



International EPI Cell Daily Evidence Digest – 12/06/2020

This Daily Evidence Digest is produced by the PHE COVID-19 Literature Digest Team as a resource for professionals working in public health. We do not accept responsibility for the availability, reliability or content of the items included in this resource and do not necessarily endorse the views expressed within them. The papers are organised under the following themes:

- Serology and immunology
- Diagnostics
- Genomics
- Epidemiology and clinical - children and pregnancy
- Epidemiology and clinical - risk factors
- Epidemiology and clinical - other
- Infection control
- Social sciences
- Modelling
- Miscellaneous
- Overviews, comments and editorials (no digest)

Please note that we are including preprints (**highlighted in red**), which are preliminary reports of work that have NOT been peer-reviewed. They should not be relied on to guide clinical practice or health-related behaviour and should NOT be reported in news media as established information.

Serology and immunology

| Publication Date | Title/URL | Journal/Article type | Digest |
|------------------|---|--|--|
| 11.06.2020 | Meta-analysis of diagnostic performance of serological tests for SARS-CoV-2 antibodies up to 25 April 2020 and public health implications | Eurosurveillance / Rapid communication | <ul style="list-style-type: none">• Review of the diagnostic accuracy of SARS-CoV-2 serological tests.• Random-effects models yielded a summary sensitivity of 82% for IgM, and 85% for IgG and total antibodies.• For specificity, the pooled estimate were 98% for IgM and 99% for IgG and total antibodies. |

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| 10.06.2020 | Perceived versus proven SARS-CoV-2-specific immune responses in health-care professionals | Infection / Article | <ul style="list-style-type: none"> • Report from the COVID-19 Contact (CoCo) Study which followed 217 frontline health-care professionals at a university hospital with weekly SARS-CoV-2-specific serology (IgA/IgG). • Study participants estimated their personal likelihood of having had a SARS-CoV-2 infection with a mean of 21%. In contrast, anti-SARS-CoV-2 IgG prevalence was about 1-2% at baseline. |
| 11.06.2020 | New IgM seroconversion and positive RT-PCR test after exposure to the virus in recovered COVID-19 patient | J Med Virol / Letter | <ul style="list-style-type: none"> • Case report of a patient recovered from COVID-19 pneumonia with positive serology, followed up by 6 negative nasopharyngeal swab-PCR tests performed along 1 month, who later on, after exposure to the virus, presented another positive RT-PCR test and a second IgM seroconversion. |
| 11.06.2020 | Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): a population-based study | The Lancet / Article | <ul style="list-style-type: none"> • Estimates weekly seroprevalence of anti-SARS-CoV-2 antibodies in the population of Geneva, Switzerland, during the epidemic. • The results suggest that most of the population of Geneva remained uninfected during this wave of the pandemic, despite the high prevalence of COVID-19 in the region (5000 reported clinical cases over <2.5 months in the population of half a million people). • Assuming that the presence of IgG antibodies is associated with immunity, these results highlight that the epidemic is far from coming to an end by means of fewer susceptible people in the population. • Further, a significantly lower seroprevalence was observed for children aged 5–9 years and adults older than 65 years, compared with those aged 10–64 years. |
| 08.06.2020 | Evaluation of the EDI enzyme linked immunosorbent assays for the detection of SARS-CoV-2 IgM and IgG antibodies in human plasma | Clin Chim Acta / Article | <ul style="list-style-type: none"> • Study to evaluate novel immunoassays for detection of SARS-CoV-2 antibodies in human plasma. • Results show high "true" vs. low "false" positivity rates for the EDI(TM) SARS-CoV-2 IgM and IgG ELISAs. |
| 10.06.2020 | IgA dominates the early neutralizing antibody response to SARS-CoV-2 | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • In a study which measured acute humoral responses to SARS-CoV-2 in 145 patients with COVID-19, early SARS-CoV-2-specific humoral responses were found to be typically dominated by antibodies of the IgA isotype. Peripheral expansion of IgA-plasmablasts with mucosal-homing potential was detected shortly after the onset of symptoms and peaked during the third week of the disease. • While the specific antibody response included IgG, IgM and IgA, the latter contributed to a much larger extent to virus neutralization, as compared to IgG. However, specific IgA serum levels notably decrease after one month of evolution. • These results represent a challenging observation given the present |

