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

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1 Advisory Committee on Immunization Practices (ACIP), USA

1.1 ACIP meeting: 26–27 June 2019

- Agenda and presentation slides of this meeting:
  https://www.cdc.gov/vaccines/acip/meetings/slides-2019-06.html
- Full minutes of the June 2019 meeting are pending. Therefore, this summary has been developed from the presentation slides and video recordings.

Human papillomavirus vaccines

- Two policy issues for consideration
  - Harmonisation of catch-up vaccination through age 26 years: Should catch-up HPV vaccination be recommended for primary prevention of HPV infection and HPV-related disease for all persons through age 26 years?
    (Working Group reached consensus)
  - Vaccination of adults older than age 26 years: Should catch-up HPV vaccination be recommended for primary prevention of HPV infection and HPV-related disease for all persons aged 27 years through 45 years?
    Two options proposed (majority and minority opinion)
- HPV vaccines have been licensed through age 45 years or older in other countries
- No country has a public health intervention program targeting adults older than 26 years
- Increasing interest from partners and stakeholders in harmonising catch-up recommendations across genders
- Licensure of 9vHPV for use in expanded age range (FDA summary basis for regulatory action)
  - Results of a randomised, double-blind, placebo-controlled trial (base study) of 4vHPV that included women aged 27–45 years
  - Observational follow-up through 10 years in a subset of women in the base study
  - A cross-study immunogenicity analysis showing statistical non-inferiority of immune responses to 4vHPV in males aged 27–45 years vs aged 16–26 years
  - Extrapolation of data to 9vHPV in individuals aged 27–45 years
- 9-valent HPV vaccine program safety and immunogenicity study in women 27–45 years
  - Most women 27–45 years of age are susceptible to infection by HPV types covered by the 9vHPV vaccine
  - The qHPV vaccine is highly efficacious in women 16–45 years of age, regardless of age and provides durable protection (up to at least 10 years)
  - The 9vHPV vaccine is highly immunogenic in women 27–45 years of age (seroconversion rates >99%) for the 9HPV types
  - The 9vHPV vaccine induces HPV antibody responses in women 27–45 years of age that are non-inferior to responses in women 16–26 years of age. Efficacy in women 27–45 years of age was previously inferred based on the overall qHPV and 9vHPV vaccine clinical data. This result further supports the efficacy of the 9vHPV vaccine in women 27–45 years of age.
  - The 9vHPV vaccine is generally well tolerated in women 27–45 years of age
  - The study supports the clinical benefit of the 9vHPV vaccine in 27–45-year-olds
- Summary of health economics results:
  - Cost per quality-adjusted life year (QALY) gained by current vaccination program <$35,000 (cost-saving in HPV-ADVISE model)
  - Adult vaccination is much less cost-effective than current program
    - Notable differences in cost-effectiveness estimates across models
      Results more consistent when standardising health economic assumptions and assumptions regarding deaths due to undiagnosed cancer
    - Uncertainties in HPV natural history and transmission dynamics preclude a precise estimate of the cost-effectiveness of vaccination of adults.
  - In context of the existing program, vaccinating adults over age 26 years would produce relatively small additional health benefits
    - Number needed to vaccinate to prevent one case of disease is ~40 times higher for adults through age 45 years than current program (for anogenital warts, CIN 2/3, and cancer)

- Summary of health economics estimates: Addressing harmonisation of catch-up vaccination through age 26 years:
  - Cost per QALY gained by harmonisation of catch-up vaccination through age 26 years (vs. current program) in HPV-ADVISE
    - $178,000 using faster progression, lower natural immunity assumptions
    - No significant gain in QALYs using slower progression, higher natural immunity assumptions
  - Results are not so favourable or unfavourable as to make a strong economic case for or against harmonisation through age 26 years
  - Cost per QALY gained by adult vaccination through age 30 years
    - Exceeds $300,000 in four of five available models
    - Exceeds $800,000 in median of 50 parameter sets in HPV-ADVISE
  - Cost per QALY gained by adult vaccination through age 45 years
    - Exceeds $400,000 in three of five available models
    - Exceeds $1,400,000 in median of 50 parameter sets in HPV-ADVISE
- Evidence to Recommendation Framework for Harmonisation of catch-up HPV vaccination through age 26 years
  - PICO question: Should catch-up HPV vaccination be recommended for primary prevention of HPV infection and HPV-related disease for all persons through age 26 years?
  - Is the problem of public health concern? Probably yes
  - How substantial are the desirable anticipated effects? Small
  - How substantial are the undesirable anticipated effects? Minimal
  - Do the desirable effects outweigh the undesirable effects? Favors intervention
  - What is the overall certainty of this evidence for the critical outcomes? Moderate (for both effectiveness and safety of the intervention)
  - Does the target population feel that the desirable effects are large relative to undesirable effects? Probably yes
  - Is there important uncertainty about or variability in how much people value the main outcomes? No important uncertainty or variability
  - Is the intervention acceptable to key stakeholders? Yes
  - Is the option a reasonable and efficient allocation of resources? Uncertain
  - Is the option feasible to implement? Yes
  - Is there sufficient information to move forward with a recommendation? Yes
  - ACIP recommends the intervention
- Evidence to Recommendations for HPV vaccination of adults older than age 26 years
  - PICO question: Should catch-up HPV vaccination be recommended for primary prevention of HPV infection and HPV-related disease for all persons ages 27 through 45 years?
  - Is the problem of public health importance? Uncertain
  - How substantial are the desirable anticipated effects? Varies
  - How substantial are the undesirable anticipated effects? Minimal
  - Do the desirable effects outweigh the undesirable effects? Unclear
  - What is the overall certainty of the evidence for the critical outcomes? Moderate (for both effectiveness and safety of the intervention)
  - Does the target population feel that the desirable effects are large relative to undesirable effects? Probably yes
  - Is there important uncertainty about or variability in how much people value the main outcomes? Possibly important uncertainty or variability
  - Is the option acceptable to key stakeholders? Uncertain
  - Is the option a reasonable and efficient allocation of resources? Probably no
  - Is the option feasible to implement? Probably yes
  - Is there sufficient information to move forward with a recommendation? Yes
  - ACIP does not recommend the intervention.
  - ACIP recommends the intervention for individuals based on shared clinical decision making
- GRADE Summary
  - Full GRADE tables were presented to ACIP in October 2018
  - Adding results from the 9vHPV observational trial presented today
  - Certainty of the evidence on benefits:

        - Efficacy: 3 RCTs of 4vHPV and/or 2vHPV
    - Immunogenicity: 3 RCTs, 6 observational trials
        - GRADE evidence level 2 (moderate quality evidence)
    - Certainty of the evidence on harms:
    - Safety: 5 RCTs, 4 observational trials
        - GRADE evidence level 2 (moderate quality evidence)
- Proposed Recommendation Text for Policy Options
    - Harmonisation of catch-up vaccination through age 26 years
      Proposed recommendation text would replace current text for catch-up: ACIP recommends catch-up vaccination for persons through age 26 years who are not adequately vaccinated
        - **All members votes YES – PASS**
    - HPV vaccination of persons older than age 26 years
      Shared clinical decision making: ACIP recommends HPV vaccination based on shared clinical decision making for individuals ages 27 through 45 years who are not adequately vaccinated. HPV vaccines are not licensed for use in adults older than age 45 years
        - **Majority voted YES – PASS**

Pneumococcal Vaccines

- Policy question: Should PCV13 be administered routinely to all immunocompetent adults aged ≥65 years in the context of indirect effects from pediatric PCV use experienced to date?
  Population: Immunocompetent adults 65 years and older
  Intervention: PCV13 in series with PPSV23, in the context of indirect effects
  Comparison(s): PPSV 23 alone, in the context of indirect effects
  Outcomes: Invasive pneumococcal disease (IPD), pneumonia, mortality, safety
- Proposed policy options:
    - ACIP recommends PCV13 for all adults ≥65 years who have not previously received PCV13. PCV13 should be given first, followed by a dose of PPSV23
    - ACIP recommends PCV13 based on shared clinical decision making for adults ≥65 years who do not have an immunocompromising condition and who have not previously received PCV13. All adults ≥65 years should receive a dose of PPSV23
    - ACIP no longer recommends PCV13 for adults ≥65 years who do not have an immunocompromising condition. All adults ≥65 years should receive a dose of PPSV23
- Indirect effects on pneumonia in adults ≥65 years old:
    - Reductions in all-cause pneumonia in adults ≥65 years old were demonstrated after pediatric PCV7 introduction in 2000
    - Analysis of Healthcare Cost and Utilisation Project (HCUP) data between 2010 and 2014 demonstrated:
        - no reductions in all-cause pneumonia
        - decline in pneumococcal pneumonia by 35% (17% to 40%) for adults 65–74 years and by 20% (8% to 40%) for adults ≥75 years
- Other indirect effects:
    - Disparities by age in PCV13-type disease reduced but not eliminated
    - Disparities in PCV-13 type IPD for Alaska Natives and Navajos versus the general population reduced but not eliminated
    - Percent reduction from indirect effects are similar among older adults with and without chronic medical conditions (including chronic heart, liver, lung disease, diabetes, alcohol abuse and cigarette smoking)
- Summary of evidence supporting PCV13 use among adults ≥65 years old in 2014:
    - Prevents IPD and non-bacteremic pneumonia
        - 75% reduction in vaccine type IPD
        - 45% reduction in vaccine-type non-bacteremic pneumonia
    - Safety demonstrated in clinical trials
    - In 2014, GRADE evaluation demonstrated strong quality evidence supporting PCV13 use in series with PPSV23 for all adults ≥65 years
- Population-level impact on invasive pneumococcal disease
    - No changes in IPD incidence since 2014

    - Non-PCV13 serotypes now make up the majority of the disease burden
- Population-level impact on PCV-13 type IPD associated deaths
    - No population-level impact on mortality associated with PCV13-type IPD since 2014
    - No changes in case fatality ratio
- Population-level impact on non-invasive and invasive pneumonia
    - Decline in non-invasive pneumonia observed between 2013 and 2014 (indirect effects)
    - No further population-level impact on non-invasive or invasive pneumonia since 2014
- Population-level impact on PCV13-type Pneumonia
    - Population-level impact on PCV13-type pneumonia and all-cause pneumonia
    - PCV13-type pneumonia ~4% of all-cause pneumonia
- Current PCV13 burden among adults ≥65 years old
    - PCV13-type IPD incidence 5/100,000 (20% of all IPD)
        - Common PCV13 serotypes (% of PCV13-types): 3 (66%), 19A (13%), 7F (13%), 19F (12%)
    - PCV13-type pneumonia incidence ~17–76/100,000 (~4% of all pneumonia)
        - Common PCV13 serotypes (% of PCV13-types): 3 (37%), 19A (28%), 6A (12%), 5 (9%), 7F (7%)
- Values and preferences of older adults regarding PCV13 use
    - Evidence: Few studies focus on older adult perceptions of PCV13 specifically
        - Pneumonia perceived as severe (more so than influenza), sometimes fatal illness
        - Low perceived personal susceptibility to pneumonia
    - Workgroup perspective: Potential protection against pneumonia likely outweighs the side effects of PCV13 for older adults
- Acceptability of continued PCV13 use
    - Limited studies assessing acceptability among stakeholders:
        - Current recommendations are confusing for providers
        - Providers recommend continuing with current recommendation
        - Keeping the current recommendations may be best programmatically if new conjugate vaccines available soon
        - Reimbursement for vaccine is still a programmatic issue
    - Frequent changes in recommendations may negatively impact the perceived importance of future adult vaccine recommendations
    - PCV13 provides individual-level protection for the remaining PCV13 disease burden
    - PCV13 provides minimal public health benefit due to the low remaining disease burden
- Feasibility considerations
    - Recommendations are complex, but integrated into many health care and public health systems
    - Frequent changes to recommendations could present implementation challenges
    - Universal age-based recommendations are easier to effectively implement than risk-based ones
    - Effective communication strategies will be needed if a policy change occurs
- Proposed policy options
    - Recommend PCV13: ACIP recommends PCV13 for all adults 65 years or older who have not previously received PCV13. PCV13 should be given first, followed by a dose of PPSV23
        - **Majority voted NO – DOES NOT PASS**
    - Shared clinical decision making: ACIP recommends PCV13 based on shared clinical decision making for adults 65 years or older who do not have an immunocompromising condition and who have not previously received PCV13. All adults 65 years or older should receive a dose of PPSV23
        - **Majority voted YES – PASS**
    - No longer recommend PCV13: ACIP no longer recommends PCV13 for adults 65 years or older who do not have an immunocompromising condition. All adults 65 years or older should receive a dose of PPSV23
        - **Majority voted NO – DOES NOT PASS**

Combination Vaccines

- Topic under consideration: Consider if the new pediatric hexavalent vaccine (DTaP-IPV-Hib-HepB) should be preferentially recommended for the American Indian/Alaska Native (AI/AN) population
    - Preferential recommendation would require ACIP vote
    - Joint venture between Merck and Sanofi Pasteur (Vaccine name: Vaxelis)

- Manufacturer has stated the vaccine will not be commercially available prior to 2021

