Paediatric Vaccines
RESEARCH REVIEW™

Making Education Easy

Issue 48 – 2021

In this issue:

Abbreviations used in this issue

4CMenB = 4-component meningococcal B vaccine
COVID-19 = coronavirus disease 2019
FDA = Food and Drug Administration
mRNA = messenger ribonucleic acid
PCV = pneumococcal conjugate vaccine
SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

Kindly Supported by

IMMUNISATION ADVISORY CENTRE
THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau

NEW ZEALAND RURAL GENERAL PRACTICE NETWORK

Welcome to the latest issue of Paediatric Vaccines Research Review.

In this issue, a US study looks at health professionals' motivations (and barriers) for correcting health misinformation on social media, a UK study confirms that COVID-19 vaccination reduces the risk of delta variant infection and accelerates viral clearance, and a review article busts the myth about mRNA vaccines and fertility. As well as the articles highlighted in this review, the latest supplement of the *Journal of Infectious Diseases* focuses on the 'triumphs of vaccination', and is certainly worth a read. In addition to my selections this month, we have a great contribution from paediatric infectious diseases specialist Dr Emma Best.

We hope you find the issue informative and look forward to any feedback you may have.

Kind regards,

Associate Professor Helen Petousis-Harris
helenpetousisharris@researchreview.co.nz

US physicians' and nurses' motivations, barriers, and recommendations for correcting health misinformation on social media

Authors: Bautista JR et al.

Summary: This US study examined health professionals' motivations and barriers for correcting health misinformation on social media. In-depth interviews were conducted with 15 registered nurses and 15 physicians. Participants were personally and professionally motivated to correct health misinformation on social media, but came up against intrapersonal, interpersonal and institutional barriers. They suggested that health care professionals should receive training for correcting misinformation on social media, including building their social media presence.

Comment (HPH): It is well established that the correction of vaccine misinformation is a vital component in the effort to reduce vaccine hesitancy and increase confidence in immunisation programmes. It is also well established that a trusted messenger is one of the most important components in this effort and health professionals score pretty high as 'trusted sources'. However, while these facts are all well and good the act of engaging to correct misinformation is deeply fraught with complexities. While a health professional engaging on social media to correct falsehoods about topics they are expert in is potentially a powerful weapon against health illiteracy, it is not for the faint hearted or ill prepared. Bullying and harassment from online trolls is just one consequence to manage. It is also problematic for some employers, who do not look favourably on staff engaged in such activities. But this is 2021 and if we want to shift the rising tide of dangerous misinformation and the associated consequences such as declines in vaccine uptake, we need to equip (through social medial training and myth correction techniques), support (ensure a safe and supportive work environment through establishing a community), and deploy our health workforce to engage with confidence and to best effect. This paper lays the matter out very clearly.

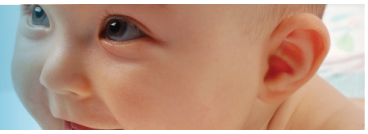
Reference: JMIR Public Health Surveill 2021;7(9):e27715
Abstract

Independent commentary provided by Associate Professor Helen Petousis-Harris

Helen is an Associate Professor in the Department of General Practice and Primary Health Care at the University of Auckland and the Director of the Vaccine Datalink and Research Group. She has a PhD in Vaccinology and is particularly interested in factors associated with vaccine safety and reactogenicity, and the performance and safety of vaccines. Helen has a blog primarily devoted to vaccines and vaccination where she often discusses vaccine myths and matters of current interest in vaccinology.

Independent commentary provided by Dr Emma Best

Dr Emma Best is a Senior Lecturer at the Department of Paediatrics, University of Auckland, a Specialist Paediatrician in Infectious Diseases at Starship Children's Hospital, and a medical advisor to the Immunisation Advisory Centre (IMAC). Her research interests include vaccine-preventable diseases, respiratory infections in children and appropriate antibiotic paediatric prescribing.



Community transmission and viral load kinetics of the SARS-CoV-2 delta (B.1.617.2) variant in vaccinated and unvaccinated individuals in the UK

Authors: Singanayagam A et al.

