Methodology

The general CPG methodology used for the entire update was the GRADE approach, following the recommended process in the DOH Manual on Practice Guideline Development. (7) The target users of the CPG would be primary care providers and policymakers. The target population of the screening test and interventions was the apparently healthy asymptomatic Filipinos.

Guideline Preparation

PHEX Phase 2 convened a Central Executive Committee comprised of a Steering Committee (SC), Oversight Committee (OC) and Central administrative staff.

Six task forces (TF) were also convened to develop their respective guidelines namely:

1. Task force on Screening for Cardiovascular Disease
2. Task Force on Screening for Neoplastic Diseases
3. Task force on Screening for Congenital and Developmental Disorders
4. Task Force on Screening for Mental Disorders and Substance Abuse
5. Task Force on Immunization – Pediatric & Adult
6. Task Force on Screening on Lifestyle Advise

Task Force chairs were identified to lead each TF. They identified and recruited the working committees namely: 1) Task force SC, 2) Technical Working Group (technical coordinator, evidence review experts, technical writer, technical meeting facilitator, and an administrative officer) 3) Consensus Panel (CP) members.

Each task force Steering Committee prioritized and finalized the guideline questions to be addressed, 2) convened the ERE and 3). convened the CP. 4). supervised the entire CPG process. Additional methods done by each task force are found in their respective manuscripts.

Due to the number of task forces involved in this project, a Central Executive Committee, led by Dr. Leonila F Dans and Dr. Marissa A Alejandria, was created. The team was composed of the central steering committee, project leaders (LFD, MMA), project managers and administrative staff. The team oversaw and coordinated with all task forces. The Central Executive Committee provided continuous administrative and technical support to the task forces including the collection of declaration of Conflict of Interest, Curriculum Vitae (CVs), preparation, collection and processing of contracts and other salary/honorarium documents, training of task force members, and technical guidance throughout the whole CPG development process. The central team ensured that the CPG methodology as recommended in the DOH Manual for CPG Development was followed. The team guided and reviewed the development of research questions and evidence summaries. (See Appendix 1 for organizational structure)

Lectures, instruction modules, technical resource and templates were prepared to guide the task force in developing the research questions, evidence synthesis, and facilitation of CP meetings. Online orientation on CPG methodology tasks, specific steps were given to the task force steering committee, technical writers, evidence reviewers, technical coordinators, and facilitators.

Prioritizing the Guideline Research Questions

Each of the 6 task forces identified, prioritized and finalized the scope and the guideline research questions. Each question included details on population, intervention, comparator, and outcomes. Additional relevant specifics such as subgroup to be considered and frequency of intervention were also included. They consulted different stakeholders in prioritizing and developing their respective guideline questions. The Central Steering Committee reviewed and approved the guideline questions prior to evidence synthesis.

Identification and prioritization of questions were mostly based on the following criteria 1. disease burden 2. public contention 3. cost-effectiveness 4. new evidence 5. potential impact 6. interest of public or care providers 7. variation in care 8. sufficiency of evidence and 9. timeliness.

Evidence Synthesis

Each task force then convened their technical working group composed of a technical coordinator, evidence review experts (ERE) and technical writer . At least one ERE was assigned a guideline question to work on supervised and guided by a technical coordinator that also functioned as second reviewer. The search strategy and inclusion criteria were based on the PICO question and are included in the evidence summaries. For each guideline question, the GRADE Adolopment process was used in gathering the evidence. It involved extracting and appraising evidence summaries of high-quality CPGs and adapting them into our own local setting by constructing an Evidence to Decision framework. (12)

A systematic search of international CPGs that directly answered the guideline question were done. We included guidelines developed by international guideline developing bodies such as the World Health Organization, the United States Prevention Task Force, the Canadian Task Force on Preventive Healthcare, National Institute for Health Care and Excellence and United Kingdom National Screening Committee Recommendations. Two independent reviewers appraised the CPG using AGREE II tool. Evidence summaries of CPG done within 5 years (2016-2021) and were deemed to have high quality (AGREE II score > 75) were included. Evidence for questions that were not covered by the above CPGs were systematically searched and appraised.

The results of the appraisal of existing CPGs and their evidence summaries determined the need for a systematic search in electronic databases (MEDLINE via PubMed, CENTRAL, Google Scholar) to do de-novo systematic reviews and meta-analysis for each question. 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, if needed.

The ERE appraised the directness, methodological validity, results, and applicability of each relevant article included. The ERE generated evidence summaries for each of the questions. Each evidence summary included evidence on the burden of the problem, and diagnostic performance, benefits, harm, and social and economic impact of the screening test/intervention.

