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: 25/05/2017 to 12/09/2017

Contents

1 Advisory Committee on Immunization Practices (ACIP), USA

1.1 ACIP meeting: 21-22 June 2017

- Agenda, presentation slides video recordings and minutes of this meeting: http://www.cdc.gov/vaccines/acip/meetings/meetings-info.html
- **Full minutes for the June 2017 meeting pending at the time of this review; therefore, this summary has been developed from the presentation slides and video recordings.**

Hepatitis A Vaccines

- Epidemiology
  - Mean age of persons hospitalised for hepatitis A (HepA) has increased significantly over the study time period (mean age 37.6 years in 2002–2003 compared to 45.5 years in 2010–2011, $P < 0.0001$).
  - Prevalence of anti-HAV has increased in younger age groups ($p<0.01$ for 6–11 and 12–19 years) and decreased in older age groups ($p<0.01$ for 40–49, 50–59 and ≥60 years) between 1999–2000 and 2009–10. Overall seroprevalence declined from 31.2% to 26.5%.
  - Sub-optimal HepA vaccination (1 or 2 doses) coverage among young children, with no routine HepA vaccination recommendation for adolescents or adults.
- Catch-up vaccination
  - Cost-effectiveness analysis of catch-up HepA vaccination among unvaccinated/partially vaccinated children found catch-up is not cost-effective at thresholds of $50,000, $100,000 or $200,000 per QALY saved, given low incidence of HepA in USA (ICER ranged from $190,000 to $725,000 per QALY).
  - Despite this, work group proposed updating the permissive recommendation to a routine catch-up recommendation for children 2–18 years, given decreasing anti-HAV seroprevalence among adults and preference compared with waiting for adulthood for universal vaccination.
  - Proposed wording: "Children and adolescents age 2-18 years who have not previously received hepatitis A vaccine should be vaccinated routinely at any age with an appropriate dose and schedule" OR "Recommended for all children aged 12 months to 18 years"
    - Changed from: "continue existing vaccination programs for ages 2-18 years"
    - Current recommendation already includes recommendation for use at age 12-23 months
  - Further work (possibly modelling) to be done before a vote on recommendation change.
- Proposed revisions to recommendations for the following groups to explicitly recommend vaccination: pregnant women with high-risk medical conditions, persons with chronic liver disease, and all residents and healthcare personnel in institutions for persons with developmental disabilities.
- Revision of recommendations for travellers to areas where HepA is endemic and post-exposure prophylaxis (PEP):
  - Healthy unvaccinated persons aged >12 months: 2 doses of HepA vaccine (6 months between doses) as PEP
  - Children <12 months and contraindicated: IG (0.02mL/kg) as PEP
  - Immunocompromised and chronic liver disease: IG (0.02mL/kg) and HepA vaccination as PEP
  - Pregnant women: 1) vaccination prior to travel continued to be recommended, 2) vaccination and IG if departing in <2 weeks, 3) IG for persons who elect not to have vaccine or are contraindicated

Influenza

- Surveillance update (regarding the 2016–17 season)
  - Moderate activity with severity indicators within range of what has been observed during previous H3N2 dominant seasons
  - A(H3N2) viruses predominated overall; influenza B viruses reported more frequently than A since late March

- Circulating viruses were similar to those contained in the 2016–17 vaccines
- Influenza vaccine effectiveness (VE) update (end-of-season estimates) from the US Flu VE Network (test-negative case-control design, N=7205):
  - Overall adjusted VE: 42% (95% CI 35 to 48); by age group – 6mo-8yrs: 61% (49 to 70), 9-17y: 35% (-1 to 34), 18-49y: 19% (-1 to 34), 50-64y: 42% (26 to 55), ≥65y: 25% (-5 to 46)
  - VE by subtype (varied by age group, VE for all ages shown here) – A/H3N2: 34% (24 to 42), A/H1N1: 54% (-11 to 81), all B: 56% (47 to 64), B/Yamagata: 55% (45 to 63), B/Victoria: 60% (31 to 77)
- Preliminary influenza vaccine effectiveness estimates (end-of-season estimates) from US Hospitalised Adult Influenza Vaccine Effectiveness Network (HAIVEN) (similar study design to above, CDC-funded study, including 10 hospitals, N=2275)
  - VE by age – ≥18 years: 30% (95% CI 11 to 46), 18-49y: 23% (-29 to 54), 50-64y: 31% (-6 to 55), ≥65y: 37% (8 to 57)
  - VE by subtype – A/H3N2: 20% (-7 to 40), B: 53% (25 to 70)
- End-of-season update: 2016–17 influenza vaccine safety monitoring
  - VAERS data show no new safety concerns detected during 2016–17
  - FDA surveillance for Guillain-Barre Syndrome (GBS) among Medicare beneficiaries found rate in the current season was very close to the historical rate (5.96/million vaccines versus 5.70/million vaccines for prior 5 seasons)
  - Vaccine Safety Datalink (VSD) analysis did not detect any statistical signals or elevated risks for pre-specified outcomes (including acute disseminated encephalomyelitis, anaphylaxis, Bell's palsy, encephalitis, GBS, seizures or transverse myelitis)
- Data on Flublok (recombinant influenza vaccine [RIV]) use in pregnancy: data from 35 pregnancies found 23 pregnancies with normal outcome, 3 spontaneous abortions, 4 elective terminations, 3 lot to follow-up and 2 study withdrawals. Passive surveillance network data from Mongolia showed no serious adverse event reported among 330 pregnant women (noting limitations of passive surveillance)
- Proposed recommendations
  - Extension of recommendation that LAIV not be used in 2017–18 seasons, awaiting further data (anticipated October 2017)
  - Afluria TIV and QIV will be offered during 2017–18 influenza seasons for persons ≥5 years
  - Recommendation for pregnant women updated to state that either IIV or RIV may be used (previously only IIV)