- Hib Epidemiology and Hib vaccines in AI/IN Native population
  - In the pre-vaccine era, Hib disease occurred at younger age among AI/AN population, compared to the general U.S. population
  - PRP-OMP vaccines achieve protective immunity in majority of infants after 1st dose
  - PRP-OMP vaccines are preferentially recommended for AI/AN population
- Current Work Group thoughts
  - The Work Group and ACIP members felt that immunogenicity data post-dose 1 is needed before ACIP could consider a preferential recommendation for the AI/AN population
- Potential benefits of the DTaP-IPV-Hib-HepB vaccine
  - Immunogenicity: Non-inferiority criteria met
    Exceptions:
    - GMC for one of five pertussis antigens (FHA) post-dose 3 – however, achieved with % vaccine response
    - GMC for one of thirteen pneumococcal antigens (PN6B) post-dose 3 – however, met non-inferiority endpoints set in PCV13 studies
  - Increased number of vaccine doses due is associated with deferring doses, leading to missed opportunities and decreased coverage **(Meyerhoff et al., 2005)**
  - Receipt of at least 1 combination vaccine independently associated with improved coverage rates (**Marshall et al., 2007)**
    - Individual vaccines as well as vaccine series (e.g. infant series)
- Potential harms of the DTaP-IPV-Hib-HepB vaccine
  - Safety: Profile consistent with component vaccines
  - Higher rate of fever, particularly compared to pentavalent regimens
    - No increase in fever-related medical events
- Potential harms: Combination vaccines (General Best Practice Guidelines for Immunisation)
  - Adverse events that might occur more frequently after administration of a combination vaccine compared with administration of separate antigens
  - Confusion and uncertainty about selection of vaccine combinations and schedules for subsequent doses
  - Reduced pathogen coverage if the combination product covers fewer types of one particular vaccine-preventable disease-causing agent
  - Extra doses of certain antigens in the combination product
  - Shorter shelf-life than in individual component vaccines
- Evidence to Recommendations Framework: Values
  - The use of a combination vaccine generally is preferred over separate injections of the equivalent component vaccines. Considerations should include provide assessment, patient preference, and the potential for adverse events (General Best Practice Guidelines for Immunisation)
  - Combination vaccines represent one solution to the issue of increased numbers of injections during single clinic visits and generally are preferred over separate injections of equivalent component vaccines (American Academy of Paediatrics)
- Evidence to Recommendations Framework: Acceptability
  - Prior evaluation of combination vaccines 2003 among Medicaid patients in Georgia showed that 85% of children received at least 1 combination vaccine in the first year of life (Marshall et al., 2007)
  - Frequency of combination vaccines and single vaccines for the infant series in multiple birth cohorts from 2014–2018
    - Use Immunisation Information Systems (IIS)
    - Evaluation assessed 2 different antigens (DTaP and Hib)
- Evidence to Recommendations Framework: Feasibility
  - Additional combination vaccine (DTaP-IPV-Hib-HepB) will not alter established vaccination schedule
  - Considerations for having additional product(s) available for booster doses
  - DTaP-IPV-Hib-HepB vaccine not commercially available prior to 2021
- Overall Work Group Interpretation

- The Work Group is supportive of including the new paediatric hexavalent vaccine (DTaP-IPV-Hib-HepB) in the VFC program as one of the available options

Rabies

- Need for updated recommendations
  - Rabies is an acute and fatal encephalomyelitis but is preventable
  - > 200,000 persons in US exposed to rabies suspect animals/year
  - > 30,000 persons receive post-exposure prophylaxis (PEP)/year
  - Rabies PEP is safe and efficacious but costs are high
  - 2008: ACIP recommendations comprehensively updated; 2010: PEP schedule updated
  - In interim, new data available and World Health Organization (WHO) updated recommendations
- Pre-exposure Prophylaxis discussions
  - Healthy adults: schedules and primary response
  - Healthy adults: duration of immunity and effectiveness
  - Healthy adults: serological monitoring (frequencies and cut-offs) and risk group recommendations
  - Special populations: determine if recommendations decided above (i.e., schedules, duration of immunity, frequency of serologic monitoring) should be different from those of healthy adults
  - Rabies vaccine safety and administration considerations
  - Miscellaneous topics including co-administration of rabies vaccine with other vaccines and anti-malarials
- Next steps:
  - Continue monthly work group calls focused on PEP
  - Continue to review systemic review of data (including unpublished and new), manufacturer input, and information that might inform decisions
  - PEP topics include:
    - Schedule
    - PrEP and PEP schedule deviations
    - Rabies Immune Globulin administration around wound vs. around wound + IM
    - Recommendations for special populations including immunocompromised
    - Internationally administered PEP
    - PEP for mass bat exposures

Influenza

- Characterisation of U.S. Influenza A (H1N1)pdm09 and B viruses collected September 30, 2018 to May 18, 2019
  - All 1,251 influenza A (H1N1)pdm09 viruses tested belong to genetic group 6B.1A
    - 96.1% were well inhibited by ferret antisera against A/Michigan/45/2015
  - All 203 B/Yamagata lineage viruses belong to the Y3 clade
    - 100% were well inhibited by ferret antisera against B/Phuket/3073/2013
  - 3 genetically and antigenically distinct B/Victoria sub-clades co-circulated
    - V1A (14.7%), V1A.1 (50.4%), V1A-3Del (34.9%)
    - The 2018–2019 Northern Hemisphere vaccines contained a B/Colorado/6/2017- like V1A.1 virus
- Characterisation of U.S. Influenza A (H3N2) viruses collected September 30, 2018 to May 18, 2019
  - Phylogenetic analysis of the HA genes of H3N2 viruses show co-circulation of multiple clades/sub-clades
  - The proportion and geographic spread of viruses belonging to clade 3C.3a increased as the season progressed
  - The 3C.3a viruses are antigenically distinguishable from the 3C.2a and 3C.2a1 virus including the A/Singapore/INFIMH-16-0019/2016(3C.2a1), a cell-propagated reference virus representing the A(H3N2) component of 2018–2019 Northern Hemisphere influenza vaccines
  - Circulation of antigenically drifted viruses can impact vaccine effectiveness
- Vaccine virus selection for 2019–2020
  - WHO and FDA Vaccines and Related Biological Products Committee Recommended Composition of Influenza Virus Vaccines for Use in the 2019–2020 Northern Hemisphere Influenza Season:
    - A/Brisbane/02/2018 (H1N1)pdm09-like virus

        - A/Kansas/14/2017 (H3N2)-like virus (3C.3a)
        - B/Colorado/06/2017-like virus (B/Victoria/2/87 lineage)
        - B/Phuket/3073/2013-like virus (B/Yamagata/16/88 lineage) – quadrivalent only
- Preliminary burden estimates during the 2018-19 flu season in the U.S
    - 37.4 million– 42.9 million flu illnesses
    - 17.3 million– 20.1 million flu medical visits
    - 531,000– 647,000 flu hospitalisations
    - 36,400– 61,200 flu deaths
- Current Influenza Activity in Australia (2018)
    - Australia's influenza season began earlier than typical this year
    - Number of reported influenza positives similar to 2017
    - Currently influenza A(H3N2) predominant
    - Multiple clades detected
        - 3C.2a1b, not 3C.3a, is the predominant clade
- The severity of the U.S. 2018–2019 influenza season was classified as moderate in all age categories
- The season was notable for 2 waves of influenza A viruses of similar magnitude, an influenza A(H1N1)pdm09 wave and an H3N2 wave
- The majority of H3N2 viruses belonged to the 3C.3a genetic group which is antigenically distinct from the 3C.2a genetic group
- The recommended H3N2 component for the 2019–20 Northern Hemisphere vaccine is an A/Kansas/14/2017-like virus, which belongs to genetic group 3C.3a
- Preliminary estimates of 2018–19 seasonal influenza vaccine effectiveness (VE) against medically attended influenza from three U.S. networks
    - Three networks: US Flu VE Network (ambulatory setting) for 6 months and older; Hospitalized Adult Influenza Vaccine Effectiveness Network (HAIVEN) (inpatient setting) for adults aged 18 years and older; New Vaccine Surveillance Network (NVSN) (inpatient setting) for children 6 months–17 years
    - Methods used across all three networks: test-negative design; comparing odds of laboratory-confirmed influenza among vaccinated vs unvaccinated patients; vaccination status: receipt of one dose (≥ 1 dose for children 6m-8 years) of any 2018–2019 seasonal flu vaccine at least 14 days prior to illness onset; sources: medical records, immunisation registries, and/or self-report only for inpatient networks)
    - Equal distribution of H1N1 and H3N2 in all networks
    - U.S. Flu VE Network adjusted vaccine effectiveness against medically attended influenza by virus subtype Nov 23, 2018– May 3 2019
        - 10,041 enrolled, 28% (n=2,795) influenza positive
        - Adjusted VE against medically attended influenza by age group – overall: 29% (95% CI: 21–35%); 6m–8years: 49% (95% CI: 38–58%); 9–17 years: 6% (95% CI: -22–27%); 18–49 years: 25% (95% CI: 10–37%); 50–64 years: 12% (95% CI: -12–31%); ≥65 years: 12% (95% CI: -29 – 41%)
        - Adjusted VE against medically attended influenza by virus subtype: A(H1N1)pdm09 = 44% (95% CI: 36–51%), A(H3N2) = 9% (95% CI: -4–20%)
        - Adjusted VE against influenza A/H3N2 by clade, U.S. Flu VE Network, 2018–2019 – All H3N2: 9% (95% CI: -4–20%); sequenced H3N2: 15% (95% CI: -1–28%); A(H3N2) clade 3C.3a: 11% (95% CI: -6–26%); A(H3N2) clade 3C.2a1: 45% (95% CI: 5–68%)
    - HAIVEN adjusted vaccine effectiveness against influenza, by age group and virus subtype Nov 2, 2018–May 3, 2019:
        - 2,873 enrolled, 16% (n=461) influenza positive
        - Adjusted VE against medically attended influenza by age group – overall 25% (95% CI: 1–41%); 18–49 years: 1% (95% CI: -58–38%); 50–64 years: 47% (95% CI: 22–63%); ≥65 years: 15% (95% CI: -24–41%)
        - Adjusted VE against medically attended influenza by virus subtype: H3N2: -43% (95% CI: -102–-2%); H1N1pdm09: 60% (95% CI: 46–71%)
    - NVSN, adjusted vaccine effectiveness against pediatric influenza hospitalization, by patient age/virus subtype Nov 7, 2018–May 13, 2019:
        - 1,481 enrolled, 13% (n=190) influenza positive

        - Adjusted VE against paediatric influenza hospitalisation by age group – overall 31% (95% CI: 5–51%); 6m–8years: 26% (95% CI: -6–49%); 9–17 years: 53% (95% CI: 5–77%)
        - Adjusted VE against paediatric influenza hospitalisation by virus subtype: H3N2: 13% (95% CI: -31–43%); H1N1pdm09: 48% (95% CI: 14–68%)
        - Overall vaccine effectiveness (influenza A or B) = 31% (95% CI: 5–51%), H3N2 = 13% (95% CI: -31 – 43%), H1N1pdm09 = 48% (95% CI: 14–68%)
    - Interpreting VE estimates for influenza A(H3N2)
        - All three networks identified no vaccine protection against predominant H3N2 virus this season, consistent with laboratory data on 3C.3a clade
        - Negative VE for H3N2 in adult inpatient network (HAIVEN) based on small number of cases and could be related to chance or bias
        - Cannot exclude possibility of alternative biological explanations
    - Next steps for finalising VE estimates
        - Updated data, vaccine verification and analysis
        - Evaluate serologic specimens and virus sequencing (U.S. Flu VE and HAIVEN)
        - Collaborating with partners to compare findings in other networks and consider possible explanations
        - Update to ACIP Influenza Working Group early fall 2019
    - Summary of 2018–2019 estimates of seasonal influenza vaccine effectiveness against medically attended influenza from three U.S. networks:
        - Overall VE was ~30% against influenza illness and hospitalisations
        - Vaccine likely prevented between ~40,000 to 90,000 hospitalisations based on previous seasons' estimates
        - Vaccine reduced A9H1N1)pdm09- associated outpatient influenza illness by 44% and hospitalisations by 48–60%
        - No significant protection against H3N2 illnesses likely due to emergence of antigenically different A(H3N2) clade 3C.3a
        - WHO has updated the A(H3N2) component of 2019–2020 Northern Hemisphere influenza vaccine
        - These VE estimates are preliminary and will be updated when final data are available
- Vaccine Adverse Event Reporting System (VAERS): Reports by vaccine type, 2018–2019 influenza season
    - IIV3 (N=150) – non-serious reports: 141 (94%); serious reports: 9 (6%); Guillain-Barre syndrome: 2 (1.3%); anaphylaxis: 0 (0%); febrile convulsion: 1 (0.7%)
    - IIV4 (N=4,890) – non-serious reports: 4,621 (94%); serious reports: 269 (6%); Guillain-Barre syndrome: 33 (0.7%); anaphylaxis: 24 (0.5%); febrile convulsion: 25 (0.5%)
    - IIV3-HD (N=2169) – non-serious reports: 2,076 (96%); serious reports: 93 (4%); Guillain-Barre syndrome: 13 (0.6%); anaphylaxis: 2 (0.1%)
    - ccIIV4 (N=1,040) – non-serious reports: 1107 (97%); serious reports: 33 (3%); Guillain-Barre syndrome: 16 (1.5%); anaphylaxis: 3 (0.3%); febrile convulsion: 0 (0%)
    - aIIV3 (N=708) – non-serious reports: 708 (98%); serious reports: 16 (2%); Guillain-Barre syndrome: 1 (0.1%); anaphylaxis: 1 (0.1%)
    - RIV4 (N=276) – non-serious reports: 268 (97%); serious reports: 8 (3%); Guillain-Barre syndrome: 4 (1.4%); anaphylaxis: 1 (0.4%)
    - LAIV4 (N=23) – non-serious reports: 22 (96%); serious reports: 1 (4%); Guillain-Barre syndrome: 0 (0%); anaphylaxis: 0 (0%); febrile convulsion: 0 (0%)
- No new safety concerns detected for IIV3, IIV4, LAIV4, IIV3-HD, ccIIV4, aIIV3, or RIV4 during the 2018–2019 influenza season
    - Surveillance for the 2019–2020 influenza season will include enhanced safety monitoring for:
        - aIIV3 (FLUAD)
        - RIV4 (Flublok Quadrivalent)
        - Pregnancy reports
        - Anaphylaxis reports in persons with history of egg allergy
- Vaccine Safety Datalink (VSD) links vaccination data to health outcome data and is used for surveillance and research
    - Rapid Cycle Analysis (RCA) in VSD

