PHILIPPINE GUIDELINES on PERIODIC HEALTH EXAMINATION (Phase 3)

Screening for Infectious Diseases

PERIODIC HEALTH EXAMINATION TASK FORCE 2022-2023

3 October 2023

Disclaimer and Contact Information

The clinical practice guideline was created for general practitioners, specialists and allied health professionals who render primary care. The Department of Health (DOH) encourages adherence to this CPG. However, variabilities exist in disease manifestations, characteristics, and values and preferences of individuals. Hence, the recommendations written herein should not restrict clinicians from using their clinical judgment and considering a patient's individual needs and preferences in decision-making.

Payers and policymakers, including hospital administrators and employers, who can utilize this CPG should not consider conformance or absence thereof as the sole basis for granting or denying financial assistance or insurance claims. Recommendations from this guideline should not be treated as strict rules upon which to base legal action.

Developers of this CPG are aware of its limitations. Evidence summaries were based on the best available scientific evidence at the time of its formulation. However, new evidence that emerged after CPG creation may affect its validity and applicability in the future.

Contact Us

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Participating Societies, Organizations, Agencies and/or Institutions

List of Abbreviations

AAFP	American Academy of Family Physicians
ADA	American Dental Association
AIDS	Acquired Immunodeficiency Syndrome
ALT	Alanine transaminase
AO	Administrative Order
aOR	Adjusted odds ratio
ART	Anti-Retroviral Therapy
ASB	Asymptomatic bacteriuria
AST	Aspartate transaminase
ATS	American Thoracic Society
CCT	Controlled clinical trial
CDC	Centers for Disease Control and Prevention
CFU	Colony-forming units
CI	Confidence Interval
CLIA	Chemiluminescent immunoassay
CP	Consensus Panel
CPG	Clinical Practice Guideline
CrI	Credible interval
CT	*Chlamydia trachomatis*
CTFPHC	Canadian Task Force on Preventive Health Care
DAA	Direct-acting antiviral
DALY	Disability adjusted life-years
DCOI	Declaration of Conflict of Interest
DMFS	Decayed, Missing, Filled, and Sound tooth surfaces
DMFT	Decayed, Missing and Filled Teeth
DOH	Department of Health
EIA	Enzyme immunoassay
ERE	Evidence Review Expert
ESCMID	European Society of Clinical Microbiology and Infectious Diseases
EtD	Evidence-to-Decision
FECT	Formalin ether concentration technique
FTA-ABS	Fluorescent Treponemal antibody absorbed test
GI	Gastrointestinal
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation
HAV	Hepatitis A virus
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HR	Hazard ratio
ICDAS	International Caries Detection and Assessment System
ICER	Incremental cost-effectiveness ratio
ICU	Intensive Care Unit
IDSA	Infectious Diseases Society of America

IGRA	Interferon-gamma release assay
INH	Isoniazid
LIA	Line immunoassay
LTBI	Latent Tuberculosis Infection
MBIA	Multiplex bead immunoassay
MSM	Men who have sex with men
NAAT	Nucleic acid amplification test
NG	*Neisseria gonorrhoeae*
NHS	National Health Service, UK
NICE	National Institute for Health and Care Excellence
NNH	Number Needed to Harm
NNS	Number Needed to Screen
NTCA	National Tuberculosis Controllers Association
OC	Oversight Committee
OR	Odds ratio
PCR	Polymerase chain reaction
PHEX	Periodic Health Examination
PI	Periodontal instrumentation
PICO	Population, Intervention, Comparator, Outcome
PID	Pelvic inflammatory disease
PLHIV	People living with HIV
PSMID	Philippine Society for Microbiology and Infectious Diseases
PWID	Persons who inject drugs
QALY	Quality-adjusted life years
RAgT	Rapid Antigen Test
RCT	Randomized controlled trial
RDT	Rapid diagnostic tests
RIF	Rifampin
RPR	Rapid Plasma Reagin
RPT	Rifapentine
RR	Relative Risk
RT-PCR	Reverse Transcriptase Polymerase Chain Reaction
SC	Steering Committee
SMART	Systematic meaningful asymptomatic repeated testing
STH	Soil-transmitted helminths
STI	Sexually transmitted infection
SVR	Sustained virologic response
TB	Tuberculosis
TPPA	Treponema pallidum particle agglutination
TST	Tuberculin skin test
UAV	Unprotected anal and vaginal intercourse
USPSTF	United States Preventive Services Task Force
UTI	Urinary tract infection
VDRL	Venereal Disease Research Laboratory
WHO	World Health Organization
WTP	Willingness to pay

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Executive Summary

This CPG is a set of eighteen (18) recommendations on screening asymptomatic, apparently healthy children and adults (see Table 1) for infectious diseases (ID) in general; specific diseases include: syphilis, chlamydia and gonorrhea, asymptomatic bacteriuria, Hepatitis A, Hepatitis C, HIV, dental infections, COVID-19, latent tuberculosis, and intestinal parasitism. The guideline is intended to be used by general practitioners and specialists in the primary care setting, allied health practitioners, policy makers, employers and administrators, funders of healthcare, other stakeholders in the health industry, and even patients. Through these recommendations, we aim to identify individuals with latent infections or early stage or those who are at risk for these diseases; to facilitate treatment; to apply preventive measures; and to improve overall outcomes for individuals and society as a whole.

The guideline development process had four general steps: (1) identification of priority research questions; (2) evidence synthesis and analysis; (3) formulation of the recommendations based on the balance of benefit, harm, values and preferences; and (4) implementation and evaluation. The process followed the GRADE approach (Grading of Recommendations, Assessment, Development, and Evaluation) including GRADE Adolopment, a systematic process of adapting evidence summaries, and the GRADE Evidence to Decision (EtD) framework.

The recommendations in this CPG shall hold and will be updated after 3 to 5 years or when new evidence arise.

Table 1. Summary of recommendations of screening for Infectious Diseases

Recommendations	Strength of recommendation	Certainty of Evidence
Question 1: Should screening for latent syphilis be routinely done among asymptomatic, apparently healthy adolescents and adults?		
Among asymptomatic, apparently healthy non-pregnant adolescents and adults, we suggest against routine screening for syphilis.	Weak	Very low
Among high-risk* asymptomatic, apparently healthy non-pregnant adolescents and adults, we recommend screening for syphilis every 6 to 12 months using rapid plasma reagin (RPR) or venereal disease research laboratory (VDRL) tests.	Strong	Moderate
Among asymptomatic, apparently healthy pregnant adolescents and adults, we recommend screening for syphilis as early as possible during pregnancy using rapid plasma reagin (RPR) or venereal disease research laboratory (VDRL) tests.	Strong	Low
Among high-risk* asymptomatic, apparently healthy pregnant adolescents and adults, we recommend screening for syphilis as early as possible during pregnancy, at 28 weeks, and at delivery using rapid plasma reagin (RPR) or venereal disease research laboratory (VDRL) tests.	Strong	Low
Question 2: Should screening for gonorrhea and chlamydia be routinely done among asymptomatic, apparently healthy adolescents and adults?		
Among asymptomatic, apparently healthy non-pregnant adolescents and adults, we suggest against routine *Chlamydia trachomatis* and *Neisseria gonorrhoeae* screening.	Weak	Very low
Among high-risk* asymptomatic, apparently healthy non-pregnant adolescents and adults, we recommend *Chlamydia trachomatis* and *Neisseria gonorrhoeae* screening using nucleic acid amplification test.	Strong	Low
Question 3: Should urinalysis or urine culture be done annually for screening for urinary tract infection among asymptomatic, apparently healthy adults?		

Among asymptomatic, apparently healthy adults, we suggest against screening for asymptomatic bacteriuria.	Weak	Very low
Among asymptomatic, apparently healthy pregnant women, we suggest screening for asymptomatic bacteriuria using urine culture.	Weak	Very low
Question 4: Should screening for Hepatitis A be routinely done among asymptomatic, apparently healthy adults?		
Among asymptomatic, apparently healthy adults, we suggest against screening for Hepatitis A.	Weak	Very Low
Question 5: Should hepatitis C screening be routinely done among asymptomatic, apparently healthy adults?		
Among asymptomatic, apparently healthy adults, we recommend against routine screening for Hepatitis C.	Strong	Very low
Among high risk* asymptomatic, apparently healthy adults, we recommend screening for Hepatitis C using serum anti-HCV.	Strong	Very low
Question 6: Should screening for HIV be routinely done among asymptomatic, apparently healthy adolescents and adults?		
Among asymptomatic, apparently healthy adolescents and adults, we recommend against routine screening for HIV.	Strong	Very low
Among high-risk* asymptomatic, apparently healthy adolescents and adults, we recommend HIV screening using a rapid diagnostic test.	Strong	Very low
Question 7: Should screening for dental infections (dental caries, periodontal diseases) be done for apparently healthy adults?		
Among asymptomatic, apparently healthy adults, we recommend annual screening for dental infections through visual inspection.	Strong	Very low
Question 8: Should COVID-19 screening test be done among asymptomatic, apparently healthy adults?		
Among asymptomatic, apparently healthy adults, we recommend against universal COVID-19 screening.	Strong	Very low
Question 9: Should screening for latent TB be done for asymptomatic apparently healthy adults?		

Among asymptomatic, apparently healthy adults, we suggest against screening for latent TB.	Weak	Very low
Among asymptomatic, apparently healthy adults, who are at high risk for TB infection, (i.e., close contacts), we suggest screening for latent TB using TST or IGRA.	Weak	Very low
Question 10: Should screening for intestinal parasitism be done among asymptomatic, apparently healthy children and adults?		
Among asymptomatic, apparently healthy children and adults, we suggest against routine screening for intestinal parasitism.	Weak	Very low

1. Introduction

The Philippine Guidelines on Periodic Health Examination (PHEX) was a CPG published in 2004.[1] It was a comprehensive guide on screening interventions committed to providing early prevention services for apparently healthy Filipinos. It was the first to offer evidence-based recommendations for screening, made possible through the combined effort of 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 (USPSTF), but tailored to the Philippine setting.

The process of updating this guideline commenced in 2021 in time to support the Universal Health Act [2], which aims to provide all Filipinos access to quality and affordable medical services starting with primary care benefits. The task of updating the PHEX was divided among several task forces, with each task force corresponding to a particular disease or risk factor.

This manuscript is dedicated for the update of recommendations on screening for infectious diseases. In this CPG, health screening aims to identify individuals with latent infection and those at risk for developing these diseases.

Infectious diseases are illnesses caused by pathogens (i.e., bacteria, viruses, fungi, parasites) or their toxic products, which can be transmitted from an infected host or the environment to a susceptible host. [3] Implementing effective screening programs is essential due to: first, infectious diseases have a significant impact on community health, with outbreaks capable of spreading rapidly and affecting a large number of individuals; and second, primary care providers have a unique opportunity to consider individual risk factors, demographics and local epidemiologic data thus they can tailor screening effort, identify infections early, initiate timely intervention and prevent further transmission within the community as well as reach individuals who may not regularly seek specialized healthcare services.

The steering committee prioritized which infectious diseases should be screened for this CPG, taking into account the following factors:

1. Burden of disease: based on the 2021 morbidity and mortality data [4] which included tuberculosis, pneumonia and COVID-19;
2. Severity of the disease and its potential to cause severe complications or death, especially if left undetected and untreated, such as HIV and urinary tract infection in pregnant patients;
3. Diseases that spread easily from person to person may require higher priority for screening, like sexually transmitted diseases;
4. Availability of effective prevention strategies, such as vaccination or behavior modification;
5. Ability to go into latency or asymptomatic carriers and could potentially lead to loss of productivity and opportunity cost such as dental infection;
6. Specific population groups that are at higher risk due to factors like age, occupation;

7. Potential impact of screening on public health, including the potential to reduce outbreaks, improve herd immunity, and decrease the overall disease burden;
8. Diseases that can be feasibly screened given the available resources that offer evidence-based significant benefits to improve patient outcomes;
9. And to prevent overdiagnosis that can lead to unnecessary medical interventions, irrational antimicrobial use, and cause anxiety and distress to individuals.

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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2. Objective, Scope, Target population and Target users

Objective

The objective of this clinical practice guideline is to provide evidence-based recommendations for the screening of asymptomatic, apparently healthy adolescent and adult Filipinos for infectious diseases at the outpatient setting, using appropriate scientific information while considering the economic implications of diagnostic tests and treatment.

Scope

The CPG shall cover screening and risk assessment of the following infectious diseases: syphilis, chlamydia and gonorrhea, asymptomatic bacteriuria, Hepatitis A, Hepatitis C, HIV, dental infections, COVID-19, LTBI, and intestinal parasitism. Although evidence on linked management is cited, the guideline does not make any recommendations for treatment of the infectious diseases discussed here.

The key clinical questions addressed by this CPG include:

Question 1. Should screening for latent syphilis be routinely done among asymptomatic, apparently healthy adolescents and adults?

Table 2. PICO table for Question 1

Population	Asymptomatic, apparently healthy adolescents and adults
Intervention	Syphilis screening
Comparator	No screening
Outcomes	Incidence of syphilis, syphilis-related morbidity and mortality, adverse events of screening, stigma reduction

Subgroups	Age group, commercial sex worker, men who have sex with men, those with high-risk sexual behavior, pregnant women

Question 2. Should screening for gonorrhea and chlamydia be routinely done among asymptomatic, apparently healthy adolescents and adults?

Table 3. PICO table for Question 2

Population	Asymptomatic, apparently healthy adolescents and adults
Intervention	Gonorrhea and Chlamydia screening
Comparator	No screening
Outcomes	Incidence of gonorrhea or chlamydia infection, infection-related morbidity and mortality, adverse events, stigma reduction
Subgroups	Age group, commercial sex worker, MSM, those with high-risk sexual behavior

Question 3. Should urinalysis or urine culture be done annually for screening for urinary tract infection among asymptomatic, apparently healthy adults?

Table 4. PICO table for Question 3

Population	Asymptomatic, apparently healthy adults
Intervention	Urinalysis or urine culture
Comparator	No screening
Outcomes	Incidence of UTI, cost of testing/treatment, adverse events, rational use of antibiotics, antimicrobial resistance
Subgroup	Pregnant women
Subgroup Outcomes	Incidence of acute pyelonephritis, premature rupture of membranes, low birth weight, preterm delivery

Question 4. Should screening for Hepatitis A be routinely done among asymptomatic, apparently healthy adults?

Table 5. PICO table for Question 4

Population	Asymptomatic, apparently healthy adults
Intervention	Hepatitis A screening
Comparator	No screening
Outcomes	Incidence of Hepatitis A, Hepatitis A-related morbidity and mortality, hospitalization, adverse events, impact on vaccination rates
Subgroups	Population at risk - food handlers, healthcare workers, travelers, daycare workers

Question 5. Should hepatitis C screening be routinely done among asymptomatic, apparently healthy adults?

Table 6. PICO table for Question 5

Population	Asymptomatic, apparently healthy adults
Intervention	Hepatitis C screening
Comparator	No screening
Outcomes	Incidence of Hepatitis C, Hepatitis C-related morbidity and mortality, incidence of liver cancer, adverse events
Subgroups	People who inject drugs (PWIDs), MSM, commercial sex workers

Question 6. Should screening for HIV be routinely done among asymptomatic, apparently healthy adolescents and adults?

Table 7. PICO table for Question 6

Population	Asymptomatic, apparently healthy adolescents and adults
Intervention	HIV screening
Comparator	No screening
Outcomes	Incidence of HIV, HIV-related morbidity and mortality, incidence of opportunistic infections, adverse events, stigma reduction, adverse events
Subgroups	Age group, commercial sex worker, MSM, PWIDs, those with high-risk sexual behavior, blood donors, migrant workers

Question 7. Should screening for dental infections (dental caries, periodontal diseases) be done for apparently healthy adults?

Table 8. PICO table for Question 7

Population	Asymptomatic, apparently healthy adults
Intervention	Screening for dental infection, frequency: once a year, linked intervention: antibiotic use, tooth extraction
Comparator	No screening
Outcomes	Incidence of dental infection, dental caries, periodontal diseases

Question 8. Should COVID-19 screening test be done among asymptomatic, apparently healthy adults?

Table 9. PICO table for Question 8

Population	Asymptomatic, apparently healthy adults
Intervention	SARS-CoV-2 Rapid Antigen Test (RAgT), SARS-CoV-2 Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR)
Comparator	No screening
Outcomes	COVID-19 related-mortality and morbidity, hospitalization, incidence of COVID, outbreak, adverse event of testing, stigma of testing, prevention of transmission, quarantine and isolation rates, early initiation of treatment
Subgroups	High-risk groups

Question 9. Should screening for latent TB be done for asymptomatic apparently healthy adults?

Table 10. PICO table for Question 9

Population	Asymptomatic, apparently healthy adolescents, and adults
Intervention	PPD Test, IGRA
Comparator	No screening
Outcomes	Incidence of TB, TB-related mortality and/or morbidity, infection prevention and control in different settings, adverse events, prevention of transmission, isolation rates, early initiation of treatment
Subgroups	Age group, smokers, household contacts of TB cases

Question 10. Should screening for intestinal parasitism be done among asymptomatic, apparently healthy children and adults?

Table 11. PICO table for Question 10

Population	Asymptomatic, apparently healthy children and adults
Intervention	Fecalysis, Kato-Katz technique, FECT, scotch tape swab technique
Comparator	No screening
Outcomes	Incidence of parasitism, adverse events, morbidity & mortality related to intestinal parasitism
Subgroups	Age group; special population- food handlers

Target Population

All recommendations are intended for asymptomatic, apparently healthy individuals. The population of interest for the recommendation for syphilis, gonorrhea and chlamydia, and HIV are for adolescents and adults; the recommendations for intestinal parasitism are for children and adults; the recommendations for asymptomatic bacteriuria (ASB), Hepatitis A, Hepatitis C, dental infections, COVID-19, and LTBI are for adults only.

Target Users

The primary audience for this Clinical Practice Guideline (CPG) comprises primary healthcare providers including general practitioners, specialists, and other medical professionals. It also extends its utility to academic medical institutions and patients. In addition, the CPG aims to equip policymakers, labor force administrators, regulatory agencies, and both government and private financial and healthcare delivery institutions in the Philippines with essential tools and strategies that will enable them to facilitate prompt healthcare access and effectively mitigate the spread of infectious diseases.

3. CPG Development Methodology

3.1 Organization of the Process

The DOH outlined the guideline development process into four phases: (1) preparatory phase; (2) evidence synthesis; (3) conversion of the evidence to recommendations (EtD step); and (4) implementation and evaluation (8).

In the preparatory phase, the Task Force Steering Committee (SC) determined the CPG objectives, scope, target audience and clinical questions. The committee formed two other working groups, the technical working group (TWG) and the consensus panel (CP). The TWG consisted of evidence review experts (EREs) tasked to review previous CPG recommendations similar to clinical questions, appraise and summarize other existing evidence, and to draft an initial recommendation based on the collected evidence. Two evidence reviewers worked on each clinical question.

The CP was composed of multi-sectoral representatives of stakeholder groups with interest and expertise relevant to the clinical questions. To ensure fairness and transparency, the composition was guided by the DOH manual. Content experts and other key stakeholders (such as policymakers, patient advocates, allied medical practitioners), and physicians from different settings (e.g., public primary care, private

practice, occupational health) were invited to nominate representatives to the CP. The invited stakeholder groups were as follows:

- Philippine College of Physicians (PCP)
- Philippine Medical Association (PMA)
- Philippine Society for Microbiology and Infectious Diseases (PSMID)
- Philippine College of Chest Physicians (PCCP)
- Philippine Academy of Family Physicians (PAFP)
- Philippine Society of Gastroenterology (PSG)
- Philippine Society of Public Health Physicians (PSPHP)
- Philippine Society of General Internal Medicine (PSGIM)
- Philippine College of Occupational Medicine (PCOM)
- Philippine Alliance of Patient Organizations (PAPO)

The CP was tasked to (1) provide inputs on the clinical questions; (2) rate the critical and important outcomes; (3) review the evidence summaries developed by the EREs; (4) discuss relevant considerations revolving around the recommendations, particularly on the aspects of feasibility, acceptability, and equity; and (5) finalize the direction, strength, and wording of the recommendation(s) for each clinical question during en banc meetings.

While the SC facilitated the entire CPG by formulating the clinical questions, forming the working groups, and guiding the TWG in its tasks, its members had no direct participation in assessing and synthesizing the evidence, generating the evidence summaries and evidence-based draft recommendations, and voting on the final recommendations during the en banc meeting.

3.2 Evidence Summaries

The clinical questions were developed using the PICO (Population, Intervention, Comparator, and Outcome) format. The EREs searched for and appraised practice guidelines related to periodic health screening, including but not limited to those developed by the Canadian Task Force on Preventive Health Care, the USPSTF, the National Institute for Health and Care Excellence, and Philippine medical organizations. When a relevant CPG published within the last 5 years was deemed of good quality using the AGREE II tool, its evidence summaries were adapted and updated with recent evidence.

In the absence of relevant Clinical Practice Guidelines (CPGs), the EREs generated original evidence summaries for each clinical question. Each evidence summary covered direct evidence that highlighted the overall benefits of screening for relevant clinical outcomes. When direct evidence is not available, the approach shifted to evaluating the accuracy of screening tests and presenting the benefits and harms of initiating early treatment for individuals already affected by the condition. This thorough process aligns seamlessly with the multi-dimensional nature of health screening, which includes conducting screening tests on seemingly healthy populations, utilizing confirmatory tests for positive screening results, and proactively introducing early therapeutic measures to prevent the progression of clinical issues.[3] Other information that may facilitate decision-making were also presented in the evidence

summaries. These included the disease burden, cost of screening and early treatment, recommendations of other groups, availability and acceptability of the tests and of treatment, feasibility, and the effects of screening on healthy equity.

To generate the needed evidence, the EREs performed a systematic search through international and local electronic databases for data among asymptomatic apparently healthy children and adults (Population) who underwent screening or no screening for infectious diseases (Intervention and Comparison) to decrease hospitalization, morbidity and mortality, reduce stigma and antimicrobial resistance and prevent transmission (Outcomes). A summary of the search strategies can be found in the Appendices.

Relevant journal articles were critically appraised by two reviewers for directness, methodological validity, magnitude and precision of the results, and applicability. RevMan and STATA were used for the quantitative synthesis of effect estimates for critical and important critical outcomes. The certainty of the evidence for each outcome and the overall certainty of evidence for each question were assessed using the GRADE approach [2] through the GradePRO software. Based on the evidence of net benefit of screening for infectious diseases on identified specific outcomes and overall certainty of that evidence, a draft recommendation was made.

Table 12. 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

3.3 Formulation of the Recommendations

The evidence summaries and draft recommendations formulated by the ERE were presented to the CP for review and finalization during the en banc videoconference meetings. This process utilized the Evidence-to-Decision or EtD framework wherein the panelists considered the evidence and its certainty while looking through equity, applicability, and feasibility lenses (Table 13) to generate the final recommendations. To facilitate the discussions during the meetings, the CP members were given the evidence summaries and were asked to fill out an online EtD from prior to the en banc meetings. The results of the EtD survey were presented after the evidence summary during the meeting.

Table 13. Detailed considerations based on the EtD framework [4]

1. Is the problem a priority?
2. How substantial are the benefits?
3. How substantial are the harms?
4. What is the overall certainty of evidence?
5. What is the balance between benefits and harms?
6. How accurate is/are the test/s?
7. 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 that is guided by the test results?
8. How large are the resource requirements (costs)?
9. What is the certainty of the evidence of resource requirements (costs)?
10. Does the cost-effectiveness of the test favor the test or the comparison?
11. What would be the impact on health equity?
12. Is/are the test/s acceptable to key stakeholders?
13. Is/are the test/s feasible to implement?