Herpes Zoster Vaccines

- Zostavax (ZVL) long-term effectiveness (review of herpes zoster [HZ] and post-herpetic neuralgia [PHN] interim results 2007–14)
  - Post-licensure commitment to FDA and EMA, 8 years of follow-up
  - Conducted within Kaiser Permanente Northern California (KPNC), 1.3 million members ≥50y during the 8 years were followed (funded by Merck)
  - Vaccine effectiveness against HZ ([diagnosis code + prescription for antiviral] OR [lab-confirmed]) – overall: 49.1% (95% CI 47.5-50.6%, p<0.001), 50-59y: 59.5% (52.7-65.4%), 60-69y: 50.5% (48.4-52.5%), 70-79y: 46.1% (43.4-48.7%), ≥80y: 47.4% (42.8-51.6%). VE high in first year post-vaccination, drops in the second year and then gradually decreases (67.5% in first year, 31.8% in 7 to <8y).
    - Data available for immunocompromised (vaccine not recommended but given for various reasons) – no difference in VE between immunocompromised and immunocompetent
  - VE against PHN (ICD and Kaiser codes) – overall: 68.7% (95% CI % 64.6-72.3%, p<0.001), 50-59y: 63.4% (10.8-84.9%), 60-69y: 71.1% (64.7-76.3%), 70-79y: 69.6% (63.4-74.7%), ≥80y: 61.6%

(50.1-70.5%). VE highest in first year (82.4%), decreases sharply in second year (66.1%), thereafter trend in waning is unclear.

- GRADE[1]: is the live attenuated herpes zoster vaccine (ZVL) safe and effective at preventing HZ?
  - Systematic review including 40 studies and case reports of SAEs and 13 reports of VZV caused by vaccine strain from 10 years of Merck's post-marketing review
  - GRADE Summary:
    - ZVL is effective in preventing HZ (level 1) and PHN (level 1)
    - No safety concerns for ZVL in real-world and clinical settings (level 1)
    - Injection-site reactions more commonly reported among vaccine recipients compared to placebo but tend to be mild (level 1)
    - ZVL effectiveness decreases 4 years post vaccination and continues to decrease year by year (level 2)
- Immunogenicity of Shingrix (HZ/su) in prior Zostavax recipients
  - Phase III, prospective, group-matched, non-randomised trial in ≥65y comparing ZVL ≥5y prior (n=215) to no previous HZ vaccine (n=215)
  - Non-inferiority of no previous HZL versus previous HZL (GMC ratio 1.04 [95%CI 0.92-1.17]) 1 month post -dose 2; similar results 3 months post-dose 2
  - Similar cellular immune responses between groups 3 months post-dose 2 and consistent with ZOE-50 trial
  - Solicited local and systemic symptoms similar between groups; unsolicited AEs vaccine-related to no vaccination also similar
- Two cost-effectiveness analyses of HZ vaccination in ≥60y developed by two different teams at Merck and GSK (a CDC model will be presented at October meeting, awaiting final price for HZ/su)
  - ZVL versus no vaccine ($/QALY) – GSK: $120,000; Merck: $125,000; sensitivity analyses (Merck only) ranged from $60,000 to $260,000 QALY
  - HZ/su versus no vaccine ($/QALY) – GSK: $12,000; Merck: $74,000; sensitivity analyses (both models) ranged from cost-saving to $150,000 per QALY
  - HZ/su versus ZVL (head-to-head): HZ/su is cost-saving relative to ZVL in both models (varied with sensitivity analyses) and in all GSK scenarios; ZVL only favoured over HZ/su in scenarios modelled by Merck with scenarios more favourable for ZVL (details on scenarios not provided)
  - Efficacy and waning immunity for 1st and waning immunity following the 2nd dose of HZ/su vaccine were the primary reasons for the difference in range of values between the two models (especially base case)
  - Important factors influencing range in overall cost effectiveness: HZ/su cost, HZ/su regimen completion, HZ incidence, cost to treat case of HZ with/without PHN, initial efficacy of single dose of HZ/su and rate of waning from HZ/su
- Policy considerations by Work Group (WG) – discussion at this meeting (vote in October 2017)
  - Should ACIP recommend HZ/su for vaccination of immunocompetent adults? – WG in favour
    - Strong evidence that vaccine is safe, efficacious and maintained protection against HZ 4 years post-vaccination, and is cost-effective under most assumptions compared to other vaccines
  - At what age should HZ/su recommendation start? –WG favoured 50 years (pending final price)
    - Based on minimal waning 4 years post-vaccination (differs from ZVL)
  - Should ACIP recommend a preference for HZ/su over ZVL? – WG majority preferred HZ/su, minority had no preference, awaiting final price and accompanying cost-effectiveness
    - HZ/su can prevent significantly more HZ and PHN than ZVL