        - Acute disseminated encephalomyelitis
        - Near real-time vaccine-safety monitoring (using sequential monitoring techniques)
        - Employs an automated analysis that uses ICD-coded diagnoses from administrative data
        - A surveillance activity (signal detection and signal refinement), which is not the same as an epidemiologic study (signal evaluation, causality assessment)
        - Requires careful thought and customisation in the design, set-up, interpretation
        - When a statistical signal occurs, CDC conducts a series of evaluations using traditional epidemiologic methods
        - Chart-confirmation of diagnoses to confirm or exclude cases as true incident cases is a key part of statistical signal assessment
        - Not all statistical signals represent a true increase in risk for an adverse event
    - Summary of VSD RCA monitoring for influenza vaccine, 2018–2019 following signal assessment and end-of-season analysis:
        - Statistical signals for anaphylaxis following IIV4 and ccIIV4 ruled out
        - Finding of an elevated risk for Bell's palsy following ccIIV4 in 4-17 year olds (RR=3.0, 95% CI: 0.31–28.8) was based on a small number of cases and doses; CDC will continue to monitor and explore options for additional analyses
        - Statistical signal for GBS following IIV3-HD (65+ years old) ruled out
        - Preliminary FDA analysis of GBS following IIV3-HD in CMS data indicate that the risk, if any, is no greater than in some previous seasons and consistent with labelled risk of Guillain-Barre syndrome
        - Final self-controlled risk interval (SCRI) analysis of confirmed febrile seizure cases showed: an elevated IRR in children aged 6–23 and 24–59 months; risk was similar in those who received IIV4 alone and those who received IIV4 simultaneously with other vaccines, including PCV13; attributable risk was less than that observed in some previous influenza seasons and less than the febrile seizure risk associated with MMR or PCV
- Influenza Work Group Considerations and Proposed 2019–20 Season recommendations:
    - Core recommendation is unchanged – Annual influenza vaccination is recommended for all persons aged 6 months and older who do not have contraindications
    - Primary update: Vaccine composition for trivalent vaccines
        - A/Brisbane/02/2018 (H1N1)pdm09-like virus updated
        - A/Kansas/14/2017 (H3N2)-like virus updated
        - B/Colorado/06/2017-like virus (Victoria lineage)
    - Vaccine composition for quadrivalent vaccines
        - Above three, plus B/Phuket/3073/2013-like virus (Yamagata lineage)
    - This year the selection of the H3N2 component by the World Health Organisation was delayed approximately by a month
    - Projected Influenza Vaccine Supply (2019–20 season)
        - AstraZeneca – distribution started early September
        - GSK – distribution started mid-August
        - Sanofi Pasteur – distribution started late August/early September
        - Seqirus – distribution started mid-August
    - 2019–20 Licensure Changes
        - Licensure changes for Afluria Quadrivalent and Fluzone Quadrivalent
        - Four IIVs expected to be available for aged 6 through 35 months
        - Dose volumes differ:

Fluarix Quadrivalent (IIV, GSK)	0.5mL
FluLaval Quadrivalent (IIV4, ID Biomedical Corp/GSK)	0.5 mL
Fluzone Quadrivalent (IIV4, Sanofi Pasteur)	0.25 mL or 0.5 mL
Afluria Quadrivalent (IIV4, Seqirus)	0.25 mL

        - Dose volume for persons aged ≥ 3 years is 0.5 mL for all IIVs
- 2019–2020 ACIP Guidance updates:
    - Timing of vaccination: Language concerning July/August vaccination moved to top paragraph. "For those requiring only one dose for the season, early vaccination (i.e., in July and August) is likely to be associated with suboptimal immunity before the end of the influenza season, particularly among older adults"

- Groups that should focus on efforts if supply is limited: Language describing health care personnel made consistent with 2011 ACIP Recommendations for the Immunisation of Health Care Personnel
- Vaccine doses needed for children aged 6 months through 8 years: Clarified to indicate that 8-year-olds needing two doses should receive second dose even if they turn 9 years of age between dose 1 and dose 2 (consistent with AAP guidance)
- Concomitant receipt of two vaccines containing novel adjuvants: Notes that given limited safety data, non-adjuvanted influenza vaccines may be considered when giving another vaccine containing a novel adjuvant; vaccination should not be delayed if a specific product is not available.
- ACIP affirms the updated statement "Prevention and Control of Seasonal Influenza with vaccines: Recommendations of the Advisory Committee on Immunisation Practices – United States 2019–20 Influenza season.
  - **All members voted YES – PASS**

Hepatitis A

- Hepatitis A catch-up vaccination
  - Hepatitis A vaccines have demonstrated safety and efficacy for over 20 years
  - Nearly the entire cohort of children aged 13–17 years assessed in 2017, living in states where vaccination was recommended in 2006, were not yet subject to the routine recommendation for childhood vaccination
  - 40% of states have a daycare or school mandate, or both, for HepA vaccination in 2018, increasing over time from hepatitis A vaccine introduction
  - 27 of 30 state immunization information systems (IIS) already routinely forecast hepatitis A vaccine as being due for an 18 year old who has never been vaccinated (American Immunisation Registry Association)
- HIV as a risk group for increased Hepatitis A virus infection severity
  - When persons with HIV(PWHIV) are co-infected with hepatitis A virus infection, they experience higher peak hepatitis A virus viral loads and a prolonged duration of hepatitis A viremia than persons without HIV infection
  - PWHIV usually respond to hepatitis A vaccination, particularly when the CD4 cell count is >200cells/mm3 and the PWHIV has a low HIV RNA viral load
  - HIV co-infection outbreak data is available for a limited number of outbreak associated states, indicating excess risk of PWHIV to hepatitis A virus infection in those states
  - Data from the medical monitoring project also indicates substantial hepatitis A virus infection among PWHIV
- Epidemiology of hepatitis A infections
  - Asymptomatic children were associated with hepatitis A virus transmission in past outbreaks
  - Recent outbreaks now primarily affect adults, causing severe disease
    - Hepatitis B, hepatitis C co-infection
    - Many cases among persons who use drugs or persons experiencing homelessness: person-to-person contact– crowding, poor hygiene; estimated tens of millions of dollars in healthcare costs
    - Men who have sex with men
  - Person-to-person spread is now the predominant mode of hepatitis A virus transmission
  - Sporadic foodborne outbreaks continue to occur
- Immunogenicity of hepatitis A vaccines
  - All licensed vaccines are highly immunogenic when administered to children and adolescents according to multiple schedules
    - 97%–100% of persons aged 2–18 years had protective levels of antibody 1 month after receiving the first dose
    - 100% had protective levels 1 month after the second dose, with high geometric mean titres
  - All licensed vaccines are highly immunogenic in persons aged >18 years when administered according to the recommended schedules
    - Protective antibody levels were identified in 94%–100% of immunocompetent adults one month after the first dose
    - After the second dose, all persons had protective levels of antibody, with high geometric mean titres
- Immunogenicity – long-term protection

- Anti-hepatitis A virus has been shown to persist in vaccine recipients for at least 22 years in adults administered inactivated vaccine as children with a three-dose schedule
- At least 20 year anti-hepatitis A virus persistence was demonstrated among adults vaccinated with a two-dose schedule as adults
- Detectable antibodies are estimated to persist for 40 years or longer based on mathematical modelling and anti-hepatitis A virus kinetic studies
- Protection following natural infection is lifelong and may also be following vaccination

- Hepatitis A vaccine safety
  - In pre-licensure trials, adverse reactions to HAVRIX, VAQTA and TWINRIX were mostly injection site reactions and mild systemic reactions
  - Postmarketing surveillance for adverse events following receipt of HepA vaccines performed primarily by two systems in the U.S.: the Vaccine Adverse Event Reporting System (VAERS) and the Vaccine Safety Datalink (VSD)
    - No unusual or unexpected safety patterns observed for any hepatitis A vaccines licensed in the U.S.
- ACIP hepatitis A vaccine recommendations: groups at increased risk of hepatitis A or severe hepatitis A virus disease:
  - Persons travelling
  - Men who have sex with men
  - Persons who use injection and non-injection drugs
  - Persons with occupational risk for infection
  - Persons who anticipate close personal contact with an international adoptee
  - Persons experiencing homelessness
  - Persons with chronic liver disease
  - Persons with HIV – *update*
- Proposed routine recommendations for children:
  - ACIP recommends hepatitis A vaccination for all children aged 12–23 months
  - ACIP recommends that all children and adolescents aged 2 through 18 years who have not previously received hepatitis A vaccine be vaccinated at any age (i.e., children and adolescents are recommended for catch-up vaccination)
- Policy question: Should hepatitis A catch-up vaccination be recommended for children aged 2–18 years?
- Evidence to Recommendations (EtR) for hepatitis A catch-up vaccination for children aged 2–18 years
  - Criteria 1: Is the problem of public health importance? Yes
  - Criteria 2: How substantial are the desirable anticipated effects? Large
  - Criteria 3: How substantial are the undesirable anticipated effects? Minimal
  - Criteria 4: Do the desirable effects outweigh the undesirable effects? Favours intervention
  - Criteria 5: What is the overall certainty of this evidence for the critical outcomes? No included studies (GRADE was not used to evaluate the evidence)
  - Criteria 6: Does the target population feel that the desirable effects are large relative to undesirable effects? Probably yes
  - Criteria 7: Is there important uncertainty about or variability in how much people value the main outcomes? Probably no important uncertainty or variability
  - Criteria 8: Is the intervention acceptable to key stakeholders? Probably yes
  - Criteria 9: Is the intervention a reasonable and efficient allocation of resources? Probably yes
  - Criteria 10: Is the intervention feasible to implement? Yes
  - Balance of consequences – Work Group Judgements: Desirable consequences probably outweigh undesirable consequences in most settings
  - There is sufficient information to move forward with a recommendation
  - ACIP recommends the intervention
- Proposed recommendation for persons with HIV: ACIP recommends that all persons with HIV aged ≥1 year be vaccinated with hepatitis A vaccine
- Policy Question: Should routine two-dose* vaccination to prevent hepatitis A virus infection be given to HIV-positive persons? (* or three doses when combination vaccine is used)
- 76% of all persons currently newly diagnosed with HIV have a risk factor for which hepatitis A vaccine is already recommended (male-to-male sexual contact; injection drug use; male-to-male sexual contact and injection drug use)