The CP voted on the wording (whether for or against screening) and the strength of each recommendation during the online en banc meeting. A consensus was reached if 75% of all CP members agreed. If consensus was not reached, questions and discussions were encouraged and another round of voting was conducted. For all the questions, in this CPG, consensus was reached after one or two rounds of voting. The strength of each recommendation (i.e., strong or weak) was determined by the CP based on the certainty of the evidence and all the factors mentioned in Table 3. A strong recommendation means that the CP is “confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects”. When the trade-offs between benefit, harm and costs are uncertain either because of the quality of the evidence or because of evidence shows that the desirable and undesirable effects are closely balanced, a weak recommendation (or suggestion) is warranted.[5]

3.4 Managing Conflicts of Interest

The PHEX Central Steering Committee developed the procedure for evaluating conflicts of interest (COIs) of all members of the guideline and a COI committee was formed to review the information based on the declaration of COI form and the curriculum vitae. Both financial and academic COI were evaluated. Individuals are then classified according to the level of participation in the guideline development. Table 14 shows the options for managing the COI.

Table 14. COI Classification and Management

Classification	**Management**	
A	Participation with no constraints;	Allowed
B	Participation is allowed with minor constraints (eg – COIs declared aloud during panel discussions);	Broadcast
C	Participation is allowed with major restrictions (eg – disallowing voting);	Manageable with major constraints
D	Participation is not allowed	Disallowed

3.5 Planning for Dissemination and Implementation

In the initial phase of planning and dissemination and implementation, the guideline developers will direct its effort in developing a comprehensive strategy for the effective introduction of the practice guideline. The stakeholders and target audience will be identified to tailor the message appropriately. Various channels will be considered to effectively disseminate the manuscript. The CPG will undergo quality screening by the DOH Evidence Generation and Management Division for recognition and implementation as a National Practice Guideline by DOH and the Philippine Health Insurance Corporation (PHIC). Included in the initial phase is the incorporation of all the recommendations in a web-based mobile application accessible to the public. The evidence summaries and the full CPG manuscript will be posted online in the DOH website and in https://phex.ph. An abridged manuscript of the CPG will be published in the Acta Medica Philippina. This will also be published in the official websites of the participating organizations.

3.6 External Review

Upon completion of the final recommendations and the CPG manuscript, three external reviewers were invited to share their insights on the processes, the output, and the planned methods of dissemination of CPG. AGREE-Recommendation EXcellence (AGREE-REX) tool was used to guide the external reviewers in their review process. The SC considered the comments of the external reviewers and kept a written record for the rationale for modifying or not modifying the CPG in response to the reviewer's comments.

References

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4. Recommendation and Evidence Summaries

4.1 Screening for Syphilis

RECOMMENDATIONS

1. **Among asymptomatic, apparently healthy non-pregnant adolescents and adults, we suggest against routine screening for syphilis.** ***(Weak recommendation, very low certainty of evidence)***

   Considerations: A recommendation against routine screening for syphilis among apparently healthy asymptomatic non-pregnant adolescents and adults was based on the lack of benefit, feasibility issues, and high cost of screening for this target population.

2. **Among high-risk* asymptomatic, apparently healthy non-pregnant adolescents and adults, we recommend screening for syphilis every 6 to 12 months using rapid plasma reagin (RPR) or venereal disease research laboratory (VDRL) tests.** ***(Strong recommendation, moderate certainty of evidence)***

   **Definition of increased risk for syphilis from Burchell 2022: HIV-positive men*

   **Definition of increased risk for syphilis from other groups: men having sex with men, unprotected sex, persons living with HIV (PLHIV), sexual contact with known case of syphilis, commercial sex workers, sexual contact with persons from countries or communities with high prevalence of syphilis and syphilis-related morbidity, prior syphilis, born to a person diagnosed with syphilis in pregnancy, multiple sexual partners, and history of sex in conjunction with illicit drug use*

   Considerations: Screening for asymptomatic non-pregnant adolescents and adults at increased risk for syphilis was strongly recommended based on benefits and cost-effectiveness of screening in the target population. Definition of individuals at increased risk for syphilis was adopted from Burchell 2022 and from other recommending groups such as the US Centers for Disease Control, Public Health Agency of Canada, British Association for Sexual Health and HIV, and HIV Medicine Association of the Infectious Disease Society of America. The recommended frequency of testing at 6 to 12 months was based on one randomized controlled trial (Burchell 2022). Repeat testing every 6 to 12 months was strongly recommended as long as the individual remains at high-risk of having the infection (i.e., high-risk exposure or high-risk sexual behavior).

3. **Among asymptomatic, apparently healthy pregnant adolescents and adults, we recommend screening for syphilis as early as possible during pregnancy using rapid plasma reagin (RPR) or venereal disease research laboratory (VDRL) tests.** ***(Strong recommendation, low certainty of evidence)***

4. **Among high-risk* asymptomatic, apparently healthy pregnant adolescents and adults, we recommend screening for syphilis as early as possible during pregnancy, at 28 weeks, and at delivery using rapid plasma reagin (RPR) or venereal disease research laboratory (VDRL) tests.** ***(Strong recommendation, low certainty of evidence)***

   **Definition of increased risk for syphilis from CDC: lives in a community with high syphilis morbidity or is at risk for syphilis acquisition during pregnancy (drug misuse, STIs during pregnancy, multiple partners, a new partner, partner with STIs)*

Considerations: Screening for syphilis in pregnant adolescents and adults regardless of risk was strongly recommended based on large benefits in terms of reduction in pregnancy-related adverse outcomes and cost-effectiveness of screening in this target population. Definition of pregnant adolescents and adults at increased risk for syphilis infection was adopted from the US Centers for Disease Control. Testing as early as possible during pregnancy and repeat testing at 28 weeks and at delivery was strongly recommended due to potential continuous exposure of pregnant adolescents and adults who remained negative for syphilis. The panel further emphasized that pregnant adolescents and adults who tested positive for syphilis should be adequately treated and repeat testing is not needed after treatment unless there is continuous high-risk exposure.

4.1.1 Burden of Syphilis

Syphilis is a sexually transmitted disease caused by the spirochete *Treponema pallidum*. The manifestations of this disease are protean with different stages progressing over time in untreated individuals.[1-4] The World Health Organization (WHO) report on global sexually transmitted infection surveillance estimates that worldwide in 2016 there were 19.9 million prevalent cases of syphilis in adolescents and adults aged 15 to 49 years and 6.3 million new cases.[5] As of 2014, the median case rate was 17.2 cases per 100,000 females and 17.7 cases per 100,000 males.[6] The highest prevalence was reported in the WHO Western Pacific region at 93 cases per 100,000 adult population.[5,7]

Cases of syphilis are increasing worldwide especially among adolescents [8] and men who have sex with men (MSM).[9] Primary and secondary syphilis cases increased by 24.5% among 15–19-year-old and by 25.4% among 20-24 year old from 2014 to 2016 in the United States.[8] Syphilis and HIV have similar modes of transmission, and infection with one may enhance the acquisition and transmission of the other. Available data from the United States Centers for Disease Control and Prevention suggest that approximately 42 percent of MSM with primary and secondary syphilis are HIV infected, compared with 8 percent of men who have sex with women and 4 percent of women.[10] According to the Sexually Transmitted Disease Surveillance of the Centers for Disease Control in 2020, syphilis cases increased by 6.8% from the documented cases in 2000-2001 compared to 2019-2020 in the United States. Cases among males who have sex with men were documented to have decreased by 2.2% but their numbers are still significant composing 50% of the identified new cases of syphilis. A higher number of syphilis cases were identified among females with a 21% increase between 2019 and 2020 and a 147% increase from 2016 to 2020. Sexual transmission is also prevalent among heterosexual relationships and interventions to address this population is also imperative.[11]

In 2016, an estimated one million pregnant women were estimated to be infected with syphilis leading to over 350,000 adverse birth outcomes.[12] Compared to pregnant women without syphilis, pregnant women with syphilis are four times more likely to develop adverse outcomes such as stillbirths and neonatal morbidities.[13] Congenital syphilis is the result of transplacental transmission of the disease from pregnant women with untreated syphilis. Neonates with congenital syphilis may be asymptomatic at birth but may also present with nasal cartilage destruction, frontal bossing, bowing of the tibia, morbilliform rash, rhinitis, and peg-shaped upper incisors. Complications include hepatosplenomegaly, seizures, and cranial nerve palsies.[14]

Cases of syphilis are increasing worldwide among pregnant women.[13,15] Congenital syphilis is also on the rise with a 15% increase from 2019 and a 254% increase from 2016 reflecting an increase in the number of pregnant women with syphilis.[11] The United States Preventive Services Task Force (USPSTF) noted that while there was a decrease in the number of congenital syphilis from 2008 to 2012, cases increased significantly by 87% from 8.4 cases per 100,000 live births in 2012 to 15.7 cases per 100,000 live births in 2016.[16]

Local data is limited; according to the Philippine Health Statistics from 2019, the mortality rate of infections with a predominantly sexual mode of transmission, including syphilis, only accounted for 10 per 100,000 population.[17]

Early treatment is advocated worldwide to prevent complications of syphilis and limit disease transmission. Full recovery is achieved after appropriate treatment; however, long term complications are expected for untreated syphilis. Antibiotic administration with a single dose of intramuscular Benzathine Penicillin is still the treatment of choice for primary and early latent syphilis. It is easily accessible and available; hence, proper treatment is easy to provide once the disease is identified.[14]

4.1.2 Benefits and Harms of Syphilis Testing

We did not find studies on the effectiveness and safety of screening program for syphilis among asymptomatic, apparently healthy population. Studies comparing the incidence of syphilis between the use of screening tests and without screening tests were also not available.

Syphilis case detection among HIV-positive men (***1 RCT, Moderate certainty of evidence***)
A pragmatic, stepped-wedge cluster randomized controlled trial (Enhanced Syphilis Screening Among HIV-Positive Men Trial or ESSAHM Trial) implemented an opt-out clinic-based intervention to routinize syphilis testing with HIV-load.[21] The trial aimed to determine the degree to which routinized syphilis screening would increase the detection of early syphilis. In four urban HIV clinics in Toronto and Ontario Canada, a total of 3,895 HIV-positive men were included in the study. Each clinic performed syphilis screening among individuals who reported risky sexual behaviors and symptoms (usual syphilis testing practice or control group) and then performed an opt-out syphilis screening along with scheduled HIV viral load monitoring (routinized syphilis testing or intervention group). The study utilized the following screening strategy: (1) screening with chemiluminescent immunoassay (CLIA), (2) additional testing was performed with rapid plasma reagin (RPR) test as well as *Treponema pallidum* particle agglutination (TPPA) test for confirmation of CLIA screening results, (3) for non-reactive or indeterminate RPR and TPPA, fluorescent treponemal antibody absorbance test was done. The trial was divided into five steps each lasting 6 months. The annualized proportion of men with newly detected early syphilis as well as early latent and latent of unknown duration increased from 0.009 in STEP 1, when all sites were in the control condition to 0.032 in STEP 5, when all sites had implemented the intervention with a corresponding time-adjusted OR of 1.44 (95% CI 0.90 to 2.31) to account for stepped-wedge cluster randomized controlled trial design. In the ESSAHM trial, syphilis screening increased substantially and resulted in testing every six months

but not every 3 months. When the trial was being designed in 2013, HIV viral load testing every 3 months was common practice; however, by the time the trial started in 2015, testing every six months had become standard.

Pregnant women and congenital syphilis (***1 Cohort study, Low certainty of evidence***)

A fair-quality observational study reviewed the implementation of free syphilis screening practices in Shenzhen, China from 2002 to 2012 (n = 2,441,237). The study implemented a medical model of prevention, treatment, management based on medical integration". The intervention included uptake of early antenatal care, universal access to active screening, reliable diagnosis and effective treatment, sexual partners tracking, detection and treatment, follow-up visits, health education to change risk behaviors, and information management of medical records. It was observed that the screening uptake for syphilis among pregnant women increased from 89.8% to 97.2%. The increase in syphilis screening was accompanied by a significant decrease in the adverse outcomes attributed to syphilis infection during pregnancy. The incidence of congenital syphilis decreased from 109.3 cases to 9.4 cases per 100,000 livebirths, the incidence of adverse pregnancy outcomes such as premature birth and low birth weight decreased from 42.7% to 19.2%, and the incidence of stillbirth and fetal loss decreased from 19.0% to 3.3%.[22]

Harms in terms of screening included inconsistencies with screening tests. Five studies documented false-positive result on treponemal tests while one study reported a false-negative result on a non-treponemal test. There are no available studies regarding the direct harm brought by treatment with penicillin (early treatment) among pregnant women.[23]

Outcomes	**No. of Studies** *(no. of participants)*	**RR (95% CI)**	**Net Benefit**	**Certainty of Evidence**
Newly Diagnosed Syphilis	1 RCT, 3,892 HIV-positive men followed over 30 months for a total of 7,471 person-years [21]	The annualized proportion of men with newly detected early syphilis as well as early latent and latent of unknown duration increased from 0.009 in STEP 1, when all sites were in the control condition to 0.032 in STEP 5, when all sites had implemented the intervention with a corresponding time-adjusted OR of 1.44 (95% CI 0.90 to 2.31) to account for stepped-wedge cluster randomized controlled trial design	Trend towards favoring screening	Moderate
Incidence of congenital syphilis	1 Cohort Study, 2,441,237 pregnant women [22]	The incidence of congenital syphilis decreased from 109.3 cases to 9.4 cases per 100 000 livebirths	Favors screening	Low
Adverse Pregnancy Outcomes	1 Cohort Study, 2,441,237 pregnant women [22]	The incidence of adverse pregnancy outcomes such as premature birth and low birth weight decreased from 42.7% to 19.2%, and the incidence of	Favors screening	Low

Outcomes	No. of Studies *(no. of participants)*	RR (95% CI)	Net Benefit	Certainty of Evidence
		stillbirth and fetal loss decreased from 19.0% to 3.3%		

4.1.3 Benefits and Harms of Early Intervention

A fair quality retrospective cohort study done in Jiangxi, China evaluated the pregnancy outcomes after treatment of maternal syphilis. A total of 4210 women were included in the study. Maternal syphilis was confirmed after testing positive for nontreponemal or treponemal tests. The pregnancy outcomes were compared between those treated and untreated for maternal syphilis as well as the difference between those adequately and inadequately treated. Adequate treatment of maternal syphilis was defined as two completed courses of penicillin at least 2 weeks apart with more than 28 days prior to delivery. The study also compared the pregnancy outcomes between those treated during the first trimester (less than 12 weeks age of gestation) versus those treated during the third trimester (>28 weeks age of gestation). The risk for stillbirth (adjusted odds ratio aOR 1.74, 95% CI 1.01-3.00, p=0.045), preterm birth (aOR 1.27, 95% CI 1.02-1.59, p=0.034), and infants with low birth weight (aOR 1.44, 95% CI 1.11-1.86, p=0.006) was higher among those with untreated maternal syphilis compared to those who were treated. Similarly, a higher risk for still birth (aOR 3.68, 95% CI 1.62-8.34, p=0.002), preterm birth (aOR 2.26, 95% CI 1.71-3.00, p<0.001), infants with low birth weight (aOR 2.23, 95% CI1.59-3.14, p<0.001), and a diagnosis of congenital syphilis (aOR 3.63, 95% CI 1.80-7.31, p<0.001) was documented among those inadequately treated versus those who were adequately treated for maternal syphilis. Lastly, a higher risk for stillbirth (aOR 4.48, 95% CI1.31-15.30, p=0.017), preterm birth (aOR 2.34, 95% CI 1.61-3.40, p<0.001), and infants with low birth weight (aOR 3.25, 95% CI 1.97-5.37, p<0.001) was noted among those who received treatment during the third trimester than those who received treatment during the first trimester of pregnancy.[24]

Outcomes	No. of Studies (no. of participants)	aOR (95% CI)	Net Benefit	Certainty of Evidence
Stillbirth	1 Cohort 4210 women [24]	Untreated vs treated 1.74 (95% CI 1.01-3.00, p=0.045)	Favors treatment	Low
		Inadequately vs adequately treated 3.68, 95% CI 1.62-8.34, p=0.002	Favors adequate treatment	Low
		Third trimester treatment vs first trimester treatment 4.48, 95% CI1.31-15.30, p=0.017	Favors first trimester treatment	Low
Preterm birth	1 Cohort 4210 women [24]	Untreated vs treated 1.27, 95% CI 1.02-1.59, p=0.034	Favors treatment	Low
		Inadequately vs adequately treated 2.26, 95% CI 1.71-3.00, p<0.001	Favors adequate treatment	Low
		Third trimester treatment vs first trimester treatment 2.34, 95% CI 1.61-3.40, p<0.001	Favors treatment	Low

Outcomes	No. of Studies (no. of participants)	aOR (95% CI)	Net Benefit	Certainty of Evidence
Low birth weight	1 Cohort 4210 women [24]	Untreated vs treated 1.44, 95% CI 1.11-1.86, p=0.006	Favors first trimester treatment	Low
		Inadequately vs adequately treated 2.23, 95% CI1.59-3.14, p<0.001	Favors adequate treatment	Low
		Third trimester treatment vs first trimester treatment 3.25, 95% CI 1.97-5.37, p<0.001	Favors first trimester treatment	Low
Congenital syphilis	1 Cohort 4210 women [24]	Inadequately vs adequately treated 3.63, 95% CI 1.80-7.31, p<0.001	Favors treatment	Low

Studies regarding outcomes with early treatment of syphilis among the non-pregnant population were not available.

4.1.4 Diagnostic Accuracy of Screening and Confirmatory Tests

There are two types of diagnostic tests for syphilis: Nontreponemal and treponemal tests. Nontreponemal tests measure the direct antibody against a lipoidal antigen. It is quantitative but non-specific. These tests include the venereal disease research laboratory test (VDRL) and the rapid plasma reagin test (RPR) which are inexpensive, may be used in disease severity monitoring, and are commonly used locally. Both only test positive after the appearance of the painless ulcer. Treponemal tests are qualitative assays that detect the immunoglobulins produced by the body against the disease. These are done using enzyme immunoassays or manual assays like fluorescent Treponemal antibody absorbed test (FTA-ABS), microhemagglutination assay for Treponema pallidum antibodies (MHA-TP), and *Treponema pallidum* particle agglutination assay (TPPA). These are used as confirmatory tests but are unable to monitor for disease severity. Syphilis is diagnosed when both the Nontreponemal and Treponemal tests are positive.[14]

Syphilis screening may be done through two algorithms: the traditional algorithm and reverse algorithm. The traditional algorithm employs the use of a Nontreponemal serology test followed by a Treponemal test for reactive specimens to confirm the diagnosis. It is cost-effective especially for resource limited settings, but it lacks specificity and relies on subjective interpretation. The reverse algorithm uses a Treponemal test first followed by a Nontreponemal test for reactive results. It is more efficient, less labor intensive, and has the ability to detect early disease, however, it has a high false positive rate in low prevalence populations and is more expensive.[18]

The high sensitivity and specificity of the different serologic exams are already established. Nontreponemal tests were evaluated in a systematic review consisting of several cross-sectional studies. VDRL had a sensitivity of 81.6% and specificity of 100% from 6 pooled studies, RPR had a sensitivity of 83.9% and specificity of 99.8% from 4 pooled studies. Among the Treponemal tests, FTA-ABS had a sensitivity of 98.1% and specificity of 96% from 3 pooled studies.[19] A cross sectional study reviewed the sensitivity and specificity of the Treponemal tests – TPPA had a sensitivity of 98.1% and specificity of 100%, Centaur-CIA had a sensitivity of 97.3%

and specificity of 95.5%, Trep-Sure EIA had a sensitivity of 98.5% and specificity of 82.6%, LIASON CIA had a sensitivity of 96.9% and specificity of 94.5%, Bioplex MBIA had a sensitivity of 96.9% and specificity of 96.7%, and INNO-LIA had a sensitivity of 96.9% and specificity of 98.5%.[20]

Population: High Risk Adults and Adolescents					
Condition: Syphilis					
Index test: **VDRL**					
Basis	Sensitivity (95% CI)	Specificity (95% CI)	Estimate of Effect per 1000 tested		Certainty of Evidence
6 cross sectional (N=3703) Tuddenham, 2020	81.6 (76.2-85.9)	100 (91.8-100)	62 (58-64)	13 (11-17)	High
Index test: **RPR**					
4 cross sectional (N=3143) Tuddenham, 2020	83.9 (79.9-86.8)	99.8 (99.4-100)	63 (60-65)	12 (10-15)	High
Index test: **FTA-ABS**					
3 cross sectional (N=2123) Park et al, 2019 Tuddenham, 2020	98.1 (96.7-98.9)	96 (76.3-99.4)	74 (73-74)	1 (1-2)	High
Index test: **TPPA**					
1 cross sectional (n=959) (Park et al, 2019)	95.4 (92.1–97.6)	100 (99.0–100)	19 (18-20)	1 (0-2)	Moderate
Index test: **Centaur CIA**					
1 cross sectional (n=959) (Park et al, 2019)	97.3 (94.6–98.9)	95.5 (93.0–97.3)	19 (19-20)	1 (0-1)	Moderate
Index test: **Trep-Sure EIA**					
1 cross sectional (n=959) (Park et al, 2019)	98.5 (96.1–99.6)	82.6 (78.4–86.1)	20 (19-20)	0 (0-1)	Moderate
Index test: **LIASON CIA**					
1 cross sectional (n=959) (Park et al, 2019)	96.9 (94.1–98.7)	94.5 (91.8–96.5)	19 (19-20)	1 (0-1)	Moderate
Index test: **Bioplex MBIA**					
1 cross sectional (n=959) (Park et al, 2019)	96.9 (94.1–98.7)	96.7 (94.4–98.2)	1 (19-20)	1 (0-1)	Moderate
Index test: **INNO-LIA**					
1 cross sectional (n=959) (Park et al, 2019)	96.9 (94.1–98.7)	98.5 (96.8–99.5)	19 (19-20)	1 (0-1)	Moderate

4.1.5 Cost Implication

There are no available studies on the cost-effectiveness of syphilis screening among pregnant and non-pregnant adolescents and adults in the Philippines. Cost effectiveness studies regarding implementation of syphilis screening among the healthy asymptomatic pregnant population and the high-risk population of males who have sex with males and those diagnosed with HIV has already been established. However, there is no data regarding the cost effectiveness of syphilis screening among the healthy, asymptomatic population.

A model regarding the cost and cost effectiveness of syphilis screening and treatment in pregnant women reviewed 8 different scenarios that could mimic the cost and health impact of syphilis. They found that syphilis screening and treatment showed significant net savings $12,261,250 compared to net costs $1,736,807 with an estimated 5,754-93,484 DALYs.[25] A model on the cost effectiveness of syphilis screening among males who have sex with males aged 15 to 64 years calculated that the cost per quality-adjusted life year gained from syphilis screening was less than $0 (cost-saving) compared to no screening, $16,100.[26]

Provided below are the costs of the available screening tests for syphilis.

