Lanznaster J., Ruethrich M.M., Borgmann S., Hower M., Wille K., Feldt T., Rieg S., Hertenstein B., Wyen C., Roemmele C., Vehreschild J.J., Jakob C.E.M., Stecher M., Kuzikov M., Zaliani A., Fröhlich H.

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Abstract

Despite available vaccinations COVID-19 case numbers around the world are still growing, and effective medications against severe cases are lacking. In this work, we developed a machine learning model which predicts mortality for COVID-19 patients using data from the multi-center 'Lean European Open Survey on SARS-CoV-2-infected patients' (LEOSS) observational study (>100 active sites in Europe, primarily in Germany), resulting into an AUC of almost 80%. We showed that molecular mechanisms related to dementia, one of the relevant predictors in our model, intersect with those associated to COVID-19. Most notably, among these molecules was tyrosine kinase 2 (TYK2), a protein that has been patented as drug target in Alzheimer's Disease but also genetically associated with severe COVID-19 outcomes. We experimentally verified that anti-cancer drugs Sorafenib and Regorafenib showed a clear anti-cytopathic effect in Caco2 and VERO-E6 cells and can thus be regarded as potential treatments against COVID-19. Altogether, our work demonstrates that interpretation of machine learning based risk models can point towards drug targets and new treatment options, which are strongly needed for COVID-19.

127. **Quantification and progress over time of specific antibodies against SARS-CoV-2 in breast milk of lactating women vaccinated with BNT162b2 Pfizer-BioNTech COVID-19 vaccine (LacCOVID)**

Esteve-Palau E., Gonzalez-Cuevas A., Guerrero M.E., Garcia-Terol C., Alvarez M.C., Garcia G., Moreno E., Medina F., Casadevall D., Diaz-Brito V.

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Abstract

Importance: To our knowledge, this is the first study to analyze long–term passage (6 months after immunization) of specific antibodies induced by BNT162b2 COVID-19 vaccine through breast milk. Objectives: Main objective: to determine SARS-CoV-2 vaccine induced antibody levels in the breast milk of lactating women 4 weeks after mRNA BNT162b2 Pfizer-BioNTech COVID-19 complete vaccination. Secondary objectives: to analyze SARS-CoV-2 antibody levels (breast milk and serum) at different time-points after vaccination, examine the correlation of SARS-CoV-2 antibody levels between serum and breast milk, describe adverse events related to vaccination (AErV) in both mothers and infants and determine the rate of COVID-19 infections. Design: Prospective cohort study between February and September 2021. Setting: Parc Sanitari Sant Joan de Déu, an urban hospital in Spain. Participants: During our health worker vaccination campaign at our hospital between January and March 2, we recruited 33 lactating women vaccinated with BNT162b2 Pfizer-BioNTech COVID-19. Results: A total of 33 volunteers were included in the study. The median (IQR) age of mothers was 38 (36-39) years and 15 (10-22) months for the infants. Primary end-point: at 4 w after second dose median (IQR) IgG-S1 levels for serum–milk pairs were 12,478 (6,870-20,801) to 50.4 (24.3-104) arbitrary units (AU) per mL. Secondary end-points: SARS-CoV-2 antibody levels at different time-points were (serum-milk): 519 (234-937) to 1 (0-2.9) AU/mL at 2w after first dose, 18,644 (9,923-29,264) to 78 (33.7-128) AU/mL at 2w, 4,094 (2,413-8,480) to 19.9 (10.8-51.9) AU/mL at 12w, and 1,350 (831-2,298) to 8.9 (7.8-31.5) at 24w after second dose. We found a positive correlation of SARS-CoV-2 antibody levels between serum and breast milk (Pearson correlation coefficient 0.68). No serious AErV were observed. We found two (6%) COVID-19 vaccine breakthrough infections. Conclusions: Pfizer-BioNTech COVID-19 vaccination is safe during breastfeeding and it transmits antibodies into breast milk with a positive correlation with serum levels, and both decrease over time in a 6-month follow-up. Infants of breastfeeding vaccinated women could be protected for at least six months after vaccination and serum determination of SARS-CoV-2 IgG-S1 could indicate the breastmilk levels of antibodies

during this period.

128. **Reducing false-positive SARS-CoV-2 diagnoses using long-range RT-qPCR**
te Velthuis A.J.W., Juozapaite D., Rigby C.V., Olendraite I., Mathur P., Dhanorkar K., Hulle V., Shah T., Jadhao V., Mutha S., Jalal H., Gopal V.
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Abstract
Quantitative polymerase chain reaction (qPCR) is a sensitive molecular method for the detection of genetic material and regarded as the gold-standard for diagnostic testing. To detect respiratory RNA virus infections, a reverse transcription (RT) step is implemented to create cDNA molecules that can serve as template in the qPCR step. However, positive RT-qPCR results can be found long after patient recovery, in part because the RT-qPCR can detect residual viral RNA genome fragments. To minimize the detection of such fragments, we here modified the RT-qPCR assay by replacing the routinely used random hexamers with an oligonucleotide that binds to the 3' end of the viral genome. We demonstrate that this method allows us to distinguish between infectious and non-infectious samples. Moreover, in clinical samples obtained over 15 days after the onset of symptoms, we observe that the modified RT-qPCR protocol yields significantly fewer positive results compared to a commercial RT-qPCR test. No significantly different results were found compared to the commercial test when SARSCoV-2 clinical samples were tested within 5 days of the onset of symptoms, suggesting that the modification has a similar sensitivity for detecting infectious viral RNA. Overall, these findings may help differentiate between false-positive, persistently positive, and reinfection cases in COVID-19 patients.

129. **The primacy of meeting public university students' essential needs during the COVID-19 pandemic: A new higher education priority**
Manze M., Lattanzio A., Larsen J., Keegan J., Freudenberg N., Jones H.E.
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Abstract
Objectives: We investigated the holistic experiences of university students during the pandemic. Participants: 38 students in a public university system in New York City (NYC) purposively selected from neighborhoods highly affected by the pandemic based on level of self-reported impact Methods: We conducted virtual in-depth interviews from May to August 2021 and analyzed data using thematic coding and constant comparison techniques informed by grounded theory. Results: Financial and social support systems, such as governmental and school resources, were critical to addressing essential needs and allowing students to persist. For those whose essential needs were met, faculty members' flexibility and students' experience with online learning were central to their academic success. Conclusions: Institutions of higher education should strengthen financial and social support systems to meet students' essential needs. Academic policies to bolster online pedagogy and faculty's flexibility can facilitate student retention and completion.

130. **Age and product dependent vaccine effectiveness against SARS-CoV-2 infection and hospitalisation among adults in Norway: A national cohort study, January – September 2021**
Starrfelt J., Buanes E.A., Juvet L.K., Lyngstad T.M., Rø G.Ø.I., Veneti L., Meijerink H.
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Abstract
Background: SARS-CoV-2 vaccines show high effectiveness against infection and (severe) disease. However, few studies estimate population level vaccine effectiveness against multiple COVID-19 outcomes, by age and including homologous and heterologous vaccine regimens. Methods: Using Cox proportional hazard models on data from 4 293 544 individuals (99% of Norwegian adults), we estimated overall, age-, and product-specific vaccine effectiveness against SARS-CoV-2 infection, hospitalisation, ICU admission and death in Norway, using data from national registries. Vaccine status was included as time-dependent variable and we adjusted for sex, pre-existing medical conditions, country of birth, county of residence, and crowded living conditions. Findings: Adjusted vaccine effectiveness among fully vaccinated is 72·1% (71·2–73·0) against SARS-CoV-2

infection, 92·9% (91·2–94·2) against hospitalisation, 95·5% (92·6–97·2) against ICU admission, and 88·0% (82·5–91·8) against death. Among partially vaccinated, the effectiveness is 24·3% (22·3–26·2) against infection and 82·7% (77·7–86·6) against hospitalisation. Vaccine effectiveness against infection is 84·7% (83·1-86·1) for heterologous mRNA vaccine regimens, 78·3% (76·8-79·7) for Spikevax (Moderna; mRNA-1273), 69·7% (68·6-70·8) for Comirnaty (Pfizer/BioNTech; BNT162b2), and 60·7% (57·5-63·6) for Vaxzevria (AstraZeneca; ChAdOx nCoV-19; AZD1222) with a mRNA dose among fully vaccinated. Interpretation: We demonstrate good protection against SARS-CoV-2 infection and severe disease in fully vaccinated, including heterologous vaccine regimens, which could facilitate rapid immunization. Partially vaccinated were less likely to get severe disease than unvaccinated, though protection against infection was not as high, which could be essential in making vaccine prioritisation policies especially when availability is limited.

131. **An outbreak inside an outbreak: rising incidence of carbapenem-resistant isolates during the COVID-19 pandemic. Report from a tertiary care center in Argentina**
Castro M.G., Ubiergo L., Vicino M., Cuevas G., Argarañá F.
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Abstract

Introduction: COVID-19 outbreaks have left us to deal with an aftermath on many fronts. In particular, disproportionate use of antibiotics, high ICU burden and longer in-hospital stays during the pandemic have been proposed to aggravate the emergency posed by carbapenem-resistant isolates (CRI), specially through carbapenemase production. However, there have been few reports worldwide regarding changes in CRI incidence and little latinamerican literature. Objective: We set out to determine whether the incidence of CRI rose in a tertiary care center in Santa Fe, Argentina during the time period with active cases of COVID-19. Methods: Analytic epidemiologic study retrospectively designed. Two time periods were defined: P1 (without active cases of COVID-19) from September, 2019 to August, 2020 and P2 (starting at the onset of the first wave of COVID-19 in this institution) from September, 2020 to June 2021. All clinically-relevant microbiological samples -those meant for diagnostic purposes- taken during the study period from patients in the Internal Medicine and Surgical wards as well as the Intensive Care Units were included. Incidence was calculated by dividing the number of CRI during each time frame by the count of patient-day during that same period, multiplied by a hundred. Results: 9,135 hospitalizations, 50,145 patient-days of analysis. A total of 7285 clinical NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice. samples were taken, with an overall positivity for CRI of 12.1% (n=883). Overall CRI incidence during P2 was 2.5 times higher than in P1 (2.52 vs 0.955/100 patient-days, p <0.001). ICU CRI incidence raised from 6.78 to 8.69/100 patient-days in P2 (p=0.006). Conclusion: We found alarming rates of CRI in our center, 2.5 times higher than previous to the first COVID-19 wave, similar to other reports worldwide. To our knowledge, this is one of the few Latin-American reports on the effect of the COVID-19 pandemic on CRI incidence.

132. **Mapping the human genetic architecture of COVID-19: An update**
Ganna A.
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Abstract

The Coronavirus Disease 2019 (COVID-19) pandemic continues to pose a major public health threat especially in countries with low vaccination rates. To better understand the biological underpinnings of SARS-CoV-2 infection and COVID-19 severity we formed the COVID19 Host Genetics Initiative. Here we present GWAS meta-analysis of up to 125,584 cases and over 2.5 million controls across 60 studies from 25 countries, adding 10 new genome-wide significant loci to the 13 we previously identified[1]. Genes in novel loci include SFTPD, MUC5B and ACE2, reveal compelling insights regarding disease susceptibility and severity.

133. **Using mobile phone data to estimate dynamic population changes and improve the understanding of a pandemic: A case study in Andorra**
Berke A., Doorley R., Alonso L., Arroyo V., Pons M., Larson K.
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Abstract

Compartmental models are often used to understand and predict the progression of an infectious disease such as COVID-19. The most basic of these models consider the total population of a region to be closed. Many incorporate human mobility into their transmission dynamics, usually based on static and aggregated data. However, mobility can change dramatically during a global pandemic as seen with COVID-19, making static data unsuitable. Recently, large mobility datasets derived from mobile devices have been used, along with COVID-19 infections data, to better understand the relationship between mobility and COVID-19. However, studies to date have relied on data that represent only a fraction of their target populations, and the data from mobile devices have been used for measuring mobility within the study region, without considering changes to the population as people enter and leave the region. This work presents a unique case study in Andorra, with comprehensive datasets that include telecoms data covering 100% of mobile subscribers in the country, and results from a serology testing program that more than 90% of the population voluntarily participated in. We use the telecoms data to both measure mobility within the country and to provide a real-time census of people entering, leaving and remaining in the country. We develop multiple SEIR (compartmental) models parameterized on these metrics and show how dynamic population metrics can improve the models. We find that total daily trips did not have predictive value in the SEIR models while country entrances did. As a secondary contribution of this work, we show how Andorra's serology testing program was likely impacted by people leaving the country. Overall, this case study suggests how using mobile phone data to measure dynamic population changes could improve studies that rely on more commonly used mobility metrics and the overall understanding of a pandemic.

134. **Neutralization breadth of SARS CoV-2 viral variants following primary series and booster SARS CoV-2 vaccines in patients with cancer**
Naranbhai V., St. Denis K.J., Lam E.C., Ofoman O., Beltran W.-G., Berrios C., Bhan A.K., Gainor J.F., Balazs A.B., Iafrate A.J.
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Abstract

Patients with cancer are more likely to have impaired immune responses to SARS CoV-2 vaccines. We studied the breadth of responses against SARS CoV-2 variants followingly primary vaccination in 178 patients with a variety of tumor types, and after booster doses in a subset. Neutralization of alpha, beta, gamma and delta SARS-CoV-2 variants was impaired relative to wildtype (Wuhan), regardless of vaccine type. Regardless of viral variant, mRNA1273 was the most immunogenic, followed by BNT162b2 and then Ad26.COV2.S. Neutralization of more variants (breadth) was associated with higher magnitude of wildtype neutralization, and increase with time since vaccination; increased age associated with lower breadth. Anti-spike binding antibody concentrations were a good surrogate for breadth (PPV=90% at >1000U/ml). Booster SARS-CoV-2 vaccines conferred enhanced breadth. These data suggest that achieving a high antibody titer is desirable to achieve broad neutralization; a single booster dose with current vaccines increases breadth of responses against variants.

135. **A prototype vaccination model for endemic Covid-19 under waning immunity and imperfect vaccine take-up**
Dagpunar J., Wu C.
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Abstract

In this paper, for an infectious disease such as Covid-19, we present a SIR model which examines the impact of waning immunity, vaccination rates, vaccine efficacy, and the proportion of the susceptible population who aspire to be vaccinated. Under an assumed constant control reproduction number, we provide simple conditions for the disease to be eliminated, and conversely for it to exhibit the more likely endemic behaviour. With regard to Covid-19, it is shown that if the control reproduction number is set to the basic reproduction number (say 6) of the dominant delta (B1.617.2) variant, vaccination alone, even under the most optimistic of assumptions about vaccine efficacy and high vaccine coverage, is very unlikely to lead to elimination of the disease. The model is not intended to be predictive but more an aid to understanding the relative importance of various biological and control parameters. For example, from a long-term perspective, it may be found that in the UK, through changes in societal behaviour (such as mask use, ventilation, and level of homeworking), without formal government interventions such as on-off lockdowns, the control reproduction number can still be maintained at a level significantly below the basic reproduction number. Even so, our simulations show that endemic behaviour ensues. The model obtains equilibrium values of the state variables such as the infection prevalence and mortality rate under various scenarios.

136. **Quantifying changes in vaccine coverage in mainstream media as a result of COVID-19 outbreak**
Christensen B., Laydon D.J., Chelkowski T., Jemielniak D., Vollmer M., Bhatt S., Krawczyk K.

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Abstract

Background: Achieving vaccine-derived herd immunity depends on public acceptance of vaccination, which in turn relies on people's understanding of its risks and benefits. The fundamental objective of public health messaging on vaccines is therefore the clear and concise communication of often complex information, and increasingly the countering of misinformation. The primary outlet shaping societal understanding is the mainstream online news media. There was widespread media coverage of the multiple vaccines that were rapidly developed in response to COVID-19. We studied vaccine coverage on the front pages of mainstream online news, using text-mining analysis to quantify the amount of information and sentiment polarization of vaccine coverage delivered to readers. Methods: We analyzed 28 million articles from 172 major news sources, across 11 countries between July 2015 and April 2021. We employed keyword-based frequency analysis to estimate the proportion of coverage given to vaccines in our dataset. We performed topic detection using BERTopic and Named Entity Recognition to identify the leading subjects and actors mentioned in the context of vaccines. We used the Vader Python module to perform sentiment polarization quantification of all our English-language articles. Results: We find that the proportion of headlines mentioning vaccines on the front pages of international major news sites increased from 0.1% to 3.8% with the outbreak of COVID-19. The absolute number of negatively polarized articles increased from a total of 6,698 before the COVID-19 outbreak 2015-2019 compared to 28,552 in 2020-2021. Overall, however, before the COVID-19 pandemic, vaccine coverage was slightly negatively polarized (57% negative) whereas with the outbreak, the coverage was primarily positively polarized (38% negative). Conclusions: Because of COVID-19, vaccines have risen from a marginal topic to a widely discussed topic on the front pages of major news outlets. Despite a perceived rise in hesitancy, the mainstream online media, i.e. the primary information source to most individuals, has been strongly positive compared to pre-pandemic vaccine news, which was mainly negative. However, the pandemic was accompanied with an order of magnitude increase in vaccine news volume that due to pre-pandemic low frequency sampling bias may contribute to a perceived negative sentiment. These results highlight the important interactions between the volume of news and overall polarisation. To the best of our knowledge, our work is the first systematic text mining study of vaccines in the context of COVID-19.

137. **COVID-19 convalescents exhibit deficient humoral and T cell responses to variant of concern Spike antigens at 12 month post-infection**

Garcia-Valtanen P., Hope C.M., Masavuli M.G., Yeow E.L., Balachandran H., Mekonnen Z.A., Al-Delfi Z., Abayasingam A., Agapiou D., Stella A.O., Aggarwal A., Gummow J., Ferguson C., O'Connor S., McCartney E.M., Lynn D.J., Maddern G., Gowans E.J., Reddi B.A.J., Shaw D., Kok-Lim C., Turville S.G., Beard M.R., Weiskopf D., Sette A., Bull R.A., Barry S.C., Grubor-Bauk B.

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Abstract

Background The duration and magnitude of SARS-CoV-2 immunity after infection, especially with regard to the emergence of new variants of concern (VoC), remains unclear. Here, immune memory to primary infection and immunity to VoC was assessed in mild-COVID-19 convalescents one year after infection and in the absence of viral re-exposure or COVID-19 vaccination. Methods Serum and PBMC were collected from mild-COVID-19 convalescents at ~6 and 12 months after a COVID-19 positive PCR (n=43) and from healthy SARS-CoV-2-seronegative controls (n=15-40). Serum titers of RBD and Spike-specific Ig were quantified by ELISA. Virus neutralisation was assessed against homologous, pseudotyped virus and homologous and VoC live viruses. Frequencies of Spike and RBD-specific memory B cells were quantified by flow cytometry. Magnitude of memory T cell responses was quantified and phenotyped by activation-induced marker assay, while T cell functionality was assessed by intracellular cytokine staining using peptides specific to homologous Spike virus antigen and four VoC Spike antigens. Findings At 12 months after mild-COVID-19, >90% of convalescents remained seropositive for RBD-IgG and 88.9% had circulating RBD-specific memory B cells. Despite this, only 51.2% convalescents had serum neutralising activity against homologous live-SARS-CoV-2 virus, which decreased to 44.2% when tested against live B.1.1.7, 4.6% against B.1.351, 11.6% against P.1 and 16.2%, against B.1.617.2 VoC. Spike and non-Spike-specific T cells were detected in >50% of convalescents with frequency values higher for Spike antigen (95% CI, 0.29-0.68% in $CD4^+$ and 0.11-0.35% in $CD8^+$ T cells), compared to non-Spike antigens. Despite the high prevalence and maintenance of Spike-specific T cells in Spike 'high-responder' convalescents at 12 months, T cell functionality, measured by cytokine expression after stimulation with Spike epitopes corresponding to VoC was severely affected. Interpretations SARS-CoV-2 immunity is retained in a significant proportion of mild COVID-19 convalescents 12 months post-infection in the absence of re-exposure to the virus. Despite this, changes in the amino acid sequence of the Spike antigen that are present in current VoC result in virus evasion of neutralising antibodies, as well as evasion of functional T cell responses.

138. **SARS-CoV-2 reinfection trends in South Africa: Analysis of routine surveillance data**

5.1.2e **J.R.C., van Schalkwyk C., Govender N., von Gottberg A., Cohen C., Groome M.J., Dushoff J., Mlisana K.,**

Moultrie H.
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Abstract

Objective To examine whether SARS-CoV-2 reinfection risk has changed through time in South Africa, in the context of the emergence of the Beta and Delta variants Design Retrospective analysis of routine epidemiological surveillance data Setting Line list data on SARS-CoV-2 with specimen receipt dates between 04 March 2020 and 30 June 2021, collected through South Africa's National Notifiable Medical Conditions Surveillance System Participants 1,551,655 individuals with laboratory-confirmed SARS-CoV-2 who had a positive test result at least 90 days prior to 30 June 2021. Individuals having sequential positive tests at least 90 days apart were considered to have suspected reinfections. Main outcome measures Incidence of suspected reinfections through time; comparison of reinfection rates to the expectation under a null model (approach 1); empirical estimates of the time-varying hazards of infection and reinfection throughout the epidemic (approach 2) Results 16,029 suspected reinfections were identified. The number of reinfections observed through the end of June 2021 is consistent with the null model of no change in reinfection risk (approach 1). Although increases in the hazard of primary infection were observed following the introduction of both the Beta and Delta variants, no corresponding increase was observed in the reinfection hazard (approach 2). Contrary to expectation, the estimated hazard ratio for reinfection versus primary infection was lower during waves driven by the Beta and Delta variants than for the first wave (relative hazard ratio for wave 2 versus wave 1: 0.75 (CI_{95}: 0.59-0.97); for wave 3 versus wave 1: 0.70 (CI_{95}: 0.55-0.90)). Although this finding may be partially explained by changes in testing availability, it is also consistent with a scenario in which variants have increased transmissibility but little or no evasion of immunity. Conclusion We conclude there is no population-wide epidemiological evidence of immune escape and recommend ongoing monitoring of these trends.

139. **Frontline healthcare workers suffering from psychosomatic disorders during COVID-19 (a pandemic) – A systematic review**
Joshi R., Agarwal N.B., Bhurani D., Khan M.A.
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Abstract

Purpose: The emergence of SARS CoV-2, has imposed high pressure on the healthcare system worldwide. As a consequence, frontline healthcare workers were impacted widely. The aim of this systematic review is to examine the impact of COVID-19 on mental status of FHW during pandemic. Methods: Databases such as PubMed, Scopus, google scholar were searched extensively from the date of inception till April 2021. All cross-sectional studies published in English assessing the mental condition and well-being of frontline caregivers during COVID-19 were included in the study. The quality assessment was done by Newcastle Ottawa scale. Results: Ten thousand eight hundred sixty-nine articles were found. After conscientious literature search, total 78 articles were included satisfying the objective of the review. The highest and lowest values for the rates of depression, anxiety and insomnia was found to be 99.51% & 6.07%, 85.7% & 73.6%, and 5.3% & 11.4%, respectively. Conclusion: It has been found that FHW were psychologically impacted by the pandemic. This could be due to lack of resources such as PPE, organizational support, inefficient relevant knowledge regarding the novel virus, its extremely indelible transmission rates, fear of contamination, stigmatization, and/or due to prevalence of ignorance by government and health policy makers.

140. **Differences in COVID-19 vaccination coverage by occupation in England: A national linked data study**
Nafilyan V., Dolby T., Finning K., Morgan J., Edge R., Glickman M., Pearce N., van Tongeren M.
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Abstract

Background: Monitoring differences in COVID-19 vaccination uptake in different groups is crucial to help inform the policy response to the pandemic. A key gap is the absence of data on uptake by occupation. Methods: Using nationwide population-level data, we calculated the proportion of people who had received two doses of a COVID-19 vaccine (assessed on 31 August 2021) by detailed occupational categories in adults aged 40-64 and estimated adjusted odds ratios to examine whether these differences were driven by occupation or other factors, such as education. We also examined whether vaccination rates differed by ability to work from home. Results: Our study population included 14,298,147 adults 40-64. Vaccination rates differed

markedly by occupation, being higher in administrative and secretarial occupations (90.8%); professional occupations (90.7%); and managers, directors and senior officials (90.6%); and lowest (83.1%) in people working in elementary occupations. We found substantial differences in vaccination rates looking at finer occupational groups even after adjusting for confounding factors, such as education. Vaccination rates were higher in occupations which can be done from home and lower in those which cannot. Many occupations with low vaccination rates also involved contact with the public or with vulnerable people Conclusions: Increasing vaccination coverage in occupations with low vaccination rates is crucial to help protecting the public and control infection, especially in occupations that cannot be done from home and involve contacts with the public. Policies such as 'work from home if you can' may only have limited future impact on hospitalisations and deaths

141. **SARS-CoV-2 Delta vaccine breakthrough transmissibility in Alachua, Florida**
Magalis B.R., Rich S., Tagliamonte M.S., Mavian C., Cash M.N., Riva A., Marini S., Amador D.M., Zhang Y., Shapiro J., Horine A., Starostik P., Pieretti M., Vega S., Lacombe A.P., Salinas J., Stevenson M., Myers P., Morris J.G., Lauzardo M., Prosperi M., Salemi M.
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Abstract

Background SARS-CoV-2 Delta variant has caused a dramatic resurgence in infections in the United Sates, raising questions regarding potential transmissibility among vaccinated individuals. Methods Between October 2020 and July 2021, we sequenced 4,439 SARS-CoV-2 full genomes, 23% of all known infections in Alachua County, Florida, including 109 vaccine breakthrough cases. Univariate and multivariate regression analyses were conducted to evaluate associations between viral load (VL) level and patient characteristics. Contact tracing and phylogenetic analysis were used to investigate direct transmissions involving vaccinated individuals. Results The majority of breakthrough sequences with lineage assignment were classified as Delta variants (74.6%) and occurred, on average, about three months (104 ± 57.5 days) after full vaccination, at the same time (June-July 2021) of Delta variant exponential spread within the county. Six Delta variant transmission pairs between fully vaccinated individuals were identified through contact tracing, three of which were confirmed by phylogenetic analysis. Delta breakthroughs exhibited broad VL values during acute infection (IQR 1.2 – 8.64 Log copies/ml), on average 38% lower than matched unvaccinated patients (3.29 – 10.81 Log copies/ml, p<0.00001). Nevertheless, 49-50% of all breakthroughs, and 56-60% of Delta-infected breakthroughs exhibited VL above the transmissibility threshold (4 Log copies/ml) irrespective of time post vaccination. Conclusions Delta infection transmissibility and general VL patterns in vaccinated individuals suggest limited levels of sterilizing immunity that need to be considered by public health policies. In particular, ongoing evaluation of vaccine boosters should address whether extra vaccine doses might curb breakthrough contribution to epidemic spread.

142. **SARS-CoV-2 RNA is enriched by orders of magnitude in solid relative to liquid wastewater at publicly owned treatment works**
Kim S., Kennedy L.C., Wolfe M.K., Criddle C.S., Duong D.H., Topol A., White B.J., Kantor R.S., Nelson K.L., Steele J.A., Langlois K., Griffith J.F., Zimmer-Faust A.G., McLellan S.L., Schussman M.K., Ammerman M., Wigginton K.R., Bakker K.M., Boehm A.B.
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Abstract

Wastewater-based epidemiology has gained attention throughout the world for detection of SARS-CoV-2 RNA in wastewater to supplement clinical testing. Methods have been developed using both the liquid and the solid fraction of wastewater, with some studies reporting higher concentrations in solids. To investigate this relationship further, we collaborated with six other laboratories to conduct a study across five publicly owned treatment works (POTWs) where both primary solids and raw wastewater influent samples were collected and quantified for SARS-CoV-2 RNA. Solids and influent samples were processed by participating laboratories using their respective methods and retrospectively paired based on date of collection. SARS-CoV-2 RNA concentrations by mass (gene copies per gram) were higher in solids than in influent by approximately three orders of magnitude. Concentrations in matched solids and influent were positively and significantly correlated at all five POTWs. RNA concentrations in both solids and influent were correlated to COVID-19 incidence rates in the sewershed and thus representative of disease burden; the solids methods appeared to produce a comparable relationship between SARS-CoV-2 RNA concentration measurements and incidence rates across all POTWs. Solids and influent methods showed comparable sensitivity, N gene detection frequency, and calculated empirical incidence rate lower limits. Analysis of solids has the advantage of using less sample volume to achieve similar sensitivity to influent methods.

143. **The role of antiviral treatment in curbing the COVID-19 pandemic: A modeling study**
Matrajt L., Brown E.R., Dimitrov D., Janes H.

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Abstract

Despite the development of safe and effective vaccines, effective treatments for COVID-19 disease are still desperately needed. Recently, two antiviral drugs have shown to be effective in reducing hospitalizations in clinical trials. In the present work, we use an agent-based mathematical model to assess the potential population impact of the use of antiviral treatments in four countries, corresponding to four current levels of vaccination coverage: Kenya, Mexico, United States (US) and Belgium, with 1.5, 38, 57 and 74% of their populations vaccinated. For each location, we varied antiviral coverage and antiviral effect in reducing viral load (25, 50, 75 or 100% reduction). Irrespective of location, widespread antiviral treatment of symptomatic infections (≥50% coverage) is expected to prevent the majority of COVID-19 deaths. Furthermore, even treating 20% of adult symptomatic infections, is expected to reduce mortality by a third in all countries, irrespective of the assumed treatment efficacy in reducing viral load. Our results suggest that early antiviral treatment is needed to mitigate transmission, with early treatment (within two days of symptoms) preventing 50% more infections compared to late treatment (started on days 3 to 5 after developing symptoms). Our results highlight the synergistic effect of vaccination and antiviral treatment: as vaccination rate increased, antiviral treatment had a bigger impact on overall transmission. These results suggest that antiviral treatments can become a strategic tool that, in combination with vaccination, can significantly control SASRS-CoV-2 transmission and reduce COVID-19 hospitalizations and deaths.

144. **Antibody decay, T cell immunity and breakthrough infections following two SARS-CoV-2 vaccine doses in infliximab- And vedolizumab-treated patients**

Lin S., Kennedy N.A., Saifuddin A., Sandoval D., Reynolds C.J., Seoane R.C., Kottoor S.H., Pieper F.P., Lin K.-M., Butler D.K., Chanchlani N., Nice R., Chee D., Bewshea C., Janjua M., McDonald T.J., Sebastian S., Alexander J.L., Constable L., Lee J.C., Murray C.D., Hart A.L., Irving P.M., Jones G.-R., Kok K.B., Lamb C.A., Lees C.W., Altmann D.M., Boyton R.J., Goodhand J.R., Powell N., Ahmad T.

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Abstract

We report SARS-CoV-2 vaccine-induced immunity and risk of breakthrough infections in patients with inflammatory bowel disease treated with infliximab, a commonly used anti-TNF drug and those treated with vedolizumab, a gut-specific antibody targeting integrin a4b7 that does not impact systemic immunity. In infliximab-treated patients, the magnitude of anti-SARS-CoV2 antibodies was reduced 4-6-fold. One fifth of both infliximab- and vedolizumab-treated patients did not mount a T cell response. Antibody half-life was shorter in infliximab-treated patients. Breakthrough SARS-CoV-2 infections occurred more frequently in infliximab-treated patients and the risk was predicted by the level of antibody response after second vaccine dose. Overall, recipients of two doses of the BNT162b2 vaccine had higher anti-SARS-CoV-2 antibody concentrations, higher seroconversion rates, shorter antibody half-life and less breakthrough infections compared to ChAdOx1 nCoV-19 vaccine recipients. Irrespective of biologic treatment, higher, more sustained antibody levels were observed in patients with a history of SARS-CoV-2 infection prior to vaccination. Patients treated with anti-TNF therapy should be offered third vaccine doses.

145. **Plasma biomarkers associated with survival and thrombosis in hospitalized COVID-19 patients**

Cabrera-Garcia D., Miltiades A., Yim P., Parsons S., Elisman K., Mansouri M.T., Wagener G., Harrison N.L.

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Abstract

Severe coronavirus disease-19 (COVID-19) has been associated with fibrin-mediated hypercoagulability and thromboembolic complications. To evaluate potential biomarkers of coagulopathy and disease severity in COVID-19, we measured plasma levels of eight biomarkers potentially associated with coagulation, fibrinolysis, and platelet function in 43 controls and 63 COVID-19 patients, including 47 patients admitted to the intensive care unit (ICU) and 16 non-ICU patients. COVID-19 patients showed significantly elevated levels of fibrinogen, tissue plasminogen activator (t-PA), and its inhibitor plasminogen activation inhibitor 1 (PAI-1), as well as ST2 (the receptor for interleukin 33) and von Willebrand factor (vWF) compared to the control group. We found that higher levels of t-PA, ST2, and vWF at the time of admission were associated with lower survival rates, and that thrombotic events were more frequent in patients with initial higher levels of vWF. These results support a predictive role of specific biomarkers such as t-PA and vWF in the pathophysiology of COVID-19. The data provide support for the case that

hypercoagulability in COVID-19 is fibrin-mediated, but also highlights the important role that vWF may play in the genesis of thromboses in the pathophysiology of COVID-19. Interventions designed to enhance fibrinolysis and reduce platelet aggregation might prove to be useful adjuncts in the treatment of coagulopathy in a subset of COVID-19 patients.

146. **A study of the benefits of vaccine mandates and vaccine passports for SARS-CoV-2**
Prosser A., Streiner D.L.
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Abstract

Objective: To evaluate the benefits of vaccine mandates and vaccine passports (VMVP) for SARS-CoV-2 by estimating the benefits of vaccination and exclusion of unvaccinated people from different settings. Methods: Quantified the benefits of vaccination using meta-analyses of randomized controlled trials (RCTs), cohort studies, and transmission studies to estimate the relative risk reduction (RRR), absolute risk reduction (ARR), and number needed to vaccinate (NNV) for transmission, infection, and severe illness/hospitalization. Estimated the baseline infection risk and the baseline transmission risks for different settings. Quantified the benefits of exclusion using these data to estimate the number of unvaccinated people needed to exclude (NNE) to prevent one transmission in different settings. Modelled how the benefits of vaccination and exclusion change as a function of baseline infection risk. Studies were identified from recent systematic reviews and a search of MEDLINE, MEDLINE In-Process, Embase, Global Health, and Google Scholar. Results: Data on infection and severe illness/hospitalization were obtained from 10 RCTs and 19 cohort studies of SARS-CoV-2 vaccines, totalling 5,575,049 vaccinated and 4,341,745 unvaccinated participants. Data from 7 transmission studies were obtained, totalling 557,020 index cases, 49,328 contacts of vaccinated index cases, and 1,294,372 contacts of unvaccinated index cases. The estimated baseline infection risk in the general population is 3.04%. The estimated breakthrough infection risk in the vaccinated population is 0.57%. Vaccines are very effective at reducing the risk of infection (RRR=88%, ARR=2.59%, NNV=39) and severe illness/hospitalization (RRR=89%, ARR=0.15%, NNV=676) in the general population. While the latter effect is small, vaccines nearly eliminate the baseline risk of severe illness/hospitalization (0.16%). Among an infected person's closest contacts (primarily household members), vaccines reduce transmission risk (RRR=41%, ARR=11.04%, NNV=9). In the general population, the effect of vaccines on transmission risk is likely very small for most settings and baseline infection risks (NNVs ≥ 1,000). Infected vaccinated people have a nontrivial transmission risk for their closest contacts (14.35%), but it is less than unvaccinated people (23.91%). The transmission risk reduction gained by excluding unvaccinated people is very small for most settings: healthcare (NNE=4,699), work/study places (NNE=2,193), meals/gatherings (NNE=531), public places (NNE=1,731), daily conversation (NNE=587), and transportation (NNE=4,699). Exclusion starts showing benefits on transmission risk for some settings when the baseline infection risk is between 10% to 20%. Conclusions: The benefits of VMVP are clear: the coercive element to these policies will likely lead to increased vaccination levels. Our study shows that higher vaccination levels will drive infections lower and almost eliminate severe illness/hospitalization from the general population. This will substantially lower the burden on healthcare systems. The benefits of exclusion are less clear. The NNEs suggest that hundreds, and even thousands, of unvaccinated people may need to be excluded from various settings to prevent one SARS-CoV-2 transmission from unvaccinated people. Therefore, consideration of the costs of exclusion is warranted, including staffing shortages from losing unvaccinated healthcare workers, unemployment/unemployability, financial hardship for unvaccinated people, and the creation of a class of citizens who are not allowed to fully participate in many areas of society.