- Hepatitis A virus infection among PWHIV: among people who a diagnosis of HIV who received outpatient HIV medical care during 2014–2017, the prevalence of a diagnosis of hepatitis A recorded in the medical record at the primary HIV care site during a 2-year period was 0.48% (95% CI= 0.26–0.70)
- What are the costs of vaccinating PWHIV?
  - A formal cost effectiveness analysis was not done for PWHIV as a risk group for HepA vaccination
  - Consider ~400,000 PWHIV, potentially unvaccinated for HepA (assume 50% vaccine uptake)
    - 200,000 × $68 = $13,600,000 (1-dose)
    - 200,000 × $136 = $27,200,000 (2-doses)
    - Vaccine administration fees range from a few dollars up to twenty dollars (best available data)
  - Other considerations:
    - Not all PWHIV will be vaccinated at the same time; cost would be spread out over time
    - Herd protection – vaccination in this high risk population would help disrupt outbreaks
  - In an outbreak response the costs associated including health care expenses and deferred activities is substantial
- Proposed recommendations for persons with HIV (PWHIV)
  - ACIP recommends that all persons with HIV aged ≥1 year be vaccinated with hepatitis A vaccine
- Hepatitis A Virus Infection – Pregnancy and Infancy
  - Review published data on hepatitis A during pregnancy
    - Associated with gestational complications (e.g. preterm labour placental abruption, premature rupture of membranes)
    - Infants born to mothers with hepatitis A virus infection are healthy (rare exceptions)
    - No increased risk of maternal or infant mortality after hepatitis A vaccination in pregnancy
- Vaccine Adverse Event Reporting System (VAERS) Study 2014 – Hepatitis A vaccination in pregnancy
  - Conclusion: This review of VAERS reports did not identify any concerning pattern of adverse events in pregnant women or their infants following maternal HepA or HepAB immunisations during pregnancy
    - Vaccine Safety Datalink (VSD) – ongoing retrospective cohort study
  - Among pregnancies ending in live births, HepA vaccine was not associated with common maternal and infant adverse events, but a potential signal for small for gestational age (SGA) births was identified)
  - The observed effect size for SGA was an absolute difference of 4% (12.3% vs. 8.3%)
    - General US prevalence estimates for SGA are approximately 10%, and up to 14% among women of Asian race (who comprised 30% of the vaccine exposed group in the study)
  - The investigators and the work group considered that this SGA finding was likely due to unmeasured confounding, and unlikely to be clinically meaningful
  - Publication of this paper is expected later this year
    - Proposed hepatitis A vaccine recommendation for pregnant women:
  - ACIP recommends that:
    - Pregnant women who are identified as being at risk for HAV infection during pregnancy or for having a severe outcome from hepatitis A virus infection (e.g., travellers, persons who use injection and non-injection drugs, persons who have occupational risk for infection, persons who anticipate close personal contact with an international adoptee, persons experiencing homelessness, persons with chronic liver disease, PWHIV) should be vaccinated during pregnancy if not previously vaccinated
      Pregnant women who are not vaccinated against HAV infection during pregnancy should be counselled concerning other methods to prevent HAV infection
- Clinical Factor Disorders– Proposed Removal of Recommendation
  - Persons who have clotting-factor disorders have been recommended to receive the HepA vaccination since 1996
  - However, the risk of hepatitis A virus infection has decreased over time, and the risk for viral transmission for persons with clotting factor disorders is considered the same as that for the general population
- No case studies of hepatitis A infections among U.S. persons with clotting factor disorders were found in the literature in the last 20 years
- Work group considerations:
  - Secondary virus reduction steps are now common instead of solvent-detergent treated

- Many of the clotting factors now in use are recombinant factors
- Source plasma is now screened for hepatitis A virus
- No longer a specific risk of HAV infection associated with clotting factor disorders; therefore this group may be removed from consideration as part of a high risk population for whom HepA vaccination is specifically recommended.

- Proposed Hepatitis A vaccine recommendations
  - ACIP recommends that all children and adolescents aged 2 through 18 years who have not previously received hepatitis A vaccine be vaccinated at any age (i.e., children and adolescents are recommended for catch-up vaccination)
  - Removal of persons with clotting factor disorder as a recommended risk group for hepatitis A vaccination
  - ACIP recommends that all persons with HIV aged ≥1 year to be vaccinated with hepatitis A vaccine
  - ACIP recommends that persons with chronic liver disease (including, but not limited to, persons with hepatitis B virus infection, hepatitis C virus infection, cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, and an alanine aminotransferase [ALT] or aspartate aminotransferase [AST] level greater than twice the upper limit of normal) should be routinely immunized against hepatitis A.
  - ACIP recommends that pregnant women who are identified as being at risk for HAV infection during pregnancy or for having a severe outcome from HAV infection (e.g., travellers, persons who use injection and non-injection drugs, persons who have occupational risk for infection, persons who anticipate close personal contact with an international adoptee, persons experiencing homelessness, persons with chronic liver disease, PWHIV) should be vaccinated during pregnancy if not previously vaccinated.
  - ACIP recommends pregnant women who are not vaccinated against HAV infection during pregnancy should be counselled concerning other methods to prevent HAV infection
  - Implementation Strategies: Settings Providing Services to Adults
    - Settings in which a high proportion of persons have risk factors for HAV infection (e.g., health care settings targeting services to people who use injection or non-injection drugs, group homes and non-residential day care facilities for developmentally disabled persons). A health care provider (HCP) may assume that unvaccinated adults age ≥19 years are at risk for HAV infection and offer hepatitis A vaccination without individual risk-factor screening if they have not previously completed vaccination
    - Hepatitis A vaccination may be offered in outreach and other settings in which services are provided to persons at risk for HAV infection (e.g., homeless shelters, syringe service programs)
    - HCP should consider implementing standing orders to identify adults recommended for hepatitis A vaccination and administer vaccination as part of routine services
    - Vaccination of staff should be considered in facilities where hygiene is difficult to maintain (e.g., group homes for developmentally disabled)
  - Recommendations for Hepatitis A Vaccination During an Outbreak
    - ACIP recommends that all unvaccinated children aged ≥1 year and adults age ≥9 years who are at risk for HAV infection (e.g., persons who use injection or non-injection drugs, persons experiencing homelessness) should receive one dose of hepatitis A vaccine during a hepatitis A outbreak
    - ACIP recommends that in the event of a community outbreak propagated by person-to-person transmission, public health officials should consider recommending administration of pre-exposure hepatitis A vaccination in close congregate settings providing services to high risk persons in the vicinity of the outbreak (e.g., persons incarcerated in correctional facilities, health care settings targeting services to people who use injection or non-injection drugs, homeless shelters, syringe service programs) dur to the risk of an outbreak in these settings and increased risk of HAV infection among persons in these settings
  - Pre-vaccination serologic testing (update)
    - Pre-vaccination serologic testing for hepatitis A immunity prior to vaccination is not recommended, but may be considered in specific settings as a way to reduce costs by not vaccinating persons who are already immune
    - Pre-vaccination serologic testing should not be a barrier to vaccination of susceptible persons, especially in populations that are difficult to access

        - If pre-vaccination serologic testing is performed, commercially available tests for total anti-HAV or IgG anti-HAV should be used
        - In population that are expected to have high rates of previous HAV infection, vaccination history should be obtained where feasible prior to testing or vaccination
        - Vaccinations should not be postponed if vaccination history cannot be obtained, if records are unavailable or if pre-vaccination testing is not feasible
    - Post-vaccination serologic testing (update)
        - Testing for the presence of anti-HAV antibody after vaccination is recommended for the persons who subsequent clinical management depends on knowledge of their immune status: PWHIV, and other immunocompromised persons (e.g., hematopoietic stem-cell transplant recipients, persons receiving chemotherapy)
        - Testing should be performed at least one month after administration of the final dose of the vaccine series with total anti-HAV or IgG anti-HAV assays
        - Persons who do not respond immunogenically to vaccination should be considered susceptible to HAV infection and counselled about precautions to prevent HAV infection and the need to obtain IG post-exposure prophylaxis for any known or likely exposure to a HAV infection
    - Revaccination
        - Re-vaccination (i.e., booster dose, challenge dose, or revaccination with a complete series) is not generally recommended for persons with a normal immune status who were vaccinated as infants, children or adults
        - Anti-HAV long-term persistence studies do not indicate a need for additional hepatitis A vaccine doses beyond the 2-dose primary vaccine series or 3-dose series if combination Hepatitis A-Hepatitis B vaccine was administered
        - For other immunocompromised persons (e.g., PWHIV, haematopoetic stem-cell transplant recipients, persons receiving chemotherapy), the ACIP has no specific guidance because limited data are available to determine the need for booster doses or revaccination with a complete series
- Proposed votes
    - ACIP recommends that all children and adolescents aged 2 through 18 years who have not previously received hepatitis A vaccine by vaccinated at any age (i.e., children and adolescents are recommended for catch-up vaccination)
        - **All members voted YES – PASS**
    - ACIP recommends that all persons with HIV aged ≥1 year be vaccinated with hepatitis A vaccine
        - **All members voted YES – PASS**
    - ACIP affirms the updated statement "Prevention of Hepatitis A Virus Infection in the United States: Recommendations of the Advisory Committee on Immunisation Practices"
        - **All members voted YES – PASS**

Meningococcal

- Meningococcal disease outbreaks
    - College students are at increased risk for serogroup B meningococcal disease and outbreaks
    - Current MenB vaccination coverage among adolescents is low (~15% of 17 year olds received ≥1 dose in 2017) but has steadily increased since vaccine licensure
    - 5 cases reported in persons who received ≥1 MenB dose to-date:
        - MenB-4C: 3 fully vaccinated, 1 partially vaccinated
        - MenB-FHbp: 1 partially vaccinated
- MenB booster doses and the rationale for today's vote
    - Although incidence of serogroup B meningococcal disease is low in the United States, a small group of individuals is at substantially elevated risk
    - ACIP recommended a MenB primary series for persons at increased risk 4 years ago.
        - Evidence presented to ACIP in February 2019 suggests waning immunity within 1–2 years
    - Serogroup B outbreaks among college students continue to occur.
        - 1 university implemented off-label/ACIP booster dose recommendations to-date.
    - No further data expected from manufacturers
        - Additional data on MenB effectiveness and duration of protection in adolescents/adults or U.S. populations may take years to generate.
- Persistence of MenB primary series against diverse serogroup B strains

  - Short-term persistence of MenB primary vaccination against diverse serogroup B strains has been assessed in several observational studies
    - Variable patterns of short-term persistence when measured up to 12 months post-vaccination
  - Seroprevalence study at Princeton University: substantial antibody waning to outbreak strain by 20 months post-vaccination with MenB-4C
- Summary of Work Group interpretation for persistence of immune response following a MenB primary series
  - Variable rate of waning observed between vaccine type and studies
  - Results from clinical trials cannot be directly compared between vaccine types
  - By 1–2 years following primary MenB vaccination, booster vaccination is indicated in persons who remain at increased risk
- Work group interpretation for persistence of immune response following a MenB booster dose:
  - Antibody persistence of a MenB booster dose is likely at least 2–3 years in healthy adolescents and adults
- Policy questions: Should persons vaccinated with a MenB primary series who remain at increased risk for serogroup B meningococcal disease receive a MenB booster dose?
- Evidence to recommendations framework: key considerations for persons at increased risk due to underlying conditions or microbiologists
  - Small group (<0.1% of U.S. population) at substantially increased risk
  - Persons with complement deficiency or complement inhibitor use have reduced MenB immunogenicity and may be at risk despite vaccination
  - MenB primary series safety demonstrated in several large evaluations in healthy persons
    - Booster doses (included repeated doses) not assessed in persons with underlying conditions
  - Survey: majority of paediatricians and family physicians would recommend MenB primary series for children aged ≥10 years at increased risk, though disparity by provider type
  - No data on cost-effectiveness
- Evidence to recommendations framework: key considerations for persons at increased risk due to a serogroup B meningococcal disease outbreak
  - 7% of serogroup B cases in the United States are outbreak-related.
    - Quebec: menB-4C 79% (95% CI: -231 to 99%) effective in persons age <20 years up to 4 years
  - Evidence suggests no impact of MenB on meningococcal carriage; herd immunity unlikely
  - Evaluations following mass vaccination campaigns during outbreaks have demonstrated the safety of MenB primary series
  - Low certainty of evidence
- Summary of Work Group deliberations for MenB booster policy options in persons at increased risk for serogroup B meningococcal disease
  - The Work Group reviewed data on:
    - Persistence of the immune response following a MenB primary series
    - Immunogenicity, persistence, and safety of a MenB booster dose
    - Results of GRADE and EtR evaluations
  - The majority of Work Group members agreed upon the need for and timing of MenB booster doses
    - A small minority felt that was insufficient evidence on safety and efficacy of MenB booster doses to inform policy options
- Work Group interpretation: Need for and timing of MenB booster doses
  - Men B booster vaccination is necessary to sustain protection against serogroup B meningococcal disease in persons who remain at increased risk
  - MenB booster dose is indicated at 1 year following completion of the primary series
    - Greater persistence is expected after the booster dose, and thus, a longer interval for repeat booster doses may be considered
  - Given the serious nature of meningococcal disease, potential benefits of MenB booster vaccination outweigh risks in person at increased risk
  - Although implementation challenges are anticipated, potential benefits of booster vaccination justify the additional implementation efforts that will be needed
- Policy proposal for MenB booster doses in persons at increased risk
  - Proposal: ACIP recommends MenB booster vaccination in persons aged ≥10 years at increased risk for serogroup B meningococcal disease who previously completed a MenB primary series

- This recommendation does not apply to persons who previously completed a MenB primary series as an adolescent based on individual clinical decision-making and who are not at increased risk for serogroup B meningococcal disease

