Paediatric Vaccines
RESEARCH REVIEW™

Making Education Easy

Issue 42 – 2020

In this issue:

Abbreviations used in this issue

CEPI = Coalition for Epidemic Preparedness Innovation
DHB = District Health Board
HPV = human papillomavirus
MeNZB = meningococcal B vaccine
MenACWY-TT = meningococcal ACWY-tetanus toxoid
MERS = Middle East respiratory syndrome
MMR = measles, mumps, and rubella
Tdap = tetanus, diphtheria, and acellular pertussis
WHO = World Health Organization

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Welcome to the latest issue of Paediatric Vaccines Research Review.

We report a number of articles related to COVID-19 this month, including the issue of vaccine hesitancy in the time of COVID-19, a report from CEPI on the development of COVID-19 vaccines, an article by Bill Gates on the global response to COVID-19, and the increasing presence of anti-vaxxers on social media. We also report the use of a third dose of MMR vaccine in young adults to improve immunity against mumps, and present positive feedback for the proposal of free maternal vaccinations at community pharmacies in NZ.

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

Kind regards,

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Vaccine confidence in the time of COVID-19

Authors: Harrison EA & Wu JW

Summary: Vaccine hesitancy has preoccupied health experts and media for the last few decades, and many professionals have proposed interdisciplinary approaches to address it. The current COVID-19 crisis may ignite a collective memory of previous struggles against infectious disease, but will it be sufficient to solve the problem of vaccine hesitancy? This article discussed vaccine hesitancy, and addressed the culture of public health. Public confidence in vaccination programmes depends on the work the programmes do for the community; the concept of public health and its programmes must be broader than the delivery of the vaccine technology itself. COVID-19 might fix the problem of vaccine hesitancy, but a failed vaccine might also lead to public backlash with devastating consequences for routine childhood vaccination.

Comment (NT): We cannot escape without COVID-19 in the conversation! I was recently asked to comment on a NZ media study asking who would accept a COVID-19 vaccine. Many were surprised by a sizeable minority who reported they would refuse any COVID-19 vaccine. Notwithstanding this was not a rigorous survey, it should not come as a surprise that many in our community are not wholeheartedly embracing vaccines. This is a very thoughtful article that takes our eyesight to a broader horizon of why there is, and will continue to be, vaccine hesitancy. Internationally, and locally, we are seeing significant societal, moral and ethical challenges for many, including rapidly rising social and financial equity gaps. On the other side we have a huge public outpouring of optimism and desperation for a vaccine(s) to solve all the problems, which it will not, no matter how good the vaccine. A very sobering message for all our linear public health thinking as the authors so rivetingly describe "*... the fantasy that vaccines could obviate the need for broader social and environmental policies*". As public health communities we can see the dilemma purely as a tension between individual autonomy and state power – but we miss the social and moral conditions in which people are asked to make choices. The authors point out that an understanding of confidence in vaccines is in many ways a gauge of how our society is collectively constructed across our state, we as individuals and within our multiple communities. Therefore, ensuring public confidence requires a much broader approach than traditional thinking. A lovely phrase from the authors is their expression of the need for "*re-imagination of the culture of public health and the essential relationships on which it depends*".

Reference: Eur J Epidemiol 2020;35(4):325-30
Abstract

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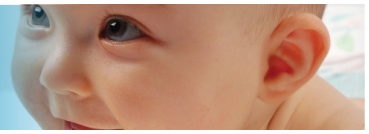


Developing COVID-19 vaccines at pandemic speed

Authors: Lurie N et al.

Summary: CEPI is an international nongovernmental organisation funded by the Wellcome Trust, the Bill and Melinda Gates Foundation, the European Commission, and 8 countries (Australia, Belgium, Canada, Ethiopia, Germany, Japan, Norway, and the UK) to support the development of vaccines on the WHO priority list. CEPI also supports development of platform technologies to prepare for "disease X" – a newly emerging epidemic disease such as COVID-19. An ideal platform supports development from viral sequencing to clinical trials in less than 16 weeks. Among the multiple platforms under development, those with the greatest potential for speed are DNA- and RNA-based platforms, followed by those for developing recombinant-subunit vaccines. As soon as China announced that a novel coronavirus had been identified as the cause of the Wuhan outbreak, CEPI contacted its partners that were developing MERS vaccines or working on novel platforms. They and others began vaccine development as soon as the first gene sequence was posted, and development is proceeding quickly. A global financing system that supports end-to-end development, large-scale manufacturing and deployment, and ensures fair allocation of vaccines is a critical component of future pandemic preparedness.