Summary: This longitudinal cohort study in the UK investigated transmission and viral load kinetics of the SARS-CoV-2 delta variant in vaccinated and unvaccinated community-dwelling individuals. Transmission risk was analysed by vaccination status for 231 contacts exposed to 162 epidemiologically linked delta variant-infected cases, and viral load trajectories from fully vaccinated individuals with delta infection (n=29) were compared with those in unvaccinated individuals with delta (n=16), alpha (B.1.1.7; n=39), and pre-alpha (n=49) infections. The secondary attack rate (SAR) in household contacts exposed to the delta variant was 25% in fully vaccinated individuals and 38% in unvaccinated individuals. Peak viral load did not differ by vaccination status or variant type, but increased modestly with age. Fully vaccinated individuals with delta variant infection had a faster mean rate of viral load decline than unvaccinated individuals with pre-alpha, alpha, or delta variant infections.

Comment (HPH): Determining the extent of viral transmission by COVID-19 vaccinated individuals is a moving feast. Variables include new variants (such as delta), waning immunity, host (age, health), and susceptibility of the contacts. While it is relatively easy to estimate the effectiveness of the vaccine in preventing infection, disease, hospitalisation and death, the matter of transmission is more complicated. For example, simply establishing if a person has become infected is insufficient and some data indicate that the virus from vaccinated individuals may be less viable than the virus from unvaccinated people. We do know that vaccinated people clear the virus faster and are therefore infectious for a shorter period. We also know that most transmission occurs in households. This study showed that if a vaccinated person brought delta into their fully vaccinated household the transmission was reduced by 40–50%. Vaccinated household members who became infected had lower viral load than unvaccinated members. These data support the importance of the mRNA COVID-19 vaccine in reducing transmission of the delta variant and further highlight the importance of vaccinating to protect others in the community.

Reference: Lancet Infect Dis 2021; published online Oct 29
Abstract

Effects of COVID-19 and mRNA vaccines on human fertility

Authors: Chen F et al.

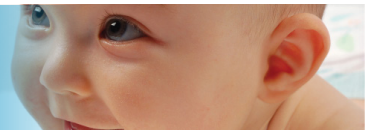
Summary: This article discussed the effects of COVID-19 and mRNA vaccines on male and female reproductive systems. Both men and women, especially pregnant women, have not been shown to have any fertility problems or increased adverse pregnancy outcomes after vaccination. In particular, the benefits of maternal antibodies transferred through the placenta outweigh any known or potential risks.

Comment (HPH): One of the most pervasive myths about the mRNA COVID-19 vaccines is the notion that they cause infertility. If one were deliberately crafting a myth that would resonate with as many communities as possible then this is a rumour that will have wings. In fact this is a theme that saw the resurgence of polio in Nigeria when people heard that the vaccine would make them sterile. The rumours behind the recent COVID vaccine-related claims are founded on 3 sources. One is a misreading of a lab study where rats were given 1333 times the human dose of mRNA vaccine and 0.1% of the dose ended up in the ovaries (hardly relevant!). Another is based on the idea that there is a similarity between the viral spike protein and a protein involved in placenta formation (syncytin-1). The original proponent speculated that this might cause antibodies to attack the pregnancy. By the way, the similarity between the two is about the same as the similarity between a bunch of flowers and a jeep! However, in contrast to the vaccine, growing evidence indicates that the SARS-CoV-2 virus may affect male fertility. This article is a useful summary of the topic and covers the current knowledge about the effect of both COVID-19 and vaccination on fertility.

Reference: Hum Reprod 2021; published online Nov 3
Abstract

RACP MyCPD Program participants can claim **one credit per hour** (maximum of 60 credits per year in Category One – Educational Activities) **for reading and evaluating Research Reviews.**

Please CLICK HERE to download CPD Information



COVID-19 breakthrough infections in vaccinated health care workers

Authors: Bergwerk M et al.

Summary: This study in Israel evaluated breakthrough SARS-CoV-2 infections among health care workers vaccinated with the Pfizer-BioNTech (BNT162b2) mRNA vaccine. 39 cases of SARS-CoV-2 breakthrough infections were documented in 1497 fully vaccinated health care workers. Neutralising antibody titres during the peri-infection period were lower in cases than in matched uninfected controls (case-to-control ratio, 0.361; 95% CI 0.165–0.787). Most breakthrough cases were mild or asymptomatic, although 19% of cases had symptoms that persisted for >6 weeks. 85% of tested samples had the B.1.1.7 (alpha) variant. 74% of case patients had a high viral load at some point during their infection.