- Current ACIP recommendations for MenB vaccines
  - In February 2015, ACIP recommended that persons aged ≥10 years at increased risk for serogroup B meningococcal disease receive a MenB primary series (Routine)
    - Includes persons with complement deficiency, complement inhibitor use, asplenia, microbiologists and individuals exposed during an outbreak
  - In June 2015, ACIP recommended that adolescents aged 16–23 years may be vaccinated with a MenB primary series based on individual clinical decision-making (preferred age of 16–18 years) (Clinical Decision Making).
- Proposed language for VOTE #1
  - For persons aged ≥ 10 years with complement deficiency, complement inhibitor use, asplenia, or who are microbiologists: ACIP recommends a MenB booster dose 1 year following completion of a MenB primary series followed by MenB booster doses every 2–3 years thereafter, for as long as increased risk remains
    - **All members voted YES – PASS**
  - For persons aged ≥ 10 years determined by public health officials to be at increased risk during an outbreak: ACIP recommends a one-time booster dose if it has been ≥1 year since completion of a MenB primary series. A booster dose interval of ≥ 6 months may be considered by public health officials depending on the specific outbreak, vaccination strategy, and projected duration of elevated risk
    - **All members voted YES – PASS**
- Additional Guidance
  - These recommendations do not apply to persons who previously completed a MenB primary series as an adolescent based on individual clinical decision-making and who are not at increased risk for serogroup B meningococcal disease
  - MenB vaccines are not interchangeable. The same product must be used for all doses
  - Collection of safety and effectiveness data for repeated booster doses of MenB vaccine in persons at increased risk for serogroup B meningococcal disease is needed for the ongoing evaluation of these recommendations by the ACIP
- Updated ACIP statement for meningococcal vaccination in the United States: Key changes
  - All existing MenACWY and MenB recommendations, as well as the proposed new recommendation for MenB booster doses, in a single document
  - Previous 'Category B' language for Men B primary vaccination in adolescents updated to "ACIP recommends a MenB primary series for individual aged 16–23 years based on shared clinical decision-making."
  - Appendices with guidance for chemoprophylaxis of close contacts and management of outbreaks no longer part of ACIP statement

Dengue

- ACIP Dengue Vaccines Work Group: Considerations and Next Steps
  - FDA Vaccine Indication
    - Persons 9–16 years of age with laboratory-confirmed previous dengue infection and living in an endemic areas
  - Policy questions for EtR: Should 3-doses of CYD-TDV (Dengvaxia) be administered routinely to persons 9–16 years of age with laboratory-confirmed previous dengue infection and living in endemic areas to prevent virologically confirmed dengue, hospitalisations and severe dengue?
  - Summary of dengue epidemiology in the U.S.
    - Dengue viruses cause increasing morbidity and mortality worldwide
    - Frequent or continuous risk for dengue in Puerto Rico, U.S. Virgin Islands and American Samoa, and some affiliated Pacific island nations
    - Limited U.S. age specific seroprevalence data: predictive value of positive IgG laboratory tests increases as prevalence increases (fewer false positives); prevalence is an important variable in cost effectiveness modelling
  - Key points on dengue disease severity

        - Severe illness can occur in infants, children and adults
        - Severe dengue often manifests as a leaky capillary syndrome which can lead to shock and death
        - Severe illness can also manifest with severe haemorrhage and/or severe organ impairment (liver, CNS, heart and other)
        - Secondary dengue infections are an established risk factor for dengue shock syndrome
        - Moderate levels of heterotypic antibody from a primary dengue infection are associated with severe disease
- Summary of CYD-TDV (Dengvaxia) efficacy and safety issues
    - Overall VE ~75% (60–85%) against VCD in seropositive 9–16 year olds
        - Increased protection against hospitalisation and severe disease
        - Protection against all four DEN serotypes (highest for DEN4)
    - Higher risk of hospitalisation and severe dengue in seronegatives – Hazard ratio for hospitalisation 1.41
        - Cumulative incidence 1.57% in vaccinated, 1.09% in controls; attributable risk, 0.48%
    - Safety profile data in vaccines and controls comparable
- Dengue virus vaccines work group discussions to date:
    - ACIP Dengue Vaccines Workgroup October 2018 to present:
        - CYD-TDV Phase III trials including long term follow up and imputed pre-vaccination serostatus analysis
        - Epidemiology of endemic dengue in the U.S.
        - Published dengue vaccine cost-effectiveness studies
        - Clinical dengue and disease severity
        - Review of EtR and GRADE framework
        - Dengue diagnostics and available IgG screening tests, target product profile
        - CYD-TDV safety and pharmacovigilance
- Available Lab Tests for Pre-Vaccination Screening
    - Systematic review of 4 rapid diagnostic tests (RDTs) by WHO (Luo et al., 2019)
        - Diagnostic tests have not been cleared by the FDA, but available in other parts of the world
        - Sensitivity ranges from 30–60%
        - Specificity ranges from 65-100% with wide confidence intervals
    - CDC landscape analysis of commercial tests including IgG ELISA tests and RDTs
    - Available tests not designed nor evaluated for detection of past infection
    - Need to evaluate tests with panels that include co-circulating flaviviruses (especially Zika virus) and flavivirus vaccinations
    - Sanofi evaluation of three lab tests available in Puerto Rico and American Samoa
- WHO Screening Test Target Product Profile Project
    - RDT, fingerstick whole blood, low cost
    - Minimum sensitivity and specificity, ≥90%
    - Description of minimal and optimal reference panel characteristics
      Optimal panel would include samples:
        - Virologically confirmed dengue at varying time points after acute infection
        - Dengue and flavivirus negatives
        - Previous flavivirus infected at varying time points
        - Dengue and previous flavivirus at varying time points
        - Variety of flavivirus vaccine recipients
- Dengue Virus Vaccines Workgroup Discussion Schedule for rest of 2019
    - Dengvaxia cost effectiveness studies
    - Acceptability
    - Implementation issues
    - GRADE analysis
    - Updates on screening laboratory tests
    - Draft recommendations
- Important Considerations in Making Recommendations on CYD-TDC (Dengvaxia)
    - Overall cost effectiveness given the unique need for pre-vaccination screening and the profile of available screening tests

- Will more complete evaluations of available laboratory tests be done and improved screening tests by available soon?
- Take into account any new seroprevalence data
- Target population acceptance and informed consent
- Feasibility and logistics of pre-vaccination screening
- Programmatic – school age target population

1.2 Newly published or updated recommendations

1.2.1 Japanese Encephalitis Vaccine: Recommendations of the Advisory Committee on Immunisation Practices

- Published in MMWR 19 July - https://www.cdc.gov/mmwr/volumes/68/rr/rr6802a1.htm
- This reports updates the 2010 recommendations from the CDC Advisory Committee on Immunization Practices (ACIP) regarding prevention of Japanese encephalitis among U.S. travelers and laboratory workers
- Recommendations for the Prevention of JE among U.S. travelers:
  - JE vaccine is recommended for persons moving to a JE-endemic country to take up residence, longer-term (e.g., ≥1 month) travellers to JE-endemic areas, and frequent travellers to JE-endemic areas
  - JE vaccine should also be considered for shorter-term (e.g., <1 month) travellers with an increased risk for JE based on planned travel duration, season, location, activities, and accommodations
  - Vaccination should be considered for travellers to JE-endemic areas who are uncertain of specific duration of travel, destinations, or activities
  - JE vaccine is not recommended for travellers with very low-risk itineraries, such as shorter-term travel limited to urban areas or travel that occurs outside of a well-defined JE virus transmission season
- Recommendations for the Prevention of JE Among Laboratory Workers
  - Vaccination is recommended for all laboratory workers with a potential for exposure to JE viruses other than SA14-14-2 JE vaccine virus
  - Vaccination generally is not required for those who work only with SA14-14-2 JE virus; however, for those working with SA14-14-2 virus at high concentrations or volumes, or passaging virus, individual risk assessments with consideration of biosafety level and vaccination should be undertaken by a local biosafety committee
  - Vaccination is not required for workers handling routine clinical samples

1.2.2 Human Papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practice

- Published in MMWR 16 August 2019 - https://www.cdc.gov/mmwr/volumes/68/wr/mm6832a3.htm
- This report updates ACIP catch-up HPV vaccination recommendations and guidance published in 2014, 2015 and 2016
- In June 2019, ACIP recommended catch-up HPV vaccination for all persons through age 26 years. ACIP did not recommend catch-up vaccination for all adults aged 27 through 45 years, but recognized that some persons who are not adequately vaccinated might be at risk for new HPV infection and might benefit from vaccination in this age range; therefore, ACIP recommended shared clinical decision-making regarding potential HPV vaccination for these persons
- Summary of Key Findings:
  - Vaccine efficacy and safety
    - Overall evidence on benefits and harms were of GRADE evidence level 2 – moderate-quality evidence
  - HPV burden of disease and impact of the vaccination program in the United States
    - Coverage with ≥1 dose of HPV vaccine was 65.5% among adolescents aged 13 through 17 years
    - Declines in prevalence of vaccine type HPV infections, anogenital warts, and cervical precancers
    - Declines among unvaccinated persons have been observed, suggesting protective herd effects

- Rationale:
  - Adolescents remain the most important focus of the HPV vaccination program in the United States
  - Recommendations harmonized across genders will simplify the immunization schedule and be more feasible to implement
  - Exposure to HPV decreases among older age groups
  - Evidence suggests that although HPV vaccination is safe for adults aged 27 through 45 years, population benefit would be minimal

1.2.3 Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2019–20 Influenza Season

- Published in MMWR August 23, 2019- https://www.cdc.gov/mmwr/volumes/68/rr/rr6803a1.htm
- This report focuses on the recommendations for use of vaccines for the prevention and control of influenza during the 2019–20 season in the United States
- Inactivated influenza vaccines, recombinant influenza vaccine, and live attenuated influenza vaccine are expected to be available for the 2019–20 season
- Standard-dose, unadjuvanted, inactivated influenza vaccines will be available in quadrivalent formulations (IIV4s). High-dose (HD-IIV3) and adjuvanted (aIIV3) inactivated influenza vaccines will be available in trivalent formulations. Recombinant (RIV4) and live attenuated influenza vaccine (LAIV4) will be available in quadrivalent formulations
- Routine annual influenza vaccination of all persons aged ≥ 6 months who do not have contraindications continues to be recommended
- No preferential recommendation is made for one influenza vaccine product over another for persons for whom more than one licensed, recommended, and appropriate product is available
- For persons aged ≥65 years, any age-appropriate IIV formulation (standard dose or high dose, trivalent or quadrivalent, unadjuvanted or adjuvanted) or RIV4 are acceptable options

1.3 New or updated recommendations – not yet published

ACIP approved the following recommendations by majority vote at its June 2019 meeting. These recommendations have been adopted by the CDC Director and will become official once published in MMWR. Information available on https://www.cdc.gov/vaccines/acip/recommendations.html

- **Human Papillomavirus (HPV) Vaccine**
  - ACIP recommends catch-up vaccination for persons through age 26 years who are not adequately vaccinated
  - ACIP recommends vaccination based on shared clinical decision making for individuals aged 27 through 45 years who are not adequately vaccinated. HPV vaccines are not licensed for use in adults older than age 45 years
- **Pneumococcal Vaccines**
  - ACIP recommends PCV13 based on shared clinical decision making for adults 65 years or older who do not have an immunocompromising condition and who have not previously received PCV13. All adults 65 years or older should receive a dose of PPSV23.
- **Influenza Vaccines**
  - ACIP recommends annual influenza vaccination is recommended for all persons aged 6 months and older who do not have contraindications.
- **Hepatitis A Vaccines**
  - ACIP recommends that all children and adolescents aged 2 through 18 years who have not previously received Hepatitis A vaccine be vaccinated routinely at any age (i.e., children and adolescents are recommended for catch-up vaccination).
  - ACIP recommends all persons with HIV aged ≥1 year be routinely vaccinated with Hepatitis A vaccine.
- **Serogroup B Meningococcal (MenB) Vaccines**
  - For persons aged ≥10 years with complement deficiency, complement inhibitor use, asplenia, or who are microbiologists:

- ACIP recommends a MenB booster dose 1 year following completion of a MenB primary series followed by MenB booster doses every 2-3 years thereafter, for as long as increased risk remains.

- For persons aged ≥10 years determined by public health officials to be at increased risk during an outbreak:
  - ACIP recommends a one-time booster dose if it has been ≥1 year since completion of a MenB primary series.
  - A booster dose interval of ≥6 months may be considered by public health officials depending on the specific outbreak, vaccination strategy, and projected duration of elevated risk.

