Philippine Clinical Practice Guidelines for Periodic Health Examination: Immunization for Adults

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ABSTRACT

Background. Immunization is very important in public health because it reduces the spread of infectious diseases. It has been an essential part of health care programs as it prevents and controls a wide range of vaccine-preventable diseases worldwide.

Objectives. The main objective of this Clinical Practice Guidelines (CPG) is to provide evidence-based recommendations on immunization for the prevention of vaccine-preventable diseases among apparently healthy adults and those with high-risk conditions.

Methods. We followed the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to CPG development recommended in the Department of Health Manual, including GRADE Adolopment and the GRADE Evidence-to-Decision or EtD frame-work. This CPG contains the systematic synthesis of scientific evidence on immunization for Cholera, *Haemophilus influenzae* type b (Hib), Hepatitis A, Herpes Zoster, Human Papillomavirus (HPV), Influenza, Japanese Encephalitis, Measles, Meningococcal, Mpox, Pneumococcal, Rabies, Tetanus, Typhoid, and Varicella in the adult population.

Results. The CPG provides forty-one (41) recommendations on prioritized questions regarding fifteen (15) vaccines.

Conclusions. The systematic review of evidence was used to assess each vaccine's efficacy, safety, and cost-effectiveness. These recommendations can be used by relevant stakeholders, particularly in the public health units, those in primary care practice and the administrative sectors involved in implementing vaccination programs.

Keywords: adult, immunization, vaccination, guidelines

A full copy of the Philippine Clinical Practice Guidelines for Periodic Health Examination: Immunization for Adults can be found at this link: https://drive.google.com/file/d/1WhZfZK1VwCB4u4eZi9z38hzO7rs7AI-t/view

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INTRODUCTION

Immunization plays a crucial role in public health by reducing the transmission of infectious diseases. Integral to healthcare programs worldwide, immunization effectively prevents and manages a diverse array of infectious illnesses such as smallpox, polio, and measles. Routine immunization programs are considered long-term cost-effective interventions by averting illnesses, thereby reducing the necessity for medical interventions. As a result, vaccines contribute to lowering healthcare expenses for individuals and governments alike.

The importance of vaccination in the country has been highlighted through the inclusion of key vaccine recommendations for healthy adults in the Philippine Guidelines on Periodic Health Examination (PHEX). PHEX is a comprehensive appraisal and synthesis of evidence, mainly on screening interventions, committed to providing early prevention services among apparently healthy Filipinos. The development of PHEX involved a collaborative effort among numerous medical and paramedical organizations, comprising over a hundred experts, researchers, and stakeholders. Inspired by models such as the Canadian and US Preventive Services Task Forces, PHEX was tailored to suit the unique healthcare landscape of the Philippines.

This clinical practice guideline (CPG) focuses on adult immunization among apparently healthy adults and those with high-risk conditions. In the guideline development, evidence-based recommendations for the prioritized vaccines were formulated using the GRADE Evidence-to-Decision (EtD) framework. The EtD framework aims to facilitate the formulation of recommendations based on specific context, essential health outcomes, benefits, and harms, while also considering equity, applicability, and feasibility.

The scope of this CPG is immunization of apparently healthy adults, as well as individuals with heightened risks and vulnerable populations susceptible to vaccine-preventable diseases. These recommendations serve as guides for healthcare professionals across various sectors, particularly those working in public health units, primary care practices, and the administrative domain of health program implementation. By providing evidence-based guidance on vaccination strategies, these guidelines aim to empower healthcare professionals to effectively address the prevention and control of vaccine-preventable diseases within their respective settings.

METHODS

Guideline Development Methodology

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to CPG development recommended in the Department of Health (DOH) Manual on Practice Guideline Development was followed.[1] The guideline development process was divided into 4 phases: 1) Preparation and Prioritization, 2) Evidence synthesis, 3) Formulation of Recommendations, and 4) External Review / CPG Appraisal. The GRADE Adolopment and Evidence-to-Decision (EtD) Framework was utilized in formulating the recommendations.[1-3]

Table 1. List of Guideline Questions

1.	Should the cholera vaccine be given to asymptomatic, apparently healthy adults?
2.	Should the Haemophilus influenzae B (HiB) vaccine be given to asymptomatic, apparently healthy adults?
3.	Should the hepatitis A vaccine be given to asymptomatic, apparently healthy adults?
4.	Should the herpes zoster vaccine be recommended to apparently healthy adults?
5.	Should the human papillomavirus vaccine be recommended to apparently healthy adults?
6.	Should the influenza vaccine be recommended to apparently healthy adults? Should the high-dose influenza vaccine be over the standard-dose influenza vaccine among older adults?
7.	Should the Japanese encephalitis vaccine be given to asymptomatic, apparently healthy adults?
8.	Should the measles-containing vaccine be given to asymptomatic, apparently healthy adults?
9.	Should the meningococcal vaccine be given to asymptomatic, apparently healthy adults?
10.	Should the monkeypox vaccine be given to asymptomatic, apparently healthy adults?
11.	Should the pneumococcal vaccine be recommended to asymptomatic, apparently healthy adults?
12.	Should the pre-exposure rabies vaccine be given to asymptomatic, apparently healthy adults?
13.	Should the tetanus vaccine be recommended to asymptomatic, apparently healthy adults?
14.	Should the typhoid vaccine be recommended to asymptomatic, apparently healthy adults?
15.	Should the varicella vaccine be given to asymptomatic, apparently healthy adults?

Guideline Preparation

In the preparation and prioritization phase, the Steering Committee defined the CPG objectives, scope, target audience, priority topics, and guideline questions (Table 1). Different stakeholders were consulted in prioritizing and developing the guideline questions. The questions were prioritized using the criteria set by the DOH.

A Technical Working Group (TWG) was formed to create the evidence summaries for each guideline question. The TWG consisted of evidence review experts (ERE) and a technical coordinator/methodologist. The evidence summaries were then presented in an *en banc* meeting to a multisectoral consensus panel (CP), which formulated the guideline recommendations.

The CP was composed of content experts on vaccination and infectious diseases, policymakers, patient advocates, and physicians from different settings (e.g., public primary care settings, private practice, occupational health settings). To ensure fairness and transparency in panel composition, the Steering Committee followed the criteria described in the DOH manual. During the *en banc* meetings, the CP prioritized critical and important outcomes (Appendix);

discussed necessary considerations relevant to each recommendation; and voted on each recommendation and its strength.

Management of Conflicts of Interest

All task force members submitted their declaration of conflict of interest (COI) and curriculum vitae. The disclosure included a 4-year period of personal potential intellectual and/or financial COI. A COI Oversight Committee (OC) reviewed and evaluated the potential conflicts of interest and gave its recommendation on how to manage them. For TF members with potential significant COIs, the members of OC conducted additional investigations with due diligence to ensure the integrity of the CPG process and the final recommendations. Members with financial COI were inhibited from voting on relevant questions. Those with non-financial COIs (such as authorship related to the CPG topic) were allowed to participate, but COIs were declared during the panel meeting and the final manuscript.

Evidence Synthesis

The evidence review questions were developed using the PICO (population, intervention, comparator, and outcome) format. The ERE searched and reviewed the evidence base and recommendations from international practice guidelines on adult immunization, which were appraised to have a ≥75% score on the Rigor domain of the AGREE tool. These included the 2018 Philippine Society for Microbiology and Infectious Diseases (PSMID) CPG for Adult Immunization, the US Advisory Committee on Immunization Practices (ACIP), and the WHO Routine Immunization Recommendations.[4-6]

The results of the appraisal of existing CPGs and their evidence summaries determined the need for a *de novo* systematic search of electronic databases (MEDLINE via PubMed, CENTRAL, Google Scholar). If there was no relevant evidence summary in the above-listed CPGs, a systematic medical literature search was done. Systematic reviews that met our inclusion criteria to answer the clinical questions were used directly to identify relevant articles and a summary of findings. If no relevant systematic review was found, *de novo* systematic reviews were conducted.

The end dates of the searches ranged from May to November of 2021 for the first set of vaccines (Herpes Zoster, Human Papillomavirus, Influenza, Measles, Pneumococcal, Tetanus, Typhoid), and from September to February 2023 for the second set of vaccines (Cholera, *Haemophilus influenzae* type b, Hepatitis A, Japanese Encephalitis, Meningococcal, Monkeypox, Rabies, Varicella). Relevant local databases and websites of medical societies were also utilized in the search. Keywords were based on PICO (MeSH and free text) set for each question. The ERE also contacted authors of related articles to verify details and identify other research studies for appraisal, when needed.

The methodological quality of the included studies was critically appraised using the standard tools, such as the Cochrane Risk of Bias tool (ROB 1.0) for randomized controlled trials (RCTs), and Painless EBM appraisal criteria or Newcastle–Ottawa Scale (NOS) for observational studies.[7-9] We used the GRADE approach to rate the certainty of evidence and the strength of recommendations (Table 2).[10]

At least two (2) reviewers worked on each evidence review question. The search strategy and inclusion criteria were based on the PICO of the evidence review question. RevMan, STATA, and GRADEPro were used for the quantitative synthesis of important clinical outcomes for each question. The ERE generated evidence summaries for each of the guideline questions. Each evidence summary included evidence on the burden of the problem, benefits, harm, and social and economic impact of the vaccination. Evidence/information that will facilitate the decision (i.e., cost of vaccine, cost-effectiveness studies, qualitative studies) was also included in the evidence summaries.