Reference: N Engl J Med 2020;382:1969-73
Abstract

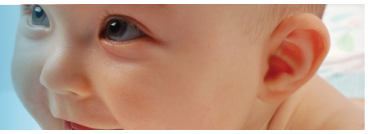
Responding to COVID-19 – a once-in-a-century pandemic?

Authors: Gates B

Summary: This article by Bill Gates on behalf of the Bill and Melinda Gates Foundation discussed the steps needed to address the COVID-19 pandemic. There are two reasons that COVID-19 is such a threat. First, it can kill healthy adults in addition to elderly people with existing health problems, and secondly it is transmitted quite efficiently. National, state, and local governments and public health agencies need to take steps to slow the spread of the virus. In addition to helping their own citizens respond, donor governments can help low- and middle-income countries (LMICs) prepare for the pandemic. It is essential that LMICs strengthen their primary health care systems in order to save lives and slow the global circulation of the virus. The world also needs to accelerate work on treatments and vaccines for COVID-19, and build a system that can develop safe, effective vaccines and antivirals, get them approved, and deliver billions of doses as fast as possible after the discovery of a fast-moving pathogen. Budgets for these efforts need to be expanded, and yet more funding is needed to improve disease surveillance and response. Finally, governments and industry need to work together to ensure that vaccines and antivirals are made available and affordable for people who are at the heart of the outbreak and in greatest need.

Reference: N Engl J Med 2020;382:1677-9
Abstract

Comment (HPH): How realistic is a COVID-19 vaccine? There is little about the development of COVID-19 vaccines that is traditional, except the general steps: Identify pathogen, identify need, develop possible vaccine candidates, test in the lab, animal models, phase I, II, and III human trials, licensure, upscale manufacture capacity, phase IV trials and postmarketing surveillance. This is the general pathway to a vaccine and traditionally it takes 10–20 years, 5 years at a pinch, and costs upwards of 1 or 2 billion dollars and is very high risk as the product could fail at any stage. This is never going to help us when a new disease emerges. So what if you were not so concerned about developing a profitable product and suddenly had the attention of the world's best scientists and technologies with over 100 candidates? Collaboration runs freely and funding is flowing. What if you could build a billion dollar manufacturing facility and start making a vaccine that has not even completed phase II trials, just in case it works? By running the essential steps toward vaccine development in parallel with each other we have made it at least possible to develop and produce effective and safe vaccines against COVID-19 with unprecedented speed (12–18 months). It is anticipated that the first vaccines may be ready to deploy in September/October this year (not in NZ, but UK, US, India and China as examples). This seems ambitious but if by some incredible run of everything going right it might happen. To roll these out safely under emergency conditions requires mature systems for monitoring the safety of the vaccine, services to deliver the vaccine and record it, effective supply chains, and a world class multi-level communications strategy. Would anyone actually be ready then, or in a year for that matter? NZ has done this successfully during the MeNZB campaign but it took a mammoth effort. There is a long road ahead of us in this space.



The online competition between pro- and anti-vaccination views

Authors: Johnson NF et al.

Summary: Opposition to vaccination with a future vaccine against SARS-CoV-2 could amplify outbreaks, as happened for measles in 2019. Social media companies are struggling to control online health dis- and misinformation during the COVID-19 pandemic. This study conducted a system-level analysis of vaccination views among nearly 100 million Facebook users from across countries, continents and languages. The investigators found that anti-vax clusters have managed to become highly entangled with undecided clusters in the main online network, whereas pro-vaccination clusters are more peripheral. They predicted that online anti-vaccination views will dominate pro-vaccination views within a decade.

