PHILIPPINE GUIDELINES on PERIODIC HEALTH EXAMINATION

PERIODIC HEALTH EXAMINATION TASK FORCE 2021

PHEx
PHILIPPINE PERIODIC HEALTH EXAMINATION

DISCLAIMER

This guideline is intended to be used by specialists, general practitioners, allied health professionals who are primary care providers. Although adherence to this guideline is encouraged by the DOH, it should not restrict the clinicians in using their clinical judgment and considering patient's values, needs and preferences while handling individual cases. Clinicians and relevant stakeholders must always exercise sound clinical decision-making as the individual patient's history and current physical status dictate and while their responses to treatment may vary. This is just the phase 1 of the Updating of the National Guidelines on Periodic Health Examination. This guideline only tackled select diseases/risk factors and screening interventions. The full spectrum of periodic health examination will be tackled in Phases 2 and 3.

Payors and policymakers, including hospital administrators and employers, can also utilize this CPG, but nonconformance to this document should not be the sole basis for granting or denying financial assistance or insurance claims. Recommendations from this guideline should not also be treated as strict rules on which to base legal action.

Developers of this CPG are aware of its limitations. Evidence summaries are based on the best available scientific evidence as of the time of its formulation. However, certain aspects of the screening may not have been addressed by the clinical trials and observational studies, and as such, evidence bases are therefore not all inclusive. Considerations on these aspects were still deemed necessary in the current contexts of primary care.

Table of Content

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ABBREVIATIONS AND ACRONYMS

ABPM	ambulatory blood pressure monitoring
ACS	American Cancer Society
ACP	American College of Physicians
ADA	American Diabetes Association
aHR	adjusted hazard ratio
AIDS	acquired immunodeficiency syndrome
AJCC	American Joint Committee on Cancer
ARB	angiotensin-receptor blocker
ASSIST	Alcohol, smoking, and substance involvement screening test
ASQ	Ages and Stages Questionnaire
AUDIT	Alcohol use disorders identification test
BMI	body mass index
BP	blood pressure
CA	cancer
CABG	coronary artery bypass grafting
CAD	coronary artery disease
CBC	complete blood count
CDC	Center for Disease Control
CHED	Commission on Higher Education
CI	confidence interval
CKD	chronic kidney disease
CP	consensus panel
CPG	clinical practice guideline
CRC	colorectal cancer
CSC	Civil Service Commission
CTFPHC	Canadian Task Force on Preventive Health Care
CV	cardiovascular
CVD	cardiovascular disease
CXR	chest X-ray
DALY	disability-adjusted life year
DOH	Department of Health
DOLE	Department of Labor and Employment
ECCD	early childhood care and development
ECG	electrocardiogram
ESRD	end-stage renal disease
FDA	Food and Drug Administration
FIT	fecal immunochemical test
FNRI	Food and Nutrition Research Institute
FOBT	fecal occult blood test
FS	flexible sigmoidoscopy
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
HbA1c	hemoglobin A1c
HDL	high-density lipoprotein
HF	heart failure
HIV	human immunodeficiency virus
HRFQ	high-risk factor questionnaire
HRQoL	health-related quality of life
HRSB	high risk sexual behavior
HPDPB	Health Policy Development and Planning Bureau
HPV	human papilloma virus

HTN	hypertension
IDA	iron deficiency anemia
IDF	International Diabetes Federation
LDL	low-density lipoprotein
LEEP	loop electrosurgical excision procedure
LMIC	lower-middle-income country
MAM	moderate acute malnutrition
MCS	mental component scale
MRI	magnetic resonance imaging
MUAC	mid-upper arm circumference
NATSAL	National Survey of Sexual Attitudes and Lifestyle
NCD	non-communicable disease
NCR	National Capital Region
NICE	National Institute for Health and Care Excellence
NSCLC	non-small cell lung cancer
OBPM	office-based blood pressure measurement
OR	odds ratio
OS	over-all survival
PAFP	Philippine Academy of Family Physicians
PCP	Philippine College of Physicians
PCOM	Philippine College of Occupational Medicine
PEDS	Parents' Evaluation of Developmental Status
PHIC	Philippine Health Insurance Corporation
PhilCAT	Philippine Coalition Against Tuberculosis
Php	Philippine peso
PHQ	Patient Health Questionnaire
PMHP	people with mental health problems
POGS	Philippine Obstetrical and Gynecological Society
PPS	Philippine Pediatric Society, Inc.
PSA	Philippine Psychiatric Association
PSGIM	Philippine Society of General Internal Medicine
PSPHP	Philippine Society of Public Health Physicians
PTB	pulmonary tuberculosis
QoL	quality of life
RCOG	Royal College of Obstetricians and Gynaecologists
RCT	randomized controlled trial
RR	relative risk
RUTF	ready-to-use therapeutic food
SAM	severe acute malnutrition
SES	socioeconomic status
Sn	Sensitivity
Sp	Specificity
SEATCA	Southeast Asia Tobacco Control Alliance
SRBBS	Sexual Risk Behavior Beliefs and Self Efficacy Scales
STD	sexually transmitted disease
STI	sexually transmitted infection
SWS	Social Weather Station
T2DM	type 2 diabetes mellitus
TB	tuberculosis
TC	total cholesterol
TNM	tumor node metastases
USD	U.S. Dollars
USPSTF	U.S. Preventive Services Task Force
VIA	Visual inspection with acetic acid
WHO	World Health Organization

WHR	waist-hip ratio
WHZ	weigh-for-height z-score
YLD	years lived with disability
YRBSS	Youth Risk Behavior Surveillance Survey

PERIODIC HEALTH EXAMINATION PHASE 1 TASK FORCE 2021

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HOW TO USE THIS DOCUMENT

This clinical practice guideline is a systematic synthesis of evidence to address sixteen questions that emerged to assist the Philippine Health Insurance Corporation. on the formulation of the PhilHealth Konsultasyong Sulit at Tama (Konsulta) Package. This package is an outpatient benefit package consisting of preventive health services. It covers health screening interventions for cervical cancer, colorectal cancer, lung cancer, pulmonary tuberculosis, chronic kidney disease, hypertension, diabetes, dyslipidemia, malnutrition, unhealthy alcohol use, tobacco smoking, high-risk sexual behavior, and developmental delay.

This guideline can be fully appreciated when read sequentially, as it appears here in the full-text manuscript. An overview of the goals and focus of this guideline can be found in the *Introduction*. The whole process of creating this CPG is written in the *Guideline Development Methods* from page 16.

The consumers of this guideline will appreciate the recommendations formulated through the supporting evidence and consensus issues that can be read starting **on page 9.** Evidence review on disease conditions precedes the review summary for risk factors. For an in-depth analysis of each evidence base, the sources are listed in the References. The Annex contains the supplementary information for the evidence, including forest plots and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) profiles for each evidence summary.

The content of this CPG is an intellectual property of the Department of Health (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.

ACKNOWLEDGMENT

This CPG on PHEX 2021 was prepared by the National Institutes of Health - Institute of Clinical Epidemiology (NIH-ICE).

This project would not have been possible without the initiative and financial support from the DOH. The DOH neither imposed any condition nor exerted any influence on the operations and the final output formulation.

The NIH-ICE undertook extensive technical work in (1) searching and synthesizing the evidence while ensuring objectivity in each stage of the process, (2) presenting the evidence in the panel discussion, and documenting and writing the final report. They were also indispensable in carrying out the legwork, coordinating among various individuals, groups, and committees, and facilitating the *en banc* meeting. The CPG Steering Committee was responsible for overall organization and management and is accountable for the quality of the CPG.

Lastly, this guideline is invaluable because of the contribution and participation of panelists from different sectors of healthcare who committed their time and effort to share their knowledge, experience, and expertise in analyzing the scientific evidence and their values and preferences in formulating the recommendations with consideration of patients and the current healthcare system in the country.

EXECUTIVE SUMMARY

This Clinical Practice Guideline for the Periodic Health Examination is an output from the joint undertaking of the Department of Health and National Institutes of Health- Institute of Clinical Epidemiology.

The CPG provides twenty three (23) recommendations on prioritized questions in the screening for certain disease conditions.

Recommendations are based on the appraisal of the best available evidence on each of the sixteen identified clinical questions. The CPG is intended to be used not only by the accredited (PhilHealth) Konsulta providers but also by other relevant stakeholders such as general practitioners and specialists in the primary care setting, employers and administrators, allied health practitioners and even patients. The guideline development process followed the widely accepted Grading of Recommendations, Assessment, Development, and Evaluation or the GRADE approach including GRADE Adolopment[1] , a systematic process of adapting evidence summaries and the GRADE Evidence to Decision or EtD[2] framework. It included 1) identification of critical questions and critical outcomes, 2) retrieval of current evidence, 3) assessment and synthesis of the evidence base for these critical questions, 4) formulation of draft recommendations, 5) convening of a multi-sectoral stakeholder panel to discuss values and preferences and assess the strength of the recommendations, and 6) planning for dissemination, implementation, impact evaluation and updating.

The recommendations in this CPG shall hold and will be updated after 3 years.

[1] Schunemann H, Wiercioch W, Brozek J, Etxeandia-Ikobaltzeta I, Mustafa R, Manja V. GRADE Evidence to Decision (EtD) frameworks for adoption, adaptation, and de novo development of trustworthy recommendations: GRADE-ADOLOPMENT. J Clin Epidemiol. 2017;81:101-10.

[2] Schunemann HJ, Mustafa R, Brozek J, Santesso N, Alonso-Coello P, Guyatt G, et al. GRADE Guidelines: 16. GRADE evidence to decision frameworks for tests in clinical practice and public health. J Clin Epidemiol. 2016;76:89-98.

SUMMARY OF RECOMMENDATIONS

Recommendation	Quality of Evidence	Strength of Panel Recommendation
Among asymptomatic apparently healthy adults 40 to 75 years with one or more CV risk factors, we suggest screening for lipid disorder using a lipid profile test.	Low	Conditional
Among asymptomatic apparently healthy adults aged 18 to 39 years, we suggest against screening for lipid disorder.	None	Conditional
Among asymptomatic apparently healthy adults, we recommend screening for hypertension.	Moderate	Strong
Among apparently healthy adults aged 40 years above or, younger if with risk factors, we recommend screening for type 2 diabetes mellitus using fasting blood sugar.	Moderate	Strong
Among apparently healthy adults aged 40 years above or, younger if with risk factors, we suggest screening for type 2 diabetes mellitus using hemoglobin A1c.	Moderate	Conditional
Among asymptomatic apparently healthy adults, we recommend using body mass index (BMI) in screening for obesity.	Moderate	Strong
Among asymptomatic apparently healthy children (6-59 months), we suggest screening for acute malnutrition using mid-upper arm circumference (MUAC) or weight-for-height z-scores.	Low	Conditional
Among asymptomatic apparently healthy adults, we recommend screening for unhealthy alcohol use and providing persons identified with risky drinking with brief behavioral counseling intervention.	Moderate	Strong

Among asymptomatic apparently healthy adolescents, we suggest screening for unhealthy alcohol use and providing persons identified with risky drinking with brief behavioral counseling intervention.	Low	Conditional
Among asymptomatic apparently healthy adolescents and adults, we suggest screening for high-risk sexual behavior.	Low	Conditional
Among all adults, we recommend that healthcare providers screen for tobacco smoking. Among all adolescents, we recommend that healthcare providers screen for tobacco smoking.	Low Very Low	Strong Strong
Among asymptomatic apparently healthy adolescents and adults, we suggest screening for depression using PHQ-9.	Low	Conditional
Among asymptomatic apparently healthy children ages 0-4 years, we recommend against screening of developmental delay using developmental screening tools.	Low	Strong
Among asymptomatic apparently healthy adults aged at least 50, we recommend to screen for colorectal cancer using annual FOBT or FIT followed by colonoscopy, when indicated.	High	Strong
Among asymptomatic women aged 21 to 65, we recommend screening for cervical cancer every three years using a Pap smear. Among asymptomatic women aged 21 to 65, we recommend screening for cervical cancer every three years using visual inspection with acetic acid as an alternative to Pap smear.	Moderate Moderate	Strong Strong

Among asymptomatic, apparently healthy adults, we recommend against the use of resting or exercise ECG to screen for coronary artery disease.	Low	Strong
Among asymptomatic apparently healthy non-pregnant adults, we suggest against routine screening of anemia using hemoglobin and/or hematocrit.	Very Low	Conditional
Among asymptomatic apparently healthy adults, we suggest against screening for chronic kidney disease using urinalysis. Among asymptomatic apparently healthy adults, we recommend against screening for chronic kidney disease using serum creatinine.	Low None	Conditional Strong
Among asymptomatic apparently healthy adults, we suggest screening for pulmonary tuberculosis using a chest X-ray.	Very Low	Conditional
Among asymptomatic apparently healthy adults, we suggest against screening for lung cancer using a chest X-ray.	Low	Conditional

1. INTRODUCTION

The Philippine Guidelines on Periodic Health Examination (PHEX) was first published in 2004.(1) It was a comprehensive appraisal and synthesis of evidence on screening interventions committed to providing early prevention services among apparently healthy Filipinos. It was a long-awaited publication and the first to offer evidence-based recommendations for screening tests made possible through the concerted effort of various medical and paramedical organizations composed of more than a hundred experts, researchers, and stakeholders.(1) It was inspired by the Canadian and the US Preventive Services Task Forces, but it was tailored to the Philippine setting.

Due to the evolving technology, scientific evidence, and health policies, there is a pressing need to update this guideline. This 2021 Philippine Guidelines will support the objectives stated in the Universal Health Care Act(2) that all Filipinos are given access to quality and affordable medical services, including primary care benefits. In a circular (3) released by Philippine Health Insurance Corporation (PhilHealth), a *Konsultasyong Sulit at Tama* (Konsulta) Package (2019) lined for implementation will cover access to quality primary care provided by an accredited Konsulta Provider. This package contains initial and follow-up primary care consultations, health screening and assessment based on life stage and health risk, and access to a set of diagnostic services and medicines. Included in the list of screening strategies are the tests tackled in this updated practice guidelines. This guideline is the first of three phases planned, and focuses on select screening interventions.

In the guideline development, evidence-based recommendations for the prioritized health screening were formulated using the GRADE Evidence-to-Decision (EtD) framework.(4, 5) The EtD framework aims to facilitate the adaptation of recommendations and decisions of experts and stakeholders based on specific contexts, essential health outcomes, benefits, and harms while looking through the equity, applicability, and feasibility lenses.

The evidence collated to answer the research questions on screening tests are used in formulating the recommendations. They can be classified into two: (1) screening for a risk factor and (2) screening for early disease. Screening for the former is directed towards determining the effective management of the condition as a risk factor, and screening for the latter is focused on the performance of the tests that will be used to detect and subsequently treat that early disease and prevent it from progressing.

Health screening also carries potential harm, for example, mislabeling the person as being ill. It can pose a threat to the psychological, social, or physical well-being and even to the individual's financial stability. Because of these probable adverse effects of screening, criteria are set to determine if screening for a particular condition can be beneficial and pragmatic. The voting panel members used these criteria (5) aligned with the EtD framework: (1) burden of illness must be high, (2) screening tests must be accurate enough, (3) early treatment must be more effective than late treatment, (4) confirmatory tests and

early management must be safe and available, and (5) costs of screening must be proportional with the potential benefit.

Aside from the regulatory agencies and policymakers in the national government, the target users of this guideline on screening strategies include primary care providers, general physicians, specialists, training institutions, payors, patients, the general public, and industry partners

References

1. Dans A, Morales D. Philippine Guidelines on Periodic Health Examination (PHEX): Effective Screening for Diseases among Apparently Healthy Filipinos. Manila: The Publications Program; 2004.
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4. Alonso-Coello P, Schünemann H, Moberg J, Brignardello-Petersen R, Davoli M, Treweek S, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction. BMJ. 2016;353:i2016.
5. Schunemann H, Wiercioch W, Brozek J, Etxeandia-Ikobaltzeta I, Mustafa R, Manja V. GRADE Evidence to Decision (EtD) frameworks for adoption, adaptation, and de novo development of trustworthy recommendations: GRADE-ADOLOPMENT. J Clin Epidemiol. 2017;81:101-10.

2. GUIDELINE DEVELOPMENT METHODOLOGY

2.1 Organization of the Process

Following the international standards, the DOH (1) outlined the guideline development process into four phases: 1) preparation and prioritization, 2) CPG generation, 3) CPG appraisal, and 4) implementation in the Manual for CPG Development [1].

In the preparation and prioritization phase, the Steering Committee set the CPG objectives, scope, target audience, and clinical questions. They identified and formed the working groups involved in creating the evidence base and finalizing the recommendations for each clinical question included.

The evidence review experts (ERE) or the technical working group were tasked to review existing CPGs, appraise and summarize the evidence, and draft the initial recommendations. The evidence summaries were then presented to the consensus panel members to finalize the recommendations.

The consensus panel comprised of multisectoral representatives tasked to review the evidence summaries and develop recommendations during the *en banc* meeting. In the meeting, they prioritized critical and important outcomes; discussed necessary considerations revolving around the recommendations and voted on each recommendation and its strength. They participated in a modified Delphi activity to decide on recommendations that were not resolved during the *en banc* meeting.

2.2 Creation of the Evidence Summaries

The clinical questions were developed using the PICO (population, intervention, comparator and outcome) format. The ERE searched and appraised international practice guidelines related to periodic health screening, including but not limited to those of the Canadian Task Force on Preventive Health Care, U.S. Preventive Services Task Force, National Institute for Health and Care Excellence. If the CPG were of good quality and done within 5 years, the evidence summaries of the CPG were adopted.

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) for the need 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.

At least two reviewers worked on each PICO question. Evidence reviewers appraised the directness, methodological validity, results, and applicability of each relevant article

included. 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 sixteen (16) 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. Evidence/information that will facilitate in the decision (i.e. cost of screening test, cost-effectiveness studies, qualitative studies) were also included in the evidence summaries. The Quality of Evidence was assessed using the GRADE approach. [2] See table 1.

Table 1. Basis for Assessing the Quality of the Evidence using 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
Factors that lower quality of the evidence are: ● Risk of bias ● Important inconsistency of results ● Some uncertainty about directness ● High probability of reporting bias ● Sparse data/Imprecision ● Publication bias Additional factors that may increase quality are: ● All plausible residual confounding, if present, would reduce the observed effect ● Evidence of a dose-response gradient ● Large effect	

2.3 Composition of the CPG Panel

The Steering Committee convened the Consensus Panel (CP), considering possible conflicts of interests of each panel member. To ensure fairness and transparency, the composition was guided by the DOH manual (1). Content and methodology experts and other key stakeholders were invited to join the CP. The key stakeholders included policymakers, patient advocates, allied medical practitioners, and physicians from different settings (e.g., public primary care settings, private practice, occupational health settings).

2.4 Formulation of the Recommendations

Draft recommendations were formulated based on the quality of evidence, trade-offs between benefit and harm, cost-effectiveness, applicability, feasibility, equity, resources and uncertainty due to research gaps. Prior to the series of online consensus panel meetings, the consensus panel received the draft recommendations together with evidence summaries based on the EtD framework shown in Table 2. These recommendations, together with the evidence summaries, were presented during the *en banc* meeting.

Table 2.Detailed considerations based on the EtD framework (3)

1. Is the problem a priority?
2. How accurate is the test?
3. How substantial are the desirable anticipated effects?
4. How substantial are the undesirable anticipated effects?
5. What is the certainty of the evidence of test accuracy?
6. What is the certainty of the evidence for any critical or important test-related direct benefits, adverse effects, or burden of the test?
7. What is the certainty of the evidence of the natural course of the condition and the effects of management guided by the test results?
8. How certain is the link between test results and management decisions?
9. What is the overall certainty of the evidence about the effects of the test?
10. Is there important uncertainty about or variability in how much people value the main outcomes, including adverse effects and burden of the test and downstream outcomes of clinical management guided by the test results?
11. Does the balance between desirable and undesirable effects favor the test or the comparison?
12. How large are the resource requirements (costs)?
13. What is the certainty of the evidence of resource requirements (costs)?
14. Does the cost-effectiveness of the test favor the test or the comparison?
15. What would be the impact on health equity?
16. Is the test acceptable to key stakeholders?
17. Is the test feasible to implement?

The recommendation for each question and its strength was determined through voting. A consensus decision was reached if 75% of all CP members agreed. (2) If consensus was not reached in the first voting, questions, and discussions were encouraged. Two further rounds of voting on an issue were conducted. Evidence-based draft recommendations were also revised based on input arrived at by consensus in the *en banc* discussions.

2.5 Managing Conflicts of Interest

The Steering Committee facilitated the whole CPG formulation process, but their members had no direct participation in assessing and synthesizing the evidence, generating the evidence summaries and evidence-based draft recommendations of the Evidence Review Experts, and voting on final recommendations during the *en banc* consensus panel review. They invited the relevant organization to nominate individuals who can become part of the consensus panel.

Each nominee was required to fill out and sign a declaration of interest form and submit their curriculum vitae. The SC screened the nominees for any possible conflict of interest that may bias their decisions. Those with significant potential COI were not allowed to join the roster of consensus panel members.

2.6 Planning for Dissemination and Implementation

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. Suggestions ranged from making guidelines available on websites, press conferences, social media sites, professional society conventions, and journal publications.

References

1. DOH, PHIC. Manual for Clinical Practice Guideline Development 2018.
2. Balshem H, Helfand M, Schünemann HJ, Oxman AD, Kunz R, Brozek J, Vist GE, Falck-Ytter Y, Meerpohl J, Norris S, Guyatt GH. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol. 2011 Apr;64(4):401-6. doi: 10.1016/j.jclinepi.2010.07.015. Epub 2011 Jan 5. PMID: 21208779.
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3. RECOMMENDATIONS AND PANEL DISCUSSION

3.1 Lipid Profile Test in Screening for Lipid Disorder

RECOMMENDATIONS

1. **Among asymptomatic apparently healthy adults aged 40 to 75 years with one or more CV risk factor*, we suggest screening for lipid disorder using a lipid profile test.** ***(conditional recommendation, low certainty evidence)*****.**

2. **Among asymptomatic apparently healthy adults aged 18 to 39 years, we suggest against screening for lipid disorder** ***(conditional recommendation, no evidence)*****.**

CV risk factors include the following:

- *Diabetes Mellitus*
- *Hypertension*
- *Smoking history*

Considerations

The consensus panel considered the following when formulating this recommendation:

- Lipid disorder is a priority in a periodic health examination.
- Benefits outweigh the risk based on the evidence presented. However, some panelists pointed out the need for further research evaluating the direct effect of screening for lipid disorders.

3.1.1 Burden of disease

Disease Frequency

In 2008, the World Health Organization (WHO) estimated that the prevalence of dyslipidemia, defined as elevated total cholesterol (TC) levels (> 190mg/dL or 5 mmol/L), in Southeast Asia was at 30.3%, much lower compared to the Western regions, such as Europe and America with prevalence rates of 53.7% and 47.7%, respectively. (1)

Based on the 2013 National Nutrition and Health Survey, a majority (71%) of Filipinos aged 20 years and above had low high-density lipoprotein (HDL) cholesterol levels. The remaining had borderline to high TC level (47.2%), borderline high to high LDL-cholesterol level (47.5%), and borderline to very high TG level (38.7%).

The national prevalence rates of all forms of dyslipidemia consistently increased from 2003 to 2013, with exceptions to high LDL, which had a slight decrease in 2008, and low HDL, which started to decrease among males in 2008 until 2013. (2)

Severity of Disease

According to a 2004 global case-control study, dyslipidemia was one of the most critical risk factors of acute myocardial infarction.(3) In 2002, 10% and 5% of the Philippines' total deaths were due to ischemic heart disease and cerebrovascular disease. In 2004 and 2009, these diseases accounted for 85.7 and 62.5 deaths per 100,000 respectively, were ranked as the top two leading causes of mortality.(4)

Social impact of the disease

Poor dietary quality, high saturated and trans-fatty acid intake, and low fruit and vegetable consumption coupled with a sedentary lifestyle and stressful environment significantly contribute to dyslipidemia, especially among adults.(5) Once diagnosed with the disease, patients also have to face barriers to access to care, such as affordability of medicine and health system support, and face threats to their productivity and economic growth. (6)

3.1.2 Benefits and Harms of Screening Tests

There were no direct studies found on lipid screening versus no lipid screening among apparently healthy and/or asymptomatic adults on mortality and other patient-important outcomes. Instead, we looked into studies on the effectiveness of management among those with dyslipidemia.

A systematic review (7) included 19 RCTs that evaluated statins' effects versus placebo or no statins among adults aged 40 to 75 years with no known CVD. Most of the trials in this review included participants based on elevated LDL-C levels, presence of diabetes, or at least the presence of one CV risk factor. This review found that the use of statins was associated with a reduced risk for all-cause mortality (RR 0.86, 95% CI 0.80 to 0.93), cardiovascular mortality (RR 0.82, 95% CI 0.71 to 0.94), ischemic stroke (RR 0.71 95% CI 0.62 to 0.82), myocardial infarction (RR 0.64, 95% CI 0.57 to 0.71), and a composite cardiovascular outcome (RR 0.70, 95% CI 0.63 to 0.78).(7)

Subgroup analysis revealed that the proportion of CVD events prevented were similar across age, sex, race, lipid level, and other risk factors. Stratification of global risk assessment also yielded similar relative risk reduction estimates (i.e., higher versus lower CVD event risk). (7)

Across the individual studies on statin use for the primary prevention of CVD, statin therapy compared to placebo was not statistically significantly associated with increased serious adverse events. There was also no evidence of increased risk for cancer or elevated aminotransferase levels using statins. (7)

Table 3 shows the summary evidence regarding the benefits and harm of statin use among adults aged 40 years and above without prior CVD events.

Table 3. Effects of statin use among adults aged 40 years and older without prior CVD events (14)

Outcomes	**No. of Studies** *(no. of participants)*	**RR (95% CI)**	**Quality**
All-cause mortality	15 RCTs *(n = 71 131)*	0.86 (0.80, 0.93)	Moderate
CV mortality	10 RCTs *(n = 65 235)*	0.69 (0.54, 0.88)	Moderate
Stroke	13 RCTs *(n = 62 863)*	0.71 (0.62, 0.82)	Moderate
Myocardial infarction	12 RCTs *(n = 68 537)*	0.64 (0.57, 0.71)	Moderate
Revascularization	7 RCTs *(n = 54 803)*	0.63 (0.56, 0.72)	Moderate
Composite CV outcomes	13 RCTs *(n = 69 215)*	0.70 (0.63, 0.78)	Moderate
Withdrawal due to adverse events	9 trials *(n = 33 589)*	0.95 (0.75, 1.21)	Moderate
Serious adverse events	7 trials *(n = 4180)*	0.99 (0.94, .04)	Moderate
Any cancer	10 trials *(n = 55 554)*	1.02 (0.90, 1.16)	Moderate
Myalgia	7 trials (n = 35 607)	0.96 (0.79, 1.16)	Moderate
Elevated aminotransferase	11 trials (n = 44 936)	1.10 (0.90, 1.35)	Moderate
Diabetes	6 trials (n = 59 083)	1.05 (0.91, 1.20)	Moderate

3.1.3 Diagnostic Performance of Screening Tests

There were no direct studies or diagnostic test accuracy reviews on lipid screening versus no lipid screening among apparently healthy and/or asymptomatic adults to predict mortality.

Currently, lipid profile is being used as an initial screening tool for lipid abnormalities and included in cardiovascular risk assessment before initiating statin therapy. (8)

3.1.4 Cost Implication

In an expert review of pharmaco-economics and outcomes research on dyslipidemia, the costs of initial diet modification as prevention strategies were estimated to be Php 5,195.88 (USD 108.00) per patient annually as compared to statin therapy, including outpatient physician visits and laboratory tests which were estimated to be Php 63,408.98 (USD1318.00) and Php 63,938.19 (USD1329.00) in primary and secondary prevention levels

per patient annually.(4) Statin therapy costs accounted for at least 90% of the total annual treatment costs and were estimated to be Php 57,202.79 (USD1189.00) per patient annually. Based on a seven-country comparison of cost-effectiveness study, annual simvastatin costs in Canada, France, and the UK were within the range of Php 28,866.00-33,677.00 (USD600.00-700.00), while the treatment cost in Spain was Php 17,656.37.00 (USD367.00).(9)

*As of November 24, 2020, 1 USD = 48.11 Php

Screening for lipid disorder using lipid profile tests among asymptomatic adults was more cost-effective than no screening based on studies conducted in the USA.(10, 11) However, among the elderly, screening for hypercholesterolemia may be more costly due to secondary illnesses and adverse effects related to treatment.(11) In a systematic review(12), a lipid profile test for screening is more cost-effective than no screening among those asymptomatic young adults and those with CVD risk. Universal screening for hyperlipidemia among children may also be cost-effective in the pediatric population; however, it may not be the most cost-efficient strategy to identify children with severe hyperlipidemia cases.(13)

An estimated annual screening cost per patient is shown in Table 4.