[1] Grading of Recommendations Assessment, Development and Evaluation. Evidence level 1: Very confident that the true effect lies close to that of the estimate of the effect. Evidence level 2: Moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

        - Key unknowns: 2 dose adherence, VE of 1 dose, long-term waning, possibility of an unexpected safety signal
    - Should prior ZVL recipients receive HZ/su? – WG agreed should be considered, awaiting final price

Varicella

- Impact of the US varicella vaccination program on the incidence of herpes zoster
    - Initial concerns (at time of debate on introduction of varicella) that incidence of HZ would increase immediately following introduction of vaccination due to reduced varicella circulation. This review examines the impact of varicella vaccination on HZ incidence 12-13 years post introduction of varicella vaccine.
    - Varicella incidence declined 97% (range: 93-98%) from 1993-95 to 2013-14 (data from 4 states) – greater reduction than coverage presumably due to herd protection
    - Increasing HZ incidence in 5 of 6 studies prior to introduction of vaccine; introduction of HZ vaccine in 2007 with moderate coverage ~30% in 2015 so impact is not expected to have a substantial effect on population incidence of HZ
    - 5 of 7 studies indicate deceleration of HZ incidence since introduction of vaccine, none indicate acceleration of HZ incidence; cannot be attributed to HZ vaccination due to poor uptake. One study shows rates in ≥65y are plateauing (Harpaz IDWeek 2015), no differences between high and low coverage states. Results in older adults (≥65y) using Medicare data show similar findings, that is, no evidence that varicella vaccination increased HZ rates, plateauing of rates from 2007 onwards and no difference between high versus low coverage (Hales et al Ann Intern Med 2013, 159:739-745). Data from 2014 show rates appear to be declining from 2014 (unpublished data). Consistent with findings from Veterans Affairs (VA) system.
    - Conclusion: No evidence that the varicella vaccination program has increased HZ rates in the general population, reason for this is unknown

Dengue epidemiology in the USA and US territories

- Dengue is highly endemic in Puerto Rico with simultaneous circulation of multiple serotypes
    - Limited seroprevalence data strongly suggest most of population has had at least one dengue infection by the second decade of life
    - During large outbreaks hundreds of hospitalisations and tens of deaths occur
- Dengue is common and may be endemic in the Virgin Islands and American Samoa and other US Pacific territories; seroprevalence data are limited
- Repeated small dengue outbreaks and local transmission since 1980s in South Texas, with seroprevalence data suggesting border crossing sub-population with significant past exposure to dengue
- Small outbreaks in South Florida since 2009 and in Hawaii since 2001

Yellow Fever Vaccines

- YF-VAX supply expected to be exhausted by July 2017; Stamaril vaccine being distributed under investigational new drug (IND) protocol in an Expanded Access Program (allows product to be used at authorised facilities in a restricted format)
- Publication: Addressing a Yellow Fever Vaccine Shortage – United States 2016–17 https://www.cdc.gov/mmwr/volumes/66/wr/mm6617e2.htm

Mumps disease and vaccine

- Characteristics of reported mumps cases and outbreaks in the US, 2017
    - Highest incidence in 18–22y, IQR=15–30y, median=23y
    - 73% with ≥2 doses of MMR; VE of 2 doses: median=88%, range: 53-95%

- 40 outbreaks known: 19 universities, 14 community-wide (9 close-knit), 7 other close contact settings (3 prison, 2 high school, 1 military facility, 1 hockey team)