Comment (HPH): What happens to vaccinated people who get COVID-19? We know that the vaccines are highly effective at preventing serious disease and death but this study provides us with some detail in a health care worker population – average age 42. Interestingly, the source of infection in all 39 cases described in this paper was an unvaccinated person and in 11 this was an unvaccinated colleague or patient. 26 cases had mild symptoms, none required hospitalisation and the remaining were asymptomatic; 6 were borderline positive. No secondary infections were traced to these cases. Also, the findings suggested that the breakthrough infections did not indicate any selection pressure for immune-evading variants. This further supports the importance of vaccinating health care workers, and also the community value of COVID-19 vaccination.

Reference: N Engl J Med 2021;385(16):1474-84
Abstract

Myopericarditis after messenger RNA coronavirus disease 2019 vaccination in adolescents 12 to 18 years of age

Authors: Das BB et al.

Summary: This cross-sectional study examined the clinical course and outcomes of adolescents who developed probable myopericarditis after vaccination with the Pfizer-BioNTech (BNT162b2) COVID-19 vaccine. 25 adolescents aged 12–18 years who were diagnosed with probable myopericarditis at 8 US centres after COVID-19 mRNA vaccination in May/June 2021 were included. 88% of cases occurred after the second dose of vaccine, and chest pain (100%) was the most common presenting symptom. Patients presented for medical attention a median 2 days after receipt of the vaccine, and all had an elevated plasma troponin level. 92% of patients had no echocardiographic abnormalities at presentation, but cardiac magnetic resonance imaging of 16 patients showed that 15 (94%) had late gadolinium enhancement consistent with myopericarditis. Most were treated with ibuprofen or an equivalent nonsteroidal anti-inflammatory drug for symptomatic relief. All patients had symptom resolution within a week.

Comment (HPH): Based on NZ data from 2008–2019, each year there are around 100–150 hospitalisations for myocarditis with a preponderance in younger males. Earlier this year myopericarditis emerged as an adverse event associated with receipt of COVID-19 mRNA vaccines. It quickly became apparent that the risk was increased after vaccination with the greatest risk among males aged 16–30 receiving their second dose – of course at this time the vaccine was not authorised for younger age groups. Several mechanisms have been proposed but nothing conclusive is yet established. Just to be clear, COVID-19 disease is associated with greater risk of myopericarditis than the vaccine and in general contrast to the vaccine-associated events, this can be severe. However, careful consideration must be given to the vaccination of a group who are at relatively low risk of severe COVID-19 and now that the vaccine has been given the go ahead for children aged 12–15 and over the question about the risk in them now needs answering. The most recent assessment by the FDA indicates that among this age group, when vaccinated, there could be expected 318 per million hospitalisations related to COVID-19 with a mean stay of 6 days prevented, compared with 156 vaccine-related hospitalisations with a mean stay of 1 day. There would be around 77,000 COVID-19 cases prevented for 186 additional cases of myocarditis. The vaccine-associated adverse events are far less and more benign that those associated with the disease. These data reinforce the generally mild nature of these vaccine-associated events in 12- to 15-year-olds, and should provide some reassurance.

Reference: J Pediatr 2021;238:26-32
Abstract

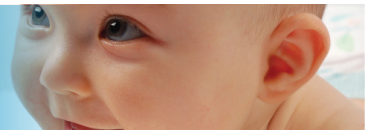
Safety, immunogenicity, and efficacy of the BNT162b2 COVID-19 vaccine in adolescents

Authors: Frenck RW et al., for the C4591001 Clinical Trial Group

Summary: This ongoing multinational study investigated the safety, immunogenicity, and efficacy of the Pfizer-BioNTech COVID-19 vaccine (BNT162b2) in adolescents. 2260 adolescents aged 12–15 years received 2 injections, 21 days apart, of 30µg BNT162b2 or placebo. BNT162b2 had a favourable safety and tolerability profile, with mainly transient mild-to-moderate reactogenicity (injection-site pain, fatigue, and headache). There were no vaccine-related serious adverse events. The geometric mean ratio of SARS-CoV-2 50% neutralising titres after dose 2 in these adolescents relative to a group aged 16–25 years was 1.76 (95% CI 1.47–2.10), which indicated a greater response in the younger cohort. The observed vaccine efficacy was 100%.