Table 2. Basis for Assessing the Quality of the Evidence using the GRADE Approach

Certainty of Evidence	Interpretation
High ⨁⨁⨁⨁	We are very confident that the true effect lies close to that of the estimate of the effect
Moderate ⨁⨁⨁◯	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low ⨁⨁◯◯	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very Low ⨁◯◯◯	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect
Strength of Recommendation	**Interpretation**
Strong	Advantages of the intervention significantly outweigh disadvantages or disadvantage of the intervention significantly outweigh advantages
Weak	Advantages of the intervention may outweigh disadvantages, disadvantages of the intervention may outweigh advantages, or the relationship between advantages and disadvantages is not clear

Table 3. Detailed Considerations Based on EtD Framework

1.	Is the problem a priority?
2.	How substantial are the desirable anticipated effects?
3.	How substantial are the undesirable anticipated effects?
4.	What is the certainty of the evidence?
5.	Is there important uncertainty about or variability in how much people value the main outcomes, including adverse effects and burden of the vaccine, and downstream outcomes of vaccination?
6.	Does the balance between desirable and undesirable effects favor the vaccine or the comparison?
7.	How large are the resource requirements (costs)?
8.	What is the certainty of the evidence of resource requirements (costs)?
9.	Does the cost-effectiveness of the vaccine favor the vaccine or the comparison?
10.	What would be the impact on health equity?
11.	Is the vaccine acceptable to key stakeholders?
12.	Is the vaccine feasible to implement?

Formulation of the Recommendations

For each guideline question, the CP was provided with the evidence summary and a draft recommendation solely based on the trade-offs between benefit and harm and the certainty of evidence. Each CP member was then asked to complete an EtD questionnaire (Table 3). The purpose of this questionnaire was for each CP member to explicitly incorporate other important factors, such as cost-effectiveness, patient values and preferences, applicability, feasibility, appropriateness, equity, and resources in their decision-making.

The strength of each recommendation (i.e., strong or weak) was determined by the panel considering all the factors mentioned above. A strong recommendation implies that the panel is *"confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects,"* while a weak recommendation means that the *"desirable effects of adherence to a recommendation probably outweigh the undesirable effects but is not confident."*[10]

The direction and strength of each recommendation were determined by a formal consensus method. Recommendations were considered to have reached consensus when ≥75% of voters agreed on the proposed recommendation. If a consensus was not reached initially, two further rounds of voting were allowed. A modified Delphi methodology was planned in case no consensus was reached during the *en banc* meetings.[11] On the rare occasion that no consensus is reached, no recommendation would be indicated in the final CPG manuscript.

Planning for Dissemination, Implementation, and Update

All recommendations and evidence summaries were posted in a web-based application (https://phex.ph). The SC discussed with relevant stakeholders, such as DOH and PhilHealth to prepare a dissemination plan that will actively promote the adoption of this guideline with strategies for copyrights. These recommendations and evidence summaries were also disseminated by the Task Force to their specific organizations. It will also be available at the DOH website. The recommendations herein shall hold until new evidence on efficacy or safety of the covered vaccines arises, or after three (3) years when contingencies dictate updating this Philippine Guidelines on Periodic Health Examination.

External Review

After the completion of the last CP meeting, three independent stakeholders (two Infectious Disease Specialists and an Internist) reviewed the draft guidelines on the content, clarity, acceptability, applicability, and feasibility of the recommendations. The AGREE-REX tool was used as a guide.[12] Comments were consolidated by the SC and addressed in the final manuscript.

RESULTS

Forty-one (41) recommendations across 15 different vaccines were formulated in this CPG. Table 4 summarizes the recommendation statements, strength of recommendations, and certainty of evidence rating.

Cholera Vaccine

Guideline Question 1. Should cholera vaccine be given to asymptomatic apparently healthy adults?

Recommendation 1.1. Among asymptomatic apparently healthy adults, we suggest AGAINST giving the oral cholera vaccine. *(Moderate certainty of evidence, weak recommendation)*

Recommendation 1.2. Among asymptomatic healthcare workers, we suggest AGAINST giving oral cholera vaccines due to insufficient evidence. *(Very low certainty of evidence, weak recommendation)*

Recommendation 1.3. Among asymptomatic apparently healthy adults traveling to cholera-endemic areas, we recommend giving the oral inactivated cholera vaccine. *(Moderate certainty of evidence, strong recommendation)*

Key findings: Cholera, caused by the toxin-producing strains of the gram-negative bacterium *Vibrio cholerae*, causes an acute secretory diarrheal disease with profound fluid and electrolyte losses in the stool.[13] In the Philippines, the DOH epidemiology bureau – Philippine health statistics recorded a total of 60 cases per 100,000 population in 2019.[14] Available vaccines for cholera include: injected cholera vaccine, oral inactivated cholera vaccine, and oral live cholera vaccine.

Injected cholera vaccines were more effective compared to placebo in reducing cholera cases (*at 7 months:* RR 0.45, 95% CI 0.38 to 0.53; *at 1 year*: RR 0.55, 95% CI 0.44 to 0.68; *at 2 years*: RR 0.58, 95% CI 0.44 to 0.75). No significant

Table 4. Summary of Recommendations for 2023 Philippine Guidelines on Periodic Health Examination: Immunization for Adults

Recommendations	Strength of Recommendation	Certainty of Evidence
Cholera		
Q1. Should the cholera vaccine be given to asymptomatic, apparently healthy adults?		
Recommendation 1.1. Among asymptomatic apparently healthy adults, we suggest AGAINST giving the oral cholera vaccine.	Weak	Moderate
Recommendation 1.2. Among asymptomatic healthcare workers, we suggest AGAINST giving the oral cholera vaccine due to insufficient evidence.	Weak	Very Low
Recommendation 1.3. Among asymptomatic apparently healthy adults traveling to cholera-endemic areas, we recommend giving oral inactivated cholera vaccine.	Strong	Moderate
***Haemophilus Influenzae* type b (Hib) vaccine**		
Q2. Should the Haemophilus influenzae type b (Hib) vaccine be given to asymptomatic, apparently healthy adults?		
Recommendation 2.1. Among asymptomatic apparently healthy adults, we recommend AGAINST giving the *Haemophilus influenzae* type b vaccine.	Strong	Low
Recommendation 2.2. Among adults with anatomical and functional asplenia, we suggest giving the *Haemophilus influenzae* type b vaccine.	Weak	Low
Recommendation 2.3. Among pregnant women, we suggest AGAINST giving the *Haemophilus influenzae* type b vaccine.	Weak	Low
Recommendation 2.4. Among asymptomatic healthcare workers, we recommend AGAINST giving the *Haemophilus influenzae* type b vaccine due to insufficient evidence.	Strong	Very Low
Hepatitis A Vaccine		
Q3. Should the hepatitis A vaccine be given to asymptomatic, apparently healthy adults?		
Recommendation 3.1. Among apparently healthy adults, we suggest giving hepatitis A vaccination using a 2-dose series (0,6 months).	Weak	Low
Herpes Zoster Vaccine		
Q4. Should the herpes zoster vaccine be recommended to apparently healthy adults?		
Recommendation 4.1. Among apparently healthy elderly aged ≥60 years old, we suggest the herpes zoster vaccine.	Weak	Low
Human Papillomavirus (HPV) Vaccine		
Q5. Should the HPV vaccine be recommended to apparently healthy adults?		
Recommendation 5.1. Among apparently healthy asymptomatic females aged 18 to 26 years who have not been vaccinated or who have not yet completed the vaccine series, we recommend HPV vaccination.	Strong	Moderate
Recommendation 5.2. Among apparently healthy asymptomatic males aged 18 to 26 years who have not been vaccinated or who have not yet completed the vaccine series, we suggest HPV vaccination.	Weak	Very Low
Recommendation 5.3. Among apparently healthy asymptomatic adults aged 27 to 45 years, we suggest AGAINST routine catch-up vaccination. The decision to vaccinate people in this age group should be made on an individual basis.	Weak	Low
Recommendation 5.4. Among pregnant patients, we suggest AGAINST HPV vaccination.	Weak	Very Low
Recommendation 5.5. Among apparently healthy asymptomatic sex workers, there is insufficient evidence to recommend for or against HPV vaccination.	N/A	Very Low
Influenza Vaccine		
Q6. Should the influenza vaccine be recommended to apparently healthy adults?		
Recommendation 6.1. Among healthy adults, pregnant women, and the elderly (≥65 years old), we suggest annual influenza vaccination using an inactivated influenza vaccine.	Weak	Low
Recommendation 6.2. Among healthcare workers, we suggest annual influenza vaccination using the inactivated influenza vaccine.	Weak	Very Low
Recommendation 6.3. High-dose inactivated influenza vaccine is not available locally, precluding the panel from making a recommendation on its use.	N/A	Very Low
Japanese Encephalitis Vaccine		
Q7. Should the Japanese encephalitis vaccine be given to asymptomatic, apparently healthy adults?		
Recommendation 7.1. Among asymptomatic apparently healthy adults, we suggest giving the Japanese encephalitis virus vaccine.	Weak	Low
Measles Vaccine		
Q8. Should the measles-containing vaccine be recommended to apparently healthy adults?		
Recommendation 8.1. Among healthy adults (non-pregnant or unvaccinated), we recommend giving the measles-containing vaccine.	Strong	Very Low

Table 4. Summary of Recommendations for 2023 Philippine Guidelines on Periodic Health Examination: Immunization for Adults *(continued)*