Table 4. Costing data on screening for dyslipidemia

Parameter	**Screening intervention**
	Lipid profile test
(A) Unit cost of screening intervention	**PhP 450.00** (14)
(B) Other direct costs associated with the implementation of the proposed screening intervention	Initial and follow-up outpatient consultations with primary care physicians or specialists (**PhP 150.00** = 2 x PhP 75.00) (14)
(C) Annual screening cost per patient	**PhP 600.00**

3.1.5 Ethical, Social, and Health Systems Impact (Equity, Acceptability, and Feasibility)

Ethical

Despite the high rate of chronic conditions among Filipinos, health research remains scarce, resulting in health disparities across the country, particularly in sustaining clinical care standards within resource-limited settings. In a rural community study to determine cholesterol testing barriers, most factors that impede early disease screening are socially determined. A financial barrier was one of the major obstacles to rural residents having their cholesterol levels screened. (15)

Based on a 2005 NEDA report, disparities in poverty continuously persist across the Philippines. Poverty incidence among the general population was estimated at 16.6%, while the proportion of poor Filipino families was estimated at 12.1%, amounting to around 3 million families in the entire year of 2018. Geographical disparities were observed in children's nutritional status across income groups, specifically dietary patterns and malnutrition. In addition, income inequality was wider in the country relative to its neighboring Asian countries.(15)

Social

In an Australian inductive analysis conducted in 2015, the health-seeking behaviors (HSB) of Filipino migrants were evaluated for health promotion. Despite the population's high rate of chronic conditions, several cultural factors came to light and were identified as hindrances to cultivating HSB.(16) The cultural practice of giving socially appropriate excuses such as 'lack of time' as a way of indirectly declining the other party without being offensive was frequently mentioned in the study as one of the barriers to HSB among Filipinos. More often than not, Filipinos were more focused on the present costs of initiating behavioral change for health promotion, while healthcare providers were more concerned with its long-term benefits. The 'bahala na' mindset, loosely translated to submissive fatalism, is also a Filipino cultural trait reflective of the previously mentioned 'time-poor' practice, which often results in the impact or presence of chronic diseases being minimized and underestimated. Lack of awareness of the nature and purpose of early screening of lifestyle diseases and their likely outcomes may have been the root cause of preserving the cultural mindset, coupled with poor comprehension about the severe implications of developing chronic diseases. Low screening rates among Filipinos for CVDs or lifestyle disease could reflect such cultural factors.(16)

Health Systems

The health system impacts that may influence the adoption or implementation of the Philippines' screening interventions are starkly manifested by the lack of infrastructure and financial and health capacities to support such programs.(17) Despite the so-called "double burden of disease" transition impacting the health system, which resulted in an unmistakable rise in NCDs among Filipinos, preventive and promotive health policies remain scarce in the country. Screening programs barely exist within the public health system (DOH, LGUs), except for a few insufficient interventions. Further, screening programs and cost-effective interventions are still excluded from the PhilHealth benefit package. Thousands of benefit recipients are still deprived of the essential medicine coverage for the management of NCDs. Such circumstances could discourage at-risk to high-risk populations with little to no financial capacities for health care.(17)

3.1.6 Recommendations from Other Groups

Primary prevention of cardiovascular disease with the use of statins

In 2016, the U.S. Preventive Services Task Force released its statement that recommends using low- to moderate-dose statins to prevent CVD events and mortality among adults with no history of cardiovascular diseases. These patients must meet the criteria that include: 1) they should be 40 to 75 years old; 2) they have one or more CVD risk factors such as

dyslipidemia, diabetes, hypertension, and smoking history; 3) and they should have a calculated 10-yr risk of cardiovascular events of 10% or greater (B Recommendation).(8)

Implementation of recommendations on statin use

Clinicians have to determine first a patient's risk of developing a cardiovascular disease event before prescribing statins. It can be done using a risk calculator or estimation tool like the Pooled Cohort Equations from the 2013 American College of Cardiology/American Heart Association (ACC/AHA) guidelines. Estimation of risk includes determining whether one or more traditional CV risk factors for CVD are present, specifically hypertension, cigarette smoking, diabetes mellitus, hyperlipidemia, premature family history of CVD, and obesity.(8)

Periodic health assessments

Periodic cardiovascular risk factor assessment for patients aged 40 to 75 years, including measurement of lipid profile (i.e., total cholesterol, LDL-C, and HDL-C levels), is required to recommend statin for the prevention of CV events. Ideal intervals of periodic cardiovascular risk assessment are uncertain, but it is reasonable to measure lipids every five years. Shorter intervals may be applied for persons whose risk assessment levels are near borderline and may warrant therapy. Longer intervals may be used for persons who are at low risk and have repeated normal lipid profiles. (8)

Screening and statin use among adults aged 21 to 39 years old

After a systematic and comprehensive search, the USPSTF has determined that there is insufficient evidence that screening for dyslipidemia among adults aged 21 to 39 had an effect of benefit on either short- or long-term cardiovascular outcomes. Furthermore, the USPSTF found no studies that looked into the impact of screening versus no screening, treatment versus no treatment, or delayed versus early initiation of statin use in adults in this age group. Thus, the USPSTF recommends neither for nor against screening for dyslipidemia in this age group. Although there is a logical basis of screening early in this age group to identify those at risk for developing early CVD or atherosclerosis, unfortunately, evidence in this age group is lacking. (8)

Adult patients aged 40 to 75 years old and a 10-yr risk score of 10% or more

The USPSTF has recommended initiating low- to moderate-dose statins for the primary prevention of CVD events and mortality in adults aged 40 to 75 years old without a history of cardiovascular disease and who have one or more traditional CVD risk factors (i.e., hypertension, cigarette smoking, diabetes mellitus, hyperlipidemia) and a calculated 10-yr CVD event risk of 10% or greater (Grade B: There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial).(15)

Adult patients aged 40 to 75 years old and a 10-yr risk score of 7.5% to 10%

The USPSTF has recommended initiating low- to moderate-dose statins for the primary prevention of CVD events and mortality in adults aged 40 to 75 years old without a history of cardiovascular disease and who have one or more traditional CVD risk factors (i.e., hypertension, cigarette smoking, diabetes mellitus, hyperlipidemia) and a calculated 10-yr CVD event risk of 7.5% to 10% (Grade C: Recommendation to selectively offer to individual

patients based on professional judgment and patient preferences. There is at least moderate certainty that the net benefit is small). (8)

Adult patients aged 76 years and above

The USPSTF stated that existing evidence is insufficient to determine if initiating statins will yield more benefits and outweigh harm for the primary prevention of CVD events and mortality among adult patients aged 76 years old above without any history of CVD. (8)

The College of Family Physicians of Canada has stated in their simplified lipid guidelines that population-based screening, including periodic health examinations for cardiac risk factors among patients without CVD, does not appear to reduce CVD or all-cause mortality (14). They recommend initiating lipid screening in patients without any history of CVD at the age of ≥40 for men and age ≥ 50 years for women based on moderate-level evidence. Frequent lipid profile testing has also been described to reflect short-term variability and minimal long-term changes in lipid levels among patients not taking any lipid-lowering therapy. It is therefore seen that frequent repeat lipid level testing is unlikely to alter the global CVD risk assessment significantly. For patients not taking any statin therapy, re-screening for lipid levels and risk re-assessment is not required more often than every five years. For patients with known or multiple risk factors, screening can be done earlier. Traditional CVD risk factors include hypertension, family history of premature CVD, diabetes, and smoking (low-level evidence). (14)

The American Diabetes Association recommends obtaining a lipid profile, including total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides, at the time of diabetes diagnosis and before starting any statin therapy. (17)

Currently, there are no recommendations for or against lipid level screening among men ages 20 to 35 or women age 20 years and older who do not have an increased risk of CVD. (18)

Also, there is a consortium of local societies that have drafted an updated Philippine Lipid Guidelines for 2020 and currently undergoing review for publication.

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3.2 Blood Pressure Measurement in Screening for Hypertension

RECOMMENDATION

Among asymptomatic apparently healthy adults, we recommend screening for hypertension *(strong recommendation, moderate certainty evidence)*.

Considerations

The consensus panel considered the following when formulating this recommendation:

- Hypertension is a priority risk factor to screen.
- Screening using blood pressure measurement was perceived as cost-effective, equitable, acceptable, and feasible.
- The evidence supporting screening was deemed to be of moderate certainty.
- Further research is still needed to assess the direct effect of screening for hypertension.

3.2.1 Burden of disease

Disease Frequency

It is estimated that 1.13 billion people are hypertensive where 2 out 3 live in low- and middle-income countries. The World Health Organization has predicted that close to 1.6 billion individuals worldwide will have elevated blood pressure by 2025.(1) Based on a nationwide survey in the Philippines, hypertension prevalence had increased from 11% in 1992 to 17.5% in 2019.(2)

Severity of Disease

Hypertension is a major cause of premature deaths worldwide. It is the leading cause of mortality and morbidity in the Philippines related to cardiovascular disease.(3) Of 590,709 deaths in 2018, 26,800 were attributed to hypertensive diseases, accounting for 4.53% of all deaths.(4) Based on the Global Burden of Disease report, hypertensive heart disease ranks 13 out of the top 48 diseases that account for the top 80% of the total disability-adjusted life years in the country. The average DALYs lost due to hypertension was 14,163.(1, 5)

Natural course of the disease

Many individuals in the general population have one or more risk factors for cardiovascular disease (CVD). Over 90 percent of CVD events occur in those with at least one risk factor.(6-8) The five leading modifiable risk factors (i.e., hypercholesterolemia, diabetes, hypertension, obesity, and smoking) are estimated to be responsible for more than half of cardiovascular mortality.(9) These risk factors exert an additive effect on the likelihood of developing coronary heart disease and other cardiovascular outcomes. The increase in CV

risk because of multiple risk factors has been seen in several Western and Asian populations. (10)

Hypertension is the most important modifiable risk factor in prevalence; contributors such as cigarette smoking, dyslipidemia, and diabetes can be controlled. It accounts for an estimated 54 percent of all strokes and 47 percent of all ischemic heart disease events globally.(11) The risk for coronary disease and stroke increases progressively with an increase in blood pressure above 115/75 mmHg. For each 20/10 mmHg increase in systolic/diastolic blood pressure, there is a doubling of coronary heart- and stroke-related mortality.(12-14)

The lifetime risk of developing CVD is significantly higher among patients with hypertension. In a cohort of over 1.25 million patients aged 30 years or older without baseline CVD, including 20 percent with baseline treated hypertension, patients with baseline hypertension had a 63.3 percent lifetime risk of developing CVD compared with a 46.1 percent risk among those with normal baseline blood pressure.(15)

The mortality rate was higher among hypertensive adults than non-hypertensive adults. Among all hypertensive participants, the age-adjusted mortality rate was 18.8 per 1000 person-years for NHANES I and 14.3 for NHANES III — higher than the rate among non-hypertensive participants (13.3 and 9.1 per 1000 person-years).(16) Uncontrolled mild to moderate hypertension is associated with atherosclerotic disease in 30% of people and organ failure in 50 % of people within 8-10 years of onset.(17) Death from ischemic heart disease or stroke gradually increases as blood pressure rises.(18)

Management of the disease

Health behavior change plays a vital role in preventing hypertension and in controlling blood pressure. A healthy lifestyle delays the onset of high blood pressure and reduces cardiovascular risks. Lifestyle modification (i.e., exercise, weight reduction, moderate alcohol intake, and stress reduction) is the first line of antihypertensive treatment. It enhances the effect of medications for blood pressure.(19)

Guidelines adopt a risk-based approach in starting antihypertensive medications. Adults use antihypertensive drug treatment and lifestyle modification with persistent hypertension who have one or more of these: target organ damage, established cardiovascular disease, renal disease, diabetes, and high cardiovascular risk. For low-risk patients (i.e., no target organ damage, low cardiovascular risk) with established hypertension, drug therapy starts at a BP threshold of $\geq$ 160/100.(20) Routine tests should be performed for all patients with hypertension: urinalysis, blood chemistry, fasting blood glucose or glycated hemoglobin, total serum cholesterol, low-density lipoprotein, high-density lipoprotein (HDL), and non-HDL cholesterol, triglycerides, and standard 12-lead electrocardiography.(21)

A BP target and drug class selection should be individualized, based on an informed, shared decision-making process between patient and health care provider, and reviewed regularly. Factors that should be considered in the decision-making include benefits and harms of therapy, tolerance, compelling indications, and adherence and maintenance feasibility. (22)

Economic impact of the disease

All cost of illness/ burden of disease studies relating to hypertension is commonly lumped with other non-communicable diseases. From a WHO report on 2019, the top four non-communicable diseases – namely cardiovascular, diabetes, cancer, and chronic respiratory, collectively cost about 4.8% of national gross domestic product (GDP), which amounts to Php 756.5 billion lost annually. An indirect cost of Php 680.8 billion was lost due to loss of workforce and reduced productivity. Overall, this translates to a 29% risk of dying prematurely (death before 70 years old) from one of the four main NCDs.(1)

A systematic review on the provider costs for CVD and related conditions in lower-middle-income countries (LMICs) found 14-unit costs for hypertension management, with drug therapy ranging from Php 106.46-Php 3,674.89 (USD2.21–USD76.29). Using general practitioners in community programs costs only Php 39.02-Php 417.63 (USD0.81–USD8.67) per patient per year, compared to annual outpatient costs to manage hypertension, ranging from Php 1,830.45-Php 27,242.06 (USD38.00 to USD565.54) per patient.(23)

*1 USD = 48.17Php as of Nov 16, 2020

Social impact of the disease

Hypertension is generally seen as an acute event rather than a chronic one, thus affecting treatment adherence.(24) One study in Asia about providers' and patients' perceptions of hypertension management noted that the patients usually found it difficult to follow needed lifestyle modifications because of unclear or insufficient information from the doctors.(25) Moreover, environmental and lifestyle factors such as stress, salt consumption, obesity, physical inactivity, alcohol intake, and smoking exacerbate hypertension.(26) It highlights that doctors should form a more personalized partnership with the patients to clarify and emphasize needed lifestyle changes, aside from prescribing antihypertensive medications.(25)

3.2.2 Benefits and Harms of Screening Tests

There were no studies found that directly investigated the effects of screening for hypertension among apparently healthy asymptomatic individuals. Instead, we looked into the effects of the management of hypertension.

Clinical trials performed over the past 30 years have shown estimates on the expected decrease in morbidity and mortality resulting from a 10 to 12 mmHg reduction in systolic pressure and a 5 to 6 mmHg reduction in diastolic pressure.(27) The recent systematic review and meta-analysis of Wei and colleagues(28) reported the benefits of 10 mm Hg systolic blood pressure in reducing important cardiovascular outcomes. Stroke patients benefited more than coronary heart disease patients in terms of BP reduction (Table 5).

Table 5.Effects of BP reduction on cardiovascular outcomes (n = 46 trials)(28)

Outcomes	RR (95% CI)	Grade Quality
CVD mortality	0.87 (0.77-0.99)	Moderate[1]
Coronary heart disease	0.95 (0.77-1.17)	Moderate[1]
Stroke	0.83 (0.72-0.97)	Moderate[1]

Revascularization	0.75 (0.50-1.13)	Moderate[1]
Overall CV events	0.86 (0.78-0.96)	Moderate[1]

1 Downgraded due to indirectness. The original research question was the effect of screening among the general population.

Assessment of the absolute risk differences showed that all five antihypertension medications were associated with greater reductions in cardiovascular events than placebo. See Table 6.

Table 6. Absolute risk differences of cardiovascular events between blood pressure-lowering drug and placebo (28)

Drug	Cardiovascular Death (95% CI)	Myocardial Infarction (95% CI)	Stroke (95% CI)	Revascularization (95% CI)	Overall CV events (95% CI)
ACEi vs. placebo	-0.005 (-0.027, 0.016)	-0.024 (-0.036, -0.011)	-0.035 (-0.070, 0.001)	-	-0.037 (-0.082, 0.009)
DH CCB vs. placebo	-0.007 (-0.011, -0.003)	-0.001 (-0.005, 0.003)	-0.016 (-0.025, -0.006)	-0.001 (-0.003, 0.0001)	-0.013 (-0.031, 0.005)
BB vs. placebo	0.005 (-0.015, 0.025)	-0.048 (-0.100, 0.003)	-0.020 (-0.048, 0.008)	-	-0.042 (-0.123, 0.039)
ARB vs. placebo	-0.000 (-0.002, 0.002)	-0.005 (-0.021, 0.011)	-0.020 (-0.041, 0.002)	-	-0.028 (-0.063, 0.007)
Diuretics vs. placebo	-0.010 (-0.022, 0.003)	-0.010 (-0.019, -0.001)	-0.021 (-0.031, -0.011)	-0.008 (-0.017, 0.0005)	-0.028 (-0.061, 0.005)

Legends: ACEi, angiotensin-converting enzyme inhibitor; DH CCB, dihydropyridine calcium channel blocker; BB, beta-blocker; ARB, angiotensin receptor blocker

The hypertension label did not affect the quality of life.(29, 30) Two studies reported contrasting effects of hypertension labeling on absenteeism.(31, 32) Most concerns were related to the tolerability of ambulatory blood pressure monitoring (ABPM) and associated discomfort(33), pain, skin irritation and bruising(30), and sleep disturbance(30, 34-36)

3.2.3 Diagnostic Performance of Screening Tests

Fifteen studies (N=11,309) evaluated the diagnostic accuracy of office-based blood pressure measurement using ambulatory blood pressure measurement as the reference standard. (Table 7) The most commonly used diagnostic threshold was an office BP of ≥140/90 mg. Office-based blood pressure measurement (OBPM) at a single visit has a pooled sensitivity of 0.54 (95% CI 0.37 to 0.70) and a pooled specificity of 0.90 (95% CI 0.84 to 0.95) for hypertension detection. Confirmatory office-based blood pressure measurement applied to a population with a previously elevated blood pressure has a pooled sensitivity 80% (95% CI 0.68 to 0.88) and a pooled specificity 55% (95% CI 0.242 to 0.66). (37)

The blood pressure measurement protocols deviated somewhat from the commonly performed protocols. No studies reported accuracy for ≥130/80 mmHg threshold. The studies mostly used a mercury sphygmomanometer, had participants rest for 5 minutes before blood pressure measurement, and used the average of multiple measurements.

Table 7. Diagnostic accuracies of BP measurements

Screening Test	Study Design	No. of Studies (Sample Size)	Results		Quality of Evidence (GRADE)
			Sensitivity (95% CI)	Specificity (95% CI)	
Office-based Blood Pressure Measurement (OBPM)	Cohort	15 studies (11,309)	0.54 (0.37-0.70)*	0.90 (0.84-0.95)*	LOW
Confirmatory Tests					
Repeat OBPM	Cohort	8 studies (53,183)	0.80 (0.68-0.88)*	0.55 (0.42-0.66)*	LOW
Home-based Blood Pressure Measurement (HBPM) confirmation	Cohort	4 studies (1,001)	0.84 (0.76-0.90)*	0.60 (0.48-0.71)*	LOW
Self-OBPM confirmation	Cohort	2 studies (698)	0.92 (0.85-0.96)	0.25 (0.16-0.35)	VERY LOW
6h (Ambulatory Blood Pressure Measurement) ABPM	Cohort	1 study (263)	0.94[a]	0.76[a]	VERY LOW

*pooled; [a] 126 were borderline hypertension; [b] 137 suspected of having white coat hypertension

3.2.4 Cost Implication

Four studies(38-41) have shown that hypertension screening among asymptomatic adults is more cost-effective than no screening or usual care, mainly if hypertension screening is conducted among those aged 45 years and older(40). Table 8 shows an estimated annual screening cost per patient based on a study in a LMIC.

Table 8. Estimated costing data on screening for hypertension

Parameter	Screening intervention
	Blood Pressure Measurement
(A) Unit cost of screening intervention	One study [a] in Nepal estimated the cost of screening and risk profiling to be Php **119.94** (USD 2.49) per case
(B) Other direct costs associated with the implementation of the proposed screening intervention	N/A
(C) Annual screening cost per patient	Php 119.94

[a] study by Aryal(42)

3.2.5 Ethical, Social, and Health Systems Impact (Equity, Acceptability, and Feasibility)

Ethical

The 2019 national survey revealed significant demographic differences in hypertension prevalence by gender, income class, location, and age group. This difference can be further exacerbated due to a lack of access to appropriate, affordable, and acceptable therapeutic options. Additionally, adults from geographically disadvantaged areas may be disadvantaged due to the distances required to reach the nearest barangay health center.(2)

Social

No studies were found on the acceptability of BP screening. Blood pressure screening is commonplace in the country.

Health Systems

Despite all efforts of governmental agencies and non-governmental organizations to improve awareness, treatment, and control rates of hypertension in the country, its prevalence has still been increasing, as shown in the national health surveys. Opportunistic screening in BP demonstrated that there was still a discomforting number of unaware hypertensives, and more than half of those receiving treatment still had uncontrolled blood pressure (BP). Regular, organized screening programs will play an essential role in diagnosing unaware hypertensives and those already on treatment but with inadequately controlled BP. (43)

3.2.6 Recommendations from Other Groups

The USPSTF and the Canadian Task Force on Preventive Health recommend screening for hypertension in adults age 18 years or older. The USPTF recommends using office blood pressure measurement (OBPM). The USPSTF recommends obtaining blood pressure measurements outside of the clinical setting for diagnostic confirmation before starting treatment. (37)

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3.3 Hemoglobin A1c or Fasting Blood Sugar in Screening for Type 2 Diabetes Mellitus

RECOMMENDATIONS

1. **Among apparently healthy adults aged 40 years above, or younger if with risk factors*, we recommend screening for type 2 diabetes mellitus using fasting blood sugar *(strong recommendation, moderate certainty evidence)*.**

2. **Among apparently healthy adults aged 40 years above, or younger if with risk factors*, we suggest screening for type 2 diabetes mellitus using hemoglobin A1c *(conditional recommendation, moderate certainty evidence)*.**

***Risk factors**

- Overweight or obese
- Maternal history of diabetes or having Gestational Diabetes Mellitus during pregnancy
- Family history of type 2 diabetes in first- or second-degree relative
- Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans, hypertension, dyslipidemia, polycystic ovary syndrome, or small-for-gestational-age birth weight)

Considerations

The consensus panel considered the following when formulating this recommendation:

- Diabetes mellitus is deemed a priority risk factor to screen and its management leads to clinically important benefits.
- Both HBa1c and FBS testing were perceived as accurate in terms of diagnostic performance.
- HBa1c and FBS are equitable, acceptable, and feasible. However, it was noted that HBA1c testing may not always be readily available in some parts of the country.
- HbA1c testing has good feedback among practitioners, but concrete evidence is still lacking. The issue that surfaced in the discussion is the standardization of HbA1c testing. Different laboratories in the country performing the HbA1c test may provide various ranges of normal or reference values.
- The panel also considered both age and risk factors in the recommendations. An apparent increase in cases of T2DM was noted starting from the age of 40, based on the national survey. However, there is also an increase seen in data from those aged below 40. Risk factors were considered across age groups, particularly in the younger than 40 years.

Remarks
The recommendation on HbA1c was deemed conditional despite moderate certainty evidence due to standardization issues in the country.

3.3.1 Burden of disease

Disease Frequency
Diabetes affects at least 285 million people worldwide, according to the International Diabetes Federation (IDF). By the year 2030, it is likely to reach 438 million cases, with two-thirds of the affected living in low-income to middle-income countries.(1) Furthermore, the increase of type 2 diabetes mellitus (T2DM) in South Asia is projected to be more than 150% between 2000 and 2035. The IDF estimated 382 million people with diabetes in 2013, exceeding its earlier predictions. More than 60% of the people with diabetes live in Asia, with almost one-half in China and India combined.(2)

Based on an IDF report, the Philippine prevalence of diabetes among adults (aged 20 to 79 years) was 6.3% (3.99 million), affecting 1 in 16 adults. However, 66.7% of adults with diabetes remain undiagnosed. (3)

Severity of Disease
Every year, almost four million deaths are directly due to diabetes, comprising 6.8% of the total global mortality. Diabetes is the fourth leading cause of disease-related death, and almost 80% of diabetes-related deaths occur in developing countries.(4)

In the Philippines, a survey conducted in 2008 reported that among 770 Filipinos with diabetes recruited from general hospitals, diabetes clinics, and referral clinics, 85% had uncontrolled diabetes (with HbA1c >7.0%).(5, 6) Almost all patients (99%) had cardiovascular complications, and other common complications involved foot complications (82%), nephropathy (81%), neuropathy (67%), and eye complications (62%).(5)

Management of the disease
There are existing local clinical practice guidelines on diabetes. However, these are already outdated. Local clinicians have been using the annually updated American Diabetes Association (ADA) diabetes guidelines to guide practice. In 2021, based on ADA guidelines, once a person is diagnosed with diabetes, diabetes self-management education and support, medical nutrition therapy, routine physical activity, smoking cessation counseling as necessary, and psychosocial care are recommended. Pharmacologic treatment is also recommended with metformin as the preferred initial pharmacologic agent for treating type 2 diabetes.(7)

Economic impact of the disease
The estimated economic burden linked with diagnosed diabetes in the US in 2012 was USD245 billion, with higher medical costs of USD176 billion and reduced productivity of USD69 billion. After adjusting for inflation, the economic costs of diabetes increased by 26%

from 2012 to 2017 due to the rise in prevalence of diabetes and the elevated cost per person with diabetes. The diabetes prevalence and medical costs are mainly among the population aged 65 years and older, impacting the growing economic cost.(6)

The estimated cost per person for one year with T2DM in 2013 in the Philippines is Php 9,874.85 (USD205.00), which is comparable with neighboring countries such as Thailand with Php 13,728.45 (USD285.00) and Indonesia with Php 8,415.30 (USD174.70). Additionally, IDF reported that the mean overall diabetes-related expenditure per person with diabetes in the Philippines has increased from Php 2,938.37 (USD61.00) in 2010 to Php 11,271.78 (USD234.00) in 2017.(8) Oral medications, insulin, and transportation cost per visit were reported to be Php 626.21 (USD13.00) per month, Php963.40 (USD20.00) per month, and Php 48.17 (USD1.00) per visit, respectively. (9)

Social impact of the disease

Poverty is related to an increase in T2DM incidence, delayed diagnosis, and inadequate diabetes care and management. Compared with those in the middle-income group, poor individuals had about a 50% higher risk of developing T2DM. Additionally, poor people with diabetes were about 50% less likely to comply with the advised diabetes examinations. A study determined that the marginalized are more at risk to develop diabetes and more likely to experience inequality of care once diabetes has developed. (10)

Diabetic patients, especially those who are overweight and obese, reported discrimination and stigma at their workplaces. The increased incidence of T2DM in Asia can be attributed to the sudden changes in lifestyle behaviors of people such as increased intakes of refined carbohydrates, more saturated and less monounsaturated fat intake, low-quality protein, and decreased fruit and vegetable intake, alongside with sedentary lifestyle.(1)

3.3.2 Benefits and Harms of Screening Tests

Peer led a systematic review of RCTs assessing screening or no screening for diabetes.(11) It included one direct study (a cluster randomized trial), the ADDITION-Cambridge research, which had 20,184 participants with high risk based on a diabetes risk score. The study was conducted in primary healthcare clinics in Eastern England. The study showed no apparent difference in all-cause mortality, diabetes-related mortality, cardiovascular mortality, and cancer mortality. Diabetes-related morbidity and health-related quality of life did not show a substantial difference. Adverse events were not reported. Overall, the certainty of the evidence is very low due to imprecision (i.e., wide confidence interval) and indirectness (included high-risk patients).

Three studies did not show any difference in harm outcomes among patients screened or not screened.(12-14)

A recent network meta-analysis on RCTs on glucose-lowering treatments included 746 RCTs with 421,346 patients.(15) As compared to placebo, SGLT-2 inhibitor and GLP-1 receptor agonist reduced all-cause mortality, CV mortality, nonfatal MI. Alpha glucosidase reduced

nonfatal MI. GLP-1 receptor agonist reduced nonfatal stroke. Sulfonylureas and basal insulin increased severe hypoglycemia as compared to placebo. These results are based on moderate to high certainty evidence.

Table 9. Effects of glucose-lowering treatments (n = 421, 346 patients)

Treatment vs. placebo	All-cause mortality OR (95% CI)	CV mortality OR (95% CI)	Nonfatal MI OR (95% CI)	Nonfatal stroke (OR, 95% CI)	Severe hypoglycemia OR (95% CI)
SGLT-2 inhibitor	0.77 (0.71,0.83)	0.84 (0.76,0.92)	0.87 (0.79,0.97)	1.01 (0.89,1.14)	0.90 (0.70,1.16)
GLP-1 receptor agonist	0.88 (0.83,0.94)	0.88 (0.80,0.96)	0.92 (0.85,0.99)	0.84 (0.76,0.93)	0.92 (0.79,1.08)
Metformin	1.03 (0.74,1.44)	0.95 (0.48,1.89)	1.14 (0.79,1.64)	1.00 (0.66,1.54)	1.64 (0.81,3.30)
SU	1.11 (0.96,1.29)	1.00 (0.80,1.26)	1.08 (0.87,1.33)	1.09 (0.86,1.40)	6.18 (4.11,9.29)
TZD	1.02 (0.87,1.20)	0.97 (0.77,1.23)	1.15 (0.84,1.56)	0.94 (0.70,1.25)	1.35 (0.89,2.05)
DPP-4 inhibitor	1.01 (0.94,1.08)	0.98 (0.89,1.09)	1.01 (0.92,1.11)	0.93 (0.82,1.05)	1.09 (0.93,1.27)
Basal insulin	1.11 (0.65,1.87)	1.13 (0.53,2.40)	1.09 (0.54,2.22)	0.84 (0.39,1.83)	2.31 (1.62,3.30)
Basal bolus insulin	0.80 (0.19,3.35)	2.23 (0.23,21.95)	0.35 (0.03,3.45)	0.62 (0.11,3.57)	2.33 (0.14,39.25)
Bolus insulin	0.98 (0.10,9.62)	0.99 (0.10,9.87)	1.23 (0.39,3.88)	0.85 (0.09,8.24)	2.67 (0.51,13.99)
Alpha glucosidase inhibitors	0.89 (0.30,2.63)	0.99 (0.21,4.70)	0.19 (0.04,0.87)	10.05 (0.81,124.59)	1.12 (0.22,5.63)
Glitinide	1.64 (0.53,5.10)	0.65 (0.11,3.75)	0.29 (0.05,1.62)	1.86 (0.28,12.54)	3.15 (0.90,11.01)

Note: There are other outcomes reported in the network meta-analysis not included in this summary.

3.3.3 Diagnostic Performance of Screening Tests

A recent systematic review and meta-analysis pooled the sensitivity and specificity of FBS and HbA1C testing.(16) HbA1c testing has a pooled sensitivity of 50.2% (95%CI 41.7% to 58.8%) and pooled specificity of 97.3% (95%CI 95.3% to 98.4%) for an HbA1C at the recommended threshold 6.5%. FBS testing has a pooled sensitivity of 59.4% (95%CI 41.7% to 58.8%) and pooled specificity of 97.3% (95%CI 95.3% to 98.4%). These analyses included 17 studies with 64,928 patients for HbA1c and 10 studies with 45,917 patients for FBS testing. The reference standard used was a 75-gram oral glucose tolerance test. The quality of evidence is moderate due to the lack of details on the population sampling method in many included studies (i.e., unclear risk in patient selection).