147. **Tenofovir disoproxil fumarate and severity of COVID-19 in people with HIV infection**
Del Amo J., Polo R., Moreno S., Martínez E., Cabello A., Iribarren J.A., Curran A., Macías J., Montero M., Dueñas C., Mariño A.I., de la Cámara S.P., Díaz A., Arribas J.R., Jarrín I., Hernán M.A.
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Abstract

Background Effective, safe, and affordable antivirals are needed for COVID-19. Tenofovir has not been studied in randomized trials despite evidence consistent with its effectiveness against COVID-19. Methods We studied HIV-positive individuals on antiretroviral therapy (ART) in 2020 at 69 HIV clinics in Spain. We collected data on sociodemographics, ART, CD4-cell count, HIV-RNA viral load, comorbidities and the following outcomes: laboratory-confirmed SARS-CoV-2 infection, COVID-19 hospitalization, intensive care unit (ICU) admission and death. We compared the 48-week risks for individuals receiving tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC), tenofovir alafenamide (TAF)/ FTC, abacavir (ABC)/lamivudine (3TC), and other regimes. All estimates were adjusted for clinical and sociodemographic characteristics via inverse probability weighting. Results Of 51,558 eligible individuals, 39.6% were on TAF/FTC, 11.9% on TDF/FTC, 26.6% on ABC/3TC, 21.8% on other regimes. There were 2,402 documented SARS-CoV-2 infections (425 hospitalizations, 45 ICU admissions, 37 deaths). Compared with TAF/FTC, the estimated risk ratios (RR) (95% CI) of hospitalization were 0.66 (0.43, 0.91) for TDF/FTC and 1.29 (1.02, 1.58) for ABC/3TC, the RRs of ICU admission were 0.28 (0.11, 0.90) for TDF/FTC and 1.39 (0.70, 2.80) for ABC/3TC, and the RRs of death were 0.37 (0.23, 1.90) for TDF/FTC and 2.02 (0.88-6.12) for ABC/3TC. The corresponding RRs of hospitalization for

TDF/FTC were 0.49 (0.24, 0.81) in individuals ≥50 years and 1.15 (0.59, 1.93) in younger individuals. Conclusion Our findings suggest that, compared with other antiretrovirals, TDF/FTC lowers COVID-19 severity among HIV-positive individuals with virological control. This protective effect may be restricted to individuals aged 50 years and older.

148. **Disparities in COVID-19 fatalities among working Californians**
Cummings K.J., Beckman J., Frederick M., Harrison R., Nguyen A., Snyder R., Chan E., Gibb K., Rodriguez A., Wong J., Murray E.L., Jain S., Vergara X.
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Abstract

Background: Information on the occupational distribution of COVID-19 mortality is limited. Objective: To characterize COVID-19 fatalities among working Californians. Design: Retrospective study of laboratory-confirmed COVID-19 fatalities with dates of death from January 1 to December 31, 2020. Setting: California. Participants: COVID-19 accounted for 8,050 (9.9%) of 81,468 fatalities among Californians 18-64 years old. Of these decedents, 2,486 (30.9%) were matched to state employment records and classified as "confirmed working." The remainder were classified as "likely working" (n=4,121 [51.2%]) or "not working" (n=1,443 [17.9%]) using death certificate and case registry data. Measurements: We calculated age-adjusted overall and occupation-specific COVID-19 mortality rates using 2019 American Community Survey denominators. Results: Confirmed and likely working COVID-19 decedents were predominantly male (76.3%), Latino (68.7%), and foreign-born (59.6%), with high school or less education (67.9%); 7.8% were Black. The overall age-adjusted COVID-19 mortality rate was 30.0 per 100,000 workers (95% confidence interval [CI], 29.3-30.8). Workers in nine occupational groups had mortality rates higher than this overall rate, including those in farming (78.0; 95% CI, 68.7-88.2); material moving (77.8; 95% CI, 70.2-85.9); construction (62.4; 95% CI, 57.7-67.4); production (60.2; 95% CI, 55.7-65.0); and transportation (57.2; 95% CI, 52.2-62.5) occupations. While occupational differences in mortality were evident across demographic groups, mortality rates were three-fold higher for male compared with female workers and three- to seven-fold higher for Latino and Black workers compared with Asian and White workers. Limitations: The requirement that fatalities be laboratory-confirmed and the use of 2019 denominator data may underestimate the occupational burden of COVID-19 mortality. Conclusion: Californians in manual labor and in-person service occupations experienced disproportionate COVID-19 mortality, with the highest rates observed among male, Latino, and Black workers.

149. **Analysis of immune escape variants from antibody-based therapeutics against Covid-19**
Focosi D., Maggi F., Franchini M., McConnell S., Casadevall A.
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Abstract

Accelerated SARS-CoV-2 evolution under selective pressure by massive deployment of neutralizing antibody-based therapeutics is a concern with potentially severe implications for public health. We review here reports of documented immune escape after treatment with monoclonal antibodies and COVID19 convalescent plasma (CCP). While the former is mainly associated with specific single amino acid mutations at residues within the receptor-binding domain (e.g., E484K/Q, Q493R, and S494P), the few cases of immune evasion after CCP were associated with recurrent deletions within the N-terminal domain of Spike protein (e.g, ΔHV69-70, ΔLGVY141-144 and ΔAL243-244). Continuous genomic monitoring of non-responders is needed to better understand immune escape frequencies and fitness of emerging variants.

150. **Rapid, reliable and robust approach for extraction-free RT-PCR based detection of SARS-CoV-2 in clinical setting to expedite large scale screening**
Dubey A., Upadhyay S., Mehta M.
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Abstract

Rapid, reliable and robust method for the detection of SARS-CoV-2 is an indispensable need for diagnostics. The development of diagnostic method will aid to address further waves of the pandemic potentially with rapid surveillance of disease; and to allay

the fears. To meet this challenge, we have developed a rapid RT-qPCR method for the detection of 3 target genes or confirmatory genes in less than 30 minutes. The assay showed 100% sensitivity and 100% specificity when tested on 120 samples. We compared a conventional extraction based method with extraction-free method, and then further reduced the run time of extraction free method. Additionally, we have validated our rapid RT-qPCR method for the assessment of pooled sample. We hereby propose a most reliable approach for the mass screening of samples with ease of operation at low cost. Finally we designed a single tube analysis method which provides qualitative as well as quantitative resultsin minimum time.

151. **Effectiveness of non-pharmaceutical measures (NPIs) on COVID-19 in Europe: A systematic literature review**
Vardavas C.I., Nikitara K., Aslanoglou K., Hilton-Boon M., Phalkey R., Leonardi-Bee J., Magiorkinis G., Katsaounou P., Pharris A., Severi E., Suk J.E.
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Abstract

Background: The study objective was to conduct a systematic review to assess the effectiveness of non-pharmaceutical interventions (NPIs) to reduce the transmission of SARS-CoV-2 in Europe during the first wave of the pandemic. Methods: We searched OVID Medline, EMBASE, and the Cochrane and Campbell Databases for Systematic Reviews published up to April 15th 2021. Focusing on community (meso-level) and society (macro-level) level NPIs, we included all study designs, while a geographic restriction was limited to the EU, UK and European Economic Area (EEA) countries. Using the PICO framework, two reviewers independently extracted data and assessed quality using appropriate quality appraisal tools. A qualitative synthesis was performed, with NPIs grouped initially by a) Physical Distancing measures, b) Case detection and management measures, and c) hygiene measures and subsequently by country. Results: Of 17,692 studies initially assessed, 45 met all inclusion criteria. Most studies (n=30) had a modelling study design, while 13 were observational, one quasi-experimental and one experimental. Evidence from across the European continent, presented by country, indicates that the implementations of physical distancing measures (i.e., lockdowns/quarantines), preferably earlier in the pandemic, reduce the number of cases and hospitalisation across settings and for which the timing and duration are essential parameters. Case detection and management measures were also identified as effective measures at certain levels of testing and incidence, while hygiene and safety measures complemented the implementation of physical distancing measures. Conclusions: This literature review represents a comprehensive assessment of the effectiveness of NPIs in Europe up to April 2021. Despite heterogeneity across studies, NPIs, as assessed within the context of this systematic review at the macro and meso level, are effective in reducing SARSCoV-2 transmission rates and COVID-19 hospitalisation rates and deaths in the European Region and may be applied as response strategies to reduce the burden of COVID-19 in forthcoming waves.

152. **A flexible data-driven framework for COVID-19 case forecasting deployed in a developing-world public health setting**
Jain S., Tiwari A., Bannur N., Deva A., Shingi S., Shah V., Kulkarni M., Deka N., Ramaswami K., Khare V., Maheshwari H., Dhavala S., Sreedharan J., White J., Merugu S., Raval A.
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Abstract

Forecasting infection case counts and estimating accurate epidemiological parameters are critical components of managing the response to a pandemic. This paper describes a modular, extensible framework for a COVID-19 forecasting system, primarily deployed during the first Covid wave in Mumbai and Jharkhand, India. We employ a variant of the SEIR compartmental model motivated by the nature of the available data and operational constraints. We estimate best fit parameters using Sequential Model-Based Optimization (SMBO), and describe the use of a novel, fast and approximate Bayesian model averaging method (ABMA) for parameter uncertainty estimation that compares well with a more rigorous Markov Chain Monte Carlo (MCMC) approach in practice. We address on-the-ground deployment challenges such as spikes in the reported input data using a novel weighted smoothing method. We describe extensive empirical analyses to evaluate the accuracy of our method on ground truth as well as against other state-of-the-art approaches. Finally, we outline deployment lessons and describe how inferred model parameters were used by government partners to interpret the state of the epidemic and how model forecasts were used to estimate staffing and planning needs essential for addressing COVID-19 hospital burden.

153. **Simultaneous identification of viruses and SARS-CoV-2 variants with programmable DNA nanobait**
Bošković F., Zhu J., Tivony R., Ohmann A., Chen K., Alawami M.F., Đorđević M., Ermann N., Dias J.P., Fairhead M., Howarth M., Baker S., Keyser U.F.
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Abstract

Respiratory infections are the major cause of death from infectious disease worldwide. The clinical presentation of many respiratory viruses is indistinguishable; therefore, diagnostic approaches that can identify multiple pathogens are essential for patient management. We aimed to address this challenge with self-assembled DNA nanobait that can simultaneously identify multiple short RNA targets. The nanobait approach relies on specific target selection via toehold-mediated strand displacement and rapid read-out via nanopore sensing. Here, we show this platform can concurrently identify several common respiratory viruses, detecting a panel of short targets of viral nucleic acids from SARS-CoV-2, respiratory syncytial virus (RSV), rhinovirus, influenza, and parainfluenza. Our nanobait could be reprogrammed to discriminate viral variants, and we identified several key SARS-CoV-2 variants with single-nucleotide resolution. We increased assay specificity with bespoke nanobait that could identify numerous short RNA targets in the same viral sample in a complex background of the human transcriptome. Notably, we found that the sequence position in the viral RNA secondary structure is critical for nanobait design. Lastly, we show that nanobait could discriminate between samples extracted from oropharyngeal swabs from negative and positive SARS-CoV-2 patients using programmable target cleavage without preamplification. Our system allows for multiplexed identification of native RNA molecules, providing a new scalable approach for diagnostics of multiple respiratory viruses in a single assay.

154. **Phase 2 dose-ranging study of the virologic efficacy and safety of the combination COVID-19 antibodies casirivimab and imdevimab in the outpatient setting**

Portal-Celhay C., Forleo-Neto E., Eagan W., Musser B.J., Davis J.D., Turner K.C., Norton T., Hooper A.T., Hamilton J.D., Pan C., Mahmood A., Baum A., Kyratsous C.A., Kim Y., Parrino J., Kampman W., Roque-Guerrero L., Stoici R., Fatakia A., Soo Y., Geba G.P., Kowal B., DiCioccio A.T., Stahl N., Lipsich L., Braunstein N., Herman G.A., Yancopoulos G.D., Weinreich D.M.

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Abstract

Background The monoclonal antibody combination casirivimab and imdevimab (REGEN-COV®) reduced viral load, hospitalisation, or death when administered 1:1 as an intravenous (IV) dose ≥1200 mg in a phase 3 COVID-19 outpatient study. Availability of subcutaneous (SC) and/or lower IV doses should increase accessibility and/or drug supplies for patients. Methods This is a double-blind, placebo-controlled study of SARS-CoV-2-infected outpatients who were asymptomatic, or symptomatic but without risk factors for severe COVID-19. Patients were randomised to single IV dose (517 patients) of REGEN-COV 300, 600, 1200 or 2400 mg or placebo; or a single SC dose (286 patients) of REGEN-COV 600 or 1200 mg or placebo. The primary endpoint was time-weighted average daily change from baseline (TWACB) in viral load from day 1 (baseline) through day 7 in patients seronegative to SARS-CoV-2 at baseline. Findings All REGEN-COV treatments showed significant ($p<0·001$ versus pooled placebo) virologic reduction through day 7. Least-squares mean differences in TWACB viral load for the treatments versus placebo ranged from –0·56 to –0·71 $\log_{10}$ copies/mL. Each REGEN-COV treatment showed significant ($p<0·001$ versus pooled placebo) and similar virologic reduction through day 7. There were no safety concerns, dose-related safety findings, grade ≥2 infusion related/hypersensitivity reactions, grade ≥3 injection-site reactions, nor fatalities. Two serious adverse events not related to COVID-19 or the study drug were reported. Interpretation: In asymptomatic and low-risk symptomatic SARS-CoV-2-infected outpatients seronegative for antibodies against SARS-CoV-2 at baseline, REGEN-COV significantly and comparably reduced viral load at all IV and SC doses.

155. **COVID-19 vaccinations: Perceptions and behaviours in people with primary ciliary dyskinesia**

Pedersen E.S.L., Mallet C.M., Lam Y.T., Bellu S., Cizeau I., Copeland F., Fernandez T.L., Manion M., Harris A., Lucas J.S., Santamaria F., Goutaki M., Kuehni C.E., Bellu S., Cizeau I., Copeland F., Dexter K., Dixon L., Fernández T.L., Grieder S., Kruljac C., Manion M., Rindlisbacher B., Silberschmidt H.

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Abstract

Primary ciliary dyskinesia (PCD) is a rare genetic disease that causes recurrent respiratory infections. People with PCD may be at high risk of severe COVID-19 and vaccination against SARS-CoV-2 is therefore important. We studied vaccination willingness, speed of vaccination uptake, side effects, and changes in social contact behavior after vaccination in people with PCD. We used data from COVID-PCD, an international participatory cohort study. A questionnaire was e-mailed to participants in May 2021 that asked about COVID-19 vaccinations. 423 participants from 31 countries replied (median age: 30 years; 261

(62%) female). Vaccination uptake and willingness was high with 273 of 287 adults (96%) being vaccinated or willing to be in June 2021; only 4% were hesitant. The most common reasons for hesitancy were fear of side effects (reported by 88%). Mild side effects were common but no participant reported severe side effects. Half of participants changed their social contact behaviour after vaccination by seeing friends and family more often. The high vaccination willingness in the study population might reflect the extraordinary effort taken by PCD support groups to inform people about COVID-19 vaccination. Clear and specific public information and involvement of representatives is important for high vaccine uptake.

156. **Vaccine effectiveness against COVID-19 related hospital admission in the Netherlands: A test-negative case-control study**

5.1.2e ., **Knol M.J., Hahné S.J.M.,** 5.1.2 5.1.2e ., **Bruijning-Verhagen P.C.J.L., Peters V., Ammerlaan H.S.M., Delsing C.E., Fransman C., Dijkstra N.G., Bresser P., Kramer H., Rusch D., bij de Vaate E.A., Veen P., Dofferhoff A., Bruns M.**

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Abstract

Introduction: Real-world vaccine effectiveness (VE) estimates are essential to identify potential groups at higher risk of break-through infections and to guide policy. We assessed the VE of COVID-19 vaccination against COVID-19 hospitalization, while adjusting and stratifying for patient characteristics. Methods: We performed a test-negative case-control study in six Dutch hospitals. The study population consisted of adults eligible for COVID-19 vaccination hospitalized between May 1 and June 28 2021 with respiratory symptoms. Cases were defined as patients who tested positive for SARS-CoV-2 by PCR during the first 48 hours of admission or within 14 days prior to hospital admission. Controls were patients tested negative at admission and did not have a positive test during the 2 weeks prior to hospitalization. VE was calculated using multivariable logistic regression, adjusting for calendar week, sex, age, comorbidity and nursing home residency. Subgroup analysis was performed for age, sex and different comorbidities. Secondary endpoints were ICU-admission and mortality. Results: 379 cases and 255 controls were included of whom 157 (18%) were vaccinated prior to admission. Five cases (1%) and 40 controls (16%) were fully vaccinated (VE: 93%; 95% CI: 81 – 98), and 40 cases (11%) and 70 controls (27%) were partially vaccinated (VE: 70%; 95% CI: 50-82). A strongly protective effect of vaccination was found in all comorbidity subgroups. No ICU-admission or mortality were reported among fully vaccinated cases. Of unvaccinated cases, mortality was 10% and 19% was admitted at the ICU Conclusion: COVID-19 vaccination provides a strong protective effect against COVID-19 related hospital admission, in patients with and without comorbidity.

157. **Genomic landscape of SARS-CoV-2 pandemic in Brazil suggests an external P.1 variant origin**

Perico C.P., de Pierri C.R., Neto G.P., Fernandes D.R., Pedrosa F.O., de Souza E.M., Raittz R.T.

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Abstract

Brazil was the epicenter of worldwide pandemics at the peak of its second wave. The genomic/proteomic perspective of the COVID-19 pandemic in Brazil can bring new light to understand the global pandemics behavior. In this study, we track SARS-CoV-2 molecular information in Brazil using real-time bioinformatics and data science strategies to provide a comparative and evolutive panorama of the lineages in the country. SWeeP vectors represented the Brazilian and worldwide genomic/proteomic data from GISAID between 02/2020 – 08/2021. Clusters were analyzed and compared with PANGO lineages. Hierarchical clustering provided phylogenetic and evolutionary analysis of the lineages, and we tracked the P.1 (Gamma) variant origin. The genomic diversity based on Chao's estimation allowed us to compare richness and coverage among Brazilian states and other representative countries. We found that epidemics in Brazil occurred in two distinct moments, with different genetic profiles. The P.1 lineages emerged in the second wave, which was more aggressive. We could not trace the origin of P.1 from the variants present in Brazil in 2020. Instead, we found evidence pointing to its external source and a possible recombinant event that may relate P.1 to the B.1.1.28 variant subset. We discussed the potential application of the pipeline for emerging variants detection and the stability of the PANGO terminology over time. The diversity analysis showed that the low coverage and unbalanced sequencing among states in Brazil could have allowed the silenty entry and dissemination of P.1 and other dangerous variants. This comparative and evolutionary analysis may help to understand the development and the consequences of the entry of variants of concern (VOC).

158. **Characterization of the humoral immune response to BNT162b2 in elderly residents of long-term care facilities five to seven months after vaccination**

Delbrück M., Hoehl S., Toptan T., Schenk B., Grikscheit K., Metzler M., Herrmann E., Ciesek S.

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Abstract

The elderly residing in long-term care facilities (LTCFs) are a group at high risk for COVID-19. Hence, monitoring of the vaccine-based immunity has a pivotal role in identifying strategies to provide optimal protection in this population. We examined the immune response to the mRNA vaccine BNT162b2 against COVID-19 five to seven months after completing a two-dose regimen. We determined significantly lower anti-SARS-CoV-2 antibody titers in 298 SARS-CoV-2 naïve residents who were at least 75 years of age (mean 51.60 BAU/ml) (median age 87 years, range 75 to 101 years) when compared to health care workers (HCWs) aged 18 to 70 years (mean 156.99 BAU/ml, $p < 0.001$). Of the SARS-CoV-2 naïve residents, 29 had detectable neutralizing antibodies against the Delta variant (9.5%), and 14 of those (48.3%) only had a borderline titer of 1:10. Of 114 HCWs, 36 (31.6%) had detectable neutralizing antibodies. In a group of 14 elderly residents who had had a PCR-confirmed breakthrough infection, the mean antibody titer was significantly higher than in the other two groups (3199.65 BAU/mL) ($p < 0.001$), and 12 (85.7%) had detectable neutralizing antibodies against the Delta variant. Our data demonstrate that 90.5% of elderly residents of LTCFs had no detectable neutralization-competent antibodies against the dominant Delta variant five to seven months after vaccination, and that neutralizing antibody titers were restored following a break-through infection. Our results suggest that both residents and health care workers in LTCFs would benefit from a booster vaccine six months after completing the two-dose schedule or earlier.

159. **Minimal in-school SARS-CoV-2 transmission with strict mitigation protocols at two independent schools in Nashville, TN**

Peetluk L.S., Rebeiro P.F., Edwards K.M., Banerjee R., Mallal S.A., Aronoff D.M., Lipworth L., Katz S.E.

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Abstract

BACKGROUND: The COVID-19 pandemic has greatly impacted school operations. To better understand the role of schools in COVID-19 transmission, we evaluated infections at two independent schools in Nashville, TN during the 2020-2021 school year. METHODS: The cumulative incidence of COVID-19 within each school, age group, and exposure setting were estimated and compared to local incidence. Primary attack rates were estimated among students quarantined for in-school close contact. RESULTS: Among 1401 students who attended school during the study period, 98 cases of COVID-19 were reported, corresponding to cumulative incidence of 7.0% (95% confidence interval (CI): 5.7-8.5). Most cases were linked to household (58%) or community (31%) transmission, with few linked to in-school transmission (11%). Overall, 619 students were quarantined, corresponding to >5000 person-days of missed school, among whom only 5 tested positive for SARS-CoV-2 during quarantine (primary attack rate: 0.8%, 95% CI: 0.3, 1.9). Weekly case rates at school were not correlated with community transmission. CONCLUSION: These results suggest that transmission of COVID-19 in schools is minimal when strict mitigation measures are used, even during periods of extensive community transmission. Strict quarantine of contacts may lead to unnecessary missed school days with minimal benefit to in-school transmission.

160. **PBPK modelling of dexamethasone in patients with COVID-19 and liver disease**

Montanha M.C., Cottura N., Booth M., Hodge D., Bunglawala F., Kinvig H., Grañana-Castillo S., Lloyd A., Khoo S., Siccardi M.

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Abstract

The aim of the study was to apply Physiologically-Based Pharmacokinetic (PBPK) modelling to predict the effect of liver disease (LD) on the pharmacokinetics (PK) of dexamethasone (DEX) in the treatment of COVID-19. A whole-body PBPK model was created to simulate 100 adult individuals aged 18-60 years. Physiological changes (e.g., plasma protein concentration, liver size, CP450 expression, hepatic blood flow) and portal vein shunt were incorporated into the LD model. The changes were implemented by using the Child-Pugh (CP) classification system. DEX was qualified using clinical data in healthy adults for both oral (PO) and intravenous (IV) administrations and similarly propranolol (PRO) and midazolam (MDZ) were qualified with PO and IV clinical data in healthy and LD adults. The qualified model was subsequently used to simulate a 6 mg PO and 20 mg IV dose of DEX in patients with varying degrees of LD, with and without shunting. The PBPK model was successfully qualified across DEX, MDZ and PRO. In contrast to healthy adults, the simulated systemic clearance of DEX decreased (35% - 60%) and the plasma concentrations increased (170% - 400%) in patients with LD. Moreover, at higher doses of DEX, the AUC ratio

between healthy/LD individuals remained comparable to lower doses. The exposure of DEX in different stages of LD was predicted through PBPK modelling, providing a rational framework to predict PK in complex clinical scenarios related to COVID-19. Model simulations suggest dose adjustments of DEX in LD patients are not necessary considering the low dose administered in the COVID-19 protocol.

161. **Viral kinetic modeling and clinical trial simulation predicts disruption of respiratory disease trials by non-pharmaceutical COVID-19 interventions**

Arsène S., Couty C., Faddeenkov I., Go N., Granjeon-Noriot S., Šmít D., Kahoul R., Illigens B., Boissel J.-P., Chevalier A., Lehr L., Pasquali C., Kulesza A.

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Abstract

Clinical research in infectious respiratory diseases has been profoundly affected by non-pharmaceutical interventions (NPIs) against COVID-19. On top of trial delays or even discontinuation which have been observed in all disease areas, NPIs altered transmission pattern of many seasonal respiratory viruses which followed regular patterns for decades before the pandemic. Clinical trial design based on pre-pandemic historical data therefore needs to be put in question. In this article, we show how knowledge-based mathematical modeling can be used to address this issue. We set up an epidemiological model of respiratory tract infection (RTI) sensitive to a time dependent between-host transmission rate and coupled this model to a mechanistic description of viral RTI episodes in an individual patient. By reducing the transmission rate when the lockdown was introduced in the United Kingdom in March 2020, we were able to reproduce the perturbed 2020 RTI disease burden data. Using this setup, we simulated several NPIs scenarios of various strength (none, mild, medium, strong) and conducted placebo-controlled in silico clinical trials in pediatric patients with recurrent RTIs (RRTI) quantifying annual RTI rate distributions. In interventional arms, virtual patients aged 1-5 years received the bacterial lysate OM-85 (approved in several countries for the prevention of pediatric RRTIs) through a pro-type I immunomodulation mechanism of action described by a physiologically based pharmacokinetics and pharmacodynamics approach (PBPK/PD). Our predictions showed that sample size estimates based on the ratio of RTI rates (or the post-hoc power of fixed sample size trials) are not majorly impacted under NPIs which are less severe (none, mild and medium NPIs) than a strict lockdown (strong NPI). However, NPIs show a stronger impact on metrics more relevant for assessing the clinical relevance of the effect such as absolute benefit. This dichotomy shows the risk that successful trials (even with their primary endpoints being met) still get challenged in risk benefit assessment during the review of market authorization. Furthermore, we found that a mild NPI scenario already affected the time to recruit significantly when sticking to eligibility criteria complying with historical data. In summary, our model predictions can help rationalize and forecast post-COVID-19 trial feasibility. They advocate for gauging absolute and relative benefit metrics as well as clinical relevance for assessing efficacy hypotheses in trial design and they question eligibility criteria misaligned with the actual disease burden.

162. **Nanopore 16S rRNA sequencing reveals alterations in nasopharyngeal microbiome and enrichment of Mycobacterium and Mycoplasma in patients with COVID 19**

Mahapatra S., Mishra R., Prasad P., Murmu K.C., Aggarwal S., Sethi M., Mohapatra P., Ghosh A., Yadav R., Dodia H., Ansari S.A., De S., Singh D., Suryawanshi A., Dash R., Senapati S., Beuria T.K., Chattopadhyay S., Syed G.H., Swain R., Raghav S.K., Parida A.

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Abstract

The coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) is a major global health concern. This virus infects the upper respiratory tract and causes pneumonia-like symptoms. So far, few studies have shown that respiratory infections alter nasopharyngeal (NP) microbiome diversity and enrich opportunistic pathogens. In this study, we have sequenced the 16S rRNA variable regions, V1 through V9, extracted from NP samples of control and COVID-19 (symptomatic and asymptomatic) participants using the Oxford Nanopore™ technology. Comprehensive bioinformatics analysis investigating the alpha/beta diversities, non-metric multidimensional scaling, correlation studies, canonical correspondence analysis, linear discriminate analysis, and dysbiosis index analysis revealed control and COVID-19-specific NP microbiomes. We observed significant dysbiosis in COVID-19 NP microbiome with abundance of opportunistic pathogens such as Cutibacterium, Corynebacterium, Oerskovia, and Cellulomonas in asymptomatic patients, and of Streptomyces and Mycobacteriaceae family in symptomatic patients. Furthermore, we observed sharp rise in enrichment of opportunistic pathogens in symptomatic patients, with abundance of Mycobacteria and Mycoplasma, which strongly correlated with the occurrences of chest pain and fever. Our findings contribute novel insights regarding emergence of opportunistic pathogens in COVID-19 patients and their relationship with symptoms, suggesting their potential role in coinfections.

163. **Unexposed populations and potential COVID-19 burden in European countries**
Chapman L.A.C., Barnard R.C., Russell T.W., Abbott S., van Zandvoort K., Davies N.G., Kucharski A.J.
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Abstract

We estimate the potential remaining COVID-19 burden in 19 European countries by estimating the proportion of each country's population that has acquired immunity to severe disease through infection or vaccination. Our results suggest that many European countries could still face a substantial burden of hospitalisations and deaths, particularly those with lower vaccine coverage, less historical transmission, and/or older populations. Continued non-pharmaceutical interventions and efforts to achieve high vaccine coverage are required in these countries to limit severe COVID-19 outcomes.

164. **Transcriptome analysis of SARS-CoV-2 naïve and recovered individuals vaccinated with inactivated vaccine**
Zhang Y., Guo X., Li C., Kou Z., Lin L., Yao M., Pang B., Zhang X., Duan Q., Tian X., Xing Y., Jiang X.
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Abstract

The urgent approval of the use of the inactivated COVID-19 vaccine is essential to reduce the threat and burden of the epidemic on global public health, however, our current understanding of the host immune response to inactivated vaccine remains limited. Herein, we performed serum IgG antibody detection and transcriptomics analysis on 20 SARS-CoV-2 naïve individuals who received multiple doses of inactivated vaccine and 5 SARS-CoV-2 recovered individuals who received single dose of inactivated vaccine. Our research revealed the important role of many innate immune pathways after vaccination, identified a significant correlation with the third dose of booster vaccine and proteasome-related genes, and found that SARS-CoV-2 recovered individuals can produces a strong immune response to a single dose of inactivated vaccine. These results help us understand the reaction mechanism of the host's molecular immune system to the inactivated vaccine, and provide a basis for the choice of vaccination strategy. Introduction Since December 2019, a new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has swept the world, causing a variety of clinical syndromes termed coronavirus disease 2019 (COVID-19)(1). The clinical manifestations of COVID-19 include fever, dry cough, fatigue, sore throat, pneumonia, diarrhea and other symptoms, and may even develop into severe pneumonia, acute respiratory distress syndrome (ARDS) or multiple organ failure(2). The World Health Organization declared a pandemic in March 2020. COVID-19 has caused considerable impacts on the global economy and public health. Although for a long time, people have relied on social distancing, hygiene measures, and repurposed drugs to coping with it, now many researchers are committed to developing safe and effective vaccines to establish herd immunity to prevent SARS-CoV-2. In view of the turmoil caused by the COVID-19 pandemic and the urgent need for effective vaccine, vaccine development can be accelerated by combining originally requested phases. The vaccine does not go through a complete approval process, but may be approved for emergency use(3). Early clinical trial results of the inactivated vaccines produced by Sinopharm and Sinovac showed a low incidence of adverse reactions and good immunogenicity(4-8). On July 22, 2020, the above two candidate inactivated vaccines were approved for use(9). These two vaccines are widely promoted and vaccinated, but the reaction mechanism of the host's molecular immune response to the inactivated vaccine is not yet fully understood, and the implementation of the third booster dose is also being actively discussed recently(10) (https://www.cdc.gov/coronavirus/2019-ncov/vaccines/booster-shot.html). In addition, the impact of prior SARS-CoV-2 infection status on vaccination response is also worthy of further analysis. These insights may provide a theoretical basis for the determination of vaccination strategies and the allocation of vaccine resources. The application of high-throughput technology to systematically scan the transcriptome response and evaluate changes in gene expression levels is very suitable for identifying immune response dynamics and gene regulatory networks. Previously, transcriptome analysis of Hantavax vaccine(11), influenza vaccine(12), VSV-EBOV vaccine(13) and BNT162b mRNA vaccine(14) have fully revealed the dynamics of the host immune response after vaccination. In this study, we characterized the PBMC transcriptome changes of SARS-CoV-2 recovered individuals receiving one dose of vaccine and healthy SARS-CoV-2 naïve individuals receiving one to three doses of vaccine respectively. This real-world study showed the changes of various cytokines and the regulation of immune pathways induced after vaccination, reveal the indispensable role of innate immune pathways, and reflect the key modules information of vaccine response in different individuals and different doses of vaccine.

165. **Humoral immune response to Covid-19 vaccination in diabetes: Age-dependent but independent of type of diabetes and glycaemic control – the prospective COVAC-DM cohort study**
Sourij C., Tripolt N.J., Aziz F., Aberer F., Forstner P., Obermayer A.M., Kojzar H., Kleinhappl B., Pferschy P.N., Mader J.K., Cvirn G., Goswami N., Wachsmuth N., Eckstein M.L., Müller A., 5.1.2e ., Lenz J., Steinberger M., Knoll L., Krause R., Stradner M., Schlenke P., Sareban N., Prietl B., Kaser S., Moser O., Steinmetz I., Sourij H.M.D.
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Abstract

Aims: Immune response to COVID-19 vaccination and a potential impact of glycaemia on antibody levels in people with diabetes remains unclear. We investigated the seroconversion following first and second COVID-19 vaccination in people with type 1 and type 2 diabetes in relation to glycaemic control prior to vaccination and analysed the response in comparison to individuals without diabetes. Materials and Methods: This prospective, multicenter cohort study analysed people with type 1 and type 2 diabetes, well (HbA1c<7.5% or <58 mmol/mol) or insufficiently (HbA1c≥7.5% or ≥58 mmol/mol) controlled and healthy controls. Roche's Elecsys anti-SARS-CoV-2 S was used to quantify anti-spike protein antibodies 7-14 days after the first and 14-21 days after the second vaccination. Results: 86 healthy controls and 161 participants with diabetes were enrolled, 150 (75 with type 1 diabetes and 75 with type 2 diabetes) were eligible for the analysis. After the first vaccination, only 52.7% in the type 1 diabetes group and 48.0% in the type 2 diabetes group showed antibody levels above the cut-off for positivity. Antibody levels after the second vaccination were similar in people with type1, type 2 diabetes and healthy controls if adjusted for age, sex and multiple testing (p>0.05). Age (r=-0.45, p<0.001) and glomerular filtration rate (r=0.28, p=0.001) were significantly associated with antibody response. Conclusions: Anti-SARS-CoV-2 S antibody levels after the second vaccination were comparable in healthy controls, people with type 1 and type 2 diabetes, irrespective of glycaemic control. Age and renal function correlated significantly with the extent of antibody levels.

166. **Favipiravir in adults with moderate to severe COVID-19: A phase 3 multicentre, randomized, double-blinded, placebo-controlled trial**

Shenoy S., Munjal S., Al Youha S., Alghounaim M., Almazeedi S., Alshamali Y., Kaszynski R.H., Al-Sabah S.

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Abstract

Aim: To assess the efficacy and safety of favipiravir in adults with moderate to severe coronavirus disease 2019 (COVID-19). Methods: In this randomized, double-blind, multicenter, phase 3 trial, adults (21-80 years) with real-time reverse transcriptase polymerase chain reaction (rRT-PCR) confirmed SARS-CoV-2 infection and presenting with moderate to severe COVID-19 and requiring hospitalization were randomized 1:1 to oral favipiravir (day 1: 1800 mg BID and days 2-10: 800 mg BID) (FPV) plus standard supportive care (SoC) versus placebo plus SoC (placebo). The primary endpoint was time to resolution of hypoxia. Results: In total, 353 patients were randomized to receive either FPV or placebo (175 and 178 in the FPV and placebo groups, respectively). Overall, 76% of the patients (240/315, 78% in FPV vs. 75% in placebo group) reached resolution of hypoxia on or before day 28. The median time to resolution of hypoxia was 7 days in the FPV group and 8 days in the placebo group. Treatment effect was not significant [Hazard ratio (HR) (95% CI): 0.991 (0.767, 1.280) (p=0.94)]. Patients in the lower NEWS-2 clinical risk subgroup were more likely to achieve shorter time to resolution of hypoxia with the median time to resolution of hypoxia of 6 days in FPV and 7 days in placebo group [HR (95% CI): 1.21 (0.847, 1.731) (p=0.29)]; shorter time to hospital discharge with a median time to discharge of 8 and 10 days in the FPV and placebo group, respectively [HR (95% CI): 1.47 (1.081, 1.997) (p=0.014)]; and shorter time to improvement by 1-point improvement over baseline in WHO 10-point clinical status score with the median time to improvement by 1-point from baseline of 6 and 7 days in the FPV and placebo group, respectively [HR (95% CI): 1.16 (0.830, 1.624) (p=0.38)] than higher NEWS-2 clinical risk subgroup. Treatment emergent adverse event (TEAEs) were experienced by 62/334 (19%) patients [35/168 (21%) patients in FPV and 27/166 (16%) in placebo group]. Hyperuricaemia/increased blood uric acid was reported in 9 (3%)/2 (1%) patients [8 (5%)/1(1%) patients in FPV and 1 (1%)/1(1%) in placebo group],which were of mild intensity and transient. Overall, 36 serious adverse events (SAEs) were reported, 20 in FPV and 16 in placebo group. Conclusion: The trial did not find favipiravir to be effective in moderate to severe, hospitalized COVID-19 patients; favourable clinical trends were observed in patients with lower NEWS-2 risk when early administration of favipiravir could be achieved.

167. **Parents' intention to vaccinate their 5-11 years old children with the COVID-19 vaccine: Rates, predictors and the role of incentives**

Shmueli L.