Recommendations	Strength of Recommendation	Certainty of Evidence
Meningococcal Vaccine		
Q9. Should the meningococcal vaccine be given to asymptomatic, apparently healthy adults?		
Recommendation 9.1. Among asymptomatic apparently healthy adults, we suggest AGAINST giving the meningococcal MenACWY vaccine.	Weak	High
Recommendation 9.2. Among asymptomatic apparently healthy young adults (18-25 years old), we suggest AGAINST giving the meningococcal MenB vaccine.	Weak	Moderate
Recommendation 9.3. Among adults with a high risk of contracting meningococcal disease*, we suggest giving the meningococcal MenACWY vaccine.	Weak	Moderate
* *Individuals living in close quarters/proximity, asplenic patients, microbiologists with increased exposure*		
Recommendation 9.4. Among adults with a high risk of contracting meningococcal disease**, we suggest giving the meningococcal MenB vaccine.	Weak	Very Low
** *young adults in crowded dormitories*		
Mpox Vaccine		
Q10. Should the mpox vaccine be given to asymptomatic, apparently healthy adults?		
Recommendation 10.1. Among apparently healthy adults, we suggest AGAINST giving the mpox vaccine.	Weak	Low
Recommendation 10.2. Among adults with high risk* for exposure to mpox, we suggest AGAINST giving a mpox vaccine.	Weak	Very Low
* *Healthcare workers responding to the monkeypox outbreak, laboratory personnel who are handling monkeypox virus, individuals with multiple sexual partners, and men having sex with men (MSM).*		
Pneumococcal		
Q11. Should the pneumococcal vaccine be recommended to apparently healthy adults?		
Recommendation 11.1. Among apparently healthy adults ≥65 years of age, we suggest the use of PCV13.	Weak	Moderate
Recommendation 11.2. Among apparently healthy adults ≥65 years of age, we recommend the use of PPSV23.	Strong	Moderate
Recommendation 11.3. Among apparently healthy adults between 18-64 years of age, we suggest the use of PCV13.	Weak	Low
Recommendation 11.4. Among apparently healthy adults between 18-64 years of age, there is insufficient evidence to recommend for or against the use of PPSV 23.	N/A	Low
Rabies Vaccine		
Q12. Should the pre-exposure rabies vaccine be given to asymptomatic, apparently healthy adults?		
Recommendation 12.1. Among asymptomatic apparently healthy adults, we suggest AGAINST giving pre-exposure rabies vaccine.	Weak	Very Low
Recommendation 12.2. Among healthcare workers with a high risk of exposure to rabies, we suggest giving the pre-exposure rabies vaccine.	Weak	Very Low
Recommendation 12.3. Among adults at high risk of exposure to rabies, we suggest giving the pre-exposure rabies vaccine.	Weak	Very Low
Tetanus Vaccine		
Q13. Should tetanus vaccine be recommended to apparently healthy adults		
Recommendation 13.1. Among healthy adults with a complete primary series, we recommend giving any tetanus-toxoid-containing vaccine every 10 years.	Strong	Low
Recommendation 13.2. Among healthy adults with unknown status or incomplete series, we suggest giving the primary series with Tdap followed by any tetanus-toxoid-containing vaccine.	Weak	Very Low
Recommendation 13.3. Among pregnant women with a complete primary series, we suggest giving any tetanus toxoid-containing vaccine during each pregnancy.	Weak	Very Low
Recommendation 13.4. Among pregnant women with unknown status or incomplete series, we suggest giving the primary series with Tdap followed by any tetanus-toxoid-containing vaccine.	Weak	Low
Typhoid Vaccine		
Q14. Should the typhoid vaccine be recommended to apparently healthy adults?		
Recommendation 14.1. Among healthy adults, we suggest the use of Vi polysaccharide intramuscular vaccine for typhoid vaccination.	Weak	Low
Recommendation 14.2. Among healthy adults, there is insufficient evidence to recommend for or against Vi-TT intramuscular vaccines.	N/A	Very Low
Recommendation 14.3. Among healthcare workers, we suggest AGAINST the routine use of typhoid vaccines.	Weak	Very Low
Varicella Vaccine		
Q15. Should the varicella vaccine be given to asymptomatic, apparently healthy adults?		
Recommendation 15.1. Among asymptomatic apparently healthy adults, we suggest AGAINST giving the varicella vaccine.	Weak	Very Low
Recommendation 15.2. Among asymptomatic healthcare workers, we suggest AGAINST giving the varicella vaccine.	Weak	Very Low

benefit was observed for cholera deaths up to 2 years (OR 0.52, 95% CI 0.26 to 1.04). However, injected cholera vaccines led to significantly milder adverse events (malaise, vomiting, unspecified local and systemic reactions) compared to placebo (RR 1.51, 95% CI 1.22 to 1.86).[15]

Oral inactivated cholera vaccines were more effective compared to placebo in reducing cholera infection up to 2 years (RR 0.36, 95% CI 0.30 to 0.44 and hospitalization rates up to 1 year after administration (RR 0.40, 95% CI 0.28 to 0.57). There was no significant benefit in terms of all-cause mortality (RR 0.83, 95% CI 0.64 to 1.08). There was inconclusive effect on cholera deaths (RR 0.73, 95% CI 0.03 to 16.41.[16-21] There was also inconclusive effect of oral inactivated cholera vaccines compared to placebo on adverse events in healthy adults (RR 1.13, 95% CI 0.88 to 1.44), among women who were pregnant during vaccination (RR 0.97, 95% CI 0.58-1.61) and among women who became pregnant after vaccination (RR 1.02, 95% CI 0.67-1.55).[19-21]

Live, oral cholera vaccines elicited an immune response after 10 days in 90.3% of vaccinees (95% CI 61.7–100%). There was an inconclusive effect in reducing cholera cases (RR 0.83, 95% CI 0.53 to 1.40), all-cause mortality (OR 1.03, 95% CI 0.82 to 1.29), and mild adverse events (RR 0.99, 95% CI 0.75 to 1.30).[22]

No studies were found that specifically involved healthcare workers.

Justification: Oral cholera vaccines were strongly recommended in cholera-endemic areas due to the moderate certainty of evidence showing their effectiveness in reducing cholera infections, and their favorable safety profile. Inactivated vaccines were prioritized over live attenuated cholera vaccines since the effectiveness of the oral live attenuated cholera vaccines is still being investigated. For injected cholera vaccine types, no recommendation was made since they are no longer available in the Philippines.

Despite having moderate certainty of evidence suggesting that oral inactivated cholera vaccines result in net benefit, the panel formulated a weak recommendation AGAINST their use for mass vaccinations. The panel considered that cholera vaccines do not appear to be more cost-effective compared to public health measures (e.g., promoting proper sanitation and providing potable water to the public and affected areas). Mass vaccination using oral inactivated cholera vaccines may be considered in outbreak situations.

A separate recommendation for healthcare workers was formulated due to their increased risk of exposure to the disease associated with working in laboratories or cholera-endemic areas. Due to the lack of evidence on the benefits of cholera vaccines for this specific population, the panel issued a weak recommendation AGAINST oral cholera vaccines.

Haemophilus Influenzae type b (Hib) Vaccine

Guideline Question 2. Should *Haemophilus influenzae* type b (Hib) vaccine be given to asymptomatic, apparently healthy adults, asplenic patients, healthcare workers, and pregnant women?

Recommendation 2.1. Among asymptomatic apparently healthy adults, we recommend AGAINST giving the Hib vaccine. *(Low certainty of evidence, strong recommendation)*

Recommendation 2.2. Among adults with anatomical and functional asplenia, we suggest giving the Hib vaccine. *(Low certainty of evidence, weak recommendation)*

Recommendation 2.3. Among pregnant women, we suggest AGAINST giving the Hib vaccine. *(Low certainty of evidence, weak recommendation)*

Recommendation 2.4. Among asymptomatic healthcare workers, we recommend AGAINST giving the Hib vaccine due to insufficient evidence. *(Very low certainty of evidence, strong recommendation)*

Key findings: *Haemophilus influenzae* type b (Hib) is a non-motile, non-spore-forming gram-negative coccobacillus commonly found in the nose and throat that can invade the body and cause meningitis, epiglottitis, pneumonia, and septic arthritis.[23] Data on the epidemiology of Hib in Asian adults are lacking. Studies on Asians have focused on children less than 5 years old. One population-based study published in 2000, done in the Philippines, showed that the annual incidence of Hib meningitis in central Manila was 95 per 100,000 children, with a high case fatality rate (11%) and high rate of complications (15%).[24]

Hib vaccination significantly increased total serum antibody concentration (anti-PRP) in healthy adults. After 1 month, 98% of vaccinated subjects reached antibody levels >1 μL/mL. After 12 months, 93% of vaccinated subjects continued to show antibody levels >1 μL/mL.[25]

In asplenic patients and pregnant women, vaccination produced antibody levels that were significantly higher than pre-vaccination levels, though the magnitude of this change varied depending on when antibody measurements were taken.[26,27] A higher proportion of infants born to vaccinated mothers reached protective antibody levels compared to those born to unvaccinated mothers. Vaccinated mothers have significantly higher total anti-PRP antibody concentrations than unvaccinated mothers (MD 8.53 μL/mL, 95% CI 5.55 to 11.51 μL/mL).[26,28,29]

No study was found specifically investigating the effects of Hib vaccination on healthcare workers.[30,31] No serious adverse events were reported in all subgroups. Only mild adverse events were observed, of which pain at the injection site was the most common.[25,26,28,32,33]

Justification: Despite evidence demonstrating an increase in immune responses from vaccination, mass Hib vaccination was NOT recommended due to the already high protection levels (i.e., antibodies for Hib) among unvaccinated individuals and the uncertainty in the data related to local seroprevalence of the disease in adults. A similar recommendation AGAINST Hib vaccination was issued for healthcare workers due to the absence of conclusive data justifying this subpopulation to be a high-risk group for contracting Hib infection.

For pregnant women, the present recommendation AGAINST Hib vaccination by the panel contrasts with the 2018 local guidelines from PSMID. Additional cohort studies beyond those considered in the PSMID CPG were considered in this CPG.

Despite the low certainty of evidence showing its effectiveness among adults with either anatomical or functional asplenia, the panel made a weak recommendation for giving the Hib vaccine to this subpopulation due to their higher risk of experiencing Hib-related disease complications.

Hepatitis A Vaccine

Guideline Question 3. Should the hepatitis A vaccine be given to asymptomatic, apparently healthy adults?