Parameter	**Screening intervention**		**Confirmatory Test**
	RPR	***VDRL***	**TP-PA**
Unit cost of screening intervention in Philippine Peso (PHP)	100-350	100	400-1500

4.1.6 Patient's Values and Preference, Equity, Acceptability, and Feasibility

There are no available studies regarding the patient's values and preference, equity, acceptability, and feasibility towards syphilis screening among healthy asymptomatic adults and adolescents during the time of this review.

A feasibility, benefits, and cost-effectiveness study was done in Thai Nguyen, Vietnam from 2012 to 2014 regarding adding universal hepatitis B virus (HBV) and syphilis screening to the routine antenatal care services. Testing coverage for HIV, HBV, and syphilis was high at 98% with 69.5% of pregnant women being tested during the second trimester. Among those tested, 0.4% had HIV, 7.8% had HBV, and 0.03% had syphilis. Only one pregnant woman was diagnosed with syphilis. She was treated with penicillin at 24 weeks age of gestation, and her infant tested negative for congenital syphilis at 8 months of life.[27] The high rate of test coverage with the inclusion of HIV, HBV, and syphilis in the routine antenatal care provided the opportunity for early treatment and avoided the congenital transmission of these diseases including syphilis.

4.1.7 Recommendations from Other Groups

Syphilis screening for adults and adolescents who are diagnosed with HIV, males who have sex with males, and those with high-risk sexual practices is recommended by the US Preventive Task Force.

For non-pregnant adolescents and adults:

Group, Year of Recommendation	Recommendation
Centers for Disease Control and Prevention (CDC), 2021	Recommends at least annual screening for sexually active MSM with confirmatory testing for individuals with reactive serology. MSM at increased risk should be screened every 3 to 6 months. Persons living with HIV who are sexually active should be screened at the first HIV evaluation, and at least annually thereafter; more frequent screening may be appropriate based on individual risk behaviors and local epidemiology. The CDC also recommends opt-out syphilis screening in correctional facilities based on the local area and institutional prevalence. In short-term facilities, screening at entry might be indicated.
Public Health Agency of Canada, 2020	Recommends screening for anyone presenting with risk factors for syphilis to prevent complications, transmission, and reinfection. Risk factors included unprotected sexual activity, including MSM; sexual contact with a known case of syphilis; sex with someone from a country/region with a high prevalence of syphilis; prior syphilis, HIV infection, or other STI; born to a person diagnosed with infectious syphilis in pregnancy; or member of a vulnerable population.
British Association for Sexual Health and HIV (BASHH), 2016	Recommends screening with confirmatory testing for individuals with positive screening tests. Recommends repeat screening for syphilis 6 and 12 weeks after a single "high risk" exposure (unprotected oral, anal, or vaginal intercourse with homosexual man, multiple partners, anonymous sex in saunas and other venues, commercial sex worker, or sex partner linked with a country where the prevalence of syphilis is known to be high). In individuals at ongoing risk due to frequent "high risk" exposures as defined above, screening as part of routine sexual health check-ups for all STIs including HIV and others is recommended, usually every 3 months and informed by sexual history.
HIV Medicine Association, Infectious Diseases Society of America, 2013	Recommends that all patients living with HIV be screened for syphilis on initiation of care and periodically thereafter, depending on risk. Risk factors that may warrant more frequent testing (i.e., every 3 to 6 months vs. annually) include having multiple partners, a history of unprotected intercourse, a history of sex in conjunction with illicit drug use, methamphetamine use, or multiple sexual partners who participate in these activities.

From: United States Preventive Services Task Force 2022

The Centers for Disease Control (CDC), American Academy of Pediatrics (AAP), and the American College of Obstetricians and Gynecologists (ACOG) recommend that all pregnant women be screened for syphilis during the first prenatal visit, at 28 weeks age of gestation, and at delivery if at high risk for syphilis. Women at high risk for

syphilis infection include those living in high-prevalence communities, those living with HIV, and those with history of incarceration, or commercial sex.[16]

Group, Year of Recommendation	Recommendation
Centers for Disease Control, 2015	All pregnant women at the first prenatal visit Retest at 28 weeks age gestation and at delivery if at high risk (lives in a community with high syphilis morbidity or is at risk for syphilis acquisition during pregnancy [drug misuse, STIs during pregnancy, multiple partners, a new partner, partner with STIs]
American College of Obstetricians and Gynecologists (ACOG), 2021	Does not recommend routine screening for syphilis for women who are not pregnant.

From: United States Preventive Services Task Force 2022

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4.2 Screening for Chlamydia and Gonorrhea

RECOMMENDATIONS

1. **Among asymptomatic, apparently healthy non-pregnant adolescents and adults, we suggest against routine *Chlamydia trachomatis* and *Neisseria gonorrhoeae* screening. *(Weak recommendation, very low certainty of evidence)***

   Considerations: A recommendation against routine screening for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* among apparently healthy asymptomatic non-pregnant adolescents and adults was based on the lack of evidence to support screening and the high cost of screening in this target population.

2. **Among high-risk* asymptomatic, apparently healthy non-pregnant adolescents and adults, we recommend *Chlamydia trachomatis* and *Neisseria gonorrhoeae* screening using nucleic acid amplification test. *(Strong recommendation, low certainty of evidence)***

   **Definition of high-risk population: men with HIV infection, non-monogamous relationship without condom use, age<25 years with 2 or more sexual partners in the past year, sex partner with active or previous STI, with previous or coexisting STI, douching within the past year, commercial sex workers, cervical ectopy (30)*

   Considerations:
   - Screening for asymptomatic non-pregnant adolescents and adults at increased risk for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* was strongly recommended based on large benefits over small harms through a targeted screening approach in this population. The panel likewise highlighted that infections in women may be asymptomatic and are left untreated. This may result to transmission to others and may lead to serious complications (i.e., infertility). The panel also expressed the need to screen sexual partners.
   - No evidence was available on the frequency of testing, which was a common limitation in the included studies. *Chlamydia trachomatis* and *Neisseria gonorrhoeae* infections have short incubation periods at less than 14 days. By placing a set schedule for screening, more asymptomatic patients may be missed. The panel recommended that the decision to screen for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* will be based on the physician's risk assessment at the time of examination. If an asymptomatic individual is considered at high-risk for infection, then screening should be done.

4.2.1 Burden of Chlamydia and Gonorrhea infection

In 2019, Chlamydia trachomatis (CT) and *Neisseria gonorrhoeae* (NG) infection resulted to 2.1% and 2.2% of Disability-adjusted life years (DALYs) from all STIs excluding HIV.[1] Based on the Global burden of disease study, in the Philippines, Chlamydia infection led to 3.39 DALYs per 100,000 among 15–49-year-old individuals while gonorrhea infection led to 3.05 DALYs per 100,000.[2] The prevalence of chlamydia on that year was 1871.8 per 100,000 for both sexes while gonococcal infection had a prevalence of 516.8 per 100,000.[1]

Chlamydia and gonorrhea infections are often difficult to detect because majority of affected individuals are asymptomatic carriers, and in cases where symptoms do present, they are usually mild or non-specific especially in females.[3,4] If ever

symptomatic, affected people usually present with urogenital symptoms which in females, commonly as cervicitis and urethritis which manifest as vaginal discharge, intermenstrual bleeding, dysuria, and/or pyuria while males may manifest with urethritis and epididymitis which manifest as urethral discharge, dysuria, testicular pain and tenderness, and/or swelling of the epididymis.[4,5] Complications of untreated infection among women are more severe and include pelvic inflammatory disease (PID), infertility, complications of pregnancy, and chronic pelvic pain.[5] Gonococcal infection may lead to disseminated disease in 0.5-3% of affected individuals and may present with tenosynovitis, dermatitis, polyarthralgia or more severely as endocarditis, meningitis, and osteomyelitis. [4]

Diagnosis of urogenital infection is performed via getting swab samples from the endocervix or vagina of women or urethral swabs in man, or by using urine specimens from both. These samples may undergo culture (gold standard), antigen detection using immunofluorescence or enzyme immunoassays or nucleic acid amplifications tests (NAAT). [3] Uncomplicated chlamydial infection may be treated by either single dose azithromycin (1g) or doxycycline (100mg twice a day) for seven days.[3] Due to an increasing rate of antimicrobial resistance, treatment recommendation for uncomplicated gonococcal infection is ceftriaxone given as a single intramuscular (IM) dose.[6] Aside from causing similar symptoms, chlamydia and gonococcal infection coexist in a significant proportion of patients and increasingly so among HIV-infected patients hence, testing for both are usually done concomitantly. [4] One study done in the Philippine General Hospital showed that 33% of newly-diagnosed HIV patients had a concomitant *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae* infection. [7]

Females who commonly present asymptomatically benefit the most from screening and treatment by reducing their risk of complications and pregnancy-related adverse outcomes whereas the benefit of screening in males is to reduce infection, transmission, and prevent reinfection of sexual partners. [3,5]

4.2.2 Benefits and Harms of Screening

Results of evidence came from a meta-analysis done in 2021, with an updated search done on October 12, 2022. [11] No additional RCTs were added to the results of the cited meta-analysis. The meta-analysis included 5 randomized controlled trials (RCTs), one controlled clinical trial (CCT), and two cohort studies that reported on the clinical outcomes of PID, ectopic pregnancy, and infertility. Data included in this evidence review was only based on RCTs and CCTs. Additionally, we excluded one RCT because the design compared home sampling for CT and conventional sampling which is another method of screening. All studies included compared intervention groups that employed screening for CT infection compared to no screening or usual care (which is usually diagnosis and treatment of CT as per local practice.) No studies investigating NG was found.

Sub-group analysis was done based on study design into universal screening and acceptors of screening. The universal screening group composed of studies that used the intention to screen design i.e. regardless of whether subjects in the screening group submitted samples for testing or not, they were included in the analysis.(12-14) Acceptors of screening subgroup are those whose design involved a 100% screening

uptake made possible because either randomization happened after sample collection (immediate screening vs delayed screening) [15] or only participants with samples were analyzed [16]. For both designs, intervention group consisted of screening of participants as compared to control groups that did not undergo (immediate) screening. One study that used the intention to screen design was also separated into a different subgroup because it only included participants identified to have risk factors for CT infection after answering a questionnaire. [14]

Risk for Pelvic Inflammatory Disease (PID) (4 RCTs, 1 CCT, n= 231, 146)
Universal screening showed no difference in risk of developing PID compared to no screening (RR 1.05, 95% CI 0.66 to 1.66) however, universal screening for high-risk individuals showed less incidence of PID with an RR of 0.43 (95% CI, 0.21-0.90). Acceptors of screening on the other hand also showed no significant difference for PID risk (RR 0.81, 95% CI 0.61 to 1.07).

Risk for Infertility (1 RCT, 1 CCT, n=43, 533)
Only two studies showed evidence for infertility. No significant difference was noted among those universally screened (RR 1.15, 95% Ci 0.94-1.40) and the acceptors of screening (RR 0.66, 95% CI 0.14 to 3.06).

Risk for Ectopic pregnancy (1 RCT, 1 CCT, n=43, 533)
Screening for CT did not seem to decrease risk for ectopic pregnancy both among those universally screened (RR 1.03 95% CI 0.67- 1.60), and those who accepted screening (RR 1.19 95% CI 0.77-1.85).

Risk for Epididymitis (2 RCTs, n=94, 865)
Two studies employing universal screening showed no conclusive evidence of effect of screening to decreasing incidence epididymitis (RR 0.91, 95% CI 0.72-1.17).

Risk of Transmission of CT and NG (1 RCT, n=7,711)
One RCT showed screening had no effect on prevalence of CT transmission by having selected participants answer a survey form prior to randomization and after study intervention (risk difference 0.90, 95% CI 0.5-1.6).

Table 14. Summary of Findings for Benefits of Screening for CT and NG

Outcomes	No. of Studies *(no. of participants)*	Effect Estimate (95% CI)	Interpretation	Certainty of Evidence
Pelvic inflammatory disease				
Universal CT screening	2 RCTs *(n=198,088)*	RR 1.05 (0.66, 1.66)	Inconclusive	Very Low
Universal CT screening- High risk group	1 RCT *(n=2607)*	RR 0.43 (0.21, 0.90)	Benefit	Low
Acceptors of universal screening	1 RCT, 1 CCT *(n= 30,451)*	RR 0.81 (0.61, 1.07)	Inconclusive	Low
Ectopic pregnancy				
Offer of universal CT screening	1 RCT *(n=15, 459)*	RR 1.03 (0.67, 1.60)	Inconclusive	Very low

Outcomes	No. of Studies *(no. of participants)*	Effect Estimate (95% CI)	Interpretation	Certainty of Evidence
Acceptors of universal screening	1 CCT *(n= 28, 074)*	RR 1.19 (0.77, 1.85)	Inconclusive	Low
Infertility				
Offer of universal CT screening	1 RCT *(n=15,459)*	RR 1.15 (0.94, 1.40)	Inconclusive	Low
Acceptors of universal screening	1 CCT *(n= 28,074)*	RR 0.66 (0.14, 3.06)	Inconclusive	Very low
Epididymitis				
Universal CT screening	2 RCTs (n= 94,865)	RR 0.91 (0.72, 1.17)	Inconclusive	Moderate
Transmission of CT- prevalence				
Universal CT screening	1 RCT, Cluster *(n=7,711)*	RD 0.90 (0.5, 1.6)	Inconclusive	Low

In the meta-analysis, harm was investigated using mostly observational studies with one RCT referencing to serious adverse event from treatment during a screening intervention. This RCT (n= 4,574 receiving treatment) showed no adverse events.

Observational studies (10 uncontrolled cohort studies) investigated psychological harm from screening or from receiving a positive diagnosis after screening for CT or NG infection. Short term observation revealed that screening for CT had no effect on general anxiety (2 cohorts, n=2,319, low certainty) but may have some increase in anxiety for their or their partner's infertility, albeit not significant (2 cohorts, n=450, very low certainty) based on validated scales for anxiety and depression. In terms of experiencing stigma, CT screening was shown to not have a significant effect in stigma manifested as low levels of overall self-esteem (2 studies, n=1990, low certainty), but some may experience emotions related to stigmatization such as embarrassment or disapproval of social circles, but the severity and duration of these symptoms are unknown.

Table 15. Summary of Findings for Harms of Screening for chlamydia and gonorrhea

Harms	No. of Studies *(no. of participants)*	Results	Interpretation	Certainty of Evidence
General anxiety	2 observational *(n=2,139)*	Lower during testing than before receiving invitation to test (change of -0.66 in Hospital Anxiety Depression Scale) Low levels of anxiety during testing visit but slight increase for those positive when they find out (Brief Symptom Inventory score 1.52 vs 1.42); for those negative, slight increase for those who turned out to be negative during their follow-up (BSI slightly increased by 0.074)	Equivalent	Low

Anxiety about infertility	2 observational *(n= 450)*	5.4% were anxious in one study In high-risk population, 20-40% of CT-negative were anxious about their chances of getting pregnant	Harm (upon receiving a positive result)	Very low
Shame/stigma symptoms	4 observational *(n= 2,542)*	2 studies using Rosenburg Self-esteem scale both reported >15 on the scale (cut-off) during testing and on follow-up 2 studies 6-18% of males and 13-14% of females felt stigmatized when test was offered; upon receiving results, both studies reported very few individuals felt shame or “dirty” (0.8-7.5%)	Equivalent	Very low
Embarrassment	4 observational *(n= 1,353)*	2 studies not embarrassing for most 18–21-year-olds (only 7% felt embarrassed) 12-17% would feel embarrassed if future testing offered in one study 3% felt embarrassed upon receiving result in one study	Harm (higher percentage of participants felt embarrassed)	Very low

4.2.3 Diagnostic Performance of Screening Test

The CDC recommends nucleic acid amplification tests (NAATs) in screening and detecting chlamydia and gonorrhea infection. In cases of child sexual assault involving boys, rectal and oropharyngeal infections among prepubescent girls, or when there is a suspected gonorrheal treatment failure, a culture and sensitivity test is warranted. [8]

In a recent meta-analysis, 39 studies were evaluated to determine the accuracy of point-of-care tests (POCTs) in detecting Chlamydia infections. Fourteen (14) of the studies showed that antigen-based detection methods had a pooled, sensitivity, specificity, and diagnostic odds ratio of 56%, 99% and 86 whereas 25 studies on NAAT-based POCTs showed the corresponding values of 94%, 99% and 1,933. [9] The values presented here were within the target product profile (TPP) for chlamydia and gonorrhea detection which was recommended by the WHO-led expert consultation panel for advancement of STI screening (for sensitivity and specificity, a minimum of 90% and value optimal of 98% for NG while >90% minimum and 100% optimal sensitivity and 98% minimum and 100% optimal specificity for CT). [10]

Table 16. Diagnostic accuracy of screening and confirmatory tests for chlamydia infection

Diagnostic Test	**Basis (# Study Design, n=)**	**Diagnostic properties**		**Certainty of Evidence**
		Sensitivity (95% CI)	Specificity (95% CI)	

Antigen-based detection test	14 observational (cohort and cross-sectional) studies (n=14,582)	0.56 (0.45-0.67)	0. 99 (0.98-0.99)	low
Nucleic acid amplification test (NAAT)-based	25 observational (cohort and cross-sectional) studies (n=27,754)	0.94 (0.91-0.96)	0.99 (0.99-0.99)	low

4.2.4 Cost Implication

STI testing in the Philippines almost always comes in packages. Large government tertiary centers don't usually have NAATs available but do have culture and sensitivity which costs around 1000-1360PHP. Packages for STI testing in private clinics may cost 4300PHP – 15,000PHP depending on the included diseases but this does not include NAATs, only rapid antigen tests. Chlamydia urine PCR alone costs around 9000PHP. FDA-approved antigen detection tests are available for online ordering costs at a minimum of 875PHP.

In one modelling study done to assess the cost-effectiveness of strategies for decreasing chlamydia prevalence, it was shown that a targeted screening approach with contact tracing was more cost-effective as compared to universal screening or targeted screening alone. [17] The mean prevalence at the 10th year of the intervention was predicted to decrease to 1.48 +/- 0.13% compared to 3.31 +/- 0.33% at baseline. At 20% efficiency of contact tracing, the incremental cost-effectiveness ratio (ICER) per QALY gained was $4,634 while it was $7,219 40% efficiency. Early treatment of partners without testing did not significantly impact overall prevalence and may cause overtreatment.

A modelling study done in the US for costs and quality-adjusted life years (QALY) lost dues to gonorrhea infection showed that in the year 2015, the discounted lifetime cost per incident was 261$ for women, 169 $ for men having sex with women (MSW), and 133$ for men having sex with men (MSM). The total population-level discounted lifetime lost with infection amounted to $150million, $54million, and $97million respectively. The higher cost in women is attributed to the chronic and long-term sequelae for gonorrhea infection (most commonly chronic pelvic pain and tubal infertility) as compared to men who present more commonly with an acute infection. [18]

Another cost effectiveness study done among adolescents and young adults in the pediatric emergency department showed that in a theoretical population of 10,000 individuals, targeted screening will result in detection and treatment of 26.4% of cases at a cost of $313,063 while universal screening will be able to successfully detect and manage 31.1% at a cost of $515,503. The ICER for screening vs no screening was $6444, and the ICER for universal vs targeted screening was $12,139. [19]

4.2.5 Patient's Values and Preference, Equity, Acceptability, and Feasibility

With the Philippines' recognition as one of the countries with the fastest growing HIV cases in Asia and the Pacific region (237% increase in annual HIV infections from

2010 to 2020), the government has issued more programs in order to address this problem including awareness of sexually transmitted infections and reduction of stigma that comes with the different STIs. [20-22] No local studies specifically address the issues of chlamydia or gonorrhea testing or the stigma that comes with infection, however local studies addressing HIV infection have shown the low uptake of testing among females (2.4% of respondents) and the presence of stigma even among healthcare workers. [23,24]

The Canadian Task force recommendation document reviewed patient values and preferences and it was shown that relative to the harms (psychosocial harm, stigmatization, etc.), the potential benefits on reproductive health and prevention of disease transmission were more important to those who were screened or wanted to be screened and this was still the case even if they were shown the current evidence and its uncertainty. [25]

4.2.6 Recommendations from Other Groups

Table 17. Recommendations from Other Groups on screening for chlamydia and gonorrhea

Group	Recommendation	Strength of recommendation and certainty of evidence
USPTF [26]	Screening for chlamydia and gonorrhea is recommended in all sexually active women 24 years and younger and in women older than 24 years old who are at an increased risk for infection. For men, there is insufficient current evidence to assess the balance of benefits and harms of screening.	Grade B Recommendation Indeterminate
CDC [27]	Follows the recommendation of the USPTF for women and men (who have sex with women) For men who have sex with men (MSM), screening is recommended at least annually for sites of contact (urethra, rectum) regardless of condom use, or every 3-6 months in the presence of additional risk factors such as multiple sexual partners, with HIV infection and/or on pre-exposure prophylaxis for HIV).	Not stated, but recommendations follow USPTF guidelines
Canadian Task Force [25]	Opportunistic screening of sexually active people younger than 30 years of age who are not known to belong to a high-risk group is recommended for annually at primary care visits using either self- or clinician collected samples.	Conditional recommendation, Very low certainty
UK National screening committee [28]	A screening test should be offered among sexually active women and other people with a womb or ovaries (e.g., transsexual, non-binaries) under 25 years old, including all their sexual partners.	Not stated

Philippines

In the Philippines, no guideline recommendation is put forth regarding screening for chlamydial and gonococcal infection. Though there is a thrust by the Department of Health for screening of sexually transmitted diseases among pregnant women, no specific focus is given to CT and NG infection, unlike syphilis and HIV. [29]

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4.3 Screening for Asymptomatic Bacteriuria

RECOMMENDATIONS

1. **Among asymptomatic, apparently healthy adults, we suggest against screening for asymptomatic bacteriuria.** ***(Weak recommendation, very low certainty of evidence)***

   Considerations: A recommendation against routine screening for asymptomatic bacteriuria among apparently healthy asymptomatic non-pregnant adults was based on the lack of substantial benefit to support screening in this population.

2. **Among asymptomatic, apparently healthy pregnant women, we suggest screening for asymptomatic bacteriuria using urine culture.** ***(Weak recommendation, very low certainty of evidence)***

   Considerations: Screening for asymptomatic bacteriuria in pregnant adults was recommended based on benefit in terms of reduction in the incidence of urinary tract infection. The panel also highlighted that there may be potential benefit in screening to prevent peripartum and congenital infections.

4.3.1 Burden of Asymptomatic Bacteriuria

Asymptomatic bacteriuria (ASB) is defined as the isolation of at least 100,000 colony-forming units (CFU)/mL of a single organism in a clean-catch voided urine from a patient without symptoms of urinary tract infection (UTI).[1] There are currently no local studies on the epidemiology of ASB in the general adult population, but a local study [2] reported a prevalence of 2.5% among pregnant Filipino patients at a tertiary government hospital (ongoing study at the time of publication).

ASB is found to be more prevalent among females than males, and poses a higher risk for future symptomatic UTI.[3,4] However, studies show that it is not associated with long-term adverse outcomes in the general adult population such as future resistance patterns, incidence of severe kidney disease, and mortality.[4,5] Contrary to the adult population, ASB among pregnant patients is associated with antepartum pyelonephritis, preterm birth and low neonatal birth weight.[6] Current treatment of ASB consists of a short-course of antibiotics based on sensitivity analyses of the urine culture and local resistance patterns.[1]

4.3.2 Benefits and Harms of Screening

We found 6 international CPGs[7-12] and 1 local CPG[1] that had recommendations on the topic of ASB. Only two CPGs[7,9] by the US Preventive Services Task Force (USPSTF) and the Canadian Task Force on Preventive Health Care (CTFPHC) were deemed adequate for adaptation. For this review, we focused on USPSTF's key questions 1 and 3: "(1) Does screening for asymptomatic bacteriuria improve health outcomes among adults, including pregnant women?; and (3) Does treatment of screen-detected asymptomatic bacteriuria improve health outcomes?", and CTFPHC

key question 1a: “What are the benefits and harms of screening compared with no screening for asymptomatic bacteriuria in pregnancy?”

