

ASVAC2022 : 8th Asian Vaccine Conference

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ABSTRACT

Aiming to further the Immunization Partners in Asia Pacific (IPAP)'s vision of a world where no one suffers from a vaccine preventable disease, the 8th Asian Vaccine Conference (ASVAC 2022) was held in Colombo, Sri Lanka and virtually from 15 to 18, September 2022 (www.asianvaccine.com). This conference followed those held in Siem Reap, Cambodia (2009), Manila, Philippines (2010), Jakarta, Indonesia (2011), Cebu, Philippines (2013), Hanoi, Vietnam (2015), Singapore (2017) and Naypyidaw and Yangon, Myanmar (2019). The ASVAC2022 themed "Immunization: in Era of Pandemics," commenced with the EPI Managers' Workshop, followed by pre-conference workshops and Vaccinology Masterclass, followed by the main conference featuring 5 plenary lectures, 6 partner-led symposia, free paper and poster presentations, and industry-supported lunch and evening sessions. There were over 1830 registered participants, with 112 attending in person and 998 virtually from 63 countries. The conference was organized by IPAP and hosted by the Vaccine and Infectious Disease Forum of Sri Lanka, Sri Lanka College of Pediatrics, Sri Lanka College of Microbiologists and College of General Practitioners of Sri Lanka, with the support of the Ministry of Health, Sri Lanka. The 9th ASVAC is scheduled to be held in Davao City, Philippines in late 2023.

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Introduction

The hybrid 8th Asian Vaccine Conference (15th to 18th September 2022) was officiated by the Minister of Health of Sri Lanka, Keheliya Rambukwella. In welcoming participants, he appreciated the efforts to share knowledge and experience from global experts in various aspects of vaccinology and expressed his gratitude to Immunization Partners in Asia-Pacific (IPAP). The power of immunization was seen clearly during the COVID-19 pandemic, where novel vaccines were produced in record time, saving millions of lives. One unfortunate result of the pandemic was increased vaccine hesitancy and the rise of the anti-vaccine lobby, and he stressed that this forum should address vaccine hesitancy in the future. Lulu Bravo (Philippines) appreciated the efforts in improving child health through immunization programs. She noted vaccine complacency can be brought about by the elimination of major childhood diseases and is of concern. The value of vaccination should be emphasized in communication and vaccine advocacy for children.

Plenary lectures

The opening plenary lecture, Equity and COVID, by Kim Mullholland (Murdoch Children's Research Institute and London School of Hygiene and Tropical Medicine)

highlighted how the past 2–3 years have been a challenging period for children. Factors such as climate change, political insecurity and war, poverty, loss of lifetime opportunities, loss of routine healthcare and failed immunization have been major contributors. The Lancet Global Health report revealed that Middle Eastern and South East Asian regions have had dramatic drops in immunization rates during the first year of the pandemic. However, although these improved with time, it is important to note that there is inequity within countries in immunization rates and access to healthcare services in certain communities which is disguised by national data. Healthcare services and immunization rates correlate with child survival. There are three markers associated with children at highest risk of death that should be considered in strategies to increase childhood immunization coverage: having a zero-dose child in the family; malnutrition in the family; and hospital admissions due to pneumonia and diarrhea. Children affected with measles have high mortality rates and outbreaks continue to occur in many countries. Measles leads to, and is exacerbated by, malnutrition and during the COVID-19 pandemic, poor vaccine coverage has increased measles susceptibility. Most of the recent developments, including the pandemic and climate change, continue to increase the gap between the rich and

poor. However, availability of vaccines provides an opportunity to bridge this gap and inequity in access to vaccines needs to be addressed in a collective manner. For this to materialize, there is a need to change the current economic model for provision of vaccines globally.

Linfa Wang (Duke-NUS Medical School, Singapore) speaking on *Bats, viruses and pandemics*, noted that a significant number of virus borne outbreaks are of zoonotic origin. Six major zoonotic virus outbreaks have occurred between 1994–2019 which were either confirmed or suspected to be of bat borne origin; Hendra virus (1994 in Australia), Nipah virus (1998–1999 in Malaysia), SARS (2002–2003 in China and 25 countries), MERS (2012 in Saudi Arabia and 26 countries), Ebola (2014 in Guinea and 6 countries) and COVID-19 (in China and over >190 countries). Up to now bat origin status has been confirmed for Hendra, Nipah and SARS viruses, whereas for MERS, Ebola and COVID-19, bat origin is suspected. Whether the bats transmitted these viruses directly to humans or through an intermediate host is currently debated. Bats harbor a significantly higher proportion of zoonotic viruses than any other mammalian species. Immune evasion by SARS CoV-2 variants of concern led to reinfection and breakthrough infections among vaccinated persons, which are less severe in disease. There was cross protection from vaccines developed against the original virus. However, the degree of cross protection differed markedly between the vaccines. Studies have shown that the presence of neutralizing antibodies against the virus protects against development of symptomatic infection. It was notable that the amount of neutralizing antibody produced by different vaccines varied significantly, with the mRNA vaccines producing the highest levels. Omicron has emerged due to immune selection and the variation observed is distant to the other variants. Therefore, it is possible to consider SARS as serotype 1, SARS-Cov-2 as serotype 2 and the Omicron variant as serotype 3. This fact is important for future development of vaccines. SARS-CoV-3 could arrive from 2 sources. Most bat viruses belong to beta corona viruses. Among the four genera of corona viruses, beta viruses are responsible for SARS1, SARS2 and MERS viruses. South East Asia is predicted to be the hotspot for the possible emergence of a SARS-CoV-3 virus. The second source of SARS-CoV-3 could be due to spill back in contrast to the usual spill over from animal sources. During spill back, the humans can spread the virus to animals, causing symptomatic infections and it would be an “unnatural” reservoir. It is possible that SARS-Cov-2 originated from bats in Asia and there may have been an intermediate host such as pangolin which enabled spill over to humans.