Recommendation 3.1. Among apparently healthy adults, we suggest giving Hepatitis A vaccination using a 2-dose series (0, 6 months). *(Low certainty of evidence, weak recommendation)*

Key findings: The hepatitis A virus (HAV) is transmitted via direct human-to-human contact or through the consumption of food and water contaminated with fecal particles. It is considered a major cause of acute viral hepatitis, which can eventually lead to acute liver failure and death. Based on 2019 data from the DOH, there were 1,047 cases of viral hepatitis recorded (1 per 100,000 Filipinos). Mortality rates associated with viral hepatitis ranged from 0.8 to 1.0 per 100,000 population, with at least 1,061 deaths in 2019. Serosurveys conducted in Southeast Asia revealed that half of the adolescents and more than 90% of 40-year-olds had anti-HAV in Malaysia and the Philippines in the 1980s, with little evidence of changes in seroprevalence in these countries.[14]

HAV outbreaks occur mainly in low-endemic regions with poor immunization rates or few previous infections.[34-37] Individuals at the highest risk for contracting the disease include persons using illegal injection drugs, those who travel to places endemic for hepatitis A, incarcerated populations, men who have sex with men, persons with occupational risk of infection, and persons at high risk for developing complications from a hepatitis A infection (e.g., patients with chronic liver disease or infected with HIV).[37,38]

Evidence from two randomized controlled trials (RCTs) indicated that inactivated hepatitis A vaccines, compared to a placebo or no vaccine, did not confer seroprotective levels of anti-HAV IgG (RR 0.01, 95% CI 0.00–0.03).

Justification: Given the low certainty of evidence on the net benefit of hepatitis A vaccination and uncertainty in the local endemicity status of the Philippines for Hepatitis A among adults, only a weak recommendation was made for hepatitis A vaccination. The panel also pointed out that estimating the actual disease burden in adults is challenging, considering the potential impact of the existing routine Hepatitis A vaccination for children. Additionally, the panel mentioned the uncertainty on the seroconversion levels that are associated with actual protection from the disease. Although the vaccine appeared to be cost-effective for countries with high endemicity for Hepatitis A, local health economic evaluations still need to be completed.

Herpes Zoster Vaccine for Adults

Guideline Question 4. Should the herpes zoster vaccine be recommended to apparently healthy adults?

Recommendation 4.1. Among apparently healthy elderly aged ≥60 years old, we suggest giving/administering the herpes zoster vaccine. *(Low certainty of evidence, weak recommendation)*

Key findings: As primary varicella infection resolves, the virus establishes latency in the dorsal root ganglia and may reactivate to cause herpes zoster or shingles. While the primary infection manifests as a generalized rash, herpes zoster presents as a vesicular rash confined to a single dermatomal distribution and is preceded by neuropathic pain for around three days.[39] Herpes zoster is often underreported and not detected early in the country. Thus, the true burden of herpes zoster locally remains unknown.

Two herpes zoster vaccine preparations are available in the global market: (a) live attenuated vaccine (ZVL) and (b) recombinant vaccine (RZV). Evidence showed higher vaccine efficacy rates with RZV. Additionally, the RZV is preferred for immunocompromised patients. However, only ZVL is currently available locally.[40,41]

ZVL, compared to placebo, significantly reduced herpes zoster incidence after 3.1 years of follow-up (RR 0.49, 95% CI 0.43, 0.56).[42] Two RCTs (n=22,022) that evaluated RZV after a 3.2-year follow-up period also showed significantly large reductions in herpes zoster incidence (RR 0.08; 95% CI 0.03 to 0.23).[43,44]

ZVL compared to placebo significantly reduced the risk for postherpetic neuralgia in persons aged 60-69 years (vaccine efficacy [VE] 65.7%, 95% CI 20.4 to 86.7), and in those ≥70 years old (VE 66.8%, 95% CI 43.3 to 81.3).[42]

Justification: The consensus panel carefully considered several factors in formulating the recommendation for herpes zoster vaccination in the Philippines. Firstly, they noted that herpes zoster cases are often underreported and not detected early in the country, leading to uncertainty about the true

burden of the disease locally. Only the live attenuated vaccine (ZVL) is accessible locally in the Philippines. Financial accessibility is also a significant concern, with the market price of herpes zoster vaccines ranging from PhP 6,000 to 7,500 per shot, or PhP 4,500 when procured in bulk. The available ZVL vaccine requires a single subcutaneous dose. Moreover, evidence regarding the cost-effectiveness of herpes zoster vaccination primarily stems from studies conducted abroad, raising questions about its applicability to the local context.

Human Papillomavirus (HPV) Vaccine

Guideline Question 5. Should the HPV vaccine be recommended to apparently healthy adults?

Recommendation 5.1. Among apparently healthy asymptomatic females aged 18 to 26 years who have not been vaccinated or who have not yet completed the vaccine series, we recommend HPV vaccination. *(Moderate certainty of evidence, strong recommendation)*

Recommendation 5.2. Among apparently healthy asymptomatic males aged 18 to 26 years who have not been vaccinated or who have not yet completed the vaccine series, we suggest HPV vaccination. *(Very low certainty of evidence, weak recommendation)*

Recommendation 5.3. Among apparently healthy asymptomatic adults aged 27 to 45 years, we suggest AGAINST routine catch-up vaccination. The decision to vaccinate people in this age group should be made on an individual basis. *(Low certainty of evidence, weak recommendation)*

Recommendation 5.4. Among pregnant patients, we suggest AGAINST HPV vaccination. *(Very low certainty of evidence, weak recommendation)*

Recommendation 5.5. Among apparently healthy asymptomatic sex workers, there is insufficient evidence to recommend for or against HPV vaccination. *(Very low certainty of evidence)*

Key findings: Human papillomavirus (HPV), a sexually transmitted pathogen, is regarded as the most common viral infection affecting the reproductive tract. Persistent infection with a specific type of HPV may lead to precancerous lesions that may eventually develop into cervical cancer in women when left untreated. It is also associated with oropharyngeal (i.e., head and neck) and anogenital (i.e., anus, vulva, vagina, and penis) cancers in both men and women.[45]

Among female patients 16 to 26 years old, quadrivalent (4vHPV) or nonavalent (9vHPV) HPV vaccination compared to placebo resulted in significant reduction in the following HPV 6, 11, 16, and 18 related outcomes: 6-month persistent infection (VE 89.0%, 95% CI 70.0, 97.0); cervical intraepithelial neoplasia (CIN) 2/3 or worse (VE 98.2%, 95% CI 93.3, 99.8); vulval intraepithelial neoplasia (VIN) 2/3 or worse (VE 100%, 95% CI 82.6, 100); and anogenital warts (VE 98.9%, 95% CI 96.1, 99.9). Among female patients 16 to 26 years old, 9vHPV compared to 4vHPV resulted in significant reduction in the following HPV 31, 33, 45, 51 and 58 related outcomes: 6-month persistent infection (VE 96.0%, 95% CI 94.6, 97.1) and CIN 2/3, VIN 2/3, or vaginal intraepithelial neoplasia (VaIN) 2/3 or worse (VE 97.4%, 95% CI 85.0, 99.9).[46-51]

Among apparently healthy female asymptomatic adults aged 27 to 45 years who have not been vaccinated previously or who have not yet completed the vaccine series, there is only 1 randomized controlled trial showing the benefit of 4vHPV vaccination in reducing 6-month persistent infection (VE 88.8%, 95% CI 76.8, 95.4).[52] RCTs on HPV vaccination excluded pregnant women; safety information in this population is limited. HPV vaccination is thus not recommended among pregnant women.[53]

Among apparently healthy asymptomatic males aged 16 to 26 years who have not been vaccinated or who have not yet completed the vaccine series, evidence was reviewed on the available clinical outcomes (i.e., 6-MPI, external genital lesion, all PeIN lesions, and anogenital warts) similarly favors HPV vaccination (4vHPV and 9vHPV). Among males 16 to 26 years old, 4vHPV compared to placebo resulted in reduction in the following HPV 6-, 11-, 16-, and 18-related outcomes: 6-month persistent infection (VE 85.6%, 95% CI 73.4, 92.9); external genital lesion (VE 90.4%, 95% CI 69.2, 98.1); condyloma acuminatum (VE 89.4, 95% CI 65.5, 97.9); anal intraepithelial neoplasia or anal cancer (VE 89.6 %, 95% CI 57.2, 98.8) [54,55]

HPV vaccination is generally safe and well-tolerated, with no significant difference in adverse events among those given HPV vaccination compared to placebo (RR 0.99, 95% CI 0.94,1.04). The risk for adverse events was similar for males and females. For all HPV vaccines, injection site reactions were the most commonly reported adverse event.[49,51,54]

There were no studies that evaluated the efficacy and safety of HPV vaccination among apparently healthy asymptomatic sex workers.

Justification: The studies included in the evidence summary were conducted internationally, raising concerns regarding their applicability to the local context. Studies showed that HPV vaccination is most effective when administered prior to an individual's sexual debut. However, the included studies did not explicitly outline how HPV naivety was determined.

While the bivalent HPV vaccine remains accessible in the country, the evidence base primarily features studies on quadrivalent and nonavalent HPV vaccines. The panel refrained from making specific recommendations regarding the preferred HPV vaccine type, emphasizing the importance of shared decision-making between patients and physicians. Factors such as HPV naivety, risk of exposure,

cost, and vaccine availability should be considered in this decision-making process.

HPV vaccination in individuals aged 16 to 26 years led to a larger benefit in females compared to males. Thus, a weak recommendation for males and a strong recommendation for females were made by the CP. For adults aged 27 to 45 years, catch-up HPV vaccination showed diminished efficacy. Therefore, the decision to vaccinate in this age group should be individualized, considering factors such as risk of exposure.

While sex workers face heightened risk of exposure, the panel unanimously agreed that there is insufficient evidence to recommend HPV vaccination in this population due to the impact of HPV naivety on vaccine efficacy and the lack of benefit among those already infected with HPV. However, the panel acknowledged that HPV vaccination may still offer some benefit to this group, particularly if the vaccine covers HPV genotypes to which the individual has not been previously exposed.

Influenza Vaccine

Guideline Question 6. Should the influenza vaccine be recommended to apparently healthy adults?