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Abstract

Background: On September 20, 2021, Pfizer announced encouraging effectiveness and safety results from their COVID-19 vaccine clinical trials in 5-11 years old children. This study aims to assess parents' perceptions and intention to vaccinate their 5-

11 years old children and to determine the socio-demographic, health-related and behavioral factors, as well as the role of incentives beyond these factors, in predicting this intention. Methods: A cross-sectional representative online survey among parents of children aged 5-11 years in Israel (n=1,012). The survey was carried out between September 23 and October 4, 2021, at a critical time, immediately after Pfizer's announcement. Two multivariate regressions were performed to determine predictors of parents' intention to vaccinate their 5-11 years old children against COVID-19 in the coming winter and how soon they intend to do so. Results: Overall, 57% of the participants reported their intention to vaccinate their 5-11 years old children against COVID-19 in the coming winter. This intention was higher for participants over the age of 40. Perceived susceptibility, perceived benefits, perceived barriers, and cues to action, as well as two incentives - vaccine availability and receiving a 'green pass' - were all significant predictors of this intention. When asked about how soon they intend to vaccinate their 5-11 years old children, 27% of the participants responded immediately; 26% within three months; and 24% within more than three months. Participants having a family member suffering from a chronic disease as well as those whose children were vaccinated against influenza in the previous winter intend to vaccinate their children sooner. Perceived susceptibility, perceived severity, perceived benefits, perceived barriers, and cues to action, were all found to be significant predictors of this sense of urgency. Similar to the intention to vaccinate children in the coming winter, while vaccine availability and receiving a 'green pass' were found to be positive significant predictors of how soon parents intend to vaccinate their children, other incentives such as monetary rewards or monetary penalties were not found to be significant predictors. Parental concerns centered around the safety of the vaccine (64%), fear of severe side effects (60%), and fear that clinical trials and the authorization process were carried out too quickly (56%). Conclusions: This study provides up-to-date information on the rates of the intention of parents to vaccinate their 5-11 years old children, how soon they intend to do so, and the predictors of those intentions, which is essential for health policy makers and healthcare providers for planning vaccination campaigns. Moreover, as vaccine safety and side effects were found to be key parental concerns, it is important to release post-approval safety data regarding the vaccine to the public as soon as such is available. Finally, our findings underscore the important role of vaccine accessibility and receiving a 'green pass' over other incentives in promoting parents' intentions to vaccinate their children.

168. **Compassionate use of REGEN-COV® in patients with COVID-19 and immunodeficiency-associated antibody disorders**

Stein D., Oviedo-Orta E., Kampman W.A., McGinniss J., Betts G., McDermott M., Holly B., Lancaster J.M., Braunstein N., Yancopoulos G.D., Weinreich D.M.

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Abstract

Background: Patients with immunodeficiency-associated antibody disorders are at a higher risk of prolonged/persistent COVID-19 infection, having no viable treatment options. Methods: This is a retrospective analysis of patients with primary and/or secondary immunodeficiency-associated antibody disorders who received casirivimab and imdevimab (REGEN-COV®) under emergency compassionate use. The objectives were to describe safety and response to REGEN-COV, with a focus on the subset of patients who had COVID-19 duration ≥21 days prior to treatment. Quantitative (change in oxygenation status and/or viral load) and/or qualitative (physician-reported clinical status) patient outcomes data are reported. Results: Outcome data are available from 64 patients who received REGEN-COV. Improvement in ≥1 outcome measure was observed in 90.6% of the overall patient group. Thirty-seven of these patients had COVID-19 duration ≥21 days prior to treatment, with a median time from RT-PCR diagnosis to REGEN-COV administration of 60.5 days. Of the 29 patients with COVID-19 duration ≥21 days prior to treatment who had available outcome data, 96.6% showed improvement in ≥1 outcome measure evaluated following use of REGEN-COV. In the 14 patients who had post-treatment RT-PCR results available, 11 (78.6%) reported a negative RT-PCR following treatment with REGEN-COV, with 5 patients (45.5%) reporting a negative RT-PCR within 5 days of treatment and 8 (72.7%) reporting a negative RT-PCR within 21 days of treatment. Conclusions: In this retrospective analysis of immunodeficient patients who were granted REGEN-COV under the compassionate use program, REGEN-COV treatment was associated with rapid viral clearance and clinical improvement in the evaluable patients with long-standing COVID-19.

169. **Validation of a rapid and sensitive SARS-CoV-2 screening system developed for pandemic-scale infection surveillance**

Dewhurst R.E., Heinrich T., Watt P., Ostergaard P., Marimon J.M., Wood D., Kõks S.

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Abstract

Without any realistic prospect of comprehensive global vaccine coverage and lasting immunity, control of pandemics such as COVID-19 will require implementation of large scale, rapid identification and isolation of infectious individuals to limit further transmission. Here, we describe an automated, high-throughput testing instrument, designed for population-scale testing for SARS-CoV-2 RNA within 25 minutes from inactivated saliva to result, and capable of reporting 3,840 results per hour. This integrated screening platform incorporates continuous flow loading of samples at random intervals to cost-effectively adjust for

fluctuations in testing demand. Protecting vulnerable populations during global pandemics requires rapid and sensitive infection surveillance of asymptomatic carriers. This "Sentinel" surveillance system offers a feasible and scalable approach to complement vaccination, to curb the spread of COVID-19 variants and future pandemics to save lives.

170. **Patient trajectories among hospitalised COVID-19 patients vaccinated with an mRNA vaccine in Norway: A register-based cohort study**
Whittaker R., Kristofferson A.B., Salamanca B.V., Seppälä E., Golestani K., Kvåle R., Watle S.V., Buanes E.A.
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Abstract

Objectives With most of the Norwegian population vaccinated against COVID-19, an increasing number and proportion of COVID-19 related hospitalisations are occurring among vaccinated patients. To support patient management and capacity planning in hospitals, we estimated the length of stay (LoS) in hospital and odds of intensive care (ICU) admission and in-hospital mortality among COVID-19 patients ≥18 years who had been vaccinated with an mRNA vaccine, compared to unvaccinated patients. Methods Using national registry data, we conducted a cohort study on SARS-CoV-2 positive patients hospitalised in Norway between 1 February and 30 September 2021, with COVID-19 as the main cause of hospitalisation. We used a Cox proportional hazards model to examine the association between vaccination status and LoS. We used logistic regression to examine the association between vaccination status and ICU admission and in-hospital mortality. Results We included 2,361 patients, including 70 (3%) partially vaccinated and 183 (8%) fully vaccinated. Fully vaccinated patients 18–79 years had a shorter LoS in hospital overall (adjusted hazard ratio for discharge: 1.35, 95%CI: 1.07–1.72), and lower odds of ICU admission (adjusted odds ratio: 0.57, 95%CI: 0.33–0.96). Similar estimates were observed when collectively analysing partially and fully vaccinated patients. We observed no difference in the LoS for patients not admitted to ICU, nor odds of in-hospital death between vaccinated and unvaccinated patients. Conclusions Vaccinated patients hospitalised with COVID-19 in Norway have a shorter LoS and lower odds of ICU admission than unvaccinated patients. These findings can support patient management and ongoing capacity planning in hospitals.

171. **Three doses of COVID-19 mRNA vaccination are safe based on adverse events reported in electronic health records**
Niesen 5.1.2e **., Pawlowski C., O'Horo J.C., Challener D.W., Silvert E., Donadio G., Lenehan P.J., Virk A., Swift M.D., Speicher L.L., Gordon J., Geyer H.L., Halamka J., Venkatakrishnan A.J., Soundararajan V., Badley A.**
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Abstract

Recent reports on waning of COVID-19 vaccine induced immunity have led to the approval and roll-out of additional dose and booster vaccinations. At risk individuals are receiving additional vaccine dose(s), in addition to the regimen that was tested in clinical trials. The risks and the adverse event profiles associated with these additional vaccine doses are currently not well understood. Here, we performed a retrospective study analyzing vaccine-associated adverse events using electronic health records (EHRs) of individuals that have received three doses of mRNA-based COVID-19 vaccines (n = 47,999). By comparing symptoms reported in 2-week time periods after each vaccine dose and in a 2-week period before the 1st vaccine dose, we assessed the risk associated with 3rd dose vaccination, for both BNT162b2 and mRNA-1273. Reporting of severe adverse events remained low after the 3rd vaccine dose, with rates of pericarditis (0.01%, 0%-0.02% 95% CI), anaphylaxis (0.00%, 0%-0.01% 95% CI), myocarditis (0.00%, 0%-0.01% 95% CI), and cerebral venous sinus thrombosis (no cases), consistent with earlier studies. Significantly more individuals (p-value < 0.05) report low-severity adverse events after their 3rd dose compared with after their 2nd dose, including fatigue (4.92% after 3rd dose vs 3.47% after 2nd dose), lymphadenopathy (2.89% vs 2.07%), nausea (2.62% vs 2.04%), headache (2.47% vs 2.07%), arthralgia (2.12% vs 1.70%), myalgia (1.99% vs 1.63%), diarrhea (1.70% vs 1.24%), fever (1.11% vs 0.81%), vomiting (1.10% vs 0.80%), and chills (0.47% vs 0.36%). Our results show that although 3rd dose vaccination against SARS-CoV-2 infection led to increased reporting of low-severity adverse events, risk of severe adverse events remained comparable to the standard 2-dose regime. This study provides support for the safety of 3rd vaccination doses of individuals that are at high-risk of severe COVID-19 and breakthrough infection.

172. **Association of alcohol consumption and frequency with loneliness: A cross-sectional study among Japanese workers during the COVID-19 pandemic**
Konno Y., Okawara M., Hino A., Nagata T., Muramatsu K., Tateishi S., Tsuji M., Ogami A., Yoshimura R., Fujino Y., Harada A., Ando H., Eguchi H., Ikegami K., Tokutsu K., Mori K., Mafune K., Kitagawa K., Nagata M., Liu N., Tanaka R., Matsugaki R., Matsuda S., Ishimaru T.
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Abstract

Background There are increasing concerns that prevention measures against coronavirus disease 2019 (COVID-19) such as social distancing and telework are leading to loneliness and poor lifestyle habits like increased alcohol consumption. The purpose of this study was to assess whether loneliness reported among workers during the COVID-19 pandemic is associated with changes in alcohol consumption. Methods The study comprised a cross-sectional, online survey of 27,036 workers between December 22 and 26, 2020. A questionnaire was used to assess loneliness, usual alcohol consumption and whether that consumption had changed. The odds ratios (ORs) were estimated by logistic regression analysis. Results A total of 2831 (10.5%) workers indicated they had increased alcohol consumption during the pandemic. Increased alcohol consumption was significantly associated with loneliness (OR=1.94, 95%CI 1.70–2.21). This association held true for those who indicated they were drinking two or more days per week (OR=1.98 95%CI 1.71–2.30) and those who drank less than one day per week (OR=1.51 95%CI 0.71–3.25). In contrast, there was no association between increased drinking and loneliness among those who indicated they hardly ever drank (OR=1.22 95%CI 0.55–2.72). Conclusions Among those with a drinking habit, increased alcohol consumption is associated with loneliness.

173. **Cumulative incidence of SARS-CoV-2 and associated risk factors among healthcare workers in the Eastern Cape, South Africa**

Stead D., Adeniyi O.V., Singata-Madliki M., Abrahams S., Batting J., Jelliman E., Parrish A.

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Abstract

Objectives: This study assesses the cumulative incidence of SARS-CoV-2 infection among healthcare workers (HCWs) during South Africa's first wave and examines the associated demographic, health-related, and occupational risk factors for infection. Methods: Multi-stage cluster sampling was used in a cross-sectional study to recruit 1,309 HCWs from two academic hospitals in the Eastern Cape, South Africa over six weeks in November and December 2020. Prior test results for SARS-CoV-2 polymerase chain reaction (PCR) and participants' characteristics were recorded while a blood sample was drawn for detection of IgG antibodies against SARS-CoV-2 nucleocapsid protein. The primary outcome measure was the SARS-CoV-2 cumulative incidence rate, defined as the combined total of positive results for either PCR or IgG antibodies, divided by the total sample. The secondary outcome was significant risk factors associated with infection. Results: Of the total participants included in the analysis (N=1295), the majority were female (81.5%), of black race (78.7%) and nurses (44.8%). A total of 390 (30.1%) HCWs had a positive SARS-CoV-2 PCR result and SARS-CoV-2 antibodies were detected in 488 (37.7%), yielding a cumulative incidence of 47.2% (n = 611). In the adjusted logistic regression model, being overweight (Adjusted odds ratio (AOR) = 2.15, 95% CI 1.44-3.20), obese (AOR = 1.37, 95% CI 1.02-1.85) and living with HIV (AOR = 1.78, 95% CI 1.38-2.08) were independently associated with SARS-CoV-2 infection. There was no significant difference in infection rates between high, medium and low COVID-19 exposure working environments. Conclusions: The high SARS-CoV-2 cumulative incidence in the cohort was surprising this early in the epidemic and probably related to exposure both in and outside the hospitals. To mitigate the impact of SARS-CoV-2 among HCWs, infection prevention and control (IPC) strategies should target community transmission in addition to screening for HIV and metabolic conditions.

174. **Waning of SARS-CoV-2 antibodies targeting the Spike protein in individuals post second dose of ChAdOx1 and BNT162b2 COVID-19 vaccines and risk of breakthrough infections: Analysis of the Virus Watch community cohort**

Aldridge R.W., Yavlinsky A., Nguyen V., Eyre M.T., Shrotri M., Navaratnam A.M.D., Beale S., Braithwaite I., Byrne T., Kovar J., Fragaszy E., Fong W.L.E., Geismar C., Patel P., Rodger A., Johnson A.M., Hayward A.

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Abstract

Background: SARS-CoV-2 vaccines stimulate production of antibodies targeting the spike protein (anti-S). The level of antibodies following vaccination and trajectories of waning may differ between vaccines influencing the level of protection, how soon protection is reduced and, consequently the optimum timing of booster doses. Methods: We measured SARS-CoV-2 anti-S titre in the context of seronegativity for SARS-CoV-2 anti-Nucleocapsid (anti-N), in samples collected between 1st July and 24th October 2021 in a subset of adults in the Virus Watch community cohort. We compared anti-S levels after BNT162b2

(BioNTech/Pfizer) or ChAdOx1 (AstraZeneca/Oxford) vaccination using time since second dose of vaccination, age, sex and clinical vulnerability to investigate antibody waning. To investigate the use of anti-S levels as a correlate of protection against SARS-CoV-2 infection, we undertook a survival analysis (Kaplan-Meier and Cox) with individuals entering 21 days after their second dose of vaccine, or first antibody test after 1st July (whichever was latest) and exiting with the outcome of SARS-Cov-2 infection or at the end of follow up 24th October 2021. We also undertook a negative test design case-control analysis of infections occurring after the second vaccine dose (breakthrough infections) to determine whether the type of vaccine affected the risk of becoming infected. Results: 24049 samples from 8858 individuals (5549 who received a second dose of ChAdOx1 and 3205 BNT162b2) who remained anti-N negative were included in the analysis of anti-S waning over time. Three weeks after the second dose of vaccine BNT162b2 mean anti-S levels were 9039 (95%CI: 7946-10905) U/ml and ChadOx1 were 1025 (95%CI: 917-1146) U/ml. For both vaccines, waning anti-S levels followed a log linear decline from three weeks after the second dose of vaccination. At 20 weeks after the second dose of vaccine, the mean anti-S levels were 1521 (95%CI: 1432-1616) U/ml for BNT162b2 and 342 (95%CI: 322-365) U/ml for ChadOx1. We identified 197 breakthrough infections and found a reduced risk of infection post second dose of vaccine for individuals with anti-S levels greater than or equal to 500 U/ml compared to those with levels under 500 U/ml (HR 0.62; 95%CIs:0.44-0.87; p=0.007). Time to reach an anti-S threshold of 500 U/ml was estimated at 96 days for ChAdOx1 and 257 days for BNT162b2. We found an increased risk of a breakthrough infection for those who received the ChAdOx1 compared to those who received BNT162b2 (OR: 1.43, 95% CIs:1.18-1.73, p<0.001). Discussion: Anti-S levels are substantially higher following the second dose of BNT162b2 compared to ChAdOx1. There is a log linear waning in levels for both vaccines following the second dose. Anti-S levels are an important correlate of protection as demonstrated by those with anti-S levels < 500U/ml following vaccination being at significantly greater risk of subsequent infection. Since anti-S levels are substantially lower in ChAdOx1 than in BNT162b2 and both decline at similar rates we would expect waning immunity to occur earlier in ChAdOx1 compared to BNT162b2. Our results showing an increased risk of breakthrough infections for those who were vaccinated with ChAdOx1 compared to BNT162b2 are in line with this hypothesis. Consistent with our data, national analyses of vaccine effectiveness also suggest that waning of immunity for infection and, to a lesser extent for severe disease, is seen earlier in ChAdOx1 than in BNT162b2. Our data demonstrate the importance of booster doses to maintain protection in the elderly and clinically vulnerable and suggest that these should be prioritised to those who received ChAdOx1 as their primary course.

175. **COVID-19: A study about the impact of coronavirus on physicians of La Plata, Argentina**
Croce M.V., Chiappa E., Moiso A., Rabassa M.E.
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Abstract

Background: In Argentina, the burden of COVID-19 on health systems and physicians was substantial with difficulties on daily triage decisions which have to be made in the context of grave shortages of basic equipment and consumables. Purpose: this study was performed to understand what physicians were experiencing during the COVID-19 pandemic in La Plata (capital city of Buenos Aires province, Argentina). Methods: A cross-sectional study was performed; a questionnaire was sent by e-mail to physicians who work in this city during November 2020. The questionnaire was made based on Medscape US and International Physicians' COVID-19 Experience Report: Risk, Burnout, Loneliness. Statistical analysis: test for normality was performed employing the Kolmogorov-Smirnov test while Chi-square test of independence to examine the relationship between sex and workplace with nominal variables. For categorical variables, Kendall's tau correlation was performed to test for independence. ANOVA was developed to examine differences between physician's age. Statistical significance was set to $p < 0.05$ in all cases. All statistical analysis was done employing SPSS Statistics, Version 24 (IBM, USA). Results: 203 physicians answered the questionnaire; the majority of physicians (96%) considered stressful their experience during pandemic and reported distress episodes being for more than 60% the most stressful of their practices, 30% presented depression and were medically treated, while 32.7% felt loneliness with 4 physicians with suicidal thoughts. Conclusion: The results highlight the need to protect the psychological well-being of the healthcare community, and to invest resources to significantly promote the mental health of professionals.

176. **Exploring associations with severe hypoxemic respiratory failure in COVID-19 patients upon admission: A model for severe hypoxemic respiratory failure in 329 unvaccinated, hospitalized COVID-19 patients**
Davis J.W., Wang B., Tomczak E., Fu C.-C., Harmouch W., Reynoso D.R., Keiser P., Cabada M.M.
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Abstract

Objective The severe acute respiratory syndrome-Coronavirus-2 (SARS-CoV-2) has caused a pandemic claiming more than 4 million lives worldwide. Overwhelming Coronavirus-Disease-2019 (COVID-19) respiratory failure placed tremendous demands on healthcare systems increasing the death toll. Cost-effective prognostic tools to characterize COVID-19 patients' likely to progress to severe hypoxemic respiratory failure are still needed. Design We conducted a retrospective cohort study to develop

a model utilizing demographic and clinical data collected in the first 12-hours admission to explore associations with severe hypoxemic respiratory failure in unvaccinated and hospitalized COVID-19 patients. Setting University based healthcare system including 6 hospitals located in the Galveston, Brazoria and Harris counties of Texas. Participants Adult patients diagnosed with COVID-19 and admitted to one of six hospitals between March 19th and June 31st, 2020. Primary outcome The primary outcome was defined as reaching a WHO ordinal scale between 6-9 at any time during admission, which corresponded to severe hypoxemic respiratory failure requiring high-flow oxygen supplementation or mechanical ventilation. Results We included 329 participants in the model cohort and 62 (18.8%) met the primary outcome. Our multivariable regression model found that lactate dehydrogenase (OR 3.38 (95% CI 2.04-5.59)), qSOFA score (OR: 2.24 (95% CI 1.22-4.12)), neutrophil to lymphocyte ratio (OR:1.08 (95% CI 1.02-1.14)), age (OR: 1.04 (95% CI 1.02-1.07)), BMI (OR: 1.08 (95% CI1.03-1.13)), oxygen saturation or admission SpO2 (OR: 0.91 (95% CI 0.83-0.99)), and admission date (OR: 0.99 (95% CI 0.98-0.99)). The final model showed an area under curve (AUC) of 0.85. The sensitivity analysis and point of influence analysis did not reveal inconsistencies. Conclusions Our study demonstrated that a combination of accessible demographic and clinical information provide a powerful predictive tool to identify subjects with CoVID-19 likely to progress to severe hypoxemic respiratory failure.

177. **Waning, boosting and a path to endemicity for SARS-CoV-2**
Keeling M.J., Thomas A., Hill E.M., Thompson R.N., Dyson L., Tildesley M.J., Moore S.
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Abstract

In many countries, an extensive vaccination programme has substantially reduced the public-health impact of SARS-CoV-2, limiting the number of hospital admissions and deaths compared to an unmitigated epidemic. Ensuring a low-risk transition from the current situation to one in which SARS-CoV-2 is endemic requires maintenance of high levels of population immunity. The observed waning of vaccine efficacy over time suggests that booster doses may be required to maintain population immunity especially in the most vulnerable groups. Here, using data and models for England, we consider the dynamics of COVID-19 over a two-year time-frame, and the role that booster vaccinations can play in mitigating the worst effects. We find that boosters are necessary to suppress the imminent wave of infections that would be generated by waning vaccine efficacy. Projecting further into the future, the optimal deployment of boosters is highly sensitive to their long-term action. If protection from boosters wanes slowly (akin to protection following infection) then a single booster dose to the over 50s may be all that is needed over the next two-years. However, if protection wanes more rapidly (akin to protection following second dose vaccination) then annual or even biannual boosters are required to limit subsequent epidemic peaks an reduce the pressure on public health services.

178. **SARS-CoV-2 testing and COVID-19 related primary care use among people with citizenship, permanent residency, and temporary immigration status in British Columbia: Cross-sectional analysis of population-based administrative data**
Wiedmeyer M., Goldenberg S., Peterson S., Wanigaratne S., Machado S., Tayyar E., Braschel M., Carrillo R., Sierra-Heredia C., Tuyisenge G., Lavergne M.R.
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Abstract

Background: Having temporary immigration status affords limited rights, workplace protections, and access to services. There is not yet research data on impacts of the COVID-19 pandemic for people with temporary immigration status in Canada. Methods: We use linked administrative data to describe SARS-CoV-2 testing, positive tests, and COVID-19 primary care service use in British Columbia from January 1, 2020, to July 31, 2021, stratified by immigration status (Citizen, Permanent Resident, Temporary Resident). We plot the rate of people tested and the rate of people confirmed positive for COVID-19 by week from April 19, 2020, to July 31, 2021, across immigration groups. Results: 4.9% of people with temporary immigration status had a positive test for SARS-CoV-2 over this period, compared to 4.0% among people with permanent residency and 2.1% among people who hold Canadian citizenship. This pattern is persistent by sex/gender, age group, neighborhood income quintile, health authority, and in both metropolitan and small urban settings. At the same time we observe lower access to testing and COVID-19 related primary care among people with temporary status. Interpretation: People with temporary immigration status in BC experience higher SARS-CoV-2 test positivity; alarmingly, this was coupled with lower access to testing and primary care. Interwoven immigration, health and occupational policies place people with temporary status in circumstances of precarity and higher health risk. Extending permanent residency status to all immigrants residing in Canada and decoupling access to health care from immigration status could reduce precarity due to temporary immigration status.

179. **Modeling COVID-19 epidemic trends and health system needs leading to projections for developing countries: A case study of Thailand**

Metchanun N., Borgemeister C., Bever C., Galick D.
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Abstract

Thailand was the first country outside China to report a COVID-19 case but had a mild impact from the outbreak especially at the beginning of the pandemic. This study systematically investigates the evolution of the COVID-19 epidemic in Thailand from January 2020 to March 2021 to uncover the COVID-19 situation in the country. By modeling all health districts throughout the country, the study found that COVID-19 contributed to an increase in excess deaths and that COVID-19 deaths might be underreported. There was a lag time in ramping up testing although testing is key to control the disease. The estimated total number of beds required by COVID-19 seems low, but it may not ensure the capacity to take care of critical cases that required ICU beds, specific medical equipment, and trained medical staff.

180. **The preparedness and response to COVID-19 in a quaternary Intensive Care Unit in Australia: Perspectives and insights from frontline critical care clinicians**
Sundararajan K., Bi P., Milazzo A., Poole A., Reddi B., Mahmood M.A.
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Abstract

Objectives: This study was conducted to explore the perspectives and opinions of Intensive Care Unit (ICU) nurses and doctors at a COVID-19 designated pandemic hospital concerning the preparedness and response to COVID-19 and to consolidate the lessons learnt for crisis/disaster management in the future. Design: A qualitative study using in-depth interviews (IDIs) and focus group discussions (FGDs). Purposeful sampling was conducted to identify participants. A semi-structured guide was utilised to facilitate in-depth interviews with individual participants. Two focus group discussions were conducted, one with the ICU doctors and another with the ICU nurses. Thematic analysis identified themes and subthemes informing about the level of preparedness, response measures, processes, and factors that were either facilitators or those that triggered challenges. Setting: ICU in a quaternary referral centre affiliated to a university teaching COVID-19 designated pandemic hospital, in Adelaide, South Australia. Participants: The participants included eight ICU doctors and eight ICU nurses for the in-depth interviews. Another sixteen clinicians participated in focus group discussions. Results: The study identified six themes relevant to preparedness for, and responses to, COVID-19. The themes included: (1) Staff competence and planning, (2) Information transfer and communication, (3) Education and skills for the safe use of PPE, (4) Team dynamics and clinical practice, (5) leadership, and (6) Managing End-of life situations and expectations of caregivers. Conclusion: Findings highlight that preparedness and response to the COVID-19 crisis were proportionate to the situation's gravity. More enablers than barriers were identified. However, opportunities for improvement were recognised in the domains of planning, logistics, self-sufficiency with equipment, operational and strategic oversight, communication, and managing end-of-life care.

181. **Internet-based health survey on loneliness and sleep-related problems among the working-age population in Japan during COVID-19**
Tesen H., Konno Y., Tateishi S., Hino A., Tsuji M., Ogami A., Nagata M., Muramatsu K., Yoshimura R., Fujino Y.
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Abstract

Background The coronavirus disease 2019 (COVID-19) pandemic has been linked to a rise in loneliness. Loneliness is associated with sleep-related problems, which in turn can be a risk factor for various psychiatric disorders. However, it is unclear whether loneliness is linked to sleep-related problems during the pandemic. Here, we studied the association between loneliness and sleep-related problems during the COVID-19 pandemic in Japan. Methods A total of 33,302 individuals who indicated they were employed were surveyed online. The survey responses of 27,036 participants were analyzed. Odds ratios (ORs) were estimated using univariate and multiple logistic regression analyses. Results Of those analyzed, 2,750 (10.2%) experienced feelings of loneliness. Further, sleep-related problems were significantly more common among those who felt lonely both in the short term (more than 3 days) and the long term (more than 3 months). The OR was much weaker after adjusting for factors related to interpersonal connections, such as family and friendships, than after adjusting for factors related to socioeconomic status. Conclusions Loneliness may be a risk factor for sleep-related problems in the COVID-19 pandemic. Having connections with family and friends may have a moderating effect on the occurrence of sleep-related problems.

182. **Forecasting the COVID-19 pandemic: Lessons learned and future directions**
Sundar S., Schwab P., Tan J.Z.H., Romero-Brufau S., Celi L.A., Wangmo D., Penna N.D.
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Abstract

The Coronavirus Disease 2019 (COVID-19) has demonstrated that accurate forecasts of infection and mortality rates are essential for informing healthcare resource allocation, designing countermeasures, implementing public health policies, and increasing public awareness. However, there exist a multitude of modeling methodologies, and their relative performances in accurately forecasting pandemic dynamics are not currently comprehensively understood. In this paper, we introduce the non-mechanistic MIT-LCP forecasting model, and assess and compare its performance to various mechanistic and non-mechanistic models that have been proposed for forecasting COVID-19 dynamics. We performed a comprehensive experimental evaluation which covered the time period of November 2020 to April 2021, in order to determine the relative performances of MIT-LCP and seven other forecasting models from the United States' Centers for Disease Control and Prevention (CDC) Forecast Hub. Our results show that there exist forecasting scenarios well-suited to both mechanistic and non-mechanistic models, with mechanistic models being particularly performant for forecasts that are further in the future when recent data may not be as informative, and non-mechanistic models being more effective with shorter prediction horizons when recent representative data is available. Improving our understanding of which forecasting approaches are more reliable, and in which forecasting scenarios, can assist effective pandemic preparation and management.

183. **Refining reproduction number estimates to account for unobserved generations of infection in emerging epidemics**
Brizzi A., O'Driscoll M., Dorigatti I.
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Abstract

Background Estimating the transmissibility of infectious diseases is key to inform situational awareness and for response planning. Several methods tend to overestimate the basic (R_0) and effective (R_t) reproduction numbers during the initial phases of an epidemic. The reasons driving the observed bias are unknown. In this work we explore the impact of incomplete observations and underreporting of the first generations of infections during the initial epidemic phase. Methods We propose a debiasing procedure which utilises a linear exponential growth model to infer unobserved initial generations of infections and apply it to EpiEstim. We assess the performance of our adjustment using simulated data, considering different levels of transmissibility and reporting rates. We also apply the proposed correction to SARS-CoV-2 incidence data reported in Italy, Sweden, the United Kingdom and the United States of America. Results In all simulation scenarios, our adjustment outperforms the original EpiEstim method. The proposed correction reduces the systematic bias and the quantification of uncertainty is more precise, as better coverage of the true R_0 values is achieved with tighter credible intervals. When applied to real world data, the proposed adjustment produces basic reproduction number estimates which closely match the estimates obtained in other studies while making use of a minimal amount of data. Conclusions The proposed adjustment refines the reproduction number estimates obtained with the current EpiEstim implementation by producing improved, more precise estimates earlier than with the original method. This has relevant public health implications.

184. **Third dose vaccine with BNT162b2 and its response on Long COVID after Breakthrough infections**
Hoque A., Rahman M.M., Imam H., Nahar N., Chowdhury F.U.H.
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Abstract

Background: Breakthrough events are not rare after emerging of Delta variant. On the other hand, long COVID is an unsolved issue where sufferers suffer a lot. Some study has shown that COVID-19 vaccine has improved some clinical and libratory parameters in long COVID. But what will be the possible measures against long COVID after the breakthrough event is still a burning question. Method: We have observed the third dose by BNT162b2 in a small group(n=20) who were diagnosed as long COVID after breakthrough infections, in Sheikh Hasina National Institute of Burn & Plastic Surgery Institute, Dhaka, Bangladesh.

CRP(C-reactive protein) and Anti S1 RBD IgG responses were measured. Result: All 20 participants in the study received both dosage of "ChAdOx1-nCoV-19" in between February 2021 to April 2021 and had breakthrough infection in the same or following month which led to long COVID syndrome. They all received a third dose of "BNT162b2". A before and after 3rd dose (14 days after) CRP from participants serum was measured. A Wilcoxon matched paired signed rank test revealed significant (P value <0.05) reduction of inflammatory marker (CRP) after receiving the 3rd vaccine dose. Pre and post 3rd dose quantitative anti S1-RBD IgG response was measured and compared that revealed significant boosting effect that clearly correlates with the CRP response. Conclusion: Coverage of vaccines all over the world is still not expected level to control this pandemic. WHO has not recommended the use of a third/booster dose of COVID vaccines. Though our results show some sort of hope for the long COVID in breakthrough events after getting the third dose more study is needed to conclude this issue.

185. **Ad26.COV2.S breakthrough infections induce high titers of antibodies capable of neutralizing variants of concern**

Kitchin D., Richardson S.I., van der Mescht M.A., Motlou T., Mzindle N., Moyo-Gwete T., Makhado Z., Ayres F., Manamela N.P., Spencer H., Lambson B., Oosthuysen B., Mennen M., Skelem S., Williams N., Ntusi N.A.B., Burgers W.A., Gray G.G., Bekker L.-G., Boswell M.T., Rossouw T.M., Ueckermann V., Moore P.L.

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Abstract

The Janssen (Johnson & Johnson) Ad26.COV2.S non-replicating viral vector vaccine, which requires only a single dose and conventional cold chain storage, is a valuable tool for COVID-19 vaccination programs in resource-limited settings. Here we show that neutralizing and binding responses to Ad26.COV2.S vaccination are stable for 6-months post-vaccination, with responses highest against the ancestral vaccine-similar D614G variant. Secondly, using longitudinal samples from individuals who experienced clinically mild breakthrough infections 3-4 months after vaccination, we show dramatically boosted binding antibodies, Fc effector function and neutralization. These responses, which are cross-reactive against diverse SARS-CoV-2 variants and SARS-CoV-1, are of similar magnitude to humoral immune responses measured in severely ill, hospitalized donors. These data highlight the significant priming capacity of Ad26.COV2.S, and have implications for population immunity in areas where the single dose Ad26.COV2.S vaccine has been deployed.

186. **Time varying association between deprivation, ethnicity and SARS-CoV-2 infections in England: A space-time study**

Padellini T., Jersakova R., Diggle P.J., Holmes C., King R.E., Lehmann B.C.L., Mallon A.-M., Nicholson G., Richardson S., Blangiardo M.

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Abstract

Background: Ethnically diverse and socio-economically deprived communities have been differentially affected by the COVID-19 pandemic in the UK. • Method: Using a multilevel regression model we assess the time-varying association between SARS-CoV-2 infections and areal level deprivation and ethnicity. We separately consider weekly test positivity rate (number of positive tests over the total number of tests) and estimated unbiased prevalence (proportion of individuals in the population who would test positive) at the Lower Tier Local Authority (LTLA) level. The model also adjusts for age, urbanicity, vaccine uptake and spatio-temporal correlation structure. • Findings: Comparing the least deprived and predominantly White areas with most deprived and predominantly non-White areas over the whole study period, the weekly positivity rate increases by 13% from 2·97% to 3·35%. Similarly, prevalence increases by 10% from 0·37% to 0·41%. Deprivation has a stronger effect until October 2020, while the effect of ethnicity becomes slightly more pronounced at the peak of the second wave and then again in May-June 2021. Not all BAME groups were equally affected: in the second wave of the pandemic, LTLAs with large South Asian populations were the most affected, whereas areas with large Black populations did not show increased values for either outcome during the entire period under analysis. • Interpretation: At the area level, IMD and BAME% are both associated with an increased COVID-19 burden in terms of prevalence (disease spread) and test positivity (disease monitoring), and the strength of association varies over the course of the pandemic. The consistency of results across the two outcome measures suggests that community level characteristics such as deprivation and ethnicity have a differential impact on disease exposure or susceptibility rather than testing access and habits.

187. **Immunity to COVID-19 in India through vaccination and natural infection**

Sarraf T.R., Maity S., Ghosh A., Bhattacharjee S., Pani A., Saha K., Chattopadhyay D., Ghosh G., Sen M.

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Abstract

In India, Corona Virus-2 Disease-2019 (COVID-19) continues to this day, although with subdued intensity, following two major waves of viral infection. Despite ongoing vaccination drives to curb the spread of COVID-19, the potential of the administered vaccines to render immune protection to the general population, and how this compares with the immune potential of natural infection remain unclear. In this study we examined correlates of immune protection (humoral and cell mediated) induced by the two vaccines Covishield and Covaxin, in individuals living in and around Kolkata, India. Additionally, we compared the vaccination induced immune response profile with that of natural infection, evaluating thereby if individuals infected during the first wave retained virus specific immunity. Our results indicate that while Covaxin generates better cell-mediated immunity toward the Delta variant of SARS-CoV-2 than Covishield, Covishield is more effective than Covaxin in inducing humoral immunity. Both Covishield and Covaxin, however, are more effective toward the wild type virus than the Delta variant. Moreover, the overall immune response resulting from natural infection in and around Kolkata is not only to a certain degree better than that generated by vaccination, especially in the case of the Delta variant, but cell mediated immunity to SARS-CoV-2 also lasts for at least ten months after the viral infection.