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| | | | uncertainty as to which kind of humoral response would optimally protect against re-infection, and whether vaccine regimens should consider boosting a potent, although, at least in blood, fading IgA response. |
| 09.06.2020 | Antibody response to infectious diseases and other factors accurately predict COVID-19 infection and severity risk 10-14 years later: a retrospective UK Biobank cohort study | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> Retrospective study of 4,510 unique participants and 7,539 testing instances from multicentre UK Biobank participants to determine the accuracy, specificity, and sensitivity of baseline data from 2006-2010 to predict COVID-19 infection and presumptive severity (i.e., testing at hospital). Among all test cases, accuracy was modest for final diagnostic models of COVID-19 infection (70.2%; AUC=0.570, CI=0.556-0.584) and severity (58.3%; AUC=0.592, CI=0.568-0.615). In the sub-group with serology, by contrast, final models predicted infection and severity with an accuracy of 93.5% (AUC=0.969, CI=0.934-1.000) and 74.4% (AUC=0.803, CI=0.663-0.943) respectively. Serological titers for infectious diseases and other risk factors could help policy makers and clinicians better identify who may get COVID-19 and require hospitalization. |

Diagnostics

| Publication Date | Title/URL | Journal/Article type | Digest |
|------------------|---|------------------------|---|
| 25.05.2020 | On the usefulness of point-of-care antibody tests for severe acute respiratory syndrome coronavirus 2 in community screening settings | Public Health / Letter | <ul style="list-style-type: none"> Letter reasoning that antibody tests should not be used in community screenings to derive public health measures such as quarantine. This is without prejudice to the importance of antibody testing for the decision to lift quarantine or other de-escalation measures. |

Genomics

| Publication Date | Title/URL | Journal/Article type | Digest |
|------------------|--|----------------------|--|
| 27.05.2020 | SARS-CoV-2 Reverse Genetics Reveals a Variable Infection Gradient in the Respiratory Tract | Cell / Article | <ul style="list-style-type: none"> A reverse genetics system was utilized to generate a GFP reporter virus to explore SARS-CoV-2 pathogenesis. High-sensitivity RNA in situ mapping revealed the highest angiotensin-converting enzyme 2 (ACE2) expression in the nose with decreasing |

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| | | | <p>expression throughout the lower respiratory tract, paralleled by a striking gradient of SARS-CoV-2 infection in proximal (high) versus distal (low) pulmonary epithelial cultures.</p> <ul style="list-style-type: none"> • The findings highlight the nasal susceptibility to SARS-CoV-2 with likely subsequent aspiration-mediated virus seeding to the lung in SARS-CoV-2 pathogenesis. |
| 09.06.2020 | Proteomic Profiling in Biracial Cohorts Implicates DC-SIGN as a Mediator of Genetic Risk in COVID-19 | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Very recent unpublished work has identified two genetic risk loci that confer greater risk for respiratory failure in COVID-19: the ABO locus and the 3p21.31 locus. • To understand how these loci might confer risk and whether this differs by race, the authors utilized proteomic profiling and genetic information from three cohorts including black and white participants to identify proteins influenced by these loci. • They observed that variants in the ABO locus are associated with levels of CD209/DC-SIGN, a known binding protein for SARS-CoV and other viruses, as well as multiple inflammatory and thrombotic proteins, while the 3p21.31 locus is associated with levels of CXCL16, a known inflammatory chemokine. |
| 09.06.2020 | Global cataloguing of variations in untranslated regions of viral genome and prediction of key host RNA binding protein-microRNA interactions modulating genome stability in SARS-CoV2 | bioRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • To have an idea of the global changes in 5- and 3-UTR sequences, the authors downloaded and analysed 8595 complete and high-coverage SARS-CoV2 genome sequence information from human host in FASTA format from Global Initiative on Sharing All Influenza Data (GISAID) from 15 different geographical regions. • Overall, they found that despite the variations in the UTR regions, binding of host RBP to them remains mostly unaltered, which further influenced the functioning of miRNAs. • These results show a possible cross-talk between host RBPs-miRNAs and viral UTR variants, which ultimately could explain the mechanism of escaping host RNA decay machinery by the virus. |
| 09.06.2020 | TMPRSS2 variants and their susceptibility to COVID-19: focus in East Asian and European populations | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • To test if epidemiological patterns may be partly determined by human genetic variation, the authors investigated the variability found in the TMPRSS2 gene in populations from different continents, since this gene is fundamental to virus access into human cells. • The functional variants revealed low diversity. The analyses of the variation in the modifiers of gene expression indicate that the European populations may have much higher levels of pulmonary expression of the TMPRSS2 gene and would be more vulnerable to infection by SARS-CoV-2. |

