Summary of recent issues considered by four national immunisation technical advisory groups (NITAGs) and WHO immunisation-related advisory committees

Prepared by the National Centre for Immunisation Research & Surveillance (NCIRS)

Period of review: 22/12/2022 – 05/05/2023

Key updates in this NITAG summary on vaccine preventable diseases of interest to Australia

COVID-19

- NACI has a preference for bivalent booster dose COVID-19 vaccines.
- NACI made a discretionary recommendation for an additional booster dose in spring of 2023 for specified individuals at increased risk of severe illness, namely those aged ≥80 years, age 65–79 years particularly if without know history of SARS-CoV-2 infection, adult residents of long-term care hones and other congregate living settings for seniors or those with complex medical care needs, and adults who are moderately to severely immunocompromised.
- ACIP endorsed a transition of the mRNA COVID-19 vaccine primary series from monovalent (original) to bivalent (original plus Omicron BA.4/5).
- ACIP updated interim clinical considerations with the simplified and flexible bivalent mRNA COVID-19 vaccination schedule for people who are not immunocompromised suggesting 1 bivalent mRNA vaccine dose for people ages ≥6 years who have not yet received a bivalent mRNA dose, regardless of COVID-19 vaccination history. While people ages ≥65 have the option to receive one additional bivalent mRNA vaccine dose.
- ACIP also updated interim clinical considerations with the flexible bivalent mRNA COVID-19 vaccination schedule for people who are immunocompromised recommending people ages ≥6 years who previously received only monovalent doses are recommended to receive 1 or 2 bivalent mRNA vaccine doses, depending on age and vaccine product. While people who previously received a bivalent mRNA vaccine dose(s) have the option to receive 1 or more additional bivalent mRNA vaccine doses.

Respiratory Syncytial Virus (RSV)

- ACIP recommended Nirsevimab a) at birth for all infants born during October to March, b) when entering first RSV season and <8 months of age for all infants born during April through September, c) for those eligible for Palivizumab in their 2nd RSV season.
- Pending licensure by FDA, ACIP will recommend vaccination with GSK RSVpreF3 vaccine and Pfizer bivalent RSVpreF vaccine in persons aged ≥65 years.
- JCVI is examining evidence on Nirsevimab and Pfizer's vaccine and awaiting results of modelling, with potential implementation in 2024/25

Pneumococcal

- JCVI did <u>not</u> preferentially recommend 15vPCV over 13vPCV and considered that 15vPCV initially be introduced as the second (booster) childhood dose before replacing 13vPCV as the first (priming) dose.

Mpox

- ACIP updated guidance to recommend vaccination in people with **HIV infection or other causes of immunosuppression** with recent or anticipate potential mpox exposure, and 2 doses JYNNEOS vaccine series **for persons aged ≥18 years at risk of mpox** during an mpox outbreak.

Meningococcal

- ACIP evaluated data from Pfizer's pentavalent meningococcal vaccine and found MenABCWY vaccine appears to be non-inferior to MenACWY+MenB based on clinical trial data presented.
- JCVI reaffirmed recommendation that children planning to travel to high-incidence meningococcal areas should be vaccinated regardless of previous receipt of meningococcal vaccine.

Poliomyelitis (Polio)

- ACIP recommended that all adults known or suspected to be unvaccinated or incompletely vaccinated against polio complete a primary vaccination series with inactivated polio vaccine (IPV) (preferring a uniform/universal rather than a risk-based recommendation of catch-up vaccination for these adults).
- WHO SAGE recommended the preferential use of novel type 2 oral poliovirus vaccine (nOPV2) for a circulating vaccine-derived poliovirus (cVDPV) type 2 outbreak response with oral vaccines, and that type 2 Sabin OPV should only be used in exceptional circumstances.

Influenza

- JCVI noted that there are policy questions on the influenza program to address before the 2023/24 season: whether or not secondary schools would be included as per JCVIs advice to roll out the programme fully to secondary schools. The latter was more cost effective than vaccinating 50–64-year-olds not in a risk group.

Contents

1 Advisory Committee on Immunisation Practices (ACIP), USA

1.1 ACIP meeting 22-24 February 2023

- Meeting agenda: https://www.cdc.gov/vaccines/acip/meetings/downloads/agenda-archive/agenda-2023-02-22-24-508.pdf
- Presentation slides: https://www.cdc.gov/vaccines/acip/meetings/slides-2023-02-22-24.html

Mpox Vaccine

- ACIP plans to discuss use of JYNNEOS in outbreaks in 2023, final recommendation expected in June 2023 for the use of 2-dose JYNNEOS for person aged <18 years and recommendations for the need of longer-term vaccination strategy for 2-dose is expected in October 2023.
- JYNNEOS post-licensure and post-authorisation vaccine safety surveillance findings to date are consistent with those observed in clinical trials. No new or unexpected safety concerns have been identified. Serious adverse events were rare among adults, and none have been identified among persons aged <18 years.
- Vaccine Adverse Event Reporting System (VAERS) and Vaccine Safety Datalink data do not suggest an increased risk for myocarditis (VAERS: Dose 1: 2.75/million, 95%CI: 0.33-9.94, Dose 2: 6.74/million, 95%CI:1.39–19.70 and Vaccine Safety Datalink: Dose 1: 27/million, 95%CI: 0.67-148, 2 Doses: 46/million, 95%CI: 1.15-254) or pericarditis (VAERS: Dose 1: 5.5/million, 95%CI: 1.50-14, Dose 2: 04.49, 95%CI: 0.54-16.23 and Vaccine Safety Datalink: Dose 1:0, 2 Doses: 0) following JYNNEOS, but the possibility of a small risk cannot be excluded.
- Incidence of Mpox among unvaccinated versus those receiving ≥1 JYNNEOS dose in USA:
    - Mpox incidence among unvaccinated individuals was 7.4 (95% CI = 6.0–9.1) times as high as persons receiving 1 dose and 9.6 (95% CI = 6.9–13.2) times as high as persons receiving 2 doses of JYNNEOS vaccine.
    - No difference observed in vaccine performance between subcutaneous and intradermal administration.
- Vaccine effectiveness (VE) of JYNNEOS against Mpox: For VE of JYNNEOS given as post-exposure prophylaxis (PEP) against mpox disease, a New York City study was used and VE of JYNNEOS given as pre-exposure prophylaxis (PrEP) against mpox disease data from 4 studies were discussed:
    - Israel single dose VE Study: Real-world effectiveness of a single dose of mpox vaccine in males (Adjusted VE (aVE): 86% (59%-95%).
    - EPIC Cosmos Case-Control Study: VE of 1 and 2 doses against mpox disease in USA (2: doses: aVE: 66% (47%- 78%); 1 dose: 36% (22%-47%).
    - Multi-jurisdictional Case-Control Study: Interim estimate of VE of 2 doses against mpox disease in 12 U.S. jurisdictions (aVE: 66% (47%- 78%).
    - New York State Case-Control Study: Preliminary estimates of VE of 1 and 2 doses against mpox disease. (2 doses: aVE: 89% (44%-98%), 1 dose: 68% (25%-86%).
- Highest protection provided by 2 doses, regardless of route of administration. Further research needed to evaluate whether immunocompromised status modulates VE and to assess duration of protection.
- Interim Clinical Considerations
    - Continued emphasis on vaccination: Mpox vaccination should continue to be offered to people with the highest potential for exposure to mpox.

- Updated guidance: People with HIV infection or other causes of immunosuppression who have had recent or anticipate potential mpox exposure should be vaccinated against mpox.

- Evidence to Recommendations (EtR) Framework:
  - Question: Does ACIP recommend the 2-dose JYNNEOS vaccine series **for persons aged 18 years and older at risk of mpox** during an mpox outbreak?
  - Desirable consequences probably outweigh undesirable consequences in most settings, suggesting recommendation of the 2-dose JYNNEOS vaccine series for persons aged 18 years and older at risk of mpox during an mpox outbreak.
- Clinical Considerations
  - In outbreak setting, vaccine is ideally given pre-exposure but may also be given as PEP, although evidence not been reviewed by ACIP for PEP at this time.
  - Complete 2-dose vaccine series should be given regardless of timing of exposure.
  - Although ACIP has not reviewed the evidence, if there are vaccine supply shortages, ID route of administration can be used.

Influenza Vaccine

- US influenza activity rose early, peaking nationally during late November/early December.

Influenza A(H3N2) viruses have predominated, with co-circulation if influenza A(H1N1)pdm09 viruses. Overall influenza activity is increased compared with the previous two seasons.

- Interim influenza VE against inpatient, emergency department (ED) and outpatient illness in the 2022-23 season:
  - New vaccine surveillance network (NVSN): Data from inpatients and ED patients aged >6 months to 17 years reported VE of 68% (95%CI: 46-81%) against paediatric hospitalisation and 42% (95% CI: 25-56%) against paediatric ED visits.
  - Flu and other viruses in the acutely ill network (IVY): Data from hospitalised adult patients and reported VE of 43% (95% CI: 30-54%) against adult hospitalisation.
  - VISION network: Data from hospitalised, ED and urgent care visits among adults and reported VE of 39% (95%CI: 31-45%) against adult hospitalisation, 44% (95%CI: 41-47%) against adult ED or urgent care visits.
  - Across three Flu VE platforms, consistent influenza VE during 2022-23 season was reported against inpatient, ED and outpatient illness among all ages, with substantial protection among important high-risk groups (ages 65+ and immunocompromised).
- Interim Estimates of 2022─23 Influenza VE from Two Studies in Wisconsin: A Test-Negative Case-Control Study (6 months -64 yrs) and a Community Cohort Study (1-17 yrs) indicate substantial vaccine-induced protection against influenza A during 2022-23 season– VE 54% against medically attended influenza A in children and working aged adults – VE 71% against symptomatic influenza A in children.
- Update on Published Estimates of LAIV4 Effectiveness:
  - LAIV4 not recommended in the U.S. for 2016-17 and 2017-18, following observation of poor effectiveness against H1N1pdm09 viruses.
  - LAIV4 again a recommended option starting in 2018-19 but its use has been low since 2018-19, precluding assessment of vaccine-specific VE.
  - LAIV VE estimates have been published from non-U.S. observational studies with VE ranging from 36%-73% from 2018 to 2022.