Recommendation 6.1. Among healthy adults, pregnant women, and elderly (≥65 years old), we suggest annual influenza vaccination using inactivated influenza vaccine. *(Low certainty of evidence, weak recommendation)*

Recommendation 6.2. Among healthcare workers, we suggest annual influenza vaccination using the inactivated influenza vaccine. *(Very low certainty of evidence, weak recommendation)*

Recommendation 6.3. High-dose inactivated influenza vaccine is not available locally, precluding the panel from making a recommendation on its use. *(Very low certainty of evidence)*

Key findings: Influenza is caused by influenza viruses, presenting as the typical flu-like symptoms. Significant morbidity and mortality are associated with viral influenza, particularly among pregnant women, adults older than 65 years of age, and people with comorbid illnesses. The most common complication is pneumonia, either from primary influenza or from secondary bacterial infection. Influenza may also cause exacerbations of underlying chronic lung disease and cardiac diseases.[56] In the Philippines, the mean annual influenza incidence rate is 5.4 per 1,000 individuals in urban regions of the country.[57]

Administration of either inactivated or intranasal influenza vaccines in healthy adults showed significant benefit in reducing laboratory-confirmed influenza (RR 0.41, 95% CI 0.36 to 0.47) and influenza-like illness (RR 0.84, 95% CI 0.75 to 0.95) compared with no vaccination. There was an inconclusive effect of inactivated influenza vaccines on hospitalization (RR 2.89, 95% CI 0.12 to 70.68). There was no significant difference in missed working days among adults given inactivated influenza vaccine compared to no vaccination (MD 0.01 days, 95% CI -0.08 to 0.09).[58]

Administration of inactivated influenza vaccine in pregnant women compared to placebo or non-influenza vaccine (such as meningococcal conjugate vaccine, pneumococcal polysaccharide vaccine) resulted in a significant reduction in infant laboratory-confirmed influenza (RR 0.64, 95% CI 0.53 to 0.78), maternal laboratory-confirmed influenza (RR 0.47, 95% CI 0.29 to 0.77), and maternal influenza-like illness (RR 0.81, 95% CI 0.67 to 0.99). There was a trend towards harm on infant mortality (RR 1.29, 95% CI 0.98 to 1.70) and serious adverse events (RR 1.08; 95% CI 0.92 to 1.28). There was an inconclusive effect on maternal mortality (RR 0.62, 95% CI 0.20 to 1.90). No significant difference was observed in infant hospitalization (RR 0.92, 95% CI 0.75 to 1.13).[59-69]

Administration of inactivated influenza vaccine in healthcare workers (HCWs) compared to no vaccine significantly reduced laboratory-confirmed influenza (RR 0.12, 95% CI 0.04 to 0.4). There was no significant difference in missed working days (MD -0.09 days, 95% CI -0.19 to 0.02). There was an inconclusive effect on influenza-like illness (RR 1.07, 95% CI 0.62 to 1.95). Inactivated influenza vaccine led to increased risk for serious adverse events (RR 5.34, 95% CI 2.12 to 13.41) among HCWs. There was no significant difference in laboratory-confirmed influenza among patients of HCWs given inactivated influenza vaccine compared to patients of HCWs with no vaccination (risk difference [RD] 0; 95% CI -0.03 to 0.03) and hospitalization (RD 0, 95% CI -0.02 to 0.02).[70-73]

Administration of inactivated influenza vaccine in the elderly significantly reduced laboratory-confirmed influenza (RR 0.44, 95% CI 0.27 to 0.71) and influenza-like illness (RR 0.64, 95% CI 0.49 to 0.84) compared to no vaccine. There was an inconclusive effect in systemic adverse events (*fever*: RR 1.58, 95% CI 0.92 to 2.71; *nausea:* RR 1.75, 95% CI 0.74 to 4.12; *general malaise*: RR 1.19, 95% CI 0.87 to 1.61). Live intranasal influenza vaccine showed a trend towards benefit in laboratory-confirmed influenza (RR 0.49, 95% CI 0.21 to 1.17), and an inconclusive effect in systemic adverse events (*general malaise:* RR 3.09, 95% CI 0.18 to 53.20; *fever:* RR 1.71; 95% CI 0.09 to 33.24.[58,74]

Administration of high-dose influenza vaccine in the elderly significantly reduced laboratory-confirmed influenza (RR 0.76, 95% CI 0.64 to 0.90), all-cause hospitalization (RR 0.93, 95% CI 0.90 to 0.96), and serious adverse events (RR 0.92, 95% CI 0.87 to 0.98) compared to standard-dose influenza vaccine. There was no significant difference in all-cause mortality (RR 0.90, 95% CI 0.95 to 1.03). There was a trend towards harm in systemic reactogenic events (RR 1.19, 95% CI 0.91 to 1.55) and a significantly increased risk for local reactogenic events (RR 1.47, 95% CI 1.26 to 1.71) with high-dose compared to standard-dose influenza vaccine.[75,76]

Justification: Annual influenza vaccination was recommended by the panel due to the evidence showing benefit, which was deemed by the CP to outweigh the potential harm. High-dose inactivated influenza vaccine is not available locally, precluding the panel from making a recommendation on its use. The panelists recognized that high-dose may be suggested over standard-dose inactivated influenza vaccine for the elderly population, whenever available. The burden of disease should be considered among other factors when choosing the appropriate dose for vaccination.

Japanese Encephalitis Vaccine

Guideline Question 7. Should the Japanese encephalitis vaccine be given to asymptomatic, apparently healthy adults?

Recommendation 7.1. Among asymptomatic apparently healthy adults, we suggest giving the Japanese encephalitis virus vaccine. *(Low certainty of evidence, weak recommendation)*

Key findings: Japanese encephalitis (JE), a vector-borne flavivirus disease, is the leading cause of viral encephalitis in Asia and is endemic in the Philippines.[77] JE virus is transmitted to humans through the bite of an infected mosquito, primarily Culex species.[78] The latest data available is the January 2023 data, wherein the Philippines had an acute meningitis/encephalitis syndrome incidence rate of 0.12 per 100,000 population, with the highest cases reported in Regions III (19 cases, 0.15/100,000) and VI (18 cases, 0.22/100,000). Regions IX (13 cases, 0.33 per 100,000) and II (13 cases, 0.24 per 100,000) had the highest incidence rates.[79] JE carries a high mortality rate of 15-40%. Permanent neurologic or psychiatric sequelae can occur in 30–50% of symptomatic cases.[80]

Six (6) RCTs investigated the effect of Japanese encephalitis virus (JE) vaccination on healthy, asymptomatic adults. All studies were performed in non-JE-endemic countries.[77,81-85] No study was found specifically investigating the effects of Japanese encephalitis virus vaccination on healthcare workers, travelers to endemic areas, or microbiologists who handle the virus.

JE vaccination resulted in high positive seroconversion rates, defined as having protective antibody levels against the JE virus, in healthy adults. After 1 month, 91-100% of vaccine recipients had positive seroconversion rates. JE vaccination was shown to provide long-lasting immunity, with vaccine recipients having protective titers even at 60 months.[83,84]

There was an inconclusive effect on local adverse events (RR 1.11, 95% CI 0.74 to 1.66) and serious adverse events (RR 1.04, 95% CI 0.45 to 2.38) among JE vaccine recipients compared to placebo. There was a trend towards benefit in the risk for systemic adverse events (RR 0.81, 95% CI 0.63 to 1.05) among JE vaccine recipients compared to placebo. Most of the adverse events observed were mild, with pain at the injection site being the most reported. Only one of the reported serious adverse events (acute viral illness 8 days after a dose of live chimeric JE vaccine) was deemed to be possibly vaccine-related. No deaths occurred in any of the studies.[84]

Justification: The CP considered that JE vaccination appears to benefit adults in terms of immunogenicity outcomes, but there were no studies showing benefit in terms of actual protection from the disease. In addition, due to the disproportionate distribution of disease burden across the country, only a weak recommendation for mass vaccination was made by the panel. In the Philippines, an increasing burden of the disease is observed, although present epidemiologic data show that cases are concentrated mostly in Regions 2, 3, 6, and 9. Local incidence is particularly high in regions where people are exposed to rice fields or other areas that are natural habitats of the Culex mosquito. Asia has been stated as a hotspot of JE infection, and the abovementioned regions in the Philippines are examples of these.

Measles Vaccine

Guideline Question 8. Should the measles-containing vaccine be recommended to apparently healthy adults?

Recommendation 8.1. Among healthy adults (non-pregnant or unvaccinated), we recommend giving the measles-containing vaccine. *(Very low certainty of evidence, strong recommendation)*

Key findings: Measles is a highly contagious acute infection characterized by fever, cough, coryza, conjunctivitis, rash, and enanthem. It may lead to severe complications such as encephalitis. In the Philippines, 2019 data showed that there were 2.31 deaths per 100,000 cases of measles.[86] A surveillance report of the DOH issued in July 2019 reported a 208% higher number of measles cases compared to the same period in 2018.[87]

The administration of two doses of measles-containing vaccine (MCV) compared to no vaccination significantly reduced measles incidence (RR 0.03, 95% CI 0.02-0.08), based on 9 observational studies conducted in children.[88] Measles seroconversion rates for people ≥7 years old ranged from 96%-100%. These results show that even if given outside the recommended age, MCV is still immunogenic.[89,90] Among healthcare workers, the administration of standard titer MCV compared to no vaccination showed a trend towards benefit in reducing all-cause mortality (RR 0.74, 95% CI 0.51 to 1.07, 4 RCTs).[91]

Evidence on the cost-effectiveness of measles-containing vaccines came from a simulated or hypothetical US birth cohort of infants and from a simulated birth cohort in East China.[92,93] The direct benefit-cost ratio of 6.06 for East China, with savings of $73.8M, and a direct benefit-cost ratio of 14.2 for the USA, with a societal benefit-cost ratio of 23, with savings of $7.6 billion.

Measles vaccination is part of the Expanded Program on Immunization of the DOH through the administration of

the MMR vaccine starting at nine months up to 12 months old, followed by a booster through the MMR vaccine given at school-age (i.e., grade levels one and seven). However, school-based vaccination efforts only reached a quarter in 2019 due to the COVID-19 pandemic. Additionally, surveillance by DOH showed low rates of fully immunized children, recording only 60% in 2020. With this, there is an expected increase in the population of measles-susceptible individuals.

Justification: Studies on the efficacy of the measles vaccine among healthy adults are lacking. The evidence involved data from the pediatric population, thereby posing applicability issues. Moreover, the included studies involved the administration of two doses of measles-containing vaccine. This may pose applicability issues since one dose is sufficient to confer lifelong immunity among adults. In clinical practice, a single dose is administered to healthy adults, while the two-dose regimen, given one month apart, is suggested only for high-risk groups, including healthcare workers.