Comment (HPH): This is pretty sobering stuff but you should see the glorious graphics! The results suggest that social media anti-vaccine clusters infiltrate greater numbers of undecided clusters and that over the next decade or so these will become the majority. This study was conducted in 2019 during a period of measles outbreaks. The authors note in the comments section that as a result of COVID-19 they are seeing a sudden further increase of activity around the same cluster ecology. Groups that spread misinformation find more favour with undecided people than expert groups do (sadly). It is noted that major public health entities are focussing in the wrong place, off to one side. The lead author of this work suggests that *"Instead of playing whack-a-mole with a global network of communities that consume and produce [mis]information, public health agencies, social media platforms and governments can use a map like ours and an entirely new set of strategies to identify where the largest theaters of online activity are and engage and neutralize those communities peddling in misinformation so harmful to the public."* Working with data scientists is an important collaboration in the management of our exploding misinfodemic.

Reference: Nature 2020; published online May 13
Abstract

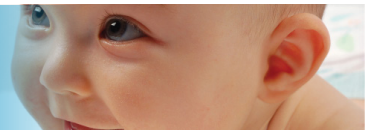
The effects of source expertise and trustworthiness on recollection: The case of vaccine misinformation

Authors: Pluviano S et al.

Summary: This study examined whether misinformation about vaccination could be effectively corrected by a perceived credible source. Two experiments were conducted, each featuring two correction conditions on vaccine misinformation. Participants were presented with a story containing information that was later retracted by a perceived credible or not so credible source. The first experiment showed that the correction reduced participants' use of the original erroneous information. The second experiment revealed that a correction from a high-trustworthy source decreased participants' reliance on misinformation, but did not positively affect their reported intent to vaccinate a child. Overall, source trustworthiness was found to be more relevant than source expertise.

Comment (NT): How do we recognise and overcome confirmation bias in our decision-making? Coping with the world and rapid multiple decision-making requires us all to use heuristics (cognitive shortcuts) such as omission bias – a tendency to prefer inaction to action, or the feelings of overconfidence regarding our own knowledge about a topic. Recognising that these heuristics occur is vital, otherwise well-meaning messages and education can fail and at times create undesirable consequences. For example, the more we directly correct a myth the more danger there is of just remembering the myth, not the correcting information. Equally, not responding to myths and false information runs the risk of allowing them to continue to run. This is another study that supports the body of evidence that the trustworthiness of the source of information is the most important factor, more important than the expertise of the source. Who is seen as trustworthy is going to vary considerably across and even within communities. As we are now focusing on more localised and tailored strategies, these approaches require a greater awareness of how to gain and maintain trustworthiness with different communities, pushing us beyond traditional health education approaches. A note of caution though, I do see there could be a real moral dilemma here, if we focus purely on trustworthiness based on emotional responses without alongside it maintaining as much rigour as possible around the credibility of messages. A complex world requires complex solutions.

Reference: Cogn Process 2020; published online Apr 24
Abstract



Clinical practices for measles-mumps-rubella vaccination among US pediatric international travelers

Authors: Hyle EP et al.

Summary: This cross-sectional study examined clinical practices for MMR vaccination in paediatric American international travellers. Of 14,602 pretravel consultations for paediatric travellers (aged 6 months to <18 years) at 29 US sites associated with Global TravEpiNet, 2864 travellers (19.6%) were eligible to receive pretravel MMR vaccination at the time of the consultation. Of these individuals, 1182 (41.3%) received the MMR vaccine and 1682 (58.7%) did not. Multivariable analysis showed that MMR vaccination-eligible paediatric travellers were less likely to be vaccinated at the pretravel consultation if they were school-aged. The most common reasons for nonvaccination were clinician decision not to administer MMR vaccine (36.9%) and guardian refusal (36.4%).

Comment (NT): One very worrying international issue with the disruption from COVID-19 shutdowns and overwhelmed health services is that many countries are already seeing significant drop offs in their childhood immunisation programmes. Measles is way more transmissible than COVID-19, and I fear we are highly likely to see large international outbreaks of measles very soon. NZ currently has no circulating measles. Our borders essentially are currently closed to measles admission and the 2-week quarantine period should pick up any possible measles cases prior to local community contact. Now feels like a good time to take stock of what we want to stop at the borders going forward, not just that "C" disease. If we are serious about keeping out measles long-term, I would advocate that we need to improve screening at our borders for measles immunisation records. While screening tourists long term will be a challenge, we should as a minimum be able to develop systems for screening all those coming to stay such as migrants and international students. While our borders are tight we should be protected, but we need an ongoing strategy to ensure this continues.