Table 10. Diagnostic accuracy of screening tests for T2DM

Screening Test	Study Design	No. of studies (n = no. of participants)	Results	Quality of Evidence (GRADE)
HbA1C (recommended threshold 6.5%)	Cohort	17 studies (n= 64,928)	Sensitivity: 50.2% (95%CI: 41.7% to 58.8%) Specificity: 97.3% (95%CI: 95.3% to 98.4%)	Moderate (risk of bias)
FBS	Cohort	10 studies (n= 45,917)	Sensitivity: 59.4% (95%CI: 41.7% to 58.8%) Specificity: 98.8% (95%CI: 96.5% to 99.6%)	

3.3.4 Cost Implication

There are no local cost-effectiveness studies on screening for type 2 DM. Studies in Asian countries showed that screening adults with diabetes using FBS (17-19) compared with no screening is cost-effective. In another study comparing FBS vs. Chinese diabetes risk score, FBS performed better in primary care settings.(20)

Table 11. Costing data on screening for type 2 DM

Parameter	Screening intervention	
	Fasting blood sugar	**HbA1c**
(A) Unit cost of screening intervention	Php 120	Php 850
(B) Other direct costs associated with the implementation of the proposed screening intervention	Cost of confirmation test (OGTT) for positive case: Php 600.00	Cost of confirmation test (OGTT) for positive case: Php 600.00
(C) Annual screening cost per patient	Php 720	Php 1450

*Published cost from Dr. Jose N. Rodriguez Memorial Hospital and Sanitarium

3.3.5 Ethical, Social, and Health Systems Impact (Equity, Acceptability, and Feasibility)

Ethical

Laboratories should satisfy the standard before HbA1c testing is done. Another consideration is that the Philippines' current capacity of health facilities does not allow this test's nationwide application. Adopting the HbA1c test for T2DM screening may only benefit people living in urban and big city areas rather than an equal distribution in the whole country. (21)

Social

A local study showed that diabetes patients receive solid family support. (91) However, knowledge about diabetes is still lacking in the country. In a survey of one region, the average score for knowledge of the condition among people diagnosed with diabetes was only 43%.(22)

Another issue highlighted previously was self-stigma and social stigma associated with the disease status, which may also affect the people's participation in the screening program. Patients tend to self-discriminate, reflect low self-esteem and self-efficacy, and tend to avoid disclosing the illness along with social withdrawal.(23) Like other screening services, T2DM screening is a "preventive service" where benefits could only be apparent in the long run. Those who are more socially deprived usually value actions that only have immediate positive outcomes; thus, they may be less likely to participate in the screening program. (19)

Health Systems

Screening for undiagnosed diabetes and pre-diabetes could give an early diagnosis and allow medical treatment to start, thus slowing down the disease. For low and middle-income countries (LMICs), including the Philippines, one of the challenges of managing diabetes is

developing effective, low-cost, and sustainable interventions to prevent or delay the onset of type 2 diabetes. Several studies have shown the cost-effectiveness of early diagnosis and management of diabetes through the use of opportunistic screening and risk assessment screening tools.(22)

However, previous evidence showed that the preparedness of the healthcare system usually is inadequate in LMICs. Screening intervention, once adopted, would result in higher demand for the healthcare system. Accordingly, the capacity in healthcare facilities includes infrastructure, and human resources should be well prepared.

Furthermore, as screening will identify more patients, the treatment capacity should be prepared. For example, the accessibility of anti-diabetic drugs and insulin should be taken into account. (24, 25)

There is only limited research on the financial burden of diabetes. Filling this gap may further help policymakers make informed decisions while developing and implementing resource planning for relevant interventions.(26)

3.3.6 Recommendations from Other Groups

Local CPG on diabetes is already outdated.(27, 28) Universal screening using laboratory tests for diabetes was not recommended. Lab test screening was recommended only for those with at least one risk factor for type 2 diabetes mellitus. HbA1C testing was not yet included in the list of recommended screening tests. Local physicians tend to follow ADA guidelines to manage patients with diabetes.

USPSTF recommended screening (including HbA1c testing) for abnormal blood glucose among adults aged 40 to 70 who are overweight or obese.(29) This recommendation is currently being updated.

ADA recommends early screening for asymptomatic adults with risk factors.(7, 30) For all people, screening is recommended to start at 45 years. Fasting plasma glucose, 2-hour plasma glucose during 75-g oral glucose tolerance test, and A1C are equally appropriate. NICE(31) and Diabetes Canada(32) also recommend fasting plasma.

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3.4 Anthropometric Measurements in Screening for Malnutrition

RECOMMENDATIONS

1. **Among asymptomatic apparently healthy adults, we recommend using body mass index in screening for obesity *(strong recommendation, moderate certainty evidence)*.**

2. **Among asymptomatic apparently healthy children (6-59 months), we suggest screening for acute malnutrition using mid-upper arm circumference or weight-for-height z-scores. *(conditional recommendation, low certainty evidence)*.**

Considerations

The consensus panel considered the following when formulating this recommendation:

- Malnutrition is a priority because of its burden.
- All panel members agreed that the benefits outweigh the undesirable effects.
- They considered the high accuracy of body mass index (BMI) for overnutrition and recognized its lack of evidence for undernutrition. The waist-hip ratio (WHR) was perceived to have low sensitivity.
- Though the evidence presented used WHO classification, the panel decided to use a cut-off score for recommendation in obesity from Asia-Pacific Classification (BMI ≥ 25 kg/m^2) that seemed more appropriate for the local setting.
- Screening for malnutrition is equitable, acceptable, and feasible.

3.4.1 Burden of disease

Disease Frequency

Prevalence of stunting (30.3%), underweight (19.1%), and wasting (5.6%) were recorded among the 20,000 Filipino children (0-59 months) in the Food and Nutrition Research Institute survey in 2018. Among older children (6 to 10 years old), stunting and underweight are still top malnutrition issues, but they seemed to decline across the years.(1) Meanwhile, nutritionally-at-risk mothers in the country are found in the marginalized sector and those below 20 years old (37.2%) with low educational attainment.(2)

To date, middle-income countries and some low-income countries, including the Philippines, are experiencing the "double burden of malnutrition."(3, 4) Although overnutrition does not appear to be as concerning as undernutrition, the trend is increasing in the country (from 8.4% in 2015 to 11.7% in 2018). It seems to be more prevalent among older children (aged 6-10 years) (1) and adolescents (5) and most pervasive among Filipino adults. Almost 40% of Filipino adults (20-50 years old) are overweight or obese based on their body mass index

in the 2018 survey.(6) In 2013, a higher prevalence of overweight or obesity was found in females (34.4%) than in males (27.6%). (7)

Severity of Disease

Undernutrition caused almost 50% of all child mortality in the last decade. Stunted, underweight, and wasted children have an increased risk of death from combined effects of nutritional problems and infectious diseases.(8)

If mothers are malnourished, their babies are more prone to infections because of their low immunological capabilities, leading to infant morbidity and mortality. Pregnant and lactating mothers in developing countries are also reported to have reduced physical performance compared with those who have average weight, affecting their productivity at work or even at home. (9)

Elevated body mass index as a characteristic of an overweight or obese adult, on the other hand, is a significant risk factor for cardiovascular diseases, metabolic disorders, and musculoskeletal disorders.(10) Meanwhile, maternal obesity is often correlated with gestational diabetes and hypertension, cesarean delivery, and pre-eclampsia. (11)

Management of the disease

Undernutrition

The national guidelines for managing acute malnutrition among children under five years (12) guided by different issues are already in place. Philippine Integrated Management of Acute Malnutrition (PIMAM) has been used in various emergency and non-emergency programs in municipalities and cities through rural health units. Inpatient and outpatient therapeutic care and targeted supplementary feeding programs start with identifying children with severe and moderate acute malnutrition using age, bilateral pitting edema assessment, and anthropometric measurements such as weight and height (weight-for-height/length), Z-scores and mid-upper arm circumference (MUAC). (12)

Overnutrition

There are already population-wide initiatives, including policies and health programs in our country. Overweight and obesity are commonly identified in outpatient clinics, workplaces, and schools through routine examinations and national surveys. (13) The health programs to address overweight and obesity among adults and children focus on creating a supportive environment towards behavior change, promoting physical activity, and a healthy diet(13). Integrating exercises through physical education classes and break routines are now being promoted in schools for children and adolescents. Although numerous programs for children and adults have been cited in the national report(14), its effectiveness in decreasing the risk of mortality and the incidence of related diseases has not been adequately studied and reported. Only in a case report included, reduction of incidence rates of diabetes (7%) and hypertension (31%) was found among 5000 employees of a national government unit because of modifying services in the office's cafeteria, gaining free access to fitness centers, and providing health programs within their community.(13)

The Philippine Association for the Study of Overweight and Obesity has also developed obesity guidelines where treatment recommendations are focused on the primary care setting. (15)

Economic impact of the disease

A regional study revealed that productivity loss and education loss from child undernutrition cost Php 328 billion in 2013. Repeating grade level requirements, reduced workforce, and premature deaths secondary to undernutrition cost the country 2.8% of our gross domestic product. If the total loss from mortality among those who would supposedly be productive members of the workforce had been prevented, the nation would have increased its productivity by Php 160 billion. (16)

Another study conducted in the Philippines on micronutrient deficiencies (MNDs), a form of malnutrition, presented that MNDs have reached substantial costs in 6-to-59-month-old children in the Philippines. The total lifetime costs amounted to direct medical expenses of Php 1.45 billion with production losses of Php29.77 billion and intangible costs of 122,138 disability-adjusted life years.(17)

On the other hand, the impact of overweight or obesity in the Philippines has been recognized because it leads to developing non-communicable diseases such as cardiovascular and metabolic disorders among adults. Economic losses may not directly come from overnutrition itself but its secondary complications.(18, 19)

Social impact of the disease

Studies have illustrated the correlation between early childhood nutrition and success in school. For example, one of the anthropometric nutritional indicators linked with schooling is the height for age.(20) A study in the Philippines suggested that severely stunted children between birth and 2 years of age had significantly lower test scores than those of non-stunted children. However, this may also be caused by substantial delay in initial enrolment, higher absenteeism, and repetition of school years among stunted children. (21)

Another strong determinant of undernutrition is poverty among young children, but this should not be the case for the nutritional outcomes among school children. Other determinants that strongly predict schoolchildren's undernutrition are household food insecurity, low maternal education, and poor health.(22)

On another side of the spectrum, a qualitative study described perceptions of being overweight and reported that women feel the social pressures to be slim with less focus on overnutrition's physical consequences.(23)

3.4.2 Benefits and Harms of Screening Tests

There is no direct study found on the effectiveness of screening for malnutrition. Available research focused on the management of the condition.

Subsequent management for undernutrition is an integrated nutrition program consisting of targeted supplemental feeding and inpatient and outpatient therapeutic care for the pediatric group where malnutrition is more prevalent and has the most considerable impact. (12, 24) On the other hand, behavioral intervention in managing overnutrition includes a healthy diet, exercise, or physical activity promotion for adults(25) and, similarly, in children with child-oriented or family-based behavior modification strategies.(26)

A recent and relatively well-conducted meta-analysis(24) reviewed 42 articles on managing severe acute malnutrition (SAM) and moderate acute malnutrition (MAM) among children in the middle- and low-income countries. They used various integrated management strategies such as ration of ready-to-use therapeutic food (RUTF), oral rehydration, antibiotics, malaria prophylaxis, immunizations, counseling mothers on child nutrition, and breastfeeding practices. The results from a RCT in this meta-analysis comparing this integrated management and standard showed a benefit in decreasing the risk of remaining malnourished (RR 0.58, 95% CI 0.42 to 0.80) after the intervention. However, there is no significant difference between integrated and standard management in terms of mortality (RR 0.93, 95% CI 0.60 to 1.45) and with unclear evidence of higher recovery in standard management than experimental (RR 1.04, 95% CI 1.00 to 1.09). Standard management differs in that it lacks counseling mothers about acceptable practices, but it has an unlimited ration of RUTF. There is also a lower risk of adverse events (i.e., fever and diarrhea) noted in the integrated management (RR 0.79, 95% CI 0.67 to 0.93). There are other different comparisons, but the evidence is still inadequate. The impact of 1) facility-based strategies according to WHO protocol compared with other protocols and 2) RUTF relative to the effect of the therapeutic milk F100 on mortality remain inconclusive.

On the other hand, lifestyle interventions are the first-line method to reduce excess adiposity, causing overweight or obesity in many people of all ages.(27-31) There is a high certainty that the risk of all-cause mortality is reduced among adults who are obese (RR 0.82, 95% CI 0.71 to 0.95) based on a systematic review and meta-analysis(25) of 34 RCTs that investigated diet change with or without exercise. However, decreasing cardiovascular events and cancer incidence among these adults remain inconclusive.(25)

3.4.3 Diagnostic Performance of Screening Tests

A recent systematic review and meta-analysis(32) has pooled sensitivity and specificity of BMI with a threshold of 25 to 30 kg/m^2 to detect overnutrition was 54.1% (95% CI 38.5 to 64.2%) and 95.4% (95% CI 90.7 to 97.8%) from data on 14,008 women of any race and ethnicity. In 11,320 men, the pooled sensitivity was slightly lower (49.6%; 95% CI 34.8 to 64.5%) and specificity was higher (97.3%; 95% CI 92.1 to 99.1%). (Table 12)

The cut-offs used by various studies in the systematic review to determine the diagnostic performance of WHR ranged from 0.74 to 0.97 in women and 0.85 to 0.96 in men. (32) The pooled sensitivity and specificity are seen in Table 12.

Table 12. Diagnostic performance of anthropometric measurement in overnutrition among adults

Test	Sensitivity (95% CI)		Specificity (95% CI)		GRADE Certainty
	Males	Females	Males	Females	
BMI	49.6% (34.8 – 64.5%)	54.1 % (38.5 – 64.2%)	97.3% (92.1 – 99.1 %)	95.4% (90.7 – 97.8%)	Low to Moderate
WHR	77.5% (70.9-83.2%)	53.1% (47.6 – 58.4%)	83.7% (80.2 – 86.8%)	77.3% (74.7 – 79.8%)	Low to Moderate

A meta-analysis aimed to determine the diagnostic accuracy of BMI at a cut-off point of 85th centile for overweight and 95th centile for obesity among children in the UK; results were almost similar to adults. BMI has a relatively low sensitivity (73.9%; 95% CI 64.2 to 81.8%) but high specificity (94.7%; 95% CI 92.2 to 96.4%) across the different subgroups for diagnosing overweight or obesity. (26)

There was no available systematic review on the diagnostic accuracy of MUAC. The following values were pooled from six different studies from India(33-35), Vietnam(36), Niger (37), and Cambodia(38). Pooled using STATA, sensitivity for MUAC at 115mm to diagnose SAM is 17% (95% CI 8 to 32%) while specificity is 99% (95% CI 99% to 100%). High heterogeneity was found across studies (I^2 = >90%). Despite the low sensitivity of MUAC, children that will be misclassified as not having SAM are nevertheless classified in moderate acute malnutrition (MAM), and essential treatment will still be provided. A meta-analysis of sensitivity and specificity values for diagnosing global acute malnutrition (37, 39) and MAM (33, 36, 38) was not possible in the software due to the limited number of studies available.

Table 13.Diagnostic performance of anthropometric measurement in malnutrition among children

	Sensitivity (95% CI)	Specificity (95% CI)	GRADE Certainty
MUAC (for undernutrition)	17% (8 - 32%)	99% (99 – 100%)	Moderate to high
BMI (for overnutrition)	73.9%(64.2 – 81.8%)	94.7%(92.2 – 96.4%)	Low to moderate

3.4.4 Cost Implication

There is no available data for cost-effective analysis of anthropometric measurements as screening intervention. Costing data is shown in Table 14.

Table 14.Estimated annual cost of using anthropometric measurements in screening for malnutrition

Parameter	Screening Intervention: Anthropometric Measurements
Unit cost of screening intervention	Not available

Parameter	Screening Intervention: Anthropometric Measurements
Other direct costs associated with the implementation of the proposed screening intervention	**Sample computation per barangay in a highly urbanized area where screening tests can be done once a year.** ● Training of 20 healthcare workers in 2 hours (professional fee and cost of materials such as pen and paper) = **Php 3,000** ● Cash incentive for BHW (assigned for every 250 children in barangay) = **Php 2,000** ● Child MUAC tape measure = Php 209* (**Php 22.06** if set at annualized cost considering 1% inflation rate in 10 remaining life years) ● SECA tape measure = Php 1,524.21* (**Php 160.93** if set at annualized cost considering 1% inflation rate in 10 remaining life years) ● SECA weighing scale = Php 36,757.33* (**Php 3,881.04** if set at annualized cost considering 1% inflation rate in 10 remaining life years) *Price used from https://1outlets.ph/go/Seca+Scales
Annual screening cost per patient	**Screening for malnutrition using anthropometric measurement in children** Annualized cost of items + BHW cash incentive + cost in training per health worker Estimated no. of children per barangay = (4,064.03 + 2,000 + 150)/250 **Php 24.86**

3.4.5 Ethical, Social, and Health Systems Impact (Equity, Acceptability, and Feasibility)

Ethical

A study in Cambodia discussed implementing a 'mid-upper arm circumference (MUAC)-only' or a 'weight-for-height-Z-scores (WHZ)-only' program to identify acute malnutrition may be unethical. It has been observed in the use of the current WHO cut-off of 115 mm for SAM screening, over 90% of children with a weight-for-height Z-score (WHZ) would have been missed. In retrospect, WHZ < -3 missed 80% of the children with a MUAC < 115 mm. It could lead to numerous children remaining undiagnosed, which could be unethical. Hence, it is recommended to use both screening interventions simultaneously. (38, 40)

Moreover, correlations of BMI and mortality rates do not often consider family history of illness, past and present history of vices (alcohol abuse and smoking), mental disorders, start and duration of obesity, and height status. Hence, the use of BMI alone for screening may lead to inaccurate diagnosis. Additional problems were observed in associating BMI with overall death rate or cardiovascular events or death rates. Based on the literature, many

obese people have no cardiovascular risk factors. In those who have, BMI does not correlate with cardiovascular events when the unforeseen effects of these factors are opted out. (41)

Social

There are no specific studies on social, cultural, or religious factors that would possibly affect anthropometric measures' acceptability in the Philippine setting. It has been used in primary care surveys for many years by the FNRI and outpatient clinics that aid the institutions and health departments in developing health programs.(1, 2, 5-7, 22, 42)

Barriers in screening for malnutrition include discomfort of disclosing poor diet, personal preferences in diet, fear of being labeled as "at-risk" to conditions as reported in an international study. These hindrances to screening may be rooted in their individual preferences, their experience of the patient-practitioner relationship, or their way of receiving the information. (43)

Another potential concern over screening for obesity and overweight is that this may increase social pressure on children and women to achieve the 'perfect body.' Moreover, recent research on BMI and suicide attempts revealed that adolescents' perception of their body weight might be more significant than their actual weight or BMI. It may result in a higher level of body dissatisfaction and body image concerns among youth, associated with lower global self-worth, more insufficient self-esteem, and greater dissatisfaction with other aspects of life.(44) However, these concerns may not necessarily apply in the local setting because of lack of evidence.

Health Systems

Continuing anthropometric measurements as screening intervention in all levels and ages provided with the mentioned cut-offs has minimal impact on human resource needs, training requirements, and infrastructure. Even teaching laypersons such as mothers using a MUAC tape is found non-inferior compared with training community health workers.(45) Tools are relatively cheap and straightforward to use. With proper instructions and visual aids, if training cannot be provided, these anthropometric measurements for screening malnutrition can be done.

3.4.6 Recommendations from Other Groups

The Canadian Task Force strongly recommends measuring BMI among healthy adults (≥ 18 years) in the primary care setting because it is better than visual estimation. It is crucial to monitor the weight over time and provide interventions as necessary.(31) Their recommendation, however, does not apply to pregnant women and people with eating disorders.

They recognized that behavioral interventions are preferred over pharmacologic interventions for overweight and obese (BMI 25 to 39.9 kg/m^2).(31) For adults with obesity (BMI 30 to 39.9 kg/m2) and are at high risk of diabetes, they strongly recommended programs targeting behavioral modifications involving a specified number of sessions over a specific duration (i.e., weeks or months) or structured behavioral interventions.

Body mass index was also strongly recommended to monitor growth among the children and youth despite a very low quality evidence since it has been in the long-standing routine in primary care and is low cost according to the Canadian Task Force.(29, 30) Their guidelines, however, focused on overnutrition among children. Although monitoring was recommended, structured interventions preventing obesity and overweight among children and adolescents were not routinely offered.(29, 30)

International guidelines, including the RCOG, recommend measuring BMI(27) on the first prenatal visit or weight(46) for women of reproductive age to manage obesity or modify their weight. Although the RCOG mentioned advising on dietary intake and physical activity promotion, they did not discuss the specific lifestyle modification strategies. However, they do consider pre-existing cultural and social beliefs on diet and weight gain. They also acknowledge possible mental health problems among women with obesity that may be aggravated by acknowledging nutrition problems.(46)

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3.5 Survey Questionnaires in Screening for High-Risk Sexual Behavior

RECOMMENDATION

Among asymptomatic apparently healthy adolescents and adults, we suggest screening for high-risk sexual behavior *(conditional recommendation, low certainty evidence)*.

Considerations

The consensus panel considered the following when formulating this recommendation:

- Most agree that high-risk sexual behavior is a priority mainly because of the rising cases of HIV.
- All agree that screening has benefits that outweigh the harmful effects (i.e., stigma) provided that health workers that will be involved are well-trained in handling those who will be identified.
- The CP perceived the screening to be inexpensive. However, professional fees and the battery of tests might incur high costs.
- All agree that screening for high-risk sexual behavior using suggested tools is equitable, acceptable, and feasible.
- Issues of privacy and confidentiality, labeling, stigma, and acceptance of the result were raised.

Remarks

This recommendation reached consensus. However, there was an abstention from the panel due to the concerns about privacy and legal issues on screening minors.

3.5.1 Burden of disease

High-risk sexual behavior is not a disease but rather a risk factor for developing many diseases and conditions. Examples of high-risk sexual behavior include 1) unprotected intercourse without male or female condom use, except in a long-term, single-partner (monogamous) relationship, 2) unprotected mouth-to-genital contact, except in a long-term monogamous relationship, 3) early sexual activity, especially before age 18, 4) having multiple sex partners, 5) having a high-risk partner (one who has multiple sex partners or other risk factors), 6) having anal sex or a partner who does, except in a long-term, single-partner (monogamous) relationship, 7) having sex with a partner who injects or has ever injected drugs, and 8) exchange of sex (sex work) for drugs or money.(1)

Disease Frequency

A national survey showed that "only one in ten sexually active Filipinos consistently uses contraceptives to avoid contracting sexually transmitted diseases (STDs) or prevent pregnancy.(2) The 2nd PhilCare Wellness Index showed that only 13.2 % said they always

used protection during sex to avoid getting STDs such as HIV. Only 12.8% admitted that they consistently used contraceptives (i.e., condoms or oral contraceptive pills) to prevent unwanted pregnancies.(3)

Among young adults (aged 18-30 years of age), only two out of ten always used protection (same as previous). (3)

Severity of Disease
The Philippines, along with Bangladesh, Pakistan, and Afghanistan, are challenged by rapidly expanding HIV epidemics. Among these, the Philippines demonstrates "the steepest rise," with new infections increasing by 200% from 2010 to 2018.(4)

Approximately 160,000 people died due to an AIDS-related illness in the region in the year 2019. Some countries experienced increases in AIDS-related deaths, including Afghanistan, Bangladesh, Indonesia, Pakistan, and the Philippines. (4)

Economic impact of the disease
Unsafe sex is the second leading cause of disability-adjusted life years (DALYs) worldwide. Hence, valid and reliable tools to assess risky sexual behaviors are necessary for implementing preventive measures. (5)

Sexually transmitted infections (STIs) constitute colossal health and economic burden for developing countries: 75–85% of the estimated 340 million annual new cases of curable STIs occur in these countries, and STIs account for 17% of economic losses because of ill health. (6)

Social impact of the disease
Healthcare providers may deliberately minimize contact with patients with HIV, reduce care for them, delay or deny treatment, or isolate these patients from others. (7)

Stigma from the diseases caused by HRSB (such as HIV, STIs), sex work, substance use, and gender and sexuality issues bring about social, economic, and legal stigma - resulting in poor health services, poor access and uptake, harassment, and abuse, discrimination and violence, poverty, and poor social or emotional wellbeing. The resulting marginalization becomes a take-off point of a vicious cycle that eventually results in poor health and sickness. (7, 8)

3.5.2 Benefits and Harms of Screening Tests

A study has shown that screening for sexual risk behavior resulted in a statistically significant increase in screening for gonorrhea, chlamydia, and syphilis.(9) The prompt diagnosis allows for treating not only the patient but also the sexual partner.(10) Gonorrhea, chlamydia, and syphilis are easily managed with the appropriate antibiotics. Early treatment of gonorrhea and chlamydia prevents complications like epididymitis that rarely may cause infertility.(11) If left untreated, gonorrhea can result in disseminated gonococcal infection, manifested as arthritis, tenosynovitis, and/or dermatitis.(12) The condition may be life-threatening. In syphilis, some patients left untreated are at risk of developing tertiary

syphilis; at this stage, the heart, blood vessels, the brain, and nervous system are affected, eventually leading to death.(12)

When high-risk sexual behaviors are screened, individuals who can benefit from voluntary counseling and testing (VCT) can be identified. Henderson and the research team in 2020 published a systematic review and meta-analysis (an update of the evidence for the USPSTF) on behavioral counseling interventions to prevent sexually transmitted infections.(13) Twenty-one out of 39 studies reported the effectiveness of behavioral counseling in preventing STI. Nineteen studies showed that behavioral intervention was significantly associated with a lower incidence of STI (overall pooled OR 0.66, 95% CI 0.54-0.81; I^2 = 74%; n = 52,072; strength of evidence moderate).(13) In terms of reducing risky behaviors and increasing protective ones, pooled results showed a lower number of episodes of unprotected intercourse (pooled mean difference, –0.94 (95%CI –1.40 to –0.48; I^2 = 16%) in those who received behavioral counseling. The result was from the meta-analysis of 14 out of 21 studies that reported a measure of unprotected intercourse, and this was statistically significant. Similarly, the pooled analysis from 13 reviews (out of 18 that said condom use) "suggested that the intervention was associated with a higher odds of condom use (OR 1.31, 95% CI 1.10-1.56; I^2 = 40%)." The strength of evidence for the outcome of protective behaviors was low. Appendix A shows the Summary of Findings from the Henderson systematic review and meta-analysis.

There was limited reporting of behavioral counseling's possible harm from seven studies investigating this (strength of evidence insufficient). (13)

One possible limitation of screening for HRSB is the social desirability bias that comes with answering a self-reported sexual risk assessment.(14) Responses may be adjusted not to create the impression of being careless concerning sex to avoid the stigma of reckless or hypersexual behavior. This stigma in itself, and the resultant marginalization, represents one of the possible harms of such screening, especially when done in settings where privacy is not keenly observed. (8)

3.5.3 Diagnostic Performance of Screening Tests

A systematic review found assessment tools for risky sexual behavior that can be carried out using questionnaires or non-questionnaire instruments.(5) For this review, only the questionnaire types are discussed.

The reviewer performed a free search for articles reporting these diagnostic accuracy measures for the screening tools listed in the Mirzaei study, but none were found. Psychometric properties and the factors they assessed were reported, as shown in the review.

The review also found two questionnaires used in large-population settings: the National Survey of Sexual Attitudes and Lifestyle (NATSAL) from the United Kingdom (UK) and the Youth Risk Behavior Surveillance Survey (YRBSS) from the United States (US). These surveys

can provide a prevalence estimate of risky sexual behaviors in the geographical locations of use. These questionnaires were found to have good reliability and validity. (15)

As to small population questionnaires, the systematic review identified nine tools identified and described in Table 15.

Table 15. Small population questionnaires: a characteristic and psychometric evaluation.(5)

Name of Tool	No. of Items	Factors Assessed	Psychometric properties
Sexual Risk Survey	23	Total of 5: sexual risk-taking with uncommitted partners, risky sex acts, impulsive sexual behaviors, intent to engage in risky sexual behaviors, and risky anal sex acts	0.88 Test-retest reliability: 0.93
Safe Sex Behavior Questionnaire (SSBQ)	27	Total of 4: protection during intercourse, avoidance of risky behaviors, avoidance of bodily fluids, and interpersonal skills	Total: 0.82 Alpha for factors between 0.52 to 0.85 Content validity index : 0.98
Sexual Health Practices Self-Efficacy Scale	20	Total of 6: Sexual relationships, sexual health care, sexual assault, safer sex, sexual equality/diversity, abstinence	Alpha of factors respectively are : 0.82, 0.81, 0.78, 0.71, 0.73
Sexual Risk Behavior Beliefs and Self Efficacy Scales (SRBBS)	26	Total of 8 Three factors for sexual risk behavior: norms about sexual intercourse, attitudes about sexual intercourse, Self-efficacy in refusing sex Five factors for protective behaviors: Norms about condom use, attitudes about condom use, self-efficacy in communication, self-efficacy in using condoms, barriers to condom use	Alpha of factors respectively are 0.78, 0.78, 0.70, 0.84, 0.87, 0.66, 0.61, 0.73
Condom use errors / Problem survey (CUES)	16	Assessments of most common problem and errors in condom use in the last three experiences	Not reported
Correct Condom Use Self Efficacy Scale (CCUSS) 7 item Alpha: 0.70	7	Questionnaire about errors and problems that might occur before, during, and after sex	Alpha 0.7
UCLA Multidimensional Condom Attitudes Scale (MCAS)	25	Total of 5: Reliability and effectiveness of condoms, pleasure associated with condoms, stigma associated with condoms, embarrassment about negotiation and use of condoms, embarrassment about purchasing condoms	Alpha between 0.71 to 0.94 for subfactors (reported separately for each sex)
Hypersexual Behavior Inventory (HBI)	19	Total of 3: Control, coping, and consequences	Total alpha: 0.90 Alpha of factors respectively are 0.78 , 0.86 and 0.78.
Hypersexual Disorder Screening Inventory (HDSI)	7	Total of 2: Recurrent and intense sexual fantasies, urges and behaviors, distress and impairment as a result of these fantasies, urges, and behaviors	Alpha: 0.88

3.5.4 Cost Implication

A few studies from 2000 onwards looked into the cost-effectiveness of screening for high-risk sexual behavior (with or without concomitant intervention), primarily done in the US. These were through text messaging survey(16), sexual health survey during emergency department (ED) visits(17), text surveys with or without interaction(18), and baseline survey and school-based educational program, Safer Choices(19). Generally, these screening interventions were deemed cost-effective.