- Review of studies of 3rd dose of MMR vaccine
  - GMTs are significantly but moderately higher after MMR3; however, 4-fold increase occurred in 6% of subjects 1 month post vaccination and 2% 1 year post vaccination (n=655). Post-vaccination titres highly correlated with baseline titres (R^2=0.81 1 month post-vax). (Parker Fiebelkorn et al Open Forum Infect Dis 2014)
  - MMR3 use in 2 outbreaks – rates of mumps were lower in MMR3 recipients than those in MMR2 recipients but not statistically significant, small number of cases post MMR3 intervention. Incremental effectiveness of MMR3: 88% (-31.9 to 98.9%). Significant decline in attack rates among 11–17 years in 1 setting. Note also MMR3 given after peak of the outbreak.
- Effectiveness of 3rd dose of MMR in a mumps outbreak in a highly vaccinated university population (ages 18-24y), Iowa, 2015–16
  - Attack rate (per 1000) was inversely proportional to the number of MMR doses received – 0 doses: 47.6, 1 dose: 32.8, 2 doses: 14.5, 3 doses: 6.7, 4+ doses: 0, p<0.0001
  - More distant receipt of MMR2 was associated with higher attack rate (HR significant for 13 or more years prior). VE of 2 doses (versus 0 doses) varied by timing of 2nd dose – recent (<13 years prior): VE=89.4% (95%CI: -2, 99%); past (13-24 years prior): VE=31.8% (-389, 91%); while CIs were wide for point estimates, the difference between recent and past VE estimates was significant p=0.0015
  - Receipt of MMR3 associated with lower risk of mumps disease, HR=0.22 (95%CI: 0.12, 0.39) p<0.0001
  - Incremental VE of 3 versus 2 doses varied by assumption of duration of immune response post-vaccination – 7 days: 60.2%, 14 days: 63.4%, 21 days: 68.4%, 28 days: 78.2%, all p<0.0001

Meningococcal Vaccines

- Meningococcal disease and vaccine response in patients receiving eculizumab
  - Case report of fatal meningococcal disease case in adolescent treated with eculizumab
    - Patient vaccinated with MenACWY and MenB vaccines ~6 months before disease onset
    - Strain non-groupable (NG) by SASG, PCR and WGS
    - Men-B-4C expected to provide protection against this strain
    - Serum from 6 healthy adults easily killed this strain
    - Normally nonpathogentic strain caused fatal illness despite vaccination
  - Data on meningococcal disease in patients receiving eculizumab 2007-present from Epi-X
    - CDC web-based communications platform to share and request preliminary health surveillance information
    - 16 cases identified from 10 jurisdictions; median age 30y (range: 16-83y); 16/16 with septicaemia, 6/16 with meningitis, all hospitalised mean 6.6 days, 1 fatality; vaccination status not known for all but not all had received vaccines
    - 5/16 NG by PCR, additional 6 NG by SASG (by PCR: 2 B, 1 C, 3 Y), 3 more NG by SASG with capsule operon defect identified by WGS. Overall 8/16 cases due to NG strains
  - Conclusion: numerous meningococcal disease cases in eculizumab recipients due to NG *N. meningitidis*
  - Breakthrough vaccination in spite of vaccination for appropriate serogroup. Opsonophagocytosis blocked or inadequate for meningococcal killing
  - Antibiotic chemoprophylaxis for duration of eculizumab treatment being considered

1.2 Newly published or updated recommendations

No new published or updated recommendations published since May 2017.

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2 Immunisation Advisory Centre (IMAC), New Zealand

2.1 PTAC Considerations

- Meeting held on 4 & 5 May 2017 - https://www.pharmac.govt.nz/assets/ptac-minutes-2017-6.pdf
- No vaccine-specific considerations; however, PTAC noted the following in regards to zoster vaccine:
  - Results of a recent retrospective cohort study of Zostavax in USA were considered. There were concerns about the generalisability to New Zealand patients. The new evidence did not change the previous recommendation that zoster vaccine be listed for vaccination in ≥65 year olds and 2-year catch-up program for persons aged 65–80 years.
  - GSK's zoster vaccine is in the pipeline, with results of the RCT to be considered when available.
- A meeting was held on 10 & 11 August 2017 – no minutes available at the time of this review but agenda does not indicate any vaccine-specific considerations

2.2 Other updates

- Antigen literature review for the NZ National Immunisation Schedule, 2017: Childhood Schedule
  - Published by IMAC July 2017, part of a series of antigen literature reviews commissioned by the Ministry of Health - http://www.immune.org.nz/sites/default/files/publications/AcRev2017_schedule_FINAL.pdf
  - Main objective is to provide information around the use of vaccines and to help inform decisions relevant to immunisation programs in NZ. Focus is on the usage, effectiveness in disease control and immunogenicity of the vaccination schedules of vaccines included on the National Immunisation Schedule for children up to the age of 5 years.

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

3.1 JCVI meeting: 7 June 2017

Agenda/draft minutes:

https://www.gov.uk/government/groups/joint-committee-on-vaccination-and-immunisation#minutes

This summary was based on the draft minutes only.

Meningococcal vaccine

- Data on immunogenicity and persistence for MenACWY vaccine was reviewed by the Meningococcal Sub-committee following a request from the Travel Sub-committee
- Based on review findings, JCVI supported boosting after five years for travellers due to waning of antibodies against MenA disease; this was less important for the routine MenACWY program in the UK