188. **De novo emergence of a remdesivir resistance mutation during treatment of persistent SARS-CoV-2 infection in an immunocompromised patient: A case report**

Gandhi 5. 5.1.2e **., Robertson A., Peña-Hernández M.A., Lin M.J., Roychoudhury P., Lu P., Fournier J., Ferguson D., Mohamed Bakhash S.A., Muenker M.C., Srivathsan A., Wunder E.A., Kerantzas N., Wang W., Pyle A., Wilen C.B., Ogbuagu O., Greninger A.L., Iwasaki A., Schulz W.L., Ko A.I.**

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Abstract

SARS-CoV-2 remdesivir resistance mutations have been generated in vitro but have not been reported in patients receiving treatment with the antiviral agent. We present a case of an immunocompromised patient with acquired B-cell deficiency who developed an indolent, protracted course of SARS-CoV-2 infection. Remdesivir therapy alleviated symptoms and produced a transient virologic response, but her course was complicated by recrudescence of high-grade viral shedding. Whole genome sequencing identified a mutation, E802D, in the nsp12 RNA-dependent RNA polymerase which was not present in pre-treatment specimens. In vitro experiments demonstrated that the mutation conferred a ~6-fold increase in remdesivir IC50 but resulted in a fitness cost in the absence of remdesivir. Sustained clinical and virologic response was achieved after treatment with casirivimab-imdevimab. Although the fitness cost observed in vitro may limit the risk posed by E802D, this case illustrates the importance of monitoring for remdesivir resistance and the potential benefit of combinatorial therapies in immunocompromised patients with SARS-CoV-2 infection.

189. **Neutralisation of the SARS-CoV-2 Delta sub-lineage AY.4.2 and B.1.617.2 + E484K by BNT162b2 mRNA vaccine-elicited sera**

Lassaunière R., Polacek C., Fonager J., Bennedbæk M., Boding L., Rasmussen M., Fomsgaard A.

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Abstract

Several factors may account for the recent increased spread of the SARS-CoV-2 Delta sublineage AY.4.2 in the United Kingdom, Romania, Poland, and Denmark. Here, we evaluate the sensitivity of AY.4.2 to neutralisation by sera from Pfizer/BioNTech (BNT162b2) vaccine recipients. AY.4.2 neutralisation was comparable to other circulating Delta lineages or sublineages. In contrast, the more rare B.1.617.2+E484K variant showed a significant >4-fold reduction in neutralisation that warrants surveillance of strains with the acquired E484K mutation.

190. **The effect of notification window length on the epidemiological impact of COVID-19 contact tracing mobile applications**

Leng T., Hill E.M., Keeling M.J., Tildesley M.J., Thompson R.N.

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Abstract

The reduction in SARS-CoV-2 transmission from contact tracing applications (apps) depends both on the number of contacts notified and on the probability that those contacts quarantine after notification. Referring to the number of days preceding a positive test that contacts are notified as an app's notification window, we use an epidemiological model of SARS-CoV-2 transmission that captures the profile of infection to consider the trade-off between notification window length and active app-usage. We focus on 5-day and 2-day windows, the lengths used by the NHS COVID-19 app in England and Wales before and after 2nd August 2021, respectively. Short windows can be more effective at reducing transmission if they are associated with higher levels of active app usage and adherence to isolation upon notification, demonstrating the importance of understanding adherence to control measures when setting notification windows for COVID-19 apps.

191. **Regional and temporal variations affect the accuracy of variant-specific SARS-CoV-2 PCR assays**
Oh C., Sashittal P., Zhou A., Wang L., El-Kebir M., Nguyen T.H.
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Abstract

Monitoring the prevalence of SARS-CoV-2 variants is necessary to make informed public health decisions during the COVID-19 pandemic. PCR assays have received global attention, facilitating rapid understanding of variant dynamics because they are more accessible and scalable than genome sequencing. However, as PCR assays target only a few mutations, their accuracy could be compromised when these mutations are not exclusive to target variants. Here we show how to design variant-specific PCR assays with high sensitivity and specificity across different geographical regions by incorporating sequences deposited in the GISAID database. Furthermore, we demonstrate that several previously developed PCR assays have decreased accuracy outside their study areas. We introduce PRIMES, an algorithm that enables the design of reliable PCR assays, as demonstrated in our experiments to track dominant SARS-CoV-2 variants in local sewage samples. Our findings will contribute to improving PCR assays for SARS-CoV-2 variant surveillance.

192. **Vaccine effectiveness of Pfizer-BioNTech and Oxford-AstraZeneca to prevent severe COVID-19 in Costa Rica by September and October 2021: A nationwide, observational study of hospitalisations prevalence**
Rosero-Bixby L.
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Abstract

Objective To estimate the dose-dependent effectiveness of coronavirus disease (COVID-19) vaccines to prevent severe illness in real-world conditions of Costa Rica, after the Delta variant became dominant. Design Observational study; secondary analysis of hospitalisation prevalence. Setting Nationwide adult population, Costa Rica. Participants All 3.67 million adults residents in Costa Rica by mid-2021. Public aggregated data of 5978 hospital records from 14th September to 20th October, 2021 and 6.1 million vaccination doses administered. Interventions Vaccination with Pfizer-BioNTech (78%) and Oxford-AstraZeneca (22%). Main outcome measures Prevalence of COVID-19-related hospitalisations Results Vaccine effectiveness to prevent hospitalisation (VEH) was estimated as 93.4% (95% confidence interval [CI]: 93.0 to 93.9) for complete vaccination and 76.7% (CI: 75.0 to 78.3) for single-dose vaccination among adults of all ages. VEH was lower and more uncertain among older adults aged 58 years and above: 92% (CI: 91% to 93%) for those who had received full vaccination and 64% (CI: 58% to 69%) for those who had received partial vaccination. Single-dose VEH declined over time during the study period, especially in the older age group. Estimates were sensitive to possible errors in the population count used to determine the residual number of unvaccinated people in groups with high vaccine coverage. Conclusion The Costa Rican vaccination programme that administered Pfizer and Oxford vaccines are highly effective to prevent COVID-19-related hospitalisations after the Delta variant had become dominant. Moreover, a single dose is reasonably effective, justifying the continuation of the national policy of postponing the application for the second dose of the Pfizer vaccine to accelerate the vaccination and increase the number of people being vaccinated. Timely monitoring of vaccine effectiveness is important to detect eventual failures and motivate the public based on information that the vaccinations are effective.

193. **Data-driven prognosis for COVID-19 patients based on symptoms and age**

Paul S., Lorin E.
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Abstract

In this article, we develop an algorithm and a computational code to extract, analyze and compress the relevant information from the publicly available database of Canadian COVID-19 patients. We digitize the symptoms, that is, we assign a label/code as an integer variable for all possible combinations of various symptoms. We introduce a digital code for individual patient and divide all patients into a myriad of groups based on symptoms and age. In addition, we develop an electronic application (app) that allows for a rapid digital prognosis of COVID-19 patients, and provides individual patient prognosis on chance of recovery, average recovery period, etc. using the information, extracted from the database. This tool is aimed to assist health specialists in their decision regarding COVID-19 patients, based on symptoms and age of the patient. This novel approach can be used to develop similar applications for other diseases.

194. **A mathematical model for repetitive behaviors of COVID-19**
Nishimoto Y., Inoue K.
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Abstract

Covid-19 pandemic waves have been hitting us again and again in the past couple years in many countries, while the reason why they come in such repetitive manners remains unexplained, which have brought us with lingering anxieties and economic stagnations. We proposed a mathematical model to describe the mechanism of the repetitive appearance of the number of new cases based upon the SIQR model in which Q (quarantined infectors) were distinguished from I (un-quarantined ones). The repetitive behavior of the pandemic was simulated by an activator-inhibitor system around a fixed point in a phase space as a kind of self-organized oscillations. Periods between each wave were confirmed to be approximately similar. Repetitive behaviors were also observed in actual Covid-19 data. Practical policies and actions were discussed on the ways to effectively control the repetition of pandemic, and proactive PCR test especially after the peak-out stage is highly recommended.

195. **The effects of the first national lockdown in England on geographical inequalities in the evolution of COVID-19 case rates: An ecological study**
Welsh C.E., Albani V., Matthews F.E., Bambra C.
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Abstract

Background Socio-economic inequalities in COVID-19 case rates have been noted worldwide. Previous studies have compared case rates over set phases. There has been no analysis of how inequalities in cases changed overtime and were shaped by national mitigation strategies (e.g. lock downs). This paper provides the first analysis of the evolution of area-level inequalities in COVID-19 cases by deprivation levels in the first wave of the pandemic (January to July 2020) in England – with a focus on the effects of the first national lockdown (March – July 2020). Methods Weekly case rates per Middle Super Output Area (MSOA, n=4412) in England from 2020-03-15 to 2020-07-04 were obtained, and characteristics of local epidemics were calculated, e.g. the highest case rate per area. Simple linear and logistic regression analyses were employed to assess the association of these metrics with index of multiple deprivation (IMD). Local authority-level (n=309) cases were used similarly in a sensitivity analysis, as these data were available daily and extended further back in time. The impact of lockdown was assessed by comparing the cumulative case rate in the most deprived 20% of MSOAs to the least deprived 20%, for the periods before the lockdown, and by the end of lockdown. Findings Less deprived areas began recording COVID-19 cases earlier than more deprived areas and were more likely to have peaked by March 2020. More deprived areas' case rates grew faster and peaked higher than less deprived areas. During the first national lockdown in the UK, the relative excess in case rates in the most deprived areas increased to 130% of that of the least deprived ones. Interpretation The pattern of disease spread in England confirm the hypothesis that initial cases of a novel infectious disease are likely to occur in more affluent communities, but more deprived areas will overtake them once national mitigation strategies begin, and bear the brunt of the total case load. The strict first national lockdown served to increase case rate inequalities in England.

196. **SARS-CoV-2 triggered excessive inflammation and abnormal energy metabolism in gut microbiota**
Zhou T., Zeng Y., Wu J., Li J., Yan J., Meng W., Han H., Feng F., He J., Zhao S., Zhou P., Wu Y., Yang Y., Han R., Jin W., 5.1.2e., Yang Y., 5.1.2e.
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Abstract

Specific roles of gut microbes in COVID-19 progression are critical. However, the circumstantial mechanism remains elusive. In this study, shotgun metagenomic or metatranscriptomic sequencing were performed on fecal samples collected from 13 COVID-19 patients and controls. We analyzed the structure of gut microbiota, identified the characteristic bacteria and selected biomarkers. Further, GO, KEGG and eggNOG annotation were employed to correlate the taxon alteration and corresponding functions. The gut microbiota of COVID-19 patients was characterized by the enrichment of opportunistic pathogens and depletion of commensals. The abundance of Bacteroides spp. displayed an inverse relationship to COVID-19 severity, whereas Actinomyces oris, Escherichia coli, and Gemmiger formicilis were positively correlated with disease severity. The genes encoding oxidoreductase were significantly enriched in SARS-CoV-2 infection. KEGG annotation indicated that the expression of ABC transporter was up regulated, while the synthesis pathway of butyrate was aberrantly reduced. Furthermore, increased metabolism of lipopolysaccharide, polyketide sugar, sphingolipids and neutral amino acids was found. These results suggested the gut microbiome of COVID-19 patients was correlated with disease severity and in a state of excessive inflammatory response. Healthy gut microbiota may enhance antiviral defenses via butyrate metabolism, whereas the accumulation of opportunistic and inflammatory bacteria may exacerbate the disease progression.

197. **Phage-like particle vaccines are highly immunogenic and protect against pathogenic coronavirus infection and disease**
Davenport B.J., Catala A., Weston S.M., Johnson R.M., Ardunay J., Hammond H.L., Dillen C., Frieman M.B., Catalano C.E., Morrison T.E.
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Abstract

The response by vaccine developers to the COVID-19 pandemic has been extraordinary with effective vaccines authorized for emergency use in the U.S. within one year of the appearance of the first COVID-19 cases. However, the emergence of SARS-CoV-2 variants and obstacles with the global rollout of new vaccines highlight the need for platforms that are amenable to rapid tuning and stable formulation to facilitate the logistics of vaccine delivery worldwide. We developed a “designer nanoparticle” platform using phage-like particles (PLPs) derived from bacteriophage lambda for multivalent display of antigens in rigorously defined ratios. Here, we engineered PLPs that display the receptor binding domain (RBD) protein from SARS-CoV-2 and MERS-CoV, alone (RBDSARS-PLPs, RBDMERS-PLPs) and in combination (hCoV-RBD PLPs). Functionalized particles possess physiochemical properties compatible with pharmaceutical standards and retain antigenicity. Following primary immunization, BALB/c mice immunized with RBDSARS- or RBDMERS-PLPs display serum RBD-specific IgG endpoint and live virus neutralization titers that, in the case of SARS-CoV-2, were comparable to those detected in convalescent plasma from infected patients. Further, these antibody levels remain elevated up to 6 months post-prime. In dose response studies, immunization with as little as one microgram of RBDSARS-PLPs elicited robust neutralizing antibody responses. Finally, animals immunized with RBDSARS-PLPs, RBDMERS-PLPs, and hCoV-RBD PLPs were protected against SARS-CoV-2 and/or MERS-CoV lung infection and disease. Collectively, these data suggest that the designer PLP system provides a platform for facile and rapid generation of single and multi-target vaccines.

198. **A self-amplifying mRNA COVID-19 vaccine drives potent and broad immune responses at low doses that protects non-human primates against SARS-CoV-2**
Rappaport A.R., Hong S.-J., Scallan C.D., Gitlin L., Akoopie A., Boucher G.R., Egorova M., Espinosa J.A., Fidanza M., Kachura M.A., Shen A., Sivko G., van Abbema A., Veres R.L., Jooss K.
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Abstract

The coronavirus disease 2019 (COVID-19) pandemic continues to spread globally, highlighting the urgent need for safe and

effective vaccines that could be rapidly mobilized to immunize large populations. We report the preclinical development of a self-amplifying mRNA (SAM) vaccine encoding a prefusion stabilized severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike glycoprotein and demonstrate potent cellular and humoral immune responses at low doses in mice and rhesus macaques. The homologous prime-boost vaccination regimen of SAM at 3, 10 and 30 μg induced potent neutralizing antibody titers in rhesus macaques following two SAM vaccinations at all dose levels, with the 10 μg dose generating geometric mean titers (GMT) 48-fold greater than the GMT of a panel of SARS-CoV-2 convalescent human sera. Spike-specific T cell responses were observed at all dose levels. SAM vaccination provided protective efficacy against SARS-CoV-2 challenge as both a homologous prime-boost and as a single boost following ChAd prime, demonstrating reduction of viral replication in both the upper and lower airways. Protection was most effective with a SAM prime-boost vaccination regimen at 10 and 30 μg and with a ChAd/SAM heterologous prime-boost regimen. The SAM vaccine is currently being evaluated in clinical trials as both a homologous prime-boost regimen at low doses and as a boost following heterologous prime.

199. **Evidence for a long-range RNA-RNA interaction between ORF8 and the downstream region of the Spike polybasic insertion of SARS-CoV-2**
Pereira F., Manzourolajdad A.
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Abstract

SARS-CoV-2 has affected people all over the world as the causative agent of COVID-19. The virus is related to the highly lethal SARS-CoV responsible for the 2002-2003 SARS outbreak in Asia. Intense research is ongoing to understand why both viruses have different spreading capacities and mortality rates. Similar to other betacoronaviruses, long-range RNA-RNA interactions occur between different parts of the viral genomic RNA, resulting in discontinuous transcription and production of various sub-genomic RNAs. These sub-genomic RNAs are then translated into different viral proteins. An important difference between both viruses is a polybasic insertion in the Spike region of SARS-CoV-2, absent in SARS-CoV. Here we show that a 26-base-pair long-range RNA-RNA interaction occurs between the genomic region downstream of the Spike insertion and ORF8 in SARS-CoV-2. Predictions suggest that the corresponding ORF8 region forms the most energetically favorable interaction with that of Spike region from amongst all possible candidate regions within SARS-CoV-2 genomic RNA. We also found signs of sequence covariation in the predicted interaction using a large dataset with 27,592 full-length SARS-CoV-2 genomes. In particular, a synonymous mutation in ORF8 accommodated for base pairing with Spike [G23675 C28045U], and a non-synonymous mutation in Spike accommodated for base pairing with ORF8 [C23679U G28042] both of which were in close proximity of one another. The predicted interactions can potentially be related to regulation of sub-genomic RNA production rates.

200. **Preventing the transmission of COVID-19 in older adults aged 60 years and above living in long-term care**
Egunsola O., Hofmeister M., Dowsett L.E., Noseworthy T., Clement F.
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Abstract

Objectives: The objective of this study was to examine the effect of measures of control and management of COVID-19, Middle East Respiratory Syndrome (MERS), and severe acute respiratory syndrome (SARS) in adults 60 years or above living in long-term care facilities. This is an update of previous work done by Rios et al. Methods: A rapid review was conducted in accordance with the Rapid Review Guide for Health Policy and Systems Research. Literature search of databases MEDLINE, Cochrane library, and pre-print servers (biorxiv/medrxiv) was conducted from July 31, 2020 to October 9, 2020. EMBASE was searched from July 31, 2020 until October 18, 2020. Titles and abstracts from public archives were identified for screening using Gordon V. Cormack and Maura R. Grossman's Continuous Active Learning® ("CAL®") tool, which uses supervised machine learning. Results: Five observational studies and one clinical practice guideline were identified. Infection prevention measures identified in this rapid review included: social distancing and isolation, personal protective equipment (PPE) use and hygiene practices, screening, training and staffing policies. The use of PPE, laboratory screening tests, sick pay to staff, self-confinement of staff within the LTCFs for 7 or more days, maintaining maximum residents' occupancy, training and social distancing significantly reduced the prevalence of COVID-19 infection among residents and/or staff of LTCFs ($p<0.05$). Practices such as hiring of temporary staff, not assigning staff to care separately for infected and uninfected residents, inability to isolate sick residents and infrequent cleaning of communal areas significantly increased the prevalence of infection among residents and/or staff of LTCFs ($p<0.05$). Conclusion: The available studies are limited to only three countries despite the global nature of the disease. The majority of these studies showed that infection control measures such as favourable staffing policies, training, screening, social distancing, isolation and use of PPE significantly improved residents and staff related outcomes. More studies exploring the effects infection prevention and control practices in long term care facilities are required.

201. **Surveillance of COVID-19 in a vaccinated population: A rapid literature review**
Egunsola O., Farkas B., Flanagan J., Salmon C., Mastikhina L., Clement F.
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Abstract

Objectives: With the availability of COVID-19 vaccines, public health focus is shifting to post-vaccination surveillance to identify breakthrough infections in vaccinated populations. Therefore, the objectives of these reviews are to identify scientific evidence and international guidance on surveillance and testing approaches to monitor the presence of the virus in a vaccinated population. Method: We searched Ovid MEDLINE®, including Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Embase, EBM Reviews - Cochrane Central Register of Controlled Trials, and EBM Reviews - Cochrane Database of Systematic Reviews. We also searched the Web of Science Core Collection. A grey literature search was also conducted. This search was limited to studies conducted since December 2020 and current to June 13th, 2021. There were no language limitations. COVID-19 surveillance studies that were published after December 2020 but did not specify whether they tested a vaccinated population were also considered for inclusion. For the international guidance review, a grey literature search was conducted, including a thorough search of Google, websites of international government organizations (e.g., Center for Disease Control and Prevention [CDC], World Health Organization [WHO]), and McMaster Health Forum (CoVID-END). This search was primarily examining surveillance guidance published since December 2020 (to capture guidance specific to vaccinations) and any relevant pre-December 2020 guidance. Results: Thirty-three studies were included for data synthesis of scientific evidence on surveillance of COVID-19. All the studies were published between April and June 2021. Twenty-one studies were from peer-reviewed journals. Five approaches to monitoring post-vaccination COVID-19 cases and emerging variants of concern were identified, including screening with reverse transcriptase polymerase chain reaction (RT-PCR) and/or a rapid antigen test, genomic surveillance, wastewater surveillance, metagenomics, and testing of air filters on public buses. For population surveillance, the following considerations and limitations were observed: variability in person-to-person testing frequency; lower sensitivity of antigen tests; timing of infections relative to PCR testing can result in missed infections; large studies may fail to identify local variations; and loss of interest in testing by participants in long follow-up studies. Through comprehensive grey literature searching, 68 international guidance documents were captured for full-text review. A total of 26 documents met the inclusion criteria and were included in our synthesis. Seven overarching surveillance methods emerged in the literature. PCR-testing was the most recommended surveillance method, followed by genomic screening, serosurveillance, wastewater surveillance, antigen testing, health record screening, and syndromic surveillance. Conclusion: Evidence for post-vaccination COVID-19 surveillance was derived from studies in partially or fully vaccinated populations. Population PCR screening, supplemented by rapid antigen tests, was the most frequently used surveillance method and also the most commonly recommended across jurisdictions. Most recent guidance on COVID-19 surveillance is not specific to vaccinated individuals, or it is in effect but has not yet been updated to reflect that. Therefore, more evidence-informed guidance on testing and surveillance approaches in a vaccinated population that incorporates all testing modalities is required.

202. **Immunogenicity and safety of the homogenous booster shot of a recombinant fusion protein vaccine (V-01) against COVID-19 in healthy adult participants primed with a two-dose regimen**
Li Y., Fang X., Pei R., Fan R., Chen S., Zeng P., Ou Z., 5.1.2e., Zhou J., Sun Z., Liu L., Peng H., Chen X., Su Z., Chen X., He J., Guan W., Hu Z., Fu Y.-X., Zhang J.
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Abstract

Background: Rising concerns over waning immunity and reduction in neutralizing activity against variants of concern (VOCs) have contributed to deploying booster doses by different strategies to tackle the COVID-19 pandemic. Preliminary findings from Phase I and II have shown that V-01, a recombinant fusion protein vaccine against COVID-19, exhibited favorable safety and immunogenicity profiles in 1060 adult participants of both younger and senior age. Herein, we aimed to assess the immunogenicity and safety for a booster dose in participants previously primed with a two-dose 10μg V-01 regimen (day 0, 21) from phase I trial, providing reassuring data for necessity and feasibility of a homogenous booster dose. Methods: We conducted a single-arm, open-label trial at the Guangdong Provincial Center for Disease Control and Prevention (Gaozhou, China). Forty-three eligible participants who were previously primed 4-5 months earlier with two-dose 10μg V-01 regimen from phase I trial received booster vaccination. We primarily assessed the immunogenicity post-booster vaccination, measured by RBD-binding antibodies using ELISA and neutralizing activity against wild-type SARS-CoV-2 and emerging variants of concern (VOCs) using neutralization assays. We secondarily assessed the safety and reactogenicity of the booster vaccination. Results: The third dose of V-01 exhibited significant boosting effects of humoral immune response in participants primed with two-dose 10μg V-01 regimen regarding both wild-type SARS-CoV-2 and VOCs. We observed a 60.4-folds increase in neutralizing titres against SARS-CoV-2 of younger adults, with GMTs of 17 (95%CI: 12-23) prior to booster vaccination in comparison to 1017 (95%CI: 732-1413) at day 14 post booster vaccination; and a 53.6-folds increase in that of older adults, with GMTs of 14 (95%CI: 9-20) before booster vaccination in comparison to 729(95%CI: 397-1339) at day 14 post-booster vaccination. The neutralizing titres against SARS-CoV-2 Delta strain also demonstrated a sharp increase from the day of pre booster vaccination to day 14 post booster vaccination, with GMTs of 11 (95%CI:8-15) versus 383 (95%CI:277-531) in younger adults (35.4-folds

increase), and 6.5(95%CI: 5-8) versus 300(95%CI:142-631) in older adults (46.0-folds increase), respectively. We also observed a considerable and consistent increase of pseudovirus neutralizing titres against emerging VOCs from day 28 post second vaccination to day 14 post booster vaccination, with GMTs of 206 (95%CI:163-259) versus 607 (95%CI: 478-771) for Alpha strain, 54 (95%CI:38-77) versus 329 (95%CI: 255-425) for Beta strain, 219 (95%CI:157-306) versus 647 (95%CI: 484-865) for Delta strain. Our preliminary findings indicate a homogenous booster dose of V-01 was safe and well-tolerated, with overall adverse reactions being absent or mild-to-moderate in severity, and no grade 3 or worse AEs were related to booster vaccination. Conclusions: A homogenous booster immunization in participants receiving a primary series of two-dose V-01 elicited a substantial humoral immune response against wild-type SARS-CoV-2 and emerging VOCs, along with a favorable safety and reactogenicity profile. Our study provided promising data for a homogenous prime-boost strategy using recombinant protein vaccine to tackle the ongoing pandemic, potentially providing broad protection against emerging VOCs and overcoming waning immunity.

203. **Causes, characteristics, and patterns of prolonged unplanned school closures prior to the COVID-19 pandemic – United States, 2011 – 2019**

Jahan F.A., Zviedrite N., Gao H., Ahmed F., Uzicanin A.

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Abstract

Introduction Outside of pandemics, there is little information about occurrence of prolonged unplanned K-12 school closures (PUSC). We describe here the reasons, characteristics, and patterns of PUSC in the United States during 8 consecutive inter-pandemic academic years, 2011-2019. Methods From August 1, 2011 through June 30, 2019, daily systematic online searches were conducted to collect data on publicly announced unplanned school closures lasting ≥1 school days in the United States. Closures were categorized as prolonged when schools were closed for ≥5 unplanned days (approximating one full workweek), excluding weekends and scheduled days off per school calendars. Results During the eight academic years, a total of 21,725 PUSCs were identified, affecting over 800,000 teachers and 13 million students that resulted in 89.9 million student-days lost. A median of 62.9% of students in PUSC-affected schools were eligible for subsidized school meals. Most affected schools were in cities (35%) and suburban areas (34%). Natural disasters (48%), adverse weather conditions (35%), and budget/teacher strikes (15%) were the most frequently cited reasons for PUSC; illness accounted for 1%, and building/facility issues, environmental issues and violence together accounted for the remaining 3%. The highest number of PUSCs occurred in Health and Human Services Regions 2, 3, 4, and 6 encompassing areas that are frequently in the path of hurricanes and tropical storms. The majority of PUSCs in these regions were attributed to a handful of hurricanes during the fall season, including hurricanes Sandy, Irma, Harvey, Florence, and Matthew. Conclusions PUSCs occur annually in the United States due to a variety of causes and are associated with a substantive loss of student-days for in-school learning. Both these prior experiences with PUSCs and those during the current COVID-19 pandemic illustrate a need for creating sustainable solutions for high-quality distance learning and innovative supplemental feeding programs nationwide, especially in disaster-prone areas.

204. **National and subnational short-term forecasting of COVID-19 in Germany and Poland, early 2021**

Bracher J., Wolffram D., Deuschel J., Görgen K., Ketterer J.L., Ullrich A., Abbott S., Barbarossa M.V., Bertsimas D., Bhatia S., Bodych M., Bosse N.I., Burgard J.P., Fiedler J., Fuhrmann J., Funk S., Gambin A., Gogolewski K., Heyder S., Hotz T., Kheifetz Y., Kirsten H., Krueger T., Krymova E., Leithäuser N., Li M.L., Meinke J.H., Miasojedow B., Mohring J., Nouvellet P., Nowosielski J.M., Ozanski T., Radwan M., Rakowski F., Scholz M., Soni S., Srivastava A., Gneiting T., Schienle M.

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Abstract

We report on the second and final part of a pre-registered forecasting study on COVID-19 cases and deaths in Germany and Poland. Fifteen independent research teams provided forecasts at lead times of one through four weeks from January through mid-April 2021. Compared to the first part (October–December 2020), the number of participating teams increased, and a number of teams started providing subnational-level forecasts. The addressed time period is characterized by rather stable nonpharmaceutical interventions in both countries, making short-term predictions more straightforward than in the first part of our study. In both countries, case counts declined initially, before rebounding due to the rise of the B.1.1.7 variant. Deaths declined through most of the study period in Germany while in Poland they increased after a prolonged plateau. Many, though not all, models outperformed a simple baseline model up to four weeks ahead, with ensemble methods showing very good relative performance. Major trend changes in reported cases, however, remained challenging to predict.

205. **SARS-CoV-2 antibody response is associated with age in convalescent outpatients**

Zhai B., Clarke K., Bauer D.L., Kupul S., Schratz L.J., Nowalk M.P., McElroy A.K., McLachlan J.B., Zimmerman R.K., Alcorn J.F.
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Abstract

COVID-19 has had an unprecedented global impact on human health. Understanding the antibody memory responses to infection is one tool needed to effectively control the pandemic. Among 173 outpatients who had virologically confirmed SARS-CoV-2 infection, we evaluated serum antibody concentrations, microneutralization activity, and enumerated SARS-CoV-2 specific B cells in convalescent blood specimens. Serum antibody concentrations were variable, allowing for stratification of the cohort into high and low responders. Serum antibody concentration was positively associated with microneutralization activity and participant age, with participants under the age of 30 showing the lowest antibody level. Neither participant sex, the timing of blood sampling following the onset of illness, nor the number of SARS-CoV-2 spike protein specific B cells correlated with serum antibody concentration. These data suggest that young adult outpatients did not generate as robust antibody memory, compared with older adults. Further, serum antibody concentration or neutralizing activity trended but did not significantly correlate with the number of SARS-CoV-2 memory B cells. These findings have direct implications for public health policy and current vaccine efforts. Knowledge gained regarding antibody memory following infection will inform the need for vaccination in those previously infected and allow for a better approximation of population-wide protective immunity.

206. **Immunogenicity of COVID-19 vaccines in patients with haematological malignancy: A systematic review and meta-analysis**
Teh J.S.K., Coussement J., Neoh Z.C.F., Spelman T., Lazarakis S., Slavin M.A., Teh B.W.
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Abstract

The objectives of this study were to assess the immunogenicity and safety of COVID-19 vaccines in patients with haematological malignancy. A systematic review and meta-analysis of clinical studies of immune responses to COVID-19 vaccination stratified by underlying malignancy and published from 1 January 2021 to 31 August 2021 was conducted using MEDLINE, EMBASE and CENTRAL. Primary outcome was the rate of seropositivity following 2 doses of COVID-19 vaccine with rates of seropositivity following 1 dose, rates of positive neutralising antibody (nAb), cellular responses and adverse events as secondary outcomes. Rates were pooled from single arm studies while rates of seropositivity were compared against the rate in healthy controls for comparator studies using a random effects model and expressed as a pooled odds ratio with 95% confidence intervals. Forty-four studies (16 mixed group, 28 disease specific) with 7064 patients were included in the analysis (2331 following first dose, 4733 following second dose). Overall seropositivity rates were 61-67% following 2 doses and 37-51% following 1 dose of COVID-19 vaccine. The lowest seropositivity rate was 51% in CLL patients and was highest in patients with acute leukaemia (93%). Following 1 dose, nAb and cellular response rates were 18-63% and 33-86% respectively. Active treatment, ongoing or recent treatment with targeted and CD-20 monoclonal antibody therapies within 12 months was associated with poor COVID-19 vaccine immune responses. New approaches to prevention are urgently required to reduce COVID-19 infection morbidity and mortality in high-risk patient groups that respond poorly to COVID-19 vaccination.

207. **The impact of heating, ventilation and air conditioning (HVAC) design features on the transmission of viruses, including the 2019 novel coronavirus (COVID-19): A systematic review of humidity**
Thornton G.M., Fleck B.A., Dandnayak D., Kroeker E., Zhong L., Hartling L.
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Abstract

The aerosol route has been a pathway for transmission of many viruses. Similarly, recent evidence has determined aerosol transmission for SARS-CoV-2 to be significant. Consequently, public health officials and professionals have sought data regarding the role of Heating, Ventilation, and Air Conditioning (HVAC) features as a means to mitigate transmission of viruses, particularly coronaviruses. Using international standards, a systematic review was conducted to comprehensively identify and synthesize research examining the effect of humidity on transmission of coronaviruses and influenza. The results from 24 relevant studies showed that: increasing from mid (40-60%) to high (>60%) relative humidity (RH) for SARS-CoV-2 was associated with decreased virus survival; although SARS-CoV-2 results appear consistent, coronaviruses do not all behave the

same; increasing from low (<40%) to mid RH for influenza was associated with decreased persistence, infectivity, viability, and survival, however effects of increased humidity from mid to high for influenza were not consistent; and medium, temperature, and exposure time were associated with inconsistency in results for both coronaviruses and influenza. Adapting HVAC humidity to mitigate virus transmission is a complex approach due to difficulties of humidity control; humidity is a feature to be considered in conjunction with other HVAC features.

208. **Ethnicity and outcomes in COVID-19 in the United Kingdom: A systematic review and meta-analysis**
Siddiq S., Ahmed S., Akram I.
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Abstract

This systematic review and meta-analysis evaluated the clinical outcomes of COVID-19 disease in the ethnic minorities of the UK in comparison to the White ethnic group. Medline, Embase, Cochrane, MedRxiv, and Prospero were searched for articles published between May 2020 to April 2021. PROSPERO ID: CRD42021248117. Fourteen studies (767177 participants) were included in the review. In the adjusted analysis, the pooled Odds Ratio (OR) for the mortality outcome was higher for the Black (1.83, 95% CI: 1.21-2.76), Asian (1.16, 95% CI: 0.85-1.57), and Mixed and Other (MO) groups (1.12, 95% CI: 1.04-1.20) compared to the White group. The adjusted and unadjusted ORs of intensive care admission were more than double for all ethnicities (OR Black 2.32, 95% CI: 1.73-3.11, Asian 2.34, 95% CI: 1.89-2.90, MO group 2.26, 95% CI: 1.64-3.11). In the adjusted analysis of mechanical ventilation need the ORs were similarly significantly raised (Black group 2.03, 95% CI: 1.80-2.29, Asian group 1.84, 95% CI: 1.20-2.80, MO 2.09, 95% CI: 1.35-3.22). This review confirmed that all ethnic groups in the UK suffered from increased disease severity and mortality with regards to COVID-19. This has urgent public health and policy implications to reduce the health disparities.

209. **Ranking the effectiveness of non-pharmaceutical interventions to counter COVID-19 in UK universities with vaccinated population**
Niu Z., Scarciotti G.
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Abstract

Several universities around the world have resumed in-person teaching after successful vaccination campaigns have covered 70/80% of the population. In this study, we combine a new compartmental model with an optimal control formulation to discover, among different non-pharmaceutical interventions, the best prevention strategy to maximize on-campus activities while keeping spread under control. Composed of two interconnected Susceptible-Exposed-Infected-Quarantined-Recovered (SEIQR) structures, the model enables staff-to-staff infections, student-to-staff cross infections, student-to-student infections, and environment-to-individual infections. Then, we model input variables representing the implementation of different non-pharmaceutical interventions and formulate and solve optimal control problems for four desired scenarios: minimum number of cases, minimum intervention, minimum non-quarantine intervention, and minimum quarantine intervention. Our results reveal the particular significance of mask wearing and social distancing in universities with vaccinated population (with proportions according to UK data). The study also reveals that quarantining infected students has a higher importance than quarantining staff. In contrast, other measures such as environmental disinfection seems to be less important.

210. **Association between long working hours and psychological distress: The effect of sick leave criteria in the workplace during the COVID-19 pandemic**
Hino A., Inoue A., Mafune K., Tsuji M., Tateishi S., Ogami A., Nagata T., Muramatsu K., Fujino Y.
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Abstract

Objective: This study investigated the effect of sick leave criteria on the association between long working hours and psychological distress. Methods: We conducted a cross-sectional survey in December 2020, and 27,032 workers completed the questionnaire. First, after testing the interaction effect of overtime work hours and sick leave criteria on psychological distress,

we conducted stratified analyses using sick leave criteria. Results: A significant interaction effect was found. When we conducted stratified analyses, the odds ratios increased with longer working hours, both with and without sick leave criteria groups; however, the risk was greater in the without sick leave criteria group, compared with the criteria group. Conclusion: We revealed that working without sick leave criteria could strengthen the association between long working hours and psychological distress during the COVID-19 pandemic.

211. **Defining the determinants of under-vaccination in migrant populations in Europe to improve routine and COVID-19 vaccine uptake: A systematic review**

Crawshaw A.F., Farah Y., Deal A., Rustage K., Hayward S.E., Carter J., Knights F., Goldsmith L.P., Campos-Matos I., Wurie F., Majeed A., Bedford H., Forster A.S., Hargreaves S.