Peter Hotez (National School of Tropical Medicine, Baylor College of Medicine and Texas Children’s Hospital) spoke on the status of global antipoverty and COVID-19 vaccines and science versus anti-science with regard to vaccination. Current drivers of the disease are varied. They include poverty, war, political instability, urbanization, deforestation, climate change, and anti-science. It has been identified that there are a number of “hot zones” for development of infectious diseases and reemergence of previously established infectious diseases. The Arabian Peninsula was one such region, where in war-torn countries like Yemen or Syria, there have been interruptions in

childhood immunizations and vector control practices with a high possibility of reemergence of vaccine preventable diseases such as polio, measles, and vector-borne diseases like leishmaniasis. For parasitic infections, a reverse vaccinology approach is being pursued in vaccine development. This method was initially tried for Sero group B meningococcal vaccines by Rino Rappuoli and his colleagues using an in-silico prediction of vaccine candidate antigens. This is followed by high throughput protein expression in bacteria such as *E. coli*. Efforts are underway to reproduce this approach for parasites, which are more complex eukaryotic organisms. The large genome size, the inadequacy of bacterial expression systems for eukaryotic antigens with low throughput protein expression, deficiencies in animal models were challenges in the development of antiparasitic vaccines. An alternative is to use a yeast expression system and is currently being pursued by several vaccine producers in the developing country vaccine manufacturers network (DCVMN). In partnership with vaccine producers in India and Indonesia, the Baylor-Texas Children’s group transferred its yeast-based technology to accelerate new recombinant protein COVID-19 vaccines that have reached almost 100 million people. This provides proof of concept that it is possible to develop and distribute vaccines by empowering DCVMN vaccine producers, such as Biological E in India or BioFarma in Indonesia.

Paul Ananth Thambyah (National University Hospital of Singapore) spoke on *the next pandemic are we prepared?* Preparing for the next pandemic will require sentinel surveillance amongst high-risk groups, such as travelers, ICU patients, immunocompromised, healthcare workers, laboratory staff etc. Surveillance cannot be confined to humans since the vast majority of emerging and reemerging infections are virus related and among these, 70% are vector borne or zoonotic. With regard to older diseases, the world is getting ready to eradicate polio and circulating polioviruses are being recognized through testing stools of patients with acute flaccid paralysis and of sewage samples. With new technology, geospatial surveillance can be carried out as has been successfully done for tuberculosis to identify hot spots of the disease. Molecular epidemiology of isolates enables tracing of index cases. Diagnostics for COVID-19 was advanced due to development of rapid antigen tests, which enabled early treatment. PCR technology revolutionized the diagnosis of infectious diseases and 16s RNA assays further expanded the scope of these tests due to the development of high throughput parallel sequencing. PCR is useful for known pathogens. Newer developments such as the next-generation sequencing will permit the early identification of new pathogens. Availability of specific viral therapeutics is an important component that needs consideration for future epidemics. With Covid-19, many therapeutics were repurposed medications; dexamethasone, nirmatrelvir, molnupiravir, remdesivir, sotrovimab. In terms of prophylaxis, oral hydroxychloroquine, ivermectin, povidone-iodine throat spray, oral zinc, vitamin C were tried in an open label parallel-randomized control trial, with hydroxychloroquine and povidone-iodine showing promise. However, WHO withdrew chloroquine from the recommended list due to suspected adverse effects. Conduct of clinical trials are critical and politics can complicate available

therapeutic choices. Vaccines against COVID-19 have had very good results, particularly the mRNA vaccines. Although COVID-19 vaccines do not stop transmission, they do prevent severe illness in adults. Vaccine equity was highlighted during this pandemic emphasizing the importance for the countries or regions to produce their own vaccines. During the COVID-19 pandemic, the incidence of influenza became very low from middle of 2020 to until end of 2021. Influenza is very likely to be the cause of the next pandemic.

Jerome Kim (International Vaccine Institute) gave the final plenary lecture, *Vaccines: What does the future hold?* The vaccines development has progressed from whole cell, live attenuated, or killed vaccines to recombinant and conjugated subunit vaccines and use of powerful adjuvants. In the recent past, reverse technology was explored for development of vaccines and more recently RNA and DNA vaccines. The Global Vaccine Action Plan of 2011–2020 has listed 27 vaccine preventable infectious diseases and among these vaccines against falciparum malaria, SARS CoV-2, dengue and RSV have completed safety trials and have promising efficacy data. With regard to COVID-19 vaccines a pan-COVID vaccine is needed in view of the rapidly mutating virus. 120 COVID-19 vaccines have been tested in human trials. The innovations include mRNA vaccines, adenoviral vector usage, DNA vaccines and use of novel adjuvants. With these new developments there is hope for old diseases, including HIV, tuberculosis and malaria (The big three). However, availability of funding will determine the outcome. There are a significant number of diseases where vaccine development initiatives are limited due to non-availability of funds, e.g. Group A streptococci, non-typhoid salmonellae, shigella, schistosomiasis. Inadequate access to vaccines is another important factor, e.g. 60% of children globally do not receive the rotavirus vaccine despite availability for 16 years. The inequity of COVID-19 vaccine distribution is a recent glaring example. Low vaccine uptake due to hesitancy has become an important challenge. Vaccine security is important for the future and can be enhanced with regional manufacturing. Adequate preparation for future pandemics is essential and, to achieve this, gaps in diagnostics, manufacturing and equity of vaccines need to be addressed.