No direct evidence was found on the benefits and harms of screening for ASB using urinalysis or urine culture, versus no screening in the general adult population. However, USPSTF cited 2 randomized controlled trials [13,14] that evaluated the benefits of antimicrobial treatment among screening-positive ASB in the general adult population, versus placebo or no treatment. We excluded 3 studies[15,17] included by the USPSTF guidelines due to indirectness with our research question. One study did not have the outcomes of interest.[15] The second RCT done in the United Kingdom[17] was excluded from this review since the study compared the effects of antimicrobial treatment on patients with ASB versus an age-matched population without significant bacteriuria. Another RCT done in Canada[16] was excluded from this review because it only recruited elderly patients with diabetes. No additional studies were found after literature search via PubMed and Cochrane Library. Furthermore, there were no identified recommendations or studies on the frequency of screening for ASB.

For the prespecified subgroup of pregnant adults, 3 observational studies (3 retrospective cohorts, n=5659)[18,20] were retrieved from USPSTF 2019 and CTFPHC 2018 guidelines. The 3 studies compared screening versus no screening for asymptomatic bacteriuria. One study[21] in the CTFPHC guideline was excluded from this review due to indirectness with the research question.

OUTCOMES

Incidence of UTI

One RCT[13] on elderly ambulatory women (n=124) reported that at 6 months of follow-up, 7.9% and 16.4% of patients developed symptomatic UTI (RR 0.48, 95% CI 0.18 to 1.33) among patients who were given antimicrobial treatment and among patients who were not given treatment, respectively. No statistical significance between the two groups (p=0.15) was reported.

Another RCT[14] (n=93) compared reinfection, relapse and persistence rates in terms of microbiologic evidence on urine cultures between elderly patients with ASB treated with ofloxacin and patients not given treatment. Results favored treatment for ASB, with reinfection, relapse and persistence rates at 0-3 months follow-up between the treatment and control groups at 15.6% and 75.9%, respectively (RR 0.21, 95% CI 0.11 to 0.38). At 4 to 6 months of follow-up, results favored treatment for ASB as well, with reinfection, relapse and persistence rates at 45% and 75.9% respectively (RR 0.60, 95% CI 0.43, 0.84). The same study reported no incidence of sepsis or shock during the 6-month follow-up period.

The certainty of evidence was downgraded to very low for serious risk of bias, indirectness and imprecision.

Cost of Testing/Treatment

No cost-effectiveness studies on screening for ASB among the general healthy population were found.

Among pregnant patients, one study published in 1995 based in the United States was found.[22] For the prevention of pyelonephritis in pregnancy, they concluded that both urine dipstick and urine culture testing were cost-beneficial compared to no screening. No other local or more recent cost-effectiveness studies were found.

Adverse Events

Two RCTs[13,14] (n=217) monitored adverse reactions to antimicrobial therapy. Two out of 127 patients (1.6%) who received antibiotics developed adverse reactions (one had vertigo, and one had upper gastrointestinal symptoms wherein both patients eventually withdrew from the study).[14] In the same study, they noted that treatment with ofloxacin did not affect SGPT, hematocrit, serum bilirubin, or blood urea levels, and there was a mild insignificant reduction in serum creatinine from 1.12mg/dL to 1.08mg/dL in the treatment groups. The certainty of evidence was downgraded to Very Low for serious risk of bias, indirectness and imprecision.

Rational use of antibiotics

No studies were found on the effects of screening for ASB versus no screening on the rational use of antibiotics.

Antimicrobial Resistance

One RCT[14] (n=93) assessed the types of microorganisms isolated in the urine specimens of cases of relapse, reinfection and persistence at 3 months of follow-up. In both intervention groups (continuous antibiotic therapy with ofloxacin and pulse antibiotic therapy with ofloxacin), there were a total of 16/29 isolated organisms (55.2%) that demonstrated resistance to ofloxacin. On the other hand, only 1 of 22 isolates (4.5%) in the control group who had relapse or persistence of bacteriuria had ofloxacin resistance. Results favored no treatment for ASB for the outcome of antimicrobial resistance (RR 12.14, 95% CI 1.74, 84.70). The certainty of evidence was downgraded to very low for serious risk of bias, indirectness and imprecision.

Table 18 shows the summary of evidence regarding the benefits and harms of screening and treatment of ASB among asymptomatic healthy adults.

Table 18. Effects of screening and treatment of ASB among asymptomatic, healthy adults

Outcomes	**No. of Studies** *(no. of participants)*	**RR (95% CI)**	**Interpretation**	**Certainty of Evidence**
Incidence of bacteriuria[a]	1 RCT *(n= 93)*	At 0-3 months: 0.21 (0.11 to 0.38) At 4-6 months: 0.60 (0.43 to 0.84)	Favors treatment for ASB	Very low
Adverse events	2 RCT *(n=217)*	*2/127 (1.6%) among patients treated with antibiotics*	Favors no treatment for ASB	Very low
Antimicrobial Resistance	1 RCT *(n=93)*	12.14 (1.74 to 84.70)	Favors no treatment for ASB	Low
Incidence of symptomatic UTI	1 RCT *(n= 124)*	0.48 (0.18 to 1.33)	Inconclusive	Very low

[a]: Reinfection, relapse and persistence of microorganism growth on urine culture

Subgroup: Pregnant Women

Incidence of UTI

For the outcome of incidence of UTI among pregnant patients, the pooled results of 3 retrospective cohort studies[18-20] (n=5659) favored screening for ASB using urine culture compared to no screening (RR 0.28, 95% CI 0.15, 0.54). There was low heterogeneity across the 3 studies (I^2=0%). Certainty of evidence is Very Low due to very serious risk of bias.

Premature rupture of membranes

One observational study (n=372) [19] compared the maternal outcome of premature rupture of membranes among patients screened for ASB versus patients who were not screened. There was no difference in risk between the two groups (RR 0.86, 95% CI 0.29, 2.50). Certainty of evidence is Very Low due to serious risk of bias and imprecision.

Low birth weight

The rates of low birth weight among patients who were screened for ASB versus patients who were not screened were retrieved from one observational study (n=372) [19] . There was no difference in risk for low birth weight between the two groups (RR 0.20, 95% CI 0.02, 1.70). The definition of low birth weight used by the study was not reported. Certainty of evidence was downgraded to Very Low due to serious risk of bias and imprecision.

Preterm Delivery

Two retrospective cohorts[19,20] (n=722) reported on the rates of preterm deliveries among patients screened for ASB versus patients who were not screened. Pooled results showed no difference in risk between the two groups (RR 1.57, 95% CI 0.78, 3.13). There was low heterogeneity across the 2 studies (I^2=34%). Certainty of evidence was downgraded to Very Low due to serious risk of bias and imprecision.

Table 19 shows the summary of evidence regarding the benefits and harms of screening and treatment of ASB among pregnant women.

Table 19. Effects of screening and treatment of asymptomatic bacteriuria among pregnant women

Outcomes	No. of Studies *(no. of participants)*	RR (95% CI)	Interpretation	Certainty of Evidence
Incidence of UTI	3 Cohorts *(n=5659)*	0.28 (0.15, 0.54)	Favors screening for ASB	Very low
Premature rupture of membranes	1 cohort *(n=372)*	0.86 (0.29, 2.50)	Inconclusive	Very Low
Low birth weight	1 cohort *(n=372)*	0.20 (0.02, 1.70)	Inconclusive	Very Low
Preterm delivery	2 cohorts *(n=722)*	1.57 (0.78, 3.13)	Inconclusive	Very Low

4.3.3 Diagnostic Performance of Screening Tests

Urine culture is the gold standard for the diagnosis of urinary tract infection.[23-25] Specific etiologic microorganisms and their resistance patterns to antibiotics are reported by urine culture and sensitivity results. Test results usually come out in 1 to 3 days, and initiation of broad-spectrum antibiotics depending on the patient's clinical presentation and local resistance patterns may be done while awaiting results. Once the diagnosis of UTI through urine culture is confirmed, appropriate antibiotics are prescribed or streamlined based on antimicrobial susceptibility results.[1]

A study on ambulatory, asymptomatic elderly men (>65 years old) assessed the diagnostic accuracy of pyuria for asymptomatic bacteriuria on the geriatric population. The reported sensitivity, specificity, positive predictive value and negative predictive value of pyuria (greater than 10 wbc/hpf) in detecting bacteriuria are 68% and 99%, 88% and 97% respectively. The prevalence of bacteriuria, defined in the study as 100,000 cfu/mL in the studied population, is around 10%.[26]

4.3.4 Cost Implication

No international and local cost-effectiveness studies on screening versus no screening for ASB among general, healthy adults were found. One US-based study published in 1995[22] found screening for ASB using urine culture or urine dipstick to prevent pyelonephritis in pregnant patients to be cost-effective, compared to no screening.

Tables 20 and 21 show the estimated costs of screening, as well as the estimated associated cost of treatment of asymptomatic bacteriuria or UTI.

Table 20. Estimated cost of screening for asymptomatic bacteriuria (as of 2022)

Parameter	**Screening intervention**	
	Urinalysis	***Urine Culture and Sensitivity Testing***
Unit cost per test of screening intervention in Philippine Peso (PHP)[a]	PHP 275[b]	PHP 1385[b]

[a]: Based on outpatient rates at a tertiary hospital in the Philippines
[b]: Urine culture and sensitivity testing is the current screening intervention of choice for asymptomatic bacteriuria. Local recommendations define ASB for asymptomatic women as two consecutive voided urine specimens with isolation of the same bacterial strain at ≥100,000cfu/mL, while only a single clean-catch voided specimen with the same quantitative count is required for diagnosis among males. However, in the absence of facilities or funds for urine culture, significant pyuria on urinalysis in 2 consecutive clean-catch midstream urine samples can be used as an alternative for screening for ASB[(1)].

Table 21. Costs of treatments associated with diagnosis of asymptomatic bacteriuria or UTI

Procedure/Treatment	**Cost**
Antibiotic treatment[a] in Philippine Peso (PHP)	PHP 168- PHP 791
Medications for supportive treatment (e.g. antipyretics, pain medications)	PHP 2.50- 4.00[b]

[a]: Estimates for total cost of treatment, assuming common oral antibiotics (cephalexin, cefuroxime, co-amoxiclav, cotrimoxazole) are used over a course of 7 days of treatment for an uncomplicated case
[b]: Estimated cost per tablet of paracetamol, to be given as needed every 4 to 6 hours depending on clinical picture

4.3.5 Patient's Values and Preference, Equity, Acceptability, and Feasibility

No studies were found on the values, preferences and social impact of asymptomatic bacteriuria and screening for ASB in the general population. For symptomatic UTI per se, a comparative study[27] that looked at the views of women and their healthcare providers on uncomplicated UTI showed different perceptions between the two groups. Almost a third of patients believed that UTIs were primarily diet-related with bacteria and personal hygiene being less likely causes, but half of the healthcare providers thought that patients knew the real causes of their UTI. Female patients were found to perceive UTI discomfort as more severe than their healthcare providers did, and they were also less concerned about its health impact than their providers. Overall, the study concluded that patients needed more education on the risk factors, prevention strategies and optimal therapy of UTI while the healthcare providers needed more knowledge on patients' perspectives and disease burden.

One systematic review in Canada[28] aimed to review ASB screening practices and patient preferences regarding ASB among pregnant women. They found that women have conflicting views on antibiotics during pregnancy with nearly half of women expressing that antibiotics should not be used, and more than half refusing to be treated for ASB. Safety concerns for the fetus and risks of teratogenic effects were cited as reasons for refusal. However, no information was provided on how these perceptions on treatment affected patients' decision-making on screening for ASB.

4.3.6 Recommendations from Other Groups

Four international practice guidelines[8,10-12] and one local practice guideline[1] all recommend against screening for asymptomatic bacteriuria in the general adult population but recommend screening using urine culture among pregnant women.

Table 22. Recommendations from other groups on screening for Asymptomatic Bacteriuria

Group	Recommendation	Strength of recommendation and certainty of evidence
AAFP 2020	"Recommends against screening for asymptomatic bacteriuria in nonpregnant adults" "Recommends screening for asymptomatic bacteriuria using urine culture in pregnant persons"	Grade D Grade B
IDSA 2019	"In healthy, premenopausal, nonpregnant women or healthy postmenopausal women, we recommend against screening for or treating ASB." "In pregnant women, we recommend screening for and treating ASB."	Strong recommendation, Moderate quality of evidence Strong recommendation, Moderate quality of evidence
NICE 2018	"...Asymptomatic bacteriuria is not routinely screened for, or treated, in women who are not pregnant, men, young people and children."	—

European Association of Urology 2017	"Do not screen or treat asymptomatic bacteriuria in: (a) Women without risk factors (b) Patients with well-regulated diabetes mellitus (c) Post-menopausal women (d) Elderly institutionalized patients (e) Patients with dysfunctional and/or reconstructed lower urinary tracts (f) Patients with renal transplants (g) Patients prior to arthroplasty surgeries (h) Patients with recurrent UTI" "Screen for and treat asymptomatic bacteriuria in pregnant women with standard short-course treatment."	Strong recommendation Weak recommendation
PSMID 2015	"Routine screening and treatment for asymptomatic bacteriuria is not recommended for healthy adults." "Screen all pregnant women for asymptomatic bacteriuria once between 9th to 17th week AOG, preferably on the 16th week AOG. A standard urine culture of clean-catch midstream urine is the test of choice in screening for asymptomatic bacteriuria."	Strong recommendation Low quality of evidence Strong recommendation High quality of evidence

[a]: AAFP recommendations are based on USPSTF guidelines.
AAFP: American Academy of Family Physicians; AOG: Age of gestation; ASB: Asymptomatic bacteriuria; IDSA: Infectious Diseases Society of America; NICE: National Institute for Health and Care Excellence; Philippine Society for Microbiology and Infectious Diseases

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4.4 Screening for Hepatitis A

RECOMMENDATION

Among asymptomatic apparently healthy adults, we suggest against screening for Hepatitis A. ***(Weak recommendation, very low certainty of evidence)***

Considerations: Hepatitis A screening is not routinely recommended in the general population including food handlers. Adherence to basic food safety practices and vaccination for individuals at increased risk are important measures to prevent the transmission of Hepatitis A virus. The panel enumerated the following as increased risk for Hepatitis A infection: international travelers (from endemic areas), men having sex with men, persons who inject drugs (PWIDs), persons who use drugs (PWUDs), occupational risk for exposure, close personal contact with an international adoptee, people experiencing homelessness, chronic liver disease, and people living with HIV (PLHIV). The panel also highlighted that risk assessment for workers should be according to job description and job process. The panel likewise emphasized on giving Hepatitis A vaccine to apparently healthy adults.

4.4.1 Burden of Hepatitis A

Hepatitis A is a highly contagious liver infection caused by the hepatitis A virus (HAV). It is prevalent worldwide, and the World Health Organization (WHO) estimates that 1.59 million cases occur each year, resulting in 39,000 deaths and 2.3 million disability-adjusted life years. [1] According to the Global Burden of Disease (GBD) 2019 database, Hepatitis A caused the heaviest burden worldwide in terms of age-standardized incidence and DALY rates among the major causes of acute viral hepatitis, with stable incidence rates from 1990 to 2019. [2] In the Philippines, the crude incidence rate in 2022 according to the DOH Epidemic-prone Disease Case Surveillance is 1.01 per 1,000,000 population, with two reported deaths due to the disease (case fatality rate of 5.8%). [3] Seroprevalence data in the country is limited, with one published study in 1986 among Filipino dentists reporting increasing seroprevalence by age: 57.1% (age 20-24), 79.3% (age 25-29), 88.0% (age 30-34) and 100% (age 35-39). [4] A 2018 study among female marriage immigrants to South Korea reported high seroprevalence among Filipinos: 77.8% (age 20-29) and 72.4% (age 30-40). [5]

Hepatitis A typically spreads through contaminated food or water. Clusters of Hepatitis A outbreaks in the country occur in various settings, with recent outbreaks attributed to consuming contaminated water and improper hygiene practices. [6,7,8] Certain populations, including daycare providers, hospital workers, and food handlers, are at risk for contracting or spreading HAV. The latter is considered a significant cause of public outbreaks of Hepatitis A. [9] Rarely, HAV infection may be transmitted via blood transfusion from infected donors during active illness. [10]

No specific treatment is available, and most hepatitis A patients fully recover. Infection usually confers life-long immunity. Adults with acute infections may have mild disease

or develop serious complications (<1%), but it is rarely fatal. [11] Hepatitis A does not cause chronic liver disease, but HAV-infected persons with underlying liver disease or HIV may have an increased risk of complications or death. [12]

Hepatitis A is vaccine-preventable. The Philippine Society of Microbiology and Infectious Diseases (PSMID) strongly recommends that adults, both immunocompetent and at risk[1], receive a 2-dose schedule of Hepatitis A vaccine. [13] Reports show that detectable protection from vaccination persists for up to at least 15 years. More recent data reveal the persistence of antibodies up to 20 years post-vaccination. [14]

4.4.2 Benefits and Harms of Screening

Our search yielded no direct evidence on the benefits or harms of screening for Hepatitis A among healthy adults in the context of periodic health examination, including outcomes relating to early detection of asymptomatic disease, effect on morbidity, hospitalization, or mortality. In most of the literature we reviewed, performing an HAV antibody test aims to diagnose patients with a high suspicion index for hepatitis A infection, in which they have already presented with symptoms compatible with hepatitis. Available seroprevalence studies utilizing anti-HAV IgG antibody tests were used among at-risk populations. We will discuss these studies in this evidence review.

General Population Undergoing Routine Screening

We found one study describing testing among adults in the context of routine health screening, but the study did not report our outcomes of interest. The outcomes were to measure seroprevalence and the association of pre-vaccination screening with the likelihood of receiving Hepatitis A vaccinations. In this observational report [20], 1,017 records of teenage and adult patients aged 16-99 were retrospectively reviewed. Testing involved IgG anti-HAV serology for routine health screening and follow-up of non-liver-related illness. Seropositivity was recorded among 68% (692/1,017) of patients. Among the seropositive patients, 103 recalled receiving passive immunization with immune serum globulin, while 8 patients received inactivated virus vaccine. Listed reasons for receipt included: post-exposure prophylaxis, travel to endemic areas, and army service. Most seropositive patients (80%) did not recall acquiring an HAV infection. The study reported that those unaware of past infection were more likely to have been vaccinated than those who were aware (26.3% vs. 7.7%; $p < 0.005$). No other outcome data were reported, including those from adult patients who tested seronegative. The authors concluded that patients who tested positive for IgG anti-HAV who were unaware of their immune status were 3.4x more

[1] Other indications include: Vaccinate any person seeking protection from HAV infection, Men having sex with men (MSM), users of injection drugs, Persons who receive clotting factor concentrates or with clotting factor disorders (e.g. hemophiliacs), Persons traveling to or working in countries that have high or intermediate endemicity of hepatitis A, Contacts of infected persons, People with chronic liver disease (because of risk of fulminant Hepatitis A), Persons for whom Hepatitis A is an occupational hazard (e.g. healthcare workers, some lab workers, food handlers)

likely to have been vaccinated unnecessarily than those who could recall a past infection.

Population at risk: Food Handlers

Most recorded instances of hepatitis A outbreaks caused by contaminated food have been traced back to individuals who handle or prepare the food and are infected with the hepatitis A virus (HAV). These individuals are typically present at the point of sale, such as in restaurants, during food preparation at schools, or at social events. A 1996 report investigating the seroprevalence of Hepatitis A among food handlers in Italy showed that there was an overall prevalence of 68.7% among 294 food handlers, with a significantly increasing trend with increasing age, ranging from 7.7% in the group aged 14-20 to 100% in the 41-50 years of age. Multiple logistic regression analysis showed a significant association in the prevalence of anti-HAV with years of activity: food handlers with ten or more years of experience have an adjusted odds ratio (OR) of 2.4 (95% CI 1.01-5.6) compared to those with a shorter period of activity. [21]

In 1983, the CDC published early recommendations for the control of Hepatitis A among food handlers. These recommendations were developed based on the epidemiologic characteristics of 20 food-borne outbreaks involving 1,000 food handlers in the USA from 1968-1980. They described that the attack rate of infected food handlers among fellow kitchen employees ranged from 2.9 to 66.7 cases per 100 workers, among other employees ranged from 0 to 8 cases per 100 workers, and all other individuals (i.e., restaurant patrons) ranged from 4.8 and 56 cases per 100 people at risk. In five of the seven outbreaks, the first patron became symptomatic within two weeks after the onset of jaundice of the source person. In one outbreak, eleven asymptomatic cases were identified by serologic testing. No further outcome data were shown in this report. There were no reported cases of a secondary wave of outbreaks. [22]

While this is the case, a new report from the US Advisory Committee on Immunization Practices (ACIP) [20] elucidated that food handlers are not at higher risk of hepatitis A because of their occupation but because they may belong to specific demographic groups at risk. Food handlers are commonly young persons and persons with lower socioeconomic status who may have a higher incidence of hepatitis A than the rest of the population.

Population at risk: Healthcare Workers (HCW)

The occupational risk of Hepatitis A among healthcare workers was reported in a 2005 systematic review of reports documenting hospital outbreaks and seroepidemiologic studies. In this review, nurses accounted for most personnel infected, with one study reporting the highest odds ratio (OR) of 2.75 (95%CI 1.79-4.21). Nurses also pose a relatively high secondary attack rate ranging from 15-41%, while the attack rates

among physicians were at 3-4%. Seroprevalence rates among HCWs were varied and wide, with physicians ranging between 5 to 79%, 8 to 88% among nurses, 4-82% among paramedical workers, and 37-88% among hospital maintenance workers. Different modes of transmission were reported: (1) transmission from an infected patient to HCW with a concurrent break in handwashing protocol, (2) food-borne infection, (3) infection through an invasive procedure such as cholecystectomy or endoscopy contaminated from non-symptomatic adult patients, (4) transmission from low socioeconomic or addicted patients, and (5) infusion of HAV-contaminated blood or blood products. [23]

Population at risk: Travelers

An observational study reported the seroprevalence of anti-HAV IgG among travelers who have no previous Hepatitis A exposure or vaccinations and compared the costs of performing pre-vaccination screening versus outright vaccination. Travelers were categorized by age, country of origin, vaccination history, and previous travel experience and were screened for anti-HAV IgG levels. A large percentage (80.0%) of the 527 travelers had previously traveled to areas of endemic hepatitis A, and 135 (32.1%) of these 420 subjects showed HAV immunity. Among travelers born in non-industrialized countries, 62 (82.7%) out of 527 have HAV immunity. This data compares to 71 (16.6%) of 428 travelers born in industrialized countries. The percentage is lower for travelers aged 50 or younger born in industrialized countries (10 out of 158, 6.3%). Considering that the cost of antibody testing was at 7.00 USD and the mean wholesale price of 2 doses of HAV vaccine at 118.90 USD, the report found that the cost of screening and vaccinating travelers was cheapest if pre-vaccination screening was limited to travelers born in non-industrialized countries and those born before 1945. [24]

Population at risk: Daycare Workers

Daycare workers are especially at risk of fecal-oral contact with very young children due to the nature of their occupation, potentially causing illness among vulnerable populations. A prevalence study among female daycare workers (n=591) was done in Belgium, comparing a reference group of blood donors (n=240). The study showed that the overall prevalence of HAV markers was more significant among exposed daycare workers at 48.4% (95% CI 44.2-52.5) personnel compared to 42.9% (95% CI 38.7-47.0) in blood donors. No other pertinent outcomes were reported in the study. [25]

Table 23 summarizes the findings for this section of the review.