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| | | | <ul style="list-style-type: none"> • By contrast, the pulmonary expression of the TMPRSS2 may be reduced in the populations from East Asia, which implies that they are less susceptible to the virus infection and, these genetic features might also favour their better outcomes. |
| 09.06.2020 | Initial Study of Human Genetic Contribution to COVID-19 Severity and Susceptibility | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Host genetic study performed by deeply sequencing and analysing 332 COVID-19 patients categorized by varying levels of severity. • This initial study of Chinese patients provides a comprehensive view of the genetic difference among the COVID-19 patient groups and highlighted genes and variants that may help guide targeted efforts in containing the outbreak. |

Epidemiology and clinical – children and pregnancy

| Publication Date | Title/URL | Journal/Article type | Digest |
|------------------|---|----------------------|---|
| 10.06.2020 | Risks to children during the covid-19 pandemic: some essential epidemiology | Bmj / Letter | <ul style="list-style-type: none"> • Short letter to inform the return-to-school quandary, presenting mortality data for 0-19 year olds showing that across France, Germany, Italy, Korea, Spain, the United Kingdom, and the United States there were 44 deaths from covid-19 in 0-19 year olds (total population 135 691 226) up to 19 May 2020. • Given all cause mortality in this age group, Covid-19 was responsible for about 0.333% of deaths of 0-19 year olds. Results were similar for each country. • A regularly updated data table including deaths by age categories and country is available at https://tinyurl.com/child-covid. |

Epidemiology and clinical - risk factors

| Publication Date | Title/URL | Journal/Article type | Digest |
|------------------|--|--|--|
| 11.06.2020 | Rapid Risk Assessment: Coronavirus disease 2019 (COVID-19) in the EU/EEA and the UK – tenth update | European Centre for Disease Control and Prevention / Rapid risk assessment | <ul style="list-style-type: none"> • Reports the risk of COVID-19 for the general population and those with risk factors for severe disease, according to the current state of knowledge on the virus and associated disease and in light of the current stage of epidemic in the EU/EEA and the UK, and provide the following: <ul style="list-style-type: none"> • Updated epidemiological and sero-epidemiological information; • Overview of response measures implemented in the EU/EEA countries |

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| | | | and the UK; • Options for response to minimise the risk of resurgence of COVID-19. |
| 10.06.2020 | Excess deaths in people with cardiovascular diseases during the COVID-19 pandemic | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Estimates of excess mortality in specific CVDs, both direct, through infection, and indirect, through changes in healthcare. • CVD service activity decreased by 60-100% compared with pre-pandemic levels in eight hospitals across China, Italy and England during the pandemic. • For total CVD(incident and prevalent), at 10% population COVID-19 rate, we estimated direct impact of 31,205 and 62,410 excess deaths in England at RR 1.5 and 2.0 respectively, and indirect effect of 49932 to 99865 excess deaths. |
| 24.04.2020 | Evaluation and Improvement of the National Early Warning Score (NEWS2) for COVID-19: a multi-hospital study | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Retrospective observational cohort study to evaluate the National Early Warning Score (NEWS2), currently recommended in the UK for risk-stratification of severe COVID-19 outcomes, and identify and validate a minimal set of common parameters taken at hospital admission that improve the score. • NEWS2 score on admission was a weak predictor of severe COVID-19 infection (AUC = 0.628). • Adding age and common blood tests (CRP, neutrophil count, estimated GFR and albumin) provided substantial improvements to a risk stratification model, particularly in relation to sensitivity, but performance was only moderate (AUC = 0.753). This finding was replicated across NHS and non-UK hospitals. |