Pneumococcal Vaccines

- In 2018–2019, the proportion of IPD caused by vaccine serotypes was:
    - 20vPCV, non-13vPCV: ~30% of IPD
    - 15vPCV, non-13vPCV: ~15% of IPD
- Additional serotypes included in higher-valency PCVs account for ~100–830 thousand outpatient visits and ~90–730 thousand antibiotic prescriptions for acute otitis media (AOM), pneumonia, and sinusitis among US children annually.
    - 15v-13vPCV serotypes: 103–168K visits and 90–148K antibiotic prescriptions
    - 20v-13vPCV serotypes: 527–831K visits and 458–731K antibiotic prescriptions
- The estimated incidence of paediatric outpatient visits and antibiotic prescriptions attributable to 20v-13vPCV serotypes is 4 – 5 times the incidence attributable to 15v-13vPCV serotypes.
- Policy questions:
    - 1: Should 20vPCV be recommended as an option for PCV vaccination according to currently recommended dosing and schedules, for U.S. children aged <2 years?
    - 2: Should 20vPCV **without 23vPPV** be recommended as an option for pneumococcal vaccination for U.S. children aged 2–18 years with underlying medical conditions that increase the risk of pneumococcal disease?
- Results of multicentre, randomised, double-blind study in the US/Puerto Rico study in infants reported that 20vPCV is well tolerated with a safety profile similar to 13vPCV. The totality of data shows 20vPCV elicits immune responses to all 20 vaccine serotypes and was well tolerated in children 15 months to < 18 years of age, including those with prior 13vPCV.
- 20vPCV currently under review by the FDA for use in paediatric population 6 weeks to <18 years of age with a target action date in April 2023.
- Cost-effectiveness analysis will be performed to address policy questions.
- Preliminary evidence to recommendation domains reported moderate benefits with minimal harm, with split consideration for benefit > harm, with moderate certainty for effectiveness and safety for policy question 1, and with very low overall certainty for policy question 2.
- Draft policy options on 20vPCV use in U.S. children for consideration by the committee. Approval is anticipated in second quarter 2023.

Meningococcal Vaccines

- Incidence of meningococcal disease declined during 2020-2021 but increased in 2022. New strains emerging in the US– predominantly affecting racial and ethnic minority groups and unclear how this will change overall epidemiology. Historically resistance in *N. meningitides* was rare, however ciprofloxacin- and penicillin-resistant serogroup Y cases detected in 2020. No cases in vaccinated individuals.
    - Unusually lethal strain of serogroup Y in on ongoing outbreak from June 2022: 11 cases, 3 deaths (27% CFR), with 10/11 cases in Black or African American persons.
- More years of data needed to understand post-COVID-19 meningococcal epidemiology.
- MenABCWY [MenB-fHbp (Trumenba) + MenACWY-TT (Nimenrix)] meningococcal vaccine (Pfizer):
    - Active immunisation of individuals 10 through 25 years of age against invasive meningococcal diseases caused by *N. meningitides* groups A, B, C, W, Y.

- Proposed dosing:
  - Administer two doses at least 6 months apart for prevention of disease caused by serogroups A, B, C, W and Y.
  - Administer one dose for prevention of disease caused by serogroups A, C, W and Y.
  - A booster dose may be administered to individuals who have previously completed a primary series with MenABCWYor MenB-fHbp vaccine or who have previously received MenACWY conjugated vaccines.
- A single dose of MenABCWY vaccine can be used as an alternative to ACWY vaccines in ACWY-naïve or primed adolescents and young adults.
  - 1 dose of MenABCWY vaccine was noninferior to 1 dose of MenACWY-CRM in ACWY-naïve participants, 82.4%-99.4% of participants had titres for serogroups ACWY above the accepted threshold after 1 dose of MenABCWY vaccine,
  - In ACWY-primed, 99.5-100% of participants had titres for serogroups ACWY above the accepted threshold after 1 dose of MenABCWY vaccine.
- MenABCWY vaccine protects against all 5 serogroups with 2 doses given 6 to 12 months apart.
  - 98.3-100% of naïve participants and 99-100% of ACWY-primed participants had titres for serogroups ABCWY above the accepted threshold following 2 doses of MenABCWY vaccine given 12 months apart.
- Booster response was observed following a dose of MenABCWY vaccine 4 years after a 2 dose primary series (0,6 months) for all 5 serogroups.
  - 100% of participants had titres for serogroups ACWY above the accepted threshold following a booster dose of MenABCWY vaccine at 4 years,
  - 95.1-100% of participants' titres for B serogroup above the accepted threshold following a booster dose of MenABCWY vaccine at 4 years,
  - 100% of ACWY-primed participants have protective titres four years after 2 doses of MenABCWY vaccine.
- If 2 doses of MenABCWY vaccine are administered at 11-12 years of age, data support that a single (booster) dose from 16 years of age can provide protection against all 5 serogroups.
- <u>Work Group Interpretation of Pfizer's MenABCWY Vaccine Clinical Trials Data: Policy questions:</u>
  - Should the pentavalent vaccine be included as an option for MenACWY/MenB vaccination in people currently recommended to receive both vaccines? (For example, 16-year-olds)
  - Should the pentavalent vaccine be included as an option for people currently recommended to receive MenACWY only? (For example, 11–12-year-olds)
  - Should the pentavalent vaccine be included as an option for people currently recommended to receive MenB only? (For example, during a serogroup B outbreak)
- Pfizer's MenABCWY vaccine appears to be non-inferior to MenACWY+MenB based on clinical trial data presented.
- Data gaps identified:
  - Data not presented on 3-dose schedule for high-risk populations.
  - Data not available in people older than 25 years.
- Next steps:
  - Reviewing additional immunologic persistence data for a single dose.

- GRADE and EtR will focus on pentavalent vaccine studies.
- Cost effectiveness study will be conducted.

Polio Vaccine

- *Policy question 1:* Should completion of a primary polio vaccination series with inactivated polio vaccine (IPV) be recommended for unvaccinated and incompletely vaccinated adults in USA?
  - Pros:
    - Allows unvaccinated adults and their health care providers to take advantage of opportunities to get vaccinated before they are at increased risk of exposure.
    - Brings adult polio vaccination policy closer in line with other routine childhood vaccines, e.g., MMR and varicella vaccines.
    - Less complicated policy to communicate and understand (i.e., recommendation doesn't change based on latest wastewater data).
  - Cons:
    - Most adults in the United States have a low risk of poliovirus exposure and paralytic polio, and most adults received primary polio vaccination series as children.
    - Demand for IPV could potentially exceed supply, particularly if a large number of adults without documentation of polio vaccination status assume they were not vaccinated, however, clinical guidance can be provided for this group.
  - Majority of work group believe pros of uniform recommendation outweigh cons; approximately 1/3 favour maintaining the current risk-based recommendation.
  - Majority recommendation: Adults who are known or suspected to be unvaccinated or incompletely vaccinated against polio should complete a primary vaccination series with IPV.
  - Clinical Considerations: In general, unless there are specific reasons to believe they were not vaccinated, most adults who were born and raised in the US can assume they were vaccinated against polio as children.
- *Policy question 2:* Should a booster IPV dose be recommended for adults in the US who have previously completed a primary polio vaccination series?
  - No data on vaccine effectiveness of primary series + booster vs. primary series only and majority of WG agreed with the current recommendation for adult IPV booster:
  - No change to recommendation, new wording for clarity: "Adults who have received a primary series of trivalent oral polio vaccine (tOPV) or IPV in any combination and who are at increased risk of poliovirus exposure may receive another dose of IPV. Available data do not indicate the need for more than a single lifetime booster dose with IPV for adults."

Respiratory Syncytial Virus (RSV) Vaccines – Paediatric/Maternal

- Economic analysis of Nirsevimab in paediatric populations was showcased by using data of US paediatric <7 months of age entering their first RSV season.
- With some limitation related to modelling and uncertain inputs such as Nirsevimab cost, QALYs lost, upper respiratory tract infection (URTI) and Palivizumab utilisation, it was concluded that Nirsevimab may be cost-effective.
  - Results sensitive to:
    - Cost per dose (Cost-Saving – 316,000 $/QALY)
    - Efficacy (75,000 - 153,000 $/QALY)

            - URTI/LRTI – Proportion of infections with LRTI
            - Or efficacy of nirsevimab against URTI
        - QALYs lost (41,000 - 125,000 $/QALY)
            - Hospitalisation, Outpatient, ED
            - Child, Parent
- Economics of Preventing Respiratory Syncytial Virus Lower Respiratory Tract Infections:
- *Policy question 1:* Should one dose of Nirsevimab be recommended:
    - a) at birth for all infants born during October to March and
    - b) for all infants born during April through September and <8 months of age when entering first RSV season?
- *Policy question 2:* Should Nirsevimab be recommended for children <20 months of age entering their second RSV season who remain at increased risk of severe disease?
- A summary report comparing models from: Sanofi and University of Michigan and CDC (UM-CDC) was showed. In Sanofi model: base case estimates for Nirsevimab cost $500/dose all infants <7 months and probabilistic sensitivity analysis (PSA), while in UM-CDC model: base case estimates for all infants <8 months, Season 1, Nirsevimab cost $300/dose.
    - $/QALY gained:
        - Season 1, infants: Sanofi model: $70,430, UM-CDC model: $102,805
        - Season 2, high risk infants: Sanofi model: $823,131, UM-CDC model: $842,139
    - $ / hospitalisation averted:
        - nirsevimab Season 1: Sanofi model: $9,387, UM-CDC model: $18,881
- Differences in key inputs among Sanofi and UM-CDC models explain differences in results:
    - Nirsevimab cost per dose, seasonality and intervention period, duration of nirservimab efficacy, hospitalisation rates and medical costs.
    - Base-case in both models:
        - Nirsevimab would significantly reduce RSV disease burden in infants.
        - Economic value of using nirsevimab in infants could be cost-effective or costly.
- Evidence to Recommendations Framework: Nirsevimab
    - 1st RSV season:
        - The WG recommends Nirsevimab a) at birth for all infants born during October to March and b) when entering first RSV season and <8 months of age for all infants born during April through September.
        - Many expressed concerns about feasibility and equity, particularly because inclusion in vaccines for children (VFC) is unknown.
        - Some WG expressed concern that at higher prices, Nirsevimab may not be a reasonable and efficient allocation of resources.
    - 2nd RSV season
        - WG would like more time to consider which infants and children would be sufficiently high risk to warrant Nirsevimab in their 2nd RSV season.
            - Limited efficacy and safety data.
            - Limited data to measure the risk of severe disease in the 2nd RSV season.
            - At this time, WG recommended Nirsevimab for those who are eligible for Palivizumab in their 2nd RSV season, since assumed to be cost effective.
            - WG will continue to evaluate other conditions.