Table 23. Summary of Seroprevalence and Attack Rates of HAV among Population at Risk

Population	Basis (# studies, N)	Seroprevalence	Secondary attack rate	Certainty of Evidence

General Population undergoing routine screening	1 observational study (n=1,017)	68%	N/A	Very low
Food Handlers	2 observational studies (n=1,294)	68.7%	4.8 to 56 cases per 100 people at risk	Very low
Healthcare Workers	1 systematic review (11,244; 23 studies)	Physicians: 5-79% Nurses: 8-88% Paramedical: 4-82% Maintenance: 37-88%	Nurses: 15-41% Physicians: 3-4%	Very low
Travelers	1 observational study (n=527)	From non-industrialized: 82.7% From industrialized: 16.6%	N/A	Very low
Daycare Workers	1 observational study (n=831)	48.4%	N/A	Very low

4.4.3 Diagnostic Performance of Screening Tests

Eliciting pertinent patient history and physical examination findings of typical Hepatitis A symptoms are considered routine diagnostic approaches for Hepatitis A. Similarly, liver function tests are used as auxiliary diagnosis, including serum measurement of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin levels. Clinical and biochemical testing, however, does not differentiate Hepatitis A from other causes of acute hepatitis, and as such, serological tests are usually needed to identify the cause.

Anti-Hepatitis IgM and IgG antibody testing

The preferred method for diagnosing hepatitis A in a patient with a compatible clinical picture is by detecting anti-hepatitis A virus (HAV) antibodies through serological assays. Anti-HAV IgM antibodies are considered main markers of acute infection, usually detected from the onset of symptoms, and remain present for approximately three months. On the other hand, anti-HAV IgG antibodies are considered markers that determine whether a person is immune to HAV by previous exposure to the virus through natural infection or vaccination. However, the test is incapable of distinguishing between the two. Nevertheless, this test has been helpful for seroprevalence studies among populations, particularly in identifying target groups for vaccination.

Diagnostic Accuracy

The clinical diagnostic accuracy of using IgM anti-HAV antibodies in diagnosing hepatitis A is generally high, with a 1982 study demonstrating 100% sensitivity, 99% specificity, and a positive predictive value of 88% during an epidemiologic outbreak investigation in a US university. [15] A recent quality improvement study in 2022 demonstrated that anti-HAV IgM antibody titer levels measuring 4.0 above correlated with a 100% positive predictive value. Low-level reactive (1.20-4.00) or equivocal (0.8-1.20) anti-HAV IgM results were associated with an alternative diagnosis other than Hepatitis A. [16] The results of the two studies were not pooled due to heterogeneity. The certainty of evidence was downgraded to low due to indirectness to the healthcare question, serious risk of bias, and inconsistency. (See Table 24)

While Hepatitis A testing is conventionally performed by analyzing serum samples using conventional assays, alternative sampling methods have been reported. Newer immunochromatographic assays (ICA or rapid tests) can provide results faster (within 15-20 minutes). In a 2018 study in Brazil, the diagnostic accuracy of a rapid test for both anti-HAV IgM and IgG antibodies was compared to enzyme immunoassay (EIA) among suspected patients and in field conditions. Anti-HAV IgM rapid tests had good sensitivity (87%, 95%CI 0.78-0.91) and specificity (80%, 0.72-0.86) compared to EIA among those suspected of Hepatitis A. Among serum samples involved in outbreak investigations, Anti-HAV IgM has good sensitivity at 81% (95%CI 68.6-90.12) and excellent specificity at 100% (95%CI 92-100), while Anti-HAV IgG has good sensitivity at 79% (95%CI 66.98-87.89) but poor specificity at 22% (95%CI 9.82-38.21). Furthermore, anti-HAV IgG rapid tests among blood donors have poor sensitivity at 49% (95%CI 36.6-61.93) but excellent specificity and positive predictive value at 100%. [17]

A study investigating samples collected from oral fluid or saliva showed excellent diagnostic accuracy specific for IgG, with sensitivity of 99% (95%CI 98.4 to 99.9) and specificity of 98% (95%CI 97.7 to 99.4). However, this method requires an extremely sensitive assay since antibody concentrations in oral fluid were estimated to be 800-1000-fold lower than those in serum and plasma. [18]

The certainty of evidence of the two studies was rated low due to reasons of indirectness to the healthcare question and serious risk of bias (confounding, allocation). (See Table 24)

Table 24. Accuracy of Anti-Hepatitis IgM antibody testing in Diagnosing Acute Hepatitis A

Anti-HAV Antibody tests	Basis (# studies, N)	Sensitivity (95% CI)	Specificity (95% CI)	Positive Predictive Value (95% CI)	Certainty of Evidence
Anti-HAV IgM Antibody Tests					

Conventional serum assays	2 observational studies (N = 234)	100%	99%	88-100%	Low
Rapid test – among suspected	1 observational study (N = 384)	87% (0.78-0.91)	80% (0.72-0.86)	-	Low
Rapid tests during outbreak setting	1 observational study (N = 103)	81% (68.6-90.12)	100% (92-100)	-	Low
Anti-HAV IgG Antibody Tests					
Rapid test – among suspected	1 observational study (N = 384)	66% (0.61-0.72)	98% (0.93-0.99)	-	Low
Rapid test during an outbreak setting	1 observational study (N = 103)	79% (66.98-87.89)	22% (9.82-38.21)	64% (52.77-74.55)	Low
Rapid test among blood donors	1 observational study (N = 96)	49% (36.6-61.93)	100% (88.78-100)	100% (89.11-100)	Low
EIA using saliva samples	1 observational study (N = 1,250)	99% (98.4 to 99.9)	98% (97.7 to 99.4)	-	Low

4.4.4 Cost Implication

The laboratory test price for Hepatitis A ranges from **500 to 700 PHP**.

Costing analysis studies involving screening for Hepatitis A among healthy adults generally evaluate the cost of different strategies involving pre-vaccination testing and outright vaccination (no screening).

In a cost-analysis done in the US, the authors assessed the cost-effectiveness of three different strategies among a cohort of adults (college, military, travelers, prison, and STD clinic): (1) *screen and defer* vaccination, (2) vaccinate without screening, and (3) *screen and begin* vaccination. They found that *vaccination without screening showed the most favorable incremental cost-effectiveness ratio* (ICER range of 17 to 162 USD per vaccine protection conferred) among all populations considered. Their sensitivity analysis showed that among travelers 65 years of age and prisoners 25 years of age, *screen and defer* become most cost-effective when serology costs are reduced by 33%. For travelers 45 years of age, *screen and defer* becomes most cost-effective when serology costs are reduced by 67%. *Screen and begin* vaccination protocol was the least cost-effective prevention protocol incurring the highest average cost-effectiveness ratio (88 to 188 USD). [30]

Regarding cost-analysis among food handlers, available evidence only concerns routine vaccination, not screening. One economic analysis concluded that routine vaccination of all food handlers would not be economical from a societal or restaurant owner's perspective. Costs in the economic model were driven by the turn-over rate of employees and the small percentage of hepatitis A cases attributable to infected

food service workers [31]. Another analysis concluded that vaccination of 100,000 food handlers in the 10 USA states with the highest incidence of hepatitis A would cost $13,969 per year of life saved [32].

4.4.5 Patient's Values and Preference, Equity, Acceptability, and Feasibility

We found no studies on patient values and preference, the screening test's impact on equity, acceptability, and feasibility.

4.4.6 Recommendations from Other Groups

There are few group, society, or country-based recommendations on routine screening among adults. They are generally related to specific contexts, such as refugee examinations, pre/post-vaccination testing, and epidemiologic investigations during outbreak situations.

Group	Recommendation
USA	**Domestic Examination of Newly Arrived Refugees:** Routine screening for hepatitis A (HAV) infection is not recommended. [26] "In some situations, testing for HAV infection may be more cost-effective than the two-dose vaccine series, although delays in receiving results and logistical challenges of repeat visits should be considered." **On pre- and post-vaccination testing:** Pre- and post-vaccination serologic testing for hepatitis A immunity before vaccination is not routinely recommended. However, it may be considered in specific settings or populations when the cost of vaccinating people who are already immune is a concern. People for whom pre-vaccination testing will likely be most cost-effective include adults who were either born in or lived for extensive periods in geographic areas that have a high or intermediate endemicity of hepatitis A. Vaccination should not be postponed if vaccination history cannot be obtained, records are unavailable, or pre-vaccination testing is not feasible. [27]
Canada	**Public Health Ontario:** Testing for hepatitis A virus (HAV) serology may be indicated for the work-up of patients with suspected acute viral hepatitis to determine the immune status (following recovery from natural infection or as a result of immunization) and as part of an epidemiologic investigation (e.g., outbreak investigation). [28]

United Kingdom (Public Health England)	**For Food Handlers, including those working in the Health and Social Care Setting:** Individuals who have had repeated fecal-oral exposure to the index case and are identified within 14 days of last exposure should be offered the vaccine, with or without HNIG, as appropriate. For post-exposure prophylaxis where human normal immunoglobulin (HNIG) is indicated, if time permits, testing for IgG antibody to the hepatitis A virus (anti-HAV IgG) may be carried out to prevent unnecessary blood product administration. [29]

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4.5 Screening for Hepatitis C

RECOMMENDATIONS

1. **Among asymptomatic, apparently healthy adults, we recommend against routine screening for Hepatitis C.** ***(Strong recommendation, very low certainty of evidence)***

   Considerations: The panel strongly recommended against routine screening for Hepatitis C because of the lack of cost-effectiveness to screen the general population.

2. **Among high risk* asymptomatic, apparently healthy adults, we recommend screening for Hepatitis C using serum anti-HCV.** ***(Strong recommendation, very low certainty of evidence)***

   **Definition of high-risk asymptomatic adult (based on studies included in this review): people who use injection drugs (PWID)*

   Considerations: The panel strongly recommended screening for Hepatitis C using serum anti-HCV among high-risk asymptomatic adults based on large benefits with minimal harms, acceptable cost-effectiveness, and importance of linkage to care. The panel further highlighted that once an individual tested positive for Hepatitis C, referral to a specialist should be made for treatment to be promptly initiated. Identified high-risk individuals were: people with HIV, people who injected drugs and shared needles, people with selected medical conditions including people receiving maintenance hemodialysis and/or people with persistently elevated alanine transaminase (ALT) levels, recipients of transfusions and organ transplants (prior to 1992), health care, emergency medical, and public safety personnel after a needle stick injury or mucosal exposure to Hepatitis C virus-positive blood, and children born to mothers with Hepatitis C infection. Routine periodic testing was recommended for people with ongoing risk factors while risk factors persist. Frequency of testing of at least once (based on IDSA guidance) to more frequent testing (i.e., annually based on US CDC guidance) for those with high-risk exposure were likewise suggested.

4.5.1 Burden of Hepatitis C

Hepatitis C virus (HCV) infection is considered as an emerging public health concern in the Philippines [1]. Worldwide, HCV infection affected an estimated 58 million people and caused 1.5 million new infections per year [2]. Global prevalence is estimated at 0.7% in 2020 [3]. In 2015, the incidence of HCV infection was 23.7 cases per 100,000 population [4]. A study reported that the prevalence rates of HCV were 0.3% and 0.9% among Filipino blood donors and overseas worker candidates, respectively [5].

Approximately 70% (55–85%) of patients with HCV will develop chronic infection [2]. About 20% will have liver cirrhosis within two decades, while three decades after infection, it is estimated that 1 to 5% will develop liver cancer [6]. In 2019, approximately 290,000 people globally have died due to chronic HCV-related liver complications, particularly liver cirrhosis, and hepatocellular carcinoma (HCC) [2].

Next to Hepatitis B infection, HCV was reported to be a significant cause of liver cirrhosis (25.87%) [7] as well as cirrhosis deaths (25.5%-26.7%) [8]. Data from a local nine-year retrospective study noted that HCV was the etiology of liver cirrhosis in 6/148

patients (4%) [9]. On the other hand, chronic HCV was identified to cause 34% of HCC in the US [10]. In a study of 53 Filipinos with HCC, HCV was reported in 10 patients [11]. Furthermore, among patients with HCV and cirrhosis, the risk of developing HCC increases, the annual incidence of HCC is estimated to be 1-4% of patients with liver cirrhosis over a 30-year period [12-13].

According to the Centers for Disease Control and Prevention, the following are at heightened risk for HCV: People with HIV infection, current or former people who inject drugs (PWIDs), people with selected medical conditions, prior recipients of transfusions or organ transplants, health care workers who had exposures to HCV-positive blood via needle sticks, sharps, or mucosal exposures, and children born to mothers with HCV infection.[14] The prevalence of HCV is also significantly higher among medical waste handlers compared to non-medical waste handlers according to studies conducted in Ethiopia and Libya. [15,16]

Among PWIDs, reported seroprevalence rates of anti-HCV were high, and ranges from 46% to 85% [17-21]. A 2002 local study done in Cebu showed that among PWID, 61/87 (70.1%) were positive for anti-HCV, while there were no commercial sex workers with positive anti-HCV. [22] Several studies done in other countries determined the seroprevalence of HCV among commercial sex workers. For the subgroup of female sex workers, report prevalence rates range from 0.6% to 42.7% [23-32], while one study on male sex workers reported an HCV prevalence rate of 3.7% [33]. A paper on HCV infections among men who have sex with men (MSM) reported that none were anti-HCV positive [34].

4.5.2 Benefits and Harms of Early Screening

We did not find any studies which directly determined the benefits and harms of early screening on mortality, liver cancer and harms or adverse events. The US Preventive Services Task Force (USPSTF) Evidence Report on Screening for Hepatitis C states that a prior review involving five studies found that risk-based screening had sensitivity of >90% and number needed to screen <20 to identify one case of HCV infection [42]. Results from one retrospective study involving 5,917 participants specified that risk-based screening and birth cohort (1946-1964) screening would identify 82% and 76% of cases of HCV, respectively [42,43] (Table 25).

Table 25. Summary table on yield of risk-based HCV screening versus birth cohort screening

Outcomes	**No. of Studies** *(no. of participants)*	**Effect estimate**	**Certainty of Evidence**
Theoretical yield (number of new diagnosed cases per test performed) of risk-based HCV screening versus birth cohort screening	1 cohort study (5,917 patients sampled from the National Health and Nutrition Examination Survey)	Risk-based screening would need to test 25% of population to identify 82% of HCV cases vs birth cohort screening would identify 76% of HCV cases	Low (effect estimate based on hypothetical birth cohort strategy)

On the other hand, according to the CDC report on the recommendations for Hepatitis C Screening among adults, based on nine studies on anti-HCV positivity prevalence, the median anti-HCV prevalence is 1.7% (range 0.02-7.9%) in the general population. Based on eleven studies on persons who use drugs, the median anti-HCV prevalence was 54.2% (range 12.7-67.1%), while for persons with HIV or sexual risks, there were

eight studies on anti-HCV positivity prevalence and the median was 5.2% (range 1.2%-32.9%) [44].

An earlier version (2013) of the USPSTF screening guidelines on Hepatitis C reviewed studies on potential harms associated with screening [45]. Potential adverse events upon receipt of a positive anti-HCV result include binge-drinking on alcohol and misconception of a positive result for other blood-borne infections (4/15 participants) [46]. The other studies reported that 44.2% (161/257) of patients had negative impact on psychological status [47] and difficulty obtaining insurance (25/44 patients) [48]. However, the certainty of these studies is low because of the study design limitations (absence of control groups, reliance on subjective recall and lack of clearly defined outcomes) [45].

4.5.3 Benefits and Harms of Early Intervention

Havens and Anderson emphasize identification and treatment of patients with HCV to avoid disease progression, morbidity and mortality. Treatment presently consists of direct-acting antiviral (DAA) medications and is reported to achieve sustained virologic response (SVR) for 12 or more weeks post-treatment in more than 99% of patients for at least 5 years.[36-38]

The USPSTF Screening Guidelines specified that no study directly addressed HCV-related mortality or morbidity and its effects on quality of life.[37] However, the guideline reviewed the evidence on benefits of treatment, specifically on DAA treatments in improving outcomes in patients with HCV infection.[37]

There were no studies which directly compared benefits of HCV screening vs no screening on the incidence of liver cancer. Indirect evidence from the USPSTF Screening Guidelines state that a retrospective cohort study by Li and colleagues showed that DAA and interferon-based therapy was associated with similar incidence of HCC that was lower compared to without antiviral therapy (incidence rate per 1000 person-years, 7.5 [95% CI, 6.5 to 8.6] and 7.9 [95% CI, 6.0 to 10.4] for antiviral therapy and 10.9 [95% CI, 9.92 to 11.97] for no therapy; p-value not reported).[37, 49]

On the other hand, a large multicenter prospective French study involving 9,895 patients showed that there was no difference between DAA therapy compared to no antiviral therapy in the risk of HCC; exposure to DAA was associated with a decrease in all-cause deaths (adjusted HR 0.48, 95% CI 0.33 to 0.70) and HCC (adjusted HR 0.66, 95% CI 0.46–0.93).[37,47]

Sustained virologic response (SVR) represents HCV eradication from the body and is often utilized as an efficacy endpoint in HCV clinical studies.[50,51] Studies included in the USPSTF evidence review [42,52-79] evaluated the association between achieving SVR versus no SVR after antiviral therapy (including interferon or DAA) with the following outcomes: all-cause mortality and hepatocellular carcinoma. Pooled hazard ratio from 13 studies [52-64] on all-cause mortality from SVR after antiviral therapy was 0.40 (95% CI 0.28-0.56), favoring treatment. On the other hand, pooled HR from 20 studies [56,57,60,65-79] included in the USPSTF evidence review on SVR on hepatocellular carcinoma was 0.29 (95% CI 0.23-0.38). The level of certainty for

both outcomes is considered to be low because of variable treatment regimens (mostly involving interferon-based treatment), non-randomized study designs, as well as varying degrees of baseline liver cirrhosis and genotypes among the included patients [42]. In terms of harms, pooled results of four trials included in the USPSTF evidence review involving a total of 2,113 participants showed a slightly increased risk (RR=1.12, 95% CI 1.02-1.24) from any adverse event (such as headache, fatigue, and gastro-intestinal side effects) with DAA compared to placebo [42]. (Table 26).

Table 26. Pooled effect estimates of benefits (decrease in all-cause mortality and hepatocellular after achieving SVR after HCV antiviral therapy) and harms of treatment (DAA versus placebo)

Outcomes	No. of Studies (no. of participants)	Effect Estimate (95% CI)	Interpretation	Certainty of Evidence
All-cause mortality	13 cohort studies (n=36,996)	Pooled Hazard Ratio 0.40 (0.28-0.56)	Benefit (Favors SVR after anti-viral therapy)	Very Low
Hepatocellular carcinoma	20 cohort studies (n=85,053)	Pooled Hazard Ratio 0.29 (0.23-0.38)	Benefit (Favors SVR after anti-viral therapy)	Very Low
Any adverse event from treatment (DAA)	4 RCTs n=(2,113)	Pooled RR 1.12 (1.02-1.24)	Harm	Moderate

A recent study by Hsu and colleagues report that PWID had a significantly lower SVR (92.2%) after DAA treatment regimens compared to non-PWID (99%, p=0.04).[80] The said study included 53 PWIDs with HCV infections in a single center in China. Similarly, a prospective study done among PWID in Italy reported SVR in 93% (162/174 patients) who were treated for HCV. It is noted that eleven patients were placed on interferon-containing regimens, while most patients (93.7%) were placed in DAA treatment regimens.[81]

4.5.4 Diagnostic Accuracy of Screening and Confirmatory Tests

Our systematic search did not find any direct evidence on screening versus no screening for HCV. Hence, indirect evidence based on the screening cascade will be presented.

Screening for HCV infection is done through anti-HCV testing (detection of viral antibodies via serological means, followed by polymerase chain reaction testing for HCV-RNA).[35-37] A positive anti-HCV test denotes current or active HCV infection, resolved past infection or may be false positive; hence HCV-RNA testing (with detection level of 25 IU/mL or lower) is used to confirm active HCV infection.[38]

The diagnostic accuracy of HCV screening via HCV antibody testing has been well established. A systematic review and meta-analysis of 21 studies by Vasquez-Molon and colleagues reported that for detection of HCV antibodies, pooled diagnostic accuracy measures of dried blood sample showed the following: sensitivity 96.1%, specificity 99.2%, positive likelihood ratio (PLR) 105, negative likelihood ratio (NLR) 0.04, diagnostic odds ratio (DOR) 2692.9.[39]

Similarly, as shown in Table 27, another meta-analysis by Tang, et al. involving five studies showed that when compared to enzyme immunoassay (EIA) as the reference standard, the pooled sensitivity and specificity of HCV antibody rapid diagnostic tests were 98% (95% CI 98-100%) and 100% (95% CI 100-100%), respectively.[40] Furthermore, among blood donors, a study done in Cambodia showed that anti-HCV rapid test versus EIA reference test had a sensitivity and specificity of 77.3% (95% CI 70.4-83.2%) and 99.8% (95% CI 99.3-100%), respectively.[41]

Table 27. Diagnostic Accuracy of HCV antibody rapid diagnostic test

Diagnostic Test	Diagnostic Accuracy		Certainty of Evidence
	Pooled Sensitivity	Pooled Specificity	
HCV antibody rapid diagnostic test (5 studies)	98% (95% CI, 98-100%)	100% (95% CI, 100-100%)	Low certainty

4.5.5 Cost Implication

HCV tests in the Philippines are available in hospitals and diagnostic facilities, with price range of PhP 450-600php and usual turn-around time of results of 2-3 days. Presently, there are no cost-effectiveness study on HCV screening in our country.

The US CDC recommendations include one report on the cost effectiveness considerations for Hepatitis C screening. Based on the analysis, an incremental cost-effectiveness ratio (ICER) of $11,378 per quality adjusted life year (QALY) was achieved for universal screening for adult patients. Furthermore, with HCV prevalence of 0.1%, estimated ICER was $36,0000 per QALY gained.[82]

On the other hand, the Canadian Task Force on Preventive Health Care recognize the resource limitations for population-based testing. The estimated cost for screening for HCV was $844 million, based on an assumed HCV prevalence of 0.2% and 70% screening uptake.[83]

4.5.6 Patient's Values and Preference, Equity, Acceptability, and Feasibility

Based on the 2018 recommendations of the Hepatology Society of the Philippines, DAAs are available in our country and regimens for treatment may vary depending on genotype, previous treatment, and presence of cirrhosis and hepatic decompensation.[84]

It is also very important to consider patient preferences with regards to screening, these include: emphasizing that screening is voluntary and should be done only with the patient's consent, educating patients on HCV infection, and allowing patients to ask questions or decline HCV screening [42] as well as potential stigma and access to health care [83].