Epidemiology and clinical – other

| Publication Date | Title/URL | Journal/Article type | Digest |
|------------------|--|--------------------------|--|
| 01.06.2020 | Assessment of Hypokalemia and Clinical Characteristics in Patients With Coronavirus Disease 2019 in Wenzhou, China | JAMA Netw Open / Article | <ul style="list-style-type: none"> • Cohort study of 175 patients with severe hypokalemia (plasma potassium <3 mmol/L), hypokalemia (plasma potassium 3-3.5 mmol/L), or normokalemia (plasma potassium >3.5 mmol/L). • Of 40 severely and critically ill patients, 34 (85%) had hypokalemia. • Patients with severe hypokalemia had statistically significantly higher body temperature and higher creatine kinase levels, higher creatine kinase-MB fraction, higher lactate dehydrogenase levels, and higher C-reactive protein levels than the patients with hypokalemia and normokalemia. |

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| | | | <ul style="list-style-type: none"> • The high prevalence of hypokalemia suggests the presence of disordered rennin-angiotensin system activity, which increases as a result of reduced counteractivity of angiotensin-converting enzyme 2, which is bound by SARS-CoV-2. |
| 01.06.2020 | Prevalence of Gastrointestinal Symptoms and Fecal Viral Shedding in Patients With Coronavirus Disease 2019: A Systematic Review and Meta-analysis | JAMA Netw Open / Systematic review | <ul style="list-style-type: none"> • Systematic review of 23 published and 6 preprint studies with a total of 4805 patients with COVID-19. • Findings suggest that 12% of patients with COVID-19 will manifest GI symptoms; however, SAR-CoV-2 shedding was observed in 40.5% of patients with confirmed SARS-CoV-2 infection. |
| 11.06.2020 | Proinflammatory Cytokines in the Olfactory Mucosa Result in COVID-19 Induced Anosmia | ACS Chem Neurosci / Article | <ul style="list-style-type: none"> • Study to explore local proinflammatory cytokine levels in the olfactory epithelium in patients with COVID-19. • Average TNF-α levels were significantly increased in the olfactory epithelium of the COVID-19 group compared to the control group ($P < 0.05$). However, no differences in IL-1β were seen between groups. • Elevated levels of the proinflammatory cytokine TNF-α were seen in the olfactory epithelium in patients with COVID-19, suggesting that direct inflammation of the olfactory epithelium could play a role in the acute olfactory loss described in many patients with COVID-19. |
| 08.05.2020 | Pre-symptomatic transmission of SARS-CoV-2 infection: a secondary analysis using published data | medRxiv (non-peer reviewed) / Meta-analysis | <ul style="list-style-type: none"> • Using 23 estimates of serial interval and five of generation time from 17 publications, simulations were generated of incubation period and of serial interval or generation time. From these, transmission times relative to symptom onset were calculated and the proportion of pre-symptomatic transmission was estimated. • Transmission time ranged from a mean of 2.91 days before symptom onset to 1.2 days after symptom onset. Proportion of pre-symptomatic transmission ranged from 42.8% to 80.6%. • Whilst contact rates between symptomatic infectious and susceptible people are likely to influence the proportion of pre-symptomatic transmission, there is substantial potential for pre-symptomatic transmission of SARS-CoV-2 in a range of different contexts. |
| 10.06.2020 | Corrigendum to Glycemic Characteristics and Clinical Outcomes of COVID-19 Patients Hospitalized in the United States | J Diabetes Sci Technol / Corrigendum | <ul style="list-style-type: none"> • Correction to an article previously highlighted in the Digest. • Two numeric values in Table 1 were incorrect in the previous published version. |