- Policy question 2 was modified: Should one dose of Nirsevimab be recommended for children <20 months of age entering their second RSV season who are eligible for Palivizumab in their second RSV season?
- Draft Interim Clinical Considerations: Nirsevimab
- For policy question 1:
  - Considerations for **timing** of administration were noted as follows:
    1) Efficacy beyond 150 days is unknown; 2) Majority of infants will only be eligible for a single dose of Nirsevimab; 3) Only 1 dose is recommended per season; 4) If Nirsevimab given too early, efficacy might wane during the RSV season; 5) For infants born during October–March, the optimal timing of Nirsevimab dosing is at birth; 6) For infants born during April-September, the ideal timing for Nirsevimab dosing is just before or near the start of the RSV season.
  - Timing and location of Nirsevimab administration were discussed as follows:
    - For infants born during Oct–Mar, shortly after birth or as soon as possible: 1) Administration in hospital prior to discharge would be optimal to ensure early protection; 2) If not given prior to discharge, administration at first visit to primary care provider, ideally within 1 week of discharge.
    - For infants born Apr–Sep: 1) Nirsevimab administration recommended during Oct-Nov (e.g., during regularly scheduled 2-, 4-, or 6-month well child visits).
  - Timing of beginning Nirsevimab administration
    - If increased RSV transmission is occurring locally in August or September, Nirsevimab could be administered to eligible infants earlier than October.
    - Local epidemiology data may be best indicator but recommend establishing evidence-based threshold.
  - Timing of ending Nirsevimab administration
    - To determine if Nirsevimab should continue to be administered to newborns shortly after birth beyond March, local jurisdictions can alter administration schedules based on local transmission conditions.
- For policy question 2:
  - Population recommended for nirsevimab when entering 2nd RSV season – same groups eligible for palivizumab when entering 2nd RSV season:
    - Children with chronic lung disease of prematurity if require medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) during the 6-month period before the start of the second RSV season–
    - Children who are profoundly immunocompromised.
    - Children with cystic fibrosis with manifestations of severe lung disease (previous hospitalisation for pulmonary exacerbation in the first year of life or abnormalities on chest XR or CT that persist when stable) or weight for length < 10th percentile.
    - Other conditions are under review.
  - Timing of nirsevimab administration for 2nd RSV season
    - Nirsevimab should be administered during October to November.
    - Nirsevimab is not recommend to be used after the 2nd RSV season.

- Safety and Efficacy of Bivalent RSV Prefusion F (RSVpreF) Vaccine in Vaccinated Mothers and their Infants
  - Data of phase 2 trial presented for Infants from birth through 6 months of age by active immunisation of pregnant individuals with RSVpreF reported RSVpreF elicits maternal neutralising titre with geometric mean ration (GMR) >12 at delivery. Infant neutralising titres remain high through 6 months.
  - MATISSE: A Phase 3 Trial to evaluate the efficacy and safety of RSVpreF in infants born to women vaccinated during pregnancy. In mothers, adverse events (AE) were 13.8 vs 13.1% and serious AE were slightly higher in the intervention group: 4.2 vs 3.7%. In the infants, any AE were:37.1 vs 34.5%), however no significant difference was found in the rates of serious AE (15.5 vs 15.2%). Premature birth and rates of babies with low birth weight was higher in the intervention group compared to placebo (5.6 vs 4.7% and 5.1 vs 4.4%) respectively.
  - RSV-Positive Severe Medically attended (MA)-LRT efficacy 90 days after birth was 81.85 (95%CI: 40.6- 96.3%) and it waned down to 69.4% (95% CI: 44.3-84.1%) 180 days after birth. For RSV-Positive MA-LRTI efficacy 90 days after birth was 57.1% (95% CI: 14.7-79.8%) and it waned down to 51.3% (95% CI: 29.4- 66.8%) 180 days after birth.
  - RSVpreF investigational vaccine was well-tolerated with a favourable benefit-risk profile for the maternal populations and their newborns.
  - Work Group considerations regarding maternal RSV vaccine
  - Policy question: Should the Pfizer RSV bivalent prefusion F vaccine be recommended for all pregnant people as a single dose given at 24–36 weeks gestation?
  - GRADE, cost-effectiveness analysis and EtR for review in June 2023, vote in October 2023.

Respiratory Syncytial Virus (RSV) Vaccines – Adult

- Considerations regarding recommendations for RSV vaccination of older adults: 1) aged ≥65 years, 2) ≥60 years.
- Note FDA has not yet completed review for the GSK adjuvanted RSVpreF3 vaccine and the Pfizer bivalent RSVpreF vaccine.
- Economic Analysis of RSV Vaccination in Older Adults
  - Cost-effectiveness analysis was done on data from adults receiving GSK and Pfizer vaccines and were compared to no vaccination. Base case assumes the age-based RSV vaccination recommendation is for age ≥65.
  - Results vary based on:
    - Vaccine Cost: ICER: ~80,000 - 385,000 $/QALY
      - Vaccine Efficacy: ICER: ~150,000 - 575,000 $/QALY
    - Ages Vaccinate: ICER: ~100,000 - 230,000 $/QALY
    - Incidence of Hospitalisation: ICER: ~30,000 - 250,000 $/QALY
  - Economics of Vaccinating U.S. Adults ≥60 years-old against RSV
  - Three models were used: GSK, Pfizer and UM-CDC.
  - Assumptions and selection of input data were crucial in differences in ICERs: 1) adjustment approach of incidence rates of hospitalisation, ER and Outpatient 2) selection of medical costs sources and data extraction approach.
  - Base-case in the 3 models: 1) Vaccination would significantly reduce RSV disease burden in older adults 2) VE clinical trials data and assumptions support impact on disease reduction •

Economic value of RSV vaccines appear to be costly and could be cost-effective 3) RSV incidence, related healthcare costs, initial VE and duration combined with reasonable vaccine price would determine the cost-effectiveness value of RSV vaccination.

- Evidence to Recommendations Framework:
- Policy questions: Should vaccination with GSK RSVpreF3 vaccine (120µg antigen + AS01E adjuvant, 1 dose IM), rather than no vaccine, be recommended in persons aged ≥60 years or ≥65? And should vaccination with Pfizer bivalent RSVpreF vaccine (120µg antigen, 1 dose IM), rather than no vaccine, be recommended in persons aged ≥60 years or ≥65?
- After reviewing EtR, WG concluded that both vaccines demonstrate significant efficacy against lower respiratory tract illness caused by RSV among older adults. However, trials were underpowered to show efficacy against RSV hospitalisation and groups at highest risk of severe RSV disease were under-represented in clinical trials.
- At least one case of inflammatory neuropathy has been observed among recipients of each investigational vaccine.
- If licensed, post licensure surveillance for both safety and vaccine effectiveness will be critical.
- WG recommended both vaccines for ≥65 but not for ≥60 year's adults.

Chikungunya Vaccine

- National surveillance data for chikungunya virus disease in US travellers reported, from 2006–2021, 4,590 cases in US travellers reported to CDC.
- Very young children and older adults have highest hospitalisation rates.
- Cases have occurred among travellers to all regions with chikungunya risk and can occur year-round.
- Literature search for articles published Jan 1, 2000 – Oct 24, 2022, describing primary data on arthralgia following chikungunya infection was shown. Among 27 studies, the rate of hospitalisation due to arthralgia varied between 0-33%, depending on the time after infection. it was difficult to provide precise estimated of arthralgia due to variation in the methodologies, case definition, included population and questionable generalisability of the results.
- Work Group Considerations:
- Mid-June 2023, WG is planning on presenting to ACIP other data relevant to recommendations. Possible licensure of a chikungunya vaccine produced by Valneva is expected in mid-Aug 2023. Mid-Oct 2023, WG will present evidence to recommendation to ACIP and in early 2024 ACIP will vote on vaccine recommendations for adult travellers and laboratory workers.

Dengue Vaccines

- Tetravalent Dengue Vaccine Candidate:
- TAK-003 is based on a live, attenuated DENV-2 virus backbone expressing E and prM proteins of all four DENV serotypes. A broad spectrum of immune responses may contribute to protection against infection, virus clearance, and prevention of severe disease.
- TIDES (DEN-301): Pivotal Phase III trial design: 20,071 children (aged 4–16 years) received either TAK-003 or placebo in a 2:1 ratio reported:
    - Long-term efficacy of TAK-003 in both baseline seronegative and seropositive participants.

    - TAK-003 is immunogenic against each of DENV-1, -2, -3, -4 serotype.
- Data from pivotal trial suggested varying TAK-003 efficacy profiles by serotype:
    - Efficacious against all four serotypes in baseline seropositive participants
    - Efficacious against DENV-1 and DENV-2 in baseline seronegative participants–
    - Among baseline seronegative participants:
        - Data suggested lack of efficacy against DENV-3. The trial did not allow assessment of DENV-4 due to low incidence.
        - Long-term follow-up did not conclude a higher risk of hospitalised or severe forms of dengue associated with TAK-003 and DENV-3 or -4 serotype.
        - Totality of data did not indicate harm.
- Safety data from integrated analysis of placebo-controlled trials showed that TAK-003 had an acceptable safety profile.
- <u>Work Group Summary and Interpretation of TAK Interpretation of TAK-003 Efficacy, Safety, and Immunogenicity Data:</u>
- VE for Virologically Confirmed Dengue (VCD): 61.2% (95%CI: 56-65.8%) overall, 64.2% (95%CI: 58.4-69.2%) in seropositive and 53.5% (95%CI: 41.6-62.9%) in seronegative.
- VE for hospitalisation: 84.1% (95%CI: 77.8-88.6%) overall, 85.9% (95%CI: 78.7-90.7%) in seropositive and 79.3% (95%CI: 63.5-88.2%) in seronegative.
- VE for Dengue haemorrhagic fever: 70% (95%CI: 31.5-86%) overall, 80.9% (95%CI: 46.3-93.2%) in seropositive and -3.4% (95%CI: -464.7-81.1%) in seronegative.
- VE for Severe Dengue: 70.2% (95%CI: -24.7-92.9%) overall, 90.2% (95%CI: 16.4-98.9%) in seropositive and -999% (95%CI: not estimated) in seronegative.
- It was concluded that TAK-003:
    - Protects seropositive recipients against VCD and hospitalisation due to any serotype.
    - Protects seronegative recipients against VCD and hospitalisation for DENV-1 or -2.
    - Does NOT protect seronegative recipients against VCD and hospitalisation for DENV-3.
    - DENV-4 assessment among seronegative children is limited by low number of events.
    - No protection against VCD for DENV-4.
    - Only one DENV-4 hospitalisation limits efficacy assessment.
    - Unsolicited, serious adverse events, and deaths similar in vaccine and placebo arms.
- <u>WG future consideration:</u>
- Vaccine efficacy against hospitalisations for DENV-4 among seronegative recipients is unknown.
- No efficacy against hospitalisations for DENV-3 among seronegative vaccine recipients compared to placebo (-87.9%; 95% CI: -573.4–47.6%).
    - Data insufficient to rule out an increased risk among vaccine recipients.
- Unclear significance of immunogenicity data because no clearly defined correlate of immune protection exists.