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2 Immunisation Advisory Centre (IMAC), New Zealand

2.1 PTAC Considerations

Meeting on 23–24 May 2019 – https://www.pharmac.govt.nz/assets/ptac-minutes-2019-05.pdf

- There were no vaccine-specific considerations at this meeting
- Minutes of the Immunisation Subcommittee meeting on 8 March 2019 were reviewed (see below)

2.2 Immunisation Subcommittee Meeting: 8 March 2019

- Minutes of the meeting –

https://www.pharmac.govt.nz/assets/ptac-immunisation-subcommittee-minutes-2019-03.pdf

Meningococcal ACWY (MenACWY) vaccine

- The subcommittee reviewed a paper from PHARMAC regarding the funding of MenACWY vaccine for: inclusion in the Pharmaceutical Schedule; adolescents aged 13-19 years; and adolescents aged 13-19 years in close living circumstances
- The Subcommittee made the following recommendations:
  - A single dose of MenACWY vaccine for children 1 year of age with a high priority, with a one year catch up programme for children 1 to 4 years of age
  - A single dose of MenACWY vaccine with a high priority at 14 years of age
  - A single dose of MenACWY vaccine for a one year catch up for adolescents and young adults. (PHARMAC staff to model catch up options for 5 to 21 years of age or 13 to 21 years of age)
  - A single dose of MenACWY vaccine with a high priority for individuals 13-25 years of age who are entrants into close living situations with a one year catch up for individuals 13-25 years of age in close living situations
- The following points were noted:
  - Over the last 5 years, a MenACWY vaccine would have covered twice as many isolates of *N. meningitidis* as targeting MenC alone
  - The UK have about half the rate of meningococcal disease of New Zealand, and other developed countries also have lower incidence rates than New Zealand: request PHARMAC consider modelling data to predict fluctuations in meningococcal disease cases following implementation of a MenACWY vaccine programme

Meningococcal B (MenB) vaccine

- The subcommittee reviewed a paper from PHARMAC regarding the funding of MenB for infants with a 2+1 dosing schedule in the Pharmaceutical Schedule, adolescents in close living situations, special groups (immunocompromised) and close contacts of cases
- The Subcommittee made the following recommendations:
  - MenB be listed with a low priority for infants with a 2+1 dosing schedule

- MenB be listed with a high priority for special groups (immunocompromised people as defined by the current meningococcal ACWY access criteria)
- MenB be listed with a medium priority for close contacts of meningococcal B cases and people who have previously had meningococcal disease of any group
- MenB be listed with a high priority for adolescents and young adults aged 13-25 years in close living situations, with a one year catch up programme

- The following points were noted:
  - MenB still accounts for the majority of New Zealand cases: considered the case fatality rate for invasive meningococcal disease be close to 4-6% in New Zealand
  - Immunisation rates for the 6 week visit were below the Ministry of Health's 95% target, and any issues with the reactogenicity of 4CMenB could adversely affect coverage
  - If 4CMenB was added to the childhood immunisation schedule, doses would be administered at 6 weeks, 3 months and in the second year of life. This would require an additional immunisation visit, probably at 12 months
  - Very high cost of 4CMenB vaccination and high cost of implementation to support such a programme

Vaccine RFP 2019

- The Subcommittee considered a paper from PHARMAC regarding the Request for Proposals (RFP): possible changes to funded vaccines that could occur from July 2020 as a result of the RFP
- The Subcommittee recommended that an additional dose of hexa-valent DTaP-IPV-HepB/Hib at 15 months of age instead of the current Hib vaccine with a high priority
  - Considered additional pertussis dose given at the 15 month visit would provide additional protection in the context of the ongoing pertussis outbreak and possible waning immunity before the next pertussis dose is given at 4 years of age
  - Hib only vaccine would need to remain listed for older children, adolescents and adults at high risk who cannot receive a combined vaccine

2.2.1 Other updates

- Boostrix now recommended from 16 weeks of every pregnancy preferably within the second trimester, but at least two weeks prior to birth - https://www.immune.org.nz/hot-topic/boostrix-now-recommended-16-weeks-every-pregnancy
- https://www.immune.org.nz/sites/default/files/resources/Written%20Resources/ProgrammePregnancyImac20190712V01Final.pdf
- PHARMAC announces Immunisation Schedule from 1 July 2020: https://www.immune.org.nz/hot-topic/pharmac-announces-immunisation-schedule-1-july-2020
- Measles overseas and in New Zealand - https://www.immune.org.nz/hot-topic/measles-overseas-and-new-zealand

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

3.1 JCVI Meeting: 5 June 2019

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

This summary was based on the draft minutes only

Coverage and attitudinal research

- The committee noted the latest coverage data from across the UK. All four countries reported on a small decline in uptake of infant vaccines over the preceding few quarters.

- The potential reasons for the small decline in coverage was likely to vary across the country, but changes in the delivery of primary care, the variable availability of call/recall systems and recruitment issues were all cited as possible contributory factors
- The uptake of maternal vaccines was reported to be good in all countries
- Shingles vaccine uptake continued to be low with between 40 and 50% of those eligible receiving the vaccine

Pneumococcal update

- The Committee considered an update on the pneumococcal programme and the Chair provided background on the programme and deliberations regarding the Committee's advice on a 1+1 childhood pneumococcal conjugate vaccination schedule using PCV13
- The Committee noted that in 2006 the PCV7 vaccine had been introduced as a 2+1 schedule. The programme had moved to the use of PCV13 vaccine in 2010. Overall, the UK was considered to have good control of PCV13 vaccine-type disease.
- In October 2017, the Committee had advised a move to a 1+1 schedule in the UK.
    - The change was confirmed by both the Minister for Public Health and Primary Care and Secretary of State for Health in April 2019
- PHE had continued to review and evaluate the likely impact of the switch to 1+1 and provided the Committee with a presentation on the latest findings. The Committee noted that:
    - when comparing post-booster dose IgG declines over time between 1+1 and 2+1 schedules, there were some serotypes which showed faster waning with the 1+1 schedule compared with the 2+1 schedule
    - waning of IgG antibody levels post-booster would not necessarily translate to a reduction in carriage protection post-booster
    - epidemiological evidence indicated protection against IPD persisted for many years post-booster, despite rapid waning of IgG levels post-booster
    - it was noted that although PPV23 vaccine produced IgG antibodies, vaccination had no impact on carriage
    - however, to explore the potential impact of these findings, PHE modelled faster waning of protection post-booster under a 1+1 schedule, using 'extreme' assumptions of duration of protection against carriage of 3 years for 1+1 and four years for a scenario where the 1st dose provides no protection against carriage or IPD compared with 5 years for the 2+1 schedule
    - under these 'extreme' assumptions of more rapid waning of protection post-booster with the 1+1 than the 2+1 schedule there was predicted to be little impact on additional IPD cases in the first five years of the programme
- The Committee noted that using a direct calculation method for additional vaccine type cases in infants, the results indicated
    - there had continued to be a decline in VT IPD in the UK (excluding serotype 3)
    - the expected number of cases with a 1+1 compared with a 2+1 schedule had been calculated using the recent VT IPD incidence, vaccine coverage and one and two dose effectiveness data, in those aged 4-14 months
    - using epidemiological data from year 2017/18, which most closely reflected recent changes, the calculation estimated only an additional 1.3 cases per year, in those aged 4-14 months, compared with the number of cases predicted if continuing with a 2+1 schedule
    - with the continued decrease in VT serotypes, it was expected this additional number of cases would continue to decline with a switch to 1+1
- The Committee agreed that the evidence presented, while of interest, provided no rationale for any change to their advice on use of a 1+1 schedule in the UK

Review of the maternal pertussis program

- The Chair reminded the Committee that in 2012 there had been an increase in pertussis disease in the population, including disease and deaths in infants too young for vaccination. The Committee had advised that an emergency maternal pertussis immunisation programme should be put in place
- Rise in pertussis activity had been observed in a number of countries, with the switch from use of whole-cell to acellular pertussis vaccines thought to be an important contributory factor due to

shorter duration of protection from disease and lower efficacy against infection of acellular pertussis vaccines

- It was considered important to note that in the UK there would be an increasing number of children who had been primed and boosted with acellular vaccines, and modelling predictions had suggested that levels of pertussis activity would remain higher going forward, when compared with pre-2012 levels
- The Committee agreed that the maternal programme had been highly successful and there had been a substantial impact on disease
    - the latest evaluation on vaccine coverage indicated that coverage using routine data sources was around 60% in the first few years of the programme, with slightly higher levels in the winter months
    - showed high levels of protection for infants whose mothers were vaccinated at least one week prior to delivery (91-93%);
    - three years after the start of the programme, showed that effectiveness remained high at around 91%
- The Committee advised that the emergency maternal programme should continue as a routine programme

Influenza

- Committee received an overview of the 2018/19 flu season from PHE and noted
    - influenza A(H1N1)pdm09 was the was the dominant subtype in circulation followed by A(H3N2) with virtually no influenza B
    - there had been a good match with the vaccine strain for A(H1N1)pdm09 and most A(H3N2) strains were characterised as belonging to the vaccine like 3C2a subclade
    - towards the end of the season, however, a small number of A(H3N2) subclade 3C3a strains were detected, which would be the subclade of next season's A(H3N2) vaccine
    - in the elderly the phased delivery of the adjuvanted vaccine meant initially a slower rate of uptake, but the final level achieved was 72%, similar to coverage in 2017/18
    - in the childhood program school year five had been added in England. Overall vaccine effectiveness (VE) for the programme was estimated to be 44.4% (95% CI: 26.8-57.7); 45.7 % (29.0- 60.1) and 35.1% (-3.7-59.3) for all flu, A(H1N1) and A(H3N2) respectively
    - VE estimates for the egg based quadrivalent vaccine in at risk groups aged 18-64 years were positive but non-significant for both influenza A subtypes for H1N1pdm09 at 67.1 (5.1, 88.6) and lower for AH3N2 at 24.2 (-123.6, 74.3);
    - In children aged 2 to 17 years old, VE for LAIV against all flu and AH1N1 were positive, at 58.6 (-4.4, 74.7) and 49.9 (-14.3, 78.0) respectively, but VE for A(H3N2) was lower and non-significant at 27.1 (-130.5, 77);
- The Committee noted that the US had experienced a late season increase in A(H3N2) subclade 3C3a, which was not contained in the 2018/19 vaccine. VE results from the US showed positive mid-season VE estimates for both A(H1N1)pdm09 and A(H3N2) however the VE estimate for A(H3N2) dropped off by the end of season
- the Committee noted that egg adaptation was likely to be a factor influencing the poor VE against A(H3N2) in those aged 2 to 64 for the egg-based vaccines (QIV and LAIV) in the UK
- Looking ahead for the 2019/20 season the Committee noted that the cell-based quadrivalent vaccine (QIVc) would be available for use in both the elderly and at risk under 65-year olds and the adjuvanted for the over 65-year olds. In addition, the high dose trivalent vaccine (TIV HD), which JCVI had advised as equally suitable to use in the elderly, was now available but was unlikely to be used as the NHS had decided not to reimburse GPs' and pharmacies' costs for this vaccine

Update from the Influenza Sub-committee

- The committee noted that an Influenza Sub-committee had met on 3 June to consider vaccines available for use in an influenza pandemic, and modelling of the impact of vaccination in different groups in different pandemic scenarios (see below)

3.2 Influenza Sub-Committee Meeting: 3 June 2019

- The committee reviewed information and data from manufacturers on their pandemic vaccine candidates to consider their potential for use as part of the UK's pandemic preparedness strategy

Presentation from Manufacturers

GlaxoSmithKline

- The vaccine is comprised of egg grown split pandemic virion antigen combined with adjuvant AS03
- The manufacturer highlighted the advantage of their adjuvanted vaccine in enhancing the immune response with antigen sparing, proven effectiveness in the 2009 pandemic, and manufacturing capacity
- In terms of the timing for the two-dose schedule only a three-week interval had been investigated
- For the avian A(H7N1) and A(H5N1) pre-pandemic vaccines the immunogenicity from one dose was similar to two doses of non-adjuvanted vaccine but not as good as for A(H1N1)pdm09
- The Committee agreed it would be important to review the issue of narcolepsy and potential association with an AS03 adjuvanted pandemic vaccine in more detail, given the potential importance of access to an immunogenic vaccine in the face of a catastrophic pandemic

Seqirus

- There are currently two pandemic vaccines licensed in the UK; Foclivia the pandemic strain matched response vaccine, which is authorised for use in an officially declared pandemic situation; and Aflunov, which is a pre-pandemic A(H5N1) zoonotic vaccine
- Other Seqirus pandemic vaccines licensed elsewhere include an alum-adjuvanted A(H5N1) pandemic vaccine (Panvax, Australia). An MF59-adjuvanted cell culture-based A(H5N1) pandemic vaccine is also under review for licensure in the US

Astra Zeneca

- The pandemic live attenuated influenza vaccine (PLAIV) is based on the nasal spray live attenuated influenza vaccine (LAIV) which has been used seasonally in the UK since 2013 for the childhood flu programme
- The Committee noted that the lower effectiveness of PLAIV A(H1N1pdm09) in adults may have been due to exposure to multiple flu antigens over time and conserved antigen T cell responses and that this might or might not be the case for other PLAIV vaccines

Vivaldi Biosciences

- There is a pandemic vaccine called deltaFLU which is administered intranasally
- So far only phase one and two clinical studies during 2009-2012 using monovalent pre-pandemic A(H5N1) (A/Vietnam/1203/04) and monovalent seasonal A(H1N1) (A/New Caledonia 20/99 and A/Brisbane 59/07) vaccines and a seasonal trivalent vaccine (A/Brisbane 59/07, A/Brisbane 10/07, B/Florida 04/06) have been completed and published

Sanofi Pasteur

- The manufacturer has a global presence and is one of the major suppliers of seasonal influenza vaccines and supplied over 210 million doses of vaccine during the last pandemic
- In addition to their egg-based pandemic vaccines, the manufacturer produces a vaccine that will use a haemagglutinin antigen identical to the pandemic strain and is made using an insect cell culture Baculovirus expression vector system platform
- The vaccine is manufactured without eggs or use of live virus and there are no biohazard safety concerns
- The manufacturer can produce both seasonal and pandemic influenza vaccines based on the Baculovirus expression system platform