Despite the very low certainty of evidence, the panelists were unanimous in recommending measles vaccine for healthy adults due to the following considerations: (1) the highly infectious nature of measles due to its airborne mode of transmission, (2) the high morbidity and mortality rates of measles infection, and (3) the expected increase in the proportion of adults susceptible to measles secondary to the low vaccination rates.

Meningococcal Vaccine

Guideline Question 9. Should the meningococcal vaccine be given to asymptomatic, apparently healthy adults?

Recommendation 9.1. Among asymptomatic apparently healthy adults, we suggest AGAINST giving the meningococcal MenACWY vaccine. *(High certainty of evidence, weak recommendation)*

Recommendation 9.2. Among asymptomatic apparently healthy young adults (18-25 years old), we suggest AGAINST giving the meningococcal MenB vaccine. *(Moderate certainty of evidence, weak recommendation)*

Recommendation 9.3. Among adults with a high risk of contracting meningococcal disease*, we suggest giving the meningococcal MenACWY vaccine. *(Moderate certainty of evidence, weak recommendation)*

Recommendation 9.4. Among adults with a high risk of contracting meningococcal disease, we suggest giving the meningococcal MenB vaccine.** *(Very low certainty of evidence, weak recommendation)*

* *individuals living in close quarters/proximity, asplenic patients, persons handling N. meningitidis isolates*

** *young adults in crowded dormitories*

Key findings: *Neisseria meningitidis* (meningococcus) is a significant source of deadly bacterial infections, frequently manifesting as meningitis or meningococcemia.[94] Invasive meningococcal disease can affect all ages, with particular predilection for infants less than 1 year old, adolescents, and the elderly.[95] Serogroups C, W, and X account for the majority of endemic and epidemic meningococcal illness.[96] The DOH Epidemiology Bureau – Philippine Health Statistics has documented 84 cases of meningococcal infections in 2019, corresponding to a rate of 0.1 per 100,000 population. The majority of the cases (73/84 or 87%) were recorded from Mindanao. The Cordillera outbreak was caused by serogroup A, whereas the other two epidemics (Davao and Makati) were caused by serogroup B.[94] The disease rate remained unchanged in 2020.

MenACWY vaccines compared to control (Tdap) resulted in a significant immune response against serogroups A, C, W, and Y 28 days post-vaccination (*MenA*: RR 8.38, 95% CI 4.48 to 15.69; *MenC*: RR 10.93, 95% CI 5.61 to 21.28; *MenW*: RR 7.54, 95% CI 4.43 to 12.84; *MenY:* RR 6.03, 95% CI 3.06 to 11.89). Although there were significantly more systemic adverse events and injection site reactions in the vaccine group at 33.2% (CI 26.7 to 40.2), no serious adverse events were reported.[97] Four observational studies of MenACWY vaccination among pregnant women showed no increased risk of pregnancy-or birth-related adverse events.[98-101]

MenB-4C vaccination compared to placebo resulted in significantly more study participants exhibiting protective antibody titer levels at 2 months (RR 1.52, 95% CI 1.37 to 1.68) and 12 months (RR 1.88, 95% CI 1.59 to 2.22) compared to placebo.[102] No serious adverse events related to the vaccine were reported.

MenB-FHbp, compared to the control group (HAV vaccine), showed benefit in terms of seroconversion at 28 days.[103] There is inconclusive evidence on the effect of MenB-FHbp vaccine compared to HAV vaccine on serious adverse events (RR 8.48, 95% CI 6.95 to 10.35).

Justification: The CP formulated a weak recommendation AGAINST giving the vaccine to all apparently healthy adults despite evidence showing that meningococcal vaccines effectively induce immune responses due to the low prevalence of the disease, low rates of infection, and high costs of vaccination. In addition, the panel considered that there are existing prophylactic interventions for those exposed to meningococcal disease.

For individuals considered to be at high risk of contracting meningococcal disease, vaccination using either MenB or MenACWY vaccines was suggested. These include individuals living in close quarters, asplenic patients, and persons handling N. meningitidis isolates (i.e., microbiologists, pathologists, etc.)

Mpox Vaccine

Guideline Question 10. Should the mpox vaccine be given to apparently healthy adults?

Recommendation 10.1 Among apparently healthy adults, we suggest AGAINST giving the mpox vaccine. *(Low certainty of evidence, weak recommendation)*

Recommendation 10.2. Among adults with high risk* of exposure to mpox, we suggest AGAINST giving the mpox vaccine. *(Very low certainty of evidence, weak recommendation)*

** Healthcare workers responding to monkeypox outbreak, laboratory personnel who are handling monkeypox virus, people with multiple sexual partners, men having sex with men (MSM)*

Key findings: Mpox (formerly monkeypox) virus is a DNA virus of the Orthopoxvirus genus that is related to the variola virus that causes smallpox. On 23 June 2022, the World Health Organization (WHO) declared mpox as an evolving threat of moderate public concern due to the increasing number of cases and affected member states.[104,105] From 01 May 2022 to 14 March 2023, a total of 86,516 mpox cases have been recorded globally, with 111 (0.13%) deaths.[106] In the Philippines, only 4 cases and zero deaths were recorded between 29 July 2022 and 22 August 2022.[104]

The current mpox outbreak mostly affected high-risk groups, including gay and bisexual men having sex with men, individuals with high-risk sexual behaviors, healthcare workers, and those working in laboratories handling the mpox virus. There are three available vaccines being used today against mpox: ACAM2000®, MVA-BN (Jynneos®, Imvamune, Imvanex), and LC16m8.

For healthy adults, one RCT showed that MVA-BN increased total and neutralizing antibody titers after 2, 4, 6, and 8 weeks and 6 months post-vaccination, with antibodies persisting even after 2 years.[106] Surveillance data for adverse events involving 987,209 individuals administered MVA-BN doses (Jynneos®) revealed only 2 cases of myocarditis within 30 days and 3 cases of anaphylaxis within 24 hours.[107]

For individuals at high risk for mpox, we adapted the evidence base consisting of 39 studies from the WHO/SAGE guidelines published on November 16, 2022. Seroconversion rates after 30 days for each vaccine type were as follows: ACAM2000 79 to 97%,LC16m8 60 to 100%, and MVA-BN 62.4%.[108-114] In terms of adverse events, 269 cases of myopericarditis were reported after ACAM2000 vaccination (8 studies, n=1,743,620). Local and systemic adverse events were frequently reported among vaccinated subjects with MVA-BN (up to 99% of vaccinees), but no reported cases of myocarditis or serious adverse events (SAEs) for this vaccine.[115,116] LC16m8 vaccine is also associated with high rates of local and systemic adverse events (up to 99% of vaccines), auto-inoculation in 0.4% of vaccinees, and no reported SAEs.[112-114]

Justification: Routine vaccination for mpox among the general population was NOT recommended due to the low burden of disease, difficulties in vaccine access, and very low certainty of evidence. DOH no longer procured mpox vaccines since documenting only 4 cases until August 2022. The commercially available vaccines are the Modified vaccinia Ankara strain (MVA-BN - ACAM2000) stockpiled by the United States and the LC16m8 stockpiled by Japan.

Mpox vaccination was also NOT recommended for individuals at high risk of exposure to mpox due to the very low certainty of evidence, and difficulties with vaccine access and implementation. The following individuals were identified as belonging to the high-risk group based on existing epidemiologic studies: healthcare workers responding to the mpox outbreak, laboratory personnel who are handling mpox virus, people with multiple sexual partners, and men having sex with men (MSM).

Pneumococcal Vaccine

Guideline Question 11. Should the pneumococcal vaccine be recommended to apparently healthy adults?

Recommendation 11.1. Among apparently healthy adults ≥65 years of age, we suggest the use of PCV13. *(Moderate certainty of evidence, weak recommendation)*

Recommendation 11.2. Among app**arently healthy adults ≥65 years of age, we recommend the use of PPSV23.** *(Moderate certainty of evidence, strong recommendation)*

Recommendation 11.3. Among apparently healthy adults between 18-64 years of age, we suggest the use of PCV13. *(Low certainty of evidence, weak recommendation)*

Recommendation 11.4. Among apparently healthy adults between 18-64 years of age, there is insufficient evidence to recommend for or against the use of PPSV23. *(Low certainty of evidence)*

Key findings: Pneumonia causes symptoms of cough, fever, chills, and difficulty of breathing. Guidelines on the role of pneumococcal vaccination for specific subgroups (immunocompromised, patients with multiple comorbidities, and high-risk patients) have been established, but data on its role among apparently healthy asymptomatic adults remains limited.[117-121]

Among immunocompetent adults ≥65 years of age, PCV13 compared to placebo decreased the incidence of pneumococcal pneumonia (RR 0.78, 95% CI 0.63 to 0.97) and invasive pneumococcal disease (RR 0.51, 95% CI 0.34 to 0.77), but had an inconclusive effect on all-cause mortality (RR 0.89; 95% CI 0.34 to 2.30).[122-124] PCV13 was associated with a greater incidence of non-serious adverse events compared to placebo (RR 1.37, 95% CI 1.08 to 1.74).[122]

Among immunocompetent adults ≥65 years of age, PPSV23 compared to placebo also significantly decreased the incidence of invasive pneumococcal disease (RR 0.27, 95% CI 0.08 to 0.90), but had an inconclusive effect on pneumococcal pneumonia (RR 0.75, 95% CI 0.35 to 1.62).[124,125] In terms of immunogenicity response (specifically measuring the opsonophagocytic activity geometric mean titers, GMTs), PCV13 was non-inferior to PPSV23 for the 12 common pneumococcal serotypes (RR 1.30, 95% CI 0.99 to 1.75). PPSV23 resulted in significantly fewer local reactions compared to PCV13 (RR 0.60, 95% CI 0.45 to 0.80).[126]

Among immunocompetent adults 18 to 64 years of age, there was a reduction in the incidence of invasive pneumococcal disease after the introduction of PCV13 compared to pre-introduction (percent reduction of 74%, 95% CI -0.78 to -0.70).[127] Local adverse events were reported in 95.8 to 96% of PCV13 recipients, which were mostly mild.[128,129] There was no impact on reducing pneumonia incidence compared to placebo.[130] Based on a Phase I/II trial, PCV13 resulted in a robust immune response among adults ≥18 years of age, with the highest responses observed in the youngest age groups. The immune response (measured using IgG levels) was comparable for PCV13 and PPSV23 vaccinees for serotypes 1, 3, and 6A, with a greater immune response seen among those 50 to 59 years old compared to those 60 to 64 years old.[131]

Justification: The evidence base included studies on immunocompetent adults without comorbidities. This contrasts with the current recommendations of the Philippine Society of Microbiology and Infectious Diseases (PSMID) and the Philippine Foundation for Vaccination (PFV) on pneumococcal vaccines, which were based on studies among immunocompetent adults with stable comorbidities. The panel noted that the outcomes were measured after a single dose of either PCV13 or PPSV23 in the studies. In clinical practice, PPSV23 is administered every five years while PCV13 is administered as a single dose.