Infection control

| Publication Date | Title/URL | Journal/Article type | Digest |
|------------------|---|--|--|
| 11.06.2020 | Face Masks Considerably Reduce COVID-19 Cases in Germany: A Synthetic Control Method Approach | IZA Institute of Labor Economics / Discussion Paper Series | <ul style="list-style-type: none"> • The authors use the synthetic control method to analyse the effect of face masks on the spread of Covid-19 in Germany, exploiting regional variation in the point in time when face masks became compulsory. • Depending on the region analysed, they found that face masks reduced the cumulative number of registered Covid-19 cases between 2.3% and 13% over a period of 10 days after they became compulsory. • Assessing the credibility of the various estimates, the authors conclude that face masks reduce the daily growth rate of reported infections by around 40%. |
| 11.06.2020 | Measuring the effectiveness of an automated text messaging active surveillance system for COVID-19 in the south of Ireland, March to April 2020 | Eurosurveillance / Rapid communication | <ul style="list-style-type: none"> • Reports the effectiveness of automated text messaging for active surveillance of asymptomatic close contacts of coronavirus disease (COVID-19) cases in the Cork/Kerry region of Ireland. • In the first 7 weeks of the COVID-19 outbreak, 1,336 close contacts received 12,421 automated texts. • Overall, 120 contacts (9.0%) reported symptoms which required referral for testing and 35 (2.6%) tested positive for COVID-19. |
| 10.06.2020 | Use of personal protective equipment against coronavirus disease 2019 by healthcare professionals in Wuhan, China: cross sectional study | BMJ / Article | <ul style="list-style-type: none"> • Cross sectional study of 420 frontline healthcare professionals who had direct contact with patients with covid-19 and performed at least one aerosol generating procedure, to examine the protective effects of appropriate personal protective equipment. • During the deployment period in Wuhan, none of the study participants reported covid-19 related symptoms. When the participants returned home, they all tested negative for SARS-CoV-2 specific nucleic acids and IgM or IgG antibodies (95% confidence interval 0.0 to 0.7%). |
| 11.06.2020 | Airborne SARS-CoV-2 is Rapidly Inactivated by Simulated Sunlight | J Infect Dis / Article | <ul style="list-style-type: none"> • In this study examining the effect of simulated sunlight, relative humidity, and suspension matrix on the stability of SARS-CoV-2 in aerosols, both simulated sunlight and matrix significantly affected the decay rate of the virus. • Relative humidity alone did not affect the decay rate; however, minor interactions between relative humidity and the other factors were observed. • These results suggest that the potential for aerosol transmission of SARS-CoV-2 may be dependent on environmental conditions, particularly sunlight. |

Social sciences

| Publication Date | Title/URL | Journal/Article type | Digest |
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| 09.06.2020 | Work-related and Personal Factors Associated with Mental Well-being during COVID-19 Response: A Survey of Health Care and Other Workers | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Observational cohort study with 5550 respondents, to measure the prevalence of stress, anxiety, depression, work-exhaustion, burnout, and decreased well-being among faculty and staff at a university and academic medical centre during the SARS-CoV-2 pandemic. • The prevalence of anxiety, depression, and work exhaustion were somewhat higher among clinicians than non-clinicians. • Among all workers, anxiety, depression, and high work exhaustion were independently associated with community or clinical exposure to COVID-19. Poor family supportive behaviours by supervisors were also associated with these outcomes. Age below 40 and a greater number of family/home stressors were also associated with poorer outcomes. |
| 09.06.2020 | Trajectories of depressive symptoms among vulnerable groups in the UK during the COVID-19 pandemic | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • In a study of 51,417 vulnerable individuals in the UK during the COVID-19 pandemic, three depressive symptoms (DST) were identified: low [N=30,850 (60%)], moderate [N=14,911 (29%)], and severe [N=5,656 (11%)] depressive symptoms. DSTs were relatively stable across the first 6 weeks of lockdown. • After adjusting for covariates, experiences of physical/psychological abuse, pre-existing mental health conditions, pre-existing physical health conditions, low social support, and low socio-economic position were significantly associated with the severe DST. • No significant association was found for ethnicity. Participants with key worker roles were less likely to experience severe depressive symptoms. Similar but smaller patterns of associations were found for the moderate DST. |
| 09.06.2020 | Changes in Solo and Partnered Sexual Behaviors during the COVID-19 Pandemic: Findings from a U.S. Probability Survey | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Nationally representative, cross-sectional survey of U.S. adults to examine past month self-reported changes in solo and partnered sexual behaviours. • Nearly half of all adults reported some kind of change, most commonly, a decrease, in their sexual behaviour in the past month. Having elementary aged children at home, past month depressive symptoms and loneliness and enacting more COVID-19 protective behaviours were associated with both reduced partnered bonding behaviours as well as reduced partnered sexual behaviours. |