<u>Varicella</u>

Health and Economic Impact of Varicella Vaccination Program in USA 1995–2019 (25 years):

- Varicella incidence declined >97%, 1990–2019.
- Varicella incidence declined in all age groups during the 2-dose program.
- Varicella hospitalisations declined 90% during 1993–2019.
- >10,500 hospitalisations are prevented now annually, including >1,250 among infants.

- Deaths practically eliminated among <20-year-olds.
- In persons aged ≥30 years, herpes zoster incidence increased during the earlier study years, with decelerations in later years.
- In children and young adults, herpes zoster incidence declined in a stepwise pattern once each age group was comprised by persons born during the varicella vaccination program.

COVID-19 Vaccines

- COVID-19 mRNA bivalent booster vaccine safety:
  - Preliminary analyses of ischemic stroke after Pfizer-BioNTech bivalent booster dose in people ages 65+ years
    - Risk of pre-specified outcomes 1–21 days following a bivalent vaccination compared with bivalent vaccinated individuals who were 22–42 days following the bivalent dose.
    - Statistical signal persistent for 8 weeks
    - Rate ratio has slowly attenuated from 1.92 to 1.36 and intermittently met signalling criteria.
  - COVID-19 mRNA bivalent booster vaccination safety –data from other monitoring systems and programs
    - No unusual or unexpected reporting patterns observed, and no evidence of a safety concern detected for ischemic stroke with either COVID-19 mRNA bivalent boosters.
  - U.S. reports to VAERS following Moderna bivalent booster COVID-19 mRNA vaccination among ages ≥5 years (as of February 6, 2023) (N=23,395).
  - Distribution by age, sex, and serious status similar regardless of manufacturer
    - Most reports (94%) were non-serious and race, ethnicity distribution comparable to monovalent COVID-19 mRNA vaccines (49% race and/or ethnicity unknown; 39% non-Hispanic white).
  - Reporting rate to VAERS of ischemic stroke/transient ischemic attack after bivalent COVID-19 mRNA vaccine in people ages ≥65 years (as of February 6, 2023): 670–970/100,000 person years.
- Update on Original COVID-19 Vaccine and COVID-19 Vaccine, Bivalent Safety
  - COVID-19 Vaccine Safety Technical (VaST) Work Group
    - The statistical signal among persons aged ≥ 65 years for ischemic stroke/transient ischemic attack (TIA) following bivalent Pfizer-BioNTech COVID-19 booster vaccination in VSD is based on limited data and has been attenuating over time. A signal has not been observed in two other U.S. active vaccine safety monitoring systems, nor in data from other countries.
    - No increased rate ratio for ischemic stroke/TIA following bivalent Moderna COVID-19 booster vaccination.
    - Previous surveillance in VSD and other U.S. systems found no evidence of increased risk of ischemic stroke/TIA after the primary series or monovalent COVID-19 booster vaccination for either Pfizer-BioNTech or Moderna products.
    - The cause of the increased rate ratio is unclear; potential contributing factors include simultaneous administration of bivalent COVID-19 booster and influenza vaccines or unmeasured confounding or bias.
    - VaST highlighted several areas for further exploration:

        - Assess the impact of recent respiratory viral illness (e.g., COVID-19, influenza) on risk of ischemic stroke/TIA.
        - Potential lower rate of ischemic stroke/TIA in the vaccinated comparator group
    - Current data in VSD do not raise additional concerns about myocarditis following bivalent COVID-19 booster vaccination.
    - WG future considerations:
    - Review of safety data is reassuring and must continue.
    - Review of healthcare data demonstrates high incidence of stroke at time of diagnosis with COVID-19 or influenza. Priorities include: 1) Increasing awareness of the risk of stroke with COVID-19 disease and influenza, 2) Continuing to encourage uptake of the bivalent COVID-19 boosters.
- The COVID-19 ACIP Work Group remains confident in current COVID19 vaccine recommendations. No changes to recommendations regarding coadministration of vaccines.
- COVID-19 vaccine effectiveness updates:
- Preliminary Estimates of Effectiveness of mRNA Vaccines in Preventing Symptomatic SARS-CoV-2 Infection Among Children Aged 3–5 Years — Increasing Community Access to Testing Program, United States, July 2022–February 2023:
    - Complete monovalent primary vaccination series helped provide protection for children aged 3–5 years against symptomatic SARS-CoV-2 infection for at least the first 4 months after vaccination.
    - Waning of monovalent Moderna primary series might occur by 3–4 months after the second dose based on point estimates (although confidence intervals overlapped).
    - CDC will continue to monitor VE in this age group, including against severe disease and for bivalent doses.
- Updates to VE of bivalent COVID-19 booster against symptomatic infection among children and adolescents aged 5-17 years and adults aged ≥18 years:
    - Bivalent booster provided added protection, though early evidence of waning of relative effectiveness.
- Updates to VE of bivalent COVID-19 booster against ED/UC encounters and hospitalisations among adults ≥18 years:
    - Bivalent boosters are helping provide additional protection against emergency department/urgent care encounters and hospitalisation.
- Benefit and risk assessment for bivalent mRNA COVID-19 vaccines
- Benefits continue to outweigh risks for primary series vaccination in all age groups.
- Benefits of bivalent booster dose vary by age, time since last dose, and COVID-19 incidence.
- Risk of myocarditis after COVID-19 vaccines likely reduced by longer interval since last dose – Additional data can better define risk after bivalent vaccines, but current data is encouraging.
- Changes in COVID-19 hospitalisation rates would impact the benefit assessment.
- Additional benefits of COVID-19 vaccines unable to be quantified in benefit-risk assessment – Likely prevention of post-COVID conditions, possible reduction in transmission, increased confidence in social interactions.
- Considerations for Future Planning:
- Immediate considerations: 1) Current COVID-19 vaccine recommendations are complex 2) Uptake of current bivalent vaccine is low 3) SARS-CoV-2 continues to evolve, but recent virus

evolution has not led to large population-level surges in cases or hospitalisations 4) Most adults have a prior infection, prior vaccination, or both 5) Hospitalisation rates are highest older adults, but remain low among people who have received a bivalent booster.

- Future considerations:
  - How frequently should people get a COVID-19 vaccine?
    - A plan for a fall booster dose could provide added protection, at a time when many would be ~1 year from last dose.
  - Are there populations who still need a primary series?
    - Children ages <2 years have higher COVID-19 hospitalisation rates than older children.
    - Children ages <4 years are less likely to have both prior infection and prior vaccination.
    - Children have frequency visits to healthcare providers.
    - The WG discussed continued primary series recommendations for young children.
    - Both age 6 months-2 years and ages 6 months-4 years were discussed without clear consensus.
  - Should older adults be recommended for >1 vaccine annually?
    - The WG emphasised the importance of older adults being up to date on current recommendations, including receiving a bivalent booster.
    - The WG discussed more frequent COVID-19 vaccine doses for older adults, and at this time felt the data were insufficient to determine a conclusion.
    - Recommendations can be updated based on data in older adults including: – Hospitalisation rates of older adults who have received a bivalent booster – Bivalent VE and patterns of waning for older adults – SARS-CoV-2 virus evolution and possibility of future immune escape variants.
  - Should immunocompromised be recommended for >1 vaccine annually?
    - The WG discussed more frequent COVID-19 vaccine doses for people with immunocompromise, and at this time felt the data were insufficient to determine a conclusion.
- Considerations for Bivalent Primary Series:
  - Does ACIP support harmonising the vaccine strain composition for mRNA COVID-19 vaccines across both primary series and booster doses: Changing the primary series from monovalent (Original) to bivalent (Original plus Omicron BA.4/5) for all ages?
  - Harmonising the primary series and booster doses could simplify the presentations, reduce administration errors, and allow continued access to primary series for unvaccinated populations.
  - The WG was supportive of a transition of the mRNA COVID-19 vaccine primary series from monovalent (original) to bivalent (original plus Omicron BA.4/5).

1.2 ACIP meeting 19 April 2023

- Meeting agenda: https://www.cdc.gov/vaccines/acip/meetings/downloads/agenda-archive/agenda-2023-04-19-508.pdf.pdf
- Presentation slides: https://www.cdc.gov/vaccines/acip/meetings/slides-2023-04-19.html

- April 18, 2023: FDA updated COVID-19 vaccine emergency use authorisations (EUAs): 1) Use of bivalent mRNA vaccines for all doses/indications administered to individuals ages 6 months and older, 2) Additional dose(s) for certain populations.
- mRNA COVID-19 bivalent booster vaccine safety update
- No safety signals were detected for ischemic stroke for primary series or monovalent boosters for Pfizer-BioNTech or Moderna COVID-19 vaccines in U.S. and global monitoring.
- Updates on VE of monovalent vaccines against symptomatic infection in children aged 6 months–4 years (Pfizer-BioNTech) and 6 months–5 years (Moderna)
- Complete monovalent primary series vaccination helped provide protection for children aged 3–5 years against symptomatic SARS-CoV-2 infection for at least the first 3 months after vaccination.
- Waning of monovalent Moderna primary series appears to occur by 4–6 months after the second dose. Initial protection and waning patterns are similar to those observed in older children and adults in the first months after vaccination.
- Waning of monovalent Pfizer-BioNTech VE against symptomatic infection could not be assessed but is also likely based on analyses in older children and adults.
- Update on bivalent vaccines against severe disease in children and adults with immunocompromising conditions:
    - People ages 6 months and older are recommended to receive 3 bivalent mRNA doses.
    - People ages 6 months and older who previously received only monovalent doses are recommended to receive 1 or 2 bivalent mRNA vaccine doses, depending on age and vaccine product.
    - People who previously received a bivalent mRNA vaccine dose(s) have the option to receive 1 or more additional bivalent mRNA vaccine doses.
- Update on bivalent vaccines against severe disease in children and adults without immunocompromising conditions:
    - Children ages 6 months–4 years are recommended to receive 2 or 3 bivalent mRNA vaccine. doses: children aged 5 years are recommended to receive 1 or 2 bivalent mRNA vaccine doses.
    - People ages 6 years and older who are unvaccinated or previously received only monovalent vaccine doses are recommended to receive 1 bivalent mRNA vaccine dose.
    - People ages 65 years and older have the option to receive 1 additional bivalent mRNA vaccine dose.
- CDC's Interim Clinical Considerations for Use of Authorised COVID-19 Vaccines will be updated with comprehensive tables of vaccine doses and dosages indicated: 1) For each age group; 2) By history of COVID-19 vaccines received, for children ages 6 months through 5 years. Revision of clinical guidance materials is underway.