IPAP partner symposia

Vaccines through the ages

This symposium, in collaboration with the International Federation of Aging, covered vaccinations across the life course ranging from children, adolescents, adults, and the older adults. Jane Barratt (International Federation of Aging) identified and discussed barriers to improving adult vaccination coverage and the need for comprehensive national immunization plans. COVID-19 brutally exposed the immediate and long-term consequences of vaccine preventable respiratory diseases (including influenza and pneumococcal pneumonia) on those most at-risk including older people and those with chronic co-morbidities such as diabetes and renal disease. Three key pillars for action to achieve immunization for all ages are to build an effective and sustained health prevention

and promotion public health strategy, key public health strategy; removing barriers to access; and ensuring equity for all. Governmental investment in infrastructure such as establishing and improving surveillance and the collection of disaggregated data to inform evolving policy is critical for success

Sybil Lizanne Bravo (Philippines) spoke on missed opportunities in vaccination in pregnancy. Vaccination in pregnancy protects both the newborn and the mother. Despite availability of effective and safe vaccines, uptake in pregnant women is suboptimal. A report from India showed that 33% of the pregnant women were not vaccinated due to non-availability of vaccines. A 2020 meta-analysis reporting factors affecting vaccination in pregnant women included accessibility and convenience, personal values and lifestyle, awareness of diseases and vaccines, social influences and emotions related to vaccination. Women are more accepting of vaccination if there is a national policy, indicating the importance of strong health systems. Social media plays an important role providing increased information on real and perceived side effects of vaccination. Healthcare recommendations, healthcare reminders, counseling and access to reliable information are important to improve vaccination programs. To reduce missed opportunities in vaccination, immunization programs require clear communication, review of vaccination policy with established contraindications, proper documentation, availability of vaccines with reliable storage systems, education of healthcare providers and vaccinators, adequate staff, and improved vaccine delivery systems.

Pornthep Chanthavanich (Mahidol University, Thailand) noted that the decision to use travel vaccines will be based on the incidence of the disease as well as the impact on the traveler. Some vaccines may have already been included in the childhood vaccination programs in the traveler's own country. The time taken to develop immunity needs to be considered when healthcare professionals advise on travel vaccines. Examples include Yellow fever and meningococcal vaccines for specific areas. It is advisable to be aware of any recent outbreaks in the travel destination before advising an appropriate vaccination schedule. Travelers should also be informed of other means of disease prevention.

Respiratory vaccines

Respiratory infections cause significant morbidity and mortality and affect all ages. Pushpa Ranjan Wijesinghe (WHO SEAR) provided an update on influenza vaccines. The WHO estimates 290,000–650,000 influenza-related deaths per year and the number is expected to rise. Influenza in pregnancy results in significant morbidity, especially in patients with co-morbidities that could be prevented by vaccination. The vaccine landscape is evolving with more vaccines being produced in developing countries like India. Availability of adjuvanted, recombinant, and high-dose vaccines for special groups has had an impact and new vaccines such as mRNA and DNA vaccines are under development. However, the withdrawal of GAVI support for influenza vaccine has slowed progress. Epidemic disease preparedness and response plans identify the importance of seasonal influenza. Seasonal vaccination is included in the Global Influenza Strategy (2019–2030) and

WHO encourages countries to include influenza vaccination in high-risk groups. The timing of vaccination and the type of vaccine depends on the country's surveillance results and not on geographical location i.e. northern or southern hemisphere. In tropical countries where there are multiple peaks of activity, the vaccination program should target the primary peak.

Cheng-Hsun Chiu (Chang Gung Memorial Hospital, Taiwan) gave an overview of the pneumococcal disease burden and vaccine uptake in Taiwan and other Asian countries. A 2022 Taiwan study reported that after the use of PCV13 vaccination for high-risk groups in 2012 and introduction to the NIP in 2015, there has been a reduction in disease caused by vaccine serotypes and culture confirmed pneumonia. This reduction included both invasive pneumococcal disease and mucosal disease. Serotype replacement has followed vaccine introduction with increases in the prevalence of non-vaccine serotypes for both carriage and disease. Country-specific and regional surveillance should be continued. All Asian countries should include PCV into their NIPs.

Since 2013, WHO has recognized that respiratory syncytial virus (RSV) vaccine development should be a priority. Lien Anh Ha Do (Australia) noted that there are 6 RSV vaccines and 2 monoclonal antibody (mAb) candidates based on the pre-F antigen in phase 3 trials. Among those candidates, mAb Nirsevimab® (Medimmune, Astra Zeneca & Sanofi Pasteur), has published its phase 3 results. It showed 70% and 73% efficacy, respectively, against medically attended visits and hospitalization associated with RSV-lower respiratory tract infections. The phase 3 trials of Nirsevimab® were conducted in 20 countries but none in Asia where the burden of disease is the highest. Of note, COVID-19 pandemic has impacted on the seasonal epidemiological characteristics of RSV and also on the immunization programs in many countries. At least, 23 million children missed out their routine vaccine including measles vaccine. As the COVID-19 restrictions are being relaxed in many countries, increasing number of RSV and measles cases have been reported. Unfortunately, children infected with measles had a 30% loss of antibody epitope binding across a range of pathogens, including RSV. After the recovery from measles infections, their new naïve B cells express immature B cell receptor (BCR) repertoires reducing B cell diversity. Therefore, children infected with measles are at high risk of having severe RSV infection. Early measles vaccination at 4 months of age could be an alternative, economic, effective and very timely approach for the current COVID-19 crisis to prevent severe RSV infection in young infants.