Influenza

- In the 2016–17 influenza season the predominant subtype was influenza A(H3N2), with some limited influenza B activity. Viruses antigenically analysed were similar to the A/HongKong/4801/2014 Northern Hemisphere 2016/17 A(H3N2) vaccine strain.
- Lab-confirmed hospitalisations and ICU admissions and excess mortality were lower than those in the previous seasons.
- Regarding influenza vaccine coverage:
  - ≥65yrs: 70.4%; <65y at-risk: 48.7%; healthcare workers: 63.4%
  - Higher uptake for paediatric program than that in the previous season (2y: 38.9%; 3y: 41.5%; 4y: 33.9%)
  - Uptake in schools: Northern Ireland: 78%; Scotland: 73%; England school year 1: 57.6%; England school year 2: 55.4%; England school year 3: 53.3%
- VE was modest for all strains in 18–64-year olds, and was lower in ≥65yrs (estimates not provided). Given the low VE in ≥65yrs particularly against H3N2, consideration of the ≥65yrs component of the influenza program is being brought forward. Data on VE from several years by age, role of immune senescence, timing of vaccination and data from ongoing incremental benefit and cost effectiveness work will be considered at the October 2017 meeting.
- VE for LAIV in children 2–17yrs was good, particularly against influenza B. Highest effectiveness was seen in those vaccinated in both 2015–16 and 2016–17. An indirect effect was being seen overall, but there was no apparent indirect protection against the most severe cases. JCVI agreed that recent findings from the elderly program meant a greater focus should be made on rolling out and improving uptake in the paediatric program.
- Modelling considering the incremental benefits of a quadrivalent vaccine program over TIV for ≥65yrs indicated that there would be a health benefit in that age group but would be limited by the indirect effects from the childhood program.
- An adjuvanted TIV for ≥65 year olds is due to be licensed in 2017 and could be used in the 2018–19 season; a high-dose influenza vaccine for the elderly is not currently available in the UK.
- JCVI noted a paper on premature mortality in adults with schizophrenia[2] and considered whether schizophrenia should be a specified risk group for influenza vaccination. The Committee agreed that those with schizophrenia in an existing risk group should be a priority for vaccination, but could not advise adding schizophrenia as a specific risk group.

HPV vaccination for adolescent boys

- Following modifications made to previous cost-effectiveness modelling work, results were unchanged, that is, with high uptake in girls there were relatively small gains in health benefits to be made by vaccinating boys, and a boys program is highly unlikely to be cost-effective.
- The main benefit of vaccinating boys was seen in the additional cervical cancer cases prevented in females; however, further work was necessary to break down the benefits in males.
- JCVI and the HPV sub-committee agreed that extension of the national HPV program to adolescent boys could not be advised on the basis that it was not a cost-effective use of health service resources. A targeted program for MSM, previously advised by JCVI, was being piloted and had received positive feedback from the medical and MSM community.
- Consideration of equality issues were not JCVI's remit, but that the Department of Health may consider these issues when developing policy, and included a number of factors to take into consideration.

[2] Olfson et al (2015) Premature Mortality Among Adults With Schizophrenia in the United States. JAMA Psychiatry 72(12):1172-81

RSV

- Ongoing modelling work looking at the impact and potential cost-effectiveness of RSV vaccination in different scenarios:
  - a static model of maternal immunisation, post-partum passive immunisation and antenatal or infant vaccination (in advanced stage)
  - a static model looking at options for immunisation of older adults (several uncertainties including disease burden in older adults, preventable mortality and whether vaccination would be required each season)
  - a dynamic model which covered all scenarios (would not be completed until 2019 at the earliest)

Hepatitis A in MSM

- Outbreaks of hepatitis A predominantly affecting young MSM in England, 545 cases reported to date. Cases had also been identified in 15 countries in Europe, Chile and USA.
- In the context of global shortage of hepatitis A vaccine, the following recommendations have been made by the PHE Incidence Management Team (agreed by JCVI):
  - Dose sparing strategies to rapidly control spread in London and limiting spread outside of London
  - A single dose of Twinrix or Havrix Junior in adults is acceptable as an outbreak control measure

3.2 Newly published or updated statement/recommendations

JCVI Interim Statement on Extending HPV Vaccination to Adolescent Boys

- July 2017, https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/630125/Extending_HPV_Vaccination.pdf
- JCVI does not recommend extension of the national HPV program to adolescent boys, based on cost-effectiveness analysis
- Issues regarding equality of access were recognised, as well as additional clinical benefits that could be derived from a gender-neutral program. These issues have been referred to the Department of Health for consideration.
- JCVI is issuing its interim findings for consultation to ensure that the most appropriate and up-to-date evidence has been used. The consultation is open for six weeks until the end of August 2017. Final advice is pending completion of the consultation.