1.3 Newly published or updated recommendations

1.3.1 Immunisation Schedule for Children and Adolescents Aged 18 Years or Younger – 2023

- MMWR; 10 February 2023: https://www.cdc.gov/mmwr/volumes/72/wr/mm7206a1.htm
- Reflects new or updated recommendations approved at 19-20 October 2022 meeting.
- Primary updates:

- Vaccine-specific changes in the 2023 immunisation schedule include new or updated ACIP recommendations for influenza vaccine, pneumococcal conjugate vaccine, measles, mumps, and rubella vaccine (MMR), and COVID-19 vaccine.
- Changes also include clarification of the recommendations for dengue vaccine, hepatitis A vaccine (HepA), hepatitis B vaccine (HepB), human papillomavirus vaccine (HPV), meningococcal serogroups A, C, W, Y vaccine (MenACWY), meningococcal serogroup B vaccine (MenB), inactivated poliovirus vaccine (IPV), and varicella vaccine.

1.3.2 Immunisation Schedule for Adults Aged 19 Years or Older – 2023

- MMWR; 10 February 2023: https://www.cdc.gov/mmwr/volumes/72/wr/mm7206a2.htm
- Reflects new or updated recommendations approved at 19-20 October 2022 meeting.
- Primary updates:
  - Vaccine-specific changes in the 2023 immunisation schedule include new or updated ACIP recommendations for influenza vaccines and pneumococcal vaccines.
  - COVID-19 vaccines have been added to the Tables and to the Notes sections summarising ACIP recommendations.
  - A new poliovirus vaccination section was also added to the Notes section to describe the use of IPV in adults who are at increased risk for exposure to polioviruses.

1.3.3 Hepatitis B Vaccine Recommendations – Screening and Testing for Hepatitis B Virus Infection

- MMWR; 10 March 2023: https://www.cdc.gov/mmwr/volumes/72/rr/rr7201a1.htm
- Updates and expands CDC's previously published Recommendations for Identification and Public Health Management of Persons with Chronic Hepatitis B Virus Infection (MMWR Recomm Rep 2008;57[No. RR-8]) regarding screening for HBV infection in the United States.
- New recommendations include hepatitis B screening using three laboratory tests at least once during a lifetime for adults aged ≥18 years.

2 Joint Committee on Vaccination and Immunisation (JCVI), UK Department of Health

2.1 JCVI meeting: 01 February 2023

- A summary of the JCVI meeting held in February is provided below
- Agenda: https://app.box.com/s/9f24lity6bqso9b6qi7c/file/1124002337426
- Draft minutes, 16 March 2023: https://app.box.com/s/iddfb4ppwkmtjusir2tc/file/1165597788909

- Matters arising and horizon scanning
  - JCVI noted that they were also specifically interested in hearing information on upcoming pertussis vaccines, MenACWYX and alternative methods of vaccine storage.
  - MSD informed JCVI that 1) their RSV monoclonal antibody product, clesrovimab, is due to finish phase three trials in 2025, 2) they can share cost effectiveness modelling data on varicella vaccination, 3) enquire about whether a recent UK outbreak of group A streptococcus might expedite plans for a varicella program.
  - A varicella model is planned which will include data from USA. A varicella sub-committee has been planned for May 2023.

- Respiratory Syncytial Virus (RSV)
  - Advice had been given to work towards to replacing Palivizumab with Nirsevimab this year. The Committee had advised that the potential for a small-scale service evaluation in a limited number of trusts should be looked at.
  - In the meantime, the modelling would be taken forward to evaluate both products (Nirsevimab and maternal vaccine by Pfizer) for potential implementation in 2024/25 and to give sufficient time for a procurement to meet the timelines for this.
  - The Committee considered both products suitable but was not ready to make a formal recommendation based on cost-effectiveness. Both products were likely to be cost effective but there was not an estimate to inform the best strategy to take or a potential tender at this time.
  - Advice on additional risk groups would require clear guidance from formal analyses but the priority was for a universal programme.
- Flu season update
  - Sentinel laboratory surveillance showed a return to more normal seasonal activity with a predominately A(H3N2) season with some A(H1N1) activity.
  - Pending final VE estimates, it might be possible to keep with the same influenza vaccine advice for 2024/25 as for 2023/24 as there were unlikely to be new products to consider by the autumn for 2024/25.
  - JCVI agreed that there were some questions on the policy for next season to address, and whether secondary schools would be included as per JCVIs advice to roll out the programme fully to secondary schools. The latter was more cost effective than vaccinating 50–64-year-olds not in a risk group. The Committee agreed It would be important to look at this issue again in June to avoid having insufficient vaccine for secondary schools until very late.
- Diphtheria: Update on outbreak amongst asylum seekers
  - Up to the end of January 2023, a total of 73 toxigenic C. diphtheriae cases had been identified amongst asylum seekers. These cases increased from September, peaking in November and decreasing in December. There have been no confirmed cases in 2023 so far.
  - Most cases have been seen in young adult males; this is generally reflective of the demographics of the population who arrive in the UK via small boats.
  - Multiple sequence types have been detected which suggests multiple importation rather than the circulation of a single strain.
  - The majority of cases were cutaneous, however there have been two respiratory presentations which required hospitalisation and treatment with antitoxin.
  - A formal review of the incident response recommended that the mass vaccination and antibiotic prophylaxis should continue until October 2023. This is planned to be reviewed at three monthly intervals looking at the interventions and epidemiology.
  - There was currently no evidence of transmission of diphtheria from the asylum seeker population to the general population, this continues to be monitored.
- Attitudinal survey
  - Findings of presentation from UKHSA on a survey of attitudes to the childhood vaccination programme amongst 1,485 parents of infants and children under 5 years of age in England. suggested that there was a high level of confidence in the vaccination programme. Participants indicated they had come across information that assured them that vaccines were important for their baby or child and that they had enough information to make an

informed decision. This had decreased from the previous survey due to the ability to access information during COVID-19 pandemic restrictions.

- Pneumococcal
  - The sub-committee agreed that the current evidence indicated 15vPCV could be used in a 1+1 schedule. This was a pragmatic decision based on incremental changes.
  - The subcommittee considered that the benefits of 15vPCV were the anticipated protection against two additional serotypes and the increased immunogenicity for serotype 3. The risks were that the immunogenicity, although non-inferior, was slightly lower for 15vPCV and there was a potential for serotype replacement disease.
  - Due to the uncertainty around the performance of 15vPCV, the committee felt that there was no advantage to using 15vPCV over 13vPCV and the two could be considered equivalent, pending any new data.
  - The subcommittee would prefer that if 15vPCV was selected for the UK programme it should be introduced initially as the booster dose i.e., complete replacement of 13vPCV in the second (booster) childhood dose before beginning to replace 13vPCV as the first (priming) dose.
  - Future considerations include modelling and cost effectiveness, and Pneumococcal vaccination in adults.
  - 15vPCV immunogenicity appeared similar to 13vPCV in a 2+1 schedule but noted that there were no 1+1 immunogenicity data to directly compare the two vaccines.
  - It was suggested that a head-to-head comparison in adults of 23vPPV and high valency conjugates, with clinical end points, was needed.
  - It was noted that a report from the WHO SAGE WG on Pneumococcal Vaccines concluded that, based on existing data, there was minimal evidence that 10/13vPCV was better than 23vPPV in protection against pneumonia (WHO SAGE meeting, October 2020). A head-to-head trial could help answer these questions. However, it was raised that if the vaccines had different serotypes, it would be difficult to compare head-to-head. In that situation, surveillance data may be more helpful in determining direct protection.
  - The subcommittee considered that the benefits of 15vPCV were the two additional serotypes and the increased immunogenicity for serotype 3. The risks were that the immunogenicity was slightly lower for 15vPCV and there was a potential for serotype replacement.
- Polio
  - There continued to be no paralytic cases of polio detected in the UK.
  - It was noted that VDPV2 continued to be detected in the US and Israel posing an ongoing risk of importation into the UK.
  - In London specific call-recall campaigns for unvaccinated or partially vaccinated children started in June. In August the JCVI had recommended a supplementary IPV booster campaign for children aged 1-9 years in London with the aim of preventing cases of paralysis and interrupting transmission. This campaign ran up until the 23rd December with around 360,000 doses delivered to the target cohort.
- Travel sub-committee
  - The sub-committee had received a presentation from Takeda on their dengue vaccine, Qdenga, which received European Medicines Agency (EMA) approval in 2022 and MHRA approval in January 2023. Qdenga is an attenuated vaccine to be made available to

travellers. The sub-committee had a few outstanding questions for Takeda, and this was planned to be discussed further in an upcoming JCVI meeting.
    - Germany's Standing Committee on Vaccination (STIKO) decision to provide a single booster dose of yellow fever vaccine at ten years for those with ongoing risk of infection was discussed. After evaluating the UK criteria for the booster dosing, the sub-committee agreed there were no changes needed. Further review was needed in relation to repeat vaccination in children under two years of age and pregnant women.
    - The Travel sub-committee are planning to make their recommendations for consideration of Vaxchora cholera vaccine at an upcoming JCVI meeting.
    - The travel sub-committee Chair confirmed that the current advice on vaccinating children who plan to travel to high-incidence meningococcal areas excluded vaccination history as a consideration, i.e., vaccination would be recommended regardless of prior vaccination.
- Pandemic flu stockpiles
    - When the pandemic vaccine stockpile had been reviewed in 2015 due to the H5N1 vaccine stock expiring, the view was that this should not be replaced.
    - Experience from the COVID-19 pandemic suggests that a H5 vaccine against a drifted clade may still prevent some cases of severe disease and death, and that even in the absence of neutralisation there still may be some protection. JCVI concluded animal data was required to determine whether the stockpile strain could be used against the drifted strain from pre-pandemic.