RevMan, STATA, and GRADEPro were used for the quantitative synthesis of important clinical outcomes for each question.

Source of the evidence would include evidence summaries from pre-identified CPG, systematic reviews, health technology assessment reports, and primary studies such as clinical trials, diagnostic accuracy studies, qualitative studies and cost-effectiveness analysis studies whenever possible or available. The certainty of evidence for the benefit and harm of an intervention was assessed according to Table 1. Over-all certainty of evidence per research question will be the lowest level based on the critical outcomes included in the decision-making.

Table 1. Basis for Assessing the Quality of the Evidence using GRADE Approach

Observational studies	**Quality of the Evidence**	**Randomized trials**
Extremely strong association and no major threats to validity	**High** (Further research unlikely to change our confidence in estimate of effect)	No serious flaws in study quality
Strong consistent association and no plausible confounders	**Moderate** (Further research is likely to have an important impact)	Serious flaws in design or execution or quasi-experimental design
No serious flaws in study quality	**Low** (Further research is very likely to have an important impact)	Very serious flaws in design or execution
Serious flaws in design and execution	**Very low** (The estimate of effect is very uncertain)	Very serious flaws and at least one other serious threat to validity
Additional factors that lower quality of the evidence are: • Important inconsistency of results • Some uncertainty about directness • High probability of reporting bias • Sparse data • Major uncertainty about directness can lower the quality by two levels Additional factors that may increase quality are: • All plausible residual confounding, if present, would reduce the observed effect • Evidence of a dose-response gradient		

The ERE systematically and exhaustively searched for and provided evidence on the following criteria whenever applicable:

- Burden of the problem
- Diagnostic performance of the screening test

- Benefits and harm of the screening test and/or subsequent management
- Economic impact and cost of the screening test
- Social and health systems impact of the screening test and/or subsequent management.

Relevant evidence that would facilitate in the decision (i.e., cost of screening test, cost-effectiveness studies, qualitative studies for patient values and preferences, accessibility, feasibility, and equity issues) were also included in the evidence summaries. The evidence gathered for each guideline question were also incorporated into the GRADE EtD framework to facilitate the decision-making process.

A draft recommendation was formulated prior to the panel meeting. The draft recommendations were formulated based solely on the evidence on the balance between benefits and harm of the screening test and the certainty of the evidence.

During this stage of development, each task force had a technical coordinator with expertise on CPG development, Evidence-Based Medicine and Evidence synthesis. The TC supervised the retrieval and appraisal of evidence, ensured methodologic rigor of the process and the accuracy and reliability of data extraction, and the construction of the draft recommendations. They also functioned as second reviewer to ERE. Practice presentations with their respective TF SC and the Central Executive Committee were organized to ensure the validity and quality of the evidence summaries prior to the consensus panel meeting.

A technical writer (TW) per task force took charge of collating the ES into an evidence base, ensuring the continuity and flow of the manuscript, standardizing the manuscript format and documenting the Consensus meeting to be included in the CPG manuscript. The TW was also responsible for incorporating the agreed recommendation and consensus issues into the final manuscript.

Formulation of Recommendations

Prior to CP Meeting

Each task force convened a 10-15 multisectoral Consensus panel and identified a technical facilitator who oversaw the deliberation and the consensus process. An online orientation session for the panelists and technical facilitators was conducted to introduce the GRADE CPG methodology, interpretation of evidence summaries, the EtD approach and the formal consensus process.

The panelists were asked to study the evidence base of the guideline research questions and asked to answer a set of questions based on the EtD framework for each guideline question. Their answers were summarized and presented during the CP meeting. Outcomes were also rated according to whether they were critical, important but not critical or of low importance for decision making by health care providers and consumers. Only important and critical outcomes were included in the evidence summaries to be considered in the decision-making. A maximum of 7 outcomes were considered and presented.

During CP Meeting

During the facilitated *en banc* consensus panel meetings, the key findings of the evidence summaries and draft recommendations were presented for deliberation. The criteria on Evidence to Decision framework on diagnostic tests by the GRADE working group were used. (17, 18)

Upon clarification and discussions, the panel voted and arrived at a recommendation. If consensus (75% of total votes) was reached before or on the third round, voting on the strength of the recommendation commenced. The CP arrived at a consensus in recommendations for all 16 questions.