- Greater COVID19 risk perception and greater COVID19 knowledge were associated with mixed effects in behaviour outcomes.

Modelling

| Publication Date | Title/URL | Journal/Article type | Digest |
|------------------|--|---------------------------------------|--|
| 09.06.2020 | Estimation of effects of contact tracing and mask adoption on COVID-19 transmission in San Francisco: a modeling study | medRxiv (non-peer reviewed) / Article | <ul style="list-style-type: none"> • Modelling study estimating that self-isolation and other practices beginning at the time of San Francisco's shelter-in-place order reduced the effective reproduction number of COVID-19 by 35.4% (95% CI, -20.1%--81.4%). • The effect of contact tracing on the effective reproduction number is estimated to be a reduction of approximately 44% times the fraction of cases that are detected, which may be modest if the detection rate is low. • The impact of cloth mask adoption on reproduction number was estimated to be approximately 8.6%, and the benefit of mask adoption may be substantially greater for essential workers and other vulnerable populations, residents return to circulating outside the home more often. |

Miscellaneous

| Publication Date | Title/URL | Journal/Article type | Digest |
|------------------|--|-------------------------------------|--|
| 12.06.2020 | First Reported Cases of SARS-CoV-2 Infection in Companion Animals - New York, March-April 2020 | MMWR Morb Mortal Wkly Rep / Article | <ul style="list-style-type: none"> • On April 22, CDC and the USDA reported cases of two domestic cats with confirmed infection with SARS-CoV-2. • These feline cases originated from separate households and were epidemiologically linked to suspected or confirmed human COVID-19 cases in their respective households. State and federal partners determined that no further transmission events to other animals or persons had occurred. Both cats fully recovered. • CDC advises persons with suspected or confirmed COVID-19 to restrict contact with animals during their illness and to monitor any animals with confirmed SARS-CoV-2 infection and separate them from other persons and animals at home. |

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| 11.06.2020 | Temperature, Humidity, and Latitude Analysis to Estimate Potential Spread and Seasonality of Coronavirus Disease 2019 (COVID-19) | JAMA Network Open / Original investigation | <ul style="list-style-type: none"> • This cohort study examined climate data from 50 cities worldwide with and without substantial community spread of COVID-19. • The distribution of substantial community outbreaks of COVID-19 along restricted latitude, temperature, and humidity measurements were consistent with the behaviour of a seasonal respiratory virus • With modelling, it may be possible to estimate areas at high risk of substantial community transmission of COVID-19. |
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Overviews, comments and editorials

| Publication Date | Title/URL | Journal/Article type |
|------------------|---|-----------------------------|
| 11.06.2020 | Have deaths from COVID-19 in Europe plateaued due to herd immunity? | The Lancet / Correspondence |
| 11.06.2020 | Potential for elimination of SAR-CoV-2 through vaccination as inspired by elimination of multiple influenza viruses through natural pandemics or mass vaccination | J Med Virol / Review |

Produced by the PHE COVID-19 Literature Digest Team