3 National Advisory Committee on Immunisation (NACI), Canada

3.1 NACI Meetings

NACI meeting Summary of Discussion landing page:
https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/meetings.html

3.1.1 NACI meeting held on 13 December 2022 (now available)

Summary of Discussion – 13 December 2022:

- Discussions and decision by NACI on COVID-19 booster program planning for the upcoming year. The committee discussed potential simplification of booster recommendations, and the need for close monitoring to enable future booster updates.

3.1.2 NACI meeting held on 23 January 2023

Summary of Discussion – 23 January 2023:

- COVID Bivalent Vaccine as Primary Series: Overview of the evidence and considerations on the potential off-label use of bivalent Omicron-containing mRNA COVID-19 vaccines in a primary series. The committee discussed evidence and preliminary ethical considerations.

3.1.3 NACI meeting held on 6-7 February 2023

Summary of Discussion – 6-7 February 2023:

- COVID bivalent vaccine as primary series: overview of new evidence and considerations on the potential off-label use of bivalent Omicron-containing mRNA COVID-19 vaccines in a primary series.

- COVID high-risk booster guidance update: The committee discussed the need for an additional booster dose for populations at highest risk of severe COVID-19 disease.

3.1.4 NACI meeting held on 7 March 2023

Summary of Discussion – 7 March 2023:

- Moderna COVID-19 bivalent BA.1 and BA.4/5 bivalent booster doses in children and adolescents 6-17 years of age: The committee discussed the evidence and potential integration of the Moderna COVID-19 bivalent booster vaccines for those 6 to 17 years of age within existing NACI COVID vaccine guidance, and the committee voted on recommendations.

3.1.5 NACI meeting held on 27-28 April 2023

- Summary of Discussion for the 27-28 April 2023 meeting not yet released.

3.2 Newly published or updated statement/recommendations

Current vaccine statements:

- Published 20 January 2023: Guidance on COVID-19 vaccine booster doses: Initial considerations for 2023

https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/guidance-covid-19-vaccine-booster-doses-initial-considerations-2023.html

  - Summary: https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/guidance-covid-19-vaccine-booster-doses-initial-considerations-2023/summary-january-20-2023.html
  - At least one booster dose should be offered to all adults 18 years of age and over and adolescents 12 to 17 years of age who are at increased risk of severe illness. *(Strong recommendation)*
  - All adults ≥65 years of age and individuals 5 to 64 years of age who are at increased risk of severe illness from COVID-19 should have received a booster dose since the start of fall 2022. For individuals who have not yet received a fall 2022 booster, it should be offered, as per the recommended interval. *(Strong recommendation)*
  - Individuals 5 to 64 years of age without risk factors for severe illness from COVID-19 may have been offered a booster dose since the start of fall 2022. Individuals who have not yet received a fall 2022 booster may still be offered one, as per the recommended interval. *(Discretionary recommendation)*
  - Bivalent Omicron-containing mRNA COVID-19 vaccines continue to be the preferred booster products for all individuals 5 years of age and over.

- Published 21 February 2023: Recommendation on Repeated Seasonal Influenza Vaccination

https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendation-repeated-seasonal-influenza-vaccination.html

  - Summary: https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/recommendation-repeated-seasonal-influenza-vaccination/summary.html
  - NACI continues to strongly recommend that the seasonal influenza vaccine and there, were no major changes to groups recommended. for vaccination.

- Published 24 February 2023: Public health level recommendations on the use of pneumococcal vaccines in adults, including the use of 15vPCV and 20vPCV

https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/public-health-level-recommendations-use-pneumococcal-vaccines-adults-including-use-15-valent-20-valent-conjugate-vaccines.html

  - Summary: https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/public-health-level-recommendations-use-pneumococcal-vaccines-adults-including-use-15-valent-20-valent-conjugate-vaccines/summary-february-2023.html
  - Economic evidence supplementary appendix: https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/public-health-level-recommendations-use-pneumococcal-vaccines-adults-including-use-15-valent-20-valent-conjugate-vaccines/economic-evidence-supplementary-appendix.html
  - For adults who have not been previously vaccinated with a pneumococcal vaccine, NACI recommends that a single dose of 20vPCVshould be offered to:
    - Adults 65 years of age and over.
    - Adults 50 to 64 years of age living with factors that place them at higher risk of pneumococcal disease.
    - Adults 18 to 49 years of age with immunocompromising conditions.
  - As a discretionary recommendation, NACI recommends:
    - A single dose of 15vPCV followed by a single dose of 23vPPV may be offered as an alternative to 20vPCV.
    - For adults 18-49 years of age with non-immunocompromising risk factors, 20vPCV and 15vPCV may be considered at clinical discretion.
  - For adults who have previously received a pneumococcal vaccine, NACI recommends that a single dose of 20vPCV:
    - Should be offered to adults 65 years of age and over who have received 23vPPV alone or both 13vPCVand 23vPPV, if it has been at least 5 years since the last dose of a pneumococcal vaccine.
  - As a discretionary recommendation, NACI recommends that a single dose of 20vPCV:
    - May be offered to adults 65 years of age and over who have received 13vPCV alone, if it has been 1 year since the last dose of 13vPCV.
    - NACI recommends that pneumococcal conjugate vaccine 20vPCV should be offered to adults 18 years old or older who received a hematopoietic stem cell transplant (HSCT) after consultation with transplant specialist. A primary series of 3 doses of PNEU-C-20 starting 3 to 9 months after transplant should be administered at least 4 weeks apart, followed by a booster dose of 20vPCV 12 to 18 months post-transplant (6 to 12 months after the last dose of 20vPCV). *(Strong recommendation)*

- Published 3 March 2023: Guidance on an additional COVID-19 booster dose in the spring of 2023 for individuals at high risk of severe illness due to COVID-19

https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/national-advisory-committee-immunization-guidance-additional-covid-19-booster-dose-spring-2023-individuals-high-risk-severe-illness-due-covid-19.html

- Summary: https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/national-advisory-committee-immunization-summary-guidance-additional-covid-19-booster-dose-spring-2023-individuals-high-risk-severe-illness-due-covid-19-march-3-2023.html
- Starting in the spring of 2023, an additional booster dose may be offered 6 or more months from the last COVID-19 vaccine dose or infection to the following individuals who are at increased risk of severe illness from COVID-19: *(Discretionary recommendation)*
  - Adults 80 years of age and older.
  - Adults 65 to 79 years of age, particularly if they do not have a known history of SARS-CoV-2 infection.
  - Adult residents of long-term care homes and other congregate living settings for seniors or those with complex medical care needs.
  - Adults 18 years of age and older who are moderately to severely immunocompromised due to an underlying condition or treatment.
- Bivalent Omicron-targeting mRNA COVID-19 vaccines continue to be the preferred booster products.
- Individuals who have not received previously recommended doses, including a primary series or fall 2022 booster dose, are recommended to receive them now.

- Published 21 March 2023: Interim guidance on the use of 15vPCV in paediatric populations https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/national-advisory-committee-immunization-interim-guidance-pneumococcal-15-valent-conjugate-vaccine-pneu-c-15-pediatric-populations.html
  - Summary: https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/national-advisory-committee-immunization-summary-interim-guidance-pneumococcal-15-valent-conjugate-vaccine-pneu-c-15-pediatric-populations-march-2023.html
  - NACI recommends that15vPCV may be used interchangeably with 13vPCV in children less than 18 years of age. A pneumococcal vaccine series may be started or completed with either vaccine. (Discretionary recommendation)
  - NACI's recommendations for the use of 23vPPVin combination with 13vPCV or 15vPCV for high-risk children remain unchanged.

4 Immunisation Advisory Centre (IMAC), New Zealand

4.1 PTAC Considerations

Meetings were held on:

- 17 – 18 November 2022; Minutes (published 20 March 2023): https://pharmac.govt.nz/assets/PTAC-meeting-record-2022-11.pdf
  - No vaccine specific considerations were discussed.
- 16 – 17 February 2023; Minutes are not yet available: https://pharmac.govt.nz/about/expert-advice/pharmacology-and-therapeutics-advisory-committee-ptac/
  - No vaccine specific applications were listed for review.

4.2 Other updates

Updates related to immunisation in New Zealand: https://www.health.govt.nz/our-work/preventative-health-wellness/immunisation/updates-immunisation

- There have been no immunisation updates since 11 August 2022.

Flu vaccine recommendation for 2023:

- https://www.influenza.org.nz/#:~:text=2023%20Influenza%20Immunisation%20Programme&text=Once%20the%20person%20is%20no,%2Ddays%20of%20self%2Disolation.&text=From%2024%20June%202021%2C%20the,be%2030%20doses%20or%20more.
    - Everyone from the age of 6 months is recommended to receive an annual influenza vaccine to reduce the spread of the virus, and for direct protection against severe illness.

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5 Immunisation updates from the World Health Organization (WHO)

5.1 WHO Position Papers

- No updates

5.2 Summary recommendation tables for routine immunisation

- Updated in March 2023: https://www.who.int/teams/immunization-vaccines-and-biologicals/policies/who-recommendations-for-routine-immunization---summary-tables

5.3 Strategic Advisory Group of Experts (SAGE) on Immunisation, WHO

See Appendix 8.1 for current list of documents on COVID-19 vaccine recommendations or technical guidance that have been updated.

Meeting landing page: https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/meetings

Meeting date: 20 – 23 March 2023

- Meeting details: https://www.who.int/news-room/events/detail/2023/03/20/default-calendar/sage_meeting_march_2023
- Agenda: https://cdn.who.int/media/docs/default-source/immunization/sage/2023/march-2023/final_sage_agenda_20-23mar2023.pdf?sfvrsn=fde2e4df_2
- Highlights: https://cdn.who.int/media/docs/default-source/immunization/sage/2023/march-2023/sage_march_2023_meeting_highlights.pdf?sfvrsn=a8e5be9_4

- Global reports
    - *Report from the department of Immunisation, Vaccines, and Biologicals*: The highest priorities for 2023-2025 are the zero-dose child agenda and routine immunisation strengthening (which includes catchup, and with special attention on measles, yellow fever, other outbreak prone diseases, and polio), preparedness and response to outbreaks, revitalisation of human papillomavirus (HPV) vaccination, integration of COVID-19 vaccination into routine immunisation and Primary Health Care (PHC), and malaria vaccine introduction in African countries.