COVID-19 vaccines

Benjamin Cowling (University of Hong Kong) addressed "COVID-19 vaccinations for children: following the evidence." Higher prevalence of infection among children was seen during delta and omicron waves. The incidence of MISC-C showed a similar pattern in the delta wave but was less with the omicron wave probably due to immunological experience. COVID-19 vaccination for children was initiated after many observational studies with regard to efficacy and safety. mRNA vaccines have been available for 12–15-year olds, from May 2021, and for 6 months to 5 years olds from June 2022.

There are several permutations of schedules, with 1–3 vaccine doses. A follow-up study in Singapore during an omicron wave showed that 24% and 0.2% of unvaccinated children had confirmed COVID infection and hospitalization, respectively. Immunobridging studies show that an additional dose of mRNA vaccine substantially improved antibody levels against the ancestral virus and omicron variant with a well-tolerated safety profile in adults who had received two doses of inactivated vaccine earlier. Further studies are needed for disease burden of long COVID-19 infection, establishing the primary vaccine series with bivalent (Omicron) vaccines and regarding frequency of boosters.

Neelika Malavige (Sri Lanka) spoke on COVID-19 vaccination in immunocompromised patients where disease severity and deaths are much higher, especially in patients with renal transplants or metastatic cancer. Patients on immunotherapeutics tend to have more severe disease and death than those on radiotherapy and chemotherapy. Studies in the United Kingdom have shown that low basal lymphocyte count and increasing age were the important determinants in the outcome of COVID-19 infection in patients with primary immunodeficiencies. A similar pattern was seen in patients with secondary immunodeficiencies. Immunodeficient patients tend to have persistent infection and have an increased risk of excreting mutated virus. Some of these mutations were similar to the viruses of concern suggesting that B.1.1.7 (alpha) and BA.1 (omicron) variants originated in an immunocompromised patient. Different types of immunocompromised patients respond differently to vaccination. Patients with solid malignancies respond similar to the normal population, unlike patients with hematological malignancies. HIV patients respond better compared to patients on immunotherapeutics or transplant recipients. Sri Lankan experience indicates that renal transplant recipients have poor seroconversion rates compared to healthy age matched controls. Another study on patients with primary immune deficiency showed that those who received mRNA vaccines had significantly higher T-cell responses compared to the inactivated vaccines. It is recommended that patients with moderate-to-severe immunodeficiencies have three vaccine doses in the primary series and two booster doses.

Anna Ong-Lim (University of Philippines) provided updates on childhood immunization during the pandemic. The direct effect of COVID-19 infection on children and adolescents is limited, but the indirect effects due to the impact on the healthcare system, economic loss, and effect on other vaccination programs have been substantial. WHO reports moderate-to-severe disruptions of routine vaccination, particularly in South-East and Western Pacific regions with high numbers of children not receiving the 1st DTP vaccine dose. The reasons include supply chain disruption, reduced availability of healthcare staff due to COVID control redeployments, public fear and transport restrictions during the pandemic. Vulnerable populations are at higher risk as they are more dependent on mass vaccination programmes and are more likely to experience service disruptions. Decisions regarding vaccination have to focus on equity of resilience rather than equity of coverage. Catch-up vaccination should

be offered to deserving communities and improvements made to healthcare information systems and disease surveillance.

Unfinished business

Daniel Chulwoo Rhee (International Vaccine Institute) presented an update on HPV vaccines focusing on the evidence toward use of a single dose. Cervical cancer is a leading cause of cancer deaths, particularly in low- and middle-income countries (LMIC). Globally, 604,000 new cases and 341,000 deaths occur each year, with 90% of the deaths occurring in LMIC. Four WHO prequalified vaccines are available: 2 bivalent; 1 quadrivalent; and 1 nonavalent. By 2022, 149 countries have initiated vaccine programs in their NIPs and the global coverage was 13%, but only 8% in the LMICs. A single-dose HPV vaccination trial in Kenya showed 0.17 incidence/100 women years in the vaccine group as compared to 6.83 in the control group. An Indian study has shown a crude attack rate of 0.05% of single-dose vaccine as compared to 2.54% in the control group. The antibody level with a single dose is lower than the 3 dose level, but still 10 times higher than the natural immunity level and remains stable for more than 10 years. The single vaccine dose ensures that more females are protected than a 2-dose vaccine especially in LMICs. WHO SAGE has recommended a 1 or 2 dose schedule for 9–14 and 15–20-year-old females and a 2 dose schedule with a 6-month interval for females over the age of 21 years. Immunocompromised individuals are recommended 3 doses or at least 2 doses. Single-dose vaccines also overcome vaccine delivery challenges with supply and demand and significant cost savings. Vaccines with currently available efficacy data or immunobridging data could be used in the single-dose schedule.