The local prevalence of pneumococcal serotypes was an important consideration for the panelists. Due to the lack of pneumococcal surveillance studies up to date, the panel used the Antimicrobial Resistance Surveillance Program Annual Report in 2020 as a basis, which showed that the locally prevailing serotypes varied per year. However, the panel also noted that the report had a small sample size and that it is an antimicrobial resistance surveillance rather than a prevalence study. Cost-effectiveness studies from different countries among adults have mixed results, with more recent studies showing that pneumococcal vaccination is not a cost-effective strategy, especially in the healthy adult population.

Despite the evidence showing PCV13 as non-inferior to PPSV23 among immunocompetent adults 65 years old and above, two panelists voted AGAINST recommending PCV13 for this age group because the serotypes covered by PCV13 are more commonly isolated in children aged ≤17 years. This was also the reason a weak recommendation was formed for PCV 13, while a strong recommendation was formed for PPSV23.

Among immunocompetent adults 18-64 years of age, PCV13 shows a decline in the incidence of invasive pneumococcal disease. However, one panelist voted AGAINST the use of PCV13 among immunocompetent adults between 18 and 64 years old due to its low efficacy in this subgroup. One study showed that PPSV23 has an inconclusive effect in reducing the incidence of pneumonia, but a benefit was shown in immunogenicity studies. Hence, the CP decided not to make a recommendation for or against PPSV23 in this age group.

Rabies Vaccine

Guideline Question 12. Should the pre-exposure rabies vaccine be given to asymptomatic, apparently healthy adults?

Recommendation 12.1. **Among asymptomatic healthy adults, we suggest AGAINST giving the pre-exposure rabies vaccine**. *(Very low certainty of evidence, weak recommendation)*

Recommendation 12.2. Among healthcare workers with a high risk of exposure to rabies, we suggest giving the pre-exposure rabies vaccine. *(Very low certainty of evidence, weak recommendation)*

Recommendation 12.3. Among adults with a high risk of exposure, we suggest giving the pre-exposure rabies vaccine. *(Very low certainty of evidence, weak recommendation)*

Key findings: Rabies, caused by rabies virus (RABV) genotype 1, carries the highest fatality rate among all viral encephalitis and is one of the most common fatal infections in the world.[132] Based on 2019 data from the DOH, animal bites were ranked 8th among the top 10 leading causes of morbidity in the Philippines, accounting for 89,082 cases or 83 per 100,000 population. There were 283 rabies deaths that year, corresponding to a mortality rate of 0.3 per 100,000 population, with most cases (n=216; 76%) occurring in adults.[14]

No studies were found comparing pre-exposure rabies vaccination with placebo or no vaccination among asymptomatic, apparently healthy adults. Indirect evidence for this guideline question was obtained from 11 RCTs that compared variations in the schedule, route, and type of pre-exposure rabies vaccination. Efficacy outcomes were expressed as geometric mean titer (GMTs) or seroconversion rates at 1 year of follow-up or less.[133-143]

In terms of vaccine schedule, an abbreviated schedule did not show a significant difference compared to the standard regimen for efficacy and safety outcomes, regardless of age, risk group, or type of rabies vaccine.[136,138,139,142] In terms of route of administration, intradermal and intramuscular routes

demonstrated similar safety and efficacy profiles.[134,135,141,143] Finally, different types of rabies vaccines (PVRV and PCECV) showed no significant difference in safety and efficacy.[140,142]

Justification. Only a weak recommendation was made for pre-exposure rabies vaccination among high-risk groups due to the very low certainty of evidence on its efficacy. The included studies in the evidence base did not specify the risk categories of the study participants. Uncertainties surrounding which geometric mean titer (GMT) levels offer protection from disease and the duration of immunity were also pointed out by the panel. Intramuscular (IM) and oral routes were deemed to be equipotent; thus, no specific recommendations on the routes were drafted.

Tetanus Vaccine

Guideline Question 13. Should the tetanus vaccine be recommended to apparently healthy adults?

Recommendation 13.1. Among healthy adults with a complete primary series, we recommend giving any tetanus-toxoid-containing vaccine every 10 years. *(Low certainty of evidence, strong recommendation)*

Recommendation 13.2. Among healthy adults with unknown status or incomplete series, we suggest giving the primary series with Tdap followed by any tetanus-toxoid-containing vaccine. *(Very low certainty of evidence, weak recommendation)*

Recommendation 13.3. Among pregnant women with a complete primary series, we suggest giving any tetanus toxoid-containing vaccine during each pregnancy. *(Very low certainty of evidence, weak recommendation)*

Recommendation 13.4. Among pregnant women with unknown status or incomplete series, we suggest giving the primary series with Tdap followed by any tetanus-toxoid-containing vaccine. *(Low certainty of evidence, weak recommendation)*

Key findings: Tetanus is caused by *Clostridium tetani*, a gram-positive spore-forming rod-shaped bacterium found in soil. Tetanus infection usually arises from skin cuts and abrasions, penetrating wounds, or drug injections.[144] In 2019, the Philippines reported only 78 cases of neonatal tetanus and 953 total cases of tetanus, but the lack of a local non-neonatal tetanus surveillance system makes underreporting of the total number of cases highly likely.[145] The DOH reported 15 cases of clinically-confirmed neonatal tetanus from January 1 to April 27, 2019.[146] Of these 15 cases, eight (53%) of the mothers were not vaccinated against tetanus, 4 (27%) had unknown vaccination status, and one (6%) had received a single dose of tetanus toxoid vaccine.

Tetanus toxoid-containing vaccination showed significant benefit in increasing immune response rates, defined as having detectable antibody levels against the tetanus antigen one month after vaccination in healthy adults. Seven immunogenicity studies showed increased immune responses from any tetanus toxoid-containing vaccine compared with another vaccine or with no comparator (VE 98.5%, 95% CI 98 to 99%).[147-153] Individuals who were given tetanus vaccination experienced a small but increased risk of grade 3 adverse events (as much as 2.4%), defined as adverse events that would cause difficulty or impairment in daily activities. The incidence of SAEs such as hospitalization, prolonged inpatient hospitalization, or disability in daily activities, was estimated at 0.4 to 1.2% among those who received the vaccine.

Justification: The panel was unanimous in recommending tetanus vaccines for healthy adults. Despite achieving the Maternal and Neonatal Tetanus Elimination (MNTE) status in 2017, the Philippines remains to have a significant burden of tetanus based on data from subsequent years. Additionally, tetanus has a high case fatality rate. Due to the high burden of disease, the CP strongly recommended tetanus vaccination among healthy adults with a complete primary series despite the low certainty of evidence.

The evidence base included studies where the participants were able to complete the primary series, posing applicability issues in the local setting. The panel noted that frequent administration of the tetanus vaccine does not provide added benefit. Further, the vaccine is more reactogenic if administered closely. In the absence of wounds, the tetanus vaccine should be given every ten years.

All but one panelist agreed with the dosing specified for the pregnant patients. The panelist who disagreed with the dosing cited that health centers currently follow a different vaccine schedule: two doses are given during the first pregnancy, and one dose is given for each of the second to fourth pregnancies. Subsequent pregnancies will no longer need tetanus vaccination once a total of five doses have been administered. However, this dosing schedule was based on the WHO recommendation wherein the evidence base was one case report.

Typhoid Vaccine

Guideline Question 14. Should the typhoid vaccine be recommended to apparently healthy adults?

Recommendation 14.1. Among healthy adults, we suggest the use of Vi polysaccharide intramuscular vaccine *(Low certainty of evidence, weak recommendation)*

Recommendation 14.2. Among healthy adults, there is insufficient evidence to recommend for or against Vi-TT intramuscular vaccines. *(Very low certainty of evidence)*

Recommendation 14.3. Among healthcare workers, we suggest AGAINST the routine use of typhoid vaccines. *(Very low certainty of evidence, weak recommendation)*

Key findings: Typhoid fever, also known as enteric fever, is a multisystemic bacteremic disease caused by *Salmonella enterica serotype* Typhi, Paratyphi A, B, and C. It is most commonly transmitted through the fecal-oral route from contaminated water or food sources. The disease is endemic in many Southeast Asian countries, most especially in areas where there is poor water and sewage sanitation. Globally, typhoid fever is estimated at 26 million cases, while paratyphoid fever is estimated at five million cases, causing 215,000 deaths each year.[154] In 2019, an estimated 52,810 (95% CI 848, 3,373) deaths were recorded in the Philippines alone.[155]

Significant benefit was observed in reducing laboratory-confirmed typhoid fever among patients living in or traveling to endemic areas who received Vi polysaccharide vaccine (RR 0.45, 95% CI 0.30 to 0.70), Ty21a oral vaccine (RR 0.50, 95% CI 0.39 to 0.65), and Vi-repa vaccine (RR 0.11, 95% CI 0.05 to 0.23) compared to placebo.[156-159] There was a trend towards benefit in reducing laboratory-confirmed typhoid fever for those who received Vi-TT Vaccine (RR 0.06, 95% CI 0.00 to 1.01), but this study was conducted among children six months to 12 years old.[159] There was a significantly increased risk for mild to severe adverse effects among those who received typhoid vaccines (RR 1.67, 95% CI 1.03 to 2.72).[160] No reported mortality and hospitalizations upon the receipt of vaccines.