Table 16 shows an estimated annual screening cost per patient in the Philippines.

Table 16. Costing for Screening for High-risk Sexual Behavior thru Text Messaging (16)

Parameter	**Screening intervention**
	Text-based Survey on Sexual Risk Behaviors
(D) Unit cost of screening intervention	Text message survey once each week for five weeks. Assume a maximum of five tries per respondent before an answer is obtained. P 1.00 x five tries/week for five weeks = Php 25.00
(E) Other direct costs associated with the implementation of the proposed screening intervention [a]	Patient cost = an average of 10 minutes per screening of a physician/nurse/social worker Php 29,277[b] = Php 30.50
(F) Annual screening cost per patient	**Php 55.50**

[a] *Cost of identifying the specific STD such as gonorrhea, chlamydia, syphilis, HIV, and treatment cost is not part of the computation. Direct and indirect costs of unwanted/unplanned pregnancy are not also included in this computation.*
[b] Based on the monthly income of a physician/nurse/social worker with a Salary grade 14

3.5.5 Ethical, Social, and Health Systems Impact (Equity, Acceptability, and Feasibility)

Ethical

An instrument that attempts to collect information on very detailed sexual history and activity puts its respondent at some degree of perceived compromise. Studies done by WHO in the Philippines and India, Indonesia, and Thailand revealed that up to 34% of respondents experienced "breaches of confidentiality" by the health providers attending to them. (20)

Adolescents and youths in disadvantaged communities, such as rural, mountainous, and other underdeveloped areas, are more likely to have higher sexual risks.(21) A properly chosen and widely-used instrument stands to benefit these populations. When screening leads to early diagnosis and treatment, the health inequity that plagues these marginalized groups may be lessened.

Social

The Philippines is a predominantly Catholic country, with an estimated 76 to 86% of the population actively practicing Catholicism.(22) Many behaviors are deemed unacceptable

and immoral, and the only sexual behavior thought to be morally appropriate is heterosexual intercourse within a monogamous marriage.(23)

Sexual risk surveys provide the prevalence of high-risk sexual behaviors. Still, since completing these calls for information about sexual debut, sexual partners, condom use, and other matters considered sensitive, participants may feel reluctant to provide truthful, complete, and accurate accounts of past behaviors because of the stigma associated with them.(24) A study that enrolled Vietnamese individuals aged 16-30 discussed that reporting sexual activities is sensitive. It was warned that the results might not accurately reflect attitudes and behaviors. (25)

Health Systems

The adoption or implementation of high-risk sexual behavior screening can ride on existing infrastructure and human resources. However, certain special concessions should be made to accommodate the sensitive nature of information being obtained. For instance, clinical record management should not allow disclosure of identity, nor shall identify information be shared, except for treatment or prevention of STIs.(26) Results of tests should not be viewable in a way that allows patient identification on a server. Thus, computer and information management teams should provide for these.

The patient's consent for disclosure must accompany referrals to other health providers. (26)

The environment for face-to-face data collection of sexual risk behaviors must be private and soundproof, precluding any overhearing or eavesdropping by either uninvolved health personnel or other patients.(26)

An appropriate way of calling in a patient would prohibit identification by others. Training of existing personnel will be necessary to assure that the survey process protects the patient's privacy, the confidentiality of data and that patients are spared from the experience of being judged or discriminated against.(26)

3.5.6 Recommendations from Other Groups

The 2013 update of the UK national guideline for consultations requiring sexual history-taking follows the 2006 version.(26) Though mainly intended for use in genitourinary medicine, it can also be applied in situations where assessments for STIs are made, including general practice. Encouraging high standards of sexual risk assessment for adults and adolescents alike targets the improvement of sexual health among these individuals. The guideline covers the following areas of inquiry and other concerns: the environment for sexual history-taking, communication skills, and thorough sexual history that delves into partners, behaviors, and practices, among many others.

Separately, the National Institute for Health and Care Excellence (NICE) in September 2016 published their first guideline on 'harmful sexual behavior among children and young

people,' to include ages 10–18.(27) It also includes individuals up to 25 years old who have special educational needs or a disability.

A search of the Canadian Task Force website on Preventive Health Care revealed upcoming screening guidelines for chlamydia and gonorrhea (2020/2021) but not for high-risk sexual behavior.(27)

The USPSTF has issued relevant recommendations on the following: screening for chlamydia and gonorrhea, screening for syphilis in nonpregnant persons and pregnant persons, screening for HIV, preexposure prophylaxis for HIV, and screening for intimate partner violence.(28)

The systematic review(13) is aligned with the recommendation on behavioral counseling for all sexually active adolescents and adults at increased risk of sexually transmitted infections. The USPSTF names in the STI screening document important information that must be captured to assess whether one is at risk or not. The factors that are listed as putting a person at risk include 1) being diagnosed with an STI in the past year, 2) inconsistent condom use, 3) having multiple sexual partners or a partner who is at high risk for STIs, and d) belonging to a population that has a high STI prevalence (individuals seeking STI testing or attending an STI clinic, sexual and gender minorities, PLHIV, injection drug use, commercial sex workers, etc.).(29)

The Centers for Disease Control (CDC), through its Division of Adolescent and School Health, "promotes environments where youth can gain fundamental health knowledge and skills, establish healthy behaviors, and connect to health services to prevent HIV, STDs, and unintended pregnancy." (30) The YRBSS monitors six categories of health-related behaviors that contribute to the leading causes of death and disability among youth and adults (one of the sexual behaviors). The CDC conducts it along with state and local governments.

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3.6 Self-Report in Screening for Tobacco Smoking

RECOMMENDATIONS

1. **Among all adults, we recommend that healthcare providers screen for tobacco smoking *(strong recommendation, low certainty evidence)*.**

2. **Among all adolescents, we recommend that healthcare providers screen for tobacco smoking *(strong recommendation, very low certainty evidence)*.**

Considerations

The consensus panel considered the following when formulating this recommendation:

- Most agreed that tobacco smoking is a priority risk factor for screening.
- The majority of the panel members favored screening, although the quality of current evidence is low to very low.
- Underreporting may be inevitable, but those who would be screened as smokers are most likely true smokers.
- The panelists agreed that screening for tobacco smoking is cost-effective, particularly in the long run.
- The majority agreed that screening for tobacco smoking is equitable, acceptable, and feasible. Equity issues in health may also be reduced if the national insurance system will cover for therapy and medicines needed for smoking cessation.
- The question was raised regarding access of adolescents to tobacco even if it is illegal. It was clarified that adolescents have access to tobacco, as reflected in the national survey. Its rampant use warrants a strong recommendation to screen including adolescents.

Remarks

Both statements were settled as strong recommendations despite low to very low certainty evidence due to the burden of the risk factor as to both health and economic aspects.

3.6.1 Burden of disease

Non-communicable diseases, such as cardiovascular diseases, cancer, diabetes, and chronic respiratory disease, kill 41 million people each year, accounting for 71% of all deaths globally. Close to 80% of NCD deaths occur in low- and middle-income countries.(1) In the Philippines, NCDs account for more than 2/3 of all deaths and are the major cause of premature death and disability.(2) Economic costs from NCDs are significant, both from direct costs of treatment and indirect costs from productivity losses. It is estimated that as much as Php 756.5 billion is lost per year, with Php 680.8 billion from losses due to reduced productivity and loss of workforce.(2)

Smoking is a major risk factor for NCDs and, in 2019, caused more than 7 million deaths worldwide, or 20.2% of all deaths in males and 5.8% in females.(3) Despite the stronger push for tobacco control strategies, particularly the tobacco excise tax in recent years, the latest WHO data still show a high age-standardized prevalence of smoking among Filipinos aged 15 years and older at 24.3% overall (41.6% in males, 7.0% in females).(2) It is similar to the 2018 National Nutrition Survey data, which reports a prevalence of 20.7% (41.3% in males and 5.8% in females) for current smoking among adults age 20 years and older and 4.0% In children aged 10 to 19 years.(4) As of 2015, 14.5% of adolescents ages 13 to 15 years (20.5% and 9.1% of male and females, respectively) were current smokers.(5)

Despite diverse approaches to economic analysis, studies consistently show significant financial and health costs from smoking borne by individuals and societal costs to the broader community. Global health expenditure and productivity losses in 2012 were estimated to amount to as much as USD 1436 billion.(6) According to the Southeast Asia Tobacco Control Alliance (SEATCA) report, the Philippines spent Php 177 billion to treat just four of over 30 tobacco-related diseases, while tobacco excise tax collections for that year were inadequate to cover this deficit. (7)

3.6.2 Benefits and Harms of Screening Tests

Direct evidence

At present, there are no studies that report the effects of screening for tobacco smoking alone on mortality, morbidity (e.g., cardiovascular events, cancer) or smoking cessation in adults, or health outcomes, prevention of smoking, or smoking cessation in children and adolescents.

Indirect evidence

Since there were no studies that provide direct evidence on the effectiveness of screening for smoking, a review of the evidence for the effectiveness of smoking cessation interventions among adults and adolescents was undertaken.

This evidence summary is based primarily on the USPSTF evidence reviews, which were appraised to be comprehensive, updated, and methodologically rigorous. In making this evidence summary, aside from reviewing and extracting the evidence from the USPSTF reviews, relevant references were also retrieved and reviewed for clarification or to extract more data when necessary.

Smoking Cessation Interventions in Adults

The USPSTF evidence synthesis for tobacco cessation interventions in adults is an overview of 64 reviews: 32 primary reviews on smoking interventions for the general adult population, 21 on specific subpopulations, and 11 ancillary reviews.(8) Most of the primary studies were Cochrane systematic reviews or meta-analyses. The methods for the search, selection, and quality assessments of the included reviews are described in more detail in the USPSTF document.(8)

There is limited evidence on the effects of smoking cessation on morbidity and mortality. A systematic review on the combination of behavioral and pharmacologic interventions reported the results of a single study that investigated the effect of an intensive, physician-based behavioral intervention.(9) The study randomized 1,445 male smokers with high cardiorespiratory risk to either an intensive stop-smoking intervention that included physician advice, written materials, and one follow-up at the health center or no intervention. It reported reductions in all-cause mortality by 7% (95% CI -20 to +9%), fatal coronary artery disease by 13% (95% CI -33 to +13%), and lung cancer by 11% (95% CI -41 to +38%), however, none of these were statistically significant.(10)

Evidence for the effectiveness of smoking cessation interventions in increasing quit rates is more robust. Systematic reviews and meta-analyses show that behavioral and pharmacologic interventions, alone or in combination, effectively increase long-term (at least 6 months) smoking cessation in the general adult population compared to no intervention or usual care (Table 17). The trials included in these systematic reviews enrolled adult smokers who were identified primarily through self-report.

Table 17. Effectiveness of selected interventions: smoking cessation at 6 or more months

Author, year	Intervention	No. of studies	No. of participants	Risk Ratio (95% CI)	I^2	Quality (GRADE)
Stead 2016 (193)	Combined pharmacotherapy and behavioral support	52 RCTs	19,488	1.83 (1.69, 1.98)	36%	high
Pharmacotherapy						
Hartmann-Boyce 2018 (194)	Nicotine replacement therapy	133 RCTs	64,640	1.55 (1.49, 1.61)	39%	high
Howes 2020 (195)	Bupropion *vs.* placebo	46 RCTs	17,866	1.64 (1.52, 1.77)	15%	high
Cahill 2016 (196)	Varenicline *vs.* placebo	27 RCTs	12,625	2.24 (2.06, 2.43)	60%	high
Behavioral Interventions						
Stead 2013 (191)	Physician advice	26 RCTs	22,239	1.76 (1.58, 1.96)	40%	moderate
Lancaster 2017 (197)	Individual Counseling alone *vs.* minimal contact control	27 RCTs	11,000	1.57 (1.40, 1.77)	50%	high
Hill-Rice 2017 (198)	Nursing intervention	44 RCTs	20,881	1.29 (1.21, 1.38)	50%	moderate
Stead 2017 (199)	Group behavioral counseling *vs.* self-help program	13 RCTs	4,395	1.88 (1.52, 2.33)	0%	moderate
Whittaker 2019 (200)	Mobile-phone based interventions *vs.* minimal support	13	14,133	1.54 (1.19, 2.00)	71%	moderate
	Text messaging + other intervention *vs.* other intervention alone	4	997	1.59 (1.09, 2.33)	0%	moderate

Author, year	Intervention	No. of studies	No. of participants	Risk Ratio (95% CI)	I^2	Quality (GRADE)
Taylor 2017 (201)	Internet (interactive and tailored) *vs.* self-help or usual care	8	6,786	1.15 (1.01, 1.30)	58%	low
Notley 2019 (202)	Incentives vs. usual care or non-incentive based intervention	30	20,060	1.49 (1.28, 1.73)	33%	high
Ussher 2019 (203)	Exercise *vs.* no exercise	21	6,607	1.08 (0.96, 1.22)	0%	low
Alternative and Complementary Therapies						
White 2014 (204)	Acupuncture vs. sham acupuncture	9	1,892	1.10 (0.86, 1.40)	23%	moderate

A systematic review and meta-analysis that included 24 randomized controlled trials on 13,141 adult participants from 11 low- to middle-income countries (LMICs) also showed that brief advice, behavioral counseling, combination bupropion and counseling, and nicotine replacement therapy were effective in promoting abstinence from smoking for at least 6 months in these settings (Table 18).(11)

Table 18. Effectiveness of selected interventions in LMICs

Intervention	Control	# of studies	# of participants	Odds Ratio (95% CI)	I^2	Quality (GRADE)
Bupropion	Placebo vs.Usual Care	2	1397	1.52 (0.67, 3.41)	72%	low
Bupropion plus Counseling	Usual Care	2	1429	12.40 (4.71, 32.65)	71%	low
Nicotine Replacement Therapy	Brief Advice vs.Usual Care	4	1230	1.76 (1.30, 2.37)	13%	moderate
Counseling	Brief Advice vs. Usual Care	8	5735	6.87 (4.18, 11.29)	67%	moderate
Brief Advice	Standard Care	4	728	2.46 (1.56, 3.88)	0%	moderate

Smoking Prevention and Cessation Interventions in Children and Adolescents

The USPSTF evidence review included 25 trials that examined the effects of primary care interventions designed to prevent tobacco use and/or promote smoking cessation on smoking prevalence and quit rates among children and adolescents. The methods for the search, selection, quality assessments and summary of the evidence are described in detail in the USPSTF document.(12)

No studies reported on health outcomes (e.g., cardiovascular, respiratory, oral, and dental health, cancer, mortality). One observational study with a long-term follow-up of 16 years found that a brief 2 to 3-minute intervention, which included asking about smoking status and counseling, administered during routine dental visits did not reduce the likelihood of smoking in adulthood (OR 0.78, 95% CI 0.56 to 1.09).(13) The study had a high risk of bias because of significant attrition—only 39% of the original sample responded to the follow-up survey and were included in the analysis.

A meta-analysis of 13 randomized controlled trials (RCTs) that included a total of 21,700 participants found that behavioral interventions prevented the initiation of smoking at six months or longer (RR 0.82, 95% CI 0.73 to 0.92, I^2=15%).(12) On the other hand, a meta-analysis of 9 RCTs on behavioral interventions to promote smoking cessation (n=2,516) found quit rates among current smokers to be similar between intervention and control groups (RR 0.97, 95% CI 0.93 to 1.01, I^2=29%).(12) Smoking prevalence was similar between treatment and control groups in trials that examined behavioral interventions for the prevention and cessation of smoking among non-smokers and smokers (RR 0.93, 95% CI 0.86 to 1.01; I^2=24%).(12) There was significant clinical heterogeneity in the populations (i.e., definitions of non-smoker/current smoker); type (e.g., counseling, educational material), target (e.g., child or parent), mode of delivery (e.g., print, phone, face-to-face), duration and intensity of the interventions, and definitions of outcomes across the different trials included in these three meta-analyses.

3.6.3 Diagnostic Performance of Screening Tests

A systematic review of 67 studies compared self-reported smoking with direct measurement of cotinine levels from biological fluids.(14) There was substantial heterogeneity in the questions that comprised self-report, the biological samples and cut-offs used for the cotinine test, and study quality (several had significant missing data), precluding pooling of results. In most studies, self-reported smoking prevalence was lower than that from direct measurement by a range of 1% to 47%, possibly indicating underreporting of smoking status.

Most studies that compare self-reports with biochemically assessed smoking status consider self-reported smoking unreliable due to significant under-reporting. However, Tennekoon and Rosenman(15) argue that biochemical assessment, which is usually regarded as the reference standard, may not be a better indicator of smoking status than self-reports. Their comparison of self-reported smoking with biochemical assessment using econometric techniques did not clearly show that one is better than the other. They suggest that instead of switching to biochemical tests, the reliability of self-report may be improved by asking a broader question to include all types of tobacco use and not just cigarette smoking.

The overall quality of evidence for the effectiveness of screening for tobacco use among adults and adolescents is low at best due to the lack of studies that provide direct evidence for its effectiveness (indirectness), the presence of risk of bias in the studies that provide indirect evidence of benefit for some outcomes (e.g., selection bias), significant heterogeneity in the types of interventions across studies (inconsistency), and imprecision of estimates for some results.

3.6.4 Cost Implication

Numerous studies have looked at the costs of smoking and the cost-effectiveness of various smoking cessation interventions.(16-20) However, there are no cost-effectiveness studies

that estimate the costs or cost-effectiveness of screening for tobacco use alone separately from smoking cessation interventions, such as brief counseling and advice. Across countries at different levels of economic development, tobacco screening and smoking cessation programs were found to be cost-effective, resulting in significant cost savings and net gains to individuals, primary care providers, and society.(19)

3.6.5 Ethical, Social, and Health Systems Impact (Equity, Acceptability, and Feasibility)

In 2015, the Social Weather Station (SWS) conducted a national survey to monitor the impact of Republic Act 1035, the Sin Tax Law of 2012. Results showed more current smokers among the poor (Economic Class D and E) compared to higher socioeconomic strata (Classes A, B, C).(5) As such, the poor, who are the most vulnerable to the adverse health and economic consequences of smoking, may benefit the most from tobacco screening and smoking cessation interventions. Screening for smoking is already part of the Department of Health's PhilPEN program(21); however, aside from brief information or advice from the rural health unit personnel (including the barangay health worker), access to effective pharmacologic treatments such as nicotine replacement therapy and other more intensive behavioral interventions may be limited.(2)

Although parental influence is a major factor, in general, peer influence plays a more important role in adolescent smoking.(22) The likelihood of smoking initiation among non-smokers increases when they belong to a "smoking clique," whereas smokers that are part of a "non-smoking clique" are more likely to quit. Furthermore, adolescents who were not part of a clique or group (isolates) were 2 to 5 times more likely to be current or daily smokers than clique members. The highest smoking rates were found among isolates in low-income schools. In contrast, smoking rates were higher among the most popular students in high-income schools. (22)

3.6.6 Recommendations from Other Groups

The Philippine College of Chest Physicians strongly recommends that every healthcare provider should document cigarette smoking during history taking in all patient visits, including pediatric populations, regardless of the reason for the consult.(23)

The USPSTF recommends that clinicians ask all adults about tobacco use, advise them to stop using tobacco, and provide behavioral interventions and US Food and Drug Administration (FDA)-approved pharmacotherapy for the cessation to nonpregnant adults who use tobacco.(24)(A recommendation)

The USPSTF recommends that primary care clinicians provide interventions, including education or brief counseling, to prevent the initiation of tobacco use among school-aged children and adolescents.(24) (B recommendation)

The Canadian Task Force on Preventive Health Care recommends asking children and youth (age 5-18 yr) or their parents about tobacco use by the child or youth and offering brief

information and advice, as appropriate, during primary care visits, to prevent and treat tobacco smoking among children and youth.(25) (weak recommendation, low-quality evidence).

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3.7 Alcohol Use Screening Tools in Screening for Unhealthy Alcohol Use

RECOMMENDATIONS

1. **Among asymptomatic apparently healthy adults, we recommend screening for unhealthy alcohol use and providing persons identified with risky drinking with brief behavioral counseling intervention *(strong recommendation, moderate certainty evidence)*.**

2. **Among asymptomatic apparently healthy adolescents, we suggest screening for unhealthy alcohol use and providing persons identified with risky drinking with brief behavioral counseling intervention *(conditional recommendation, low certainty evidence)*.**

Considerations

The consensus panel considered the following when formulating this recommendation:

- Unhealthy alcohol use is deemed a priority risk factor to screen.
- The benefits of screening for unhealthy alcohol use outweigh the undesirable effects presented in the evidence.
- The panel recognized that screening tools' diagnostic performance depends on the age group being screened and the instrument being used.
- All agreed that using screening tools is cost-effective, and large savings can be made.
- Moreover, screening for unhealthy alcohol consumption using screening tools presented was perceived to be equitable, acceptable, and feasible.
- The brief behavioral counseling intervention is included in the recommendation because it is usually combined with opportunistic screening in the evidence presented. Screening and brief intervention for unhealthy alcohol use commonly entails two elements (1) screening in a primary care setting and (2) a low-intensity, short duration counseling intervention for 10 to 15 minutes, including advice and feedback on drinking behavior.
- An identified dilemma in screening lies in its results and implications, such as reporting to an authority.

3.7.1 Burden of disease

Disease Frequency

In 2016, 43% of the population worldwide are current drinkers, while more than a quarter (26.5%) of the 15 to 19 years old or 155 million adolescents are current drinkers. (1)

In the Philippines, the prevalence of heavy episodic drinking (those consuming at least 60 grams or more of pure alcohol on at least one occasion in the past 30 days) is more than 8 million or 12.1% of the population (15 years old and above). Heavy episodic drinking is six

times more prevalent among males at 21.7% than females at 3.5%.(2) Among adolescents, 20.8% are current drinkers (consumed alcoholic beverages in the previous 12-month period) — the majority are males.(2)

Around 2.4% of the population had harmful use of alcohol. The prevalence of alcohol use disorders and alcohol dependence in the country are higher at 5.3% and 2.9%, respectively than the reported prevalence in the country's corresponding Western Pacific Region (4.7% and 2.3%). More males are diagnosed with alcohol use disorders (8.8% vs. 1.8% among females) and alcohol dependence (5.2% vs. 0.7% among females). (3)

Severity of Disease

Alcohol caused around 3 million deaths globally in 2016 from 230 different ICD-10 codes. It was responsible for 7.2% of all premature mortality worldwide and 132.6 million disability-adjusted life years (DALYs) of the global disease burden. (4)

The younger population and men are disproportionately affected by alcohol compared to older age groups and women. (2) Alcohol use during pregnancy is also a preventable cause of congenital disabilities and developmental disabilities.(5) Alcohol use is associated with poor pregnancy outcomes, such as the increased risk of miscarriage, premature birth, stillbirth, and sudden infant death syndrome.(6)

There was a 15.1% decrease in the country's age-standardized alcohol-attributable death rates and a 13% decrease in the age-standardized alcohol-attributable DALYs, comparing data from 2010 and 2016. This trend was opposite in the southeast Asian countries.(7)

However, in a report from a 2019 study by the national government, this still means that out of every 100,000 Filipinos with alcohol addiction, 4,431 deaths would occur due to liver cirrhosis in 2020; 2,714 deaths would occur from mouth, colorectal, and breast cancers; 16,418 deaths would occur from hypertensive diseases, and 8,526 deaths would occur from tuberculosis.(8)

Economic impact of the disease

Its impact on an individual level, aside from money spent on alcohol, would mean lower wages (caused by missed work or decreased productivity on the job), loss of employment opportunities, increased medical expenses for illness and accidents, the cost for material damages, and legal cost of drink-related offenses. Indirectly, it also affects society due to premature death, morbidity, and unemployment.(2)

The economic burden of alcohol on society accounts for 0.45% to 5.44% of gross domestic product.(9) In the Philippines, alcohol abuse costs the government Php 200 billion annually. A significant portion is allocated to treat Filipinos with alcohol problems, and the rest is on law enforcement costs and burial costs for alcohol-related deaths.(8)

Social impact of the disease

Social consequences associated with alcohol use may include workplace problems, family problems, poverty, and violence.(1) It leads to absences in work, lower performance, and

decreased productivity which may further cause unemployment. A meta-analysis in 2019 (n=92,730) showed that alcohol consumption is associated with impaired work performance. Although the systematic review presented low quality evidence due to precision issues, it still supports targeting alcohol consumption to improve employees' health and productivity.(10)

Drinking also impairs a person's ability to function as a parent, a spouse or partner, contributor to the household. Children are most affected and are at higher risk of developing injuries, depression, anxiety disorders, problems with cognitive and verbal skills, and parental abuse or neglect. They are also more likely to have alcohol use disorder themselves.(11, 12)

Meta-analyses show a positive relationship between alcohol use and violence, including intimate partner violence for both males and females.(12, 13) In a local study , alcohol plays a role in criminal activities and violence. Murder and physical injury are found to have a significant relationship to alcohol consumption.(14)

People who binge drink are more likely to engage in unprotected sex and multiple sex partners. These, in turn, increases the risk of unintended pregnancy and sexually transmitted infections, including HIV. (2, 15)

3.7.2 Benefits and Harms of Screening Tests

No studies identified the direct effect of screening for unhealthy alcohol on reducing alcohol use or improving health outcomes such as morbidity or mortality.

To evaluate the effectiveness and harm of the screening (indirectly), this evidence summary used different studies on the counseling interventions on alcohol use among the screen-detected population. In an evidence review done in 2018 (68 studies; n=36,528), the most commonly reported alcohol use outcome is the number of drinks per week, and on average, the counseling interventions were associated with a decrease in the number of drinks per week (weighted mean difference -1.59 (95% CI -2.15 to -1.03)(16); 32 trials and 37 analysis groups, n = 15,974, I^2=62.8%) after 6-12 months.

The counseling intervention was also associated with a 40% reduction in the odds of exceeding the recommended drinking limits at 6 to 12 months of follow up: OR 0.60 (95% CI 0.53-0.67); (15 trials; 16 groups; n = 9,760; I^2 = 24%); and a 33% reduction in the odds of reporting episodes of heavy use at 6 to 12 months follow up: OR 0.67 (95% CI 0.58-0.77); (12 trials; 14 groups; n=8,108; I^2 = 24%).

Another systematic review (69 studies, n=33,642) published in 2018 shows that participants drank less alcohol after brief intervention with a mean difference of -20 grams/week less than those in control (95% CI -28 to -12, I^2 = 73%). However, brief interventions do not have as much impact with decreasing the frequency of binge drinking per week (mean difference of -0.08, 95% CI -0.14 to -0.02; n= 6,946); reducing the drinking days per week (mean difference of -0.13, 95% CI -0.23 to -0.04, n= 5,469); nor decreasing

the drinking intensity (mean difference of -0.18 g/drinking day, 95% CI -3.09 to 2.73; n=3,128).

Eight studies (n= 4,533) reported death among adults which showed statistically not significant reduction in all-cause mortality (OR 0.64, 95% CI 0.34-1.19); (I^2=0%). However, this result is underpowered as most of the trials did not report mortality despite not having deaths. Table 19 summarizes the benefits of alcohol screening.

Table 19. Summary of outcomes on the benefits of alcohol management

Outcome	Mean Difference (95% CI)	OR (95% CI)	No. of Participants (Studies)	Quality of Evidence (GRADE)
Number of drinks per week	-1.59* (-2.15 to -1.03)	-	15,974 (32)	Low (adolescents) Moderate (adults)
Quantity of drinks/week in grams	-20 (-28 to -12)	-	15,197 (34)	Moderate
Proportion exceeding the recommended drinking limits	-	0.60 (0.53-0.67)	9,760 (15)	Low (adolescents) Moderate (adults)
Proportion reporting heavy use episodes	-	0.67 (0.58-0.77)	8,108 (12)	Low (adolescents) Moderate (adults)
Frequency of binge drinking per week	-0.08 (-0.14 to -0.02)	-	6,946 (15)	Moderate
Drinking days per week	-0.13 (-0.23 to -0.04)	-	5,469 (11)	Moderate
All-cause mortality	-	0.64 (0.34-1.19)	4,533 (8)	Low (adults)

* weighted mean difference

Some postulated possible harms of undergoing alcohol screening among adolescents and adults include stigma, being labeled and discriminated against, privacy concerns, and disruption of the patient-provider relationship. However, there were no studies identified that directly examined the harms of screening for alcohol use. In the systematic review, there were five studies with very low quality evidence that reported adverse events while in two studies there were none. In contrast, in one study, the intervention group had increased binge drinking for women. In the other two studies, their adverse events were, but their results were like the control group.

3.7.3 Diagnostic Performance of Screening Tests

A systematic review involving 314,466 patients reviewed screening and behavioral counseling interventions to reduce unhealthy alcohol use (which includes the spectrum of risky drinking to alcohol use disorder) in adolescents and adults.(17) Numerous brief screening instruments (one- or two-item questions, Alcohol Use Disorders Identification

Test or AUDIT-C, AUDIT, and Alcohol, Smoking, and Substance Involvement Screening Test or ASSIST) can detect unhealthy alcohol use with acceptable sensitivity and specificity.

Among adolescents (12-18 years old), with insufficient evidence (having just one study available, n=225), the sensitivity of the AUDIT-C and AUDIT to identify unhealthy alcohol use ranges from 0.73 to 0.79 (95% CI ranges 0.60-0.93) and a specificity of 0.79-0.81 (95% CI 0.73-0.86).

Among adults (18 years old and above), with high quality of evidence, brief (1-3 items) screeners have a sensitivity of 0.65-0.92 (95% CI, 0.43-0.98) and specificity of 0.66-1.0 (95% CI, 0.59-1.00) of assessing unhealthy alcohol use among adults. AUDIT and AUDIT-C have almost similar sensitivities and specificities.

A subgroup analysis among the young adults (18-25 years old) showed alcohol screening tools have a sensitivity range of 0.80-0.88 (95% CI ranges 0.71-0.88) and a specificity range of 0.70-0.97 (95% CI ranges 0.64-0.88) for unhealthy alcohol use. On the other hand, among the older adult subgroup (≥65 years old), these screening tools have a sensitivity of 0.64-0.97 (95% CI ranges 0.61-0.99) and a specificity of 0.7-1.0 (95% CI ranges 0.65-1.0).