Ooi Eng Eong (Duke-NUS Medical School, Singapore) gave updates on dengue vaccines and reported that 19% of the patients with dengue could develop chronic sequelae. Sanofi's chimeric vaccine by has been recommended for patients with previous dengue infection. Takeda's live attenuated recombinant vaccine has found no evidence of risk in patients without previous dengue infection. NIH/Butantan/Merck vaccine trials have been completed and are being evaluated. The importance of T-cells in dengue infection was shown in several case reports of immunocompromised patients who had been on immunosuppressives for a long time and had excreted the dengue virus for more than 9 months. These patients had neutralizing antibodies but no T-cells. Dengue needs both cell mediated and humoral immune responses for control. Current vaccines are promising but the issues related to differences in seronegative and seropositive populations have to be addressed with a strong implementation plan and long-term post-marketing surveillance. Dengue vaccine alone will not control dengue, and other measures are needed such as vector control and specific antivirals.

Somia Iqtadar (Pakistan) spoke to challenges in the control of polio that include co-circulation of WPV1 and cVDPV2, restarting supplementary immunization and surveillance activities in countries with wild polio circulation which had been halted during the COVID-19 pandemic, and otherwise ambitious program goals to suppress circulation of virus which could not be attained. In 2022 two countries (Pakistan and

Afghanistan) reported wild polio cases, as compared to 168 countries in 1988. A coordinated approach to the elimination of polio is required in these 2 countries with strong vaccination programs, uninterrupted supply of vaccines, targeted vaccine campaigns and joint data analysis. International Health Regulation protocols are needed to ensure vaccination for travelers. The importance of community involvement and political support was emphasized.

Enteric vaccines

Julia Lynch (International Vaccine Institute) presented an update on cholera vaccines – past, present and future. Cholera cases may be under-reported in developing countries. Large outbreaks in Haiti and Yemen have received global attention. Injectable cholera vaccines had been in use for more than 70 years but had moderate efficacy (50%) for short duration. The whole cell inactivated vaccines when combined with cholera toxin B have shown 85% efficacy for 6–9 months compared to 58% with the whole cell inactivated vaccine. However, a 3-year follow-up showed similar efficacy for both vaccines (50 and 52%, respectively). A combined vaccine (whole cell + rCTB) is pre-qualified by WHO but is expensive and complex to administer. It is a very successful travel vaccine. An O139 strain was added to the four antigen whole cell inactivated vaccine and resulting in another WHO prequalified vaccine that is inexpensive at less than 2 USD per dose and easy to administer. This Oral Cholera Vaccine (OCV) is available in a Gavi funded stockpile and is used in control of outbreaks, globally. Meta-analysis has shown a much higher effectiveness (76%) when compared to efficacy (58%) after 2 doses possibly due to herd immunity leading to reduction of transmission. As demand for OCV currently exceeds production capability, additional manufacturers and new vaccines have to be identified for increased production of OCV to maintain the stockpile. New vaccines for populations should have higher efficacy in infants and young children, should be single dose and inexpensive with a longer duration of protection. Several new vaccines are in development including a conjugate vaccine which could be more ideal for young children as it will elicit long-lasting T-cell responses with a single dose.

Aziza Mwisongo (PATH) spoke on typhoid conjugate vaccines: experiences from early introducers. More than 40 million children were vaccinated with the typhoid conjugate vaccine (TCV) from November 2019. WHO has prequalified 2 TCVs – Typbar-TCV and TYPHIBEV, and GAVI extends support for inclusion in immunization schedules. This vaccine is easily introduced into existing schedules and has been proven to be safe and immunogenic.

Carl Kirkwood (Bill and Melinda Gates Foundation) updated on the status of oral rotavirus vaccines. Rotavirus vaccines have been introduced into national immunization programs of at least 115 countries across the globe. These have had a real impact in every setting with significant reductions in rotavirus-related mortality and morbidity observed. However, despite the major progress, an estimated 71 million children or 53% of the world's infant population are without access to rotavirus vaccines. The countries with low coverage

include countries in Asia and Africa. The COVID-19 pandemic has affected all vaccination programs, with a 9% drop in uptake in South-East Asia with DTP coverage. Four live oral rotavirus vaccines have been pre-qualified by WHO. WHO SAGE has reaffirmed rotavirus vaccines should be included in all NIPs as a priority. Recent programmatic challenges were mainly associated with vaccine supply, which impacted more than 20 countries. These were due to a product being removed from GAVI support, and production and delivery issues leading to product switches, delayed introduction and stock outs. Post-marketing surveillance data in 25 countries have shown significant impact of rotavirus vaccination. Africa has reported a 50% decline in rotavirus associated hospitalizations, and significant reductions in diarrheal associated mortality and even all cause diarrhea. Overall, rotavirus vaccination programs have had enormous successes in reducing the diarrheal disease burden in all settings that have introduced vaccine.

Communication and advocacy

Latest strategies in communicating vaccine safety were presented by Pramod Jog (D.Y. Patil Medical College, Pune, India). Negative information spreads rapidly depending on contacts, communication networks and well-wishers. Healthcare practitioners have to be firm and confident in delivering their safety messages and address any concerns especially with regard to perceived risks. Lois Privor-Dumm (John Hopkins Bloomberg School of Public Health) presented on communicating the impact of COVID-19 in childhood immunization. Vaccine hesitancy has increased due to the COVID-19 pandemic. Immunization agenda 2030: was delivered by Charlotte Mbuh (Geneva Learning Foundation, Switzerland). There are seven strategic priorities: commitment and demand; coverage and equity; life course and integration; outbreaks and emergencies; supply and sustainability; research and innovation. Julian Savulescu (National University of Singapore) spoke on the ethics of challenge studies to fast track vaccine development. Challenge studies are morally and ethically required in vaccine development to prevent morbidity and mortality. There should be valid scientific rationale for developing universal vaccines and testing vaccines with pandemic potential or for blocking transmission such as COVID-19. Challenge studies should avoid vulnerable and socially disadvantaged groups and if they are included additional measures should be taken to protect their rights.