Comment (EB): This is an important study demonstrating the safety and efficacy of the current COVID mRNA vaccine in those aged 12–15 years, a vaccine now widely in use in many countries for this age group. As seen in older teens and young adults, it is a reactogenic vaccine with headache and/or fatigue commonly reported in the first 1–2 days, although slightly less frequently amongst 12- to 15-year-olds compared with those aged 16–25 years. The increased rate of peri/myocarditis observed post-marketing after mRNA vaccines (particularly in males aged <30 years) wasn't detected in this relatively small study. This month has also seen the publication of a BNT162b2 COVID-19 vaccine trial for children aged 5–11 years with 1500 children receiving one-third of the adult/teen dose in a 3-week apart regimen. Comparable to older children, the mRNA vaccine is equivalently immunogenic in young children and young adults, with slightly less frequently seen mild post-vaccine side effects. The vaccine now awaits Medsafe approval in NZ. With the current delta outbreak there have been much higher rates of COVID infection in children; amongst 5500 COVID cases, one-third are aged less than 20 years, of whom half are aged 10 years or less. Yet when compared with older or even younger adults, hospital level care for children remains exceptionally uncommon, even with delta. Balancing health and non-health vaccine benefits, including potential to limit intergenerational transmission, prevent school disruption and inequitable disease burden in Māori and Pacific communities means that vaccinating school-age children is likely to have a role in Aotearoa NZ COVID control.

Reference: N Engl J Med 2021;385:239-50
Abstract



Effectiveness of pneumococcal vaccination against hospitalized pneumococcal pneumonia in older adults

Authors: Heo JY et al.

Summary: This prospective multicentre study in Korea investigated the effectiveness of the 13-valent PCV (PCV13) and the 23-valent pneumococcal polysaccharide vaccine (PPV23) against pneumococcal pneumonia in older adults. 1525 adults aged ≥65 years hospitalised with community-acquired pneumonia (CAP) between September 2015 and August 2017 were included. 167 (11.0%) cases were identified as pneumococcal CAP. The adjusted vaccine effectiveness (VE) of pneumococcal vaccines against pneumococcal CAP was not statistically significant (40.0% for PCV13 and 11.0% for PPV23). However, in a subgroup of patients aged 65–74 years, sequential PCV13/PPV23 vaccination had the highest adjusted VE (80.3%), followed by single-dose PCV13 (66.4%) and PPV23 (18.5%).

Comment (EB): Despite the large disease burden of non-bacteraemic CAP in older adults, pneumococcal vaccines are not funded in Aotearoa NZ other than for adults at highest risk of invasive pneumococcal disease such as individuals with asplenia, cochlear implants or severe immunosuppression following transplantation. PCV13 is useful in older adults to protect from serotype-specific pneumococcal CAP. However with infant PCV programmes, additional benefit of PCV use in older adults is less clear and PPV23 alone is suggested by some (e.g. Centers for Disease Control and Prevention). In this Korean study, vaccine effectiveness to protect against pneumococcal pneumonia was only shown in those aged 65–74 years (not in older age groups) and with sequential use PCV13/PPV23 in preference to either alone. Presence of any medical risk factors such as chronic respiratory, heart, renal disease and/or smoking are known to add to risk of pneumococcal pneumonia alongside older age. Is it time to consider a sequential PCV13/PPV23 vaccination policy in 'high-risk' adults alongside PCV13 for infants in view of emergent serotypes, disparity in disease burden amongst Māori adults compared with non-Māori, and the likelihood of resurgent seasonal respiratory viruses when borders open next year?

Reference: J Infect Dis 2021; published online Sep 19
Abstract

Unravelling the impact of pneumococcal conjugate vaccines on ambulatory antibiotic drug consumption in young children

Authors: Danino D et al.