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4 National Advisory Committee on Immunization (NACI), Canada

A meeting was conducted on 7–8 June 2017 and 27–28 September 2017 in Ottawa, Ontario; however, the summaries of discussions have not been released at the time of this review. The latest available summary was for their October 2016 meeting, which is available at https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/immunization/national-advisory-committee-on-immunization-naci.html#oct2016

Newly published or updated statement/recommendations

4.1.1 Updated recommendations on HPV vaccines: 9vHPV vaccine 2-dose immunisation schedule and the use of HPV vaccines in immunocompromised populations

- Published in May 2017 – https://www.canada.ca/en/public-health/services/publications/healthy-living/updated-recommendations-human-papillomavirus-immunization-schedule-immunocompromised-populations.html
- Accompanied by a literature review on HPV immunisation of immunocompromised populations, published May 2017 – https://www.canada.ca/en/public-health/services/publications/healthy-living/literature-review-human-papillomavirus-immunization-immunocompromised-populations.html
- Summary of recommendations:
  - In immunocompetent 9–14-year-old girls and boys, 9vHPV should be offered in either a 2-dose (minimum 24 weeks between doses) or 3-dose schedule.
  - In immunocompetent girls and boys aged ≥15 years, 9vHPV should be offered in a 3-dose schedule. (NACI notes that there is evidence from India that 2 doses of 4vHPV may be immunogenic in females aged 10–18 years, and will continue to monitor emerging evidence on optimal scheduling.)
  - In immunocompromised populations, a 3-dose schedule should be administered.
  - HPV immunisation may be completed with 2vHPV, 4vHPV or 9vHPV in females and 4vHPV or 9vHPV in males. Where possible, the same vaccine should be used to complete the series.

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5 Immunisation updates from the World Health Organization (WHO)

5.1 Strategic Advisory Group of Experts (SAGE) on Immunization, WHO

There has not been a SAGE meeting since its April 2017 meeting, which was covered in the previous NITAG report. SAGE will meet again in October 2017. A summary of position papers published since the last summary is below.

5.1.1 Diphtheria vaccines: WHO position paper (August 2017)

http://www.who.int/immunization/policy/position_papers/wer_31_diphtheria_updated_position_paper.pdf?ua=1

WHO position

- All children worldwide should be immunised against diphtheria, with a primary series of 3 doses of diphtheria toxoid-containing vaccine. The first dose may be administered as early as 6 weeks of age, with subsequent doses given with an interval of at least 4 weeks between doses and the 3rd dose completed by 6 months of age. Booster doses should be given in combination with tetanus toxoid at 12-23 months, 4–7 years and 9–15 years, using age-appropriate vaccine formulations.
- For previously unimmunised or partially vaccinated children, the 3-dose diphtheria toxoid-containing vaccine series should be completed. Two subsequent booster doses using Td or Tdap combination vaccines are needed with an interval of at least 1 year between doses.
- Vaccination during pregnancy is not necessary to protect neonatal infants against diphtheria, but diphtheria-containing vaccines combined with pertussis and tetanus can be used to protect young infants against tetanus and pertussis.
- Diphtheria toxoid-containing vaccines can be used in immunocompromised persons including HIV-infected individuals.

5.1.2 Cholera vaccines: WHO position paper (August 2017)

http://apps.who.int/iris/bitstream/10665/258763/1/WER9234.pdf?ua=1

WHO position

- Cholera prevention and control should be a priority in areas at risk for cholera or where endemic cholera is present. Vaccination with oral cholera vaccine (OCV) should not disrupt the provision of other high-priority health interventions to control or prevent cholera outbreaks.
- A series of criteria were listed for consideration to guide the decision to vaccinate, including risk to targeted populations and risk of spread, programmatic capacity and implementation of previous OCV campaigns. Vaccination of the entire population in cholera-endemic countries is not warranted, and should be guided by an assessment of cholera risk and targeted to hotspots.
- Revaccination is recommended where there is continued risk of *V. cholera* infection.
- Cholera vaccines can be co-administered with other injectable or orally administered vaccines.
- Pregnant and lactating women and HIV-infected individuals should be included in OCV campaigns.

5.1.3 Hepatitis B vaccines: WHO position paper (July 2017)

http://apps.who.int/iris/bitstream/10665/255841/1/WER9227.pdf?ua=1

WHO position

- All national programs should include a monovalent hepatitis B vaccine birth dose. WHO also recommends that all infants receive a late birth dose during first contact with healthcare providers at any time up to the time of the next dose of the primary schedule.
- Two recommended schedules for infants are considered appropriate:
  - a 3-dose schedule of hepatitis B vaccine, with the first dose (monovalent) being given at birth and the second and third (monovalent or as part of a combined vaccine) given at the same time as the first and third doses of DTP-containing vaccine
  - 4 doses, where a monovalent birth dose is followed by 3 (monovalent or combined vaccine) doses, usually given with other routine infant vaccines
  - Interval between doses should be at least 4 weeks
- No evidence to support the need for a booster dose
- For low birth weight or premature infants, a birth dose should be given. This dose should not count towards the primary 3-dose series.
- Priority for catch-up should be given to younger age groups when the risk of infection is highest
- High-risk groups include patients who frequently require blood or blood products, dialysis patients, diabetes patients, recipients of solid organ transplantation, persons with chronic liver disease including those with hepatitis C, persons with HIV infection, prisoners, injecting drug users, household and sexual contacts of persons with chronic HBV infection, MSM, persons with multiple sexual partners, as well as healthcare workers and others who may be exposed to blood, blood products or other potentially infectious body fluids during their work.
- HIV-positive individuals should be vaccinated as early as possible in the course of HIV infection.
- Serological surveys of HBV surface antigen (HBsAg) prevalence will serve as the primary tool to measure the impact of vaccination and verify the achievement of hepatitis B control goals.