Summary of discussion with manufacturers

- Timelines for currently available pandemic vaccines to the UK appear to be five to six months and only egg culture derived products- AS03 and MF59 adjuvanted inactivated vaccines and the live attenuated influenza vaccine look likely to be available for the next few years
- Cell culture/recombinant technologies avoid the issue of egg adaption and have the potential for higher/quicker potential yields. Recombinant technologies bypass some of the safety/security issues related to manufacture as live virus is not used
- Advantages of egg cultured vaccines are that the method is tried and tested and can also provide high yields especially if more than one manufacturer is used

- Some of the challenges in using eggs in manufacturing pandemic vaccines include the range of yields using highly pathogenic avian strains which have to be attenuated and making a master seed that will grow adequately in eggs. Master seeds also have to be shipped to the manufacturers of egg-based vaccines
- The use of adjuvants allows for antigen sparing and broader protection. The issue of safety, however, was an important consideration, given the experience with Pandemrix in 2009 and the potential association of narcolepsy, and the limited data on the use of MF59 in children
- Currently there are no cell culture pandemic products available to the UK and there is no indication when one might be available to the UK
- The Committee agreed it would be helpful to better understand regulatory requirements including what is involved pre-pandemic to get a mock up licence on a formulation, and then what the requirements are for a licence variation in the event of a pandemic, which may differ depending on the type of pandemic vaccine product
- The Committee agreed there was also the need to be more specific in comparing the timelines for production, setting aside regulatory delays, in how long it would take to produce a certain number of doses from a master seed/strain

Pandemic modelling work – PHE

- Committee noted that PHE had been commissioned by DHSC to conduct a modelling study of the health and economic impact of vaccination strategies to support the formulation of advice on influenza pandemic preparedness to the Government
- The Committee noted the following findings
    - a 1918 type pandemic would have a much greater impact on morbidity and mortality than a 2009 type pandemic and the overall impact of both would be reduced by slowing transmission over a two-week period to create a second wave
    - Only a vaccine available at 6 weeks had an impact on incidence reduction during the single wave pandemics modelled. In that scenario an uptake as low as 10% had a substantial reduction in incidence (single dose)
    - with a two wave 2009 type pandemic there would be a small reduction in incidence for a vaccine available at 6 months with a 70% vaccine efficacy
    - A paediatric strategy had the greatest incidence reduction for all pandemic scenarios except a single wave 1918 type pandemic where targeting high risk groups prevented more hospitalisations
    - increasing efficacy to 70% had the largest reduction in all scenarios whilst increasing uptake only really impacts on a 2009 type pandemic
- The Committee noted that a vaccine available at 6 months would only impact on the tail end of a second wave of a 2009 type pandemic starting in October. In general, a vaccine available at 6 months was unlikely to have an impact for most of the scenarios modelled so far
- The Committee noted that PHE planned to look at other pandemic scenarios and conduct sensitivity analyses on a range of factors including, timing of the pandemic, the duration of the pandemic, vaccine effectiveness and age-specific susceptibility
- The Committee noted that based on current manufacturing timescales, vaccination might only be of use in the event of a second wave occurring. Such a scenario could occur naturally with a pandemic starting in March/April, like in the 2009 pandemic, which had two waves interrupted by the school summer holidays, or be forced by population-distancing measures such as mass school closure and/or people staying at home
- The Committee considered that it would be sensible not to have a pandemic preparedness strategy based on vaccine supply from only one manufacturer. Of the products currently available, there was the option to tailor their use to specific groups based on the characteristics of the vaccine

3.3 Newly published or updated statement/recommendations

3.3.1 Updated guidance for UK immunization schedule – Green Book chapter 11

- Updated 16 September 2019 - https://www.gov.uk/government/publications/immunisation-schedule-the-green-book-chapter-11

- Updated with changes to the childhood immunization schedule, including eligibility for the Human Papilloma Virus (HPV) vaccine

3.3.2 Updated guidance for human papillomavirus (HPV) – Green Book chapter 18a

- Updated 12 July 2019 – https://www.gov.uk/government/publications/human-papillomavirus-hpv-the-green-book-chapter-18a
- Updated HPV chapter in preparation for the introduction of the HPV universal program

3.3.3 Updated guidance for typhoid – Green Book chapter 33

- Updated 20 June 2019- https://www.gov.uk/government/publications/typhoid-the-green-book-chapter-33
- Updated chapter to include information on the background and epidemiology of the disease

3.3.4 Updated guidance for varicella – Green Book chapter 34

- Updated 26 June 2019- https://www.gov.uk/government/publications/varicella-the-green-book-chapter-34
- Added link to the updated guidelines on post exposure prophylaxis (PEP) for varicella/shingles: advice for health professionals (June 2019)

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4 National Advisory Committee on Immunization (NACI), Canada

Note: The most recent meeting was conducted 5-6 June 2019 in Ottawa, Ontario; however, the summary of discussions has not yet been released. Summary of discussions was made available for meetings from October 2016 through to February 2019. Decisions and recommendations from February 2018 to February 2019 meetings are summarised below.
https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/immunization/national-advisory-committee-on-immunization-naci.html

4.1 NACI Meetings

4.1.1 February 7-8, 2018, Ottawa, Ontario

Split vs Sub-unit Influenza Vaccine: Rapid Review

- The methodology, results, and conclusions of the literature review on vaccine effectiveness and immunogenicity of subunit versus split virus inactivated influenza vaccine were presented for NACI approval
- The initial database search retrieved 30 records after removal of duplicates; only three of these studies met inclusion criteria. After post-hoc adjustments to the study protocol, 41 unique studies were retrieved from the database search and eight were deemed eligible for inclusion based on the revised eligibility criteria
- Decision: NACI approved the literature review

4.1.2 June 6-7, 2018, Ottawa, Ontario

Meningococcal Working Group

- The literature review methodology and key findings on the efficacy/effectiveness, immunogenicity and safety of Trumenba were presented
- NACI was also presented the draft Statement on 'The Use of Trumenba for the Prevention of Meningococcal B Disease'. The recommendations were approved by NACI

Measles Post-Exposure Prophylaxis (PEP) Recommendations

- The Canadian Communicable Disease Report (CCDR) Summary of the Measles PEP Recommendations was presented for approval. The summary was approved

Afluria Tetra Supplemental Statement

- The supplementary 'Statement on the use of Afluria Tetra in adults and children' was presented for review and comments on the proposed recommendation. The Statement was approved by NACI

4.1.3 September 26-27, 2018 Meeting, Ottawa, Ontario

Ethics, Equity, Feasibility and Acceptability (EEFA) – piloting and framework

- NACI was presented the draft EEFA framework as well as an overview of the next steps, which included obtaining NACI approval to pilot this framework. The framework was approved for piloting

Rabies Working Group (WG)

- NACI approval of the interim guidance to the Department of National Defence (DND) on accelerated rabies pre-exposure prophylaxis (PrEP) regimens was sought. DND is seeking this guidance due to accelerated deployment schedules of its troops. NACI approved the interim guidance
- The WG will begin developing updated recommendations on the use of rabies vaccine for PrEP, post-exposure prophylaxis (PEP), and in the context of PEP, guidance on the use of rabies immune globulin separately once this interim guidance to the DND is completed

4.1.4 February 6-7, 2019 Meeting, Ottawa, Ontario

Live Attenuated Influenza Vaccine (LAIV) in HIV-infected individuals

- Recommendations on the use of LAIV in HIV-infected Individuals presented for NACI review and approval. The guidance objective was to review the efficacy and effectiveness, immunogenicity, and safety evidence on LAIV use in HIV-infected individuals and to provide updated guidance on the use of LAIV in this population
- Decision: The Influenza Working Group will revise the statement according to NACI feedback received and an updated version will be brought to NACI for approval at the June 2019 meeting

Economics – Interim guidelines

- The Economic Task Group Technical Leads provided a presentation to the committee on the Interim Guidelines for conducting economic evaluations
- The purpose of these Interim Guidelines is to inform best practices for conducting de novo economic evaluations of vaccines in Canada
- This is to ensure the economic information is standardized, credible, and relevant for decision-makers in Canada's publicly funded health care system.
- The interim guidelines for economic evaluations of vaccines were approved by NACI.

4.2 Newly published or updated statement/recommendations

4.2.1 NACI Statement on Seasonal Influenza Vaccine for 2019–2020

- Published May 2019 – https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/healthy-living/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2019-2020/NACI_Stmt_on_Seasonal_Influenza_Vaccine_2019-2020_v12.3_EN.pdf

New influenza vaccine product

- NACI has concluded that Afluria® Tetra (Seqirus) has a comparable safety and immunogenicity profile to already authorized quadrivalent inactivated influenza vaccines
- NACI recommends that Afluria Tetra may be considered among the quadrivalent inactivated influenza vaccines offered to adults and children 5 years of age and older (Discretionary NACI

Recommendation). Refer to the NACI Supplemental Statement on Afluria® Tetra for additional information supporting this recommendation

Comparative effectiveness and immunogenicity of subunit and split virus inactivated influenza vaccines in adults 65 years of age and older

- Unadjuvanted subunit and split virus inactivated influenza vaccines are two commonly used types of seasonal influenza vaccines in Canada
- NACI has concluded (based on a systematic review of the literature) that there is insufficient evidence at this time on the comparative effectiveness and immunogenicity of unadjuvanted subunit and split virus inactivated influenza vaccines in adults 65 years of age and older to support specific recommendations on the differential use of these vaccines (Grade I Evidence). Refer to the NACI Literature Review on the Comparative Effectiveness and Immunogenicity of Subunit and Split Virus Inactivated Influenza Vaccines in Adults 65 Years of Age and Older for additional information supporting this conclusion.

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5 Immunisation updates from the World Health Organization (WHO)

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

No new meetings

5.2 Updated WHO Vaccine Position Papers

No new meetings

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

- 5–6 June, 2019 Geneva, Switzerland. Full meeting report available at: https://apps.who.int/iris/bitstream/handle/10665/325850/WER9428-309-316-en-fr.pdf?ua=1

Safety of Ebola virus vaccines

- There are currently 2 licensed Ebola vaccines: a single-dose Ad5-EBOV vaccine in China and a 2-dose rVSV/Ad5 vaccine licensed in the Russian Federation “for emergency use”
- The Ad5-EBOV (China) and the rVSV/ Ad5 vectored vaccine (Russian Federation) “for emergency use” were licensed on the basis of tests in animal models and data on human immunogenicity from phase 1 and 2 clinical trials, which included studies in African populations
- There are 2 investigational vaccines, the rVSV-ZEBOV vaccine made by Merck and the Ad26.ZEBOV/MVA-BN-Filo vaccine by Janssen
- The rVSV-ZEBOV was evaluated in several phase 2 and 3 clinical studies in over 15 000 people
    - Interim data on the impact of the vaccine used in ring vaccination strategy during the outbreak in the DRC confirmed high vaccine efficacy
    - Preclinical data showed no toxic effects in mice, rats or non-human primates and no neurovirulence in non-human primates
    - However, rVSV-ZEBOV is neurotropic in neonatal mice
    - Vaccine elicits innate immune responses and adaptive immune responses within 7–14 days
    - Safety of the vaccine was evaluated in 8 phase 1 clinical trials in various countries and populations and in 5 phase 2 and 3 studies in Liberia (PREVAIL), Sierra Leone (STRIVE), Guinea (Ebola Ça Suffit! and Frontline Workers) and in Canada, Spain and the USA
    - The results of an integrated analysis of the double-blinded trials showed SAEs in 3.4% of vaccine recipients and 7.8% of placebo recipients (1-year follow up)
    - Data on the safety and efficacy of the rVSV-ZEBOV vaccine in infants (<1 year) are not available
    - GACVS noted that more data are needed on the pregnancy outcomes. Concern was expressed about the possible implications of viral shedding and viraemia, the latter especially in infants

- The effectiveness of the Ad26.ZEBOV/MVA-BN-Filo vaccine made by Janssen is based on studies in non-human primates in phase 1 and 2 clinical safety and immunogenicity trials
    - A phase 3 study is planned
    - Data on the safety of this vaccine are available for about 4000 people

Development of the Global Vaccine Safety Blueprint 2.0

- Preliminary findings from 2 surveys of global stakeholders discussed in preparation for the next version of the vaccine safety blueprint ("Blueprint 2.0")
- Survey replies are still being analysed, but, overall, progress appears to have been made, and many of the findings resemble those of the 2011 landscape analysis, including requests for more training and harmonized methods
- When the analysis is complete, the results will be shared with GACVS and the working group drafting the Blueprint 2.0
- The plan for Blueprint 2.0 is to establish a drafting group of technical experts who will collaborate and identify core subjects, form and lead subgroups of subject matter experts and create a draft after discussions, iterations and a stakeholder meeting during the next few months.
- GACVS will review the draft document at its meeting in December 2019 to obtain WHO clearance and SAGE endorsement in spring 2020
- GACVS suggested that Blueprint 2.0 be aligned with the Immunization Agenda 2030 and be a technical (and living) document. The new version should apply to all countries and not just LMICs