Table 20. Diagnostic accuracy of screening tools (AUDIT and AUDIT-C) for unhealthy alcohol use

Screening tool	K	n	Sensitivity	95% CI	Specificity	95% CI
Adolescents						
AUDIT-C	1	225	0.73	0.60-0.93	0.81	0.74-0.86
AUDIT	1	225	0.79	0.66-0.87	0.79	0.73-0.85
Adults						
One or two item	8	48,211	0.65-0.90	0.58-0.91*	0.68-1.0	0.64-1.0
AUDIT-C	8	9,447	0.74-0.92^	0.62-0.98*	0.66-0.89^	0.59-0.92
AUDIT	9	9,832	0.68-0.91	0.43-0.96	0.75-0.96	0.63-0.98
Young Adults						
AUDIT-C	1	401	0.80-0.82^	0.71-0.88*	0.82-0.88^	0.74-0.88
AUDIT	2	703	0.82-0.88	0.76-0.79	0.70-0.97	0.64-0.84
Older Adults						
One or two item	2	9,138	0.64-0.97	0.61-0.99*	0.7-1.0	0.65-1.00*
AUDIT-C	1	517	0.94	0.88-0.97	0.8	0.76-0.84
AUDIT	1	517	0.86	0.78-0.91	0.87	0.83-0.90

K = no . of studies; n = no. of participants; ^more than one value reported because data was presented by subgroups (e.g., sex, race)
*Adapted from the USPSTF Systematic Review (19) O'Connor et al., 2018, page 127 and Summary of Evidence Table page 131-134
[1] information around the administration of the screening test and reference standard often not well reported (order of tests, blinding of the interviewer to the results of the index test while administering the reference standard)

3.7.4 Cost Implication

In studies done in high-income countries like the United States, Canada, and Japan, alcohol screening followed by the brief intervention was found to be cost-effective. The same

screening and brief intervention are also cost-effective in middle-income countries such as South Africa.

Table 21. Costing data on screening for unhealthy alcohol use

Parameter	Screening intervention	
	Alcohol Use Disorders Identification Test (AUDIT)	**Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST)**
A. Unit cost of screening intervention	Free [a]	Free[b]
B. Other direct costs associated with the implementation of the proposed screening intervention	Patient cost = an average of 2 minutes per screening (31) of a physician/nurse/social worker Php 29,277[c] = Php 6.10	Patient cost = an average of 10 minutes per screening (27) of a physician/nurse/social worker Php 29,277[c] = Php 30.50 Supplies: Paper = Php 5.00 Pen = Php 5.00
C. Annual screening cost per patient ***Formula: A + B***	Php 6.10	Php 40.50

[a] AUDIT test and manual are free
[b] ASSIST tool and manual is downloadable for free
[c] based on the monthly income of a physician/nurse/social worker with a Salary grade 14

3.7.5 Ethical, Social, and Health Systems Impact (Equity, Acceptability, and Feasibility)

Ethical

There are no issues on equity in terms of doing the screening for alcohol use.

Social

Self-reported alcohol use, such as using AUDIT or ASSIST, has limitations. Respondents may be reluctant to provide an accurate description of their behaviors due to the social stigma and stereotypes associated with drinking alcohol, more so drinking excessively. Bias response is crucial to any survey, as it focuses mainly on the respondents' information.(15) It would be especially true among adolescents and pregnant where alcohol use is highly stigmatized.(18-20)

Moreover, alcoholism is not considered a medical problem among Filipinos such that most Filipinos with alcohol problems do not consult nor get any medical treatment at all.(1)

Alcohol is also widely used in the country. There are no action plans or policies regarding alcohol problems or community-level support from the government for persons with alcohol

problems. There are also no alcohol restrictions set on alcohol outlet density, availability at public events, serving intoxicated persons, and no legally binding alcohol advertising and sponsorship regulation. (21)

Health Systems

In a local study(21), it was noted that the health workers had poor baseline knowledge on effective and safe treatment methods for alcohol problems because they do not provide these services. Implementing the alcohol screening would mean having to train health care workers, including doctors, nurses, social workers, counselors, to deliver the service. Another factor to consider for alcohol screening is the management of these patients since screening would identify more patients with alcohol use disorder. Another huge concern is that alcohol abuse or dependency treatment is generally excluded from the National Health Insurance Program's coverage only, with certain exceptions.(22)

3.7.6 Recommendations from Other Groups

With moderate certainty, the USPSTF recommends that screening for alcohol use disorder and providing persons engaged in risky or hazardous drinking with brief behavioral counseling interventions in primary care settings in adults 18 years or older have a moderate net benefit. On the other hand, there is insufficient evidence to assess the balance of benefits and harms of screening and brief behavioral counseling interventions for alcohol use in adolescents 12-17 years old. (17)

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3.8 Fecal Occult Blood Test and Colonoscopy in Screening for Colorectal Cancer

RECOMMENDATION

Among asymptomatic apparently healthy adults aged at least 50, we recommend to screen for colorectal cancer using annual FOBT or FIT, followed by colonoscopy, when indicated. ***(strong recommendation, high certainty evidence)*****.**

Considerations

The consensus panel considered the following when formulating this recommendation:

- Colorectal cancer (CRC) screening was deemed in the periodic health examination. Screening for colorectal cancer had net benefits and uses accurate tests. However, the high cost of colonoscopy included in the screening pathway was raised as a concern. The consensus panel perceived the certainty of evidence to be high.
- Individuals age 50 years were considered because of the prevalence of colorectal cancer in the age group.
- Panelists recognized that only fecal occult blood test (FOBT) has more direct evidence compared with the fecal immunochemical test (FIT).
- Panel members also have taken into account the challenge in FOBT procedures that need three tests. Utilizing a single test may result in a high false-positive rate because of its interaction with the patient's diet.
- Panelists agreed that FOBT, FIT, and colonoscopy are acceptable and feasible. Inequity issues arise in using colonoscopy. Although it is widely available in the country, practitioners trained to use colonoscopy may be limited, particularly in remote areas. They also considered the cost of performing colonoscopy.
- Aside from its feasibility, FIT was also perceived to be more accurate than FOBT based on the evidence presented.

3.8.1 Burden of disease

Disease Frequency

In the Philippines, colorectal cancer (CRC) is the third leading malignancy for both sexes, with rapid increases in incident cases from 5,787 in 2010, 9,625 in 2015, and 17,634 in 2020.(1) It is now the second most common cancer in Filipino men and the third most common cancer in Filipino women. Age-standardized incidence rates per sex are 23.7 per 100,000 and 15.1 per 100,000 for men and women, respectively.(2)

Severity of Disease

Mortality from CRC is on the rise in the country, with an average annual percentage change of 5.7 (95% 4.7-6.7).(3) In 2020, CRC was the third-leading cause of cancer-related deaths for both Filipino men and women with an age-standardized mortality rate of 10.1 per

100,000.(2) The five-year relative survival rate of CRC patients in Metro Manila was 40.2% using data from 1993 to 2002, which is significantly lower compared to Filipino-Americans (62.3%) and Caucasians (64%) in the United States.(4, 5) Moreover, decreased survival rate may be attributed to late stage in the diagnosis caused by delays in consultation, diagnosis, and intervention.(4, 6)

Natural course of the disease

CRC is hypothesized to develop from adenomas which are benign tumors that may become malignant. It is presumed that the time for a polyp to grow into a malignant tumor is ten years, during which a patient with a differentiating tumor may be asymptomatic.(7, 8) There is a paucity of symptoms in early CRC. The symptoms may manifest over time depending on tumor location, size, and presence of metastasis. They may include occult to overt bleeding, non-specific abdominal pain, alternating constipation and diarrhea, abdominal distention, weight loss, and anorexia.(9) Prognosis is related to stage at initial diagnosis, with the American Joint Committee on Cancer (AJCC) Tumor Node Metastases (TNM) staging as the most commonly used staging algorithm. The five-year overall survival (OS) ranges from 92% in stage I to 11% in stage IV.(10) Patients with stage II and III disease have a wider range of prognosis, particularly in those who receive adjuvant chemotherapy, with a five-year OS between 50% to 90%, with OS affected by age, sex, primary tumor location, tumor grade, number of positive lymph node, lymphovascular and perineural invasion, presence of bowel obstruction or perforation and adjuvant treatment.(11)

Management of the disease

Further management depends on the results of confirmatory tests. When polyps are detected, these can be characterized, removed, and sent to histopathology. The type of polyp, size, and number determine the frequency of colonoscopies to be recommended. On the other hand, tumors can be managed according to size and depth of tumor invasion, either endoscopically or surgically. Finally, a patient may undergo chemotherapy or combination chemoradiation therapy, depending on final staging.

Economic impact of the disease

CRC is costly. In 2015, the Association of Southeast Asian Nations Costs in Oncology (ACTION) reported that 48% of families with a member with newly diagnosed cancer face financial catastrophe within the first year of treatment. In a similar study using the Philippine data set, it was reported that 40.6% of Filipino households struggle financially after a cancer diagnosis.(1) Cost of cancer treatment worldwide in 2009 amounted to approximately Php 10.446 trillion (USD217 billion) with Php 1.877 trillion (USD39 billion) colorectal treatment expenditure. The cost per patient increased with the stage of CRC ranging from Php 160,957.65 (RM13,672) for stage I to Php 329,308.62 (RM 27,972) for stage IV.(12)

Social impact of the disease

Patients with CRC experience poor social involvement that has an impact on the patients and their families. For patients diagnosed with stage IV disease, their scores for emotional functioning were significantly lower. Patients and their caregivers may also experience fear, anxiety, depression, and anger. Patients with low scores on health-related quality-of-life

scales were more often recommended to receive special attention from healthcare providers and their families as supportive care strategies.(13)

The number of patients diagnosed is rising, but survival rates are also improving. These numbers have implications for health services, patients and their families, and society.(14) However, studies show inequalities among socioeconomic groups, with the marginalized sector having a significantly worse prognosis after diagnosis.(15)

3.8.2 Benefits and Harms of Screening Tests

Based on five RCTs (n=404,396) that used intention-to-treat analyses, screening with FOBT (Hemoccult II) resulted in a reduction of CRC-specific mortality compared to no screening, with a pooled relative risk (RR) of 0.82 (95% CI 0.76 to 0.89) for both annual and biennial screening and relative risk of 0.87 (95% CI 0.82 to 0.91) for biennial screening alone. The single study involving annual FOBT showed a marked reduction of CRC-related mortality (RR 0.67; 95% CI 0.56 to 0.80). These studies involved 2 to 9 rounds of screening with a range of 11 to 30 years follow-up. (16-20)

There were no randomized trials involving screening with FIT compared to no screening on the outcome of mortality. One fair quality prospective cohort in Taiwan with 5,417,699 participants aged 50 to 69 years showed that screening biennial FIT was associated with lower CRC mortality than no screening with RR 0.9 (95% CI 0.84 to 0.95) when adjusted for self-selection bias and increasing CRC incidence over time.(21)

There were no harms directly related to testing for fecal occult blood. However, several studies presented complications arising from diagnostic colonoscopies following an abnormal stool test. Based on 11 studies of colonoscopy conducted after abnormal FOBT/FIT (n=78,793), the pooled estimate was 17.5 serious bleeding per 10,000 (95% CI 7.6 to 27.5; I^2=89.3%). The pooled estimate of perforations following abnormal FOBT or FIT was 5.7 per 10,000 procedures (95% CI 2.8 to 9.7; I^2=47.8%).(22)

3.8.3 Diagnostic Performance of Screening Tests

Diagnostic Accuracy of FOBT in detecting CRC

In resource-limited countries, FOBT is the first choice for screening.(23) The guaiac-based test detects the pseudo-peroxidase activity of hemoglobin. Dietary restrictions before the test are recommended to the detriment of decreased compliance and adherence. Moreover, since sensitivity is increased by repeated testing, a complete FOBT is comprised of three separate bowel movement samples, with two samples from each stool.(24) FIT is a newer type of FOBT that uses antibodies to detect the globin portion of human hemoglobin. It avoids the limitations encountered with FOBT with the added benefit of increased sensitivity and specificity. (25-27) Both tests, upon yielding positive results, require further testing, often in the form of direct visualization tests such as colonoscopy or flexible sigmoidoscopy.

Based on five prospective, fair quality studies, two of which used colonoscopy as a reference standard (n=3,503) and three with cancer registry as a reference standard (n=15,969), the sensitivity of guaiac-based FOBT ranged from 0.50 to 0.79 (95% CI 0.01 to 0.99) (28) and specificity ranged from 0.87 to 0.98 (95% CI 0.86 to 0.99) for detecting colorectal carcinoma. (27, 29-31) All five studies involved average-risk individuals with ages ranging from 50 to 80 years. No subgroups by age, sex, race, or ethnicity were reported. (22)

Diagnostic Accuracy of FIT in detecting CRC

The studies on FIT are largely heterogeneous, owing not only to the wide variety of manufacturers, test cutoffs, analysis methods, and test kits available but also to the type of study and settings. Forty-five studies were reviewed in the updated evidence synthesis of the USPSTF. Twenty-eight studies were cross-sectional using one-time FIT with sample sizes ranging from 307 to 21,805. Seventeen studies were conducted under a screening program, and their population ranged from 2,235 to 956,005 individuals. Most studies recruited participants 40 or older and were average-risk, excluding those with the first-degree relative with CRC. The most commonly used FITs were part of the OC-Sensor family (Polymedco in the US or Eiken Chemical outside the US). The studies on the OC Sensor family were pooled and presented. In 26 studies, FIT was followed by a colonoscopy for all participants regardless of the FIT results. Nineteen studies used a combination of cancer registries for all participants and direct visualization for participants with abnormal FIT results. Nine studies were rated as good quality, with the rest of the studies at higher risk of bias in terms of differential verification, unclear or absence of blinding of the FIT results for those performing the colonoscopy, unclear methods of patient selection, and patient attrition (unreadable screening tests).

Nine studies (n=34,352) of the OC-Sensor FIT family with a colonoscopy as the reference standard for all participants and using the manufacturer-recommended cut-off of 20ug Hb/g feces showed a pooled sensitivity of 74% (95% CI 64% to 83%; I^2=31.6%) and specificity of 94% (95% CI 93% to 96%; I^2=96.6%) in detecting CRC. (10, 21, 24, 26, 28, 31-35). Seven studies (n=2,468,638) using OC-Sensor tests at a cutoff of 20ug Hb/g feces to detect CRC with cancer registry follow-up to identify CRC yielded a pooled sensitivity of 81% (95% CI 74% to 88%, I^2=98.6%) and a specificity of 95% (95% CI 94 to 96%, I^2=98.5%).(36-42) Nine other FIT brands were assessed in 11 studies with colonoscopy as the reference standard.(25, 26, 29, 31-33, 43-48) Pooling results for OC Light among these from three studies showed that this test has a sensitivity of 81% (95% CI 70% to 91%; I^2=0) and a specificity of 0.93 (95% CI 0.91-0.96; I^2=99%). (33, 37, 44) The sensitivity range for other FITs was 50% to 97% (95% CI ranges, 90 to 100%) with specificity ranging from 83% to 97% (95% CI ranges, 82% to 97%). There were no clear patterns identified for differential accuracies by tumor location or stage, age, sex, race, ethnicity, or family history.

3.8.4 Cost Implication

Cost-effectiveness studies(49-56) from different countries showed that screening strategies for colorectal cancer (i.e., annual FOBT, FOBT followed by colonoscopy, FOBT and HRFQ, annual FIT, colonoscopy, annual FIT, and colonoscopy) were cost-effective compared with

no screening. Table 22 shows an estimated annual screening cost per patient in Php using FOBT or FIT.

Table 22. Estimated annual cost of screening for CRC using FOBT/FIT

Parameter	Screening intervention		
	FOBT yearly	**FIT yearly**	**Colonoscopy every 10 years**
(A) Unit cost of screening intervention in Philippine Peso (Php)	Php 570 (3 samples at 190/sample)	Php 405	Php 8817
(B) Other direct costs associated with the implementation of the proposed screening intervention in Philippine Peso	Php 30 (3 stool containers at 10/piece	Php 10	Php 6720 (PhilHealth professional fee)
(C) Annual screening cost per patient in Philippine Peso	Php 600	Php 415	Php 15,537

Values based on the 2018 cost-utility study conducted in the Philippines. (291)

3.8.5 Ethical, Social, and Health Systems Impact (Equity, Acceptability, and Feasibility)

Ethical

A study in colorectal cancer screening shows inequities in access to cancer care and screening in general. Factors such as income, education, level, age, location of residence, and immigration status affect screening intervention. Low income has been associated with poorer survival rates for several cancers, including CRC.(57) Access to healthcare has a substantial impact on screening behavior. Patients who have health insurance and regular access to care were more likely to have received CRC screening.(58) Differential availability of screening resources has also limited the uptake of screening programs. The success of a nationwide screening program relies on the availability of facilities for both the initial screening test and the subsequent tests and treatment.

Social

Many factors influence participation in CRC screening, and these range from personal health beliefs, familial contributions to decision making, educational attainment, low household income, and cultural and social stigma.(39, 59-61) Since an FOBT or FIT is non-invasive, patients may be more amenable to comply with this procedure. However, access to the secondary visualization tests must be made available for patients who tested positive. Geographic factors and the maldistribution of specialist care may hinder the adoption of these initial screening tools for CRC. These socio-cultural and geographic factors must be considered in implementing a national CRC program.

Health Systems

To improve CRC screening implementation and rates, improving access to health care through systematic interventions must be done. Strategies may include increasing health insurance coverage and ensuring patients' consistent follow-up with their primary care providers.(58) Facilities should be constructed to provide access and availability of the screening test, proper referral system for the confirmatory testing and procedures, and continuing management for detected cancers. Evidence-based interventions such as patient education regarding the screening and distribution of free FOBT kits can significantly increase screening rates. However, it can only be achieved if intervention is widely implemented.(62) Health care providers play a crucial role in the acceptability of the screening intervention. Increasing awareness of the benefits of screening and reducing the perceived barriers would increase screening uptake.(39)

3.8.6 Recommendations from Other Groups

Multiple organizations worldwide agree on the importance and benefit of CRC screening. Guidelines, however, differ in terms of recommended screening strategies and optimal age to initiate and terminate screening. In 2017, the Philippine Society of Gastroenterology and the Philippine Society of Digestive Endoscopy consensus guidelines recommended screening for CRC in average-risk individuals using a fecal occult blood test (FOBT), preferably fecal immunochemical test (FIT), flexible sigmoidoscopy (FS), and colonoscopy. It begins at the age of 50 up to 75; older patients are individualized by predicted life expectancy and risk factors. They also recommended the performance of colonoscopy for patients with abnormal findings on screening.(63)

In the US, multiple organizations, including the American Cancer Society (ACS), USPSTF, US Multi-Society Task Force of Colorectal Cancer, and the American College of Gastroenterology, agree that the recommended options for screening for CRC include colonoscopy every ten years, annual high-sensitivity guaiac FOBT or FIT, and FS every 5 to 10 years. Notable differences in international guidelines include: 1) an earlier onset of screening at 45 years as a conditional recommendation by the ACS, 2) modalities for screening, and 3) age to stop screening, spans from 75 to 85 years of age. (22, 64)

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3.9 Pap Smear or Visual Inspection with Acetic Acid in Screening for Cervical Cancer

RECOMMENDATIONS

1. **Among asymptomatic women aged 21 to 65, we recommend screening for cervical cancer every three years using a Pap smear *(strong recommendation, moderate certainty evidence)*.**

2. **Among asymptomatic women aged 21 to 65, we recommend screening for cervical cancer every three years using visual inspection with acetic acid as an alternative to Pap smear *(strong recommendation, moderate certainty evidence)*.**

Considerations

The consensus panel considered the following when formulating this recommendation:

- Cervical cancer is a priority disease in the periodic health examination.
- All agreed that the net effect favors screening.
- The majority agreed that the screening tools for cervical cancer are accurate (good diagnostic performance).
- Despite relatively expensive confirmatory tests, experts in the panel perceived that screening for cervical cancer is cost-effective.
- The panel members also believed that screening for cervical CA would need an infrastructure to implement confirmatory tests and treatment. An issue of inequity was raised because of limited coverage and is sometimes not an option for women because of the out-of-pocket expenses incurred. .
- Most of the panel members believed that screening using Pap smear or VIA has moderate certainty evidence.
- The question on considering the history of sexual activities in the recommendation was also discussed. The evidence presented that age suffices as it was also considered in other guidelines. Epidemiologically, cervical cancer rarely occurs before 21 years old regardless of sexual history.
- Panelists also agreed not to place a specific recommendation on using these screening tools followed by colposcopy. Not all abnormalities found in Pap smears or VIA will lead to testing using colposcopy.

3.9.1 Burden of disease

Disease Frequency

In 2019, the Philippines had 141,021 new cancer cases and 86,337 cancer deaths. In 2018, cervical cancer incidence and mortality rates were 5.1% and 4.7%, respectively.(1) Cervical

cancer is included in the top 10 leading sites of new cancer cases and deaths. The estimated age-standardized national incidence rate was 16 per 100,000 in 2012. Two (1.6) out of 100 women would have had a likelihood of getting cervical cancer before the age of 75.(2) Estimates would show that cervical cancer incidence is the least in the 15-19 and 20-24 age groups, with 5 and 27 cases only in 2018. Furthermore, the age-specific rates of cervical cancer rise beginning at age 25 years old and peak in the 55-59 age group.(3) This trend observed with age was also seen in the US; only 1% of cervical cancer cases were detected among women younger than 20.(4) Notably, the Philippines has a lower incidence/mortality ratio than high-income countries/regions.(5)

Severity of Disease

Local studies(5, 6) were consistent with systematic reviews(7) that showed the significant impact of cervical cancer on patients' physical symptoms, psychological health, and sexual function.

Natural course of the disease

The natural course of cervical cancer has been described as each woman undergoes monthly transitions between health states representing the true underlying health. The factors considered are HPV infection status, precancer histological grade (i.e., CIN2 or CIN3), and stage of invasive cancer (i.e., local, regional, or distant). The precancer locations (CIN2 and CIN3) are observed as non-sequential health states with distinct cervical cancer progression probabilities.(8) Inadequate management of CIN3 in women leads to a crude incidence of cervical cancer of 823 per 100,000 woman years (95% CI 630, 1074) — ten times the crude cancer incidence — among those with adequate or probable adequate treatment. Inadequately treated CIN3 would result in 8.5%, 12.6%, 18.4%, and 20.7% of women with cervical cancer after 5, 10, 20, and 30 years, respectively.(9) There is some form of regression from a precancer status to a lower histological grade or a normal cervix at younger ages. In one study(10), of 95 women aged 13 to 24 years with CIN2 on histology, 38% cleared by the first year of follow-up, 63% by the second year, and 68% by the third year. The age of first intercourse is one of the significant predictors of the risk of CIN2 regression (aHR=1.25, 95% CI 1.06, 1.48).

Management of early disease

Based on the guidelines of the Society of Gynecologic Oncologists of the Philippines 2008 (as cited in a local study)(11), the standard of treatment for cervical cancer is complete radiotherapy concurrent with chemotherapy (concurrent chemoradiation). However, for patients who are unable to receive chemotherapy, radiation alone is acceptable. Various surgical options are suggested for each stage of disease, such as extrafascial hysterectomy (for stage IA1), radical hysterectomy (for stage IA2-IIA) with or without bilateral salpingo-oophorectomy with pelvic lymphadenectomy, radical vaginal hysterectomy (stage IB1-IIA with low risk for parametrial or nodal metastasis, no evidence of metastasis, and with pelvic organ prolapse). Subsequently, patients may undergo adjuvant chemoradiation in the presence of surgical and pathologic prognostic factors. The presence of a tumor in the vaginal cuff or less than 2 cm tumor-free margin requires additional brachytherapy. In biopsy-proven metastasis, systemic chemotherapy and individualized radiotherapy are recommended.

Economic impact of the disease

Treatment access and affordability likely pose barriers to a considerable number of patients. Cancer care services, including treatment facilities, are mainly provided by private institutions, with government hospitals and clinics accounting for only a fraction of the total number of hospitals in the NCR. Although public institutions offer subsidized services, diagnostic procedures and treatment regimens are still costly for an average Filipino.(12) (Comparing baseline and twelve months after a cancer diagnosis, Filipino cancer patients experienced a decrease in income, a change in employment type, and a reduction in paid work. Furthermore, 40.6% experienced financial catastrophe at the end of this period.(13)

Social impact of the disease

Cervical cancer is often associated with sexually transmitted infections. Given the sexual nature of cervical cancer and the cultural stigma, parents and other family members may not have engaged in these discussions at a time when many positive health behaviors emerge during the stage of adolescence, a critical developmental period concerning health and illness.(13)

3.9.2 Benefits and Harms of Screening Tests

Direct evidence on VIA and cervical cytology testing's impact came from a cluster randomized trial in India(14), which randomized women aged 30-59 years by clusters to the VIA group, cytology testing, and control groups. Those in the control group received routine care and advice on seeking screening at local hospitals. In contrast, those in the intervention groups received a card containing a single-round screening schedule and place. Colposcopy was done for women with a positive screening test. Women with colposcopic findings of low-grade or high-grade lesions received treatment options, including immediate cryotherapy, loop electrosurgical excision procedure (LEEP), or conization. Women with suspected invasive cancer were referred to a hospital for surgery, radiotherapy, or both. After eight years of follow-up, this study found that cervical cancer screening with cytology testing had a significant benefit in reducing the incidence of stage 2+ cervical cancer (Table 23).

Table 23.Effect of VIA and cytology testing on cervical cancer incidence and death (314)

Outcome	Cytology Testing*	VIA*
Cervical cancer incidence	RR 1.27 (95% CI 1.00, 1.61)	RR 1.23 (95% CI 0.97, 1.56)
Stage 2+ cervical cancer incidence	RR 0.69 (95% CI 0.50, 0.97)**	RR 0.97 (95% CI 0.71, 1.31)
Death	RR 0.83 (95% CI 0.58, 1.19)	RR = 0.81 (95% CI 0.57,1.16)

**Compared to no screening. **Significant difference*

A decision analysis conducted for the 2018 cervical cancer screening guidelines of the USPSTF (315) further emphasized the benefits of cytology testing compared to no screening. Cytology testing started at age 21 and performed every three years resulted in a decrease in cervical cancer cases and deaths (Table 24).

Table 24. Outcomes of cytology testing (starting at age 21 and every three years) versus no screening for cervical cancer (15)

Outcomes (per 1,000 women)	No screening	Cytology-based screening
False positives	0	484
Cervical cancer cases	18.86	2.34
Cervical cancer deaths	8.34	0.76

3.9.3 Diagnostic Performance of Screening Tests

A high-quality systematic review(16) was found for the diagnostic accuracy of visual inspection with acetic acid (VIA) and cervical cytology (Pap smear), compared to colposcopy with or without biopsy. Eleven (11) studies were included for these comparisons, with a total of 12,089 participants. The pooled sensitivity and specificity values for VIA and Pap smear appear similar (Table 25).

Table 25. Diagnostic accuracy of VIA and Pap smear, compared with colposcopy with or without biopsy (316)

	Visual inspection with acetic acid (VIA)	Cervical cytology (Pap smear)
Sensitivity	0.77 (95% CI 0.66, 0.85)	0.84 (95% CI 0.76, 0.90)
Specificity	0.82 (95% CI 0.67, 0.91)	0.88 (95% CI 0.79, 0.93)

3.9.4 Cost Implication

Two local economic evaluations of cervical cancer screening concluded that VIA is more advantageous than Pap smear in terms of cost. In a nationwide randomized controlled trial(17) of four alternative cervical cancer screening methods, visual inspection with acetic acid (VIA) was a cost-effective and cost-beneficial screening method in the Philippine setting. They reported a cost of PhP 476 per woman screened and a net benefit of Php 810 million to Php 3.13 billion.

A cost-utility analysis with semi-Markov modeling using country-specific epidemiologic, cost, and clinical parameters(18) revealed that VIA was the most cost-saving screening strategy among the different coverage situations. Pap smear was not cost-effective due to its high cost. Its incremental cost-effectiveness ratio was Php 61,059 per quality-adjusted life-year. The most efficient screening option will be performing VIA at 35 to 45 years old done every five years. The cost increases as the age range of women targeted for screening is widened, and the frequency of testing is increased from three to six times per lifetime. Comparing VIA and Pap smear screening every five years, from 35 to 55 years old, the budget impact is PhP 94 million and PhP 182 million, respectively.

Aside from the screening tests' cost impact, it is also essential to consider the costs of confirmatory colposcopy, biopsy, and various treatments. Table 26 shows the costing parameters used in the cost-utility analysis above.(18) Take note that the charges were mainly based on the PhilHealth packages and will likely be different in other healthcare settings (i.e., private hospitals, etc.).