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Abstract

Diverse migrant populations in Europe are at risk of under-immunisation and have recently shown lower levels of COVID-19 vaccination intent and uptake. Understanding the determinants of vaccine uptake in migrants is critical to address immediate COVID-19 vaccination inequities, and longer-term will help improve coverage for routine vaccinations, aligning with the goals of the new Immunisation Agenda 2030. We did a systematic review following PRISMA guidelines and using a PICOS framework (PROSPERO CRD42020219214; MEDLINE, CINAHL, PsycINFO databases, 1 January 2000 – 14 September 2021) exploring barriers and facilitators to vaccine uptake and determinants of under-vaccination in migrants in the EU/EEA, UK, and Switzerland. We categorised barriers/facilitators using the '5As' Determinants of Vaccine Uptake Taxonomy. 5259 data sources were screened, with 67 studies included from 16 countries, representing 366,529 migrants. Access barriers were most commonly reported (language, literacy and communication barriers; practical and legal barriers to accessing/delivering vaccination services; service barriers, including lack of specific guidelines and knowledge of healthcare professionals) for key vaccines including MMR, DTP, HPV, influenza, polio, COVID-19 vaccines. Acceptance barriers were mostly reported in Eastern European and Muslim communities for HPV, measles, and influenza vaccines. We identified 23 determinants of under-vaccination in migrants, including geographical origin (where 25/26 (96%) studies showed significance) – particularly African/Eastern European origin; recent migration; being a refugee/asylum seeker; higher income; parental education level; no healthcare contact in the past year; and lower language skills. Facilitators of migrants' vaccine uptake included tailored vaccination messaging, community outreach and 'nudging' interventions. Migrants' barriers to accessing healthcare are already well documented, and this review confirms their role in limiting vaccine uptake. These data hold immediate relevance to strengthening vaccination programmes in high-income countries, including for COVID-19. Our findings suggested that targeted, evidence-informed strategies are needed to address access and acceptance barriers to vaccination in migrants, including the development of migrant-sensitive and adaptable vaccination services and systems, unambiguous public health messaging, and coproduction of tailored interventions.

212. **Stable cell clones harboring self-replicating SARS-CoV-2 RNAs for drug screen**

Liu S., Chou C.-K., Wu W.W., Luan B., Wang T.T.

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Abstract

The development of antivirals against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been hampered by the lack of efficient cell-based replication systems that are amenable to high-throughput screens in biosafety level 2 laboratories. Here we report that stable cell clones harboring autonomously replicating SARS-CoV-2 RNAs without S, M, E genes can be efficiently derived from the baby hamster kidney (BHK-21) cell line when a pair of mutations were introduced into the non-structural protein 1 (Nsp1) of SARS-CoV-2 to ameliorate cellular toxicity associated with virus replication. In a proof-of-concept experiment we screened a 273-compound library using replicon cells and identified three compounds as novel inhibitors of SARS-CoV-2 replication. Altogether, this work establishes a robust, cell-based system for genetic and functional analyses of SARS-CoV-2 replication and for the development of antiviral drugs.

213. **Accelerated decline of genome heterogeneity in the SARS-CoV-2 coronavirus**

Oliver J.L., Bernaola-Galván P., Perfectti F., Gómez-Martín C., Verdú M., Moya A.

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Abstract

In the brief time since the outbreak of the COVID-19 pandemic, and despite its proofreading mechanism, the SARS-CoV-2 coronavirus has accumulated a significant amount of genetic variability through recombination and mutation events. To test evolutionary trends that could inform us on the adaptive process of the virus to its human host, we summarize all this variability in the Sequence Compositional Complexity (SCC), a measure of genome heterogeneity that captures the mutational and recombinational changes accumulated by a nucleotide sequence along time. Despite the brief time elapsed, we detected many differences in the number and length of compositional domains, as well as in their nucleotide frequencies, in more than 12,000 high-quality coronavirus genomes from across the globe. These differences in SCC are phylogenetically structured, as revealed by significant phylogenetic signal. Phylogenetic ridge regression shows that SCC followed a generalized decreasing trend along the ongoing process of pathogen evolution. In contrast, SCC evolutionary rate increased with time, showing that it accelerates toward the present. In addition, a low rate set of genomes was detected in all the genome groups, suggesting the existence of a stepwise distribution of rates, a strong indication of selection in favor of different dominant strains. Coronavirus variants reveal an exacerbation of this trend: non-significant SCC regression, low phylogenetic signal and, concomitantly, a threefold increase in the evolutionary rate. Altogether, these results show an accelerated decline of genome heterogeneity along with the SARS-CoV-2 pandemic expansion, a process that might be related to viral adaptation to the human host, perhaps paralleling the transformation of the current pandemic to epidemic.

214. **Structural basis of main proteases of coronavirus bound to drug candidate PF-07321332**
Li J., Lin C., Zhou X., Zhong F., Zeng P., Yang Y., Zhang Y., Yu B., Fan X., McCormick P.J., Fu R., Fu Y., Jiang H., Zhang J.
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Abstract

The high mutation rate of COVID-19 and the prevalence of multiple variants strongly support the need for pharmacological options to complement vaccine strategies. One region that appears highly conserved among different genus of coronaviruses is the substrate binding site of the main protease (M^{pro} or $3CL^{pro}$), making it an attractive target for the development of broad-spectrum drugs for multiple coronaviruses. PF-07321332 developed by Pfizer is the first orally administered inhibitor targeting the main protease of SARS-CoV-2, which also has shown potency against other coronaviruses. Here we report three crystal structures of main protease of SARS-CoV-2, SARS-CoV and MERS-CoV bound to the inhibitor PF-07321332. The structures reveal a ligand-binding site that is conserved among SARS-CoV-2, SARS-CoV and MERS-CoV, providing insights into the mechanism of inhibition of viral replication. The long and narrow cavity in the cleft between domains I and II of main protease harbors multiple inhibitor binding sites, where PF-07321332 occupies subsites S1, S2 and S4 and appears more restricted compared with other inhibitors. A detailed analysis of these structures illuminated key structural determinants essential for inhibition and elucidated the binding mode of action of main proteases from different coronaviruses. Given the importance of main protease for the treatment of SARS-CoV-2 infection, insights derived from this study should accelerate the design of safer and more effective antivirals.

215. **SARS-COV-2 Delta variant displays moderate resistance to neutralizing antibodies and spike protein properties of higher soluble ACE2 sensitivity, enhanced cleavage and fusogenic activity**
Neerukonda S.N., Vassell R., Lusvarghi S., Wang R., Echegaray F., Bentley L., Eakin A.E., Erlandson K.J., Katzelnick L.C., Weiss C.D., Wang W.
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Abstract

The SARS-CoV-2 B.1.617 lineage variants, Kappa (B.1.617.1) and Delta (B.1.617.2, AY) emerged during the second wave of infections in India, but the Delta variants have become dominant worldwide and continue to evolve. The spike proteins of B.1.617.1, B.1.617.2, and AY.1 variants have several substitutions in the receptor binding domain (RBD), including L452R+E484Q, L452R+T478K, and K417N+L452R+T478K, respectively, that could potentially reduce effectiveness of therapeutic antibodies and current vaccines. Here we compared B.1.617 variants, and their single and double RBD substitutions for resistance to neutralization by convalescent sera, mRNA vaccine-elicited sera, and therapeutic neutralizing antibodies using a pseudovirus neutralization assay. Pseudoviruses with the B.1.617.1, B.1.617.2, and AY.1 spike showed a modest 1.5 to 4.4-fold reduction in neutralization titer by convalescent sera and vaccine-elicited sera. In comparison, similar modest reductions were also observed for pseudoviruses with C.37, P.1, R.1, and B.1.526 spikes, but seven- and sixteen-fold reduction for vaccine-elicited and convalescent sera, respectively, was seen for pseudoviruses with the B.1.351 spike. Four of twenty-three

therapeutic neutralizing antibodies showed either complete or partial loss of neutralization against B.1.617.2 pseudoviruses due to the L452R substitution, whereas six of twenty-three therapeutic neutralizing antibodies showed either complete or partial loss of neutralization against B.1.617.1 pseudoviruses due to either the E484Q or L452R substitution. Against AY.1 pseudoviruses, the L452R and K417N substitutions accounted for the loss of neutralization by four antibodies and one antibody, respectively, whereas one antibody lost potency that could not be fully accounted for by a single RBD substitution. The modest resistance of B.1.617 variants to vaccine-elicited sera suggest that current mRNA-based vaccines will likely remain effective in protecting against B.1.617 variants, but the therapeutic antibodies need to be carefully selected based on their resistance profiles. Finally, the spike proteins of B.1.617 variants are more efficiently cleaved due to the P681R substitution, and the spike of Delta variants exhibited greater sensitivity to soluble ACE2 neutralization, as well as fusogenic activity, which may contribute to enhanced spread of Delta variants.

216. **Molecular signature of postmortem lung tissue from COVID-19 patients suggests distinct trajectories driving mortality**

Budhraja A., Basu A., Gheware A., Abhilash D., Rajagopala S., Pakala S., Sumit M., Ray A., Arulselvi S., Mathur P., Nambirajan A., Kumar S., Gupta R., Wig N., Trikha A., Guleria R., Sarkar C., Gupta I., Jain D.

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Abstract

The precise molecular mechanisms behind severe life-threatening lung abnormalities during severe SARS-CoV-2 infections are still unclear. To address this challenge, we performed whole transcriptome sequencing of lung autopsies from 31 patients suffering from severe COVID-19 related complications and 10 uninfected controls. Using a metatranscriptome analysis of lung tissue samples we identified the existence of two distinct molecular signatures of lethal COVID-19. The dominant "classical" signature (n=23) showed upregulation of unfolded protein response, steroid biosynthesis and complement activation supported by massive metabolic reprogramming leading to characteristic lung damage. The rarer signature (n=8) potentially representing "Cytokine Release Syndrome" (CRS) showed upregulation of IL1 cytokines such CCL19 but absence of complement activation and muted inflammation. Further, dissecting expression of individual genes within enriched pathways for patient signature suggests heterogeneity in host response to the primary infection. We found that the majority of patients cleared the SARS-CoV-2 infection, but all suffered from acute dysbiosis with characteristic enrichment of opportunistic pathogens such as Gordonia bronchialis in "classical" patients and Staphylococcus warneri in CRS patients. Our results suggest two distinct models of lung pathology in severe COVID-19 patients that can be identified through the status of the complement activation, presence of specific cytokines and characteristic microbiome. This information can be used to design personalized therapy to treat COVID-19 related complications corresponding to patient signature such as using the identified drug molecules or mitigating specific secondary infections.

217. **An interactome landscape of SARS-CoV-2 virus-human protein-protein interactions by protein sequence-based multi-label classifiers**

Lee H.-J.

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Abstract

The new coronavirus species, SARS-CoV-2, caused an unprecedented global pandemic of COVID-19 disease since late December 2019. A comprehensive characterization of protein-protein interactions (PPIs) between SARS-CoV-2 and human cells is a key to understanding the infection and preventing the disease. Here we present a novel approach to predict virus-host PPIs by multi-label machine learning classifiers of random forests and XGBoost using amino acid composition profiles of virus and human proteins. Our models harness a large-scale database of Viruses.STRING with >80,000 virus-host PPIs along with evidence scores for multi-level evidence prediction, which is distinct from predicting binary interactions in previous studies. Our multi-label classifiers are based on 5 evidence levels binned from evidence scores. Our best model of XGBoost achieves 74% AUC and 68% accuracy on average in 10-fold cross validation. The most important amino acids are cysteine and histidine. In addition, our model predicts experimental PPIs with higher evidence level than text mining-based PPIs. We then predict evidence levels of ~2,000 SARS-CoV-2 virus-human PPIs from public experimental proteomics data. Interactions with SARS-CoV-2 Nsp7b show high evidence. We also predict evidence levels of all pairwise PPIs of ~550,000 between the SARS-CoV-2 and human proteomes to provide a draft virus-host interactome landscape for SARS-CoV-2 infection in humans in a comprehensive and unbiased way in silico. Most human proteins from 140 highest evidence predictions interact with SARS-CoV-2 Nsp7, Nsp1, and ORF14, with significant enrichment in the top 2 pathways of vascular smooth muscle contraction (CALD1, NPR2, CALML3) and Myc targets (CBX3, PES1). Our prediction also suggests that histone H2A components are targeted by multiple SARS-CoV-2 proteins.

218. **A SARS-CoV-2 variant of concern triggers Fc effector function with increased cross-reactivity**
Richardson S.I., Manamela N.P., Motsoeneng B.M., Kaldine H., Ayres F., Makhado Z., Mennen M., Skelem S., Williams N., Sullivan N.J., Misasi J., Gray G.G., Bekker L.-G., Ueckermann V., Rossouw T.M., Boswell M.T., Ntusi N.A.B., Burgers W.A., Moore P.L.
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Abstract

SARS-CoV-2 variants of concern (VOCs) exhibit escape from neutralizing antibodies, causing concern about vaccine effectiveness. However, while non-neutralizing cytotoxic functions of antibodies are associated with decreased disease severity and vaccine protection, Fc effector function escape from VOCs is poorly defined. Furthermore, whether VOCs trigger Fc functions with altered specificity, as has been reported for neutralization, is unknown. Here, we demonstrate that the Beta VOC partially evades Fc effector activity in individuals infected with the original (D614G) variant. However, not all functions are equivalently affected, suggesting differential targeting by antibodies mediating distinct Fc functions. Furthermore, Beta infection triggered responses with significantly improved Fc cross-reactivity against global VOCs compared to either D614G infected or Ad26.COV2.S vaccinated individuals. This suggests that, as for neutralization, the infecting spike sequence impacts Fc effector function. These data have important implications for vaccine strategies that incorporate VOCs, suggesting these may induce broader Fc effector responses.

219. **Longitudinal changes of cardiac and aortic imaging phenotypes following COVID-19 in the UK biobank cohort**
Bai W., Raman B., Petersen S.E., Neubauer S., Raisi-Estabragh Z., Aung N., Harvey N.C., Allen N., Collins R., Matthews P.M.
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Abstract

Case studies conducted after recovery from acute infection with SARS-CoV-2 have frequently identified abnormalities on CMR imaging, suggesting the possibility that SARSCoV-2 infection commonly leads to cardiac pathology. However, these observations have not been able to distinguish between associations that reflect pre-existing cardiac abnormalities (that might confer a greater likelihood of more severe infection) from those that arise as consequences of infection. To address this question, UK Biobank volunteers (n=1285; 54.5% women; mean age at baseline, 59.8 years old; 96.3% white) who attended an imaging assessment including cardiac magnetic resonance (CMR) before the start of the COVID-19 pandemic were invited to attend a second imaging assessment in 2021. Cases with evidence of previous SARS-CoV-2 infection were identified through linkage to PCR-testing or other medical records, or a positive antibody lateral flow test; n=640 in data available on 22 Sep 2021) and were matched to controls with no evidence of previous infection (n=645). The majority of these infections were milder and did not involve hospitalisation. Measures of cardiac and aortic structure and function were derived from the CMR images obtained on the cases before and after SARS-CoV-2 infection from images for the controls obtained over the same time interval using a previously validated, automated algorithm. Cases and controls had similar cardiac and aortic imaging phenotypes at their first imaging assessment. Changes between CMR imaging measures in cases before and after infection were not significantly different from those in the matched control group. Additional adjustment for comorbidities made no material difference to the results. While these results are preliminary and limited to imaging metrics derived from automated analyses, they do not suggest clinically significant persistent cardiac pathology in the UK Biobank population after generally milder (non-hospitalised) SARS-CoV-2 infection.

220. **Costly miscommunication: College students with disabilities' perceptions of COVID-19 vaccine costs**
Taylor Z.W., Charran C.
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Abstract

Institutions of higher education have mandated COVID-19 vaccinations for students wishing to return to an on-campus, in-person learning experience. However, college students with disabilities (SWDs) may be hesitant to take a COVID-19 vaccine for a variety of reasons, possibly delaying or denying these students' access to higher education. Yet, an under-researched aspect of COVID-19 vaccinations and related communication is whether college students with disabilities understand that the COVID-

19 vaccine is free and whether that understanding varies by intersectional identities. As a result, this study's research team surveyed 245 college students with disabilities to explore these students' knowledge of vaccine costs and whether differences exist between groups. Data suggests many college students with disabilities do not know that COVID-19 vaccinations are free: White/Caucasian SWDs were most aware of COVID-19 vaccines being free (23.6%), while Latinx students were least aware (1.3%). Moreover, women were more aware of free COVID-19 vaccines (14.8%) than men (11.4%), first generation college students were more aware (15.6%) than non-first generation college students (12.2%), and full-time students (19%) were more aware than part-time students (8.9%). Overall, less than 25% of SWDs understood that COVID-19 vaccines are free. Implications for health communication, vaccine awareness, and higher education policy are addressed.

221. **Evaluation of a machine learning approach utilizing wearable data for prediction of SARS-CoV-2 infection in healthcare workers**

Hirten R.P., Tomalin L., Danieletto M., Golden E., Zweig M., Kaur S., Helmus D., Biello A., Pyzik R., Bottinger E.P., Keefer L., Charney D., Nadkarni G.N., Suarez-Farinas M., Fayad Z.A.

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Abstract

Importance: Passive and non-invasive identification of SARS-CoV-2 infection remains a challenge. Widespread use of wearable devices represents an opportunity to leverage physiological metrics and fill this knowledge gap. Objective: To determine whether a machine learning model can detect SARS-CoV-2 infection from physiological metrics collected from wearable devices. Design: A multicenter observational study enrolling health care workers with remote follow-up. Setting: Seven hospitals from the Mount Sinai Health System in New York City Participants: Eligibility criteria included health care workers who were ≥18 years, employees of one of the participating hospitals, with at least an iPhone series 6, and willing to wear an Apple Watch Series 4 or higher. We excluded participants with underlying autoimmune/inflammatory diseases, and medications known to interfere with autonomic function. We enrolled participants between April 29th, 2020, and March 2nd, 2021, and followed them for a median of 73 days (range, 3-253 days). Participants provided patient-reported outcome measures through a custom smartphone application and wore an Apple Watch, collecting heart rate variability and heart rate data, throughout the follow-up period. Exposure: Participants were exposed to SARS-CoV-2 infection over time due to ongoing community spread. Main Outcome and Measure: The primary outcome was SARS-CoV-2 infection, defined as ±7 days from a self-reported positive SARS-CoV-2 nasal PCR test. Results: We enrolled 407 participants with 49 (12%) having a positive SARS-CoV-2 test during follow-up. We examined five machine-learning approaches and found that gradient-boosting machines (GBM) had the most favorable 10-CV performance. Across all testing sets, our GBM model predicted SARS-CoV-2 infection with an average area under the receiver operating characteristic (auROC)=85% (Confidence Interval 83-88%). The model was calibrated to improve sensitivity over specificity, achieving an average sensitivity of 76% (CI ±~4%) and specificity of 84% (CI ±~0.4%). The most important predictors included parameters describing the circadian HRV mean (MESOR) and peak-timing (acrophase), and age. Conclusions and Relevance: We show that a tree-based ML algorithm applied to physiological metrics passively collected from a wearable device can identify and predict SARS-CoV2 infection. Utilizing physiological metrics from wearable devices may improve screening methods and infection tracking.

222. **Inhaled corticosteroids for outpatients with COVID-19: A meta-analysis**

Lee T.C., Bortolussi-Courval É., Belga S., Daneman N., Chan A.K., Hanula R., Ezer N., McDonald E.G.

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Abstract

The role of inhaled corticosteroids for outpatient COVID-19 is evolving. We meta-analyzed reported clinical trials and estimated probability of any effect and number needed to treat of 50 or 20 for symptom resolution by day 14 [100%, 99.8%, 93.1%] and hospitalization [89.3%, 72.9%, 26.7%] respectively.

223. **Association between teleworking frequency and work functioning impairment: A nationwide cross-sectional study of Japanese full-time employees**

Yamashita S., Ishimaru T., Nagata T., Tateishi S., Hino A., Tsuji M., Ikegami K., Muramatsu K., Fujino Y.

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Abstract

Objective: We examined the impact of teleworking frequency, including influencing factors and work functioning impairment. Methods: This online cross-sectional study was conducted using a self-administered questionnaire among 27,036 full-time Japanese workers. We used the Work Functioning Impairment Scale to measure work functioning impairment and performed multilevel logistic regression analysis. Results: We observed higher odds for work functioning impairment among employees who teleworked 4 or more days a week compared with those almost never teleworked: odds ratio (OR) 1.18, 95% confidence interval (CI) 1.07–1.3. After adjusting for influencing factors (teleworking preference, changes in working time, and commuting time), there was no significant association between teleworking frequency and work functioning impairment (OR 0.93, 95% CI 0.82–1.05). Conclusions: Frequent telework may cause work functioning impairment; this can be explained by the impact of influencing factors.

224. **Cellular and humoral Immune response to mRNA COVID-19 vaccination in subjects with chronic lymphocytic leukemia**

Lyski Z.L., Kim M.S., Lee D.X., Raué H.-P., Raghunathan V., Griffin J., Ryan D., Brunton A.E., Curlin M.E., Slifka M.K., Messer W.B., Spurgeon S.E.

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Abstract

Chronic Lymphocytic Leukemia (CLL) is predominantly a B-lymphocyte leukemia associated with immune defects that are often exacerbated by CLL directed therapies. SARS-CoV-2 infection poses a significant risk of illness or mortality to CLL patients, and while SARS-CoV-2 vaccines are highly effective in immunocompetent individuals, efficacy varies substantially in immunocompromised patients, including those with CLL. To date, studies of COVID-19 vaccine immune responses in immunocompromised hosts have largely relied on semi-quantitative antibody titers that only partially characterize vaccine-elicited immune responses and do not measure B or T-cell specific responses that may also play a protective role in vaccinees. Here, we report RBD-specific antibody as well as B-cell and T-cell responses in an observational cohort of sixteen CLL subjects who received mRNA vaccination against SARS-CoV-2, finding a strong association between CLL treatment and vaccine immunogenicity, with important implications for vaccination timing in the context of CLL treatment or recovery from prior treatment.

225. **A high-throughput, automated, cell-free expression and screening platform for antibody discovery**

Hunt A.C., Vögeli B., Kightlinger W.K., Yoesep D.J., Krüger A., Jewett M.C.

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Abstract

Antibody discovery is bottlenecked by the individual expression and evaluation of antigen-specific hits. Here, we address this gap by developing an automated workflow combining cell-free DNA template generation, protein synthesis, and high-throughput binding measurements of antibody fragments in a process that takes hours rather than weeks. We apply this workflow to 119 published SARS-CoV-2 neutralizing antibodies and demonstrate rapid identification of the most potent antibody candidates.

226. **Autoantibodies detected in MIS-C patients due to administration of intravenous immunoglobulin**

Burbelo P.D., Castagnoli R., Shimizu C., Delmonte O.M., Dobbs K., Discepolo V., Lo Vecchio A., Guarino A., Licciardi F., Ramenghi U., Rey E., Vial M.C., Marseglia G.L., Licari A., Montagna D., Rossi C., Montealegre Sanchez G.A., Barron K., Warner B.M., Chiorini J.A., Espinosa Y., Noguera L., Dropulic L., Truong M., Gerstbacher D., Mató S., Kanegaye J., Tremoulet A.H., Eisenstein E.M., Su H.C., Imberti L., Poli M.C., Burns J.C., Notarangelo L.D., Cohen J.I., Abe N., Bryl A., Donofrio-Odmann J.J., Ekpenyong A., Gardiner M., Gutglass D.J., Nguyen M.B., Ulrich S.

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Abstract

The autoantibody profile associated with known autoimmune diseases in patients with COVID-19 or multisystem inflammatory syndrome in children (MIS-C) remains poorly defined. Here we show that adults with COVID-19 had a moderate prevalence of autoantibodies against the lung antigen KCNRG, and SLE-associated Smith autoantigen. Children with COVID-19 rarely had autoantibodies; one of 59 children had GAD65 autoantibodies associated with acute insulin-dependent diabetes. While autoantibodies associated with SLE/Sjögren's syndrome (Ro52, Ro60, and La) and/or autoimmune gastritis (gastric ATPase) were detected in 74% (40/54) of MIS-C patients, further analysis of these patients and of children with Kawasaki disease (KD), showed that the administration of intravenous immunoglobulin (IVIG) was largely responsible for detection of these autoantibodies in both groups of patients. Monitoring in vivo decay of the autoantibodies in MIS-C children showed that the IVIG-derived Ro52, Ro60, and La autoantibodies declined to undetectable levels by 45-60 days, but gastric ATPase autoantibodies declined more slowly requiring >100 days until undetectable. Together these findings demonstrate that administration of high-dose IVIG is responsible for the detection of several autoantibodies in MIS-C and KD. Further studies are needed to investigate autoantibody production in MIS-C patients, independently from IVIG administration.

227. **Plasma markers of neurologic injury and systemic inflammation in individuals with self-reported neurologic post-acute sequelae of SARS-CoV-2 infection (PASC)**

Peluso M.J., Sans H.M., Forman C.A., Nylander A.N., Ho H.-E., Lu S., Goldberg S.A., Hoh R., Tai V., Munter S.E., Chenna A., Yee B.C., Winslow J.W., Petropoulos C.J., Martin J.N., Kelly J.D., Durstenfeld M.S., Hsue P.Y., Hunt P.W., Greene M., Chow F.C., Hellmuth J., Henrich T.J., Glidden D.V., Deeks S.G.

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Abstract

Background: The biologic mechanisms underlying neurologic post-acute-sequelae of SARS-CoV-2 infection (PASC) are incompletely understood. Methods: We measured markers of neuronal injury (glial fibrillary acidic protein [GFAP], neurofilament light chain [NfL]) and soluble markers of inflammation among a cohort of people with prior confirmed SARS-CoV-2 infection at early and late recovery following the initial illness (defined as less than and greater than 90 days, respectively). The primary clinical outcome was the presence of self-reported central nervous system (CNS) PASC symptoms during the late recovery timepoint. We compared fold-changes in marker values between those with and without CNS PASC symptoms using linear mixed effects models and examined relationships between neurologic and immunologic markers using rank linear correlations. Results: Of 121 individuals, 52 reported CNS PASC symptoms. During early recovery, those who went on to report CNS PASC symptoms had elevations in GFAP (1.3-fold higher mean ratio, 95% CI 1.04-1.63, p=0.02), but not NfL (1.06-fold higher mean ratio, 95% CI 0.89-1.26, p=0.54). During late recovery, neither GFAP nor NfL levels were elevated among those with CNS PASC symptoms. Although absolute levels of NfL did not differ, those who reported CNS PASC symptoms demonstrated a stronger downward trend over time in comparison to those who did not report CNS PASC symptoms (p=0.041). Those who went on to report CNS PASC also exhibited elevations in IL-6 (48% higher during early recovery and 38% higher during late recovery), MCP-1 (19% higher during early recovery), and TNF-alpha (19% higher during early recovery and 13% higher during late recovery). GFAP and NfL correlated with levels of several immune activation markers during early recovery; these correlations were attenuated during late recovery. Conclusions: Self-reported neurologic symptoms present >90 days following SARS-CoV-2 infection are associated with elevations in markers of neurologic injury and inflammation at early recovery timepoints, suggesting that early injury can result in long-term disease. The correlation of GFAP and NfL with markers of systemic immune activation suggests one possible mechanism that might contribute to these symptoms. Additional work is needed to better characterize these processes and to identify interventions to prevent or treat this condition.

228. **Cohort study of Covid-19 vaccine effectiveness among healthcare workers in Finland, December 2020 - October 2021**

Poukka E., Baum U., Palmu A.A., Lehtonen T.O., Salo H., Nohynek H., Leino T.

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Abstract

Recently, Covid-19 vaccine effectiveness has decreased especially against mild disease due to emergence of the Delta variant and waning protection. In this register-based study among healthcare workers in Finland, the vaccine effectiveness of two-dose mRNA vaccine series against SARS-CoV-2 infection decreased from 82% (95% CI 79-85%) 14-90 days after vaccination to 53% (43-62%) after 6 months. Similar trend was observed for other series. Waning was not observed against Covid-19 hospitalization. These results facilitate decision-making of booster doses for healthcare workers.

229. **Spatialized epidemiological forecasting applied to Covid-19 pandemic at departmental scale in France**
Oliver M., Georges D., Prieur C.
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Abstract

In this paper, we present a spatialized extension of a SIR model that accounts for undetected infections and recoveries as well as the load on hospital services. The spatialized compartmental model we introduce is governed by a set of partial differential equations (PDEs) defined on a spatial domain with complex boundary. We propose to solve the set of PDEs defining our model by using a meshless numerical method based on a finite difference scheme in which the spatial operators are approximated by using radial basis functions. Such an approach is reputed as flexible for solving problems on complex domains. Then we calibrate our model on the French department of Isère during the first period of lockdown, using daily reports of hospital occupancy in France. Our methodology allows to simulate the spread of Covid-19 pandemic at a departmental level, and for each compartment. However, the simulation cost prevents from online short-term forecast. Therefore, we propose to rely on reduced order modeling tools to compute short-term forecasts of infection number. The strategy consists in learning a time-dependent reduced order model with few compartments from a collection of evaluations of our spatialized detailed model, varying initial conditions and parameter values. A set of reduced bases is learnt in an offline phase while the projection on each reduced basis and the selection of the best projection is performed online, allowing short-term forecast of the global number of infected individuals in the department.

230. **Influence of heterogeneous age-group contact patterns on critical vaccination rates for herd immunity to SARS-CoV-2**
Saldaña J., Scoglio C.
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Abstract

Currently, several western countries have more than half of their population fully vaccinated against COVID-19. At the same time, some of them are experiencing a fourth or even a fifth wave of cases, most of them concentrated in sectors of the populations whose vaccination coverage is lower than the average. So, the initial scenario of vaccine prioritization has given way to a new one where achieving herd immunity is the primary concern. Using an age-structured vaccination model with waning immunity, we show that, under a limited supply of vaccines, a vaccination strategy based on minimizing the basic reproduction number allows for the deployment of a number of vaccine doses lower than the one required for maximizing the vaccination coverage. Such minimization is achieved by giving greater protection to those age groups that, for a given social contact pattern, have smaller fractions of susceptible individuals at the endemic equilibrium without vaccination, that is, to those groups that are more vulnerable to infection.

231. **Primary care diagnosis and treatment of attention-deficit/hyperactivity disorder in school-aged children: Trends and disparities during the COVID-19 pandemic**
Bannett Y., Dahlen A., Huffman L.C., Feldman H.M.
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Abstract

Importance: Little is known about changes in health care in the first year of the pandemic for the large population of school-aged children with attention-deficit/hyperactivity disorder (ADHD), who were especially impacted by lockdowns, school closures, and remote learning. Objective: To assess temporal trends in rates of primary care provider (PCP) diagnosis and treatment of school-aged children with ADHD in the first year of the COVID-19 pandemic as compared to pre-pandemic years, and to investigate disparities in care. Method: We retrospectively analyzed electronic health records from all primary care visits (in-person and telehealth) of children ages 6-17 years seen between 01/2016 and 03/2021 in a community-based primary healthcare network in California (n=77,298 patients). Study Outcomes: (1) # of primary care visits, (2) # of visits with ADHD diagnosis (ADHD-related visits), (3) # of first ADHD diagnoses, (4) # of PCP prescriptions for ADHD medications (stimulants, alpha-2 agonists, atomoxetine), (5) # of first PCP prescriptions of ADHD medications. Interrupted time-series analysis evaluated changes in rates of study outcomes during 4 quarters of the pandemic year (3/15/2020-3/15/2021) compared to pre-pandemic years. Patient

demographic characteristics were compared pre-pandemic to pandemic year. Results: In the first quarter (Q1) of the pandemic year, all primary care visits dropped by 62% (CI 54.9-67.2%); ADHD-related visits dropped by 33% (95% CI 22.2-43.6%). In Q2-4, while all primary care visits remained significantly below pre-pandemic rates, ADHD-related visits returned to pre-pandemic rates. Conversely, rates of first ADHD diagnoses remained at half of pre-pandemic rates throughout the year (Q1-4). ADHD medication prescription rates remained stable throughout the pandemic year. The proportion of patients living in low-income neighborhoods who received ADHD-related care (ADHD-related visits and first ADHD diagnoses) were lower during the pandemic year compared to pre-pandemic years. Females comprised a higher proportion of first ADHD diagnoses compared to pre-pandemic years (34% vs. 28%, absolute standardized difference=0.13, p=0.03). Conclusion: Ongoing treatment for school-aged children with ADHD was maintained during the pandemic, especially in children from high-income families. Socioeconomic differences in ADHD-related care emphasize the need to improve access to care for all children with ADHD in the ongoing pandemic and beyond.

232. **Safety and immunogenicity of heterologous and homologous inactivated and adenoviral-vectored COVID-19 vaccines in healthy adults**

Wanlapakorn N., Suntronwong N., Phowatthanasathian H., Yorsaeng R., Vichaiwattana P., Thongmee T., Auphimai C., Srimuan D., Thatsanatorn T., Assawakosri S., Kanokudom S., Sudhinaraset N., Poovorawan Y.

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Abstract

In light of intermittent supply shortages of individual vaccines and evidence of rare but serious adverse events after vaccination, heterologous regimens for COVID-19 vaccines have gained significant interest. This study aims to assess the reactogenicity and immunogenicity of the heterologous adenoviral vector vaccine regimen (ChAdOx1-S, AstraZeneca; hereafter referred to as AZ) and the inactivated vaccine regimen (CoronaVac; hereafter referred to as CV) regimen in healthy Thai adults immunized between June and September 2021. Our study showed that adverse events following homologous CV-CV and AZ-AZ, and heterologous CV-AZ and AZ-CV combinations, were mild and well tolerated overall. Receptor-binding domain (RBD)-specific antibody responses and neutralizing activities against wild-type and variants of concern after two-dose vaccination were higher in the heterologous CV-AZ and homologous AZ-AZ groups compared to the CV-CV and AZ-CV groups. Conversely, the spike-specific IgA response was detected only in the CV-AZ group after two doses of vaccination. The total interferon gamma response was detected in both the CV-AZ and AZ-CV groups after the two-dose vaccination. Given the shorter completion time of two doses, heterologous CoronaVac followed by ChAdOx1-S can be considered as an alternative regimen to homologous efficacy-proven ChAdOx1-S in countries with circulating variants. Additional studies on the efficacy and durability of immune responses induced by heterologous vaccine regimens are warranted.

233. **SARS-CoV-2 aerosol transmission indoors: A closer look at viral load, infectivity, the effectiveness of preventive measures and a simple approach for practical recommendations**

Kriegel M., Hartmann A., Buchholz U., Seifried J., Baumgarte S., Gastmeier P.

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Abstract

Currently, airborne transmission is seen as the most important transmission path for SARSCoV-2. In this investigation, a classic dose-response model is used on the one hand to find out retrospectively the probable viral load of the infectious source patient at the time of transmission in 25 documented outbreaks. We showed that an infection due to airborne transmission at a distance from the infectious person was probably only possible in the 25 outbreaks examined, with attack rates of 4-100%, if the viral load had been higher than 1E+08 viral copies/ml. This demonstrates that the viral load estimated from the swab might overestimate a person's infectivity via aerosol, because a person is generally considered infectious, independent of the transmission way, when the viral load from the swab is 1E+06 viral copies/ml. On the other hand, a possible approach is presented to predict the probable situational Attack Rate (PARs) of a group of persons in a room through aerosol particles emitted by an infectious source patient. Four main categories of influence on the risk of infection are formed: First the emitted viruses, depending on the viral load and the amount of respiratory particles, and necessary number of reproducible viruses for infection, second the room-specific data and duration of stay of the group of people, third the activity of the exposed persons, and fourth the effect of personal protection (e.g. wearing masks from infectious and/or susceptible person). Furthermore, a simplified method is presented to calculate either the maximum possible number of persons in a room, so that probably a maximum of one person becomes infected when an infectious person is in the room, or the $PAR_{s,simple}$ for a given number of persons, ventilation rate and time of occupancy. We additionally show, taking into account organizational preventive measures, which person-related virus-free supply air flow rates are necessary to keep the number of newly infected persons to less than 1. The simple approach makes it easy to derive preventive organizational and ventilation measures. Our results show that the volume flow rate or a person-related flow rate is a much more effective parameter to evaluate ventilation for infection prevention than the air change rate. We suggest to monitor the CO_2 concentration as an easy to implement and valid measurement system for indoor spaces.

Finally, we show that of the three measures, besides of wearing masks and increasing ventilation, testing contributes the most to the joint protective effect. This corresponds to the classic approach to implement protection concepts: preventing the source from entering the room and emitting viruses at all. In summary, a layered approach of different measures is recommended to mutually compensate for possible failures of any one measure (e.g. incorrect execution of tests, incorrect fit of masks or irregular window opening), to increase the degree of protection and thus reduce the risk of transmission of SARS-CoV-2.

234. **Severity and inpatient mortality of COVID-19 pneumonia from Beta variant infection: A clinical cohort study in Cape Town, South Africa**

Boloko L., Lifson A., Little F., de Wet T., Papavarnavas N., Marais G., Hsiao N.-Y., Rosslee M.-J., Doolabh D., Iranzadeh A., Williamson C., Dlamini S., Mendelson M., Ntusi N., Wilkinson R.J., Hussey H., Davies M.-A., Meintjes G., Wasserman S.