Reference: JAMA Pediatr 2020;174(2):e194515
Abstract

Long-term antibody persistence after a booster dose of quadrivalent meningococcal ACWY-tetanus toxoid conjugate vaccine in healthy 5-year-old children

Authors: Vesikar T et al.

Summary: This study measured antibody persistence after booster dosing of MenACWY-TT conjugate vaccine in children. 159 children were vaccinated at age 12–23 months then received a booster dose 4 years later. This study assessed antibody persistence at 2–6 years post-booster against each of the 4 meningococcal serogroups. The percentages of children with rabbit serum bactericidal antibody (rSBA) titers ≥1:8 ranged from 96.7% to 100% across serogroups at 2 years post-booster and from 71.6% to 94.0% at 6 years post-booster. rSBA geometric mean titers decreased from year 2 to 4 and generally remained stable thereafter. The percentages of children with human serum bactericidal antibody titers ≥1:4 ranged from 70.0% to 100% across serogroups at 2 years post-booster and from 58.5% to 98.5% at 6 years post-booster.

Comment (NT): It is nice to be able to get back to some 'bread and butter' vaccinology questions. NZ does not yet have a national childhood meningococcal vaccination programme, except for individuals with particularly high-risk medical conditions. For others, vaccine can be purchased on the private market. If there was a universal national programme the approach would be to aim for herd immunity; in the absence of that, vaccination is about offering protection specifically just to the vaccinated individual. Hence the importance of the question of how quickly does vaccination protection wane. Many people assume that a vaccine offers long-lasting protection, but meningococcal vaccines do not and the general rule of thumb is that for persisting protection, boosters around every 3–5 years are necessary. Meningococcal is a rapidly progressive illness so maintaining high antibody levels is essential to ensure effective response, therefore waning immunity is a significant concern. This study can lend confidence to the advice that from being given a toddler vaccination with MenACWY-TT (Nimenrix®), persisting high antibody levels are seen for up to 6 years. A note of caution is that for meningococcal conjugates we cannot assume all brands act the same.

Reference: Vaccine 2020;38(22):3902-8
Abstract

A third dose of measles-mumps-rubella vaccine to improve immunity against mumps in young adults

Authors: Kaaijk P et al.

Summary: This study investigated antibody responses after a third dose of MMR vaccine (MMR3) in 150 young adults. Levels of immunoglobulin G, anti-vaccine strain, and anti-outbreak strain antibodies were increased by a factor of 1.65, 1.34, and 1.35, respectively, 4 weeks after receiving the third dose. Levels had declined when measured 1 year later, but remained higher than baseline levels by a factor of 1.37, 1.15, and 1.27, respectively. Significantly more participants were protected against mumps virus infection up to 1 year after vaccination, and had antibody levels above the presumed threshold for herd immunity.

Comment (NT): While it has been an excellent efficient approach to combine the mumps vaccine with measles and rubella, all 3 components do not act the same. It is well recognised that the mumps component has waning immunity much more rapidly than measles or rubella. On the positive side, fully vaccinated individuals (received 2 doses) who do get breakthrough mumps disease have much lower rates of severe disease than the unvaccinated, but it is not zero. Reported rates of mumps complications in fully vaccinated individuals who go on to get disease are around 3%, of which three-quarters are orchitis. Hence the question about whether a third dose of mumps-containing vaccine should be recommended. If we had high enough vaccination coverage in a community for herd immunity, mumps would be eliminated and this would not be a problem. This is estimated to require around 90–92% vaccination coverage (or immunity gained from having the disease) across the community. We currently do not have this rate in all groups in our community, particularly in adolescents and young adults. Hence the ongoing mumps outbreaks around NZ. The best long-term solution is to get MMR1 and MMR2 rates high enough and mumps will be eliminated. Another compelling reason for getting on with our measles catch-up programme. However, while we still have significant community immunity gaps with ongoing outbreaks, it seems sensible to offer MMR3 in outbreak situations to reduce disease.

Reference: J Infect Dis 2020;221(6):902-9
Abstract

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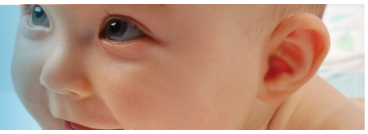

A qualitative study of views and experiences of women and health care professionals about free maternal vaccinations administered at community pharmacies

Authors: Gauld N et al.