Industry symposia

The GSK symposium on vaccination in the elderly looked at the risks of vaccine preventable disease in aging populations and the related immunological challenges in this age group. The elderly benefit from influenza, herpes zoster and pneumococcal vaccines. The importance of herd immunity was stressed; for example, vaccinating young children with the live attenuated intranasal influenza vaccine reduced the incidence of influenza in all age groups in the United Kingdom. Immune senescence, an age-related decline in immunity leads to a reduction in immune response to vaccines in the elderly. There are a number of approaches to address this issue,

including increasing the antigen load, use of new adjuvants and alternate routes of administration. Takeda's symposium on dengue and the TAK-003 dengue vaccine provided details of the burden of dengue, the clinical scenario and the 4.5-year vaccine trial data. In 2019, WHO declared dengue to be one of the 10 global threats. Data indicated that the age distribution of dengue fever (DF) and dengue hemorrhagic fever (DHF) was shifting from children to an older age group. Data was presented regarding management of patients with DF and DHF in Sri Lanka, where the case fatality rate has decreased to 0.1% in 2022. It was reiterated that early diagnosis of DF and DHF and proper treatment of DHF would reduce mortality. The long-term clinical data of TAK-003 confirmed a favorable benefit/risk profile with no important safety risks identified. The MSD symposium highlighted pneumococcal disease, including invasive as well as community-acquired pneumonia in the elderly. Immune senescence as well as a low-grade inflammatory state "inflammaging" reduce the ability of the elderly to mount an immune response. Data from Australia show that the introduction of vaccination leads to a great reduction in pneumococcal disease below 4 years, but not in other age groups. In spite of the conjugate vaccines containing the serotype, the incidence of serotype 3 was still present in Australia. The rates of pneumococcal disease were reported to be lower in Asia, compared Europe. The Astra Zeneca symposium was on COVID-19 vaccination in the era of Omicron. While protection against symptomatic COVID-19 wanes rapidly after vaccination, protection against severe disease was maintained with the viral vector and mRNA vaccines. There was equivalent protection against the Omicron strain with both the viral vector and mRNA vaccines. There was no difference between homologous and heterologous boosting. The Sanofi symposium on childhood immunization highlighted the use of combination vaccines to improve compliance.

Pre-congress workshops

Update on pneumococcal vaccine development

Organised by The Asian Strategic Alliance for Pneumococcal disease prevention (ASAP), this workshop invited pharmaceutical companies to give updates on new pneumococcal vaccine developments. Egemen Ozbilgili (Vaccine Regional Lead, Pfizer emerging markets/Asia) spoke about the legacy of PCV7/13 with regard to real-world experience after 25 years and also shared the development program of PCV 20. Olakunle Oladehin (Regional Medical Lead: Emerging Markets: GSK vaccines), highlighted the purpose of adding different carrier proteins, DT for 19F and TT for 18C, while continuing PD protein from NTHi for other serotypes included in GSK's PCV 10. A new technique called MAPS (Multiple Antigen presenting System) platform is being used to make new pneumococcal vaccines that can incorporate multiple antigens into a single vaccine. Jin Oh Kim (Regional Director of Medical Affairs Vaccines: MSD Asia Pacific region), summarized clinical data on their two new vaccines, PCV 15 for children and adults and PCV 21 for adults and shared results of initial clinical trials in children, adults and the immunocompromised. Nitin Shah talked about the new

PCV10 from Serum Institute India where ST4 and ST18C have been replaced by 6A and 19A based on global distribution of pneumococcal serotypes. Safety and immunogenicity results were compared with other existing PCV vaccines.

Pre-congress workshop on HPV vaccination in Asia; demand, delivery, and latest recommendations

Kirthini Muralidharan (Johns Hopkins Bloomberg School of Public Health) overviewed HPV in Asia and the poor introduction of vaccines in the most needy Asian countries. Daniel Chulawee Rhee (International Vaccine Institute) shared results of vaccine trials with single-dose HPV vaccination which has validated WHO's recommendation of single-dose vaccine for LMIC countries that have not yet introduced HPV vaccination into their NIP due to financial constraints. Didik Setiawan (Indonesia) presented the HPV vaccine policy in Indonesia, where phase-by-phase regional introduction is in progress. Kurnia Eka Wijaywanti (Indonesia) expressed concerns over their findings on knowledge and attitudes on HPV vaccines in the Indonesian community.