4.5.7 Recommendations from Other Groups

Group	Recommendation	Strength of Recommendation & Certainty of Evidence

Hepatology Society of the Philippines	"Screening with serum anti-HCV should be done for patients at risk for acquiring the disease. Testing for anti-HCV should not be routinely performed as a pre-requisite for employment"	Strong recommendation; Moderate Quality of Evidence
US Preventive Services Task Force	"Screen adults aged 18-79 years with anti-HCV antibody testing followed by confirmatory PCR" "The USPSTF also suggests that clinicians consider screening persons younger than 18 years old and older than 79 years who are at high risk for infection (e.g., those with past or current injection drug use)."	B-Recommendation, Moderate Certainty of Evidence
Canadian Task Force on Preventive Health Care	"We recommend against screening for HCV in adults who are not at elevated risk."	Strong Recommendation, Very Low Quality of Evidence
American Association for Study of Liver Diseases – Infectious Disease Society of America	"A one-time HCV test is recommended in asymptomatic persons in the 1945-1965 birth cohort and other persons based on exposures, behavior and conditions that increase risk for HCV infection."	Class I Recommendation, Level B Evidence

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4.6 Screening for HIV

RECOMMENDATIONS

1. **Among asymptomatic, apparently healthy adolescents and adults, we recommend against routine screening for HIV.** ***(Strong recommendation, very low certainty of evidence)***

   Considerations: The panel strongly recommended against routine screening for HIV among asymptomatic apparently healthy adolescents and adults. The panel maintained that HIV screening is multidimensional. Psychological harm of screening should be considered specially among individuals who are at low risk for HIV infection. The panel further emphasized that physicians should identify a compelling reason to request HIV screening for low-risk individuals. The panel likewise cited that routine screening will also be costly for those who do not really need to undergo testing.

2. **Among high-risk* asymptomatic, apparently healthy adolescents and adults, we recommend HIV screening using a rapid diagnostic test.** ***(Strong recommendation, very low certainty of evidence)***

   Philippine DOH Definition of high-risk: *HIV testing shall be routinely offered and promoted to the following (a) key populations including adolescents (b) high-risk individuals who have not been tested recently (c) partners, infants and children of people living with HIV (PLHIV), (d) patients showing signs and symptoms consistent with AIDS defining illness (e) patients with sexually transmitted infections, (f) patients with Hepatitis B and C, (g) patients with undernutrition not responsive to interventions, (h) all confirmed tuberculosis patients, and (i) all pregnant women regardless of risk. Key population: MSM, people in prisons and other closed settings, people who inject drugs, sex workers, and transgender men and women.*

   Considerations: The panel strongly recommended routine screening for HIV among high-risk individuals based on (1) large benefits and trivial harms of screening in terms of early detection and prevention of transmission, and (2) the clear benefits of early treatment. The panel further recommended that individuals who will undergo testing should receive pre-testing counselling.

4.6.1 Burden of HIV infection

Over the years, HIV cases in the Philippines have risen dramatically with an increase in the incidence of 237% in annual new HIV infections from 2010 to 2020.[1] Although the Philippine prevalence remained to be less than 1%, the HIV/Acquired Immunodeficiency Syndrome (AIDS) and Anti-Retroviral Therapy (ART) Registry of the Philippines reported a total of 105,794 confirmed HIV cases in the country-wide registry as of September 2022. Almost 29% of HIV-positive population were in the age group of 15-24 years old with more than half of the cases between 25-34 years old.[2] In an effort to mitigate this burden, the Philippine Department of Health (DOH) issued Administrative Order 2022-0035 which integrates multiple approaches to HIV testing services which includes community- and facility-based HIV testing, self-testing, and index testing.[3]

The World Health Organization (WHO) defines HIV as an infection that attacks the body's immune system specifically the white blood cells called CD4 cells. The condition may eventually weaken the patient's immune status leading to opportunistic

infections and diseases.[4] To date, there is no effective vaccine that prevents and protects against HIV infection. Primary treatment for HIV infection is still a combination of ARTs which lower the risk of both AIDS-defining and non-AIDS-defining complications and reduce the risk of HIV transmission.[5]

Early detection of HIV infection plays a central role in potentially reducing transmission and HIV-related morbidity and mortality. Identification of asymptomatic HIV-positive individuals at potentially higher CD4 counts before they develop into an advanced immune-deficiency state could decrease HIV-related morbidity and mortality.[6] Moreover, early detection of HIV infection could also institute early initiation of therapy to further reduce the risk of transmission and to prevent AIDS-related complications.[7]

4.6.2 Benefits and Harms of Screening

We found no direct studies on the benefits and harms of HIV screening compared with no screening among asymptomatic, apparently healthy adolescents and adults.

Indirect evidence for benefits of screening was derived from one systematic review and meta-analysis of observational studies which compared the prevalence of high-risk sexual behaviors among HIV-positive individuals[13] and one modelling study which estimated the relative contribution of HIV-positive individuals who were aware compared with unaware of their HIV status in sexually transmitting new HIV infections to at-risk partners in the US[14].

In 2005, Marks and colleagues performed a systematic review and meta-analysis which compared the prevalence of high-risk sexual behaviors in HIV-positive individuals aware of their serostatus with that of HIV-positive individuals unaware of their HIV status in the US [13]. A total of 11 studies from 1988 to 2003 with a total of 4,522 individuals were included in the meta-analysis. The analysis, which integrated all 11 independent study findings, indicated that the prevalence of unprotected anal and vaginal intercourse (UAV) with any partner was lower by 68% (95% CI 59% to 76%) among HIV-positive individuals aware of their serostatus when compared with HIV-positive individuals unaware of their serostatus. The study concluded that the prevalence of UAV as a high-risk sexual behavior is substantially reduced after individuals become aware they are HIV-positive. Findings in the study emphasized on the importance of HIV testing to reduce exposure to and potential transmission of HIV from HIV-positive individuals unaware that they are infected.

A modeling study in 2006 by the US CDC Division for HIV/AIDS Prevention [14] estimated the relative contribution of individuals who were aware compared with individuals who were unaware of their HIV-positive status in sexually transmitting new HIV infections to at-risk partners in the US. In this study, the proportion of sexually transmitted HIV from unaware individuals was estimated to range from 0.54 to 0.70. Using a conservative approach, Marks and colleagues estimated that out of 32,000

cases (an estimated 80% of 40,000 new HIV infections transmitted through sexual intercourse), about 17,280 sexual transmissions could be from HIV-positive individuals unaware of their serostatus. This translated to a transmission rate of 6.9% among HIV-positive individuals unaware of their serostatus compared to a transmission rate of only 2.0% from HIV-positive individuals aware of their serostatus. Thus, transmission rate could be 3.5 times higher from HIV-positive individuals unaware of their serostatus. The study highlighted the benefit of intensifying HIV testing and counseling to increase the number of HIV-positive individuals who are aware of their infection. If all individuals unaware of their infection would know their serostatus and a UAV prevalence with at-risk partners reduced by 68% (based on empirical data from the meta-analysis[13]), then new sexual infections could theoretically be reduced from 17,280 to 5,530 among HIV-positive unaware individuals. This reduction could represent a 36% reduction in the overall number of new sexual infections per year (from 32,000 to 20,250). Certainty of evidence was downgraded to very low due to indirectness in the population.

Table 28. Benefits of Screening for HIV

Outcome	Basis	Effect Estimate	Interpretation	Certainty of Evidence
Prevalence of high-risk sexual behavior, in particular, UAV	11 cross-sectional and cohort studies[13] (n=4,522)	-68% (95% CI -75% to -59%)	68% lower high-risk sexual behavior in HIV-positive aware individuals compared with unaware individuals	Very Low
Sexual transmission of HIV	1 modelling Study[14]	6.9% transmission rate with HIV-positive unaware individuals compared with 2.0% transmission rate from HIV-positive aware individual.	Transmission rate could be 3.5 times higher in HIV-positive unaware individuals when compared with HIV-positive aware individuals	Very Low

4.6.3 Benefits and Harms of Early Intervention

Benefits of Early Versus Deferred (or Delayed) ART Initiation

We found four RCTs [15-18] which investigated on the efficacy and safety of early versus deferred (or delayed) initiation of ART. These trials were the HIV Prevention Trials Network (HPTN) Trial [15], Strategies for Management of Antiretroviral Therapy

(SMART) Trial [16], the International Network for Strategic Initiatives in Global HIV Trials Strategic Timing of Antiretroviral Treatment (INSIGHT START) Trial [17] and the TEMPRANO ANRS Trial [18]. The trials included a total of 8,984 HIV-positive adolescents and adults. The SMART Trial [16] included adolescents and adults aged 13 years old and older while the HPTN Trial [15], INSIGHT START Trial [17], and TEMPRANO ANRS Trial [18] included adults aged at least 18 years old. Study participants in all of the four trials were from low-middle income [15,18] to high income countries [16,17] which included Thailand, India, Australia, Israel, Europe, and North America. Interventions in all four trials were early versus deferred (or delayed) ART initiation. In two trials, HPTN Trial [15] and SMART Trial [16], early ART initiation was defined as CD4 count >350 to 500 cells/mm^3 while deferred (or delayed) ART initiation was defined as CD4 count <250 cells/mm^3. In two trials, INSIGHT START Trial [17] and TEMPRANO ANRS Trial [18], early ART initiation was defined as CD4 count >500 cells/mm^3 while deferred (or delayed) ART initiation was defined as CD4 count <350 cells/mm^3. Outcomes investigated were primary composite outcomes which included all-cause mortality, acquired immunodeficiency syndrome (AIDS)-related and non-AIDS-related events, and opportunistic disease, all-cause mortality, AIDS-related events, incidence of tuberculosis, incidence of opportunistic infections, linked HIV transmission, and serious adverse events defined as grade 3 or 4 adverse events. Pooled results from four RCTs [15-18] showed that early ART initiation significantly reduced primary composite outcomes (RR 0.53, 95% CI,0.44-0.64; High certainty). Certainty of evidence was high.

Table 29. Primary Composite Outcomes for Early versus Deferred (or Delayed) ART Initiation

Outcome	Basis	Effect Estimate (95% CI)	Interpretation	Certainty of Evidence	Importance
Primary Composite Outcomes	4 RCTs (n=8,984)	RR 0.53 (0.44 to 0.64) I^2=0%	BENEFIT (Favors Early ART)	High	Critical

Results from four trials [15-18] showed significant reduction in all-cause mortality (RR 0.39, 95% CI 0.19-0.80; Moderate certainty), AIDS-related events (RR 0.47, 95% CI 0.31-0.71; Moderate certainty), and incidence of tuberculosis (RR 0.47; 95% 0.34-0.65; High Certainty) with early ART initiation when compared to deferred (or delayed) ART initiation. Effect of early ART initiation when compared to deferred (or delayed) ART initiation was inconclusive in terms of incidence of bacterial infection (RR 0.67; 95% 0.30-1.52; Low Certainty). Certainty of evidence for all-cause mortality and AIDS-related events was downgraded to moderate due to inconsistency from substantial heterogeneity (I^2>50%). Certainty of evidence for incidence of bacterial infections was downgraded to low due to imprecision and inconsistency from substantial heterogeneity (I^2>50%).

Table 30. Pooled Analysis of Other Clinical Outcomes for Early versus Deferred (or Delayed) ART Initiation

Outcome	Basis	Effect Estimate (95% CI)	Interpretation	Certainty of Evidence	Importance
All-cause mortality	4 RCTs (n=8,984)	RR 0.39 (0.19 to 0.80) I^2=76%	BENEFIT (Favors Early ART)	Moderate	Critical
AIDS-related events	4 RCTs (n=8,984)	RR 0.47 (0.31 to 0.71) I^2=60%	BENEFIT (Favors Early ART)	Moderate	Critical
Incidence of tuberculosis	4 RCTs (n=8,984)	RR 0.47 (0.34 to 0.65) I^2=0%	BENEFIT (Favors Early ART)	High	Critical
Incidence of bacterial infection	4 RCTs (n=8,984)	RR 0.67 (0.30 to 1.52) I^2=74%	INCONCLUSIVE	Low	Critical
Linked transmission	1 RCT [21] (n=1,763)	HR 0.07 (0.02-0.22)	BENEFIT (Favors Early ART)	Moderate	Critical

The HPTN Trial [15] further reported that the initiation of early ART significantly decreased the risk of HIV-linked transmission to uninfected sex partners when compared with deferred (or delayed) ART initiation (HR 0.07, 95% CI 0.02 to 0.22; Moderate certainty). In this study, reported hazard ratios were calculated from univariate and multivariate Cox regression analysis stratified according to study site. The multivariate model included early versus delayed ART therapy, baseline CD4 count per 100 CD4 increment, baseline viral load, sex (male versus female), and baseline condom use (100% versus <100%). Certainty of evidence was downgraded to moderate due to low event rates.

Harms of Early Versus Deferred (or Delayed) ART Initiation

From four trials [15-18], effect of early compared with deferred (or delayed) ART initiation on the risk of grade 3 or 4 adverse events was inconclusive (RR 0.94, 95% CI, 0.80-1.11; Moderate certainty). Risk estimates were imprecise regardless of the level of CD4 counts. The most commonly reported adverse events were bacterial infections, gastrointestinal, metabolism, nutrition disorders, and hematologic in both the early and deferred (or delayed) ART initiation groups. Certainty of evidence was downgraded due to imprecision.

Table 31. Serious Adverse Events for Early versus Deferred (or Delayed) ART Initiation

Outcome	Basis	Effect Estimate (95% CI)	Interpretation	Certainty of Evidence	Importance
Grade 3 or 4 Adverse Events	4 RCTs (n=8,984)	RR 0.94 (0.80 to 1.11) I^2=0%	INCONCLUSIVE	Moderate	Critical

Table 32. Clinical Outcomes on the Effects of Early versus Deferred (or Delayed) ART Initiation in the 4 RCTs According on the Level of CD4 Counts

Studies (No. of Participants)	Primary Composite Outcomes	All-cause Mortality	AIDS-related events	Incidence of Tuberculosis	Incidence of Bacterial Infection	HIV transmission
CD4 >500 cells/mm^3						
INSIGHT START Trial 2015 (n=4,685)	RR 0.44 (95% CI, 0.31-0.63) Definition: All-cause mortality, serious AIDS-related events, and serious non-AIDS-related events	RR 0.58 (95% CI 0.29-1.18)	RR 0.28 (95% CI 0.16-0.51)	RR 0.30 (95% CI 0.12-0.76)	RR 0.39 (95% CI 0.21-0.73)	NR
TEMPRANO ANRS Trial 2015 (n=2,056)	RR 0.57 (95% CI, 0.43-0.77) *Definition: All-cause mortality, progression to AIDS, AIDS- defining cancer, or non-AIDS-defining invasive disease*	RR 0.19 (95% CI 0.12-0.30)	RR 0.50 (95% CI 0.33-0.76)	RR 0.50 (95% CI 0.32-0.79)	RR 0.39 (95% CI 0.21-0.71)	NR
CD4 >350 cells/mm^3						
HPTN Trial 2011 (n=1,763)	RR 0.61 (95% CI, 0.42-0.89) *Definition: All cause-mortality, serious AIDS-related, and serious non-AIDS related events*	RR 0.76 (95% CI 0.34-1.73)	RR 0.69 (95% CI 0.49-0.97)	RR 0.51 (95% CI 0.29-0.91)	RR 1.45 (95% CI 0.72-2.91)	HR 0.04 (95% CI 0.01 – 0.28) *Definition: Linked HIV transmission 5.5-year follow-up*
SMART Trial 2008 Subgroup Analysis (n=477)	RR 0.31 (95% CI, 0.11-0.83) *Definition: All-cause mortality or opportunistic disease*	RR 0.31 (95% CI 0.11-0.83)	RR 0.33 (95% CI 0.11-1.03)	RR 0.31 (95% CI 0.03-2.91)	RR 4.58 (95% CI 0.22-94.89)	NR

Abbreviations: ANRS, Agence Nationale de Researche sur le SIDA; **HPTN**, HIV Prevention Trial Network; **NR**, Not Reported; **RR**, Relative Risk**; SMART**, Strategies for Management of Antiretroviral Therapy; **START**, Strategic Timing of Antiretroviral Treatment

Optimal HIV Screening and Testing Frequency

Evidence for optimal HIV screening and testing intervals among HIV-negative individuals from various risk groups was examined by K. Timmerman et al [19] in 2018. In a systematic review of 27 articles, HIV testing intervals in the general population, men having sex with men, PWIDs, and sex workers were synthesized and analyzed. Studies included in the systematic review were modelling studies with economic inputs. Optimal testing intervals across different risk groups ranged from one-time testing for the general population to every three months for high-risk populations. In the general population, testing frequency ranged from every three months, annually, every two years, every three years, every five to ten years, and one-time testing based on an individual's risk and prevailing incidence of HIV. The most common testing strategy identified in the general population was a one-time testing strategy for low-risk individuals in a low prevalence setting (i.e., <1% HIV prevalence). On the other hand, individuals who belong to high-risk groups, testing frequency ranged from every three months, every six months, and annually. The most common testing strategy identified in the high-risk population was every three months to annually. Despite the lack of consistency in the findings to identify an optimal HIV testing interval for specific risk populations, results of the review are still consistent with the recommendations by the US CDC on HIV screening for gay, bisexual, and other MSM. According to US CDC, pragmatic experience and expert opinion support the recommendation of HIV testing among high-risk individuals from once per year to more frequent intervals.

4.6.4 Diagnostic Accuracy of Screening Tests

At present, the Philippine DOH utilizes three algorithms in HIV testing: (1) using a combination of rapid diagnostic tests (RDT) and enzyme immunoassays, (2) using an immunoassay or an RDT, then confirmed by immunochromatographic tests, and (3) using a test with the lowest number of false positives based on the validation study.[8] The WHO recommends that all HIV testing algorithms achieve at least 99% positive predictive value and use a combination of tests with >99% sensitivity and >98% specificity. [9-11]

A 2018 diagnostic accuracy systematic review and meta-analysis compared RDTs for HIV and Western Blot for screening of HIV.[12] RDTs included in the review were Capillus HIV-1/HIV-2, Determine HIV-1/2, Serocard HIV, HIV Check 1+2, Serodia HIV, and Genie II HIV-1/HIV-2 as index tests. Western blot was used as the gold standard. The review reported sensitivity and specificity values from 20 studies with a total of 27,343 individuals tested. Tests were performed in the general population (volunteers, blood donors, and antenatal clinics) and high-risk individuals (high-risk men having sex with men or MSM). In the pooled analysis, RDTs showed a sensitivity of 99.8% (95% CI 99.10% to 100%; Moderate certainty) and specificity of 99.8% (95% CI 99.4% to 99.90%; Moderate certainty). Certainty of evidence was downgraded to moderate due to inconsistency from heterogeneity.

Table 33. Diagnostic Accuracy of Rapid Diagnostic Tests (Index Test) versus Western Blot (Gold Standard)

Basis	Sensitivity (95% CI)	Specificity (95% CI)	Effect per 1,000 individuals tested				Certainty of Evidence
			True Positive	False Positive	True Negative	False Negative	
Low Probability: At 1% (Overall HIV Prevalence in the Philippines)[a]							
20 studies[b] (n=27,343)	0.998 (0.991-1.000)	0.998 (0.994-0.999)	10 (10 to 10)	2 (1 to 6)	988 (984 to 989)	0 (0 to0)	Moderate
High Probability: At 15% (HIV Prevalence in High-risk Individual i.e., MSM)[c]							
20 studies[b] (n=27,343)	0.998 (0.991-1.000)	0.998 (0.994-0.999)	150 (149 to 150)	2 (1 to 5)	848 (845 to 849)	0 (0 to 1)	Moderate

[a]Overall prevalence data <1% from Philippine DOH [b]COMBINED RT ASSAYS included Capillus HIV-1/HIV-2, Determine HIV-1/2 and Mixed Assays (Serocard HIV, HIV Check 1+2, Serodia HIV, and Genie II HIV-1/HIV-2) [c]Estimated Prevalence of HIV among high-risk individuals i.e., men having sex with men from Thailand (https://www.uptodate.com/contents/global-epidemiology-of-hivinfection?source=history_widget)

4.6.5 Cost Implication

In high HIV prevalence setting, it was demonstrated that the cost-effectiveness of routine versus targeted testing yields a higher positivity rate.[20] But even in the setting of <1% prevalence of HIV infection, in the era of antiretroviral therapy, the cost-benefit and cost-effectiveness are also observed. Sanders et al demonstrated <50,000 USD per quality-adjusted life-year for voluntary screening. Furthermore, the advantage of early detection among screened HIV-positive individuals is a reduction in the annual HIV transmission rate by 21%. This is mainly due to a reduction in the risk behavior and HIV infectivity with the initiation of an anti-retroviral agent.[21,22] In previous USPSTF guidelines, the analysis supports the cost-effectiveness of HIV screening in settings with low or average HIV prevalence.[23]

In the information briefs of DOH for HIV testing, they presented the estimated cost of rapid diagnostic tests and confirmatory tests with a shorter turnaround time using RDT of 10-30 minutes compared to 7-21 days in the western blot. Costs vary on the brands of test kits.[24]

Table 34. The DOH Costing of Rapid Diagnostic Test and Confirmatory Test for HIV

	Rapid Diagnostic Tests		Western Blot
Type of Assay	Immunochromatographic	Qualitative Immunoassay	Qualitative Immunoassay
Description	Antibodies for HIV type 1, subtype O and HIV type 2: IgG, IgM, IgA	HIV Antibodies Type 1 & 2 HIV Type 1 p24 Ag	HIV antibodies type 1 and 2
Estimated Cost	PhP 50 to 1,500	PhP 150	Php 3500

4.6.6 Patient's Values and Preference, Equity, Acceptability, and Feasibility

The Philippines qualifies to the WHO definition of low HIV-burden settings as an HIV national prevalence of less than 5%.[25] In a low HIV-burden, a practical approach in

our local setting for clinicians is to adequately screen patients with clinical indicators of HIV or individuals who are at increased risk for exposure to HIV infection than doing a mandatory screening for all age group. The DOH AO 2017-0019 provided updated guidelines to standardize HIV testing services in health facilities. HIV testing shall be routinely offered and promoted to the following [26]: (a) key populations including adolescents (b) high-risk individuals who have not been tested recently (c) partners, infants and children of people living with HIV (PLHIV), (d) patients showing signs and symptoms consistent with AIDS defining illness I patients with sexually transmitted infections, (f) patients with Hepatitis B and C, (g) patients with undernutrition not responsive to interventions, (h) all confirmed tuberculosis patients, and (i) all pregnant women regardless of risk. Key population was defined as males who are having sex with a male (MSM), people in prisons and other closed settings, people who inject drugs, sex workers, and transgender men and women. It is recommended to do this every 3 months of retesting for key populations and annually for their casual or intimate partners or PLHIV. Furthermore, it was stipulated that appropriate pre- and post-HIV test counseling shall be implemented for all clients.[27]

Furthermore, the WHO recommends a convenient approach to HIV testing services. HIV self-testing (HIVST) is an accurate and feasible strategy to increase the acceptance of HIV testing among key populations. However, no clear implementing guidelines have been set in the country, and have to identify regulatory issues concerning this test, privacy and adequate linkage to care.[28] The nature of HIV testing is also complex considering that all testing should adhere to WHO's essential 5 Cs (Consent, Confidentiality, Counselling, Correct test results, Connection/linkage to prevention, care, and treatment). In low HIV burden settings, HIV testing is offered in a targeted population. Those who have symptoms or medical conditions relating to HIV infection are tested in facility-based HIV testing services (HTS). Another concern is one of the age groups that is increasing in number in the Philippines is the younger population. Programs should focus on screening this vulnerable generation and revisit the consenting age for HIV testing.