Table 26. Costs of confirmatory test and treatments associated with cervical cancer (18)

Procedure	Cost (Php)
Colposcopy/ Biopsy	1,120
Cryotherapy	1,500
Loop Electrosurgical Extraction Procedure	12,644.54
Cold Knife Conisation	8,100.36
Simple Hysterectomy	41,362.67

3.9.5 Ethical, Social, and Health Systems Impact (Equity, Acceptability, and Feasibility)

Ethical

Access to health facilities and healthcare workers will likely be unequally distributed, considering the archipelagic geography of the country and the concentration of these facilities and workers in major cities.(2) Additionally, socioeconomic status (SES) generates variations in cervical cancer screening, irrespective of the country's level of development. Disparities caused by different ethnicity, education, urbanization, and income are still present worldwide. The impact of education and geographical area on screening uptake has been proven significant. Occupation is a standard indicator for SES and was considered a predictor for screening uptake since unemployed women were less likely to receive a Pap test.(19)

Social

One local study(20) found that VIA and Pap smear seem to be acceptable screening methods for cervical cancer, with mean acceptability scores ranging from 1.82 to 1.95 (scale: 1 – very comfortable, 5 – much discomfort). Lack of awareness on cervical cancer, problems in patient compliance on follow-up and treatment, and social stigma on reproductive health problems are some issues that potentially have an impact on the acceptability of cervical cancer screening in the country.(6, 11, 21-24)

Health Systems

The government cancer screening infrastructure is patchy at best, with intermittent supplies, training service provision.(17) Simultaneously, there are no sanctions or incentives for the private healthcare delivery sector related to cancer screening. Cervical cancer screening was opportunistic, using visual inspection.(25) Infrastructure, technical expertise, and regular tracking of women who test positive improve screening units, provide advanced training to nurses and physician screening personnel, create strategies for the compliance of target women, and cover health insurance for preventive services.(20)

The National Integrated Cancer Control Act (RA 11215) and its Implementing Rules and Regulations (DOH MC No. 2019-0036) include cancer screening as one of the many responsibilities of key stakeholders such as the National Cancer Control Council, DOH Cancer Control Division, PhilHealth, local government units and other concerned government agencies (i.e., DOLE, CSC, CHED, etc.). This law also designates May as the annual cancer awareness campaign for cervical cancer. Furthermore, Expanded Primary Care Benefit is one of the outpatient benefits available for PhilHealth members belonging to the following

groups: employed members, lifetime members, and senior citizens. Pap smear (as applicable) is included in the essential services for the following age groups: 10 to 19, 20 to 60, above 60 years.(26)

3.9.6 Recommendations from Other Groups

Two international USPSTF(27) and American Cancer Society(28) and two local (Philippine Society for Cervical Pathology and Colposcopy(29) and Philippine Cancer Society(30) guidelines recommend cervical cytology screening every three years with a stop age of 65 years. The 2020 ACS guideline recommended a start age of 25 years, while the 2018 USPSTF and PSCPC were similar in recommending to start cervical cancer screening at age 21. However, the PCS recommended starting screening at age 21 or within two years of onset of sexual activity. It is also of note that the primary recommendation of international guidelines (2018 USPSTF and 2020 ACS) for cervical cancer screening would be with the use of HPV testing every five years.

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3.10 Chest X-ray in Screening for Lung Cancer

RECOMMENDATION

Among asymptomatic apparently healthy adults, we suggest against screening for lung cancer using a chest X-ray *(conditional recommendation, low certainty evidence)*.

Considerations

The consensus panel considered the following when formulating this recommendation.

- Although lung cancer is a priority in screening apparently healthy adults, the majority agreed that the net effect of using chest X-ray for screening was not convincing.
- Screening entails considerable cost for the confirmatory tests or the post-screening work-up. Furthermore, screening using chest X-ray is not cost-effective among the general or asymptomatic population.
- The cost of these procedures, including the post-screening, is too expensive for marginalized sectors. Availability of chest X-ray in different parts of the country was also raised as a concern.

3.10.1 Burden of disease

Disease Frequency

According to the WHO 2020 data, lung cancer accounted for 12.5% of the 153,751 newly diagnosed cancer cases in the Philippines. The risk percentage of developing cancer before the age of 75 was 16.5%. Among males, lung cancer was the most common cancer and accounted for one-third of all cases.(1)

An increasing trend of lung cancer incidence was observed from 2000 to 2008 based on the Lung Center of the Philippines Registry Data. Older age consistently posed a higher risk of the disease, with most cases being diagnosed starting from the age of 40. About 50% of lung cancer cases in the registry data were reported to occur during the sixth decade of life.(2)

Severity of Disease

Lung cancer was attributable to 18.4% of the total number of cancer-related deaths in the Philippines or 17,063 individuals.(1) Emotional, spiritual, financial, physical preparation, and acceptance concerning lung cancer diagnosis can also be very stressful for the patient, significantly affecting one's overall quality of life (QoL).(2, 3)

Natural course of the disease

Lung cancer generally has a poor prognosis that largely depends on the disease stage and the given treatment strategies. Over 50% of people diagnosed with lung cancer die within one year of diagnosis, and only about 18% survive, on average, after five years.(4, 5) With the current TNM staging system for non-small cell lung cancer (NSCLC), five-year survival

rates are estimated to range from 73% for early-stage (Stage IA) disease to as low as 13% in advanced (stage IV) cases. The five-year survival rates have slightly improved with chemo- and radiotherapy but remain low at < 25%.(6) Newer advancements in genetics and biomarkers testing, immunotherapy, and other targeted therapies toward the mechanisms of tumor development, growth, and metastasis also show promise in improving survival.(4) Overall mortality from lung cancer has been steadily declining in the last 15 years, especially for NSCLC and men, most likely due to the reduction of lung cancer incidence and the development of these newer treatments. (7)

Management of the disease

No local clinical practice guidelines have been developed yet on the diagnosis and management of lung cancer.

In the Pan-Asian adaptation of the European Society for Medical Oncology (ESMO) CPGs, systemic therapy that promotes smoking cessation and considers patient's preferences, age, comorbidities, and histological findings or molecular pathology is recommended to all patients with advanced metastatic NSCLC.(8) Contrast-enhanced CT scans of the chest, upper abdomen, and brain are recommended for patients with locally advanced unresectable tumors before initiating concurrent chemoradiotherapy.(9)

For localized small-cell lung cancer (SCLC) (T1-4, N0-3, M0), combined concurrent chemoradiotherapy, surgery followed by four cycles of adjuvant chemo/radiotherapy, or prophylactic cranial irradiation (PCI) are considered depending on the patient's characteristics. On the other hand, palliative chemotherapy is recommended for metastatic (stage IV) SCLC**.** (10)

Economic impact of the disease

The burden of disease caused by lung cancer in 2015 in the Philippines was 38,594 DALYs, as per a discount rate of 3%, with an increasing trend seen among individuals aged 45-79 years old. The DALY rate in the country was estimated to be 0.4 DALYs per 1,000 person-years. When calculated without the discount rate, the calculated burden of disease substantially increased to 50,977 DALYs. Individuals aged 70-79 years had the highest calculated burden of disease at 4.7 DALYs per 1,000-years.

Based on the 2018 Philippine Costs in Oncology (PESO) study, the mean combined Month 3 and Month 12 out-of-pocket health expenditures of Filipino cancer patients were Php 181,789.00 with indirect costs, such as transportation fees, meals, and outside caregiver salaries, having the highest share of Month 12 expenditures at Php 70,510.20 followed by medication expenses at Php 51,138.42. Hospitalization costs ranged from no fees to Php 9,885.57.(11) Treatment for lung cancer is associated with a catastrophic financial burden. Chemotherapy alone costs within the range of Php 50,000 to Php 120,000 per month. Medicines were estimated to cost monthly as much as Php 100,000 or more.(12)

Social impact of the disease

Compared to the other types of cancer, lung cancer is associated with the most intense and distressing symptoms considered to be detrimental to a patient's QoL. As the QoL decreases

due to poorly managed symptoms, patient care complexity arises, affecting the patient's family or caregiver. Several studies found that family caregivers feel unsupported by health care professionals and frequently risk their physical, mental, and social well-being in the process. (13)

3.10.2 Benefits and Harms of Screening Tests

Data on the benefits and harms of CXR screening for lung cancer was found from three systematic reviews of moderate-to-high quality.(14-17) No new additional studies were found after an updated search on March 11, 2021.

Lung cancer mortality

Five RCTs [Kaiser Foundation(18-20), PLCO(21, 22) North London(23, 24), Czech(25), Mayo Lung Project (14, 26, 27)] and a controlled trial [Erfurt County Study (28)] provided the effect of CXR screening on lung cancer-related deaths.

Two RCTs (PLCO, Kaiser Study) demonstrated no significant difference in lung cancer mortality between participants who received annual CXR screening versus those with no formalized screening (RR 0.99, 95% CI 0.92 to 1.07; I^2=0%). Analysis of 13-year follow-up data in the PLCO trial showed no significant reduction in lung cancer mortality with CXR screening (RR 0.99, 95% CI 0.87 to 1.22).

Similarly, two studies (Erfurt County Study, North London Study) showed no significant advantage of frequent CXR screening (every six months) compared to CXR done only every one to two years in terms of lung cancer mortality (RR 0.85, 95% CI 0.63 to 1.14; I^2=67%). Adding sputum cytology with frequent CXR screening (every four to six months) was also not seen to reduce lung cancer deaths (RR 1.12, 95% CI 1.00-1.26; I^2=0%).

All-cause mortality

Five studies (Mayo Lung Project, Czech, Kaiser, PLCO, Erfurt County Study) reported all-cause mortality data. No significant results were noted in the studies (PLCO, Kaiser Study) that compared annual CXR screening versus no screening(18-22) (RR 0.98, 95% CI 0.96 to 1.00; I^2=0%), more frequent versus less frequent CXR screening(28) (RR 0.96 (95% CI 0.93 to 1.00), and more frequent versus less frequent CXR with SC (25, 27)(RR 1.08, 95% CI 0.96 to 1.22; I^2=47%).

Lung cancer stage at diagnosis

Four studies (PLCO, Czech Study, Mayo Lung Project, Erfurt County Study) reported data on lung cancer stage at diagnosis.

Early Stage (I & II NSCLC)

Based on a RCT (PLCO) with good quality, a higher proportion of early stages (I & II) NSCLCs were detected in the group that received annual CXR screening compared to the group without formalized screening (39.7% vs. 34.9%) with RR 1.14 (95% CI 1.03 to 1.25). More frequent CXR screening also identified more early stage NSCLCs (77.8% vs. 63.2%) with RR

1.23 (95% CI 1.04 to 1.46). The same benefit was noted with frequent CXR plus SC screening (49.0% vs. 36.0%), showing a pooled RR of 1.34 (95% CI 1.03 to 1.73; I^2=38%).

Late Stage (III & IV NSCLC)
In the PLCO study, a significantly lower proportion of late-stage lung cancers were detected among participants who received annual CXR screening versus no screening (RR 0.93, 95% CI 0.87 to 0.98). Less frequent CXR screening showed a relative increase of 40% (RR 0.60, 95% CI 0.39-0.92) to detect late-stage cancer. A similar effect favoring less frequent CXR plus SC screening was observed in two RCTs (RR 0.79, 95% CI 0.69 to 0.91; I^2=0%).

Invasive follow-up procedures may include fine-needle aspiration biopsy, fine-needle aspiration cytology, video-assisted thoracoscopic surgery, thoracotomy, bronchoscopy, mediastinoscopy, or surgical resection. Harms of using chest x-ray for screening may result from these follow-up procedures.

Deaths
Data from five RCTs --- Memorial-Sloan Study(29), Erfurt County Study, Mayo Lung Project, Czech Study, National lung screening trial or NLST research team --- and one prospective cohort study (PREDICA Cohort) (30) showed that a total of 44 patients died out of 1,111 who underwent invasive follow-up procedures following CXR screening with or without sputum cytology. This translates to about 40 deaths per 1,000 patients (95% CI 2.0 to 6.0) undergoing invasive follow-up testing.

Complications
One large RCT (NLST) comparing CXR with LDCT screening reported that of the 279 patients who were CXR-positive, 65 (23.3%) had at least one complication—24 (8.6%) with major, 35 (12.5%) intermediate, and 6 (2.2%) minor complications.(359) In the PLCO trial, complications were present in 54 of 12,718 (0.4%) CXR-positive subjects following an invasive diagnostic procedure. The degree and type of complications were not specified, but authors mentioned pneumothorax (29%) and atelectasis (15%) as the most common ones.(22)

Infections
A RCT (Lung Screening Study) that involved 1,658 participants in the CXR arm and 1,660 in the low-dose CT scan provided data on infection resulting from invasive follow-up procedures.(31) Thirty-five out of 621 (5.6%) patients in the CXR arm who underwent invasive follow-up procedures developed an infection. In the PLCO trial, infections were observed in 7 out of 12,718 (0.001%) CXR screen-positive subjects. (22)

Quality of life
In a sub-study of the PLCO trial that involved administering the 12-item short-form questionnaire (SF-12) to 149 participants in the CXR screening and 179 usual care group, no difference was found after screening in the domain of physical health (MD -0.28, 95% CI -1.48 to 0.93). However, a significant difference was noted in mental health composite scores (MD 1.19, 95% CI 0.20 to 2.17), with better scores recorded for those in the no-screening

group.(32) Another RCT involving 1,424 subjects showed a significant change toward poorer quality of life after detecting a lung nodule from CXR screening (0.940 vs. 0.877, p=0.022), as measured using the Euro QoL 5-Dimension Index (EQ-5D).(33)

Anxiety
No study was found assessing the relationship between CXR screening and anxiety levels.

Overdiagnosis (detection of lung cancers that will not otherwise cause symptoms throughout the person's lifetime or result in death)

Data from the two low-certainty RCTs on CXR+SC screening (Mayo Lung Project, Memorial Sloan-Kettering Study) estimated an overdiagnosis rate between 2.3%-16.3%. Using a shorter cut-off for tumor volume doubling time (300 vs. 400 days) tended to result in higher estimates. (34)

Invasive procedures following a false positive result
Based on four observational studies that screened a total of 81,819 individuals, 139 (0.17%) underwent major invasive diagnostic procedures (e.g., thoracotomy, video-assisted thoracoscopic surgery, surgical resection, etc.). In contrast, 192 (0.23%) had minor follow-up procedures (e.g., fine-needle aspiration biopsy/cytology, bronchoscopy, thoracic or lymph node biopsy). It translated to an absolute number of 2.73 per 1,000 subjects (95% CI 0.96 to 4.51) with benign conditions undergoing major invasive procedures and 2.30 per 1,000 subjects (95% CI 1.49-3.11) for minor invasive procedures.

Subgroup analysis for harm and benefit

Benefit
The PLCO trial found no significant differences in lung cancer mortality when participants stratified according to smoking status such as never smokers (RR 0.94, 95% CI 0.69 to 1.29), former smokers (RR 1.02, 95% CI 0.91 to 1.15), current smokers (RR 0.99, 95% CI 0.88 to 1.12). No significant differences were also found when stratified according to gender —men with RR 1.02, 95% CI 0.92 to 1.13, and women with RR 0.92, 95% CI 0.81 to 1.06. Subgroup analysis according to age is not possible in the PLCO trial as they only enrolled older participants (55-74 years old).

Harm
None of the included harm studies conducted or reported results for overdiagnosis, mortality, or significant complications in subgroup analyses based on age, gender, and/or smoking history. Consequently, there is no evidence on which to base a response to this question.

3.10.3 Diagnostic Performance of Screening Tests

Pooled estimates could not be derived due to a low number of studies and heterogeneity across studies.

Moderate-quality evidence from two extensive observational studies from Japan reported the results of mass chest X-ray screening done to 236,392 individuals aged 40 years or older from the general population.(35) One study that used miniature CXR as index test (35) estimated the sensitivity of CXR at 57% (95% CI 45 to 68%), while another study using indirect radiography obtained a sensitivity estimate of 70% (95% CI 63 to 77%). Both studies involved histology and other diagnostic methods (e.g., CT, bronchoscopy, exploratory thoracotomy) as the gold standard for lung cancer diagnosis. However, these methods were only done for patients with a high index of suspicion for lung cancer on CXR.

3.10.4 Cost Implication

Three(22, 36, 37) out of five studies found that lung cancer screening using CXR was not statistically different compared with no screening in decreasing mortality related to lung cancer among asymptomatic adults with or without risk factors. These studies also showed possible burdens from the increased workload of radiologists and harm from overdiagnosis.(22, 37) The other groups of researchers believed that an annual chest x-ray, however, is more cost-effective among adults who are heavy smokers (i.e., more than ten pack-years) than no screening at all.(30, 38) Table 27 shows an estimated annual screening cost per patient with different factors taken into account.

Table 27. Costing data on chest x-ray as a screening tool

Parameter	**Screening intervention**
	Chest X-ray
A. Unit cost of screening intervention	**Php 350.00 (39)**
B. Other direct costs associated with the implementation of the proposed screening intervention	Initial and follow-up outpatient consultations with primary care physicians or specialists **(Php 150.00 = 2 x Php 75.00) (40)** According to the Clinical Treatment Guidelines of the Philippine Cancer Society, it is recommended for lung cancer suspects to undergo a CT scan of the chest, abdomen, and adrenal glands as it is considered to be the most valuable and highly sensitive among all modalities and confirmatory tests in determining the characteristics of lung cancer. (41) 1. **CT scan of chest (Php 5,500.00 = 1 x Php 5,500.00)** (39) 2. **CT scan of abdomen (Php 8,100.00 = 1 x Php 8,100.00)**(39) 3. **CT scan of adrenal glands (Php 8,450.00 = 1 x Php 8,450.00)** (39)

C. Annual screening cost per patient	**Php 22,550.00**

3.10.5 Ethical, Social, and Health Systems Impact (Equity, Acceptability, and Feasibility)

Ethical

A patient's socioeconomic status could heavily influence most healthcare providers in deciding whether to conduct lung cancer screening. Providers recognized the heavier burden on rural and minority patients' well-being due to their financial incapacities to access post-screening interventions such as surgeries and cancer treatments, which could be prohibitive and unethical for them. Additionally, they recognized the substantial costs incurred by these patients, such as travel fees and lost income from taking occupational day-offs. Despite the availability of health maintenance organizations, many are still classified as self-paying, either uninsured or uninsurable. When the country is unable to implement free screenings with complimentary transport, mobile or one-stop health centers, or full health insurance coverage, these circumstances promote racial, ethnic, and socioeconomic disparities in sustaining the clinical standards of cancer care. (4)

Radiologists committing errors when interpreting radiographic examinations has become precariously common, according to literature. Plain film chest X-ray screening, which is the most common radiological modality used in diagnosis, reportedly has an average error rate of 30%. False positives and overdiagnosis could present not only complications but also ethical and medicolegal issues to the patient. If the radiologist does not adequately disclose the said potential harms since a positive result, regardless if falsely interpreted, it would necessitate greater financial costs and health hazards to the patient due to increased radiation exposure from additional confirmatory tests. (42)

Social

One study describing Filipinos' online search behaviors related to lung cancer revealed that Filipinos had a steady interest in learning about its etiology, symptoms, and management in the last decade.(43) However, a formal qualitative study on the social, behavioral, and cultural determinants of participation in a lung cancer screening program in the Philippines still needs to be done to identify the most efficient strategies to promote and improve lung cancer screening participation, especially among high-risk groups. A cross-sectional US study concluded that the determinants of cancer perceived risk and worries vary depending on cancer risk. The effect of higher income, age, and insurance status was mainly observed among low-risk groups but not in the high-risk groups (e.g., ever smokers, minorities).(44)

Health Systems

A cost-effectiveness analysis including assessment of the availability of such equipment and health care staff who would interpret CXR results of this strategy is necessary to inform PhilHealth and other key stakeholders.

3.10.6 Recommendations from Other Groups

The Canadian Task Force on Preventive Health Care (2016), and USPSTF (2013; 2020) recommend against using chest x-ray as a screening test for lung cancer.(16, 45) On the other hand, the National Institute for Health and Care Excellence (NICE) recommends offering an urgent chest x-ray to assess lung cancer in people over 40 years old with a smoking history and presenting with two or more symptoms.(46)

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3.11 Chest Radiography in Screening for Pulmonary Tuberculosis

RECOMMENDATION

Among asymptomatic apparently healthy adults, we suggest screening for pulmonary tuberculosis using a chest X-ray *(conditional recommendation, very low certainty evidence)*.

Considerations

The consensus panel considered the following when formulating this recommendation:

- Pulmonary tuberculosis should be prioritized in periodic health examination because of the burden of the disease in the country.
- Although screening for PTB seems beneficial, the responses varied when the panel was asked about the clear net effect that will favor screening. The desirable effects were perceived to be small because there were no RCTs found that evaluated the effect of screening for TB on cure rate, TB-related mortality, and all-cause mortality.
- The majority agreed that chest X-ray was accurate in detecting cases of pulmonary tuberculosis. In spite of high accuracy, uncertainty to recommend chest x-ray arose in the discussion when being compared with sputum microscopy because sputum examination is more commonly available in rural health units, especially in far-flung areas than chest X-ray. The challenge acknowledged in the sputum test is expectoration from asymptomatic and apparently healthy individuals. A panel member argued that a technique could be used to facilitate sputum production and expectoration.
- A high false-positive rate in chest x-ray seemed also alarming to a panel member considering the negative social stigma attached to PTB.
- Two panel members who expressed disagreement in suggesting chest radiographs in screening opt to use assessment of symptoms.
- Chest X-ray is also currently utilized as a requirement in school enrollment and employment to screen for tuberculosis and disease surveillance in the workplace. The suggestion of using a chest X-ray is also currently aligned with the recommendations of PhilCAT.

3.11.1 Burden of disease

Disease Frequency

Tuberculosis is one of the leading causes of morbidity and mortality in the Philippines. The prevalence of TB in the Philippines is 1,159 per 100,000 population, indicating that at least 1 million Filipinos may have the disease.(1)

Severity of Disease
In 2010, tuberculosis was the sixth leading cause of mortality in the country, with a mortality rate of 26.3 deaths per 100,000 population, accounting for 5.1% of the total deaths in the country. (2)

In 2018, it was estimated that 26,600 people died due to tuberculosis, of which 600 people were infected with HIV.(3) Other risk factors of tuberculosis were previous TB infection, aged over 65, smoking for more than five years, and even poverty. One study also reported that diabetes and residents in an urban setting were significant risk factors.(3)

Natural course of the disease
The burden of pulmonary TB among adult Filipinos has not declined and is significantly associated with previous tuberculosis treatment, diabetes mellitus, smoking, poverty, and living in an urban area.(3) In 2019, tuberculosis was ranked 7 in the top 10 causes of death and disability in our country.(3)

Though adults are primarily affected, over one-quarter of TB patients in the Philippines are children, adolescents, and young adults. It has implications in the long term as they age and contribute to the high prevalence of latent TB infection.(4)

Based on a systematic review from the pre-chemotherapy era, untreated smear-positive tuberculosis (HIV negative) has a 10-year case fatality reportedly between 53% and 86%, with a weighted mean of 70%. For both smear-positive and smear-negative tuberculosis, the duration of tuberculosis from onset to either cure or death is approximately three years.(5)

Management of the disease
The recommended regimen for tuberculosis treatment includes a two-month intensive phase of isoniazid, rifampin, pyrazinamide, and ethambutol followed by a four-month regimen of isoniazid or rifampin.(6, 7)

People infected with tuberculosis need to take the drugs as prescribed. If they take initially but stop too soon, they may either become sick again or become drug-resistant.(8)

Economic impact of the disease
A recent study in Cavite, Philippines, reported that the incurred cost of TB patients during treatment was Php 15,462.57 (321 USD) for drug-susceptible TB and Php 113, 488.52 (2356 USD) for MDR-TB.(9) To date, the TB DOTS (Tuberculosis Directly Observed Treatment Short-course) package is shouldered by Philippine Health Insurance Corporation (PhilHealth). It includes service fees, drugs and medicines, and follow-up sputum smears. However, PhilHealth currently just pays Php 4,000 for the entire treatment of TB.(10)

Social impact of the disease
According to the National TB prevalence survey in 1997, TB was higher than malnourished and diabetic. Moreover, TB is twice higher in the urban poor than that of the general population in Metro Manila.(11)

Moreover, patients with tuberculosis often experience social stigma and discrimination from the general population. In the Philippines, patients with TB are often discriminated against in their community, school, or work.(12) The 1997 National Prevalence Survey revealed that 50% of the patients with TB-like symptoms do not seek medical help because TB is viewed as a "shameful and unclean disease." A study reports that some TB patients would label their health condition with less stigmatizing terms such as "just cough" or "intense cough." Other patients isolate themselves from the general population to avoid transmitting the disease and avoid stigma.(13)

3.11.2 Benefits and Harms of Screening Tests

The 2021 WHO consolidated guidelines(14) on TB screening reviewed the evidence on the effectiveness of screening for active TB in the general population. No randomized controlled trials were found that evaluated the effect of screening for tuberculosis on cure rate, tuberculosis-related mortality, and all-cause mortality.

Treatment success

Three observational studies(15-17)(N=2,224) found that the proportion of cases with treatment success may be similar between patients found through active screening and passive screening (OR = 1.02, 95%CI 0.69 to 1.50).

Case mortality

Four observational studies(15-18) (N= 2,501) found there may be no difference in the proportion of cases who died between patients found through active screening and standard case detection.

Severity of TB cases at the time of diagnosis

Three observational studies(16, 17, 19) (N = 1,578) found that there may be fewer severe tuberculosis cases (smear grade 2+ and 3+) identified through active screening compared to those detected through passive screening.

Prevalence of tuberculosis and latent tuberculosis in children

Two cluster randomized controlled trials(20, 21) (N= 173,981) that evaluated active case finding compared to passive case finding gave conflicting results. These trials, however, had different approaches to case finding. The ZAMSTAR trial(21) (N= 90,601) conducted in Zambia and South Africa showed that active case finding involving community mobilization and open laboratory access at health centers did not significantly decrease tuberculosis prevalence (OR 1.36, 95%CI 0.59 to 3.14) and latent tuberculosis prevalence (OR 1.36, 95%CI 0.59 to 3.14) in children. The ACT3 trial (394) (N = 83,830) in Vietnam was able to decrease tuberculosis prevalence (OR 0.55, 95%CI 0.39 to 0.77) and latent tuberculosis prevalence in children (OR 0.50, 95%CI 0.32 to 0.78) by utilizing a door-to-door approach (with or without symptoms) compared to passive case finding.

Table 28. Effects of active TB case finding compared to passive TB case finding

Outcomes	Odds Ratio (95% CI)	Grade
Treatment success (3 observational studies, N=2,224)	1.02 (0.69 to 1.50)	Very low
Case mortality (4 observational studies, N = 2,501)	0.91 (0.57 to 1.46)	Very low
Smear grade 2+ and 3+ (3 observational studies, N = 1,578)	0.42 (0.32 to 0.55)	Very low
Tuberculosis prevalence (community mobilization) (1 RCT, N= 90,601)	1.09 (0.86 to 1.40)	Low
Tuberculosis prevalence (door-to-door) (1 RCT, N = 83,830)	0.55 (0.39 to 0.77)	Low
Latent tuberculosis prevalence (community mobilization) (1 RCT, N = 10,103)	1.36 (0.59 to 3.14)	Low
Latent tuberculosis prevalence (door-to-door) (1 RCT, N = 1,484)	0.50 (0.32 to 0.78)	Low

Harms of screening tests involve false positive and false negative cases. Using the pooled sensitivity and specificity for x-ray (any abnormality)(14) and TB prevalence in the Philippines(1), we estimated the number of false-positive and false-negative cases in a 100,000 Filipino population. See Table 29. If screening was done using chest X-ray, around 12,849 of 100,000 individuals may be mislabeled to have tuberculosis, while the number of cases that will be missed is approximately 70 cases in 100,000.

Table 29. False-positive and negative cases in a 100,000 Filipino population

	Number of results per 100,000 patients tested (95% CI)
	Prevalence 1.159% Point estimate from Philippine NTPS 2016 data
True positives	**1089** (997 to 1136)
False negatives	**70** (23 to 162)
True negatives	**85992** (79073 to 90934)
False positives	**12849** (7907 to 19768)

3.11.3 Diagnostic Performance of Screening Test

The 2021 WHO consolidated guidelines on TB screening(14) included an analysis of the accuracy of chest x-ray in the general population. Based on a review of 22 cross-sectional studies, the pooled sensitivity and specificity of CXR were estimated at 94% (95% CI 92 to 96%) and 89% (95% CI 85 to 92%). The GRADE rating for this body of evidence was downgraded to very low sensitivity due to concerns regarding the serious risk of bias and inconsistency and low specificity due to serious imprecision and inconsistency.

Philippine Data

Compared to international data, higher sensitivity and lower specificity estimates were reported locally. The National TB Prevalence Survey in 2016(1) provided the sensitivity (100%; 95% CI 98.2 to 100%), and specificity (65.7%; 95% CI 65 to 66.5%) of CXR when used for screening asymptomatic patients with risk factors. At-risk groups involved healthcare workers, contacts of TB patients, those ever treated for TB (i.e., with a history of previous TB treatment), people living with HIV (PLHIV), elderly (>60 years old), diabetics, smokers, urban and rural poor, all those with immunosuppressive medical conditions, and people in congregate settings.

When the analysis was restricted to asymptomatic patients without risk factors, sensitivity remained unchanged at 100% (95% CI 98.8 to 100%), while specificity and positive likelihood ratios increased to 73% (95% CI 72.5 to 73.4%) and 3.7 (95% CI 3.64 to 3.76), respectively. Chest x-ray screening alone identified 98.2% cases (430/438 available chest x-rays) compared to 32.2% (150/466) identified by symptom screening alone. During active case finding scenarios, screening for TB cases using symptoms alone would have missed one-to two-thirds of bacteriologically confirmed pulmonary TB cases.