Vaccinology Masterclass

The ASVAC Vaccinology Masterclass in 2022 was one of the most successful events in the conference. Over 112 local participants attended in-person and over 200 participants from other countries in the Asia Pacific region attended virtually. This is the third edition of the Masterclass following those held in ASVAC 2017 and ASVAC 2019. While the program lasted less than six hours, it covered all the essentials of vaccinology from the history of vaccines, the impact of vaccination, the basic vaccine immunology and the role of adjuvants to the future of vaccines. Mathu Santhosham from Johns Hopkins University inaugurated the session with the history of vaccines and the impact of vaccination. He quoted instances where vaccines have resolved conflicts and disputes between countries. Philippe Buchy summarized the principles of basic vaccine immunology and emphasized the role of adjuvants. He also highlighted the importance of vaccine preventable disease surveillance in implementing vaccine strategies. Alberta di Pasquale (Singapore) covered vaccine clinical development from research to post licensure validation. She emphasized that vaccine candidates go through several phases of clinical testing in thousands of people to demonstrate a favorable benefit/risk profile. Zulkifli Ismail from Malaysia expressed concerns over the rapidly increasing vaccine hesitancy, especially following the COVID-19 pandemic. He explained how Malaysia has worked to reduce vaccine hesitancy using various formats including social media and community involvements through the "Immunize4life" programme. Vaccines for various ages was another interesting session where renowned speakers gave an overview of vaccination in infancy, children, adolescents, pregnancy and the elderly. Elizabeth Gallardo (Pediatric Infectious Disease Society of the Philippines) highlighted key issues of vaccination of neonates and infants, including timing and efficacy of different vaccines. Pramod Jog (D.Y. Patil Medical College, Pune, India) noted that immunization is becoming more important in adolescents for

various reasons: diseases with higher morbidity (Hep A, Varicella); diseases with higher incidence (mumps, meningococcal); emergence of new infections (Covid-19); epidemiological age shift (diphtheria, measles); the need to boost waning immune response (diphtheria, tetanus, pertussis); appearance during adulthood (HPV); or for future protection (congenital rubella syndrome). Sybil Lizanne Bravo (Philippines) discussed how mortality and morbidity of some diseases in mothers and neonates can be prevented by routine vaccination of pregnant women with Tdap and influenza and stressed that live vaccines should be avoided when possible. Jean-Pierre Michel (Geneva University Medical School, Switzerland) gave the final lecture of the session covering vaccination of older adults. Global expansion of the elderly population has seen increased mortality from vaccine preventable diseases in this age group. Their poorer immune response is one of many reasons to vaccinate the elderly. Priority vaccination of older adults during COVID-19 pandemic saved millions of lives since SARS CoV-2 mortality was highest in the elderly. Herd immunity also prevents disease in elderly. Recent data shows that influenza and pneumococcal vaccination indirectly reduces mortality due to non-communicable diseases such as cardiovascular disease and stroke. Influenza vaccine also reduces dementia in the elderly. However global vaccine coverage of elderly is very low even in high income settings. In the segment on practical application of vaccinology, Sri Lanka, as conference host, presented two interesting case scenarios. The first highlighted the importance of taking a history of cow's milk and red meat allergy before giving any live vaccines especially MMR and JE vaccines. The second scenario emphasized the need of taking a history of prior sibling deaths in early infancy prior to BCG vaccine administration. The Masterclass concluded with an informative lecture on the future of vaccines by Jerome Kim (International Vaccine Institute), which shed light on overcoming the inequity of vaccine delivery in the future. Daniel Goh, coordinator of the Masterclass, gave the concluding remarks.

Asia Pacific EPI managers meeting

Held on September 15 and organized by The Vaccine and Infectious Diseases Forum of Sri Lanka, the meeting was opened by the Forum's president Geethani Galagoda. Susie Perera, the Deputy Director General of Health Services, Ministry of Health Sri Lanka was the Chief Guest. Ranjan Wijesinghe (WHO SEARO) started the opening session on influenza and pneumococcal vaccines covering influenza disease burden and vaccine uptake in SEARO. The burden of disease is an important tool for quantifying influenza as a public health problem. However, as many do not seek healthcare, the estimates are invariably low and number of influenza deaths are likely to be higher. Among SEARO and WPRO countries, only Bhutan and Thailand have included influenza vaccine in their NIP. During the COVID-19 pandemic, due to the impact of public health measures such as lockdown and mandatory use of facemasks, influenza transmission has been low. However, once these measures were relaxed there have been epidemics of influenza. Hence, the additional burden on vulnerable populations and health

systems were recognized and SAGE's interim recommendations for influenza vaccination during the COVID-19 pandemic were issued. Cheng-Hsun Chiu (Chang Gung Memorial Hospital, Taiwan) overviewed the pneumococcal conjugate vaccine (PCV) in Taiwan and other Asian Countries in the region. During the update on rotavirus vaccines in the Asia Pacific, Tony Nelson (School of Medicine, The Chinese University of Hong Kong, Shenzhen) stated that, during the pre-vaccination era, 185,000 children less than 5 years died globally every year due to rotavirus-associated disease and over 1/3 of child deaths due to diarrhea were caused by rotavirus. Following introduction of the vaccine, mortality reduced by 31% in under 1 year of age and 42% in under 5 years of age. In addition, hospitalization and emergency department visits due rotavirus disease reduced by 80% in under 1-year age group and by 67% in under 5-year age group. Hospitalizations due to acute gastroenteritis were also reduced by 38%. WHO 2013 position paper recommended removal of the age restriction of rotavirus vaccine and the 2021 update describes other prequalified rotavirus vaccines. Key messages in 2021 include the recognition of rotavirus vaccine as a priority vaccine in South Asia, South Eastern Asia and Sub Saharan Africa. Although, continued surveillance is important, lack of data should not stop introduction of rotavirus vaccine. Especially since circulating strains should not drive vaccine selection due to heterologous protection offered by the vaccine. Cervical Cancer burden and HPV vaccine uptake WPRO/SEARO was discussed by Paba Palihawadana (WHO Indonesia). In SEARO, HPV vaccine is in the NIP of 14% of the countries, namely Bhutan, Maldives, Myanmar, Sri Lanka and Thailand whereas in WPRO it is 52%. Limitations for wider introduction are the relative high cost, supply issues, effect of COVID-19 response activities, challenges with new vaccine introduction in upper-middle-income countries which are not eligible for GAVI support and lack of the required laboratory-based surveillance. Samitha Ginige (Sri Lanka) overviewed the integrated immunization programme: Overcoming challenges during pandemics, focusing on Sri Lanka. Sri Lanka does not have separate immunization units as in some other countries. The immunization service is part of the service provided by the preventive health care section (PHC) as well as the curative care section and free universal healthcare services are available for both. PHC delivery system, since its inception uses a polyclinic approach. This approach has enabled high immunization coverage for relatively less cost and effort, more opportunities for health care workers to interact with the communities and gain more community acceptance and trust, more opportunities to follow up clients in the field and optimal utilization of available resources at field level. During the COVID-19 pandemic, the national goal was to provide free vaccine up to the last citizen and nationwide vaccination by the fastest possible means. However, during this time the coverage of NIP as measured by the administration of the 3rd dose DPT vaccine decreased to 81% globally and 82% in SEAR. However, in Sri Lanka, it was maintained above 96%. During the presentation on COVID-19 vaccine deployment in the SEAR and perspectives for roll-out, Jayantha Liyanage