- *Update from Gavi, the Vaccine Alliance*: The Gavi "must-win" priorities for 2023 include the restoration of routine immunisation, expansion of malaria vaccination, the relaunch of HPV vaccination, and support for targeted COVID-19 vaccination and its integration with other health services. Gavi will continue to support the introduction and use of inactivated poliovirus vaccine (IPV) and preventive and outbreak response vaccination for measles and rubella in eligible countries.
- *Regional reports with a focus on measles*: All WHO regions have observed an increase in measles cases in 2022 and the accumulation of immunity gaps has increased the risk of outbreaks. SAGE noted the need to review and update policies on age eligibility for measles vaccination to enable catch-up, accelerate the development and use of new technologies and innovations, and review the evidence to support policy recommendations for vaccination of infants below six months and during pregnancy.

- Partnering with regions and countries to identify priority pathogens for new vaccines
  - Consensus that tuberculosis, human immunodeficiency virus (HIV), and pathogens that exhibit high levels of antimicrobial resistance such as *Klebsiella pneumoniae* are important across all regions.
  - Other pathogens targets including *Streptococcus pyogenes* (Group A streptococcus), Shigella, and respiratory syncytial virus (RSV) were identified as important by four or more regions and *Plasmodium falciparum* by the African region.
- COVID-19 – Roadmap for COVID-19 vaccination in the Omicron era
  - Key recommendations in the updated roadmap comprise:
  - (i) administration of additional booster doses (beyond the first booster dose) for high-priority groups, including frontline health workers 12 months after the previous booster dose;
  - (ii) additional booster doses are not routinely recommended for the medium risk group;
  - (iii) administration of a booster dose during pregnancy if the last dose was given more than 6 months earlier; and
  - (iv) considering the primary series and booster dose for healthy children 4 and adolescents only within country context, including disease burden in this age group, cost-effectiveness, other health or programmatic priorities, and opportunity costs.
- Tuberculosis (TB)
  - Regarding the status of new tuberculosis vaccine candidates intended for adults and adolescents, several candidates are in late-stage clinical trials and a few vaccines could receive regulatory authorization within 3 years.
  - SAGE was provided with preliminary clinical trial data on a promising TB vaccine candidate for adults and adolescents – M72/AS01$_E$.
  - SAGE proposed that a cluster randomised trial to assess the potential indirect effect of M72/AS01E be considered in parallel to the phase 3 trial, and studies to accelerate recommendations for use in adolescents below 15 years of age, ease implementation and improve cost-effectiveness.
- Polio
  - Previous recommendation of conducting quality outbreak response without delay.
  - SAGE recommended the preferential use of novel type 2 oral poliovirus vaccine (nOPV2) for a circulating vaccine-derived poliovirus (cVDPV) type 2 outbreak response with oral vaccines, and that type 2 Sabin OPV should only be used in exceptional circumstances.

- SAGE recommended in areas of persistent poliovirus circulation, an additional IPV (full or fractional dose) campaign should be conducted to supplement OPV campaigns as a means to enhance mucosal immunity and reduce the likelihood of ongoing poliovirus circulation. (This is on the basis that IPV may boost immunity in the intestinal mucosa among individuals previously immunised with oral poliovirus vaccine, although it has long been recognised that IPV is incapable of inducing a strong mucosal response on its own. Indeed, mucosal protection appears to be stronger following a booster dose of IPV than oral poliovirus vaccine, especially in older children.)
- Recommended a flexible approach using nOPV2 for outbreak response in shorter than 4-week intervals but maintaining a minimum 1-week interval if dictated by programme needs.

- Malaria vaccination
  - SAGE concurred with the SAGE and Malaria Policy Advisory Group (MPAG) Working Group (WG) on malaria vaccines proposal to allow for flexibility in the immunisation schedule and to reduce the minimum interval between the doses 3 and 4 to 6 months to optimise impact in areas of highly seasonal malaria transmission or perennial transmission with seasonal peaks.
  - The SAGE MPAG WG is in the process of reviewing the R21 Matrix M malaria vaccine, which is in the late stages of clinical development. Initial results presented appear promising. The safety of the vaccine will be reviewed by the WHO Global Advisory Committee on Vaccine Safety (GACVS).

5.4 Meeting of the Global Advisory Committee on Vaccine Safety (GACVS)

- GACVS Committee Reports landing page: https://www.who.int/groups/global-advisory-committee-on-vaccine-safety/committee-reports

- **Second joint meeting (hybrid) of the WHO Global Advisory Committee on Vaccine Safety and the WHO Advisory Committee on Safety of Medicinal Products meeting on 14 – 16 December 2022**
- Full report (published 17 April 2023): https://www.who.int/publications/i/item/who-wer9809-83-92
  - Overview of mpox (monkeypox) vaccines and safety surveillance
  - The safety profile of ACAM2000 includes risks for myocarditis and pericarditis and many of the risks associated with replication-competent smallpox vaccines. The safety of the third-generation vaccine, MVA-BN, has similar rates of adverse events observed in vaccinia-naive and previously vaccinated individuals. The safety of this vaccine has been assessed in special populations (e.g. people with HIV or atopic dermatitis, children, and pregnant and breastfeeding women), and no safety concerns were identified; however, the study sample size was small. The safety assessment of intradermal administration of the MVA-BN vaccine showed an increased rate of local reactogenicity reactions. The second third generation vaccine, Lc16m8, has been used mainly in Japan, and 2 recent studies in Japan and the USA reported no safety concerns.
  - The post-marketing data available for MVA-BN show no safety concerns, but there are gaps in knowledge on its safety and benefit–risk, and more data are needed on specific

populations, such as children; pregnant women; populations outside Australia, Europe and the USA; immunocompromised populations; and people who were previously vaccinated.

- In 2022, after administration of more than 1 million MVA-BN doses, the safety profile, assessed predominantly in adult males, was good for both subcutaneous and intradermal administration and consistent with the safety profile reported in clinical trials. Although the rates of local adverse events after intradermal administration were higher than those after subcutaneous administration, none were serious. No safety signal has been observed for an excess risk of myocarditis or pericarditis.
- COVID-19
- Most work winding down, however, continue to monitor safety signals. In particular, the long-term impact of signals, such as COVID-19 vaccine-related myocarditis, pregnancy outcomes and Guillain-Barré syndrome, as well as the safety of new COVID-19 vaccines as they are rolled out.
- Updates on monitoring safety during pregnancy and breastfeeding projects: Pregnancy Exposure Registries Landscape Analysis and the COVID-19 pregnancy cohort study
- Plan to finalise the report in the first quarter of 2023 and to submit a manuscript describing the project in the second or third quarter of 2023.
- Update on nOPV2 vaccine safety
- By early December 2022, 525 million doses of nOPV2 had been administered in 25 countries since its first use in March 2021. Most of the doses have been used in Nigeria, especially in northern Nigeria.
- To date, only one sample (3 isolates from same sample) from Uganda out of a total of 600 has shown reversion at the primary attenuation sites (domain V and cre).
- Data from field use show that about 70% of countries have no evidence of breakthrough transmission after 2 vaccination campaigns, similar to experience with Sabin OPV2.
- After administration of 253 million doses, the rate of AESI reports per 100 000 doses administered was lower than background rates reported in the published literature, and the rate of VAPP (0.002 per 100 000 children vaccinated) was lower than would be expected with the Sabin vaccine (0.025 0.4 per 100 000 doses).
- No safety concerns had been detected. Also noted that no genetic mutations or reversions of concern had been observed.
- Innovative approaches in monitoring AEFIs
- The PVG team contracted the Australian National Centre for Immunisation Research and Surveillance to develop a rate sheet for COVID-19 vaccines. The initial sheet will include 5 known serious reactions: myocarditis or pericarditis, thrombosis with thrombocytopenia syndrome, Guillain-Barré syndrome, immune thrombocytopenia and anaphylaxis. These events will be assessed for each COVID-19 vaccine on the WHO list for emergency use. In addition, the rates of common local and systemic adverse reactions will be summarized from evidence provided by clinical trials.
- The concept of a project for a business intelligence dashboard for monitoring serious AEFI reporting rates from data on WHO–UNICEF Joint Reporting Forms (JRFs) and UMC's VigiBase data was demonstrated. The expected benefits include an open, transparent resource that will be available on the WHO-HQ PVG website and near real-time monitoring of the Immunization Agenda IA2030 framework indicator for serious AEFI reporting rates per million population. GACVS cautioned that, if such a dashboard were in the public

domain, it could be misinterpreted and misused, and they recommended that it be available only to relevant stakeholders via restricted access.

5.5 WHO Regional Committee for the Western Pacific meeting

- Regional Committee meeting page: https://www.who.int/westernpacific/about/governance/regional-committee
- **24 – 28 October 2022, 73rd session (Manila, Philippines): - Re-included as Final report now available:** https://www.who.int/westernpacific/about/governance/regional-committee/session-73
- Agenda: https://www.who.int/docs/default-source/wpro---documents/regional-committee/session-73/wpr-rc73-1-provisional-agenda.pdf?sfvrsn=c652c79a_1
- Summary report from the Chairperson: https://www.who.int/docs/default-source/wpro---documents/regional-committee/session-73/rc73-report-of-the-chairperson.pdf?sfvrsn=da7b1a59_1
- The Final report of the Regional Committee: https://apps.who.int/iris/bitstream/handle/10665/366387/WPR-RC073-15-FinRep-2022-en.pdf?sfvrsn=877007b4_1
- Topics covered: cervical cancer, mental health, non-communicable disease prevention and control, primary health care, climate change and environmental health.
- There was broad recognition of the need to scale up HPV screening, vaccination and treatment, specifically by organising catch-up campaigns and incorporating the HPV vaccine into national immunisation schedules.
- The HPV vaccine must be included in national immunisation programmes to vaccinate 90% of girls before the age of 15 and protect the next generations.
- High rates of COVID-19 immunisation coverage had been achieved throughout the Region, particularly among health workers and older populations.