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Abstract

Background The SARS-CoV-2 Beta variant, associated with immune escape and higher transmissibility, drove a more severe second COVID-19 wave in South Africa. Individual patient level characteristics and outcomes with the Beta variant are not well characterized. Methods We performed a retrospective cohort study comparing disease severity and inpatient mortality of COVID-19 pneumonia between the first and second wave periods at a referral hospital in Cape Town, South Africa. Beta variant infection was confirmed by genomic sequencing. Outcomes were analyzed with logistic regression and accelerated failure time models. Results 1,182 patients were included: 571 during the first wave period and 611 from the second wave. Beta variant accounted for 97% of infections in the second wave. There was no difference in crude in-hospital mortality between wave periods (first wave 22.2%, second wave 22.1%; p = 0.9). Time to death was decreased with higher weekly hospital admissions (16%; 95% CI, 8 to 24 for every 50-patient increase), age (18%; 95% CI, 12 to 24 for every 10-year increase) and hypertension (31%; 95% CI, 12 to 46). Corticosteroid use delayed time to death by 2-fold (95% CI, 1.5 to 3.0). Admission during the second wave decreased time to death after adjustment for other predictors, but this did not reach statistical significance (24%; 95% CI, 47 to -2). There was no effect of HIV on survival. Conclusions There was a trend towards earlier mortality during the second COVID-19 wave driven by the Beta variant, suggesting a possible biological basis. Use of oral prednisone was strongly protective.

235. **Measuring college students' with disabilities attitudes toward taking COVID-19 vaccines**

Taylor Z.W., Charran C.

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Abstract

This survey explores attitudes of 245 currently enrolled college students with disabilities regarding their comfort taking a COVID-19 vaccine. Results suggest most college students with disabilities are willing to take a COVID-19 vaccine if their institution requires it to return to campus in subsequent semesters. However, many students with disabilities would not feel comfortable with a vaccine mandate mid-semester and would consider withdrawing, especially among older students with disabilities and first-generation college students with disabilities. Implications for postsecondary policy and leadership are addressed.

236. **Estimation of the basic reproduction number of COVID-19 from the incubation period distribution**

Basnarkov L., Tomovski I., Avram F.

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Abstract

Background The estimates of future course of spreading of the SARS-CoV-2 virus are frequently based on Markovian models in which the transitions between the compartments are exponentially distributed. Specifically, the basic reproduction number R_0 is also determined from formulae where it is related to the parameters of such models. The observations show that the start of infectivity of an individual appears nearly at the same time as the onset of symptoms, while the distribution of the incubation period is not an exponential. Methods We propose a method for estimation of R_0 for COVID-19 based on the empirical

incubation period distribution and assumed very short infectivity period that lasts only few days around the onset of symptoms. It is tested on daily new cases in six major countries in Europe, in the first wave of epidemic in spring, 2020. Results The calculations show that even if the infectivity starts two days before the onset of symptoms and stops immediately when they appear, the value of R_0 is larger than that from the classical, Markovian approach. For more realistic cases, when only individuals with mild symptoms spread the virus for few days after onset of symptoms, the respective values are even larger. Conclusions The calculations of R_0 and other characteristics of spreading of COVID-19 based on the classical, Markovian approaches should be taken very cautiously. Instead, non-Markovian models with general distribution functions of transition between compartments should be considered as more appropriate.

237. **Whole-blood DNA methylation analysis reveals respiratory environmental traits involved in COVID-19 severity following SARS-CoV-2 infection**

Barturen G., Carnero-Montoro E., Martínez-Bueno M., Rojo-Rello S., Sobrino B., Alcántara-Domínguez C., Bernardo D., Alarcón-Riquelme M.E.

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Abstract

SARS-CoV-2 causes a severe inflammatory syndrome (COVID-19) leading, in many cases, to bilateral pneumonia, severe dyspnea and in ~5% of these, death. DNA methylation is known to play an important role in the regulation of the immune processes behind COVID-19 progression, however it has not been studied in depth, yet. In this study, we aim to evaluate the implication of DNA methylation in COVID-19 progression by means of a genome-wide DNA methylation analysis combined with DNA genotyping. The results reveal the existence of epigenomic regulation of functional pathways associated with COVID-19 progression and mediated by genetic loci. We found an environmental trait-related signature that discriminates mild from severe cases, and regulates IL-6 expression via the transcription factor CEBP. The analyses suggest that an interaction between environmental contribution, genetics and epigenetics might be playing a role in triggering the cytokine storm described in the most severe cases.

238. **Determinants of pre-vaccination antibody responses to SARS-CoV-2: A population-based longitudinal study (COVIDENCE UK)**

Talaei M., Faustini S., Holt H., Jolliffe D.A., Vivaldi G., Greenig M., Perdek N., Maltby S., Symons J., Davies G.A., 5.1.2e 5.1.2c **., Griffiths C.J., Kee F., Sheikh A., Richter A.G., Shaheen S.O., Martineau A.R.**

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Abstract

Background: Prospective population-based studies investigating multiple determinants of pre-vaccination antibody responses to SARS-CoV-2 are lacking. Methods: We did a prospective population-based study in SARS-CoV-2 vaccine-naive UK adults between May 1 and Nov 2, 2020. Information on 88 potential risk factors was obtained through online questionnaires, and combined IgG/IgA/IgM responses to SARS-CoV-2 spike glycoprotein were determined in dried blood spots. We used logistic and linear regression to estimate adjusted odds ratios (aORs) and adjusted geometric mean ratios (aGMRs) for potential determinants of SARS-CoV-2 seropositivity (all participants) and antibody titres (seropositive participants only), respectively. Results: 1696 (15.2%) of 11,130 participants were seropositive. Factors independently associated with increased risk included frontline health/care occupation (aOR 1.86, 95% CI 1.49-2.33), international travel (1.22, 1.08-1.37), BMI >30 vs <25 kg/m^2 (1.22, 1.05-1.42), Asian/Asian British vs White ethnicity (1.65, 1.10-2.47), and alcohol consumption ≥15 vs 0 units/week (1.26, 1.06-1.49). Light physical exercise associated with decreased risk (0.80, 0.69-0.93, for ≥10 vs 0-4 h/week). Higher titres associated with frontline health/care occupation (aGMR 1.26, 95% CI 1.13-1.41), international travel (1.10, 1.04-1.16), BMI >30 vs <25 kg/m^2 (1.09, 1.01-1.17), and Asian/Asian British vs White ethnicity (1.23, 1.03-1.46); these associations were not substantially attenuated by adjustment for disease severity. Conclusions: Higher alcohol consumption and reduced physical exercise represent new modifiable risk factors for SARS-CoV-2 infection. Recognised associations between Asian/Asian British ethnic origin and obesity and increased risk of SARS-CoV-2 seropositivity were independent of other sociodemographic, clinical, or behavioural factors investigated.

239. **Use cases for COVID-19 screening and surveillance with rapid antigen-detecting tests: A systematic review**

Anand A., Bigio J., MacLean E., Underwood T., Pai N.P., Carmona S., Schumacher S.G., Toporowski A.

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Abstract

Introduction: Testing is critical to controlling the COVID-19 pandemic. Antigen-detecting rapid diagnostic tests (Ag-RDTs) that can be used at the point of care have the potential to increase access to COVID-19 testing, particularly in settings with limited laboratory capacity. This systematic review synthesized literature on specific use cases and performance of Ag-RDTs for detecting SARSCoV-2, for the first comprehensive assessment of Ag-RDT use in real-world settings. Methods: We searched three databases (PubMed, EMBASE and medRxiv) up to 12 April 2021 for publications on Ag-RDT use for large-scale screening, irrespective of symptoms, and surveillance of COVID-19, excluding studies of only presumptive COVID-19 patients. We tabulated data on the study setting, populations, type of test, diagnostic performance and operational findings. We assessed risk of bias using QUADAS-2 and an adapted tool for prevalence studies. Results: From 4313 citations, 39 studies conducted in asymptomatic and symptomatic adults were included. Study sample sizes varied from 40 to >5 million. Of 39 studies, 37 (94.9%) investigated lateral flow Ag-RDTs and two (5.1%) investigated multiplex sandwich chemiluminescent enzyme immunoassay Ag-RDTs. Six categories of testing (screening/surveillance) initiatives were identified: mass screening (n=13), targeted screening (n=11), healthcare entry testing (n=6), at-home testing (n=4), surveillance (n=4) and prevalence survey (n=1). Across studies, Ag-RDT sensitivity varied from 40% to 100%. Ag-RDTs were noted as convenient, easy-to-use and low cost, with a rapid turnaround time and high user acceptability. Risk of bias was generally low or unclear across the studies. Conclusion: This systematic review demonstrates the use of Ag-RDTs across a wide range of real-world settings for screening and surveillance of COVID-19 in both symptomatic and asymptomatic individuals. Ag-RDTs were overall found to be easy-to-use, low cost and rapid tools, when consideration is given to their implementation and interpretation. The review was funded by FIND, the global alliance for diagnostics.

240. **Effectiveness of COVID-19 vaccines and post-vaccination SARS-COV 2 infection, hospitalization, and mortality: A systematic review and meta-analysis of observational studies**

Rahmani K., Shavaleh R., Forouhi M., Disfani H.F., Kamandi M., Dezfuli A.A.Z., Oskooi R.K., Foogerdi M., Soltani M.

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Abstract

Introduction & Objective: Vaccination is one of the most important and effective ways of preventing infectious diseases, and has recently been used in the COVID-19 epidemic and pandemic. The present meta-analysis study aimed to evaluate the effectiveness of COVID-19 vaccines in reducing the incidence of infection, hospitalization, and mortality in observational studies. Materials and Methods: A systematic search was performed independently in Scopus, PubMed, ProQuest, and Google Scholar electronic databases as well as Preprint servers using the keywords under study. The heterogeneity of the studies was assessed using I^2 and χ^2 statistics, according to which the I^2 of > 50% and P -value <0.1 was reported as heterogeneity of the studies. In addition, the Pooled Vaccine Effectiveness (PVE) obtained from the studies was calculated by converting (1- Pooled estimate × 100%) based on the type of outcome. Results: A total of 54 records were included in this meta-analysis. The rate of PVE against SARS-COV 2 infection was about 71% (OR = 0.29, 95% CI: 0.23-0.36) in the first dose and 87% (OR = 0.13, 95% CI: 0.08-0.21) in the second, and the highest effectiveness in the first and second doses was that of BNT162b2 mRNA and combined studies. The PVE versus COVID-19-associated hospitalization was 73% (OR = 0.27, 95% CI: 0.18-0.41) in the first dose and 89% (OR = 0.11, 95% CI: 0.07-0.17) in the second. mRNA-1273 and combined studies in the first dose and ChAdOx1 and mRNA-1273 in the second dose had the highest effectiveness. Regarding the COVID-19-related mortality, PVE was about 28% (HR = 0.39, 95% CI: 0.23-0.45) in the first dose and 89% (HR = 0.11, 95% CI: 0.03-0.43) in the second. Conclusion: The evidence obtained from this study showed that the effectiveness of BNT162b2 mRNA, mRNA-1273, and ChAdOx1 in the first and second doses, and even combined studies were associated with increased effectiveness against SARS-COV2 infection, hospitalization, and death from COVID-19. In addition, considering that the second dose was significantly more efficient than the first one, a booster dose injection could be effective in high-risk individuals. On the other hand, it was important to observe other prevention considerations in the first days after taking the first dose.

241. **The basic reproduction number of COVID-19 across Africa**

Iyaniwura S.A., Rabiu M., David J.F., Kong J.D.

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Abstract

The pandemic of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) took the world by surprise. Following the first outbreak of COVID-19 in December 2019, several models have been developed to study and understand its transmission dynamics. Although the spread of COVID-19 is being slowed down by vaccination and other interventions, there is still a need to

have a clear understanding of the evolution of the pandemic across countries, states and communities. To this end, there is a need to have a clearer picture of the initial spread of the disease in different regions. In this project, we used a simple SEIR model and a Bayesian inference framework to estimate the basic reproduction number of COVID-19 across Africa. Our estimates vary between 1.98 (Sudan) and 9.66 (Mauritius), with a median of 3.67 (90% CrI: 3.31 - 4.12). The estimates provided in this paper will help to inform COVID-19 modeling in the respective countries/regions.

242. **Multiplex solid-phase RPA coupled CRISPR-based visual detection of SARS-CoV-2**
Qin X., Zhou Y., Paul R., Wu Y., 5.1.2e.
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Abstract

COVID-19 has challenged the world's public health and led to over 4.5 million deaths. A rapid, sensitive, and cost-effective point-of-care virus detection device is crucial to the control and surveillance of the contagious severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic. Here we demonstrate a solid phase isothermal recombinase polymerase amplification coupled CRISPR-based (spRPA-CRISPR) assay for on-chip multiplexed, sensitive and visual COVID-19 DNA detection. By targeting the SARS-CoV-2 structure protein encoded genomes, two specific genes were simultaneously detected with the control sample without cross-interaction with other sequences. The endpoint signal can be directly visualized for rapid detection of COVID-19. The amplified target sequences were immobilized on the one-pot device surface and detected using the mixed Cas12a-crRNA collateral cleavage of reporter released fluorescent signal when specific genes were recognized. The system was tested with samples of a broad range of concentrations (20 to $2x10^5$ copies) and showed analytical sensitivity down to 20 copies per reaction. Furthermore, a low-cost LED UV flashlight (~$12) was used to provide a visible SARS-CoV-2 detection signal of the spRPA-CRISPR assay which could be purchased online easily. Thus, our platform provides a sensitive and easy-to-read multiplexed gene detection method with the capacity to specifically identify low concentration genes. Similar CRISPR biosensor chips can support a broad range of applications such as HPV DNA detection, influenza SARS-CoV-2 multiplex detection, and other infectious disease testing assays.

243. **A RCT of a third dose CoronaVac or BNT162b2 vaccine in adults with two doses of CoronaVac**
Mok C.K.P., Cheng S.M.S., Chen C., Yiu K., Chan T.-O., Lai K.C., Ling K.C., Sun Y., Ho L.L., Peiris M., Hui D.S.
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Abstract

Background. Poor immunogenicity and antibody waning were found in vaccinees of CoronaVac. There is lack of randomized controlled trial (RCT) data to compare the immunogenicity and safety of schedules using homologous and heterologous vaccine as a booster dose. Methods. We randomly assigned adults who had received 2 doses of CoronaVac with low antibody response to receive an additional booster dose of either BNT162b2 or CoronaVac. The local and systemic adverse reactions were recorded. Levels of SARS-CoV-2 neutralizing and spike binding antibody in plasma were measured. Findings. At one month after the third dose of vaccine, BNT162b2 vaccines elicited significantly higher surrogate virus neutralizing test (sVNT), spike receptor binding, spike N terminal domain binding, spike S2 domain binding levels than CoronaVac. More participants from the BNT162b2 group reported injection site pain and swelling as well as fatigue and muscle pain than those who received CoronaVac as the third dose. The mean results of the sVNT against the wild type, beta, gamma and delta variants in the BNT162b2 boosted group was 96.83%, 92.29%, 92.51% and 95.33% respectively which were significantly higher than the CoronaVac boosted group (Wild type: 57.75%; Beta: 38.79 %; Gamma: 32.22%; Delta: 48.87%) Conclusion. Our RCT study shows that BNT162b2 booster dose for those people who poorly responded to the previous vaccination of CoronaVac is significantly more immunogenic than a CoronaVac booster. BNT162b2 also elicits higher levels of SARS-CoV-2 specific neutralizing antibodies to different variants of concern. The adverse reactions were only mild and short-lived.

244. **The impact of the initial and 2nd national COVID-19 lockdown on mental health in young people with and without pre-existing depressive symptoms**
Joensen A., Danielsen S., Andersen P.K., Groot J., Strandberg-Larsen K.
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Abstract

Background: The evidence on mental well-being and loneliness among young people during the initial lockdown is mixed, and little is known about the long-lasting impact of the sequential lockdowns. We examine changes in young people's mental health from before to during the initial and second more prolonged lockdown, and whether women and those with pre-existing depressive symptoms were disproportionally impacted. Methods: Participants reported on mental health indicators in an ongoing 18-year data collection in the Danish National Birth Cohort and in a COVID-19 survey, including 8 data points: 7 in the initial lockdown, and 1 year post. Changes in quality of life (QoL), mental well-being, and loneliness were estimated with random effect linear regressions on longitudinal data (N=32,985), and linear regressions on repeated cross-sections (N=28,579). Findings: Interim deterioration in mental well-being and loneliness was observed during the initial lockdown, and only in those without pre-existing depressive symptoms. During the second lockdown, a modest deterioration was again observed for mental well-being and loneliness. QoL likewise only declined among those without pre-existing symptoms, where women showed a greater decline than men. QoL did not normalise during the initial lockdown and remained at lower levels during the second lockdown. These findings were not replicated in the repeated cross-sections. Interpretation: Except for an interim decrease in mental health during lockdown, and only in those without pre-existing depressive symptoms, this study's findings do not suggest a substantial detrimental impact of the lockdowns. Potential methodological differences in-between studies are a possible explanation for the mixed evidence. Funding: The Velux Foundation

245. **Downsizing of contact tracing during COVID-19 vaccine roll-out**

Martignoni M.M., Renault J., Baafi J., Hurford A.

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Abstract

Contact tracing is a key component of successful management of COVID-19. Contacts of infected individuals are asked to quarantine, which can significantly slow down (or prevent) community spread. Contact tracing is particularly effective when infections are detected quickly (e.g., through rapid testing), when contacts are traced with high probability, when the initial number of cases is low, and when social distancing and border restrictions are in place. However, the magnitude of the individual contribution of these factors in reducing epidemic spread and the impact of vaccination in determining contact tracing outputs is not fully understood. We present a delayed differential equation model to investigate how vaccine roll-out and the relaxation of social distancing requirements affect contact tracing practises. We provide an analytical criteria to determine the minimal contact tracing efficiency (defined as the the probability of identifying and quarantining contacts of symptomatic individuals) required to keep an outbreak under control, with respect to the contact rate and vaccination status of the population. Additionally, we consider how delays in outbreak detection and increased case importation rates affect the number of contacts to be traced daily. We show that in vaccinated communities a lower contact tracing efficiency is required to avoid uncontrolled epidemic spread, and delayed outbreak detection and relaxation of border restrictions do not lead to a significantly higher risk of overwhelming contact tracing. We find that investing in testing programs, rather than increasing the contact tracing capacity, has a larger impact in determining whether an outbreak will be controllable. This is because early detection activates contact tracing, which will slow, and eventually reverse exponential growth, while the contact tracing capacity is a threshold that will easily become overwhelmed if exponential growth is not curbed. Finally, we evaluate quarantine effectiveness during vaccine roll-out, by considering the proportion of people that will develop an infection while in isolation in relation to the vaccination status of the population and for different viral variants. We show that quarantine effectiveness decreases with increasing proportion of fully vaccinated individuals, and increases in the presence of more transmissible variants. These results suggest that a cost-effective approach during vaccine roll-out is to establish different quarantine rules for vaccinated and unvaccinated individuals, where rules should depend on viral transmissibility. Altogether, our study provides quantitative information for contact tracing downsizing during vaccine roll-out, to guide COVID-19 exit strategies.

246. **Investigating the relationship between interventions, contact patterns, and SARS-CoV-2 transmissibility**

Trentini F., Manna A., Balbo N., Marziano V., Guzzetta G., Merler S., Ajelli M., Poletti P., Melegaro A.

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Abstract

Background After a rapid upsurge of COVID-19 cases in Italy during the fall of 2020, the government introduced a three-tiered restriction system aimed at increasing physical distancing. The Ministry of Health, after periodic epidemiological risk assessments, assigned a tier to each of the 21 Italian regions and autonomous provinces (AP). It is still unclear to what extent these different measures altered mixing patterns and how quickly the population adapted their social interactions to continuous changes in restrictions. Methods and findings We conducted a survey between July 2020 and March 2021 to monitor changes in social contact patterns among individuals in the metropolitan city of Milan, Italy, which was hardly hit by the second wave of COVID-19 pandemic. The number of contacts during periods characterized by different levels of restrictions was analyzed

through negative binomial regression models and age-specific contact matrices were estimated under the different tiers. Relying on the empirically estimated mixing patterns, we quantified relative changes in SARS-CoV-2 transmission potential associated with the different tiers. As tighter restrictions were implemented during the fall of 2020, a progressive reduction in the mean number of contacts recorded by study participants was observed: from 16.4% under mild restrictions (yellow tier), to 45.6% under strong restrictions (red tier). Higher restrictions levels were also found to increase the relative contribution of contacts occurring within the household. The SARS-CoV-2 reproduction number was estimated to decrease by 18.7% (95%CI: 4.6-30.8), 33.4% (95%CI: 22.7-43.2), and 50.2% (95%CI: 40.9-57.7) under the yellow, orange, and red tiers, respectively. Conclusions Our results give an important quantification of the expected contribution of different restriction levels in shaping social contacts and decreasing the transmission potential of SARS-CoV-2. These estimates can find an operational use in anticipating the effect that the implementation of these tiered restriction can have on SARS-CoV-2 reproduction number under an evolving epidemiological situation.

247. **REACT-1 round 15 interim report: High and rising prevalence of SARS-CoV-2 infection in England from end of September 2021 followed by a fall in late October 2021**

Chadeau-Hyam M., Eales O., Bodinier B., Wang H., Haw D., Whitaker M., Walters C.E., Atchison C., Diggle P.J., Page A.J., Ashby D., Barclay W., Taylor G., Cooke G., Ward H., Darzi A., Donnelly C.A., Elliott P.

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Abstract

Background: The third wave of COVID-19 in England coincided with the rapid spread of the Delta variant of SARS-CoV-2 from the end of May 2021. Case incidence data from the national testing programme (Pillar 2) in England may be affected by changes in testing behaviour and other biases. Community surveys may provide important contextual information to inform policy and the public health response. Methods: We estimated patterns of community prevalence of SARS-CoV-2 infection in England using RT-PCR swab-positivity, demographic and other risk factor data from round 15 (interim) of the REal-time Assessment of Community Transmission-1 (REACT-1) study (round 15a, carried out from 19 to 29 October 2021). We compared these findings with those from round 14 (9 to 27 September 2021). Results: During mid- to late-October 2021 (round 15a) weighted prevalence was 1.72% (1.61%, 1.84%) compared to 0.83% (0.76%, 0.89%) in September 2021 (round 14). The overall reproduction number (R) from round 14 to round 15a was 1.12 (1.11, 1.14) with increases in prevalence over this period (September to October) across age groups and regions except Yorkshire and The Humber. However, within round 15a (mid- to late-October) there was evidence of a fall in prevalence with R of 0.76 (0.65, 0.88). The highest weighted prevalence was observed among children aged 5 to 12 years at 5.85% (5.10%, 6.70%) and 13 to 17 years at 5.75% (5.02%, 6.57%). At regional level, there was an almost four-fold increase in weighted prevalence in South West from round 14 at 0.59% (0.43%,0.80%) to round 15a at 2.18% (1.84%, 2.58%), with highest smoothed prevalence at subregional level also found in South West in round 15a. Age, sex, key worker status, and presence of children in the home jointly contributed to the risk of swab-positivity. Among the 126 sequenced positive swabs obtained up until 23 October, all were Delta variant; 13 (10.3%) were identified as the AY.4.2 sub-lineage. Discussion: We observed the highest overall prevalence of swab-positivity seen in the REACT-1 study in England to date in round 15a (October 2021), with a two-fold rise in swab-positivity from round 14 (September 2021). Despite evidence of a fall in prevalence from mid- to late-October 2021, prevalence remains high, particularly in school-aged children, with evidence also of higher prevalence in households with one or more children. Thus, vaccination of children aged 12 and over remains a high priority (with possible extension to children aged 5-12) to help reduce within-household transmission and disruptions to education, as well as among adults, to lessen the risk of serious disease among those infected.

248. **A combination of variant genotypes at two loci in the APOL1 gene is associated with adverse outcomes in SARS-CoV-2: A UK Biobank study**

Adamson W., Noyes H., Beckett-Hill G., Cooper A., MacLeod A.

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Abstract

The risk of hospitalisation or death from Covid-19 in the UK is disproportionately higher in black ethnic populations than others for reasons that are not fully understood[1]. In people of African ancestry, variants of the APOL1 gene (G1 and G2) have been associated with risk of a number of non-communicable diseases, such as chronic kidney disease[2,3,4,5] and the infectious disease, African sleeping sickness[6]. Here we test the hypothesis that adverse Covid-19 outcomes are also associated with these variants. Using data from Black UK Biobank participants, we used Firth's Bias-Reduced Logistic Regression in R to identify APOL1 genotypes that were associated with either hospitalisation or death. APOL1 G1/G2 compound heterozygotes were associated with hospitalisation (OR = 2.4 95% CI: 1.2-4.5) p = 0.010) and death (OR = 5.4, 95% CI: 1.8-15.4, p = 0.004) compared to individuals not carrying the variants. This support hypotheses proposing APOL1 genotype (specifically G1/G2) is a significant contributory factor in the increased rates of poor Covid-19 outcomes observed in people of African ancestry. This has implications for both at the individual and population level by identifying those at higher risk of severe Covid-19 who would

benefit from early vaccination and treatment. This is especially relevant to geographical regions where APOL1 G1/G2 genotypes are common such as West and Central Africa[6] and their diaspora.

249. **The Brief Observation of Symptoms of Autism (BOSA): Development of a new adapted assessment measure for remote telehealth administration through COVID-19 and beyond**

Dow D., Holbrook A., Toolan C., McDonald N., Sterrett K., Rosen N., Kim S.H., Lord C.

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Abstract

Interest in telehealth assessment for autism has increased due to COVID-19 and subsequent expansion of remote psychological services, though options that are easy for clinicians to adopt and available through the lifespan are limited. The Brief Observation of Symptoms of Autism (BOSA) provides a social context with standardized materials and activities that can be coded by clinicians trained in the Autism Diagnostic Observation Schedule (ADOS). The current project examined psychometric properties to determine optimal use for each BOSA version. Three hundred and seven participants with 453 BOSAs were included to determine best performing items for algorithms, validity, sensitivity, specificity, recommended cut-offs, and proposed ranges of concern. While preliminary, the BOSA provides a promising new option for telehealth-administered assessment for autism.

250. **Equipment-free detection of SARS-CoV-2 and Variants of Concern using Cas13**

Arizti-Sanz J., Bradley A.D., Zhang Y.B., Boehm C.K., Freije C.A., Grunberg M.E., Kosoko-Thoroddsen T.-S.F., Welch N.L., Pillai P.P., Mantena S., Kim G., Uwanibe J.N., John O.G., Eromon P.E., Kocher G., Gross R., Lee J.S., Hensley L.E., Happi C.T., Johnson J., Sabeti P.C., Myhrvold C.

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Abstract

The COVID-19 pandemic, and the recent rise and widespread transmission of SARS-CoV-2 Variants of Concern (VOCs), have demonstrated the need for ubiquitous nucleic acid testing outside of centralized clinical laboratories. Here, we develop SHINEv2, a Cas13-based nucleic acid diagnostic that combines quick and ambient temperature sample processing and lyophilized reagents to greatly simplify the test procedure and assay distribution. We benchmarked a SHINEv2 assay for SARS-CoV-2 detection against state-of-the-art antigen-capture tests using 96 patient samples, demonstrating 50-fold greater sensitivity and 100% specificity. We designed SHINEv2 assays for discriminating the Alpha, Beta, Gamma and Delta VOCs, which can be read out visually using lateral flow technology. We further demonstrate that our assays can be performed without any equipment in less than 90 minutes. SHINEv2 represents an important advance towards rapid nucleic acid tests that can be performed in any location.

251. **Interferon pathway lupus risk alleles modulate risk of death from acute COVID-19**

Nln I., Fernandez-Ruiz R., Wampler Muskardin T.L., Paredes J.L., Blazer A.D., Tuminello S., Attur M., Iturrate E., Petrilli C.M., Abramson S.B., Chakravarti A., Niewold T.B.

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Abstract

Type I interferon (IFN) is critical in our defense against viral infections. Increased type I IFN pathway activation is a genetic risk factor for systemic lupus erythematosus (SLE), and a number of common risk alleles contribute to the high IFN trait. We hypothesized that these common gain-of-function IFN pathway alleles may be associated with protection from mortality in acute COVID-19. We studied patients admitted with acute COVID-19 (756 European-American and 398 African-American ancestry). Ancestral backgrounds were analyzed separately, and mortality after acute COVID-19 was the primary outcome. In European-American ancestry, we found that a haplotype of interferon regulatory factor 5 (IRF5) and alleles of protein kinase cGMP-dependent 1 (PRKG1) were associated with mortality from COVID-19. Interestingly, these were much stronger risk factors in younger patients (OR=29.2 for PRKG1 in ages 45-54). Variants in the IRF7 and IRF8 genes were associated with mortality from COVID-19 in African-American subjects, and these genetic effects were more pronounced in older subjects. Combining genetic

information with blood biomarker data such as C-reactive protein, troponin, and D-dimer resulted in significantly improved predictive capacity, and in both ancestral backgrounds the risk genotypes were most relevant in those with positive biomarkers (OR for death between 14 and 111 in high risk genetic/biomarker groups). This study confirms the critical role of the IFN pathway in defense against COVID-19 and viral infections, and supports the idea that some common SLE risk alleles exert protective effects in anti-viral immunity. Background We find that a number of IFN pathway lupus risk alleles significantly impact mortality following COVID-19 infection. These data support the idea that type I IFN pathway risk alleles for autoimmune disease may persist in high frequency in modern human populations due to a benefit in our defense against viral infections. Translational Significance We develop multivariate prediction models which combine genetics and known biomarkers of severity to result in greatly improved prediction of mortality in acute COVID-19. The specific associated alleles provide some clues about key points in our defense against COVID-19.

252. **Using portable air purifiers to reduce airborne transmission of infectious respiratory viruses – a computational fluid dynamics study**

Guo L., Torii R., Epstein R., Rubin J., Reid J.P., Li H., Ducci A., Balachandran R., Tiwari M.K., Ventikos Y., Lovat L.B.
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Abstract

Aerosols and droplets generated from expiratory events play a critical role in the transmission of infectious respiratory viruses. Increasingly robust evidence has suggested the crucial role of fine aerosols in airborne transmission of respiratory diseases, which is now widely regarded as an important transmission path of COVID-19. In this report, we used CFD modelling to investigate the efficiency of using portable air purifiers containing HEPA filters to reduce airborne aerosols in hospitals and serve as a potential retrofit mitigation strategy. We used a consulting room to set up our simulations because currently the clearance time between consultations is the controlling factor that limits the patient turnover rate. The results suggest the inlet/suction of the air purifier unit should be lifted above the floor to achieve better clearance efficiency, with up to 40% improvement possible. If multiple air purifiers are used, the combined efficiency can increase to 62%. This work provides practical guidance on a mitigation strategy that can be easily implemented in an expedient, cost-effective and rapid manner, and paves the way for developing more science-informed strategies to mitigate the airborne transmission of respiratory infections in hospitals.

253. **SARS-CoV-2 infection induces cross-reactive autoantibodies against angiotensin II**

Briquez P.S., Rouhani S.J., Yu J., Pyzer A.R., Trujillo J., Dugan H.L., Stamper C.T., Changrob S., Sperling A.I., Wilson P.C., Gajewski T.F., Hubbell J.A., Swartz M.A.
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Abstract

Patients infected with the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) can experience life-threatening respiratory distress, blood pressure dysregulation and thrombosis. This is thought to be associated with an impaired activity of angiotensin-converting enzyme-2 (ACE-2), which is the main entry receptor of SARS-CoV-2 and which also tightly regulates blood pressure by converting the vasoconstrictive peptide angiotensin II (AngII) to a vasopressor peptide. Here, we show that a significant proportion of hospitalized COVID-19 patients developed autoantibodies against AngII, whose presence correlates with lower blood oxygenation, blood pressure dysregulation, and overall higher disease severity. Anti-AngII antibodies can develop upon specific immune reaction to the SARS-CoV-2 proteins Spike or RBD, to which they can cross-bind, suggesting some epitope mimicry between AngII and Spike/RBD. These results provide important insights on how an immune reaction against SARS-CoV-2 can impair blood pressure regulation.

254. **Comparison of antibody levels in Response to SARS-CoV-2 infection and vaccination type in a midwestern cohort**

Remy L., Tomomori-Sato C., Conkright-Fincham J., Wiedemann L.M., Conaway J.W., Unruh J.R.
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Abstract

We present preliminary data in an ongoing observational study reporting SARS-CoV-2 spike protein reactive antibody levels from a convenience cohort of over 250 individuals in Kansas City. We observe stable antibody levels over one year in individuals who recovered from COVID19 infection caused by SARS-CoV-2. By comparison, our data reveals even higher antibody levels from naïve individuals vaccinated with Pfizer or Moderna vaccines and slightly lower levels from Johnson & Johnson (J&J) recipients. For all vaccines, inoculation after recovery resulted in higher antibody levels than vaccination alone. Responses to Pfizer and Moderna vaccines decreased over time from high initial levels but at the time of publication remain higher than those for recovered or J&J recipients. Within our limited cohort we only see slight demographic trends including higher antibody levels in recovered female vs. male individuals. Booster doses and breakthrough infections both result in rapid increases in antibody levels.

255. **Model-estimated relationship between elementary school-related SARS-CoV-2 transmission, mitigation interventions, and vaccination coverage across community incidence levels**

Giardina J., Bilinski A., Fitzpatrick M.C., Kendall E.A., Linas B.P., Salomon J., Ciaranello A.L.

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Abstract

Background While CDC guidance for K-12 schools recommends indoor masking regardless of vaccination status, final decisions about masking in schools will be made at the local and state level. The impact of the removal of mask restrictions, however, on COVID-19 outcomes for elementary students, educators/staff, and their households is not well known. Methods We used a previously published agent-based dynamic transmission model of SARS-CoV-2 in K-12 schools to simulate an elementary school with 638 students across 12 scenarios: combinations of three viral infectiousness levels (reflecting wild-type virus, alpha variant, and delta variant) and four student vaccination levels (0%, 25%, 50% and 70% coverage). For each scenario, we varied observed community COVID-19 incidence (0 to 50 cases/100,000 people/day) and mitigation effectiveness (0-100% reduction to in-school secondary attack rate), and evaluated two outcomes over a 30 day period: (1) the probability of at least one in-school transmission, and (2) average increase in total infections among students, educators/staff, and their household members associated with moving from more to less intensive mitigation measures. Results Over 30 days in the simulated elementary school, the probability of at least one in-school SARSCoV-2 transmission and the number of estimated additional infections in the immediate school community associated with changes in mitigation measures varied widely. In one scenario with the delta variant and no student vaccination, assuming that baseline mitigation measures of simple ventilation and handwashing reduce the secondary attack rate by 40%, if decision-makers seek to keep the monthly probability of an in-school transmission below 50%, additional mitigation (e.g., masking) would need to be added at a community incidence of approximately 2/100,000/day. Once students are vaccinated, thresholds shift substantially higher. Limitations The interpretation of model results should be limited by the uncertainty in many of the parameters, including the effectiveness of individual mitigation interventions and vaccine efficacy against the delta variant, and the limited scope of the model beyond the school community. Additionally, the assumed case detection rate (33% of cases detected) may be too high in areas with decreased testing capacity. Conclusion Despite the assumption of high adult vaccination, the risks of both in-school SARS-CoV-2 transmission and resulting infections among students, educators/staff, and their household members remain high when the delta variant predominates and students are unvaccinated. Mitigation measures or vaccinations for students can substantially reduce these risks. These findings underscore the potential role for responsive plans, where mitigation is deployed based on local COVID-19 incidence and vaccine uptake.

256. **Epidemiological characteristics of the B.1.526 SARS-CoV-2 variant**

Yang W., Greene S.K., Peterson E.R., Li W., Mathes R., Graf L., Lall R., Hughes S., Wang J., Fine A.

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Abstract

To characterize the epidemiological properties of the B.1.526 SARS-CoV-2 variant of interest, here we utilized nine epidemiological and population datasets and model-inference methods to reconstruct SARS-CoV-2 transmission dynamics in New York City, where B.1.526 emerged. We estimated that B.1.526 had a moderate increase (15-25%) in transmissibility and could escape immunity in 0-10% of previously infected individuals. In addition, B.1.526 substantially increased the infection-fatality risk (IFR) among adults 65 or older by >60% during Nov 2020 – Apr 2021, compared to baseline risk estimated for preexisting variants. Overall, findings suggest that new variants like B.1.526 likely spread in the population weeks prior to detection and that partial immune escape (e.g., resistance to therapeutic antibodies) could offset prior medical advances and increase IFR. Early preparedness for and close monitoring of SARS-CoV-2 variants, their epidemiological characteristics, and disease severity are thus crucial to COVID-19 response as it remains a global public health threat.