3.11.4 Cost Implication

Universal tuberculosis screening using chest X-ray in 2 years was shown to be a cost-effective strategy compared to no screening in Korea among asymptomatic adults aged 40 years and above. (22)

Table 30. Costing data on screening tuberculosis

Parameter	**Screening intervention**
	Chest X-ray
(A) Unit cost of screening intervention	Php 235 (17)
(B) Other direct costs associated with the implementation of the proposed screening intervention	1) Professional fee: Php 45 (17) 2) Direct Sputum Smear Microscopy: Php 641.14 (13.31 USD) (18) 3) Xpert assay: Php 836.71 (17.37 USD) (18) Total : **Php 1,522.84**

Parameter	Screening intervention
	Chest X-ray
(C) Annual screening cost per patient	Php 1, 757.84

3.11.5 Ethical, Social, and Health Systems Impact (Equity, Acceptability, and Feasibility)

Ethical

The availability of chest X-rays is limited to only selected hospitals and primary care centers. It is not accessible to the majority of primary care health facilities. In the Philippines, Luzon, including NCR, has the highest physical access to diagnostic imaging equipment, while Mindanao has the least access.(23) This limits the capacity to conduct effective TB screening. As such, presumptive TB cases will then be referred to other facilities, leading to high costs for patients, delayed diagnosis and care, and high early loss to follow-up.(1)

Social

Studies report that tuberculosis is more prevalent in males and the older population. Tuberculosis is also twice higher in poor urban settlements than in the general population in Metro Manila. Thus, screening for tuberculosis must be prioritized in high-risk and vulnerable groups, including men, the elderly, those in poverty, and dwellers in urban slums to increase case detection.(1, 2, 24, 25)

Moreover, there is a strong social stigma and discrimination against patients with tuberculosis because it is a highly contagious disease. Tuberculosis is often associated with HIV, poverty, low social class, malnutrition, or disreputable behavior. To avoid such stigma, patients tend to seek help first from private practitioners. The stigma and socioeconomic impact of TB also affect the at-risk individuals' decision to undergo TB screening. They result in a delay in diagnosis, treatment compliance, and increased costs to patients.(26)

Health Systems

The Philippines TB Joint Program Review reports that chest x-ray is limited to selected hospitals and primary care centers.(2) Most primary care health facilities do not have access to chest x-ray machines and radiologists to interpret the x-ray films. Differences are observed in the density of diagnostic imaging equipment across the regions of the country. Luzon, including NCR, has the highest physical access to x-ray and MRI equipment, while Mindanao has the least access.(23) This results in the delay of TB diagnosis. There will be a need to refer the patient to another healthcare facility with complete equipment and eventually delay treatment, resulting in higher costs. In such a scenario, areas with a high prevalence rate for tuberculosis should be given priority for implementation. Moreover, as reflected in some of the cost-effectiveness studies listed above, screening of tuberculosis using chest x-ray examination may be feasible but not economical in areas with a low TB incidence. (27, 28)

Screening for active TB cases may be more economically wise if the focus is given to selected high-risk groups (targeted screening). The WHO's 2013 guidelines on systematic screening for active TB include strong recommendations for screening of 1) household contacts and other close contacts of patients with active TB, 2) people living with HIV, and 3) current and former workers in workplaces with silica exposure. It is, however, worth noting that the guidelines state that direct evidence underlying these strong recommendations was insufficient, and the recommendations were mainly influenced by the views of the members of the guideline development group.(29)

3.11.6 Recommendations from Other Groups

WHO *Consolidated Guidelines on Tuberculosis 2021* (14) suggest doing systematic screening for TB among the general population in areas with an estimated TB prevalence of 0.5% or higher (conditional recommendation, low certainty of evidence). Screening may include using a symptom screen, chest X-ray, or molecular WHO-recommended rapid diagnostic tests, alone or in combination (conditional recommendation, very low certainty of evidence for test accuracy).

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3.12 Resting ECG or Exercise ECG in Screening for Coronary Artery Disease

RECOMMENDATION

Among asymptomatic apparently healthy adults, we recommend against the use of resting or exercise ECG to screen for coronary artery disease *(strong recommendation, low certainty evidence)*.

Considerations

The consensus panel considered the following when formulating this recommendation.

- All members of the CP agreed that coronary artery disease is a priority in screening healthy adults. However, the majority decided that the desirable effects of ECG are small to trivial. The panelists' opinions varied in terms of its undesirable effects. Screening may lead to undergoing invasive procedures, thus, may be associated with additional risk and high economic burdens. The majority favored no screening because these undesirable effects outweigh the perceived benefit.
- They noted that the diagnostic performance of exercise ECG in detecting CAD is imprecise and has low to very low quality of evidence.
- Absence of data on resting ECG and cost of exercise ECG or a treadmill test were also highlighted in the decision-making.
- Some panel members further examined the implications of not recommending even the use of exercise ECG. A CP member raised a question of how to thoroughly examine fitness to work if exercise ECG will not be recommended to provide cardiovascular clearance. The panel member argued that the suggestion of using physical examination and history taking might not provide reliable results for obtaining clearance for cardiovascular diseases.

3.12.1 Burden of disease

Disease Frequency

According to the Philippine Statistics Authority Report in 2017, ischemic heart diseases were the leading causes of death in males and females, 50 503 and 33 617 deaths, respectively (405). From a 2015 survey, the overall prevalence of coronary disease in the Philippines was 0.9%. The prevalence also increased across age groups and was highest among females at 1.1%. Notably, the coronary disease was higher among adults in urban areas (1.2%) than those in rural areas (0.6%), with its prevalence increasing with wealth. (1)

Severity of Disease

The risk factors of coronary artery disease include hypertension, diabetes, hypercholesterolemia, and smoking(2). One study reported that approximately 69% of CAD

patients have comorbidities like hypertension or diabetes. The physical and mental component scores of health-related quality of life (HRQoL) were better in patients without any morbidity. Moreover, female and lower educated patients had significantly lower physical and mental component scores, resulting in lower HRQoL.(3)

Natural course of the disease

A 1972 cohort study(4) described the natural course of disease of 246 patients with ischemic heart disease diagnosed through coronary arteriography. Among patients with no vessel disease (defined as no obstruction >50% of a major vessel), 3 out of 98 patients (3.1%) died at a mean follow-up of 22 months. Among those with one vessel disease, 4.3% died at a mean follow-up of 20 months, while 27.5% of patients with the two-vessel and three-vessel disease died.(4)

More recent prognosis studies report the outcomes of patients with coronary artery disease who received standard treatment (medications and revascularization). By 10 years, 52.9% of patients had developed at least one recurrent ischemic event. The mortality rate was 20.9% at 10 years.(5)

Management of the disease

Based on the 2014 Philippine Heart Association Guidelines on the Management of Coronary Artery Disease, lifestyle modification, control and treatment of risk factors, and pharmacologic therapy form the cornerstone of the management of CAD.(6) Lifestyle modifications include changes in dietary habits, engaging in regular physical activity, and smoking cessation. Risk factors that need to be controlled are hypertension, dyslipidemia, diabetes mellitus, obesity, and psychosocial distress. Pharmacologic therapy for CAD include aspirin or clopidogrel, and statins. ACE inhibitors or angiotensin receptor blockers (ARBs) are also recommended, especially in patients with concomitant heart failure, hypertension, or diabetes mellitus. Beta-blockers or calcium channel blockers are recommended first-line treatment to reduce symptoms of angina. Revascularization through percutaneous coronary intervention or coronary artery bypass surgery is recommended for patients with a high risk of mortality (i.e., high-risk coronary anatomy, moderate/severe left ventricular dysfunction).(6) International guidelines have similar recommendations. The 2019 European Society of Cardiology recommends modification, control of risk factors, and pharmacologic treatment. Pharmacologic treatment includes antiplatelet drugs (aspirin or clopidogrel), consideration for statin treatment irrespective of LDL-cholesterol levels, and ACE-inhibitors/ARBs for those with coexisting hypertension, heart failure, diabetes. Revascularization is recommended when angina persists despite medical treatment.(7)

Economic impact of the disease

Coronary artery bypass grafting (CABG), popularly known as heart bypass surgery, is performed to treat patients with severe coronary artery disease, leading to coronary artery-related deaths. The average cost of CABG in the Philippines amounts to around P700,000.00 to P1,000,000.00, while PhilHealth coverage for CABG for Qualified PhilHealth members can avail of the maximum coverage of P550,000.00.(8)

Social impact of the disease

Since coronary artery disease is a chronic disease, it constrains the patients' physical, emotional, and social functions, significantly affecting their adherence to treatment recommendations.(3) Psychosocial factors like low socio-economic status, lack of social support and social isolation, chronic work or family stress, and negative emotions, including depression and anxiety, significantly contribute to the development and outcome of CAD.(9) One study reported that fatigue was the most severe CAD symptom, which causes less physical activities and social interactions. Depression was also evident in patients with CAD and was associated with severe symptom experience and low perceived social support.(10) Another social implication of having coronary artery disease includes loss of employment, relocation due to job loss, or the need to be closer to health care centers.(11)

3.12.2 Benefits and Harms of Screening Tests

There were no trials found for resting ECG. Two RCTs involving 1,151 asymptomatic adults aged 50-75 years old with diabetes mellitus (high-risk population) were included for exercise ECG. Both trials reported no significant reduction in mortality, myocardial infarction, heart failure, or stroke among participants who underwent screening compared to no screening.(12, 13) Subgroup analysis from one trial showed no significant difference in outcome based on sex, age, and cardiovascular risk.(13)

Based on the results of 1 RCT (which was 1 of the 2 RCTs included in the benefits of screening with ECG in improving health outcomes), 20 of 262 participants in the screened group had exercise ECG abnormalities. Out of the 20, 17 underwent coronary angiography. Out of the 17, 12 underwent revascularization. One out of 12 patients who underwent revascularization had a non-fatal acute myocardial infarction three days after the procedure.(13)

The harms of screening with ECG include the conduct of unnecessary invasive confirmatory procedures if ECG abnormalities are detected, overtreatment, and labeling. The harms of invasive confirmatory testing include unnecessary radiation exposure with an increased risk of cancer, contrast-induced nephropathy, allergic reactions to the contrast agent, bleeding, arrhythmia, anxiety, and cost. The harms of overtreatment include adverse medication effects such as gastrointestinal bleeding and liver damage and the economic burden of buying medications. Studies report that up to 3% of asymptomatic individuals with abnormal exercise ECG results undergo coronary angiography, and up to 0.5% undergo revascularization, even though revascularization has not been shown to reduce CAD-related events in asymptomatic individuals.(14)

3.12.3 Diagnostic Performance of Screening Tests

Resting ECG

No studies were found that directly provided the sensitivity and specificity of resting ECG in detecting CAD.

Exercise ECG

There are no recently conducted systematic reviews on the use of exercise ECG for screening asymptomatic adults for CAD. The last systematic review was completed in 2012. (15)

Nine studies evaluated the use of exercise ECG as screening for CAD among asymptomatic adults.(16-24)

The pooled sensitivity is 75% (95% CI 67 to 81%) while the pooled specificity is 56% (95% CI 32 to 78%) based on 6 studies (n=1,040).(16-18, 20-22) The other three studies were not included in the pooled analysis due to insufficient data.(19, 23, 24)

3.12.4 Cost Implication

One cost-effectiveness study in Japan evaluated screening for coronary artery disease versus no screening on asymptomatic type 2 diabetes patients and other atherogenic risk factors. They report that screening was cost-effective for high-risk diabetes patients.(25) We did not find studies that evaluate the cost-effectiveness of screening for CAD in the general population. Estimated costing data on screening for CAD per patient is shown in Table 31.

Table 31. Costing data on screening for CAD

Parameter	**Screening intervention**
	Electrocardiogram
(A) Unit cost of screening intervention	ECG at Heart Station: **Php 400**
(B) Other direct costs associated with the implementation of the proposed screening intervention	According to the 2014 Clinical Practice Guidelines, initial laboratory tests are recommended to establish cardiovascular risk factors: • Fasting lipid profile (total cholesterol, high density lipoprotein, low density lipoprotein, triglyceride levels): **Php 1, 140** • Fasting glucose and/or glycated hemoglobin(HbA1c) level: **Php 650** • Oral glucose tolerance test if fasting glucose and HbA1c are inconclusive: **Php 400** • Complete blood count: **Php 250** • Creatinine level with an estimation of glomerular filtration rate: **Php 140** • Biochemical markers of myocardial injury (Troponin T or I) if clinical evaluation suggests Acute Coronary Syndrome: **Php 800** • Thyroid hormone levels if with clinical suspicion of a thyroid disorder: **Php 550** • Liver function tests early after beginning statin therapy: **Php 560** A chest x-ray is recommended in patients with signs or symptoms of congestive heart failure, aortic dissection and/or aneurysm, valvular heart disease, pericardial disease, or pulmonary disease: **Php 365** Transthoracic two-dimensional and Doppler echocardiography is recommended in the initial evaluation of all patients: **Php 3, 600**

	Ambulatory ECG monitoring is recommended in patients with suspected arrhythmia and vasospastic angina: **Php 2, 200** (26, 27) Other direct costs total: **Php 10, 655**
(C) Annual screening cost per patient	Assuming that all additional tests are performed, the total annual screening cost would be **Php 11, 055**

3.12.5 Ethical, Social, and Health Systems Impact (Equity, Acceptability, and Feasibility)

Ethical

People from LMICs who suffer from cardiovascular diseases and other non-communicable diseases have less access to effective and equitable health care services. As a result, people from LMICs are detected late in the disease, resulting in lower quality of life.

Another issue on equity is that some companies require applicants to undergo ECG as a pre-employment requirement. Those with abnormal ECG results may be required to undergo coronary angiography and possible revascularization before employment, which is paid out-of-pocket by the individual applicant.

Social

Screening of coronary artery disease using electrocardiogram is a common practice in the Philippines. As with other screening interventions, the lack of awareness of the importance of screening and early diagnosis may have repercussions of less access to services to detect and manage chronic diseases. There may also be significant implications for those diagnosed with cardiac disease, including insurance, employment, and mental health issues.(28)

Health Systems

Although the prevalence and incurred costs of cardiovascular diseases are high in developing countries, healthcare resources are not prioritized. For CAD specifically, adequate infrastructure for interpretation of ECG results according to expert guidelines, including a pathway to treatment, is essential. Moreover, a substantial number of people will require follow-up tests, and the person conducting screening must be prepared to counsel patients with an abnormal result. (28)

3.12.6 Recommendations from Other Groups

In 2011, the USPSTF recommended screening with resting or exercise ECG to detect CAD among asymptomatic low-risk adults. Given the minimal incremental benefit and the potential harms of screening, the USPSTF concluded with moderate certainty that the potential harm equals or outweighs the potential benefits among asymptomatic low-risk adults. For intermediate or high-risk asymptomatic adults, the USPSTF concluded that the balance of benefits and harms could not be determined due to lack of evidence. Individuals

are considered low risk if their risk for 10-year risk of a CAD-related event is <10%, intermediate risk if their risk is 10-20%, and high risk is >20%.(14)

For individuals in occupations that can endanger others' safety, such as pilots and heavy equipment operators, the USPSTF states that evidence is insufficient to determine the balance of benefits and harms of screening with ECG.(14)

In 2018, the USPSTF updated its recommendations on the use of resting or exercise ECGs for screening. In this report, the focus was the use of ECG for screening for cardiovascular disease risk compared with conventional risk factor assessment. They concluded that screening with exercise ECG did not improve health outcomes, even if higher risk populations (those with diabetes mellitus) were screened.(29)

The European Society of Cardiology 2019 guidelines state that there is limited data on managing asymptomatic individuals with positive screening test results due to a lack of evidence demonstrating improved prognosis following appropriate management.(7)

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3.13 Urinalysis and Serum Creatinine in Screening for Chronic Kidney Disease

RECOMMENDATIONS

1. **Among asymptomatic apparently healthy adults, we suggest against screening for chronic kidney disease using urinalysis *(conditional recommendation, low certainty evidence)*.**

2. **Among asymptomatic apparently healthy adults, we recommend against screening for chronic kidney disease using serum creatinine *(strong recommendation, no evidence)*.**

Considerations

The consensus panel considered the following when formulating this recommendation:

- Given the burden of the disease, chronic kidney disease should be prioritized.
- Majority, however, agreed based on the net effects of the test that they do not favor screening. They acknowledged the low sensitivity values of urine dipstick and no diagnostic study to be used as evidence on serum creatinine. Moreover, even if these screening tests are not expensive and widely available, further work-up to ascertain the case of CKD and treatment of these cases will be costly. Accessibility to treatment services for CKD also remains a challenge.

3.13.1 Burden of disease

Disease Frequency

The global burden of the disease shows there were three times more people from low-middle-income countries (LMICS) with CKD (387.5 million) than high-income countries (109.9 million).(1) In the Philippines, the overall prevalence of CKD among Filipino adults (N=19,513) in 2013 was 3.2% (95% CI: 2.9-3.6%).(2)

Severity of Disease

According to the Philippine Health Statistics 2016 report, diseases of the genitourinary system are the ninth leading cause of mortality in the Philippines, with about 23,526 total deaths per 100,000 population of both sexes and all ages. (3)

In 2017, CKD was ranked as the twelfth (12^{th}) leading cause of mortality worldwide. Between 1990 and 2017, the global all-age CKD mortality rate increased by 41.5%, with 1.2 million deaths recorded in 2017. The age-standardized mortality rate remained stable within the period, with a slight change of 2.8% (2.8%, -1.5 to 6.3).(4)

The quality of life (QoL) of patients with CKD progressively decreases with more advanced disease stages. Low family income and hemoglobin levels were considered predictors of worse QoL in both physical and mental component summaries among CKD patients.

Natural course of the disease

Excess mortality associated with renal failure is mainly due to the increased risk of cardiovascular disease. An investigation of the causes of death related to CKD in Alberta revealed that the primary cause of mortality was cardiovascular failure (including an increase in heart failure and valvular disease). The unadjusted proportion of patients who died from cardiovascular disease increased with decreasing eGFR (i.e., 21% of patients with proteinuria had 45-59.9 ml/min/1.73m^2;44 % of patients with an eGFR of ≥60 had 15–29.9 ml/min/1.73 m^2). The proportion of deaths from infection also increased but not those from cancer.(3)

Management of the disease

Routine screening of CKD among the general population is not recommended in major guidelines unless patients have high risk or with the presence of comorbidities or risk factors that include diabetes, hypertension, and other cardiovascular diseases.(5) Thus, CKD management in its early stage is usually focused on treating these risk factors or comorbidities, leading to complications or progression of CKD.

Treatment recommendations include but are not limited to diabetes medications (e.g., metformin, sodium-glucose co-transporter-2 inhibitors, or glucagon-like peptide-1 receptor agonists), antihypertensives (e.g., angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers), lipid-lowering agents, and nutritional support.(6)

Economic impact of the disease

The population of end-stage renal disease or ESRD dialysis-dependent patients in Asia is increasing at a rate highest in the world. The annual growth in China, the Philippines, and Malaysia is more than 10% and is even likely to increase further due to progressive aging and rising incidences of diabetes and hypertension among Asians.(7)

Globally, ESRD is a leading cause of poverty due to the associated catastrophic health expenditures. Based on a systematic analysis for the global burden of CKD, 35.8 million disease-adjusted life years (DALYs) were recorded in 2017, about a third of which was due to diabetic nephropathy.(4) In 2010, only 27% of patients globally in need of renal replacement therapy received it, with only about 2% to 5% of the proportion coming from countries classified as low to lower-middle-income classes.(8) About 7.7% of the total universal health coverage (UHC) budget in the Philippines was spent on renal replacement therapy alone, amounting to Php 91.4 B (~USD 1.9 B), despite having only 0.03% of the UHC beneficiaries as dialysis patients. (442) (As of November 24, 2020, USD1 = Php 48.11)

Social impact of the disease

CKD is of particular interest in the study of health inequalities as, like many chronic diseases, there is a marked social gradient in the incidence of the disease. Factors of social disadvantage, including neighborhood deprivation, low income, low socioeconomic status

(SES), and minority ethnicity, are strongly associated with higher CKD rates. There is also consistent evidence that disadvantaged individuals with CKD have more inadequate access to quality treatment, including kidney transplantation.(9)

Moreover, in most policies implemented for ESRD care and training of healthcare professionals, the ethical issues associated with ESRD and resource-limited countries are infrequently considered. Most lower-income countries do not have full UHC, which often results in inequitable access to care, health outcomes, resources, and potential exclusion from patient care, especially for those below the poverty line. Other ethical issues prevalent among resource-limited settings are the existing disparities in sustaining clinical standards of care to compensate for the partial government coverage. Such circumstances could impose emotional and moral burdens as well as ethical dilemmas on patients, families, healthcare workers, and policymakers, particularly in the aspect of end-of-life decision-making and provision of patient care.(10)

3.13.2 Benefits and Harms of Screening Tests

A systematic review found no studies on the benefits of urinary dipstick screening. The authors found no evidence to assess the benefits and harms of screening using a urinary dipstick in general populations and patients in hospitals.(11)

There was one RCT on the treatment of screen-detected early CKD in asymptomatic apparently healthy patients in the general population. A substudy (N=864) from the larger PREVEND study screened for albuminuria in the general Dutch population (PREVEND IT study), then treated those with urinary albumin excretion rate between 15 to 300 mg/d, blood pressure <160/100 mm Hg, and plasma cholesterol <8.0 mmol/L, with fosinopril, an angiotensin-converting enzyme inhibitor, and pravastatin, a lipid-lowering drug, to prevent cardiovascular events. Mean follow-up was 46 ($\pm$7) months, with CV events occurring in 45 (5.2%) subjects. There was no significant difference between CV events in patients treated with fosinopril compared to the placebo group (RR 0.60, 95% CI 0.21 to 1.74), pravastatin versus placebo (RR 0.92, 95% CI 0.45 to 1.89), and fosinopril plus pravastatin versus placebo (RR 0.53, 95% CI 0.18 to 1.58).

3.13.3 Diagnostic Performance of Screening Tests

Urinalysis (Albuminuria)

Four observational studies were found that determined the diagnostic accuracy of urine dipstick protein in detecting urine protein, with cutoffs at trace and higher or 1+ and higher, compared to urine albumin to creatinine ratio (ACR) >30 mg/g and >300 mg/g. Pooled sensitivity was 82%, (95% CI 42,97) to the cutoff of 1+ or higher using ACR>300 mg/g as reference standard. (12-15)

A cross-sectional study using data obtained from a nationwide community-based health examination program in 2008 for adults aged 40 to 74 (N=538,846) in Japan showed that

the sensitivity of the urine dipstick protein using a cutoff of 1+ or higher compared to a diagnosis of CKD was 28.6% (95% CI 28.3, 28.9) and with a high specificity of 100%.(16)

Another community-based prospective cohort study in Japan (N=69,238) showed sensitivity for urine dipstick protein to be 6.9% (95% CI 6.4 to 7.4), and specificity was 97% (95% CI 96.9 to 97.1), with eGFR<60 ml/min/1.73 sqm as the reference standard.(17)

Serum Creatinine

We found no studies that compared serum creatinine to any reference standard to screen CKD in asymptomatic apparently healthy individuals.

3.13.4 Cost Implication

Three studies were found which reviewed the cost-effectiveness of universal screening for CKD through urinalysis with dipstick and serum creatinine assay versus no screening. These three studies (Japan, China, Korea) found that screening is cost-effective in high-risk patients, hence, could be instrumental in countries with a high prevalence of the disease. (18-21) Moreover, a systematic review of cost-effectiveness studies published in 2014 suggested that screening may not be cost-effective in the general population, except in situations in which screening could be added to mandatory health check-ups or when rates of CKD progression were rapid, and RAAS inhibitors could be considered highly effective for renal and cardiovascular risk reduction. With these findings, given that the screening for CKD in the general population without risk stratification and targeted treatment is unlikely to be cost-effective, prioritizing general screening with older patients or patients most likely vulnerable to the disease may show a better approach for screening.(22)

Table 32. Costing data on as a screening tool

Parameter	Screening intervention
(A) Unit cost of screening intervention	Urinalysis 50.00 Php Serum creatinine 90.00 Php (23)
(B) Other direct costs associated with the implementation of the proposed screening intervention	Patient cost = an average of 10 minutes per screening (27) of a physician/nurse/social worker Php 29,277[1] = Php 30.50
(C) Screening cost per patient	Php 170.50

3.13.5 Ethical, Social, and Health Systems Impact (Equity, Acceptability, and Feasibility)

Ethical

The implementation of the international KDIGO-aligned urinalysis and creatinine-based screening guidelines in LMICs is not well-studied, especially in rural areas, and therefore remains uncertain in the context of cost-effectiveness due to geographical constraints, cost, timeliness/ reliability, and durability issues, and lack of access to health infrastructures even at the primary care level. (24)

It is essential to consider the treatment status of any country before implementing the national screening guidelines to prevent counterproductive results such as increasing the anxiety the screened individual might suffer due to lack of post-screening interventions. This patient suffering being heightened emotionally and mentally too early (also known as the lead-time bias) does not promote greater happiness of an individual or a society from an ethical point of view.(25)

Social

Since CKD is known as a 'major but poorly understood health burden' in LMICs(26) and is also a 'silent killer' NCD, Filipinos tend not to prioritize CKD screening until clinical signs and symptoms worsen. It happens among affected populations when 1) they are already diagnosed with other NCDs such as cardiovascular diseases; 2) financially incapable of paying for additional health expenditures, 3) lacking in proper awareness about CKD prevention such as proper lifestyle and diet, and education about the disease, in general, and/or 4) are residing in rural areas where laboratory facilities and healthcare professions needed for CKD testing are not widely accessible.

Health Systems

The poor and disproportionate referral systems and human resources evident among LMICs continuously present challenges toearly CKD detection, treatment, and management. Untreated CKD poses a risk for developing the ESRD and cardiovascular diseases (CVDs) that remain as leading causes of mortality in LMICs.(1)

International KDIGO-aligned CKD screening guidelines usually require access to specialized laboratory facilities for testing, even with the initial screening tests such as serum creatinine assessment assays. The lack of government funding and training requirements for CKD screening among national health systems and healthcare professionals in LMICs bar patients, particularly in rural and resource-limited areas, from early CKD diagnosis and management and integrated patient care.(24)

3.13.6 Recommendations from Other Groups

No CPGs recommended screening for CKD in asymptomatic persons without risk factors. The international guidelines such as NICE 2014, ACP 2013, and USPSTF 2012 explicitly advised against it. Most guidelines recommended screening in persons with risk factors like diabetes, hypertension, cardiovascular disease, or positive family history for ESRD.(6, 27) The 2019 US Veterans Affair Clinical Practice Guideline for the Management of Chronic Kidney Disease concluded that there is insufficient evidence to recommend screening for or against CKD in the general population.(5)

Based on a synopsis of the Evidence-based Clinical Practice Guidelines for Chronic Kidney Disease 2018 (original article in Japanese), the examination of proteinuria/albuminuria is recommended in the specific health check-ups and guidance programs in Japan because proteinuria/albuminuria is associated with increased risks of all-cause mortality, CVD onset, and renal impairment.

Screening in those with other risk factors such as age, ethnicity, obesity, and HIV status is not consistently recommended.

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3.14 Hemoglobin and Hematocrit in Screening for Anemia

RECOMMENDATION

Among asymptomatic apparently healthy non-pregnant adults, we suggest against routine screening of anemia using hemoglobin and/or hematocrit *(conditional recommendation, very low certainty evidence)*.

Considerations

The consensus panel considered the following when formulating this recommendation.

- Most panel members perceived that screening for anemia may or may not be prioritized, with most members favoring no screening.
- Although blood tests are considered useful in detecting certain diseases and are relatively acceptable and accessible as a screening procedure, the CP focused on the very low certainty of evidence and costly additional workup, particularly in private settings.
- The CP's discussion revolved around the implications of this recommendation that may implicitly suggest against the use of CBC in annual physical examination. They emphasized that CBC is not mandated by law to be part of physical examination and is only part of the usual practice. Panelists who abstained from voting cited the use of CBC in surveillance and monitoring of workers who are at risk for occupational diseases (e.g., lead toxicity among employees of battery manufacturing companies, anemia among jeepney drivers).
- This conditional recommendation suggests that a CBC can be done mainly in situations wherein there is a risk for developing certain conditions.

3.14.1 Burden of disease

Disease Frequency

Anemia is considered a major public health concern worldwide, with a high prevalence in Africa and South East Asia. It affects 43% of children below five years old, 38% of pregnant women, and 29% of non-pregnant women worldwide.(1, 2) In the Philippines, iron deficiency anemia (IDA) affects a large portion of infants (40.5%), pregnant women (26.4%), lactating women (16.7%), and elderly males (23.0%).(3)

According to the 2018 National Nutritional Survey, anemia affects 8.3% of adults aged 20-59 and 20.2% of elderly adults aged 60 years old and older.(4)

Severity of Disease

Anemia in pregnant women and adolescent girls results from nutrition-related causes, inflammatory or infectious diseases, and blood loss. It causes a decreased quality of life in

older adults, functional limitations, increased risk of developing dementia, fatigue, increased risk of falling, and increased depressive symptoms.(5) In patients with heart failure (HF), anemia is recognized as critical comorbidity leading to poor outcomes.(6) It is estimated that up to a fifth of maternal deaths in nine low-income Asian countries, 65, 000 deaths annually, are caused by severe iron deficiency anemia.(7)

Economic impact of the disease

South Asia, the region with the highest prevalence of IDA, loses Php 240.7 billion (USD5 billion) annually to iron deficiency and ~2% in economic growth. Iron supplements for a full pregnancy cost Php 96.27 (~USD2). Annual iodine and iron fortification costs are Php 2.41 (USD0.05) and Php 4.81 (USD0.10) per person, respectively.(7) In patients with T2DM, annual treatment costs were higher for patients with anemia, Php 47,317.20 (USD983) than non-anemic patients, Php30,325.37 (USD630).(8) There are also indirect costs such as disability payments, reduced productivity at work, and travel expenses for healthcare appointments.(9) However, there is currently no data for Southeast Asia.

Social impact of the disease

Most correlational studies have found associations between IDA and low cognitive and motor development and behavioral problems. Longitudinal studies consistently indicate that children who are anemic in infancy continue to have lower cognition, poor school performance, and more behavior problems into middle childhood.(10) In addition, there is considerable evidence that anemia is associated with a large number of socioeconomic and biomedical disadvantages that can affect children's development. Some patients with chronic fatigue may also be at risk for withdrawal from daily life and major depression.(11)

3.14.2 Benefits and Harms of Screening Tests

No studies were found that directly evaluated the effectiveness of anemia screening using hemoglobin and hematocrit.

A systematic review(12) examined the benefits and harm of iron therapy in anemic patients and found no significant benefit in mortality, proportion requiring blood transfusion, length of hospital stay, hemoglobin, quality of life, and serious adverse events.

Based on a systematic review of observational studies(13), adverse effects of venipuncture include vasovagal reactions (3.4%), pain and bruising (including hematoma, 14.2%), and nerve injury (less than 0.04%). In outpatient settings, reported vasovagal reactions including diaphoresis or near syncope, syncope, convulsive syncope, and ventricular tachycardia. In hospital phlebotomy clinics, patients reported feeling very faint or extremely faint and losing consciousness; phlebotomists used strategies in managing fainting symptoms. Of 56 patients who incurred a nerve injury, around 22 patients recovered within three days, 17 recovered within 3 to 29 days, 13 recovered within 1 to 3 months, two patients recovered within 3 to 6 months, while two patients had more than six months recovery period requiring physical consultation with one of them having a residual neurologic deficit.

3.14.3 Diagnostic Performance of Screening Tests

Anemia is defined as a low red cell mass.(14) In a routine blood test, anemia is reported as low hemoglobin or hematocrit. The gold standard test to diagnose iron-deficiency anemia is a Prussian blue stain of a bone marrow aspirate smear(15), but this is rarely done. There is no definite study on independent diagnostic sensitivity and specificity of a routine complete blood count in the diagnosis of iron deficiency anemia.