The CP considered the balance between harm and benefit, certainty of evidence, costs, acceptability, feasibility, appropriateness, and equity in making the recommendation and its strength. The CP needed to decide on the direction of the recommendation [whether to recommend for or against] and the strength of recommendation [whether weak or strong]. Usually high or moderate certainty of evidence will result into a strong recommendation and low or very low certainty of evidence will lead to a weak recommendation.

All meetings were done remotely via Zoom. When no consensus was reached during the remote meetings, modified Delphi approach was used to extend the voting process if additional evidence or issues were introduced that might change the votes to reach a consensus. Strong recommendation means that desirable effects of intervention clearly outweigh undesirable effects, or clearly do not while weak recommendations means that trade-offs are less certain, either because of low quality evidence or because evidence suggests desirable and undesirable effects are closely balanced. *(21)* In case of discrepant decisions with the certainty of evidence, the CP was asked to explicitly justify the recommendations and this was documented under consensus issues in the final manuscript of the CPG.

Management of Conflict of Interest

The Central Executive Committee convened an Oversight Committee (OC) whose task was to thoroughly review the declaration of conflict of interest (DCOI) of each of the Task Force members particularly the Consensus Panelists (CP) and make recommendations on how to manage the COI. For TF members with potential significant COIs, the member of OC conducted additional investigations with due diligence to ensure the integrity of the CPG process and the final recommendations.

All task force members submitted a DCOI and their curriculum vitae (CV) prior to the initiation of guideline development process. The disclosure included a 4-year period of personal potential intellectual and/or financial conflicts of interest (COI).

Management of the COI of the Consensus Panel, Technical Coordinators, and Task Force Steering Committees were deliberated and decided by the OC, using the pre-agreed criteria (See Appendix 5). The OC decision was then forwarded to the Task Force Steering Committee for appropriate action. The OC members were invited to attend the CP meetings for due diligence if the OC recommendations were actually being followed.

Web-based Application Development

An online and mobile application was developed to allow users to generate a patient specific primary care plan based on age, sex, occupation and other patient characteristics.

Computer programmers were recruited to develop the web-based application for PHEX. The Steering Committee, headed by Dr. Antonio Dans, led the development of the software application.

The scope and features of the website are as follows:

1. Content Management System (CMS) – used for managing and editing the application and web portal
2. Mobile and Desktop responsive – website adopts to the browser screen size of the user

3. Website portal – will be mobile responsive; also used for generating list of recommendations to users

The website structure has 2 parts: 1) CMS which included the login page, home page, edit page (guidelines, list of recommendations and list of diseases) and 2) the main website which included the following: home/search page and the recommendations page where they are categorized as guidelines, list of recommendations and list of diseases.

The development method used was rapid application and software development wherein it followed 4 processes: 1) analysis and quick design 2) build - demonstrate – refine 3) testing and 4) implementation

Regular meetings were held to discuss the goals and plans for the webpage. During the planning stage, requirements, content and delivery milestones were discussed, then the minimum viable product (MVP) was defined and the target launch date identified. Succeeding meetings then focused on the webpage design, development, testing, deployment and support.

Continuous updating of the website will be done as new recommendations are made.

External Review

Each task force was requested to have the final manuscripts reviewed by independent stakeholders, who were not members of the Task Force. Some task force SC opted to present to relevant societies for their comments and suggestions.

Feedback on the process

The Central Executive Committee conducted post-CP meeting feedback sessions per task force. The TF steering committee and the technical working group expressed their opinion, experiences, difficulties, and suggestions regarding the whole CPG development process. This included best practices and ways to move forward.

Dissemination and update plans

The Central Executive Committee is coordinating with the DOH in the dissemination of these guidelines. Aside from developing an online software application, the DOH enumerated the following steps to enhance uptake.

- Releasing a DOH memo to notify all stakeholders of the publication
- Publicizing the National CPGs through the DOH newsletter and alerts to appropriate agencies
- Issuing of a press release, releasing news articles, and utilizing social media accounts
- Creating tri-media advertisements (print, television, and radio)
- Organizing a press launch to allow information exchange between media and the guideline development groups
- Organizing a dissemination forum
- Conducting conferences, trainings, and implementation workshops
- Speaking engagements by experts in appropriate forums for the benefit of stakeholders and the general public
- Creating information, education, and communication materials for laymen and patients
- All strong recommendations in this guideline can be used for monitoring and auditing practices in institutions. This can be converted to key performance indicators and it can also be used in creating clinical pathways.

The plan for another update on the topics covered in this Phase 2 CPG was at the latest every 3-5 years. When new studies relevant to the topic are published in the interval, updates can be scheduled earlier.