4.6.7 Recommendations from Other Groups

Group	Recommendation	Certainty of Evidence and Strength of Recommendation
WHO 2021 [29]	In low HIV-burden settings, HIV testing should be offered for: (a) adults, adolescents or children who present in clinical settings with signs and symptoms or medical conditions that could indicate HIV infection, including TB, viral hepatitis and sexually transmitted infections (b) HIV-exposed children and symptomatic infants and children (c) key populations and their partners (d) pregnant women	Strong Recommendation, Low Quality of Evidence

USPSTF 2019 [30]	Clinicians should screen for HIV infection in adolescents and adults aged 15 to 65 years. Younger adolescents and older adults who are at increased risk of infection should also be screened.	GRADE A Recommendation, High Certainty
US CDC 2006 [31]	In all healthcare settings, screening for HIV infection should be performed routinely for all patients aged of 13 to 64. Healthcare providers should initiate screening unless the documented prevalence of undiagnosed HIV infection is <0.1%. In the absence of existing data for HIV prevalence, health care providers should initiate voluntary HIV screening until they establish that the diagnostic yield is <1 per 1000 patients screened, at which point such screening is no longer warranted. All patients initiating treatment for TB should be screened routinely for HIV infection. All patients seeking treatment for STDs, including all patients attending STD clinics, should be screened routinely for HIV during each visit for a new complaint, regardless of whether the patient is known or suspect ted to have specific behavior risk for HIV infection.	Not Stated
Canadian Task Force on Preventive Health Care 2003 [32]	Canadian practitioners should consider testing those with clinical indicators of HIV or with factors that increase the risk for exposure to HIV infection, focusing on higher-prevalence groups such as men who have sex with men, people who inject drugs and people from HIV-endemic countries. Although some Canadian jurisdictions have moved to recommend routine screening in certain settings (e.g., primary and/or emergency care) in response to their local HIV epidemiology, it is important to note that this practice is not yet supported by direct evidence. In the opinion of the Canadian Task Force on Preventive Health Care, primary care practitioners in Canada should continue to offer HIV counseling and testing to individuals who may be at increased risk for exposure to HIV, given the potential benefits of timely detection. Pregnant women should continue to be screened for HIV as per existing guidelines.	Consensus Statement (Adopted from the USPSTF Recommendation)

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4.7 Screening for Dental Infections

RECOMMENDATION

Among asymptomatic, apparently healthy adults, we recommend annual screening for dental infections through visual inspection. ***(Strong recommendation, very low certainty of evidence)***

Considerations:

- The panel strongly recommended annual screening for dental infections to emphasize oral health recognizing the burden of dental infections and the negative impact of poor oral health on the overall wellbeing of an individual including its effect on one's productivity in school and at work. The panel likewise raised that there are legislations in Occupational Health and Safety in relation to dental health in support of this recommendation. The Rules and Regulations and Standards Requirements for Occupational Dental Health Services prescribed under the Philippine Labor Code of 1974 and the Philippine Department of Health Administrative Orders No. 7 and 306 signed December 9, 1976 and August 21, 1978, and Administrative Order No. 3 signed February 4, 1998 as amended mandate the conduct of complete and thorough oral examination of workers for pre-employment physical examination and certification whether the worker is "orally fit or not" and the conduct of oral examination of workers during employment at least once a year in a non-hazardous workplace and periodic oral examination as may be deemed necessary.
- The consensus panel agreed on an annual interval for screening to essentially detect asymptomatic dental infections.
- The current recommendation on screening for dental infection through visual inspection is expected to be performed by primary care providers with appropriate referral to dentists for further evaluation and management.

4.7.1 Background

The Oral Health Program of Department of Health in the Philippines provides services such as oral examination, education and counseling on good oral hygiene, diet and adverse effects of tobacco/smoking and alcohol and sweetened beverages & food, gum treatment, oral prophylaxis and scaling, permanent filling, and atraumatic restorative treatment (ART) to adults aged 20 to 59 years old [1]. There is no universally recognized definition of the term 'routine dental check-up'. It can involve many of the following dental services such as clinical history taking and examination, the provision of advice, charting (including assessment and recording of any malocclusion and monitoring of periodontal status), explanation of the risks, as well as the costs, of any required treatment and reporting or recording [2].

The primary purpose of the dental clinical examination is to detect the signs and symptoms of oral disease: in particular, dental caries, periodontal disease, as well as oral cancer. The clinical examination basically requires visual inspection of the teeth and surrounding structures using a plane mouth mirror. Radiography, for detection of approximal caries, and fiberoptics is not recommended in the initial screening and may be useful to further assess the extent and reduce the underestimation of already identified dental lesions and caries [3]. Radiography and newer modalities for diagnosis of dental pathology such as fiberoptics and laser fluorescence will not be

discussed as they require additional cost and were found to have not enough data to show a difference of efficacy with visual inspection [4, 5].
Many dental practitioners provide regular prophylactic scaling and polishing for patients at low risk of developing periodontal disease. “Routine scale and polish” treatment generally means scaling or polishing, or both, of the crown and root surfaces of the teeth to remove local irritational factors (plaque, calculus, debris and staining). This procedure does not involve periodontal surgery or any form of supplementary periodontal therapy [6].

A 'recall visit' is defined as "the planned, unprecipitated return of a patient who, when last seen was in good oral health" [7]. Since the definition indicates a patient of previously good health, this definition can also be applied to 'routine dental check-up' or an 'oral health review' of a patient who has no apparent dental complaints and is healthy. The 'recall interval' is the period, in months or years, or the regularity of follow up examinations. No study was found that specifically evaluates the value of a first dental consult, as it is assumed (in available studies) that a dental consult will happen for all adults at some point in their life course.

Regular oral health risk assessment among children is recommended at age of 6 months or eruption of first tooth and every 6 months thereafter [8]. By the time the individual reaches adulthood, there is no definite guideline as to regularity and necessity of oral health screening in asymptomatic, apparently well adults. While it was customary for dentists in the National Health Service of the United Kingdom to follow up their patients in a 6-monthly interval, newer guidelines were made to base the recall interval on a risk-based assessment [7]. In the improvement of oral health with the mandated delivery of enhanced dental services especially among developed countries, those who cannot afford such services carry the bulk of oral diseases [9]. These variations in the distribution of dental disease within populations, associated with dissimilarities in the risk of developing oral disease between individual patients cannot be adequately addressed by a uniformly fixed recall interval and best favors a personalized examiner-dependent risk-based approach as to need and frequency of follow up.

The provision of non-complex procedures delivered by dental practitioners such as routine dental check-ups, scaling and polishing, and other associated interventions compose most of the total direct expenditure on oral health. Decisions about when and how frequently to recall patients for routine dental check-ups influence not only the health care cost but also the dentists’ workloads and capacity to streamline services to more serious dental conditions. The impact of the consultation frequency or “recall interval” on the timely detection and intervention of new onset oral illnesses and the risk for iatrogenic over-diagnosis and over-treatment is also affected. The value of following-up patients who were previously assessed as low risk for dental pathology or, equally, to screen asymptomatic or apparently healthy adults is put to question. This evidence summary will focus on the benefits and harm of the regularity of routine visual inspection or “dental recall interval” in the screening for dental infection in apparently well adults.

4.7.2 Burden of Dental Illness

Oral health is fundamental to the overall health of an individual that supports day to day function such as breathing, eating, talking, social interaction, and physical hygiene and appearance. Oral disease is recognized as a major global health burden with almost half of the world's population (45% or 3.5 billion people) suffering from oral diseases, most of which are people living in low- and middle-income countries [9, 10]. Dental caries and periodontal disease are among the most common chronic diseases. According to the WHO Global Oral Health Status Report (GOHSR), untreated dental caries is the single most common condition globally, affecting an estimated 2.5 billion people. Severe gum disease, a major cause of total tooth loss, is estimated to affect 1 billion people worldwide [9].

In 1998, an estimate of about 92.4% of Filipinos have dental caries and 78% have periodontal diseases. Majority of local surveys on dental health focus on the pediatric population. According to the DOH, the average number of Decayed, Missing and Filled Teeth (DMFT) of 12-year-old Filipinos was higher at 4.48 than the WHO standards of 3 DMFT and below [11].

According to the 2006 National Oral Health Survey (NOHS), 97.1% of six-year-old children suffer from tooth decay, around 78.4% suffer from dental caries, 49.7% had dentinogenic infection presentations, while 74% of twelve-year-old children suffer from gingivitis. These early manifestations of dental conditions may complicate into irreversible periodontal disease in adolescence and adulthood, if not treated early.

Dental caries and periodontal diseases are the 2 most common oral diseases among Filipinos. Although they are not fatal diseases, they weaken bodily immunity and predispose the individual to serious conditions such as endocarditis, gastro-intestinal diseases, orofacial and/or neurologic infection, and chronic oral discomfort and malfunction. Speech disturbance and chronic recurrent dental pain may affect work performance, nutrition, social interactions, income, and self-esteem. Late detection and treatment require more complicated investigation and intervention such as tooth extraction, antimicrobial coverage, fluoride varnishes, topical solutions, and/ or rinses, chlorhexidine varnishes, topicals, and/ or rinses, combined chlorhexidine-fluoride applications, occlusal sealants, subgingival iodine irrigation, ultrasonic scaling, and other approaches. These procedures may be invasive and costly [9, 10, 11].

Among the 194 countries evaluated in the GOHSR, it was estimated that the total direct expenditure for oral diseases from the public and private sectors' oral health care services (except for oral cancer) amounted to 387 billion US dollars, or a global average of about 50 US dollars per capita, in 2019. This comprises about 4.8% of the global direct health expenditures. At the same time, productivity losses from oral diseases were estimated at 42 US dollars per capita, or a total of around 323 billion US dollars globally [9].

4.7.3 Benefits and Harms of Dental Screening

a. Dental Recall Interval

The need to discriminate dental consult intervals for each individual patient, tailored to meet the patient's needs, based on an assessment of disease levels and risk of or from dental disease was emphasized by the National Institute for Health and Care

Excellence in England and Wales [12]. This is indirectly supported by a few systematic studies that showed very low certainty of evidence in observational studies that explored the benefits and harm of various recall interval schemes (every 6, 12, or 24 months, etc.) as to dental outcome [13, 14]. These reviews consistently have similar findings of poorly reported, heterogenous studies that widely vary in characteristics and the direction of effect (e.g., varying dental check frequencies on measures of caries in deciduous mixed or permanent dentition, periodontal disease or oral cancer in permanent dentition).

A systematic review of 29 studies aimed to review the effectiveness of routine dental checks of different recall frequencies in adults and children. All of the studies include participants who have deciduous, mixed and permanent dentition (population); having gone through various intervals of “routine dental check” (intervention); with observed outcomes of caries, periodontal disease, quality of life, and oral cancer. It concluded that there is no existing high-quality evidence to support or refute the practice of encouraging six-monthly dental checks in adults and children [13].

Another systematic review examined the evidence behind the rationale of a “one-recall-interval-fits-all” protocol, specifically a six-month recall interval (intervention) on caries incidence (outcome). There were 7 articles reviewed that met the inclusion criteria. The studies notably differed in outcome and outcome measurements. One randomized controlled trial showed no significant differences in oral health between patients recalled every 12 months and those recalled every 24 months. One nonrandomized controlled trial found that a 2 to 3-month recall interval significantly reduced the incidence and recurrence of caries while another nonrandomized trial compared caries increments from 3-, 6- and 12-month recall intervals with no significant differences. Two retrospective studies showed that a specific recall interval did not alter caries incidence significantly while a cross-sectional study determined that a six-month recall interval was associated with more restored teeth but less active caries. The differing recall intervals observed with varying outcomes led the authors of this review to conclude that there is weak evidence for using a one-recall interval-fits-all protocol to reduce caries [14].

Two randomized control trials (RCT) were similar to the characteristics of the research question. Although no RCT was found that compared the oral health outcome of unscreened and screened healthy asymptomatic adults. These RCTs aimed to find out which routine dental recall interval is best suited for individuals who were initially examined as low-risk individuals or are considered healthy at initial dental consult. These studies were evaluated thoroughly in a regularly updated Cochrane review on Recall Intervals for Oral Health in Primary Care Patients, the latest of which was published in the year 2020 [15].

One RCT was conducted in a public dental service clinic in Norway among 3 groups of participants aged 3 to 5 years old, 16 to 18 years old, and 18 to 20 years old who received routine dental care from the clinic. The study included a total of 185 patients and excluded those classified as ‘high risk’. Random allocation of recall interval schedule was done in each subgroup between recall at 12 and 24 months while the other recall is at 24 months. The process of random allocation and concealment was

not elaborated. The incremental number of decayed, missing, filled, and sound tooth surfaces (DMFS) as well as length of time per consult were recorded in each visit [16].

The second RCT was a multicenter trial of 2372 participants from 51 general dental practices across the UK, among low-risk adults (aged18 years and older) who had visited their dentist within the previous two years, and who received dental care, including dental examination. Participants were randomized to receive a dental check-up at 6-monthly, 24-monthly or risk-based recall intervals. The following comparisons were evaluated: risk-based versus 6-month recall; risk-based versus 24-month recall; and a 24-month versus 6-month recall. The main outcome measures observed were dental caries as categorized by the International Caries Detection and Assessment System (ICDAS), percentage of sites with gingival bleeding on probing, oral health-related quality of life (OHRQoL), and cost-effectiveness [17]. Risk-based approach is decided upon by the attending dentist and is guided by the recommendations of the National Institute of for Clinical Excellence Guidelines (NICE) on dental recall interval for low-risk individuals [12].

Dental Caries at 24-month versus 12-month recall at 2 years follow-up (1 RCT, N= 49, very low certainty of evidence)
There is very low certainty of evidence that there is an important difference in caries occurrence among adults assigned to either a 24-month or a 12-month dental follow-up or recall. For 18- to 20-year-olds with permanent teeth, the mean difference (MD) in DMFS increment was 1.8 (95% CI -2.09 to 5.69; 49 participants). The presence of dental caries by virtue of the DMFS were assessed as the only clinical outcome in this study [16].

Dental caries at Risk-based recall versus 6-month recall at 4 years follow-up (1 RCT, N= 1486, high certainty of evidence)
There is high-certainty evidence that there is little to no difference between risk-based and 6-month recall intervals for the number of tooth surfaces with any caries at 4 years follow-up (ICDAS 1 to 6; MD 0.15, 95% CI −0.77 to 1.07) [17].

Gingival bleeding at Risk-based recall versus 6-month recall at 4 years' follow-up (1 RCT, N= 1473, moderate certainty of evidence)
There is moderate-certainty evidence that there is little to no difference between risk-based and 6-month recall intervals for the outcome of proportion of sites with gingival bleeding (MD 0.47, 95% CI -1.76 to 2.70) [17].

Dental caries at 24-month recall versus 6-month recall at 4 years' follow-up (1 RCT, N= 273, low certainty of evidence)
There is moderate-certainty evidence that there is little to no difference between 24-month and 6-month recall intervals for the outcome of number of tooth surfaces with any caries (MD 0.60, 95% CI −1.32 to 2.5) [17].

Gingival bleeding at 24-month recall versus 6-month recall at 4 years' follow-up (1 RCT, N= 271, low certainty of evidence)
There is low-certainty evidence that there is an important difference between 24-month and 6-month recall intervals for the outcome of proportion of sites with gingival bleeding (MD 1.2, 95% CI −3.8 to 6.2) [17].

Dental caries at Risk-based recall versus 24-month recall at 4 years' follow-up (1 RCT, N= 281, low certainty of evidence)
There is low-certainty evidence that there is an important difference between risk-based and 24- month recall intervals for the outcome of number of tooth surfaces with any caries (MD -1.4, 95% CI −3.49 to 0.69) [17].

Gingival bleeding at Risk-based recall versus 24-month recall at 4 years' follow-up (1 RCT, N= 295, low certainty of evidence)
There is low- certainty evidence that there is an important difference between risk-based and 24- month recall intervals for the outcome of percentage of sites with gingival bleeding (MD -1.2, 95% CI −5.7 to 3.3) [17].

Table 35. GRADE Summary of Findings for RCTs on Recall Interval

Critical Outcome		**Basis**	**Effect Size**	**95% CI**	**Interpretation**	**Summary of Evidence**
2 years follow up: 24-months vs 12 months recall	Dental Caries	49	MD 1.8	-2.09, 5.69	Inconclusive	Very low certainty of evidence
4 years follow up: Risk-based recall vs 6-months recall	Dental caries	1486	MD 0.15	−0.77, 1.07	Inconclusive	Moderate certainty of evidence
	Gingival bleeding	1473	MD 0.47	−1.76, 2.70	Inconclusive	Moderate certainty of evidence
4 years follow up: 24-months recall vs 6 months recall	Dental caries	273	MD 0.6	−1.32, 2.5	Inconclusive	Low certainty of evidence
	Gingival bleeding	271	MD 1.2	−3.8, 6.2	Inconclusive	Low certainty of evidence
4 years follow up: Risk-based recall vs 24-months recall	Dental caries	281	MD -1.4	−3.49, 0.69	Inconclusive	Low certainty of evidence
	Gingival bleeding	295	MD -1.2	−5.7, 3.3	Inconclusive	Low certainty of evidence

b. Prophylactic Treatment vs No Treatment

Dental plaque formation is not a disease by itself, but it is the most important risk factor for developing periodontitis. Dentists address this by routinely performing periodontal instrumentation (PI) or scaling and polishing even to low-risk patients. The evidence of the clinical effectiveness and optimal frequency of periodontal instrumentation is

unclear, wherein there is insufficient evidence to determine the effects of routine PI treatments [6]. A similar research question explores the effects of prophylactic dental treatment to patients assessed as low risk for dental disease.

There were 2 RCTs found that examined the effect of prophylactic dental treatment of routing scaling and polishing or otherwise known as periodontal instrumentation versus no treatment. Both included participants who scored low in the Basic Periodontal Index (BPE) at 0-3 and are considered healthy. The first was published in 2011 by Jones et al [19], which included 307 healthy adults in a practice-based parallel randomized controlled trial with 24-month follow-up. Participants were randomly assigned to 3 groups (6-month, 12-month, or 24-month interval between scale and polish). The primary outcome was gingival bleeding and were recorded by examiners blinded to the allocation.

The 2nd RCT tested the clinical effectiveness and assessed the economic value of personalized oral health advise (OHA) versus routine OHA, 12-monthly PI (scale and polish) compared with 6-monthly PI, and no PI compared with 6-monthly PI. It was a multicenter, pragmatic split-plot, randomized open trial with a cluster factorial design (for the OHA comparison) and blinded outcome evaluation with 3 years' follow-up and a within-trial cost–benefit analysis [18].

Gingivitis at 6-monthly PI vs no PI (2 RCTs, N= 1087, low certainty of evidence)
There is low-certainty evidence that there is little to no difference between 6- monthly PI vs no PI for the outcome of gingivitis measured as mean proportion of bleeding sites per patient (MD -0.24, 95% CI -3.16 to 2.68). [18, 19]

Calculus formation at 6-monthly PI vs no PI (2 RCTs, N= 1086, low certainty of evidence)
There is low-certainty evidence that there is little to no difference between 6-monthly PI vs no PI for the outcome of calculus formation (MD -0.29, 95% CI -0.56 to 0.02).[19]

Plaque formation at 6-monthly PI vs no PI (1 RCT, N= 207, low certainty of evidence)
There is low-certainty of evidence that there is little to no difference between 6-monthly PI vs no PI for the outcome of plaque formation measured as mean proportion of plaque per patient (MD 0.04, 95% CI -0.05 to 0.13). [19]

Gingivitis at 12-monthly PI vs no PI (2 RCTs, N= 1091, low certainty of evidence)
There is low-certainty evidence that there is little to no difference between a 12 monthly PI vs no PI for the outcome of gingivitis measured as mean proportion of bleeding sites per patient (MD -1.09, 95% CI -4.08 to 1.91). [18,19]

Calculus formation at 12-monthly PI vs no PI (2 RCTs, N= 1089, low certainty of evidence)
There is low-certainty evidence that there is little to no difference between a 12 monthly PI vs no PI for the outcome of calculus formation (MD -0.09, 95% CI -0.36 1to 0.18). [19]

Plaque formation at 12-monthly PI vs no PI (1 RCT, N= 200, low certainty of evidence)
There is low-certainty of evidence that there is little to no difference between 12-monthly PI vs no PI for the outcome of plaque formation measured as mean proportion of plaque per patient (MD = 0.00, 95% CI -0.09 to 0.09). [19]

Table 36. GRADE Summary of Findings for RCTs on prophylactic PI

Critical Outcome		**Basis (N)**	**Effect Size**	**95% CI**	**Interpretation**	**Summary of Evidence**
6 monthly PI vs no PI	Gingivitis	1087	MD -0.24	-3.16, 2.68	Inconclusive	Low certainty of evidence
	Calculus	1086	MD -0.29	−0.56, -0.02	Favors 6 months	Low certainty of evidence
	Plaque	207	MD 0.04	−0.05, 0.13	Inconclusive	Low certainty of evidence
12 monthly PI vs no PI	Gingivitis	1091	MD -1.09	-4.08, 1.91	Inconclusive	Low certainty of evidence
	Calculus	1089	MD -0.09	-0.36, 0.18	No difference	Low certainty of evidence
	Plaque	200	MD 0	−0.09, 0.09	No difference	Low certainty of evidence

4.7.4 Resource Implication

a. Economic Evaluations on Different Recall Intervals

The multi-center RCT on recall interval, discussed previously, also performed a within-trial economic evaluation by assessing the willingness to pay (WTP) of patients for dental recall interval and dental health outcomes, WTP for dental health outcomes only, and QALYs. The cost values collected were NHS dental costs, all NHS costs and participant costs from dental claims data, and annual participant completed questionnaires. QALYs were derived from the responses to the annual participant completed EQ-5D-3L questionnaire and valued according to UK general population tariffs. An online discrete choice experiment (DCE) was used to estimate WTP tariffs which were matched to frequency of recall interval, instances of bleeding on brushing and number of caries observed in the trial. The results showed that willingness to pay by the general population were in favor of avoiding progressive levels of dental decay and bleeding gums as well as more frequent recalls. When restricting the scope of benefit valuation to dental outcomes only (such as for bleeding on brushing and caries experience only), 24-month recall is the best strategy, with a high probability of positive net dental health benefit ranging between 65% and 99%. [15]

An economic evaluation used a Markov decision analysis modelling exercise to arrive at an incremental cost-effectiveness analysis of the various dental check recall policies in different dental clinics across the United Kingdom. Effectiveness of the policies are reflected by the decay experience (DMFT) among children aged 1–6 years with only deciduous dentition, and among children/adults aged 12–80 years with only permanent dentition (DMFT). The assumption was that dental checks, not aided by radiography, are effective for identifying gross decay because these surveys are based on clinical diagnoses of gross caries by dental practitioners. Calculations were done on the cost and effectiveness measures for different policies on the frequency of routine dental checks, where effectiveness was measured in terms of the number of teeth free from decay, extraction, or fillings. The results indicated that the most effective but also the highest cost strategy is always 3-monthly intervals for dental checks (for both deciduous and permanent dentition). However, a move from a 6-monthly to a 3-monthly interval is associated with a sharp increase in cost per patient with only a modest increase in effectiveness. Therefore, as frequency of recall goes up, so does the economic cost for health [13].

b. Economic Evaluation on Different Periodontal Instrumentation Frequency

A within-trial cost–benefit analysis was also performed by Ramsay et al, which assessed the costs and benefits (in monetary terms) of each policy compared with standard care (no PI with 6-monthly PI). Routinely collected dental claims data were gathered, while patient-answered questionnaires determined additional participant costs, including private care, self-purchased products, and time and travel costs. A discrete choice experiment (DCE) was also administered online, to estimate WTP. Results of this economic evaluation demonstrated that participants valued and were willing to pay for prophylactic procedures such as routine scaling and polishing both at 6 and 12 monthly frequency despite having bigger financial cost [18].