257. **Rapid transmission of coronavirus disease 2019 within a religious sect in South Korea: a mathematical modeling study**
Kim J.-H., Lee H., Won Y.S., Son W.-S., Im J.
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Abstract

Rapid transmission of coronavirus disease 2019 (COVID-19) was observed in the Shincheonji Church of Jesus, a religious sect in South Korea. The index case was confirmed on February 18, 2020 in Daegu City, and within two weeks, 3,081 connected cases were identified. Doubling times during these initial stages (i.e., February 18 – March 2) of the outbreak were less than 2 days. A stochastic model fitted to the time series of confirmed cases suggests that the basic reproduction number (t_0) of COVID-19 was 8.5 [95% credible interval (CrI): 6.3, 10.9] among the church members, whereas (t_0 = 1.9 [95% CrI: 0.4, 4.4]) in the rest of the population of Daegu City. The model also suggests that there were already 4 [95% CrI: 2, 11] undetected cases of COVID-19 on February 7 when the index case reportedly presented symptoms. The Shincheonji Church cluster is likely to be emblematic of other outbreak-prone populations where t_0 of COVID-19 is higher. Understanding and subsequently limiting the risk of transmission in such high-risk places is key to effective control.

258. **Preventable deaths from SARS-CoV-2 in England and Wales: A systematic case series of coroners' reports during the COVID-19 pandemic**
Swift B., Heneghan C., Aronson J.K., Howard D.J., Richards G.C.
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Abstract

Objectives To examine coroners' Prevention of Future Deaths reports (PFDs) to identify deaths involving SARS-CoV-2 that coroners deemed preventable. Design Consecutive case series. Setting England and Wales. Participants Patients reported in 510 PFDs dated between 01 January 2020 and 28 June 2021, collected from the UK's Courts and Tribunals Judiciary website using web scraping to create an openly available database, https://preventabledeathstracker.net/. Main outcome measures Concerns reported by coroners. Public and Patient Involvement Patients and members of the public were not involved in this study. Results SARS-CoV-2 was involved in 23 deaths reported by coroners in PFDs. Twelve deaths were indirectly related to the COVID-19 pandemic, defined as those that were not medically caused by SARS-CoV-2, but were associated with mitigation measures. In 11 cases the coroner explicitly reported that COVID-19 had directly caused death. There was geographical variation in the reporting of PFDs; most (39%) were written by coroners in the North-West of England. The coroners raised 56 concerns, problems in communication being the most common (30%), followed by failure to follow protocols (23%). Organizations in the National Health Service (NHS) were sent the most PFDs (51%), followed by the Government (26%), but responses to PFDs by these organizations were poor. Conclusions PFDs contain a rich source of information on preventable deaths that has previously been difficult to examine systematically. Our openly available tool (https://preventabledeathstracker.net/) streamlines this process and has identified many concerns raised by coroners that should be addressed during the Government's inquiry into the handling of the COVID-19 pandemic, so that mistakes made are less likely to be repeated.

259. **How an election can be safely planned and conducted during a pandemic: Decision support based on a discrete event model**
Weibrecht N., Rößler M., Bicher M., Emrich Š., Zauner G., Popper N.
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Abstract

In 2020, the ongoing COVID-19 pandemic caused major limitations for any aspect of social life and in specific for all events that require a gathering of people. While most events of this kind can be postponed or cancelled, democratic elections are key elements of any democratic regime and should be upheld if at all possible. Consequently, proper planning is required to establish the highest possible level of safety to both voters and scrutineers. In this paper, we present the novel and innovative way how the municipal council and district council elections in Vienna were planned and conducted using an discrete event simulation model. Key target of this process was to avoid queues in front of polling stations to reduce the risk of related infection

clusters. In cooperation with a hygiene expert, we defined necessary precautions that should be met during the election in order to avoid the spread of COVID-19. In a next step, a simulation model was established and parametrized and validated using data from previous elections. Furthermore, the planned conditions were simulated to see whether excessive queues in front of any polling stations could form, as these could on the one hand act as an infection herd, and on the other hand, turn voters away. Our simulation identified some polling stations where long queues could emerge. However, splitting up these electoral branches resulted in a smooth election across all of Vienna. Looking back, the election did not lead to a significant increase of COVID-19 incidences. Therefore, it can be concluded that careful planning led to a safe election, despite the pandemic.

260. **Monday effect on confirmed cases of COVID-19 in Japan**

Nakagawa K., Kanatani T.
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Abstract

We examined the phenomenon of fewer new confirmed cases of COVID-19 on Mondays in Japan, which we refer to as the Monday effect, and reveal the details of this effect. Specifically, we estimated the difference between the number of new positive cases that decreased over the weekend and the number of new confirmed cases that decreased at the beginning of the week. In Japan, prefectures aggregate and announce the number of confirmed daily cases. This analysis allows us to examine whether there is a Monday effect in each prefecture. We show that the Monday effect is due to the decreased number of inspections on the weekend appearing at the beginning of the week due to a time lag. Our results indicate that the administrative system causes delays in some prefectures, and that some prefectures are less likely to conduct screenings on holidays. Our results also suggest that delays generally occur in prefectures with a population of over 2 million. Congestion, Reporting delay, Public health, COVID-19

261. **Identifying Louisiana communities at the crossroads of environmental and social vulnerability, COVID-19, and asthma**

Bakshi A., van Doren A., Maser C., Aubin K., Stewart C., Soileau S., Friedman K., Williams A.
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Abstract

The COVID-19 pandemic has disproportionately affected the socially and environmentally vulnerable, including through indirect effects on other health conditions. Asthma is one such condition, which may be exacerbated by both prolonged adverse in-home exposures if quarantining in unhealthy homes and prolonged outdoor exposures if the ambient air quality is unhealthy or hazardous. As both are often the case in Environmental Justice (EJ) communities, here we have analyzed data at the census tract (CT) level for Louisiana to assess any correlation between social and environmental vulnerability, and health issues like COVID-19 and asthma. Higher Social Vulnerability Index (SVI), Particulate Matter less than 2.5 μm in diameter ($PM_{2.5}$) and Ozone levels were associated with higher rates of cumulative COVID-19 incidence at various time points during the pandemic, as well as higher average annual asthma hospitalization rates and estimated asthma prevalence. Further, cumulative COVID-19 incidence during the first three months of the pandemic was moderately correlated with both asthma hospitalizations and estimated prevalence, suggesting similar underlying factors may be affecting both conditions. Additionally, 137 CTs were identified where social and environmental vulnerabilities co-existed, of which 75 (55%) had high estimated prevalence of asthma. These areas are likely to benefit from asthma outreach that considers both social and environmental risk factors. Fifteen out of the 137 CTs (11%) not only had higher estimated prevalence of asthma but also a high burden of COVID-19. Further research in these areas may help to elucidate any common social determinants of health that underlie both asthma and COVID-19 burdens, as well as better clarify the possible role of the environment as related to the COVID-19 burden in Louisiana.

262. **An Open Repository of Real-Time COVID-19 Indicators**

Reinhart A., Brooks L., Jahja M., Rumack A., Tang J., Agrawal S., Saeed W.A., Arnold T., Basu A., Bien J., Cabrera Á.A., Chin A., Chua E.J., Clark B., Colquhoun S., DeFries N., Farrow D.C., Forlizzi J., Grabman J., Gratzl S., Green A., Haff G., Han R., Harwood K., Hu A.J., Hyde R., Hyun S., Joshi A., Kim J., Kuznetsov A., Motte-Kerr W.L., Lee Y.J., Lee K., Lipton Z.C., Liu M.X., Mackey L., Mazaitis K., McDonald D.J., McGuinness P., Narasimhan B., O'Brien M.P., Oliveira N.L., Patil P., Perer A., Politsch C.A., Rajanala S., Rucker D., Scott C., Shah N.H., Shankar V., Sharpnack J., Shemetov D., Simon N., Smith B.Y., Srivastava V., Tan S., Tibshirani R., Tuzhilina E., van Nortwick A.K., Ventura V., Wasserman L., Weaver B., Weiss J.C., Whitman S., Williams K., Rosenfeld R., Tibshirani R.J.
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Abstract

The COVID-19 pandemic presented enormous data challenges in the United States. Policy makers, epidemiological modelers, and health researchers all require up-to-date data on the pandemic and relevant public behavior, ideally at fine spatial and temporal resolution. The COVIDcast API is our attempt to fill this need: operational since April 2020, it provides open access to both traditional public health surveillance signals (cases, deaths, and hospitalizations) and many auxiliary indicators of COVID-19 activity, such as signals extracted from de-identified medical claims data, massive online surveys, cell phone mobility data, and internet search trends. These are available at a fine geographic resolution (mostly at the county level) and are updated daily. The COVIDcast API also tracks all revisions to historical data, allowing modelers to account for the frequent revisions and backfill that are common for many public health data sources. All of the data is available in a common format through the API and accompanying R and Python software packages. This paper describes the data sources and signals, and provides examples demonstrating that the auxiliary signals in the COVIDcast API present information relevant to tracking COVID activity, augmenting traditional public health reporting and empowering research and decision-making.

263. **Appropriate relaxation of non-pharmaceutical interventions minimizes the risk of a resurgence in SARS-CoV-2 infections in spite of the Delta variant**

Koslow W., Kühn M.J., Binder S., Klitz M., Abele D., Basermann A., Meyer-Hermann M.

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Abstract

We analyze the relaxation of non-pharmaceutical interventions (NPIs) under an increasing number of vaccinations in Germany. For the spread of SARS-CoV-2 we employ a SIR-type model that accounts for age-dependence and includes realistic contact patterns between age groups. The implementation of NPIs occurs on changed contact patterns, improved isolation, or reduced infectiousness when, e.g., wearing masks. We account for spatial heterogeneity and commuting activities in between regions in Germany, and the testing of commuters is considered as a further NPI. We include the ongoing vaccination process and analyze the effect of the B.1.617.2 (Delta) variant, which is considered to be 40% – 60% more infectious then the currently dominant B.1.1.7 (Alpha) variant. We explore different opening scenarios under the ongoing vaccination process by assuming that local restrictions are either lifted in early July or August with or without continued wearing of masks and testing. Our results indicate that we can counteract the resurgence of SARS-CoV-2 despite the Delta variant with appropriate timing for the relaxation of NPIs. In all cases, however, school children are hit the hardest.

264. **Transmission networks of SARS-CoV-2 in coastal Kenya during the first two waves: a retrospective genomic study**

Agoti C.N., Ochola-Oyier L.I., Mohammed K.S., Lambisia A.W., de Laurent Z., Morobe J.M., Mburu M.W., Omuoyo D.O., Ongera E.M., Ndwiga L., Maitha E., Kitole B., Suleiman T., Mwakinangu M., Nyambu J., Otieno J., Salim B., Musyoki J., Murunga N., Otieno E., Kiiru J., Kasera K., Amoth P., Mwangangi M., Aman R., Kinyanjui S., Warimwe G., Phan M., Agweyu A., Cotten M., Barasa E., Tsofa B., Nokes D.J., Bejon P., Githinji G.

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Abstract

Background: The transmission networks of SARS-CoV-2 in sub-Saharan Africa remain poorly understood. Methods: We undertook phylogenetic analysis of 747 SARS-CoV-2 positive samples collected across six counties in coastal Kenya during the first two waves (March 2020 - February 2021). Viral imports and exports from the region were inferred using ancestral state reconstruction (ASR) approach. Results: The genomes were classified into 35 Pango lineages, six of which accounted for 79% of the sequenced infections: B.1 (49%), B.1.535 (11%), B.1.530 (6%), B.1.549 (4%), B.1.333 (4%) and B.1.1 (4%). Four identified lineages were Kenya specific. In a contemporaneous global subsample, 990 lineages were documented, 261 for Africa and 97 for Eastern Africa. ASR analysis identified >300 virus location transition events during the period, these comprising: 69 viral imports into Coastal Kenya; 93 viral exports from coastal Kenya; and 191 inter-county import/export events. Most international viral imports (58%) and exports (92%) occurred through Mombasa City, a key touristic and commercial Coastal Kenya center; and many occurred prior to June 2020, when stringent local COVID-19 restriction measures were enforced. After this period, local virus transmission dominated, and distinct local phylogenies were seen. Conclusions: Our analysis supports moving control strategies from a focus on international travel to local transmission.

265. **Predictors of black fungus fear during the COVID-19 pandemic among the Bangladeshi health workers: a cross-sectional study**
Hasan Md.K., Kabir H., Rahman M., Roy A.K., Akter S., Mitra D.K.
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Abstract

The emergence of mucormycosis cases amid the COVID-19 pandemic; fear associated with mucormycosis may turn out to be a terrifying public health issue. This study aimed to assess the association between fear and insomnia status and other predictors of mucormycosis among Bangladeshi healthcare workers. Methods From 25 May 2021 to 05 June 2021, a cross-sectional study was carried out among healthcare workers. A total of 422 healthcare workers participated in this study. A semi-structured online questionnaire was used for data collection during the COVID-19 pandemic, followed by convenient and snowball sampling methods. A multivariable linear regression model was fitted to assess the association between fear and insomnia status and other predictors of mucormycosis. Results The results indicated that the respondents with insomnia status had a higher score of mucormycosis fear than not having insomnia (β = 3.91, 95% CI: 2.49, 5.33, p <0.001), significantly. Alongside the increased knowledge score of mucormycosis, the average score of fear increased significantly(β = 0.35, 95% CI: 0.20, 0.50, p <0.001). The gender, profession, and death of friends and family members due to COVID-19 significantly affected mucormycosis fear score increment. Conclusions This is the first study that focused on assessing the association between mucormycosis fear and insomnia status among the health care workers so far. These study findings recommend emphasizing the mental health aspects and ensuring support to the healthcare workers to better tackle the ongoing public health crisis.

266. **Whole-genome sequencing of SARS-COV-2 showed wide spread of B.1.525 in February 2021 in Libya**
Alhudiri I.M., Ramadan A.M., Ibrahim K.M., Abdalla A., Eljilani M., Salem M.A., Elgheriani H.M., El Meshri S.E., Elzagheid A.
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Abstract

Alpha (B.1.1.7) SARS-COV-2 variant was detected in September 2020 in minks and humans in Denmark and UK. This variant has several mutations in the spike region (S) which could increase the transmissibility of the virus 43-90% over previously circulating variants. The National Center for Disease Control (NCDC) announced on 24th February 2021 a 25% frequency of B.1.1.7 strain in Libya using a reverse-transcriptase quantitative PCR assay. This assay relies on the specific identification of the H69-V70 deletion in S gene which causes its failure of amplification (SGTF). This deletion is not specific for B.1.1.7; but is also characteristic of two other SARS-COV-2 variants. This study aimed to estimate the frequency of B.1.1.7 and identify other variants circulating in Libya in February 2021. We performed whole genome sequencing of 67 positive SARS-COV-2 samples collected on 25th February 2021 in Libya which were also tested by RT-qPCR for SGTF. Our results showed that 55% of samples had mutations specific to B.1.525 strain and only ~3% of samples belonged to B.1.1.7. These findings suggested that B.1.525 was spreading widely in Libya. The use of such RT-qPCR assay although useful to track some variants, it cannot discriminate between variants with H69-V70 deletion. RT-qPCR assays could be multiplexed to identify multiple variants and screen samples prior to sequencing. We emphasize on the need for providing whole-genome sequencing to the main COVID-19 diagnostic laboratories in Libya as well as establishing international collaboration for building capacity and advancing research in this time of the pandemic.

267. **Mathematical modelling of SARS-CoV-2 variant outbreaks reveals their probability of extinction**
Schiøler H., Knudsen T., Brøndum R.F., Stoustrup J., Bøgsted M.
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Abstract

When a virus spreads, it may mutate into, e.g., vaccine resistant or fast spreading lineages, as was the case for the Danish Cluster-5 mink variant (belonging to the B.1.1.298 lineage), the British B.1.1.7 lineage, and the South African B.1.351 lineage of the SARS-CoV-2 virus. A way to handle such spreads is through a containment strategy, where the population in the affected area is isolated until the spread has been stopped. Under such circumstances, it is important to monitor whether the mutated virus is extinct via massive testing for the virus sub-type. If successful, the strategy will lead to lower and lower numbers of the

sub-type, and it will eventually die out. An important question is, for how long time one should wait to be sure the sub-type is extinct? We use a hidden Markov model for infection spread and an approximation of a two stage sampling scheme to infer the probability of extinction. The potential of the method is illustrated via a simulation study. Finally, the model is used to assess the Danish containment strategy when SARS-CoV-2 spread from mink to man during the summer of 2020, including the Cluster-5 sub-type. In order to avoid further spread and mink being a large animal virus reservoir, this situation led to the isolation of seven municipalities in the Northern part of the country, the culling of the entire Danish 17 million large mink population, and a bill to interim ban Danish mink production until the end of 2021.

268. **Epigenome-wide DNA methylation profiling of healthy COVID-19 recoverees reveals a unique signature in circulating immune cells**
Huoman J., Sayyab S., Apostolou E., Karlsson L., Porcile L., Rizwan M., Sharma S., Das J., Rosén A., Lerm M.
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Abstract

Background: Epigenetic alterations upon microbial challenge have been described as both a defence strategy and a result of pathogenic manipulation. While most COVID-19 studies focus on inflammatory and immune-mediated responses, little is known about epigenetic modifications in response to SARS-CoV-2 infection. Methods: Epigenome-wide DNA methylation patterns from COVID-19 convalescents were compared to uninfected controls from before and after the pandemic. Peripheral blood mononuclear cell (PBMC) DNA was extracted from uninfected controls, COVID-19 convalescents and symptom-free individuals with SARS-CoV-2-specific T cell-responses, as well as from PBMCs stimulated in vitro with SARS-CoV-2. Subsequently, the Illumina MethylationEPIC 850K array was performed, and statistical/bioinformatic analyses comprised differential DNA methylation, pathway over-representation and module identification analyses. Results: Differential DNA methylation patterns distinguished COVID-19 convalescents from uninfected controls, with similar results in an experimental SARS-CoV-2 infection model. A SARS-CoV-2-induced module was identified in vivo, comprising 66 genes of which six (TP53, INS, HSPA4, SP1, ESR1 and FAS) were present in corresponding in vitro analyses. Over-representation analyses revealed involvement in Wnt, muscarinic acetylcholine receptor signalling and gonadotropin-releasing hormone receptor pathways. Furthermore, numerous differentially methylated and network genes from both settings interacted with the SARS-CoV-2 interactome. Conclusions: Altered DNA methylation patterns of COVID-19 convalescents suggest recovery from mild-to-moderate SARS-CoV-2 infection leaves longstanding epigenetic traces. As in vitro SARS-CoV-2 infection corroborated in vivo exposure results, this indicates DNA methylation is involved in immune cell responses to challenge with this virus. Future studies should determine whether this reflects host-induced protective antiviral defence or targeted viral hijacking to evade host defence.

269. **Public opinion on a mandatory COVID-19 vaccination policy in France: A cross sectional survey**
Gagneux-Brunon A., Botelho-Nevers E., Bonneton M., Peretti-Watel P., Verger P., Launay O., Ward J.K.
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Abstract

Objectives: Reaching the last pockets of unvaccinated people is challenging, and has led to consider COVID-19 mandatory vaccination. Our aim was to assess attitudes toward COVID-19 mandatory vaccination in France before the announcement and factors associated with opposition to this type of policy. Methods: Between the 10th and the 23rd of May 2021, we conducted a cross-sectional online survey among a representative sample of the French population aged 18 and over and a specific sample of the French Senior Population over 65. Results: Among 3,056 respondents, 1,314 (43.0 %) were in favor of mandatory COVID-19 vaccination, 1,281 (41.9 %) were opposed to such a policy, and 461 (15.1 %) were undecided. Among opponents to COVID-19 mandatory vaccination for the general population, 385 (30.05 %) were in favor of a mandatory COVID-19 vaccination for healthcare workers (HCWs). In multivariate analysis, age groups 18-24 years, and 25-34 years were significantly more opposed than the reference group (>75 years old) with respective adjusted odds ratio (aOR) and 95 % confidence interval (95 % CI) 4.67 (1.73-12.61) and 3.74 (1.57-8.93). No intention of getting COVID-19 vaccine was strongly associated with opposition to mandatory vaccination with aOR 10.67 (95 % CI 6.41-17.76). In comparison with partisans of the center, partisans of the far left and green parties were more likely to be opposed to COVID-19 mandatory vaccine with respective aOR (95 % CI) 1;89 (1.06-3.38) and 2.08 (1.14-3.81). Conclusion: Attitudes toward mandatory COVID-19 vaccination are split in the French general population, and the debate might become politicized.

270. **Tracing and testing multiple generations of contacts to COVID-19 cases: Cost-benefit tradeoffs**
Kim J., Chen X., Nikpey H., Rubin H., Bidokhti S.S., Sarkar S.
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Abstract

Traditional contact tracing for COVID-19 tests the direct contacts of those who test positive even if the contacts do not show any symptom. But, by the time an infected individual is tested, the infection starting from the person may have infected a chain of individuals. Hence, why should the testing stop at direct contacts, and not test secondary, tertiary contacts or even contacts further down? One deterrent in testing long chains of individuals right away may be that it substantially increases the testing load, or does it? We investigate the costs and benefits of such multi-hop contact tracing for different number of hops. Considering a large number of contact topologies, spanning synthetic networks of divergent characteristics and those constructed from recorded interactions, we show that the cost-benefit tradeoff can be characterized in terms of a single measurable attribute, the initial epidemic growth rate. Once this growth rate crosses a threshold, multi-hop contact tracing substantially reduces the outbreak size compared to traditional contact tracing. Multi-hop even incurs a lower cost compared to the traditional contact tracing for a large range of values of the growth rate. The cost-benefit tradeoffs and the choice of the number of hops can be classified into three phases, with sharp transitions between them, depending on the value of the growth rate. The need for choosing a larger number of hops becomes greater as the growth rate increases or the environment becomes less conducive toward containing the disease.

271. **Association between preference and e-learning readiness among the Bangladeshi female nursing students in the COVID-19 pandemic: a cross-sectional study**

Kabir H., Tonmon T.T., Hasan Md.K., Biswas L., Chowdhury Md.A.H., Islam M.D., Rahman M., Mitra D.K.
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Abstract

Background The COVID-19 pandemic jeopardized the traditional academic learning calendars due to the closing of all educational institutions across the globe. To keep up with the flow of learning, most of the educational institutions shifted toward e-learning. However, the students' e-learning preference for various subdomains of e-learning readiness did not identify, particularly among the female nursing students' for a developing country like Bangladesh, where those domains pose serious challenges. Results A cross-sectional study was conducted among the female nursing students' perceived e-learning readiness in subdomains of readiness; availability, technology use, self-confidence, and acceptance. The findings of the study revealed that the prevalence of preference for e-learning was 43.46%. The students did not prefer e-learning compared to 'prefer group' has significantly less availability of technology (β = -3.01, 95% CI: -4.46, -1.56), less use of technology (β = - 3.08, 95% CI: -5.11, -1.06), less self-confidence (β = -4.50, 95% CI: -7.02, -1.98), less acceptance (β = -5.96, 95% CI: -7.76, -4.16) and less training need (β = -1.86, 95% CI: -2.67, - 1.06). The age, degree, residence, parents' highest education, having a single room, having any eye problems were significantly associated with the variation of availability of technology, use of technology, self-confidence, acceptance, and training need of e-learning. Conclusions The outcomes of the study could be helpful while developing an effective and productive e-learning infrastructure regarding the preparedness of nursing colleges for the continuation of academia in any adverse circumstances like the COVID-19 pandemic.

272. **COVID-19 pandemic dynamics in India, the SARS-CoV-2 Delta variant, and implications for vaccination**

Yang W., Shaman J.
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Abstract

Background: The COVID-19 Delta pandemic wave in India surged and declined within 3 months; cases then remained low despite the continued spread of Delta elsewhere. Here we aim to estimate key epidemiological characteristics of the Delta variant based on data from India and examine the underpinnings of its dynamics. Methods: We utilize multiple datasets and model-inference methods to reconstruct COVID-19 pandemic dynamics in India during March 2020 – June 2021. We further use model estimates to retrospectively predict cases and deaths during July – mid-Oct 2021, under various vaccination and vaccine effectiveness (VE) settings to estimate the impact of vaccination and VE for non-Delta-infection recoverees. Findings: We estimate that Delta escaped immunity in 34.6% (95% CI: 0 – 64.2%) of individuals with prior wildtype infection and was 57.0% (95% CI: 37.9 – 75.6%) more infectious than wildtype SARS-CoV-2. Models assuming higher VE among those with prior non-Delta infection, particularly after the 1st dose, generated more accurate predictions than those assuming no such increases (best-performing VE setting: 90/95% vs. 30/67% baseline for the 1st/2nd dose). Counterfactual modeling indicates that high vaccination coverage for 1st vaccine-dose in India (~50% by mid-Oct 2021) combined with the boosting of VE among recoverees averted

around 60% of infections during July – mid-Oct 2021. Interpretation: Non-pharmaceutical interventions, infection seasonality, and high coverage of 1-dose vaccination likely all contributed to pandemic dynamics in India during 2021. Given the shortage of COVID-19 vaccines globally and boosting of VE, for populations with high prior infection rates, prioritizing the first vaccine-dose may protect more people.

273. **Can auxiliary indicators improve COVID-19 forecasting and hotspot prediction?**
McDonald D.J., Bien J., Green A., Hu A.J., DeFries N., Hyun S., Oliveira N.L., Sharpnack J., Tang J., Tibshirani R., Ventura V., Wasserman L., Tibshirani R.J.
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Abstract

Short-term forecasts of traditional streams from public health reporting (such as cases, hospitalizations, and deaths) are a key input to public health decision-making during a pandemic. Since early 2020, our research group has worked with data partners to collect, curate, and make publicly available numerous real-time COVID-19 indicators, providing multiple views of pandemic activity in the U.S. This paper studies the utility of five such indicators—derived from de-identified medical insurance claims, self-reported symptoms from online surveys, and COVID-related Google search activity—from a forecasting perspective. For each indicator, we ask whether its inclusion in an autoregressive (AR) model leads to improved predictive accuracy relative to the same model excluding it. Such an AR model, without external features, is already competitive with many top COVID-19 forecasting models in use today. Our analysis reveals that (a) inclusion of each of these five indicators improves on the overall predictive accuracy of the AR model; (b) predictive gains are in general most pronounced during times in which COVID cases are trending in "flat" or "down" directions; (c) one indicator, based on Google searches, seems to be particularly helpful during "up" trends.

274. **Incidence of venous thrombotic events and events of special interest in a retrospective cohort of commercially-insured US patients**
Weller S.C., Porterfield L., Davis J.W., Wilkinson G.S., Chen L., Baillargeon J.
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Abstract

Objective: To estimate the US incidence of thrombotic events and related rare diagnoses. Design: Claims-based retrospective cohort study of incidence. Setting: US commercial health insurance administrative claims database. Participants: Adults 25-65 years of age between 2015 and 2019 with a minimum of 12 consecutive thrombosis-free months of continuous enrollment beginning 2014 were selected. Main Outcomes: Age (10-year intervals) and sex stratum specific incidence rates per 100,000 person-years were determined for: venous thromboembolism (VTE), cerebral venous thrombosis (CVT), and other major venous thrombotic events, and events of special interest, including immune thrombocytopenic purpura (ITP), hemolytic-uremic syndrome (HUS), and heparin-induced thrombocytopenia (HIT). Results: Of 13,249,229 enrollees (half female/male), incidence of venous thromboembolic events (DVT, PE, CVT, or other major venous thrombotic conditions) was 247.89 per 100,000 person-years (95% CI: 245.96, 249.84). Incidence of VTE was 213.79 with ICD codes alone (95% CI: 211.99, 215.59) and 127.18 (95% CI: 125.80, 128.58) when also requiring a filled anticoagulation prescription. Incidence was 6.37 for CVT (95% CI: 6.07, 6.69), 26.06 for ITP (95% CI: 25.44, 26.78), 0.94 for HUS (95% CI: 0.82, 1.06), and 4.82 for HIT (95% CI: 4.56, 5.10). The co-occurrence of CVT with either ITP or HIT (diagnoses within 14 days of one another) was 0.090 (95% CI: 0.06, 0.13). Incidence tended to increase with age and was higher for women under 55. Incidence for CVT, HUS, and CVT with ITP or HIT was higher for women in all age groups. Incidence of PE and CVT increased significantly over the five-year period, while DVT rates decreased. Conclusions: These results are the first US estimates for incidence of thrombotic and rare events of interest in a large, commercially-insured US population. Findings provide a critically important reference for determining excess morbidity associated with COVID-19 and more generally for vaccine pharmacovigilance.

275. **A clinical observational analysis of aerosol emissions from dental procedures**
Dudding T., Sheikh S., Gregson F., Haworth J., Haworth S., Main B.G., Shrimpton A.J., Hamilton F.W., Ireland A.J., Maskell N.A., Reid J.P., Bzdek B.R., Gormley M.
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Abstract

Aerosol generating procedures (AGPs) are defined as any procedure releasing airborne particles <5 μm in size from the respiratory tract. There remains uncertainty about which dental procedures constitute AGPs. We quantified the aerosol number concentration generated during a range of periodontal, oral surgery and orthodontic procedures using an aerodynamic particle sizer, which measures aerosol number concentrations and size distribution across the 0.5–20 μm diameter size range. Measurements were conducted in an environment with a sufficiently low background to detect a patient's cough, enabling confident identification of aerosol. Phantom head control experiments for each procedure were performed under the same conditions as a comparison. Where aerosol was detected during a patient procedure, we assessed whether the size distribution could be explained by the non-salivary contaminated instrument source in the respective phantom head control procedure using a two-sided unpaired t-test (comparing the mode widths (log) and peak positions ($D_{P,C}$)). The aerosol size distribution provided a robust fingerprint of aerosol emission from a source. 41 patients underwent fifteen different dental procedures. For nine procedures, no aerosol was detected above background. Where aerosol was detected, the percentage of procedure time that aerosol was observed above background ranged from 12.7% for ultrasonic scaling, to 42.9% for 3-in-1 air + water syringe. For ultrasonic scaling, 3-in-1 syringe use and surgical drilling, the aerosol size distribution matched the non-salivary contaminated instrument source, with no unexplained aerosol. High and slow speed drilling produced aerosol from patient procedures with different size distributions to those measured from the phantom head controls (mode widths log(σ)) and peaks ($D_{P,C}$), $p < 0.002$) and, therefore, may pose a greater risk of salivary contamination. This study provides evidence for sources of aerosol generation during common dental procedures, enabling more informed evaluation of risk and appropriate mitigation strategies.

276. **Inferring global-scale temporal latent topics from news reports to predict public health interventions for COVID-19**

Wen Z., Powell G., Chafi I., Buckeridge D., Li Y.

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Abstract

Summary The COVID-19 pandemic has highlighted the importance of non-pharmacological interventions (NPI) for controlling epidemics of emerging infectious diseases. Despite their importance, NPI have been monitored mainly through the manual efforts of volunteers. This approach hinders measurement of the NPI effectiveness and development of evidence to guide their use to control the global pandemic. We present EpiTopics, a machine learning approach to support automation of the NPI prediction and monitoring at both the document-level and country-level by mining the vast amount of unlabelled news reports on COVID-19. EpiTopics uses a 3-stage, transfer-learning algorithm to classify documents according to NPI categories, relying on topic modelling to support result interpretation. We identified 25 interpretable topics under 4 distinct and coherent COVID-related themes. Importantly, the use of these topics resulted in significant improvements over alternative automated methods in predicting the NPIs in labelled documents and in predicting country-level NPIs for 42 countries.

277. **Prevalence of long-term effects in individuals diagnosed with COVID-19: an updated living systematic review**

Domingo F.R., Waddell L.A., Cheung A.M., Cooper C.L., Belcourt V.J., Zuckermann A.M.E., Corrin T., Ahmad R., Boland L., Laprise C., Idzerda L., Khan A., Morissette K., Garcia A.J.

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Abstract

Objective: Post COVID-19 condition refers to persisting or recurring symptoms weeks after acute COVID-19 illness which can significantly impact quality of life and health systems. It is important to understand the manifestation and magnitude of this condition. The objective of this living systematic review is to summarize the prevalence of symptoms and sequelae reported by people ≥4 weeks after COVID-19 diagnosis. Design: Systematic review, meta-analysis and narrative synthesis. Data sources: Embase, Medline, PsychInfo, Cochrane Central and select grey literature up to April 14, 2021. Methods: We adapted a previous search strategy used by the U.K. National Institute for Health and Care Excellence and updated it to search for new literature. Two reviewers screened references independently; one extracted data and assessed risk of bias and certainty of the evidence while another verified them. Prevalence data from laboratory-confirmed populations were meta-analyzed using a random effects model and synthesized separately in the short-term (4-12 weeks) and long-term (>12 weeks) periods after diagnosis. Data from clinically-diagnosed populations were synthesized narratively. Results: Of the 4444 unique citations, 84 observational studies met our inclusion criteria. Over 100 post COVID-19 symptoms and sequelae were reported. Sixty-one percent (95% CI: 44-76%, low certainty) and 53% (95% CI: 41-65%, low certainty) of laboratory-confirmed individuals reported persistence or presence of one or more symptoms in the short- and long-term periods, respectively. The most prevalent symptoms in both periods included: fatigue, general pain or discomfort, shortness of breath, cognitive impairment and mental health symptoms. Conclusions: A

substantial proportion of individuals reported a variety of symptoms ≥4 weeks after COVID-19 diagnosis. Due to gaps in the research base, and the low certainty of the evidence currently available, further research is needed to determine the true burden of post COVID-19 condition in the general population and in specific subgroups.

278. **COVID Oximetry @home: Evaluation of patient outcomes**
Boniface M., Burns D., Duckworth C., Ahmed M., Duruiheoma F., Armitage H., Ratcliffe N., Duffy J., O'Keeffe C., Inada-Kim M.
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Abstract

Background: COVID-19 has placed unprecedented demands on hospitals. A clinical service, COVID Oximetry @home (CO@h) was launched in November 2020 to support remote monitoring of COVID-19 patients in the community. Remote monitoring through CO@h aims to identify early patient deterioration and provide timely escalation for cases of silent hypoxia, while reducing the burden on secondary care. Methods: We conducted a retrospective service evaluation of COVID-19 patients onboarded to CO@h from November 2020 to March 2021 in the North Hampshire (UK) community led service (a collaboration of 15 GP practices covering 230,000 people). We have compared outcomes for patients admitted to Basingstoke & North Hampshire Hospital who were CO@h patients (COVID-19 patients with home monitoring of SpO_2 (n=115)), with non-CO@h patients (those directly admitted without being monitored by CO@h (n=633)). Crude and adjusted odds ratio analysis was performed to evaluate the effects of CO@h on patient outcomes of 30-day mortality, ICU admission and hospital length of stay greater than 3, 7, 14, and 28 days. Results: Adjusted odds ratios for CO@h show an association with a reduction for several adverse patient outcome: 30-day hospital mortality (p<0.001 OR 0.21 95% CI 0.08-0.47), hospital length of stay larger than 3 days (p<0.05, OR 0.62 95% CI 0.39-1.00), 7 days (p<0.001 OR 0.35 95% CI 0.22-0.54), 14 days (p<0.001 OR 0.22 95% CI 0.11-0.41), and 28 days (p<0.05 OR 0.21 95% CI 0.05-0.59). No significant reduction ICU admission was observed (p>0.05 OR 0.43 95% CI 0.15-1.04). Within 30 days of hospital admission, there were no hospital readmissions for those on the CO@h service as opposed to 8.7% readmissions for those not on the service. Conclusions: We have demonstrated a significant association between CO@h and better patient outcomes; most notably a reduction in the odds of hospital lengths of stays longer than 7, 14 and 28 days and 30-day hospital mortality.

279. **A time series analysis and predictive modeling of COVID-19 impacts in the African American community**
Oladunni T., Tossou S., Denis M., Ososanya E., Adesina J.
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Abstract

Background: Sometimes in 2019, there was an outbreak of coronavirus pandemic. Data shows that the virus has infected millions of people and claimed thousands of lives. Vaccination and other non-pharmacological interventions have brought a relief; however, COVID-19 left some indelible marks. This work focuses on a time series analysis and prediction of COVID-19 fatality rates in the Black community. Decision makers will find the work useful in building a robust architecture for a resilient pandemic preparedness and responsiveness against the next pandemic. Method: Our analysis of COVID-19 cases and deaths spans March 2020 to December 2020. Assuming there was no vaccine and other factors remained the same, we hypothesized that COVID-19 disproportionality would have continued. To test our hypothesis, COVID-19 forecasting cases and deaths models were built for the total population as well as the Black population. Holt and Holt-Winters exponential smoothing forecast methodologies were used for the forecast modeling. Forecasting accuracy was based on Mean Absolute Percentage Error (MAPE). Furthermore, we designed, developed, and evaluated a fatality rate predictive model for a Black county. Considering the number of ethnic groups in the USA, a Black county was defined as any county in the USA that at least 45% of its population are Blacks. Five learning algorithms were trained and evaluated. Dataset was a merger of datasets obtained from John Hopkins COVID-19 repository, US Census Bureau and US Center for Disease Control and Prevention. Results and Conclusion: Time series analysis shows that there exists a strong evidence of COVID-19 disproportionate impacts in the states investigated. Using 9 different criteria for performance comparison, our predictive modeling showed that decision tree model has a slight edge over other models. Our experiment suggests that Blacks and senior citizens with pre-existing condition living in Georgia State are the most vulnerable to COVID-19.