Summary: This NZ study explored the views and experiences of women and health care professionals regarding funded maternal vaccinations in community pharmacies. Women in late pregnancy or with an infant, and midwives, pharmacists, and general practice staff were approached to participate. A total of 53 women and health care professionals were interviewed, and most of them had positive views about funded maternal vaccinations in community pharmacies.

Comment (HPH): A barrier to higher vaccine uptake of vaccines given to adolescents and adults is easy access. Such vaccines include Tdap, HPV, influenza, vaccines for pregnant women, and private market vaccines such as meningococcal. Pharmacists are a relatively untapped resource in this space yet they are the health professional that people see most often. In the last few years a growing number of pharmacies in NZ have been offering immunisation services. Nationally pharmacists are funded to administer maternal flu vaccine. In 2016, Waikato DHB funded pharmacist-administrated pertussis vaccine for pregnant women. Qualitative research suggests that access to pertussis vaccine in pharmacies was associated with a larger increase in overall uptake. Adding to this, the study presented here shows that the strategy is generally well accepted among pregnant women, midwives, pharmacists, and general practice staff. Given our relatively low uptake of maternal pertussis vaccine, this seems like a very obvious way to reduce access issues for maternal pertussis vaccination.

Reference: Vaccines 2020;8(2):152
Abstract

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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. She is the Chair of the WHO Global Advisory Committee on Vaccine Safety (GACVS).

Independent commentary provided by Associate Professor Nikki Turner.

Nikki is an academic General Practitioner. She currently lives in Wellington and works as an Associate Professor for the University of Auckland in the Department of General Practice and Primary Care, as honorary Associate Professor for the University of Otago Wellington and part-time as a General Practitioner in Wellington.
Her roles include Director of Immunisation Advisory Centre (IMAC) at the University of Auckland. She is a member of the WHO Strategic Advisory Group of Experts (SAGE) committee on immunisation which is the principle advisory group to the WHO for vaccines and immunisation. She is also the chair of the WHO measles and rubella elimination subcommittee. Nikki's academic interests are in primary health care, preventive child health and immunisation and she continues to work part-time as a General Practitioner for NUHS Broadway clinic in Strathmore, Wellington.

The state of vaccine safety science: Systematic reviews of the evidence

Authors: Dudley MZ et al.

Summary: This article discussed possible causal associations of adverse events following immunisation (AEFI) reported by the Institute of Medicine in 2012 and the Agency for Healthcare Research and Quality in 2014. A causal association was found for 12 of 46 AEFI examined. The adverse events included anaphylaxis, arthralgia or arthritis (acute, mild and transient), deltoid bursitis after improper vaccine administration, disseminated varicella infection in immune-deficient individuals, encephalitis, febrile seizures, Guillain-Barré syndrome, hepatitis in immune-deficient individuals, herpes zoster, immune thrombocytopenic purpura (ITP), meningitis, and syncope. These adverse reactions were mostly rare or very rare, other than mild acute and transient arthralgia/arthritis, which is common in women after rubella vaccine. Overall, vaccines were found to have an excellent safety profile.

Comment (HPH): Serious events causally related to modern routinely administered vaccines are extremely rare. Some are so rare as to be impossible to assess with enough accuracy as to be sure. By and large, if the risk is more than 1 in a million we know about it. This is the penultimate summary of the state of the safety of vaccines. 46 different adverse events following immunisation were assessed. The review updates the very elderly previous penultimate summary that was published by the US Institute of Medicine in 2012. Of the vaccines relevant to NZ, anaphylaxis is always a risk, arthralgia or arthritis after influenza and MMR vaccines, deltoid bursitis due to incorrect administration, disseminated varicella infection, hepatitis, herpes zoster, and meningitis in people with supressed immune systems after varicella vaccine, febrile seizures after several vaccines, and ITP after MMR. As you can see, most things on the list are avoidable by not using varicella vaccine in immune-suppressed people and not poking needles into shoulders. Anyway, this will be a very useful resource for the next few years.

Reference: Lancet Infect Dis 2020;20(5):e80-9
Abstract

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