5.1.4 Use of fractional doses for Yellow Fever (June 2017)

http://apps.who.int/iris/bitstream/10665/255748/1/WER9225.pdf?ua=1

WHO position

- Addendum to the corresponding vaccine position paper on yellow fever (YF) vaccines (July 2013); addresses potential use of fractional dose YF (fYF) in the context of emergency supply shortages.
- A fractional YF vaccine dose can be used as part of an emergency response to an outbreak if there is shortage of full-dose YF vaccine that exceeds the capacity of the global stockpile.

- As soon as the YF vaccine supply situation can meet the immediate need, the use of fYF vaccination should be replaced by standard full-dose YF vaccination.
- The minimum dose administered should preferentially contain 3000 IU/dose, but no less than 1000 IU/dose, and the minimum volume of the dose should not be less than 0.1mL because of practical difficulties delivering dose volumes smaller than this.

5.2 Updates from 26th meeting of the Technical Advisory Group on Immunization and Vaccine-Preventable Diseases in the Western Pacific Region

- 13–16 June 2017, Manila, Philippines. Full meeting report available at: http://iris.wpro.who.int/bitstream/handle/10665.1/13645/RS-2017-GE-40-PHL-eng.pdf?ua=1
- The Western Pacific Region is on track to achieve most Global Vaccine Action Plan (GVAP) targets. WPRO aims to use the *Global Routine Immunization Strategies and Practices* (GRISP) document to guide countries in sustaining program gains, accelerating progress towards regional and global immunisation goals and addressing the needs of hard-to-reach and marginalised populations.
- Regional goal of reducing HBsAg seroprevalence among 5-year-old children to less than 1% by 2017 has been achieved.
- WPRO is developing a regional framework for triple elimination of mother-to-child transmission of HIV, hepatitis B and syphilis, using the shared maternal, newborn and child health intervention platform during antenatal, delivery and postnatal care.
- New regional strategy for measles and rubella elimination with operational targets for 2017–20.
- Regional priorities for polio eradication include achieving/maintaining high level of population immunity, addressing shortage of IPV supply, expanding environmental surveillance in priority countries and proceeding with polio transition. Once OPV is withdrawn, SAGE recommends giving at least 2 full or fractional doses of IPV to all children. Interruptions in supply of IPV may occur due to shortages, and introduction of IPV in Mongolia and Vietnam has been postponed until 2018.
- Importance of strengthening platforms to administer vaccines in the second year of life was emphasised, with key features of a strong platform discussed.

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

- 7–8 June 2017, Geneva, Switzerland. Full meeting report available at: http://apps.who.int/iris/bitstream/10665/255870/1/WER9228.pdf?ua=1
- The anti-malaria vaccine (RTS,S), which received a positive scientific opinion by the EMA in January 2016, will be implemented through pilot programs in Ghana, Kenya and Malawi. Phase III and IV studies are planned.
- A systematic review of published literature on BCG vaccine safety is underway.
- GACVS reviewed new studies examining the safety of HPV vaccines and concluded there was no evidence to suggest a causal association between HPV vaccine and GBS, CRPS, POTS, other syndromes characterised by pain and motor dysfunction, autoimmune conditions and adverse pregnancy outcomes. A WHO commissioned systematic review of SAEs following HPV vaccines found no difference in rates of selected SAEs between exposed and unexposed populations. GACVS reaffirmed the safety of HPV vaccines, noting that since licensure there have been no new adverse events of concern based on many very large, high-quality studies.
- A template for reviewing the safety profile of new vaccines is being developed and was discussed; a revised version will be posted on the GACVS website after final endorsement.

5.4 Meeting of the Immunization and Vaccine-related Implementation Research Advisory Committee (IVIR-AC)

- 1–2 February 2017, Annecy, France. Summary and conclusions available at: http://www.who.int/immunization/research/committees/WER9215_IVIR_Feb2017.pdf?ua=1

- Examination of modelling methods for measles mortality, hepatitis B vaccine impact comparison and typhoid vaccine impact and economic model – findings discussed with specific recommendations for improvement.
- Reporting guide for observational influenza vaccine effectiveness:
  - Development of a reporting guide for observational influenza VE studies is planned, given that these studies are susceptible to bias (should not be construed as requirements for publication).
  - Estimates of VE should be accompanied with analysis of antigenic matching of circulating strains, vaccine formulations, availability and access insofar as possible, and acknowledged in limitations if data are unavailable.
  - As a first step, the guide should focus on reporting VE studies; it may then also consider implications for enhancing test-negative study designs based on the study aims and available data of investigators.
  - The potential for extending these recommendations for VE studies for other vaccines was recognised. Collaboration with other groups (e.g. STROBE) may be helpful.