280. **Clinical outcomes and cost-effectiveness of COVID-19 vaccination in South Africa**
Reddy K.P., Fitzmaurice K.P., Scott J.A., Harling G., Lessells R.J., Panella C., Shebl F.M., Freedberg K.A., Siedner M.J.
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Abstract

Low- and middle-income countries are implementing COVID-19 vaccination strategies in light of varying vaccine efficacies and costs, supply shortages, and resource constraints. Here, we use a microsimulation model to evaluate clinical outcomes and cost-effectiveness of a COVID-19 vaccination program in South Africa. We varied vaccination coverage, pace, acceptance, effectiveness, and cost as well as epidemic dynamics. Providing vaccines to at least 40% of the population and prioritizing vaccine rollout prevented >9 million infections and >73,000 deaths and reduced costs due to fewer hospitalizations. Model results were most sensitive to assumptions about epidemic growth and prevalence of prior immunity to SARSCoV-2, though the vaccination program still provided high value and decreased both deaths and health care costs across a wide range of assumptions. Vaccination program implementation factors, including prompt procurement, distribution, and rollout, are likely more influential than characteristics of the vaccine itself in maximizing public health benefits and economic efficiency.

281. **Disordered eating and self-harm as risk factors for poorer mental health during the COVID-19 pandemic: A UK-based birth cohort study**
Warne N., Heron J., Mars B., Kwong A.S.F., Solmi F., Pearson R., Moran P., Bould H.
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Abstract

Background: Young adults and especially those with pre-existing mental health conditions, such as disordered eating and self-harm, appear to be at greater risk of developing metal health problems during the COVID-19 pandemic. However, it is unclear whether this increased risk is affected by any changes in lockdown restrictions, and whether any lifestyle changes could moderate this increased risk. Methods: In a longitudinal UK-based birth cohort (The Avon Longitudinal Study of Parents and Children, ALSPAC) we assessed the relationship between pre-pandemic measures of disordered eating and self-harm and mental health during the COVID-19 pandemic in 2,657 young adults. Regression models examined the relationship between self-reported disordered eating, self-harm, and both disordered eating and self-harm at age 25 years and depressive symptoms, anxiety symptoms and mental wellbeing during a period of eased restrictions in the COVID-19 pandemic (May-July 2020) when participants were aged 27-29 years. Analyses were adjusted for sex, questionnaire completion date, pre-pandemic socioeconomic disadvantage and pre-pandemic mental health and wellbeing. We also examined whether lifestyle changes (sleep, exercise, alcohol, visiting green space, eating, talking with family/friends, hobbies, relaxation) in the initial UK lockdown (April-May 2020) moderated these associations. Results: Pre-existing disordered eating, self-harm and comorbid disordered eating and self-harm were all associated with the reporting of a higher frequency of depressive symptoms and anxiety symptoms, and poorer mental wellbeing during the pandemic compared to individuals without disordered eating and self-harm. Associations remained when adjusting for pre-pandemic mental health measures. There was little evidence that interactions between disordered eating and self-harm exposures and lifestyle change moderators affected pandemic mental health and wellbeing. Conclusions: Young adults with pre-pandemic disordered eating, self-harm and comorbid disordered eating and self-harm were at increased risk for developing symptoms of depression, anxiety and poor mental wellbeing during the COVID-19 pandemic, even when accounting for pre-pandemic mental health. Lifestyle changes during the pandemic do not appear to alter this risk. A greater focus on rapid and responsive service provision is essential to reduce the impact of the pandemic on the mental health of these already vulnerable individuals.

282. **Examining the factor structure of the DSM-5 level 1 cross-cutting symptom measure**
Gibbons A., Farmer C., Shaw J.S., Chung J.Y.
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Abstract

Objectives: The DSM-5 Level 1 Cross-Cutting Symptom Measure (DSM-XC) is a transdiagnostic mental health symptom measure that has shown promise in informing clinical diagnostic evaluations and as a screening tool for research. However, few studies have assessed the latent dimensionality of the DSM-XC. We examined the factor structure of the DSM-XC in a large convenience sample of participants with varying degrees of psychological health. Methods: Participants (n=3533) enrolled in a protocol conducted at the National Institute of Mental Health (NCT04339790). We used a factor analytic framework to evaluate an existing two-factor solution (Lace & Merz, 2020) and two additional candidate solutions. Results: The Lace and Merz solution had acceptable fit. Exploratory factor analysis yielded two candidate solutions: a six-factor (characterized as mood, worry, activation, somatic, thoughts, and substance use) and a bifactor (general factor of non-specific psychopathology, residual factors characterized as internalizing and thought disorder), which both had good fit and full measurement invariance across age, sex,

and enrollment date. Conclusions: Our findings confirm that the DSM-XC may be conceptualized as a multidimensional instrument and provide a scoring solution for researchers who wish to measure distinct constructs. Future research on the psychometric profile of the DSM-XC is needed, focused on the validity of these candidate solutions and their performance across research populations and settings.

283. **Affordable and time-effective high throughput screening of SARS-CoV-2 variants using denaturing high-performance liquid chromatography analysis**
Turba M.E., Mion D., Papadimitriou S., Taddei F., Dirani G., Sambri V., Gentilini F.
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Abstract

Mutations in the receptor binding domain (RBD) region of SARS-CoV-2 have been shown to impact the infectivity, pathogenicity and transmissibility of new variants of concern (VOC). Even more worrisome, those mutations have the potential of causing immune escape, undermining the population immunity induced by ongoing mass vaccination programs. Gap statement The massive parallel sequencing techniques have taken a lead role in the detection strategies of the new variants. Nevertheless, they are still cumbersome and labour-demanding. There is an urgent need for novel strategies and techniques aimed at the surveillance of the active emergence and spread of the VOC. Aim The aim of this study was to provide a quick, cheap and straightforward Denaturing High-Performance Liquid Chromatography (DHPLC) method for the prompt identification of the SARSCoV-2 VOC. Methodology Two PCRs were designed to target the RBD region, spanning residues N417 through N501 of the Spike protein. Furthermore, a DHPLC screening analysis was set up. The screening consisted of mixing the unknown sample with a standard sample of a known variant, denaturing at high temperature, renaturing at room temperature followed by a 2-minute run using the WAVE DHPLC system to detect the heteroduplexes which invariably originate whenever the unknown sample has a nucleotide difference with respect to the standard used. Results The workflow was able to readily detect new variants including the P.1, the B.1.585 and the B.1. 617.2 lineages at a very affordable cost. The DHPLC analysis was robust being able to identify variants even in case of samples with very unbalanced target concentration including those samples at the limit of detection. Conclusions This approach has the potential of greatly expediting surveillance of the SARS-CoV-2 variants.

284. **Risk factors associated with severe outcomes of COVID-19: A systematic rapid review to inform national guidance on vaccine prioritization in Canada**
Gates M., Pillay J., Wingert A., Guitard S., Rahman S., Zakher B., Gates A., Hartling L.
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Abstract

Background: To inform vaccine prioritization guidance in Canada, we systematically reviewed evidence on the magnitude of association between risk factors and severe outcomes of COVID-19. The urgent nature of this review necessitated an adapted methodology, which may serve as an exemplar for reviews undertaken under strict timelines. Methods: We updated our existing review by searching online databases and websites for cohort studies providing multivariate adjusted associations. After piloting, one author screened studies and extracted data. Two authors estimated the magnitude of association between exposures and outcomes as little-to-no (odds, risk, or hazard ratio <2.0, or >0.50 for reduction), large (2.0-3.9, or 0.50-0.26 for reduction), or very large (≥4.0, or ≤0.25 for reduction), and rated the evidence certainty using GRADE. Results: Of 11,734 unique records we included 134 reports. There is probably (moderate certainty) at least a large increase in mortality from COVID-19 among people aged 60-69 vs. <60 years (11 studies, n=517,217), with ≥2 vs. no comorbidities (4 studies, n=189,608), and for people with (vs. without): Down syndrome (1 study, n>8 million), type 1 and 2 diabetes (1 study, n>8 million), end-stage kidney disease (1 study, n>8 million), motor neuron disease, multiple sclerosis, myasthenia gravis, or Huntington's disease (as a grouping; 1 study, n>8 million). The magnitude of association with mortality is probably very large for Down syndrome and may (low certainty) be very large for age 60-69 years, and diabetes. There is probably little-to-no increase in severe outcomes with several cardiovascular and respiratory conditions, and for adult males vs. females. Conclusion: There is strong evidence to support at least a large increase in mortality from COVID-19 among older adults aged 60 to 69 years versus <60 years; people having two or more versus no comorbidities; and for people affected by several pre-existing conditions. The methodology employed in this review may provide an important exemplar for future syntheses undertaken under urgent timelines.

285. **Rapid evaluation of COVID-19 vaccine effectiveness against VOC/VOIs by genetic mismatch**
Cao L., Lou J., Zheng H., Zhao S., Mok C.K.P., Chan R.W.Y., Chong M.K.C., Chen Z., Wong E.L.Y., Chan P.K.S., Zee B.C.-Y., Yeoh E.K., Wang M.H.
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Abstract

Timely evaluation of the protective effects of COVID-19 vaccines is challenging but urgently needed to inform the pandemic control planning. Based on vaccine efficacy/effectiveness (VE) data of 11 vaccine products and 297,055 SARS-CoV-2 sequences collected in 20 regions, we analyzed the relationship between genetic mismatch of circulating viruses against the vaccine strain and VE. Variations from technology platforms are controlled by a mixed-effects model. We found that the genetic mismatch measured on the RBD is highly predictive for vaccine protection and accounted for 72.0% (p-value < 0.01) of the VE change. The NTD and S protein also demonstrate significant but weaker per amino acid substitution association with VE (p-values < 0.01). The model is applied to predict vaccine protection of existing vaccines against new genetic variants and is validated by independent cohort studies. The estimated VE against the delta variant is 79.3% (95% prediction interval: 67.0 – 92.1) using the mRNA platform, and an independent survey reported a close match of 83.0%; against the beta variant (B.1.351) the predicted VE is 53.8% (95% prediction interval: 39.9 – 67.4) using the viral-vector vaccines, and an observational study reported a close match of 48.0%. Genetic mismatch provides an accurate prediction for vaccine protection and offers a rapid evaluation method against novel variants to facilitate vaccine deployment and public health responses.

286. **Multifactorial seroprofiling dissects the contribution of pre-existing human coronaviruses responses to SARS-CoV-2 immunity**

Abela I.A., Pasin C., Schwarzmüller M., Epp S., Sickmann M.E., Schanz M.M., Rusert P., Weber J., Schmutz S., Audigé A., Maliqi L., Hunziker A., Hesselman M.C., Niklaus C.R., Gottschalk J., Schindler E., Wepf A., Karrer U., Wolfensberger A., Rampini S.K., Meyer Sauteur P.M., Berger C., Huber M., Böni J., Braun D.L., Marconato M., Manz M.G., Frey B.M., Günthard H.F., Kouyos R.D., Trkola A.

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Abstract

Determination of SARS-CoV-2 antibody responses in the context of pre-existing immunity to circulating human coronavirus (HCoV) is critical to understanding protective immunity. Here we perform a multifactorial analysis of SARS-CoV-2 and HCoV antibody responses in pre-pandemic (N=825) and SARS-CoV-2-infected donors (N=389) using a custom-designed multiplex ABCORA assay. ABCORA seroprofiling, when combined with computational modeling, enables accurate definition of SARS-CoV-2 seroconversion and prediction of neutralization activity, and reveals intriguing interrelations with HCoV immunity. Specifically, higher HCoV antibody levels in SARS-CoV-2-negative donors suggest that preexisting HCoV immunity may provide protection against SARS-CoV-2 acquisition. In those infected, higher HCoV activity is associated with elevated SARS-CoV-2 responses, indicating cross-stimulation. Most importantly, HCoV immunity may impact disease severity, as patients with high HCoV reactivity are less likely to require hospitalization. Collectively, this evidence points to HCoV immunity promoting the rapid development of SARS-CoV-2-specific immunity, underscoring the importance of exploring cross-protective responses for comprehensive coronavirus prevention.

287. **Post-COVID-19 syndrome in outpatients: A cohort study**

Desgranges F., Tadini E., Munting A., Regina J., Filippidis P., Viala B., Karachalias E., Suttels V., Haefliger D., Kampouri E., van Singer M., Tschopp J., Stettler L.R., Schaad S., Brahier T., Hugli O., Chabloz Y.M., Gouveia A., Opota O., Carron P.-N., Guery B., Papadimitriou-Olivgeris M., Boillat-Blanco N.

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Abstract

Background After mild COVID-19, some outpatients experience persistent symptoms. However, data are scarce and prospective studies are urgently needed. Objectives To characterize the post-COVID-19 syndrome after mild COVID-19 and identify predictors. Participants Outpatients with symptoms suggestive of COVID-19 with (1) PCR-confirmed COVID-19 (COVID-positive) or (2) SARS-CoV-2 negative PCR (COVID-negative). Design Monocentric cohort study with prospective phone interview between more than three months to ten months after initial visit to the emergency department and outpatient clinics. Main Measures Data of the initial visits were extracted from the electronic medical file. Predefined persistent symptoms were assessed through a structured phone interview. Associations between long-term symptoms and PCR results, as well as predictors of persistent symptoms among COVID-positive, were evaluated by multivariate logistic regression adjusted for age, gender, smoking, comorbidities, and timing of the survey. Key results The study population consisted of 418 COVID-positive and 89 COVID-negative patients, mostly young adults (median age of 41 versus 36 years in COVID-positive and COVID-negative,

respectively; p=0.020) and health care workers (67% versus 82%; p=0.006). Median time between the initial visit and the phone survey was 150 days in COVID-positive and 242 days in COVID-negative patients. Persistent symptoms were reported by 223 (53%) COVID-positive and 33 (37%) COVID-negative patients (p=0.006). Overall, 21% COVID-positive and 15% COVID-negative patients (p=0.182) attended care for this purpose. Four surveyed symptoms were independently associated with COVID-19: fatigue (adjusted odds ratio [or] 2.14, 95%CI 1.04-4.41), smell/taste disorder (26.5, 3.46-202), dyspnea (2.81, 1.10-7.16) and memory impairment (5.71, 1.53-21.3). Among COVID-positive, female gender (1.67, 1.09-2.56) and overweight/obesity (1.67, 1.10-2.56) were predictors of persistent symptoms. Conclusions More than half of COVID-positive outpatients report persistent symptoms up to ten months after a mild disease. Only 4 of 14 symptoms were associated with COVID-19 status. The symptoms and predictors of the post-COVID-19 syndrome need further characterization as this condition places a significant burden on society.

288. **Impaired immune signaling and changes in the lung microbiome precede secondary bacterial pneumonia in COVID-19**

Tsitsiklis A., Zha B.S., Byrne A., DeVoe C., Rackaityte E., Levan S., Sunshine S., Mick E., Ghale R., Love C., Tarashansky A.J., Pisco A., Albright J., Jauregui A., Sarma A., Neff N., Serpa P.H., Deiss T.J., Kistler A., Carrillo S., Ansel K.M., Leligdowicz A., Christenson S., Detweiler A., Jones N.G., Wu B., Darmanis S., Lynch S.V., DeRisi J.L., Matthay M.A., Hendrickson C.M., Kangelaris K.N., Krummel M.F., Woodruff P.G., Erle D.J., Rosenberg O., Calfee C.S., Langelier C.R.

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Abstract

Secondary bacterial infections, including ventilator-associated pneumonia (VAP), lead to worse clinical outcomes and increased mortality following viral respiratory infections including in patients with coronavirus disease 2019 (COVID-19). Using a combination of tracheal aspirate bulk and single-cell RNA sequencing we assessed lower respiratory tract immune responses and microbiome dynamics in 23 COVID-19 patients, 10 of whom developed VAP, and eight critically ill uninfected controls. At a median of three days (range: 2-4 days) before VAP onset we observed a transcriptional signature of bacterial infection. At a median of 15 days prior to VAP onset (range: 8-38 days), we observed a striking impairment in immune signaling in COVID-19 patients who developed VAP. Longitudinal metatranscriptomic analysis revealed disruption of lung microbiome community composition in patients with VAP, providing a connection between dysregulated immune signaling and outgrowth of opportunistic pathogens. These findings suggest that COVID-19 patients who develop VAP have impaired antibacterial immune defense detectable weeks before secondary infection onset.

289. **The effect of COVID-19 vaccination in Italy and perspectives for "living with the virus"**

Marziano V., Guzzetta G., Mammone A., Riccardo F., Poletti P., Trentini F., Manica M., Siddu A., Bella A., Stefanelli P., Pezzotti P., Ajelli M., Brusaferro S., Rezza G., Merler S.

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Abstract

Vaccination campaigns against COVID-19 are allowing the progressive release of physical distancing restrictions in many countries. However, the global spread of the highly transmissible Delta variant has likely suppressed the residual chances of SARS-CoV-2 elimination through herd immunity alone. Here we assess the impact of the vaccination program in Italy since its start on December 27, 2020 and evaluate possible prospects for reopening the society while at the same time keeping COVID-19 under control. To this aim, we propose a mathematical modeling framework where levels of social activity are adjusted to match the time-series of the net reproduction number as estimated from surveillance data. We compared the estimated level of social contacts, number of deaths, and transmission potential with those of a counterfactual scenario where the same epidemic trajectory is obtained in absence of vaccination. We then evaluate the prospective impact of different scenarios of vaccination coverage and different social activity levels on SARS-CoV-2 reproduction number. We estimate that by June 30, 2021, the COVID-19 vaccination program allowed the resumption of about half the social contacts that were recorded in pre-pandemic times; in absence of vaccination, only about one third could have been resumed to obtain the same number of cases, with the added cost of about 12,100 (95%CI: 6,600-21,000) extra deaths (+27%; 95%CI: 15-47%) between December 27, 2020 and June 30, 2021. We show that the negative effect of the Delta variant diffusion in July was entirely offset by vaccination in the month of July and August 2021. Finally, we estimate that a complete return to the pre-pandemic life could be safely attained only if >90%, including children from 5 years on, will be vaccinated using mRNA vaccines developed in 2020. In any case, increasing the vaccination coverage will allow further margins for societal reopening even in absence of a pediatric vaccine. These results may support the definition of vaccination targets for countries that have already achieved a broad population coverage.

290. **Show us the data: Global COVID-19 Wastewater monitoring efforts, equity, and gaps**
Naughton C.C., Roman F.A., Alvarado A.G.F., Tariqi A.Q., Deeming M.A., Bibby K., Bivins A., Rose J.B., Medema G., Ahmed W., Katsivelis P., Allan V., Sinclair R., Zhang Y., Kinyua M.N.
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Abstract

A year since the declaration of the global coronavirus disease 2019 (COVID-19) pandemic there were over 110 million cases and 2.5 million deaths. Learning from methods to track community spread of other viruses such as poliovirus, environmental virologists and those in the wastewater based epidemiology (WBE) field quickly adapted their existing methods to detect SARS-CoV-2 RNA in wastewater. Unlike COVID-19 case and mortality data, there was not a global dashboard to track wastewater monitoring of SARS-CoV-2 RNA worldwide. This study provides a one year review of the "COVIDPoops19" global dashboard of universities, sites, and countries monitoring SARS-CoV-2 RNA in wastewater. Methods to assemble the dashboard combined standard literature review, direct submissions, and daily, social media keyword searches. Over 200 universities, 1,000 sites, and 55 countries with 59 dashboards monitor wastewater for SARS-CoV-2 RNA. However, monitoring is primarily in high-income countries (65%) with less access to this valuable tool in low and middle income countries (35%). Data are not widely shared publicly or accessible to researchers to further inform public health actions, perform meta-analysis, better coordinate, and determine equitable distribution of monitoring sites. For WBE to be used to its full potential during COVID-19 and beyond, show us the data.

291. **A novel benchmark for COVID-19 pandemic testing effectiveness enables the accurate prediction of new intensive care unit admissions**
Nikoloudis D., Kountouras D., Hiona A.
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Abstract

The positivity rate of testing is currently used both as a benchmark of testing adequacy and for assessing the evolution of the COVID-19 pandemic. However, since the former is a prerequisite for the latter, its interpretation is often conflicting. We propose as a benchmark for COVID-19 testing effectiveness a new metric, termed 'Severity Detection Rate' (SDR), that represents the daily needs for new Intensive Care Unit (ICU) admissions, per 100 cases detected (t-i) days ago, per 10,000 tests performed (t-i) days ago. Based on the announced COVID-19 monitoring data in Greece from May 2020 until August 2021, we show that beyond a certain threshold of daily tests, SDR reaches a plateau of very low variability that begins to reflect testing adequacy. Due to the stabilization of SDR, it was possible to predict with great accuracy the daily needs for new ICU admissions, 12 days ahead of each testing data point, over a period of 10 months, with Pearson $r = 0.98$ ($p = 10^{-197}$), RMSE = 7,16. We strongly believe that this metric will help guide the timely decisions of both scientists and government officials to tackle pandemic spread and prevent ICU overload by setting effective testing requirements for accurate pandemic monitoring. We propose further study of this novel metric with data from more countries to confirm the validity of the current findings.

292. **Stochastic social behavior coupled to 2 COVID-19 dynamics leads to waves, 3 plateaus and an endemic state**
Tkachenko A.V., Maslov S., Wang T., Elbanna A., Wong G.N., Goldenfeld N.
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Abstract

It is well recognized that population heterogeneity plays an important role in the spread of epidemics. While individual variations in social activity are often assumed to be persistent, i.e. constant in time, here we discuss the consequences of dynamic heterogeneity. By integrating the stochastic dynamics of social activity into traditional epidemiological models we demonstrate the emergence of a new long timescale governing the epidemic, in broad agreement with empirical data. Our Stochastic Social Activity model captures multiple features of real-life epidemics such as COVID-19, including prolonged plateaus and multiple waves, which are transiently suppressed due to the dynamic nature of social activity. The existence of a long timescale due to the interplay between epidemic and social dynamics provides a unifying picture of how a fast-paced epidemic typically will transition to an endemic state.

293. **Current state of COVID-19 knowledge, attitude, practices, and associated factors among Bangladeshi food handlers from various food industries**
Jubayer Md.F., Kayshar Md.S., Kabir Md.F., Arifin Md.S., Limon Md.T.I., Uddin Md.N., Al-Emran Md.
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Abstract

While people around the world are terrified of the global pandemic coronavirus disease 2019 (COVID-19) and are dying for a permanent solution, undertaking preventive safety measures are said to be the most effective way to stay away from it. People's adherences to these measures are broadly dependent on their knowledge, attitude, and practices (KAP). People working in the food industries must be extra cautious during this time because they are in close proximity to consumable items. The present study was designed to evaluate food handlers' knowledge, attitude, and practices regarding COVID-19 in different food industries in Bangladesh. A number of 400 food handlers from 15 food industries took part in this online-based study. The information was collected from the participants through a questionnaire prepared in Google form. With a correct response rate of about 90% on average (knowledge 89.7%, attitude 93%, practices 88.2%), the participants showed an acceptable of KAP regarding COVID-19. Education and working experiences had a significant association with the total KAP scores ($p < 0.05$). The findings may assist public health professionals and practitioners in developing targeted strategies for implementing such studies in other industrial sectors and taking appropriate measures based on the KAP studies.

294. **Timeliness of provisional United States mortality data releases during the COVID-19 pandemic: delays associated with electronic death registration system and weekly mortality**
Rosenbaum J.E., Stillo M., Graves N., Rivera R.
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Abstract

All-cause mortality counts allow public health authorities to identify populations experiencing excess deaths from pandemics, natural disasters, and other emergencies. Delays in the completeness of mortality counts may contribute to misinformation because death counts take weeks to become accurate. We estimate the timeliness of all-cause mortality releases during the Covid-19 pandemic for the dates 3 April to 5 September 2020 by estimating the number of weekly data releases of the NCHS Fluview Mortality Surveillance System until mortality comes within 99% of the counts in the 19 March 19 2021 provisional mortality data release. States' mortality counts take 5 weeks at median (interquartile range 4-7 weeks) to completion. The fastest states were Maine, New Hampshire, Vermont, New York, Utah, Idaho, and Hawaii. States that had not adopted the electronic death registration system (EDRS) were 4.8 weeks slower to achieve complete mortality counts, and each weekly death per 10^8 was associated with a 0.8 week delay. Emergency planning should improve the timeliness of mortality data by improving state vital statistics digital infrastructure.

295. **Development of a rapid point-of-care test that measures neutralizing antibodies to SARS-CoV-2**
Lake D.F., Roeder A.J., Kaleta E., Jasbi P., Pfeffer K., Koelbel C., Periasamy S., Kuzmina N., Bukreyev A., Grys T.E., Wu L., Mills J.R., McAulay K., Gonzalez-Moa M., Seit-Nebi A., Svarovsky S.
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Abstract

Background: After receiving a COVID-19 vaccine, most recipients want to know if they are protected from infection and for how long. Since neutralizing antibodies are a correlate of protection, we developed a lateral flow assay (LFA) that measures levels of neutralizing antibodies from a drop of blood. The LFA is based on the principle that neutralizing antibodies block binding of the receptor-binding domain (RBD) to angiotensin-converting enzyme 2 (ACE2). Methods: The ability of the LFA was assessed to correctly measure neutralization of sera, plasma or whole blood from patients with COVID-19 using SARS-CoV-2 microneutralization assays. We also determined if the LFA distinguished patients with seasonal respiratory viruses from patients with COVID-19. To demonstrate the usefulness of the LFA, we tested previously infected and non-infected COVID-19 vaccine recipients at baseline and after first and second vaccine doses. Results: The LFA compared favorably with SARS-CoV-2 microneutralization assays with an area under the ROC curve of 98%. Sera obtained from patients with seasonal coronaviruses

did not show neutralizing activity in the LFA. After a single mRNA vaccine dose, 87% of previously infected individuals demonstrated high levels of neutralizing antibodies. However, if individuals were not previously infected only 24% demonstrated high levels of neutralizing antibodies after one vaccine dose. A second dose boosted neutralizing antibody levels just 8% higher in previously infected individuals, but over 63% higher in non-infected individuals. Conclusions: A rapid, semi-quantitative, highly portable and inexpensive neutralizing antibody test might be useful for monitoring rise and fall in vaccine-induced neutralizing antibodies to COVID-19.

296. **Test-trace-isolate-quarantine (TTIQ) intervention strategies after symptomatic COVID-19 case identification**
Ashcroft P., Lehtinen S., Bonhoeffer S.
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Abstract

The test-trace-isolate-quarantine (TTIQ) strategy, where confirmed-positive pathogen carriers are isolated from the community and their recent close contacts are identified and pre-emptively quarantined, is used to break chains of transmission during a disease outbreak. The protocol is frequently followed after an individual presents with disease symptoms, at which point they will be tested for the pathogen. This TTIQ strategy, along with hygiene and social distancing measures, make up the non-pharmaceutical interventions that are utilised to suppress the ongoing COVID-19 pandemic. Here we develop a tractable mathematical model of disease transmission and the TTIQ intervention to quantify how the probability of detecting and isolating a case following symptom onset, the fraction of contacts that are identified and quarantined, and the delays inherent to these processes impact epidemic growth. In the model, the timing of disease transmission and symptom onset, as well as the frequency of asymptomatic cases, is based on empirical distributions of SARS-CoV-2 infection dynamics, while the isolation of confirmed cases and quarantine of their contacts is implemented by truncating their respective infectious periods. We find that a successful TTIQ strategy requires intensive testing: the majority of transmission is prevented by isolating symptomatic individuals and doing so in a short amount of time. Despite the lesser impact, additional contact tracing and quarantine increases the parameter space in which an epidemic is controllable and is necessary to control epidemics with a high reproductive number. TTIQ could remain an important intervention for the foreseeable future of the COVID-19 pandemic due to slow vaccine rollout and highly-transmissible variants with the potential for vaccine escape. Our results can be used to assess how TTIQ can be improved and optimised, and the methodology represents an improvement over previous quantification methods that is applicable to future epidemic scenarios.

297. **Use of artificial intelligence on spatio-temporal data to generate insights during COVID-19 pandemic: A review**
Jayatilaka G., Hassan J., Marikkar U., Perera R., Sritharan S., Weligampola H., Ekanayake M., Godaliyadda R., Ekanayake P., Herath V., Godaliyadda G.M.D., Rathnayake A., Dharmaratne S.D., Ekanayake J.
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Abstract

The COVID-19 pandemic, within a short time span, has had a significant impact on every aspect of life in almost every country on the planet. As it evolved from a local epidemic isolated to certain regions of China, to the deadliest pandemic since the influenza outbreak of 1918, scientists all over the world have only amplified their efforts to combat it. In that battle, Artificial Intelligence, or AI, with its wide ranging capabilities and versatility, has played a vital role and thus has had a sizable impact. In this review, we present a comprehensive analysis of the use of AI techniques for spatio-temporal modeling and forecasting and impact modeling on diverse populations as it relates to COVID-19. Furthermore, we catalogue the articles in these areas based on spatio-temporal modeling, intrinsic parameters, extrinsic parameters, dynamic parameters and multivariate inputs (to ascertain the penetration of AI usage in each sub area). The manner in which AI is used and the associated techniques utilized vary for each body of work. Majority of articles use deep learning models, compartment models, stochastic methods and numerous statistical methods. We conclude by listing potential paths of research for which AI based techniques can be used for greater impact in tackling the pandemic.

298. **SARS-CoV-2 epidemic after social and economic reopening in three US states reveals shifts in age structure and clinical characteristics**
Wikle N., Tran T.N.-A., Gentilesco B., Leighow S.M., Albert J., Strong E.R., Brinda K., Inam H., Yang F., Hossain S., Chan P., Hanage W.P., Messick M., Pritchard J.R., Hanks E.M., Boni M.F.
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Abstract

In the United States, state-level re-openings in spring 2020 presented an opportunity for the resurgence of SARS-CoV-2 transmission. One important question during this time was whether human contact and mixing patterns could increase gradually without increasing viral transmission, the rationale being that new mixing patterns would likely be associated with improved distancing, masking, and hygiene practices. A second key question to follow during this time was whether clinical characteristics of the epidemic would improve after the initial surge of cases. Here, we analyze age-structured case, hospitalization, and death time series from three states – Rhode Island, Massachusetts, and Pennsylvania – that had successful reopenings in May 2020 without summer waves of infection. Using a Bayesian inference framework on eleven daily data streams and flexible daily population contact parameters, we show that population-average mixing rates dropped by >50% during the lockdown period in March/April, and that the correlation between overall population mobility and transmission-capable mobility was broken in May as these states partially re-opened. We estimate the reporting rates (fraction of symptomatic cases reporting to health system) at 96.0% (RI), 72.1% (MA), and 75.5% (PA); in Rhode Island, when accounting for cases caught through general-population screening programs, the reporting rate estimate is 94.5%. We show that elderly individuals were less able to reduce contacts during the lockdown period when compared to younger individuals. Attack rate estimates through August 31 2020 are 6.4% (95% CI: 5.8% – 7.3%) of the total population infected for Rhode Island, 5.7% (95% CI: 5.0% – 6.8%) in Massachusetts, and 3.7% (95% CI: 3.1% – 4.5%) in Pennsylvania, with some validation available through published seroprevalence studies. Infection fatality rates (IFR) estimates for the spring epidemic are higher in our analysis (>2%) than previously reported values, likely resulting from the epidemics in these three states affecting the most vulnerable sub-populations, especially the most vulnerable of the ≥80 age group.

299. **Potential reduction in transmission of COVID-19 by digital contact tracing systems: A modelling study**
Plank M.J., James A., Lustig A., Steyn N., Binny R.N., Hendy S.C.
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Abstract

Background. Digital tools are being developed to support contact tracing as part of the global effort to control the spread of COVID-19. These include smartphone apps, Bluetooth-based proximity detection, location tracking, and automatic exposure notification features. Evidence on the effectiveness of alternative approaches to digital contact tracing is so far limited. Methods. We use an age-structured branching process model of the transmission of COVID-19 in different settings to estimate the potential of manual contact tracing and digital tracing systems to help control the epidemic. We investigate the effect of the uptake rate and proportion of contacts recorded by the digital system on key model outputs: the effective reproduction number, the mean outbreak size after 30 days, and the probability of elimination. Results. Effective manual contact tracing can reduce the effective reproduction number from 2.4 to around 1.5. The addition of a digital tracing system with a high uptake rate over 75% could further reduce the effective reproduction number to around 1.1. Fully automated digital tracing without manual contact tracing is predicted to be much less effective. Conclusions. For digital tracing systems to make a significant contribution to the control of COVID-19, they need be designed in close conjunction with public health agencies to support and complement manual contact tracing by trained professionals.

300. **Benchmarking deep learning models and automated model design for COVID-19 detection with chest CT scans**
He X., Wang S., Shi S., Chu X., Tang J., Liu X., Yan C., Zhang J., Ding G.
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Abstract

—COVID-19 pandemic has spread all over the world for months. As its transmissibility and high pathogenicity seriously threaten people's lives, the accurate and fast detection of the COVID-19 infection is crucial. Although many recent studies have shown that deep learning based solutions can help detect COVID-19 based on chest CT scans, there lacks a consistent and systematic comparison and evaluation on these techniques. In this paper, we first build a clean and segmented CT dataset called Clean-CC-CCII by fixing the errors and removing some noises in a large CT scan dataset CC-CCII with three classes: novel coronavirus pneumonia (NCP), common pneumonia (CP), and normal controls (Normal). After cleaning, our dataset consists of a total of 340,190 slices of 3,993 scans from 2,698 patients. Then we benchmark and compare the performance of a series of state-of-the-art (SOTA) 3D and 2D convolutional neural networks (CNNs). The results show that 3D CNNs outperform 2D CNNs in general. With extensive effort of hyperparameter tuning, we find that the 3D CNN model DenseNet3D121 achieves the highest accuracy of 88.63% (F1-score is 88.14% and AUC is 0.940), and another 3D CNN model ResNet3D34 achieves the best AUC of 0.959 (accuracy is 87.83% and F1-score is 86.04%). We further demonstrate that the mixup data augmentation technique can largely improve the model performance. At last, we design an automated deep learning methodology to generate a lightweight deep

learning model MNas3DNet41 that achieves an accuracy of 87.14%, F1-score of 87.25%, and AUC of 0.957, which are on par with the best models made by AI experts. The automated deep learning design is a promising methodology that can help health-care professionals develop effective deep learning models using their private data sets. Our Clean-CC-CCII dataset and source code are available at: https://github.com/HKBUHPML/HKBU_HPML_COVID-19.

301. **A flexible statistical framework for estimating excess mortality**
Acosta R.J., Irizarry R.A.
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Abstract

Quantifying the impact of natural disasters or epidemics is critical for guiding policy decisions and interventions. When the effects of an event are long-lasting and difficult to detect in the short term, the accumulated effects can be devastating. Mortality is one of the most reliably measured health outcomes, partly due to its unambiguous definition. As a result, excess mortality estimates are an increasingly effective approach for quantifying the effect of an event. However, the fact that indirect effects are often characterized by small, but enduring, increases in mortality rates present a statistical challenge. This is compounded by sources of variability introduced by demographic changes, secular trends, seasonal and day of the week effects, and natural variation. Here we present a model that accounts for these sources of variability and characterizes concerning increases in mortality rates with smooth functions of time that provide statistical power. The model permits discontinuities in the smooth functions to model sudden increases due to direct effects. We implement a flexible estimation approach that permits both surveillance of concerning increases in mortality rates and careful characterization of the effect of a past event. We demonstrate our tools' utility by estimating excess mortality after hurricanes in the United States and Puerto Rico. We use Hurricane Maria as a case study to show appealing properties that are unique to our method compared to current approaches. Finally, we show the flexibility of our approach by detecting and quantifying the 2014 Chikungunya outbreak in Puerto Rico and the COVID-19 pandemic in the United States. We make our tools available through the excessmort R package available from https://cran.r-project.org/web/packages/excessmort/.

302. **Current state and predicting future scenario of COVID-19 pandemic for highly infected nations**
Patil N.L.
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Abstract

Since the first report of COVID-19 from Wuhan China, the virus has rapidly spread across the globe now presently reported in 177 countries with positive cases crossing 400 thousand and rising. In the current study, prediction is made for highly infected countries by a simple and novel method using only cumulative positive cases reported. The rate of infection per week (R^w) coefficient delineated three phases for the current COVID-19 pandemic. All the countries under study have passed Phase 1 and are currently in Phase 2 except for South Korea which is in Phase 3. Early detection with rapid and large-scale testing helps in controlling the COVID-19 pandemic. Staying in Phase 2 for longer period would lead to increase in COVID-19 positive cases.

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