Use of distributed data networks

- Distributed networks are independent groups with a common goal – in this case, investigation of concerns about vaccine safety
- GACVS was informed about a new global vaccine data network (GVDN), the aim of which is to establish a network of collaborators with capacity in vaccine data linkage, supported by a central coordinating entity. The network would foster inclusion and mentor organizations that wish to link data in order to assess the effects of vaccines
- An inaugural meeting was held in Annecy (France) in January 2018
- The meeting reached agreement on a collaborative model for conducting studies of vaccine safety, efficacy and risk– benefit; a governance model that ensures full participation of sites and efficient development of study protocols; data models to protect individual privacy but allow collaborative agreements on common data models (standardization of data to allow pooling of results); and a pilot study to investigate the link between influenza vaccines and Guillain–Barré syndrome

Communication about the safety of human papillomavirus vaccines

- A GACVS subgroup on vaccine safety communication has studied selected vaccine communication crises, including that associated with Dengvaxia in the Philippines, measles, mumps and rubella (MMR) vaccine in Samoa and Sudan and HPV vaccine in 5 countries
- At this meeting, case studies of communication about HPV vaccine were examined
- The case studies reviewed demonstrate that crises can be mitigated when key stakeholders are involved and proactive communications are established immediately.
- In Samoa (MMR), there was prompt communication among the relevant authorities and appropriate investigations, but initial attempts to hide the vaccination error and blaming individuals rather than conducting systemic analyses were detrimental to the vaccine program. The public was not informed of the reasons for the event
- Lack of preparedness, insufficient crisis response and strategic communication capacity, limited financial and human resources and insufficient media relations negatively affect vaccine uptake, while a swift response and good coordination among stakeholders have positive effects

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

- 12 – 14 March, 2019 Geneva, Switzerland. Full meeting report available at:
- https://www.who.int/immunization/research/committees/Meeting_report_IVIR_AC_March2019.pdf
- WER available at https://apps.who.int/iris/bitstream/handle/10665/312312/WER9419.pdf?ua=1

WHO/UNICEF Estimates of National Immunization Coverage (WUENIC) methods and estimates

- Since 2000 the WHO and UNICEF have made annual estimates of national infant immunization coverage for selected vaccines
- The WUENIC are based on data officially reported to WHO and UNICEF by Member States, surveys and other data reported in the published and grey literature.
- A review of the WUENIC methodology, exploring alternative methods and inputs as well as improving upon existing processes, was started
- Given the time constraints before any new methods can be adopted we should continue to rely on the current WUENIC methods in the near future
- A problem in estimating coverage is there is no gold standard against which different methods can be compared therefore there will still be need for human judgement
- While coverage is important, it is no substitute for actual measurement of disease reduction as a result of immunization
- IVIR-AC recommends setting up an IVIR-AC WG to allow continuing dialogue between IVIR-AC and the WUENIC WG on the best ways to estimate vaccine coverage

Human Papillomavirus (HPV) vaccine coverage methods

- Until now the production of comparable coverage estimates has been limited by the many changes in the recommendations and the variety of national HPV vaccination policies. Notably, differences do not only occur between countries, but within the same country over the years
- WHO has developed two measures of HPV vaccine coverage: One indicator was receipt of complete HPV vaccination by 15 years of age. The other was receipt of complete immunization according to country recommendations for age at receipt of HPV vaccines.
- IVIR-AC was asked to comment on the methodology to develop these estimates, which is based on the available data collected through the JRF and additional data sources. IVIR-AC was furthermore asked for suggestions on how to calculate uncertainty
- IVIR-AC agrees that both indicators are valuable, but full data (number of doses received by a person by age and year) collected in JRF should be made available, as well as a quality assessment of the data

Market Information for Access Methodology (MI4A) for HPV vaccines

- The MI4A was launched by WHO to contribute to the achievement of Sustainable Development Goal 3.8 (Universal Health Coverage target) by enhancing access to safe, effective, quality, and affordable vaccines for all
- IVIR-AC was requested to comment on the methodology, data and assumptions underlying the estimates of global demand and supply
- The methods are transparent, reasonable and replicable. Each piece (pricing, supply and demand) is important - the most useful analyses will require all three pieces
- The model uses coverage estimates of existing vaccines to project use of new vaccines. Efforts should be made to validate demand forecasts by looking at past introduction of new vaccines and their relationship to use of vaccines already in use at the time of the new introductions

Ebola Epidemiological modeling

- IVIR-AC was asked to comment on whether the model is valid to determine the optimal Ebola vaccine strategies in an outbreak setting in terms of the model design, parameters, attributes and the assumptions given the sparsity of data available
- IVIR-AC believes that the model is useful for the forward projection of the number of cases, estimates of number of cases averted, and demand for vaccine supplies for various control strategies (e.g. ring vaccination, contact tracing and isolation, etc). The Committee sees the value of the combination of model outputs and empirical data to inform response activities
- There are numerous strengths of the model parameters (e.g. vaccine efficacy based on trial data as well as continuing assessments of vaccine effectiveness) and attributes (e.g. temporal changes in transmission dynamics (e.g. time to admission to health care facilities) and vaccine operations depend on regular revision of data)

WHO guide on vaccine delivery costs

- WHO is considering the development of a Guide on Vaccine Delivery Costs
- IVIR-AC recommends for a WHO guide to be developed requires some careful consideration, given the availability of existing guides and tools.
- IVIR-AC recommends EPI National Immunization Programme Managers are included in the development of the guide

Measles Rubella vaccines investment case

- IVIR-AC and SAGE WGs previously recommended that a second modelling group be invited to assess global measles eradication. In response, a second measles and rubella modelling consortium is being proposed incorporating 2 measles models, 2 rubella models and 1 or 2 subnational models. The proposed work of the Vaccine Impact Modelling Consortium was presented to IVIR-AC with the request to comment on the proposed plan of work
- IVIR-AC believes the proposed modelling will be a tremendous help in efforts to eliminate and potentially eradicate measles/rubella. The current ongoing approach has the potential to overcome some of the concerns with earlier models. The timelines are tight but feasible
- IVIR-AC recommends that modelling groups need to lay out the assumptions behind each model (e.g. herd immunity thresholds, vaccine effectiveness of MCV1, MCV2 etc.)
- IVIR-AC noted that in the future there is a need to move towards models adapted to sub-national geography and sub-populations and further work is required on heterogeneity of vaccine coverage

Enteric disease burden estimation

- the Institute for Health Metrics and Evaluation (IHME) and the Johns Hopkins University Maternal and Child Epidemiology Estimate (MCEE) models were compared to identify commonalities and divergences in the methods and assumptions, with an initial focus on diarrhoeal deaths due to each pathogen (etiology)
- IVIR-AC was asked to comment on the proposed approach to comparing and characterizing the IHME and MCEE data in order to identify key variables in the models, on the review of forensic data analysis and on the validity, scope, methodology and scientific approach for the proposed systematic reviews
- the Institute for Health Metrics and Evaluation (IHME) and the Johns Hopkins University Maternal and Child Epidemiology Estimate (MCEE) models were compared to identify commonalities and divergences in the methods and assumptions, with an initial focus on diarrhoeal deaths due to each pathogen (etiology)
- IVIR-AC was asked to comment on the proposed approach to comparing and characterizing the IHME and MCEE data in order to identify key variables in the models, on the review of forensic data analysis and on the validity, scope, methodology and scientific approach for the proposed systematic reviews
- IVIR-AC agrees with the approach proposed and highlights the importance of multiple models and model comparison exercises for better understanding the methodology for estimating disease burden.
- IVIR-AC recommends better understanding of the margin of error in mortality estimates that policy-makers are prepared to accept in prioritizing development of vaccine candidates
- IVIR-AC considers that inclusion of search terms related to death and case fatality rates for the systematic review might bias the search towards studies in which deaths occurred, and other search terms, e.g. related to hospitalization, should be included

5.5 Meeting of the Product Development for Vaccines Advisory Committee (PDVAC)

- 26 – 28 June 2019, Geneva, Switzerland. Presentations and executive summary available at: https://www.who.int/immunization/research/meetings_workshops/pdvac_june19/en/index1.html

Next generation malaria

- The Malaria Vaccine Advisory Committee (MALVAC) is being reconvened to help WHO formulate updated guidance about public health targets and priority activities in malaria vaccine R&D

- Progress in translational science is being made in development of blood stage malaria vaccine candidates, in man-to-mosquito challenge models, and in the development of monoclonal antibodies targeting malaria antigens

Human Immunodeficiency virus (HIV)

- PDVAC endorsed the need for WHO to develop consensus regarding Preferred Product Characteristics (PPC) for HIV vaccines and broadly neutralizing antibodies (BNAbs), particularly for LMIC use
- PDVAC proposed evaluating the relative benefits and trade-offs of the vaccine and BNAbs candidates by using a total systems effectiveness approach to ascertain information

Next-generation (universal) influenza

- PDVAC noted the rapid progress being made in this area
- PDVAC suggested that WHO should review the current PPCs for Next-generation Influenza Vaccines that were produced in 2017 to ensure that this guidance is still appropriate and relevant
- Noted that PPCs need to be specific for the major target populations, particularly young children, pregnant women, and the elderly

Enterotoxigenic E.coli

- Vaccine pipeline has declined significantly since this pathogen was prioritized by PDVAC in 2016
- Phase IIb efficacy data for an oral vaccine candidate in adults is imminent

Shigella

- Vaccine pipeline remains diverse with both oral (live attenuated and formalin inactivated) and parenteral (subunit based) approaches evaluated in clinical studies

Group A Streptococcus (GAS)

- In February 2019, the Australian government pledged 35M AUD to develop a vaccine to combat the disease. In recent months, important progress has been seen in the establishment of a standard GAS Controlled Human Infection Model (CHIM)
- A global GAS vaccine consortium has been established, with aims being to support implementation of recommendations articulated in the WHO GAS vaccine R&D Technical Roadmap

Sexually Transmitted Infections (STI)

- Only HSV and Chlamydia vaccine candidates are in clinical development
- WHO convened a stakeholder consultation to discuss the potential public value of a gonococcal vaccine
- WHO will develop PPC guidance for gonorrhoea vaccines
- In 2019, the first Chlamydia vaccine candidate in decades completed phase I clinical studies (NCT02787109). The Statens Serum Institute, Denmark, is planning to commence a phase 2a study with their CTH552:CAF01 candidate later in 2019

Respiratory syncytial virus (RSV)

- Nineteen RSV vaccine candidates are in clinical development, across six different manufacturing platforms, in pregnant women, pediatric and elderly populations
- The vaccine candidates for maternal immunization are the most advanced

Tuberculosis

- PDVAC expressed that the M72/AS01 Phase IIb efficacy signal warrants progression to late stage development including phase III evaluation, without delay
- PDVAC further iterated the urgency for WHO to convene stakeholders to proactively determine the late stage development approach, and licensure, policy and access strategy for this vaccine, in the event that favorable results are confirmed

- The status of TB vaccine development, and in particular the M72/AS01 candidate should be presented to SAGE in the coming year to determine data and evidence that will support policy consideration

Group B Streptococcus (GBS)

- The GBS vaccine pipeline includes 2 candidate vaccines being evaluated in humans, and preclinical candidates
- In collaboration with the LSHTM, WHO is developing global economic investment case for GBS vaccines
- PDVAC recommendation to identify and collect data that could inform post licensure study design during early phase clinical studies, to reduce the time and financial burden of vaccine effectiveness studies

5.6 Global Immunization News and other items and resources

- Latest news available here: http://www.who.int/immunization/gin/en/

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6 Other items

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

New/updated registrations for vaccines:

- Vaxigrip Tetra is indicated for use in people ≥ 6 months of age for the prevention of influenza disease caused by the two influenza A virus subtypes and the two influenza B virus types contained in the vaccine
- Influvac Tetra is now indicated for use in people ≥ 3 years of age [previously Influvac Tetra was registered for use in people aged ≥18 years]
- Fluquadri is now indicated for use in people ≥ 6 months of age [previously Fluquadri was registered for use in people aged ≥3 years]

6.2 Global measles outbreaks

- WHO reports that measles outbreaks continue to spread rapidly around the world - there have been almost three times as many cases reported to date in 2019 as there were at this same time last year
- The Democratic Republic of the Congo, Madagascar and Ukraine have reported the highest numbers of cases this year. However, cases have dramatically decreased in Madagascar in the past several months as a result of nationwide emergency measles vaccine campaigns
- Major outbreaks are ongoing in Angola, Cameroon, Chad, Kazakhstan, Nigeria, Philippines, South Sudan, Sudan and Thailand
- Global vaccine coverage of 1 dose of MMR stands at 86%; second dose coverage is 69% (according to WHO and UNICEF coverage data released in July 2019)
- For more information, see:
- https://www.who.int/immunization/newsroom/new-measles-data-august-2019/en/
- https://www.cdc.gov/globalhealth/measles/globalmeaslesoutbreaks.htm

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7 Upcoming meetings and agendas

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

- 23–24 October 2019

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

- 22–23 August 2019
- 20–21 February 2020

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)

- 5–6 June 2019
- 25–26 September 2019

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

- 8–10 October 2019
- 31 March–2 April 2020
- 6 October – 8 October 2020