5.5 Global Immunization News

Available here: http://www.who.int/immunization/gin/en/

- Publication on Japanese Encephalitis surveillance and immunisation in WPRO - https://www.cdc.gov/mmwr/volumes/66/wr/mm6622a3.htm

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6 Other items

6.1 Updates from TGA

- New/updated registrations for vaccines:
  - Menveo: PI amended 3 July 2017. Updated dosing schedules (specifically adding new schedules for infants and children). ARTG effective from 05 September 2017.
  - Gardasil 9: 2 dose schedule registered, no PI available.
- No recent media releases related to vaccinations.

6.2 Journal of Infectious Diseases supplement issue: Polio Endgame & Legacy-Implementation, Best Practices and Lessons Learned

- Volume 216, Issue Suppl_1, 1 July 2017 https://academic.oup.com/jid/issue/216/suppl_1
- 51 articles published in this supplement to serve as a resource and reference on how to implement large-scale, globally synchronised public health activities within ambitious timelines. Provides valuable insights for other initiatives looking to do the same.
- Some pertinent articles:
  - Menning et al. Communications, Immunization, and Polio Vaccines: Lessons From a Global Perspective on Generating Political Will, Informing Decision-Making and Planning, and Engaging Local Support. pp.S24-S32.
  - Ba-Nguz et al. The Role of National Immunization Technical Advisory Groups (NITAGs) in the Introduction of Inactivated Polio Vaccine: Experience of the Indonesia and Uganda NITAGs. pp.S109-S113.
  - Dolan et al. Administering Multiple Injectable Vaccines During a Single Visit—Summary of Findings From the Accelerated Introduction of Inactivated Polio Vaccine Globally. pp.S152-S160.
  - Mulders et al. Expansion of Surveillance for Vaccine-preventable Diseases: Building on the Global Polio Laboratory Network and the Global Measles and Rubella Laboratory Network Platforms. pp.S324-S330.

- Guirguis et al. Placing Human Behavior at the Center of the Fight to Eradicate Polio: Lessons Learned and Their Application to Other Life-Saving Interventions. pp.S331-S336.

7 Upcoming meetings and agendas

ACIP, USA (http://www.cdc.gov/vaccines/acip/meetings/upcoming-dates.html)

- 25-26 October 2017
- 21-22 February 2018

PTAC, New Zealand (https://www.pharmac.govt.nz/about/committees/ptac/)

- 9 & 10 November 2017
- 8 & 9 February 2018

JCVI, UK (https://www.gov.uk/government/policy-advisory-groups/joint-committee-on-vaccination-and-immunisation)

- Future meeting dates pending, but usually the 1st Wednesday of February, June and October

NACI, Canada (http://www.phac-aspc.gc.ca/naci-ccni/meetings-reunions-eng.php)

- 7-8 February 2018
- 6-7 June 2018

SAGE WHO (http://www.who.int/immunization/sage/future_meetings/en/)

- 17-19 October 2017
- 17-19 April 2018

Abbreviation List

ACIP	Advisory Committee on Immunization Practices, USA
CDC	Centers for Disease Control and Prevention
EMA	European Medicines Agency
FDA	Food and Drug Administration
GBS	Guillain-Barré Syndrome
GMT	Geometric Mean Titers
GRADE	Grading of Recommendation Assessment, Development and Evaluation
GSK	GlaxoSmithKline
HAV	Hepatitis A Vaccine
HepA	Hepatitis A
HepB	Hepatitis B
HPV	Human Papillomavirus
HZ	Herpes Zoster
ICD	International Classification of Diseases
ICER	Incremental cost-effectiveness ratio
IVIR-AC	Immunization and Vaccine-related Implementation Research Advisory Committee
ICU	Intensive Care Unit
IIV	Inactivated Influenza Vaccine
IMAC NZ	Immunisation Advisory Centre New Zealand
IND	Investigational New Drug
IQR	Interquartile range
JCIV UK	Joint Committee on Vaccination and Immunisation UK
KPNC	Kaiser Permanente Northern California
LAIV	Live Attenuated Influenza Vaccine
MMR	Measles, Mumps and Rubella
MSM	MSM Men Who Have Sex With Men
NACI	National Advisory Committee on Immunization Canada
NITAG	National Immunisation Technical Advisory Group
PEP	Post-exposure Prophylaxis
PHN	Post-herpetic Neuralgia
QALY	Quality-adjusted life year
QIV	Quadrivalent Influenza Vaccine
RCT	Randomised Controlled Trial
RIV	Recombinant Influenza Vaccine
RSV	Respiratory Syncytial Virus
SAGE	Strategic Advisory Group of Experts
SASG	Slide Agglutination
PCR	Polymerase Chain Reaction
PTAC NZ	Pharmacology and Therapeutics Advisory Committee (New Zealand)
TGA	Therapeutic Goods Administration
TIV	Trivalent Influenza Vaccine
VA	Veterans Affairs (The US Department of Veterans Affairs)
VAERS	Vaccine Adverse Event Reporting System
VSD	Vaccine Safety Datalink
WGS	Whole Genome Sequencing
WHO	World Health Organization
YF	Yellow Fever
ZVL	Live Attenuated Herpes Zoster Vaccine