(WHO, India) mentioned that out of the 11 countries in SEAR, 10 countries are administering COVID-19 vaccines with 6 countries offering the vaccine to the 5 to 11 years age group and only 4 countries providing the second booster. Bhutan is the most successful country with 92% of the population receiving one dose, 89% receiving 2 doses and 74% receiving booster doses. WHO Global COVID-19 vaccination strategy was updated in July 2022, as many at-risk people were unvaccinated (primary and/or booster doses), significant transmission reduction with current vaccines is difficult and immunization coverage is declining. In this, the first priority is to protect 100% of health care workers and elderly and other priority groups with existing vaccines. In the updated WHO SAGE recommendations issued in August 2022, guidance on administration of second booster dose is given. DPT vaccine has led to a dramatic reduction in the incidence of diphtheria, whooping cough and tetanus. HT Wickramasinghe (Sri Lanka), discussed a study carried out in Sri Lanka, where the vaccine coverage is very high. A reduction of anti-pertussis IgG was seen in the 8–11 year group compared to the 4–11 year group in this study. But there was a rise in titer in 12–15 year group demonstrating that there may be natural infection in the community. Similar data are also available from Israel, Netherlands and Turkey. In the study done in Turkey, individuals up to the age of 60 years were studied and most of the adults did not show adequate antibodies. In a study carried out in Germany, it was demonstrated that priming with the whole cell vaccine and booster doses with acellular vaccine confers better immunity. Maternal antibodies could protect the young infants from pertussis and vaccinating pregnant mothers with Tdap will lead to protection in over 90% of the infants up to 2 months, which is the most vulnerable group for fatal infection. CDC recommends vaccinating pregnant women between 27 to 38 weeks gestation to provide the maximum benefit. Booster doses are recommended in adolescence and repeated every 10 years. Furthermore, WHO recommends vaccination in pregnant women, through the NIP in countries where there is high or increasing infant morbidity or mortality due to pertussis. However, these recommendations are not enforced by WHO, as the antibody and cell mediated assays are not validated to predict protection and the mucosal immunity is not taken into account. In Sri Lanka, there is a high coverage of immunization in all regions of the country, the incidence of pertussis is very low and diphtheria and neonatal tetanus are absent. Similar findings are observed in other countries such as Bhutan and Maldives. This indicates that sustainable and equitable vaccination covering more than 95% of the children in all regions of a country prevents the need of vaccinating more individuals in other age groups. Ananda Amarasinghe (WHO, Philippines) highlighted some of the adverse reactions that led to low vaccine confidence and uptake, such as 2 deaths due to rubella vaccine in Sri Lanka and neonatal deaths due to birth dose of hepatitis B in Vietnam. Vaccine hesitancy develops due to complacency, confidence and convenience. Therefore, immunization programs should overcome behavioral and social drivers toward hesitancy by improving motivation for vaccination and addressing practical issue to minimize inconvenience and

low confidence. There were country updates from Indonesia, Philippines, Malaysia, Pakistan, and Thailand. These reports focused on the new vaccines introduced in the EPI of each country during the recent past and the rationale for introduction, impact of the COVID pandemic on the EPI of each country and strategies used to implement COVID vaccines.

Summary

Headwinds continue to thwart the IPAP vision of a world where no-one should die from a vaccine preventable disease. Since ASVAC 2017, there has been increasing concern about growing vaccine hesitancy. This trend has rapidly accelerated post COVID-19 with an increase in lack of vaccine confidence, vaccine hesitancy, and anti-vaccine sentiments. Reasons for this increasing trend in the face of COVID-19 seem counter-intuitive. Surely the speed of development and effectiveness of the new COVID-19 vaccines should have inspired populations to enthusiastically embrace the new vaccines? Although the majority are getting COVID-19 vaccines, some are raising doubts about the safety of COVID-19 vaccines and the value of vaccines in general. New strategies and better communication are needed to reverse this trend. Equity has been another recurring theme of this ASVAC conference, and lack of equity

during COVID-19 was raised on many occasions. Large sections of the global population are still denied vaccines because of financial and related barriers. These issues need to be resolved. We need a world where, not only should no-one be denied access to vaccines because of cost, and where everyone values and wants the benefits that vaccines offer. Much work still needs to be done.

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