3.14.4 Cost Implication

Anemia screening was investigated among colorectal surgery patients(16), and in another study(17), hematocrit screening and CBC screening were investigated among adult patients receiving antiretroviral therapy. In both cases, they are cost-saving, reducing the number of red cell units to be transfused and reducing the disability-adjusted life years (DALY).(16, 17) However, these studies were not done among the general population. Table 33 shows an annual screening cost per patient and its considerations.

Table 33.Costing data on screening anemia

Parameter	Screening Intervention
	Complete Blood Count
(G) Unit cost of screening intervention	In one of the PhilHealth Accredited hospitals (Western Visayas Medical Center-Iloilo or WVMC), the costs are as follows: ● CBC – Php 250
Other direct costs associated with the implementation of the proposed screening intervention	If CBC shows anemia, additional tests may be done to determine the cause of anemia. Some of these may include: ● Reticulocyte count – Php 150 (WVMC) ● Ferritin level – Php 585 (Southern Philippines Medical Center) ● Peripheral blood smear – Php 450 (WVMC) ● Hemoglobin electrophoresis – Php 275 (Jose Reyes Memorial Medical Center)
(H) Annual screening cost per patient	Php 250 for screening, Php 1460 for possible workup

3.14.5 Ethical, Social, and Health Systems Impact (Equity, Acceptability, and Feasibility)

Ethical

There are large variations and inequities in terms of infrastructure, equipment, essential drugs, and staffing. The inequitable distribution of clinical laboratories in provincial areas remains unresolved. There are geographically disadvantaged areas that require the patient to travel long distances to reach the nearest health center. Therefore, screening may benefit more people living in urban areas compared to rural areas. Dispensing of appropriate healthcare is inequitably distributed among various socio-economic sectors. (18, 19)

Social

Even though it is not well studied, the harms for screening anemia are likely minor. Potential harms of screening, such as false-positive results, anxiety, and the cost it will incur to the patient, may affect the patient's acceptability and participation in the screening program. The screening program should be clinically, socially, and ethically acceptable to both the health professionals and the public.(19)

Health Systems

In developing countries, the cost and interference from infectious conditions make it challenging to assess iron status. A control strategy should be carried out. Information in the distribution of health staff and facilities, community organization, transport and storage facilities, the management structure of primary health care, including supplies and budgeting, is needed. Adequate staffing and facilities should be available before the commencement of the screening program. Health technicians should be universally and intensively trained to minimize individual variability of screening results.

As screening will diagnose more patients, and even though treatment is quite simple, the treatment capacity should be prepared. In areas where moderate or severe iron deficiency anemia exists, an anemia control strategy that is direct, inexpensive, and more effective should be incorporated into the country's health system. (20, 21)

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3.15 Depression Screening and Assessment Tools in Screening for Depression

RECOMMENDATION

Among asymptomatic apparently healthy adolescents and adults, we suggest screening for depression using PHQ-9 ***(conditional recommendation, low certainty evidence)*****.**

Considerations

The consensus panel considered the following when formulating this recommendation.

- The majority of the expert panel members agreed that depression is a priority in periodic health examinations primarily because of its alarming increase in cases.
- They perceived the net effects of screening for depression lead to more benefit than harm. However, a group representative pointed out the stigma that will inevitably surface and should be addressed.
- The recommendation was also rooted in the screening outcomes measured, such as suicide rates, the remission rate of depression, and suicidal ideations.
- Panelists recognized the accuracy of Patient Health Questionnaire PHQ-9 and were uncertain in PHQ-2 in terms of diagnostic performance.
- Factors such as the lack of specialists who can provide intervention were raised.
- The cost of training the non-specialist was also anticipated to result in moderate costs.
- All agree that screening using PHQ-9 is equitable, acceptable, and feasible, but the accessibility of depression management should be improved for it to be entirely equitable.
- Certainty of evidence was seen as low.

3.15.1 Burden of disease

Disease Frequency

There is limited data on the prevalence of depression in the Philippines.(1) In 2008, the World Health Organization (WHO) ranked major depression as the third cause of disease burden and projected that it would rank first by 2030. The global data show an estimated prevalence of depression to be 3.44%, ranging from 2% to 6%.(2) The WHO estimated that 3.3 million Filipinos had a depressive disorder in 2017. (3)

An increase in the prevalence of depression was further seen during the COVID-19 pandemic. A meta-analysis showed the prevalence to have jumped from 3.44% in 2017 to a pooled estimate of 25% (95% CI 18% to 33%; I^2=99.6%, p<0.001). (4)

In a recent survey done in 12 countries (n= 24,849), the Philippines has the highest prevalence for suicidal ideation, wherein 3.1% of local respondents reported suicidal ideation nearly every day.(5)

Severity of Disease

Major depression is a common illness that severely limits psychosocial functioning and diminishes the quality of life. The lifetime risk of depression is three times higher (15 to 18%), with almost 1 in 5 people experiencing one episode at some point in their lifetime.(6)

Large cohort studies (n=1,203,734 participants) have shown that rates of suicide attempts and deaths increase with escalating responses to item 9 of PHQ-9, a screening tool for depression (HR 2.99, 95% CI 1.92 to 4.65).(7, 8) Another study (n= 939,268) has shown that those who reported suicidal ideation nearly every day were 4.9 to 8.2 times more likely to attempt suicide and 3.3 to 10.8 times more likely to die within 30 days of the completed PHQ-9 compared to those without suicidal thoughts.(9)

Economic impact of the disease

Globally, depression was among the top three leading causes of non-fatal health loss, which contributed to 7.4% of all years lived with disability (YLD). Among the Filipinos, depression contributed to about 6.2% of YLD in 2015.(3)

The government does not subsidize outpatient cases, and patients need to pay 100% of the cost from their pocket.(10) The government's total expenditure on mental health as a percentage of total government health expenditure is 0.22%.(3)

Social impact of the disease

Depression influences various aspects of a patient's life, including work, social functioning, and health.(11) Moreover, severe depression and anxiety might lead to self-harm and suicide.

A qualitative study was conducted on the stigma experienced by people with mental health problems (PMHP). Participants emphasized that they were facing stigma because of cultural traits such as the perception of a mental health problem as a disease of the family. Moreover, individuals are concerned about the sense of shame, reduced social networks, and opportunities for PMHP, and their adherence to Asian values of conformity to norms where mental illness is considered unacceptable. These issues have threatened the economic survival of their entire family and exacerbated their mental health problem. Filipinos are also prevented from seeking help by their sense of resilience and self-reliance, as explored in qualitative studies.(12, 13)

3.15.2 Benefits and Harms of Screening Tests

There are benefits in screening for depression in adults in areas with adequate systems ensuring an accurate diagnosis. An evidence review(14) found nine trials (n = 3,814) that showed a higher number of remissions in those screened (RR 1.23, 95%CI 1.12 to 1.36).(15)

One study also showed gains from newly-identified depression with 47% remission *vs.* 28% at the end of 12 months (RR 1.71, 95%CI 1.13 to 2.57).(16)

Five studies reported quality of life as outcomes. The largest trial (n=1,356) reported a significant improvement in the mental component scale (MCS) of patients who went through a quality improvement program with a 12-month mean MCS score of 40.9 (SD 0.48) *vs.* 39.3 (SD 0.62), p=0.04.(17) The remaining four with 860 participants failed to show any significant difference between the control and the intervention. There were no trials that reported suicide-related outcomes. (15)

The magnitude of harm in screening for depression in adults is small to none.(15, 16)

3.15.3 Diagnostic Performance of Screening Tests

PHQ-9 is a depression module that scores each of the nine DSM-IV criteria from "0" (not at all) to "3" (nearly every day). Aside from screening and diagnosis, it allows for monitoring the condition. PHQ-2 measures the first two items of PHQ-9 and is scored the same way. Its primary purpose is to screen for depression among individuals who experience depressed mood and anhedonia over the past two weeks. Should the score signify signs of depression, i.e., scores of 3 or greater, PHQ-9 is performed. A Filipino version of the PHQ-9 is translated by the Mapi Research Institute from Pfizer and recently validated in a study(18) on Filipino migrant domestic workers in Macao.

There were systematic reviews that pooled the Patient Health Questionnaires' diagnostic accuracy (PHQ) as screening tools for depression. The pooled sensitivity of PHQ-9 is 78.8% (95%CI 77% to 80%), and the pooled specificity is 84.9% (95%CI 84% to 85%) at a cut-off score of 10 out of a possible score of 27.(19) The pooled sensitivity of PHQ-2, on the other hand, is 65.2%% (95%CI 64% to 67%); pooled specificity is 87.3% (95%CI 87% to 88%) at a cut-off score of 3 out of a possible score of 6.(20)

3.15.4 Cost Implication

Jiao and colleagues examined the cost-effectiveness of universal two-stage screening with the PHQ-2 and PHQ-9 in New York City, followed by collaborative care for those who were screened positive.(21) The incremental cost-effectiveness of the interventions over the average lifespan of a 20-year-old adult in NYC is approximately USD1,726 per QALY gained (95% plausible interval: cost-saving, USD10,594/QALY gained). They concluded that two-stage screening coupled with collaborative care for depression in the clinical setting appears to be significantly less expensive than most clinical preventive interventions, such as HIV screening in high-risk patients.(21) We did not find any studies conducted in the Philippines nor low and middle-income countries. Table 34 shows an annual screening cost per patient based on factors known in the local setting.

Table 34. Costing data on screening for depression

Parameter	Screening intervention

(A) Unit cost of screening intervention	Free[a]
(B) Other direct costs associated with the implementation of the proposed screening intervention	Patient cost = An average of 10 minutes per screening of a physician/nurse/social worker Php 29,277[b] = Php 30.50
(C) Annual screening cost per patient	Php 30.50

[a] PHQ questionnaire is downloadable for free
[b] Based on the monthly income of a physician/nurse/social worker with a Salary grade of 14

3.15.5 Ethical, Social, and Health Systems Impact (Equity, Acceptability, and Feasibility)

Ethical

Currently, mental health care is not readily available at the primary care level, and people in the local community could not resolve the PMHP's mental health crisis. For fair distribution to be in place, health infrastructures and human health resources should be available at the primary care level. (13)

Social

The stigma around people with depression and mental health issues is rampant, which creates a significant barrier for Filipino to seek professional help and recover.(22) A survey done in 16 countries cited that the Philippines had the second-highest proportion of citizens who agreed that PMHP should not be hired for a job even if they are qualified. Additionally, the belief that mental health problems can be transmitted among relatives pushes families of PMHP to deny the existence of mental health issues and people in the community to distance themselves from PMHP. It highlights the discrimination against people with mental health problems in the country which may prevent them from getting screened, as it might even threaten their economic survival. Without adequate stigma-reduction strategies in place, this could exacerbate mental health problems for PMHP.(13)

Health Systems

Mental healthcare in the Philippines faces continued challenges, including underinvestment, lack of mental health professionals, and underdeveloped community mental health services. Although the recent legislation (Mental Health Act) has —for the first time — provided a legal framework for the delivery of comprehensive mental healthcare, economic restrictions preventing people from accessing mental healthcare should be considered to enable the population to access appropriate care when required equitably. Increased investment is urgently needed to improve the training and recruitment of psychiatrists, nurses, psychologists, social workers, and other multidisciplinary team members.(1)

3.15.6 Recommendations from Other Groups

The National Institute for Health and Care Excellence (NICE) Guidelines maintain their 2013 recommendations for screening for those who may have depression followed by assessment and initial management by a competent professional. There was no mention of screening on asymptomatic healthy individuals.

The USPSTF recommends screening in the general adult population, including pregnant and postpartum women, with adequate systems to ensure accurate diagnosis, effective treatment, and appropriate follow-up.(15) The American College of Physicians (ACP) 2009 supported this recommendation.

The Canadian Task Force on Preventive Health Care (CTFPHC) 2013, on the other hand, does not recommend routine screening for depression in adults at average risk of depression or in adults in subgroups of the population who may be at an increased risk of depression due to the very low quality of evidence on the benefits and harms.(15) They have concerns about the potential harms of screening (e.g., false positives, unnecessary treatment, stigma and labeling, and appropriate use of limited resources). The task force is currently updating its guidelines and will release them by 2022.(23)

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3.16 Developmental Delay Screening Tools in Screening for Developmental Delay

RECOMMENDATION

Among asymptomatic apparently healthy children, we recommend against screening of developmental delay using developmental delay screening tools *(strong recommendation, low certainty evidence)*.

Considerations

The consensus panel considered the following when formulating this recommendation.

- All members of the panel agreed that developmental delay should be prioritized in periodic health examination.
- Majority agreed that screening for developmental delays has desirable effects when screening leads to early intervention services. However, the panel members were undecided on the issue of undesirable effects of these screening tests due to lack of direct evidence. Most of the panel members also perceived that the tests from the evidence presented are inaccurate.
- The recommendation was revised from using developmental delay screening tools among children with apparent delay and known risk factors to not using these tools among children who are apparently healthy and asymptomatic after the clarifications on the population presented in the evidence.

Remarks

Although the use of these standardized screening tools is not recommended, practitioners are not discouraged to use caregivers' report or routine physical examination and history taking which may include questions relevant in detecting possible delays in developmental milestones.

3.16.1 Burden of disease

Disease Frequency

Developmental delay is a condition in which a child is not achieving skills (i.e., not reaching developmental milestones; performance 1.5 standard deviations or more below age-expected norms) at the expected time.(1) Delays can occur in social/emotional, communication, motor, and/or cognitive domains. They can be transitory or, if they continue, can be diagnosed as a developmental disability. Developmental disability, on the other hand, refers to a group of conditions (formally diagnosed) due to impairment in physical, learning, language, or behavior areas.(2)

In the Philippines, the percentage of developmental delay ranged from 9.0 - 15.1 % among children between 0 - 96 months(3), which is roughly around 2-3 million (based on the latest population census of Filipino children)(4). Globally, approximately 52.9 million children

younger than five years had developmental disabilities. In the Philippines, an estimated 1,014,332 children below five years have some form of developmental disabilities.(5)

Severity of Disease

The Global Burden of Disease Study of 2016(5) estimated the years lived with disabilities (YLDs) among children with developmental disabilities and showed an increase from 3.8 million in 1990 to 3.9 million in 2016. These disabilities accounted for 13.3% of the 29.3 million YLDs for all health conditions among children younger than five years in 2016. In the Philippines, a similar trend was seen from 53,972 (1990) to 63,694 (2016), with 550.6 YLDs per 100,000 as of 2016.(5)

Natural course of the disease

Developmental delays can be transitory or may continue to be diagnosed as a developmental disability. Developmental disability is an umbrella term for a group of conditions that begin during the developmental period and usually last throughout a person's lifetime, resulting in impairments in physical, learning, language, and/or social-emotional areas(6); hence, screening early for developmental delays is essential.

Screening tools for developmental delays are the brief standardized tool that aids the identification of children at risk of a developmental disorder.(7) Screening provides an initial step towards confirmatory diagnostic tests or procedures to confirm a diagnosis of developmental disability and provision of needed early intervention services.

Children who are not screened for developmental delay earlier run the risk of various functional limitations due to impaired motor development(8), poor academic performance(8, 9), behavioral problems(9), delayed language development(10), and difficulties in adaptive functioning(8-11) to name a few.

Management of the disease

Supporting young children to achieve optimal developmental potential is a fundamental human right necessary for sustainable development.(12) The recommendations relate to 1) providing responsive care and activities for early learning during the first three years of life; 2) including responsive care and early education as part of interventions for optimal nutrition of infants and young children, and 3) integrating psychosocial interventions to support maternal mental health into early childhood health and development services. Specialists involved in managing children with developmental delay may include developmental pediatricians, neurologists, speech therapists, physical therapists, occupational therapists, and early intervention providers.(13)

Economic impact of the disease

An extensive literature documents the direct and indirect costs to families associated with childhood disabilities. However, these are mostly in developed and/or Western countries. Nevertheless, it can inform the Philippines of similar trends, albeit contextualized to the local settings. For example, estimates of the costs to families ranged from 108 to 8,472 USD per year.(14) These costs may depend on the type and severity of the condition and availability of health and social care benefits. Taking into account the indirect costs, the estimated

economic cost of raising a child with disability may go up to 30,500 USD per year. Lifetime cost has been postulated at around USD 1million in developed countries.(15)

Social impact of the disease

The social impact of developmental disabilities may be classified into those affecting the child and the families. Among Filipino families, the social implications of raising a child with a developmental disability have been suggested to influence parental stress(16), affect the quality of life of parents(17) and even the siblings(18). There are limited studies that explore the social impact of developmental disabilities among children. However, international studies provide scenarios for us to believe that developmental disabilities may influence how they participate and are accepted in the community and society.(19) Their families may eventually reject individuals with developmental disabilities, have limited socialization, are given up or institutionalized, limited community participation and mobility, and experience loneliness.

3.16.2 Benefits and Harms of Screening Tests

This review did not find any evidence from RCTs or controlled cohort studies to show that screening for developmental delay in children aged one to four years with no known developmental concerns improved health outcomes. There is no evidence that commonly used screening tools would consistently identify otherwise unrecognized cases. The low specificity of these tools would lead to a high proportion of false positives.(20) However, screening with standardized developmental delay screening tools: 1) increased the likelihood of identification of developmental delay; 2) increased the likelihood of the child receiving a referral for specialist or multidisciplinary evaluation for developmental delay (and reduced the time to referral for such evaluation); 3) increased eligibility for federally funded early intervention services; and better academic performance.(21) Nevertheless, what is known is that early screening leads to early confirmation of disability and intervention.(22) The evidence supports the effectiveness of early intervention services on various childhood outcomes across different developmental disabilities.(23-25)

The evidence on the benefits of universal screening for developmental delay among children between 1-4 years is scarce. The CTFPHC(20) found moderate evidence on universal screening benefits (leading to earlier referral to specialized services) on higher and earlier intervention rates among children screened for developmental delay.(26) They found universal screening, specifically for language delay, insufficient evidence on the benefit in academic performance.(27) Overall, while developmental screening may lead to an earlier referral to early interventions and specialized services, the evidence on the long-term benefits of universal screening in children 1-4 years is, at present, inconclusive.(20, 21, 28)

No direct evidence was found on the harms of screening and treatment for children with developmental delay.(21, 29) Nevertheless, the reviewed evidence recommends that developmental screening should be conducted for children with known risks or apparent developmental delay(10, 20, 30) and monitored using developmental surveillance tools regularly (i.e., 18 and 24 or 30 months)(10, 30) Children who screened positive should be

immediately referred to early intervention services to improve development and academic performance.(10, 20, 30)

3.16.3 Diagnostic Performance of Screening Tests

The CTFPHC considered indirect evidence on the accuracy of screening tools used to assess developmental delay in children aged one to four years with no known developmental concerns based on one systematic review.(21, 29) They found evidence to support the accuracy of two screening tools (in primary care settings): Ages and Stages Questionnaire-36 (ASQ) and the Parents' Evaluation of Developmental Status (PEDS). (Table 35) The child's parent should answer both tools. Between the ASQ and PEDS, only the PEDS has a known Filipino version that can be used in the Philippine setting.

Table 35. Diagnostic accuracy of screening tests for developmental delay

Screening Test	Study Design	# of Studies & Sample Size	Results	Quality of Evidence (GRADE)
ASQ*	Cohort	4; 1,001	Sensitivity: 55.0% (95% CI: 47.1% to 66.7%) Specificity: 86.0% (95% CI: 38.6% to 94.3%) Positive Likelihood Ratio 4.2 (95% CI: 1.1 to 8.2) Negative Likelihood Ratio 0.61 (95% CI: 0.47 to 0.86)	LOW
PEDS	Cohort	1; 331	Sensitivity: 41.1% (95% CI: 24.7% to 59.3%) Specificity: 89.3% (95% CI: 85.1% to 92.5%) Positive Likelihood Ratio 3.8 (95% CI: 95% CI: 2.3 to 6.4) Negative Likelihood Ratio 0.66 (95% CI: 0.5 to 0.88)	VERY LOW

*Results reported for ASQ are medians

The quality of evidence ratings is mainly due to biases across studies, indirect evidence, and imprecision.(21, 28, 29) All of the evidence is from indirect evidence of single study outcomes (cross-sectional studies) and hence limited by lack of studies reporting the test properties' outcomes. The CTFPHC assessed the ASQ3 as having a moderate sensitivity but low specificity across age groups. In contrast, PEDS generally had either a low sensitivity or specificity depending on the age group when the cut-off of one atypical finding was used as a positive result.(20) When a cut-off of two abnormal findings was used as a positive result, in both cases, the specificity improved, but the sensitivity dropped to below acceptable levels. The GRADE quality of PEDS is lower than ASQ due to only having one study included for analysis, which can contribute to imprecision. Reference standards varied across studies.(20)

Table 36. Index tests and reference tests used in studies

Study	Indexed Test	Reference Test
Gollenberg 2009	ASQ	BSID-II
Limbos 2011	ASQ and PEDS	Bayley Scales of Infant Development; Wechsler Preschool and Primary Scale of Intelligence; Vineland Adaptive Behavior Scales; Preschool Language Scale
Rydz 2006	ASQ	BDI

Steenis 2015	ASQ	BSID-III

*ASQ = Ages and Stages Questionnaire; BSID= Bayley Scales of Infant Development; BDI= Beck Depression Index

In the Philippines, we found evidence on using a locally developed developmental monitoring tool, the Early Childhood Care and Developmental Checklist(31), currently being used by the Department of Social Welfare and Development and the Department of Education for children ages 0-5. No evidence supports its diagnostic accuracy and psychometric properties. However, the technical manual of the ECCD outlines its development, where the tool was tested in a sample of 10,915 Filipino children across different regions in the country.(32) The table below presents a summary of reviewed evidence on the available developmental screening tests.

Table 37. Description of screening tests for developmental delays

Screening Test	Author	Number of Items	Type of Test	Language	Administration Time	Cost
Ages and Stages Questionnaire[A]	Squires & Bricker, 2009	30 items (5 domains)	Parent-Answered	English	10-15 minutes	Training Assessment Test
Parent Evaluation of Development Status[A]	Glascoe, 1997	10 items (7 domains)	Parent-Answered	English, Tagalog; Visaya	5 minutes	Training Assessment Test
Early Childhood and Care Developmental Checklist[B]	Ledesma, 2002	109 items (7 domains)	Standardized Test *Administered by a trained individual	English, Tagalog (unofficial)	45 minutes	None

Note: A - intended to be a screening tool; B - intended to be a monitoring tool; developed and validated specifically for Filipino Children; can be administered by teachers, rural health midwives, child development and daycare workers, caregivers after being trained.

The current evidence recommends that: 1) validated developmental screening tools should be used, and 2) a parent-completed tool should be used initially instead of a directly administered tool.(20)

3.16.4 Cost Implication

The evidence did not find any studies on the question of cost-effectiveness and feasibility of screening for DD in preschool children aged 1 to 4 years.(20, 21, 29) Annual cost of screening for developmental delay per patient was estimated based on known factors in the country. (Table 38)

Table 38. Estimated annual cost of screening for developmental delay

Parameter	Screening Intervention
	Developmental Delay Screening Tools
Unit cost of screening intervention	Developmental screening on average can be estimated to be at PhP 240.75.(32)
Other direct costs associated with the implementation of the proposed screening intervention	● Training for health workers (per individual; can be done via online training)[1]: Php 9,052.50 ○ Roughly, it is estimated that the training for screening (1 BHW: 1 child): Php 146.00

	● Developmental Screening Complete Set[2] (PEDS- Filipino) 1 Pad Response Form (50 forms) and 1 Pad Score/Interpretation Forms (50 forms) at PhP 3177.90: Php 63.558
(A) Annual screening cost per patient	**Php 450.308** (PhP 240.75 + PhP 146.00 + PhP 63.558) **Php 450.308** ● (PhP 240.75 + PhP 146.00 + PhP 63.558)

3.16.5 Ethical, Social, and Health Systems Impact (Equity, Acceptability, and Feasibility)

Ethical

Disparities in overall health and well-being may stem in early childhood.(33) Stressors in early childhood can disrupt neurologic, metabolic, and immunologic systems, leading to poorer developmental outcomes. These stressors can result from vulnerabilities related to socio-economic disparities. Although health, social care, and education programs that serve young children and their families and communities offer opportunities to foster sensitive relationships and environments, these systems also fragment their efforts because of limitations that limit the age ranges they can serve and the types of services they can provide.(34) Exposure to hardship and stressors such as poverty, lack of protection and stability in the home setting, and lack of access to quality early education can have a negative effect on the development of young children.(33)

The health and social inequality affecting people with disabilities (PWD) in the Philippines has resulted in low participation (less than 2 percent) in the national government's conditional cash transfer program.(35) Possible reasons for the low level of involvement are: 1) the Filipino culture of disability; 2) the omission of PWDs from the initial development of the Poverty Reduction National Housing Targeting Scheme, the framework responsible for identifying beneficiaries of the program; and 3) conditions that are not significant and sensitive to PWDs.

Likewise, the language in which developmental delay screening tools are presented should be considered. The English language is commonly used in developing screening tools. Children from families with limited English proficiency can face socio-economic conditions related to increased developmental delays and diminished involvement in early care and education programs.(36) Thus, it has been suggested that improved translation and interpretation resources may decrease disparities. However, there are limited available Filipino translations of assessment tools used by rehabilitation professions(16), let alone developmental delay screening tools.

Social

Disability-related health and social interventions in the Philippines could be more difficult due to the cultural structure of disability.(35) The community continues to be significantly reflected in the Filipino household in recognizing disabilities. The country's apparent poverty and the Filipinos' religious values gave rise to the option of finding alternative types

of medicine instead of medical assistance. Active health-seeking habits may be undermined if personal values influence the external attitudes of families. Lack of recognition of the disorder and explicit cooperation could lead families to hide and separate from the group, making it more difficult for disability advocates to locate them extensively and assist them.

Health Systems

Implementing a universal screening intervention program in the Philippines will need to have a thorough understanding of the rehabilitation process and the issues surrounding it. Rehabilitation, in general, is considered tertiary and specialized care; thus, universal screening for developmental delay will necessitate a primary care approach(37), which has been followed in the Philippines since the 1970's.(38) The screening for the developmental delay has been part of a community-based rehabilitation approach.(38) This entails training barangay health workers to become community-based rehabilitation workers who can screen community members, including young children who may have developmental delays. (39) It can be seen as a cost-effective approach to implementing developmental delay screening in young children since evaluation by rehabilitation professionals (i.e., physical therapists, occupational therapists, speech therapists, physiatrists, developmental pediatricians) can be costly.

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4. RESEARCH IMPLICATIONS

Many research questions from the identified clinical questions in this CPG were unanswered in terms of benefits and harms of screening, equity, applicability, and feasibility. Direct evidence is still lacking to aid in providing definite recommendations for screening certain conditions using the tests. Screening for anemia using hemoglobin and hematocrit, screening CAD using resting ECG, screening for developmental delay using standardized tools, screening for a lipid disorder, screening for PTB using chest x-ray are screening strategies that lack direct evidence to ascertain their benefits among the general population.

Generating direct evidence (screening *vs.* no screening) may be difficult. Because of this challenge, in some instances, establishing the diagnostic performance of tests as indirect evidence can be adequate. However, specific tests' accuracy in detecting early diseases and preventing them from developing into a chronic or more severe state is still not investigated. For example, there are still no studies showing diagnostic performance of a (1) routine CBC in diagnosing iron deficiency anemia, (2) resting ECG in apparently healthy individuals or those with risk factors for CAD, and (3) serum creatinine in identifying CKD among patients. Psychometric properties of some standardized tools used to detect developmental delays such as ECCD among apparently healthy children have not been established even if the government currently uses them in the primary care setting.

Conducting studies on some cases, such as high-risk sexual behavior among adults and adolescents, is also challenging; thus, they may not always be available. It poses ethical concerns in generating evidence from research due to reports of breaches of confidentiality. Other issues that need ethical safeguards in the studies are handling possible incidental reports of rape.

There have been cost-effectiveness studies available for screening the diseases included in this CPG, but most of them are conducted in Western countries. For conditions with a burden that has been recently increasing, such as depression and developmental delays, cost-effectiveness research is still not adequately investigated in LMICs.

Social science research also plays a vital role in examining the impact of the diseases. However, few qualitative studies were found to provide a holistic view of the impact of screening for some conditions. For example, although there have been cases of suicide rates because of the negative impact of being labeled as obese in women of reproductive age in other countries, it has not been examined in the Philippines. Qualitative studies can also provide information on motivators or determinants among the general population in participating in a screening program despite the probable harm of stigma and mislabeling afterward.

Examining needs and monitoring implementation of screening programs were also found to be not well-established even if, in some conditions, guidelines and programs are already in place. Some examples are capacity mapping for screening depression at the community level

and the effects of screening acute malnutrition. Perspectives and experiences of clinical practitioners and other stakeholders directly involved in screening programs are rarely reported in studies.

Many research questions emerged from collating the evidence for this CPG and can be explored further. Filling in these gaps can provide a clearer picture of the impact of screening programs using previously mentioned tests and may influence the recommendations for updating this guideline.

5. DISSEMINATION AND IMPLEMENTATION

A full copy of this document will be sent to the Department of Health for transmittal and publication. The Disease Prevention and Control Bureau will transmit copies of this CPG to the Philippine Health Insurance Corporation (PHIC) and health maintenance organizations (HMOs) and NGOs involved in a periodic health examination.

The DOH planned to develop a simplified version of this CPG and made it available in the format that will be ready for reproduction and dissemination to the patients in different health care settings. It will also be available for interested parties who might visit the DOH website.

6. APPLICABILITY ISSUES

The PHEX Task Force accentuates some caveats of this CPG using equity and applicability lenses. Comprehensive history taking, physical examination, and monitoring are essential parts of evaluating risk factors and the probability of developing diseases. This CPG does not necessarily supersede the consumers' (i.e., health professionals, hospital administrators, employers, payors, patients) values, settings, and circumstances.

Although this CPG intends to influence the direction of health policies for the general population, it should not be the sole basis for recreating or abolishing practices that aim to improve the health conditions of many Filipinos, particularly those part of the workforce.

7. UPDATING OF THE GUIDELINES

The recommendations herein shall hold until such time that new evidence on screening, diagnosing or managing various risk factors and diseases emerges and contingencies dictate updating this Philippine Guidelines on Periodic Health Examination. This guideline will be updated after 3 years.