Summary: This time-series analysis in Israel evaluated the impact of PCVs on antibiotic use in young children. Dispensed antibiotic prescription (DAP) rates for children under 5 years of age were examined over a 13-year period (including 4 pre-PCV years). Of 1,090,870 DAPs (mostly amoxicillin or amoxicillin-clavulanate), 57% were for children under 2 years of age. DAP rates abruptly declined after PCV7/PCV13 implementation, reaching a plateau within 5 years. Age <2 years and Bedouin ethnicity were significantly associated with higher pre-PCV DAPs but with faster and greater decline in DAPs post-PCV.

Comment (EB): Overall reduction in antibiotic use is a major strategy to contain antibiotic resistance. In young children, respiratory tract infections are the commonest reason for antibiotic prescription. By decreasing respiratory tract infections (particularly acute otitis media and community-acquired pneumonia), PCVs are one of the tools against antibiotic resistance. This study over 13 years in Israel shows an overall decline in antibiotics dispensed after PCV implementation, more marked in children from more socioeconomically deprived groups where prescribing was highest prior. At the same time azithromycin consumption slightly increased although it contributed only 14% of all dispensed antibiotics. Although there is evidence of initial impact with PCV the effect plateaued and the increase in another antibiotic class, such as a broad macrolide, is concerning. Just as in NZ, it seems that community antibiotic consumption is not driven solely by rate of respiratory tract infection, but that parent and prescriber expectations/behaviour, healthcare access, prescribing guidelines and restrictions on certain antibiotics will all have a part to play.

Reference: Clin Infect Dis 2021;73(7):1268-78
Abstract

First real-world evidence of meningococcal group B vaccine, 4CMenB, protection against meningococcal group W disease

Authors: Ladhani SN et al.

Summary: In September 2015, the UK introduced the meningococcal group B vaccine 4CMenB into the national infant immunisation programme alongside an emergency adolescent meningococcal ACWY (MenACWY) programme to control a national outbreak of group W (MenW) disease. This study analysed the number of MenW cases reported in the 4 years before versus the 4 years after implementation of both vaccines. Poisson models showed 69% and 52% fewer MenW cases than predicted among age-cohorts that were fully- and partly-eligible for 4CMenB, respectively. 138 MenW cases were reported in children under 5 years of age. It was estimated that 4CMenB directly prevented 98 cases, while the MenACWY programme indirectly prevented an additional 114 (conservative) to 899 (extreme) cases over 4 years. Disease severity was similar in 4CMenB-immunised and unimmunised children.

Comment (EB): The protein-based 4CMenB vaccine contains 4 targets from meningococcal bacteria including adhesin A, factor H binding protein, Neisserial heparin-binding antigen, and NZ MenB epidemic strain outer membrane protein. These vaccine targets are found not only on MenB but also on other meningococcal serogroups including emergent serogroup MenW. The UK has already reported the impact of their 2+1 infant 4CMenB schedule and reductions in infant MenB disease. This paper shows expected cases of infant MenW cases were also prevented in the 4CMenB eligible infants from cross serogroup protection. In NZ, meningococcal disease has been gradually increasing since 2014, comprised almost entirely of serogroups B and W. 60% of cases occur in those aged <20 and over one-third are aged <5 years. Although rates were dampened by COVID pandemic measures, cases were seen again particularly after our 2021 winter surge of respiratory syncytial virus. We continue to have high rates of invasive meningococcal disease compared with other developed countries. Earlier this year Pharmac funded 4CMenB for only medically high-risk individuals and cases/contacts of those with meningococcal disease – a strategy which will have no meaningful population-level impact nor control on overall burden of meningococcal disease in NZ that is borne by otherwise healthy children and young people.

Reference: Clin Infect Dis 2021;73(7):e1661-8
Abstract

CLICK HERE to read previous issues of Paediatric Vaccines Research Review

This Research Review has been endorsed by The Royal New Zealand College of General Practitioners (RNZCGP) and has been approved for up to 1 CME credit for the General Practice Educational Programme (GPEP) and Continuing Professional Development (CPD) purposes. You can record your CME credits in your **RNZCGP Dashboard**

Time spent reading this publication has been approved for CNE by The College of Nurses Aotearoa (NZ) for RNs and NPs. For more information on how to claim CNE hours please **CLICK HERE**.