No RCTs evaluated the efficacy of typhoid vaccines specifically in healthcare workers (HCWs). Very low certainty evidence from a case series suggests that the typhoid vaccine may not sufficiently provide protection of HCWs from the disease.[161]

Justification: Typhoid fever is endemic in the Philippines; thus, the panel emphasized the importance of typhoid vaccination among healthy adults in the country. However, issues were raised on the efficacy, availability, and financial accessibility of typhoid vaccines. Among the four types of typhoid vaccine, only the Vi polysaccharide intramuscular vaccine and the Vi-TT intramuscular vaccine are available locally. The panel was unanimous in recommending the Vi polysaccharide vaccine among healthy adults, but this was a weak recommendation due to the small magnitude of benefit and high cost.

For Vi-TT, the CP unanimously decided that there is insufficient evidence to recommend for or against Vi-TT because no direct studies evaluated Vi-TT in healthy adults. The available study evaluated the Vi-TT conjugate vaccine in children, with very low certainty of evidence and indirectness. The unavailability and lack of local experience on the Ty21 oral vaccine and Vi-rEPA intramuscular vaccine precluded the panel from making recommendations on these vaccines. Additionally, there is an expected shortage of the Ty21 oral vaccine because its manufacturing was temporarily stopped in December 2020 for undisclosed reasons.

The typhoid vaccine does not offer 100% protection. The panel highlighted the importance of other preventive measures such as access to safe water, adequate sanitation, and hygienic food preparation. These preventive measures were also the reason the panel was unanimous AGAINST routine typhoid vaccination among healthcare workers. Despite the risk of exposure of this group to typhoid fever, transmission could be prevented by proper hygiene and occupational safety measures.

Varicella Vaccine

Guideline Question 15. Should the varicella vaccine be given to asymptomatic, apparently healthy adults?

Recommendation 15.1. Among asymptomatic apparently healthy adults, we suggest AGAINST giving the varicella vaccine. *(Very low certainty of evidence, weak recommendation)*

Recommendation 15.2. Among asymptomatic healthcare workers, we suggest AGAINST giving the varicella vaccine. *(Very low certainty of evidence, weak recommendation)*

Key findings: Varicella-zoster virus (VZV) is a Herpesviridae virus responsible for two clinical disorders, namely varicella and herpes zoster. Varicella, often known as chickenpox, is the main illness and is caused by exposure to an infected person.[162] Serious complications can occur, most commonly in infants, adults, and immunocompromised people. These include secondary bacterial infections of skin lesions, which at times can lead to bacteremia/sepsis, pneumonia, cerebellar ataxia, encephalitis, and hemorrhagic conditions. Rarely (about 1 in 40,000 varicella cases), these complications may result in death.[163] Data from the Philippine Health Statistics 2011 documented a total of 14,080 varicella cases or a rate of 32.4% per 100,000 population for all ages, with 47 total deaths across all ages (<0.01% per 100,000 population). Among ages 15 and above, the total number of deaths is 38 (<0.01% per 100,000 population). Varicella is listed as one of the ten leading causes of morbidity since 1989.[164]

The incidence of breakthrough varicella infection among vaccine recipients occurred in 7% of healthy adults and 9% of healthcare workers.[165,166] These participants received two doses of the varicella vaccine within an interval of 4 to 12 weeks. Among those with reported exposures, the proportion of subjects who developed varicella ranged from 9 to 21% in healthy adults[167-169] and 3 to 17% in healthcare workers.[166] Seroconversion rate was reported at 92 to 99% among healthy adults. Among healthcare workers, the pooled seroconversion rates were 95% for the short-term group (1-2 months post-vaccination), 94% for the medium-term group (5-6 months post-vaccination), and 81% for the long-term group (>6 months post-vaccination).

No serious adverse events were reported in the studies. Only mild adverse events were observed, including local or injection-site related reactions, fever, varicella or zoster-like rash, headache, facial spasm, sore throat, chills, muscle pain, and an increase in body temperature.

Justification: A weak recommendation AGAINST the routine vaccination of healthy adults was made by the panel due to the lack of epidemiological studies on the burden of varicella disease among adults. In addition, the available evidence exhibited high uncertainty in the ability of vaccination to provide adequate levels of protection for disease prevention. However, some clinicians in the panel reported that more severe disease presentation may occur in adults compared to children. The panel also noted that there are other costs to be considered, including lost workdays when adults would take care of a family member with varicella, as well as being at high risk of contracting the virus when exposed to afflicted family members.

DISCUSSION

This CPG contains systematic syntheses of evidence on adult immunization. The CPG provides forty-one (41) recommendations on prioritized questions in the immunization of apparently healthy Filipino adults. Recommendations are based on the appraisal of the best available evidence for the fifteen clinical questions. The CPG is intended to be used by general practitioners and specialists in the primary care setting, policy makers, employers and administrators, allied health practitioners, and patients.

The PHEX Task Force underscores the importance of considering certain factors in the choice to recommend vaccination, including equity and applicability. When assessing individuals' eligibility for vaccination, vaccine availability, age, eligibility criteria, medical history, current health status, potential contraindications, and drug interactions should be considered. Although this CPG aims to give guidance to health professionals, hospital administrators, employers, payors, and patients, the recommendations are not intended to supersede individuals' values and preferences. The task force recognizes that implementation of the recommendations may vary depending on the given context. In addition, this CPG should not serve as the sole basis for instituting or discontinuing practices aimed at enhancing the health outcomes of many Filipinos, particularly the workforce.

This guideline integrates the best available evidence as well as the clinical expertise and values of stakeholders to provide reliable recommendations. We also considered in the discussions the limitations in different areas, such as access to vaccines and the required logistics in the immunization process. This CPG provides evidence-based guidelines so that healthcare providers can make informed decisions regarding immunizations and counsel patients on when and how often the vaccines should be administered.

We have purposefully narrowed the scope of this CPG to apparently healthy individuals. The guideline will also be updated periodically; however, CPG development takes time, and guidelines may lag behind the most recent evidence. We encourage stakeholders to stay updated with the latest research and be aware of any emerging evidence that may impact immunization practices. This document also does not address individual patient variations (allergies, comorbidities, past infection, etc.), healthcare providers should consider individual factors when applying the guidelines to ensure personalized care.

Research Gaps

Although there were available studies on the efficacy and safety of the vaccines among apparently healthy adults, the efficacy outcomes for some vaccines were based on immunogenicity and seroconversion findings only and not prevention of disease (e.g., Japanese encephalitis vaccine, rabies vaccine, *Haemophilus influenzae* type b), which reduced the certainty of evidence. For some questions, the available evidence did not use a placebo control group. There were also limited RCTs specifically enrolling healthcare workers. Some of the RCTs that were available are more than 20 years old, such as those on the Hib vaccine. No studies were found comparing pre-exposure rabies vaccination with placebo or no vaccination among asymptomatic, apparently healthy adults. No RCTs were also found comparing varicella vaccination with no vaccination or placebo.

More vaccine trials should be conducted using clinical outcomes to improve the evidence. Future studies could also investigate the resources required and the cost-effectiveness of the vaccines, especially in our country.

CONCLUSIONS

The systematic review of evidence was used to assess each vaccine's efficacy, safety, and cost-effectiveness. These recommendations can be used by relevant stakeholders, particularly in the public health units, those in primary care practice, and the administrative sectors of the implementation of vaccination programs.

Disclaimer

This guideline is intended to be used by general practitioners, specialists, and health professionals who are primary care providers. Although adherence to this guideline is encouraged, it should not restrict the primary care providers from using their sound clinical judgment in handling individual cases. Payors and policymakers, including hospital administrators and employers, can also utilize this CPG, but this document should not be the sole basis for evaluating insurance claims. Recommendations from the PHEX app and the guidelines therein should also not be treated as strict rules on which to base legal action.

The content of this CPG is the intellectual property of the DOH. Kindly provide the proper citations when using any part of this document in lectures, research papers, and any other format presented to the public. The electronic version of this material can be accessed online on the DOH website.

Queries, suggestions, and other concerns regarding this CPG may be directed to the DOH office by email.

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All authors certified fulfillment of ICMJE authorship criteria.

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APPENDIX

Critical Outcomes

Cholera vaccine	Incidence of cholera, all-cause mortality, mortality from cholera, adverse events, hospitalization, immunogenicity
Haemophilus influenzae B vaccine	Immunogenicity, adverse events
Hepatitis A vaccine	Incidence of hepatitis A, immunogenicity, adverse events, all-cause mortality
Herpes zoster vaccine	Incidence of herpes zoster, adverse events
High-dose inactivated influenza vaccine	Incidence of influenza, all-cause mortality, all-cause hospitalization, adverse events
Human papilloma virus vaccine	Persistent infection, incidence of cancer, incidence of anogenital warts, adverse events, death
Influenza vaccine	Incidence of influenza, influenza-like illness, hospitalization, adverse events, infant hospitalization, infant mortality, all-cause mortality
Japanese encephalitis vaccine	Immunogenicity, adverse events
Measles vaccine	Death, immunogenicity, adverse events, and incidence of measles
Meningococcal vaccine	Adverse events, immunogenicity
Mpox vaccine	Immunogenicity, adverse events
Pneumococcal vaccine	All-cause mortality, community-acquired pneumonia incidence, incidence of invasive pneumococcal disease, pneumococcal pneumonia, adverse events, immunogenicity
Rabies vaccine	Immunogenicity, adverse events
Tetanus vaccine	Immunogenicity, adverse events,
Typhoid vaccine	Incidence of typhoid fever, adverse events
Varicella vaccine	Immunogenicity, incidence of break-through infection, varicella attack rate

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