5.6 Global immunisation news (GIN) and other items and resources

- GIN landing page: https://www.who.int/teams/immunization-vaccines-and-biologicals/about/newsletter
- Statement of the thirty-fourth Polio IHR Emergency Committee (2 Feb 2023): https://www.who.int/news/item/02-02-2023-statement-of-the-thirty-fourth-polio-ihr-emergency-committee
- Fourth meeting of the International Health Regulations (2005) (IHR) Emergency Committee on the Multi-Country Outbreak of monkeypox (mpox) (15 Feb 2023): https://www.who.int/news/item/15-02-2023-fourth-meeting-of-the-international-health-regulations-(2005)-(ihr)-emergency-committee-on-the-multi-country-outbreak-of-monkeypox-(mpox)
- Communicating with caregivers about the Human Papillomavirus vaccination: a tool to build confidence in communication skills among health workers (16 Feb 2023): https://www.who.int/publications/i/item/WHO-EURO-2023-6865-46631-67769

- Communicating with caregivers about the Human Papillomavirus vaccination: facilitator's guide (16 Feb 2023): https://www.who.int/publications/i/item/WHO-EURO-2023-6839-46605-67665
- WHO Technical Advisory Group – candidate vaccine prioritization. Summary of the evaluations and recommendations on the four Marburg vaccines (4 Apr 2023): https://www.who.int/publications/m/item/who-technical-advisory-group---candidate-vaccine-prioritization.--summary-of-the-evaluations-and-recommendations-on-the-four-marburg-vaccines

5.7 Other items of relevance to vaccine preventable diseases

- Immunisation and Vaccine related Implementation Research Advisory Committee (IVIR-AC) meeting on 13-16 February 2023
  - Final minutes (published in Weekly Epidemiological Record on 31 March 2023): https://www.who.int/publications/i/item/who-wer9813-127-144
  - COVID-19
  - Identified 3 core areas in which mathematical modelling studies are critical to filling evidence gaps and informing vaccination strategies, namely: 1) shifting vaccine prioritisation in the presence of high infection-derived immunity; 2) the cost effectiveness of COVID-19 vaccination compared to other vaccines; and 3) the impact of variants of concern on vaccination priorities.
  - Dengue vaccine review
  - Takeda's TAK-003 is currently undergoing SAGE's rigorous evidence review process in preparation for policy consideration at the SAGE meeting in September 2023. Also reviewing Sanofi Pasteur's licensed dengue vaccine11 Dengvaxia® (CYDTDV).
  - Explore alternative modes of action for the vaccine, including: 1) assume that the vaccine would mimic a primary infection and that the first post-vaccination infection would have a higher probability of being severe; and 2) assume that the vaccine is a DENV2 vaccine with only temporary cross-protection against the other types.
  - Explore the impact of vaccination strategies with less optimistic assumptions about efficacy, including relaxing the assumption that efficacy is lifelong and that it is not serotype-specific. Scenarios where vaccine induces no or very low efficacy against DENV3 or DENV4 should be explored.
  - When evaluating the additional value of catch-up campaigns, focus on longer time horizons and explore lower vaccine coverages.
  - Explore a broader range of vaccine coverages, including very low coverages. Also, for any targeted age cohort, data-informed potentially achievable vaccine coverages should be explicitly evaluated.
  - Potentially account for demographic dynamics, especially when focusing on longer time horizons.
  - Explore and report on uncertainties regarding parameter estimates. Make explicit the sources of uncertainty addressed in the modelling exercise.
  - Demonstrate that the model can reproduce the trial results.
  - In the construction of archetypes, consider incorporating 3 aspects, namely: dengue epidemiology; demography (population size, growth and structure); and health system

characteristics such as robustness and capacity as these have an impact on disease management, reporting and potentially achievable vaccine coverage. (Note that the modelled disease progression and severity structure should be adjusted if archetypes include health system capacity, as access to care will differ).
    - Maternal and Neonatal Tetanus Elimination (MNTE)
    - Concluded that pre-validation without an LQAS-CS survey and audit of TTCV SIA coverage without an LQAS-CS survey were appropriate to address the challenges to MNTE assessment in conflict-affected areas.
    - Stressed the importance of using the standard approach – pre-validation followed by LQASCS survey – wherever feasible.
    - Estimating the value of vaccines in preventing antimicrobial resistance (AMR)
    - The approach to estimating vaccine impact on antimicrobial usage by focusing on syndromes and pathogen-specific reductions due to vaccination is appropriate but may not fully account for potential vaccine impact.
    - Also consider changes to public and prescriber perceptions of what causes a particular syndrome, which are more difficult to quantify and predict.
    - Model predictions for the impact of vaccines on antimicrobial usage should be validated against data from clinical trials and post-licensure vaccine impact evaluations.
    - Typhoid conjugate vaccine micro-array patches full value of vaccine assessment
    - Water, sanitation and hygiene (WASH) indicators are not reliable predictors of variation in typhoid incidence across countries, and other factors are likely to vary at the subnational level that may be correlated with typhoid incidence and that are not accounted for in the subnational analysis.
    - Relevant additional data sources may be worth exploring within the extended cost-effectiveness analysis framework: recent typhoid cost-of-illness studies have provided estimates of the percentage of families facing catastrophic health expenditures from typhoid.
- Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) meeting on 16-17 March 2023: https://www.who.int/news/item/14-04-2023-report-of-the-meeting-of-the-who-technical-advisory-group-on-covid-19-vaccine-composition-(tag-co-vac)-held-on-16-17-march-2023
    - Purposes of the meeting: (1) to review the evidence on the performance of updated COVID-19 vaccines that incorporate descendent lineages of Omicron as a booster dose; (2) to establish timelines for COVID-19 vaccine composition recommendations in 2023.
    - Both BA.1- and BA.4/5-containing bivalent mRNA vaccines enhance the magnitude and elicit greater breadth of cross-reactive immune responses to SARS-CoV-2 variants when used as a booster dose, as compared to the index virus-based vaccines.
    - There is in vitro evidence to show that immune imprinting, also known as original antigenic sin – a phenomenon in which immune memory recall biases the immune response towards previously encountered antigen – occurs with repeated exposure to the same antigen. However, the clinical impact of immune imprinting in observational epidemiological studies to date is unclear, due to limited data and the possibility of bias.
    - Achieving broader cross-reactive vaccine-induced immune responses remains prudent in the context of continued SARS-CoV-2 evolution. Further recommendations on any updates will be issued by the TAG-CO-VAC following the May 2023 meeting.
- Disease Outbreak News (DONs): https://www.who.int/emergencies/disease-outbreak-news

See Appendix 8.1 for updated COVID-19 vaccine recommendations or technical guidance.

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6 Other items

6.1 Published information on assessment and registration of vaccines in Australia by TGA

6.1.1 Public summary documents

- Provisional Registrations of COVID-19 vaccines: https://www.tga.gov.au/covid-19-vaccine-provisional-registrations
- Other COVID-19 related updates: https://www.tga.gov.au/products/covid-19/covid-19-vaccines
- Live vaccines – what are the contraindications? (4 May 2023): https://www.tga.gov.au/news/safety-updates/live-vaccines-what-are-contraindications
    - Reminder that live vaccines should not be given to people who are significantly immunocompromised or pregnant. This is particularly the case for the herpes zoster vaccine Zostavax – and the Japanese encephalitis (JE) vaccine – Imojev.
    - People who are significantly immunocompromised should not receive live vaccines due to the risk of unchecked infection. However, people with HIV who are mildly immunocompromised can receive MMR (measles-mumps-rubella), varicella and zoster vaccines with further advice from their doctor.
    - In general, pregnant women should not receive live vaccines and should be advised not to become pregnant within 28 days of receiving a live vaccine.
    - Updated guidelines from ATAGI now recommend that Shingrix is preferentially used over Zostavax in immunocompetent adults. Zostavax is contraindicated in people with current or recent severe immunocompromising conditions from a medical condition or treatment.
    - Imojev, the live vaccine for JE, should not be given to children under 9 months of age and is contraindicated in immunocompromised individuals and women who are pregnant or breastfeeding.

6.1.2 TGA media releases

- Media releases and statements landing page: https://www.tga.gov.au/resources/article

Note: only key updates are provided in this summary

- TGA grants provisional approval to Pfizer's COVID-19 bivalent (COMIRNATY Original/Omicron BA.4-5 COVID-19 vaccine) booster dose vaccine (23 January 2023): https://www.tga.gov.au/news/media-releases/tga-grants-provisional-approval-pfizers-covid-19-bivalent-comirnaty-originalomicron-ba4-5-covid-19-vaccine-booster-dose-vaccine
- TGA grants provisional approval to Moderna's COVID-19 bivalent (SPIKEVAX Bivalent Original/Omicron BA.4-5) booster dose vaccine (20 February 2023): https://www.tga.gov.au/news/media-releases/tga-grants-provisional-approval-modernas-covid-19-bivalent-spikevax-bivalent-originalomicron-ba4-5-booster-dose-vaccine
- Moderna's COVID-19 vaccine SPIKEVAX receives approval for full registration (24 April 2023): https://www.tga.gov.au/news/media-releases/modernas-covid-19-vaccine-spikevax-receives-approval-full-registration

7 Upcoming meetings and agendas

ACIP, USA (https://www.cdc.gov/vaccines/acip/meetings/index.html)
- 2023: 21-22 June; 25-26 October
- 2024: 28-29 February; 26-27 June; 23-24 October

PTAC, New Zealand https://pharmac.govt.nz/about/expert-advice/pharmacology-and-therapeutics-advisory-committee-ptac/)
- 2023 meeting dates: 18-19 May; 17-18 August; 16-17 November

JCVI, UK (https://www.gov.uk/government/policy-advisory-groups/joint-committee-on-vaccination-and-immunisation)
- Next full committee meeting: 2 June 2023
- Other future meeting dates pending, but usually the 1st Wednesday of February, June and October

NACI, Canada (https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/meetings.html)
- 2023: 27-28 April; 5-6 June; 27-28 September; 15-16 November

SAGE WHO (https://www.who.int/groups/strategic-advisory-group-of-experts-on-immunization/meetings)
- 2023: 25-28 September
- 2024: 18-21 March; 23-26 September

WHO-GACVS (https://www.who.int/vaccine_safety/committee/en/)
- The date of the next GACVS meeting has not yet been announced.

WPRO
- 16 – 20 October 2023 in Manila, Philippines

ACV (https://www.tga.gov.au/committee/advisory-committee-vaccines-acv)
- 2023: 7 June; 2 August; 4 October

8 Appendix

8.1 COVID-19 related reports, guidelines and publications by WHO

Technical Guidance Publications: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance-publications

General COVID-19 vaccination

- COVID-19 Vaccine Delivery Partnership - January 2023 (27 February 2023): https://www.who.int/publications/m/item/covid-19-vaccine-delivery-partnership-january-2023
- WHO SAGE Roadmap for prioritizing uses of COVID-19 vaccines (30 March 2023): https://www.who.int/publications/i/item/WHO-2019-nCoV-Vaccines-SAGE-Roadmap
- Guidance on operational microplanning for COVID-19 vaccination, revised 2 May 2023 (2 May 2023): https://www.who.int/publications/i/item/WHO-2019-nCoV-vaccination-microplanning-2023.1
- Global Convening on COVID-19 Vaccination Monitoring and Related System Strengthening (2 May 2023): https://www.who.int/publications/m/item/global-convening-on-covid-19-vaccination-monitoring-and-related-system-strengthening