Table 37 demonstrates the estimated range of costs of a routine dental visit and for common dental services in the rural and urban areas of the country.

Table 37. Estimated cost of a routine dental visit and common dental interventions

Parameter	**Consultation Fee**	**Consultation Fee with prophylactic treatments**	**Restoration Procedures** (for dental caries; per tooth)	**Radiographic Services per shot**
Unit cost in Philippine Peso (PHP)	500 to 1500	1500 to 6000	1000 to 8500	500 to 1200

4.7.5 Patient's Values and Preference, Equity, Acceptability, and Feasibility

The economic evaluations mentioned above suggested willingness of patients to adhere to a 6-month follow-up interval or any prophylactic procedures even at increased frequency. However, the scenario may be altogether different in the Philippines. The South-East Asia Region and the Western Pacific Region have the highest case numbers of oral diseases among the WHO regions. Along with the

Philippines, these countries belong to the lower to middle income bracket and have large population sizes.

As in other areas of health, the economic stability of a country strongly influences the burden of oral diseases. The apparent social gradients cause a disproportional vulnerability among disadvantaged population groups throughout the life course. These groups, which include low-income households, people living with disabilities, older people, refugees, people in prison or living in remote and rural communities, children and people from minority and/or other socially marginalized groups, have less access to oral health services [6].

A policy analysis on the oral health of Filipinos emphasized the weight of the oral health problem in the country. It demonstrated how all areas in public health needs improvement to be able to provide accessible dental services and effectively address the common problems of dental caries and periodontal diseases in the country. A shortage of dentists and oral health auxiliaries as well as maldistribution of workforce favoring urbanized areas and immigration is a stark contrast to the high oral health demand. Essential medicine such as fluoride and fluoridation has been observed to effectively decrease caries worldwide and is yet to be integrated into a widely accepted public health program in the country. Outpatient dental health services, which is the most commonly availed dental service, is not covered by PhilHealth benefits. Thus, one must take a chance for consult in a public hospital/ clinic or proceed to a privately owned service provider and pay out of pocket for a dental consultation [19].

With this current situation, it is not expected to see oral health as priority for the common Filipino patient. For health services as fundamental as a dental consultation to take place, one must take on the responsibility of paying out-of-pocket until such a time that oral health is finally well supported in public health policies to provide free dental screening and consult for all.

4.7.6 Recommendations from Other Groups

Table 38. Recommendations from Groups on Dental Screening

Group	Recommendation	Strength of Recommendation and Certainty of Evidence
American Dental Association (ADA)	A patient's recall interval and cleaning should be patterned on the risk of disease specific for the individual.	Recommend
National Health Service, UK (NHS)	Does not explicitly recommend a periodic recall interval, and openly supports risk-based approach. Supports a personalized plan for dental cleaning.	Suggest

Both ADA and NHS emphasized the lack of reliable data to support regularity of dental consults or extent of prophylactic treatment for adult patients. The RCTs mentioned above were also cited as reasons for favoring a risk-based approach in advising dental screening and consult and a personalized plan for routine cleaning and prophylactic procedures. Although their previous practice ranges from every 3 to 6 months follow-

up with varied routine dental procedures administered, most dentists are now more inclined towards a risk assessment of the patient's needs and follows-up the patient according to the risk assessment of the patient [17, 19].

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4.8 Screening for COVID-19

RECOMMENDATION

Among asymptomatic, apparently healthy adults, we recommend against universal COVID-19 screening. ***(Strong recommendation, very low certainty of evidence)***

Considerations: The panel strongly recommended against universal screening based on increased harms in the form of anxiety and stigma, and in terms of negative economic impacts which include cost of testing, loss of productivity, and loss of income. The panel further agreed on implementing risk-based screening instead of universal screening.

4.8.1 Burden of COVID-19

The first outbreak of COVID-19 was reported in December 2019 in Wuhan, China. In the Philippines, the first case of COVID-19 was reported on 30 January 2020 (1). The first local transmission of COVID-19 was confirmed on 07 March 2020. In 2020, COVID-19 was included in the list of top causes of death in the Philippines. In 2021, the Philippines was considered to have the highest cumulative COVID-19 cases and deaths in Southeast Asia (2, 3). As of 25 Mar 2023, the total confirmed cases of COVID-19 were reported as 4,079,992, 66,322 deaths and 13.7% cumulative positivity rate (4). COVID-19 symptoms and severity range from mild to critical. The most common symptoms in patients with mild disease are low fever and slight asthenia, without pneumonia. The prognosis was reported to be good in most people. However, increased risk for severe disease, hospitalization or intensive care unit admission, poor outcomes and mortality was found in elderly patients, obese, and those with chronic diseases (5, 6). In a living systematic review, in 84 screening studies, the interquartile range of asymptomatic COVID-19 patients was 20% to 65% (prediction interval 4% to 94%). As compared to symptomatic individuals, people exposed to asymptomatic individuals were less likely to become infected with COVID-19. However, it was also estimated that the transmissibility of COVID-19 infection from asymptomatic patients ranges from <15% to 69% (7).

4.8.2 Benefits and Harms of COVID-19 Screening

Efficacy Outcomes

SARS-CoV-2 Rapid Antigen Test (RAgT): Community-based Screening versus No Screening

Outcome: Hospital Admission (1 Before-After Study, n=668,243, Very Low Certainty of Evidence)

On 02 December 2020, the national lockdown in Liverpool city was ended and entered a less stringent restriction (Tier 2) (8). Community antigen testing conducted in the Liverpool city on 03 December 2020 and was expanded to the wider Liverpool City Region using the systematic meaningful asymptomatic repeated testing (SMART) approach. The COVID-SMART had three components, one is to test-to-protect' vulnerable people and settings, second is 'test-to-release' which are the contacts of confirmed infected people sooner from quarantine than the stipulated period and the 'test-to-enable' careful return to restricted activities to improve public health, social

fabric, and the economy. The study has tested 668,243 (45%) residents aged five years and older using SARS-CoV-2 rapid antigen lateral flow test at a testing center or through a universal access home test kit between 03 December 2020 to 31st July 2021(8). The study used synthetic controls from the other regions of UK where COVID-SMART was not yet implemented. As the synthetic control group were in tighter restrictions (Tier 3) and Tier 3 was reported to reduce hospital admission rate by 15% (95% CI: 11% to 19%), the study adjusted the analysis to remove the effect of the Tier 3 restrictions. It should also be noted that the report was done before 16 August 2021 when people fully vaccinated or aged under 18 years were no longer required to self-isolate if identified as a close contact of a positive COVID-19 case. Results showed that the Liverpool study where the community testing was conducted ahead of the control areas (Dec. 3, 2020 to Jan. 2, 2022), had statistically significantly reduced the hospital admission to 32% (95% CI: -39% to -22%, p-value=0.001). This 32% reduction is equivalent to 391 fewer hospital admissions (8). Due to the observational nature of the study and the possibility of spill-over effects the certainty of evidence was graded as very low. We did not find any evidence for other outcomes such as COVID-19 related mortality and morbidity, incidence of COVID-19 outbreaks, adverse events of testing, stigma of testing, prevention of transmission, quarantine and isolation rates and early initiation of treatment.

Table 39. Effect of Rapid Antigen test for COVID-19 in Screening Asymptomatic Individuals

Critical Outcomes	No and Type of Studies, Total Participants)	Effect Size 95% CI	Certainty of Evidence
Hospital Admission	1 Before and After Study (n=668,243)	Reduction of 32% (95% CI -39% to -22%)	Very Low

SARS-CoV-2 Reverse Transcriptase Polymerase Chain Reaction (RT-PCR): Screening versus No Screening

We did not find direct evidence that compared screening using RT-PCR as compared to no screening in asymptomatic and apparently healthy individuals. Instead, we found an interim analysis of a cohort study that compared screening using RT-PCR test vs non-screening in asymptomatic cancer patients.

Need for oxygen, Hospital Admission, Need for ICU and Mortality (1 Cohort Study, n=76 *Very Low Certainty of Evidence)*

In the interim analysis of the study, the patients that were not screened in the hospital had higher odds for need for oxygen (OR 16.2; 95%CI 2.2-117.1), hospital admission (OR 31.5; 95% CI: 3.1-317.8), need for ICU (OR 23, 95% CI: 2.4-223.8) and mortality (OR 8.8 95% CI: 1.2-65.5) as compared to those who were screened in the institution (9). None of the patients included in the study were vaccinated. The certainty of evidence was graded very low due to high risk of bias and indirectness. The study was specific for cancer patients. The study was an unplanned interim analysis and observational, thus there is a possibility of selection bias. Also, the study has a wide confidence interval.

Table 40. Effect of RT-PCR testing for COVID-19 in Asymptomatic Cancer Patients

Critical Outcomes	No and Type of Studies, Total Participants	Effect Size 95% CI	Certainty of Evidence

Need for O2	1 Cohort Study (n=76)	OR 16.2 (95% CI 2.20 to 117.1)	Very Low
Hospital Admission	1 Cohort Study (n=76)	OR 31.5 (95% CI 3.10 to 317.8)	Very Low
Need for ICU Admission	1 Cohort Study (n=76)	OR 23 (95% CI 2.40 to 223.8)	Very Low
Mortality	1 Cohort Study (n=76)	OR 8.8 (95% CI 1.20 to 65.5)	Very Low

Stigma of Testing, Prevention of Transmission, Quarantine and Isolation Rates, and Early Initiation of Treatment

We did not find any evidence for other outcomes such as incidence of COVID-19 outbreaks, adverse events of testing, stigma of testing, prevention of transmission, quarantine and isolation rates and early initiation of treatment.

Safety Outcomes

No direct evidence was found that reported the safety outcomes of using rapid antigen test or RT-PCR test for screening for COVID-19. Instead, we found a review that reported complications of nasopharyngeal testing (11). The review has included 29 articles. The complications reported were 16 cases of retained swabs due to swab fracture during the examination, 10 cases of epistaxis, 10 cases of cerebrospinal fluid (CSF) leakage, 3 cases of nasal septal or pharyngeal abscess and 1 case of ethmoidal silent sinus syndrome (11).

Other Subgroups

We found no direct evidence on other subgroups such as patients with known exposure being admitted for other (non-COVID-19) medical condition and health care workers.

4.8.3 Diagnostic Accuracy of SARS-CoV-2 Rapid Antigen Test (SARS-CoV-2 RAgT) and SARS-CoV-2 Reverse Transcriptase-Polymerase Chain Reaction (SARS-CoV-2 RT-PCR)

a. Diagnostic Accuracy of SARS-CoV-2 RAgT

Asymptomatic Individuals with Known COVID-19 Exposure

Based on the Infectious Disease of Society of America (IDSA) guidelines that included 59 studies that compared rapid antigen test to the reference standard Nucleic Acid Amplification Tests (NAAT), the reported pooled sensitivity was 63% (95% CI: 56% to 69%) and the pooled specificity was 100% (95% CI: 100% to 100%) (12). They have graded the certainty of evidence for sensitivity as moderate due to inconsistency, and high for specificity due to large effect (12).

The authors also estimated the effect of the test in 1000 patients using the prevalence rate of 1%, 5% and 10%, among 1000 patients tested with antigen test (12), as shown in Table 42.

Table 41. Diagnostic Accuracy of SARS-CoV-2 RAgT for Asymptomatic COVID-19 (With Known Exposure)

Measures of diagnostic accuracy	No. and Type of Studies, Total Participants	Effect Size 95% CI	Certainty of Evidence
Sensitivity	59 studies (n=4,553)	63% (95% CI: 56% to 69%)	Moderate
Specificity	59 studies (n=4,553)	100% (95% CI: 100% to 100%)	High

Table 42. Estimate of Effect per 1000 tested with SARS-CoV-2 RAgT for Asymptomatic COVID-19 (With Known Exposure)

Test result	Number of results per 1,000 patients tested (95% CI)		
	Prevalence at 1%	Prevalence at 5%	Prevalence at 10%
True positives	6 (6 to 7)	32 (28 to 34)	63 (56 to 69)
False negatives	4 (3 to 4)	18 (16 to 22)	37 (31 to 44)
True negatives	990 (990 to 990)	950 (950 to 950)	900 (900 to 900)
False positives	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)

Any Asymptomatic Individual with or without COVID-19 Exposure

A 2022 Cochrane systematic review and meta-analysis investigated on the diagnostic accuracy of SARS-CoV-2 rapid antigen test compared with SARS-COV-2 RT-PCR among asymptomatic community-based individuals. The review included 50 studies with 40,956 test applications. Pooled analysis showed a sensitivity of 54.7% (95% CI 47.7% to 61.6%) and a specificity of 99.5% (95% CI 99.4% to 99.6%). Certainty of evidence was downgraded to moderate due to high risk of bias because of participant selection, and participant flow and timing of diagnostic tests (13).

Table 43. Diagnostic Accuracy of SARS-CoV-2 RAgT for Asymptomatic COVID-19 (With or Without Known Exposure)

Measures of diagnostic accuracy	No. and Type of Studies, Total Participants	Effect Size 95% CI	Certainty of Evidence
Sensitivity	50 studies (n=40,956)	54.7% (95% CI 47.7 to 61.6)	Moderate
Specificity	50 studies (n=40,956)	99.5 (95% CI 99.4 to 99.6)	Moderate

Table 44. Estimate of Effect per 1000 tested with SARS-CoV-2 RAgT for Asymptomatic COVID-19 (With or Without Known Exposure)

Test result	Number of results per 1,000 patients tested (95% CI)		
	Prevalence at 1%	Prevalence at 5%	Prevalence at 10%
True positives	5 (5 to 6)	27 (24 to 31)	55 (48 to 62)
False negatives	5 (4 to 5)	23 (19 to 26)	45 (38 to 52)
True negatives	985 (984 to 986)	945 (944 to 946)	896 (895 to 896)
False positives	5 (4 to 6)	5 (4 to 6)	4 (4 to 5)

b. Diagnostic Accuracy of SARS-CoV-2 RT-PCR (Gold Standard for COVID-19)

Asymptomatic Individuals with known COVID-19 exposure

Based on the IDSA guidelines, they did not find diagnostic test accuracy for SARS-COV-2 NAATs in asymptomatic individuals (14). Instead, they based their evidence in

symptomatic patients as asymptomatic and pre-symptomatic patients may have similar viral loads and shedding compared to those who are symptomatic. The sensitivity of NAAT was reported as 75% (95% CI: 55% to 95%) while the specificity was reported as 99% (95% CI: 99% to 100%). They have graded the certainty of evidence as very low due to indirectness and small number of patients included (14).

Table 45. Diagnostic Accuracy of RT-PCR test for COVID-19

Measures of diagnostic accuracy	No. and Type of Studies, Total Participants	Effect Size 95% CI	Certainty of Evidence
Sensitivity	6 studies n=385	75% (95% CI: 55% to 95%)	Very Low
Specificity	2 studies n=457	99% (95% CI: 99% to 100%).	Very Low

Table 46. Estimate of Effect per 1000 tested with RT-PCR For COVID-19

Test result	Number of results per 1,000 patients tested (95% CI)		
	Prevalence of 1%	Prevalence of 5%	Prevalence of 10%
True positives	8 (6 to 10)	38 (28 to 48)	75 (55 to 95)
False negatives	2 (0 to 4)	12 (2 to 22)	25 (5 to 45)
True negatives	980 (980 to 990)	941 (941 to 950)	891 (891 to 908)
False positives	10 (0 to 10)	9 (0 to 9)	9 (0 to 9)

4.8.4 Resource Implication

There were no local studies regarding the cost-effectiveness of screening tests for COVID-19 in the Philippines. In 2022, the DOH set the price cap on rapid antigen test to Php 660 and the cost for self-administered rapid antigen test to Php 350 (15). Meanwhile RT-PCR price was capped to Php 2,450 and Php 2,800 for GeneXpert. See Table below for estimated cost of screening for COVID-19 [16].

Table 47. Estimated cost of screening for COVID-19

Parameter	Screening intervention	
	SARS-CoV-2 RAgT	SARS-CoV-2 RT-PCR
Unit cost of screening intervention	Antigen Rapid test Php 350 Operational Cost Php 250 10% allowable mark-up Php 60 Final Cost (Price Cap) Php 660	Public laboratories: Php 2,800 for plate-based Php 2,450 for GeneXpert Private laboratories: Php 3,360 for plate-based, Php 2,940 for GeneXpert 1,000 on top of testing costs

4.8.5 Patient's Values and Preference, Equity, Acceptability, and Feasibility

In a survey conducted in the Philippines which included 147 participants, the willingness to be tested for COVID-19 despite being asymptomatic is due to the desire of the participants to have peace of mind [17]. When grouped by age, the most compelling reasons for willingness to get tested for COVID-19 in patients aged 53-59 are the test being free and the nearness of the testing facility. For patients age >60, the compelling reasons are: "Personally knowing people who have undergone testing, the desire to have peace of mind that he/she does not have COVID-19, the desire to

be a good example to others and the desire to be reassured that his infection preventive practices are keeping him/her COVID-free" [17].

In Canada, they conducted a large screening program in the workplace (rapid antigen test twice a week) [18]. They have reported a sharp increase in the number of people voluntarily screened for COVID-19 during the third wave in Canada (April to May 2021). However, after the wave, although more organizations had joined the screening program, the number of people screened flattened out. The organizations reported that since many people have been vaccinated, they opt not to be tested. The authors sent out a survey to 163 people and received 116 (71%) responses. Among the participants, 68% were very satisfied with the screening program, 31% were satisfied, and only 1 participant was dissatisfied [18].

4.8.6 Recommendations from Other Groups

In 4 guidelines (IDSA [12, 13] WHO [18], and ESCMID [19]), screening of asymptomatic individuals was recommended in specific situations only such as exposure to COVID-19 confirmed cases, frequently exposed population, high incidence of infection, hospital admission (high community transmission rate of SARS-CoV-2 and/or with low vaccination coverage), and hospitalization of immunocompromised individuals (regardless of the transmission rate of SARS-CoV-2 and extent of vaccination coverage). The WHO did not recommend the use of widespread screening of asymptomatic individuals due to the significant costs associated with it and the lack of data on its operational effectiveness [19].

Table 48. Recommendation from Other Groups For COVID-19 Screening Test Among Asymptomatic Apparently Healthy Individuals

Guidelines	Ag test/RT-PCR test	Recommendation	Strength of recommendation and certainty of evidence
A. Asymptomatic with known exposure			
[1] Infectious Disease of Society of America (IDSA) (12, 14)	RT-PCR	"The IDSA panel suggests SARS-CoV-2 RNA testing in asymptomatic individuals who are either known or suspected to have been exposed to COVID-19"	conditional recommendation, very low certainty of evidence
	Antigen Test	"For asymptomatic individuals with known exposure to SARS-CoV-2 infection, the IDSA panel suggests using a single (i.e., one-time) Ag test over no testing in specific situations"	conditional recommendation, moderate certainty evidence
	RT-PCR vs Antigen test	a. "For asymptomatic individuals with known exposure to SARS-CoV-2 infection, the IDSA panel suggests using a single standard NAAT (i.e., rapid RT-PCR or laboratory-based NAAT) over a single rapid Ag test b. "In asymptomatic individuals with a known exposure to SARS-CoV-2, if standard NAAT testing or results are not available in a timely manner and a first Ag test is negative, the IDSA panel suggests repeat Ag testing"	a. conditional recommendation, low certainty evidence b. *conditional recommendation, very low certainty evidence*
[2] World Health Organization (WHO), 2021 (19)	RT-PCR/Antigen test	a. "Testing of asymptomatic individuals with NAAT or Ag-RDTs is currently recommended only for specific groups	Not mentioned

		including contacts of confirmed or probable COVID-19 cases” b. Widespread screening of asymptomatic individuals is not a currently recommended strategy due to the significant costs associated with it and the lack of data on its operational effectiveness.	
[3] European Society of Clinical Microbiology and Infectious Diseases (ESCMID), 2022 (20)	Did not specify	In the health care setting (testing vs quarantine only): a. “The panel suggests immediately testing asymptomatic hospitalized patients who have had high-risk-exposure contacts with SARS-CoV-2 cases, along with isolation in a separate room and close follow-up for symptoms. If negative, patients should be tested again at 5-7 days after contact, regardless of vaccination status b. “The panel suggests immediately testing residents of long-term care facilities who have had high-risk-exposure contact with SARS-CoV-2 cases, along with isolation in a separate room and close follow-up for symptoms, regardless of vaccination status. The panel suggests testing immediately (at least 2 days after the contact) and, if negative, testing again at 5-7 days after contact	a. Strong recommendation, Quality of evidence (QoE): very low b. strong recommendation, QoE: very low
B. Asymptomatic With No Known Exposure For Hospital Admission			
1) Infectious Disease of Society of America (IDSA) (14)	RT PCR	“The IDSA panel suggests against SARS-CoV-2 RNA testing in asymptomatic individuals with no known contact with COVID-19 who are being hospitalized in areas with a low prevalence of COVID-19 in the community”	conditional recommendation, very low certainty of evidence
2) European Society of Clinical Microbiology and Infectious Diseases (ESCMID), 2022 (20)	Did not Specify	a. The panel suggests universal testing of asymptomatic patients on hospital admission in areas with a high community transmission rate of SARS-CoV-2 and/or with low vaccination coverage	a. conditional recommendation, QoE: low b. conditional recommendation, QoE: low

		b. The panel suggests universal testing of asymptomatic individuals who have been transferred between facilities in areas with a high community transmission rate of SARS-CoV-2 and/or with low vaccination coverage c. The panel suggests universal testing of asymptomatic patients at admission in settings where immunocompromised individuals are hospitalized, regardless of the transmission rate of SARSCoV-2 and extent of vaccination coverage d. The panel suggests testing of asymptomatic vulnerable individuals who have been transferred between facilities or residents before admission to an LTCF regardless of the community transmission rate of SARS-CoV-2 and extent of vaccination coverage	c. conditional recommendation, QoE: very low d. conditional recommendation, QoE: low
C. Asymptomatic Individuals Who Will Undergo Surgery			
1) Infectious Disease of Society of America (IDSA) (14)	RT PCR	a. "The IDSA panel suggests SARS-CoV-2 RNA testing in asymptomatic individuals (without known exposure to COVID-19) who are undergoing major time-sensitive surgeries b. "The IDSA panel suggests against SARS-CoV-2 RNA testing in asymptomatic individuals without a known exposure to COVID-19 who are undergoing a time-sensitive aerosol generating procedure (e.g., bronchoscopy) when PPE is available." c. "The IDSA panel suggests SARS-CoV-2 RNA testing in asymptomatic individuals without a known exposure to COVID-19 who are undergoing a time-sensitive aerosol generating procedure (e.g., bronchoscopy) when PPE is limited, and testing is available"	a. *conditional recommendation, very low certainty of evidence* b. *conditional recommendation, very low certainty of evidence* *c. conditional recommendation, very low certainty of evidence*

2) European Society of Clinical Microbiology and Infectious Diseases (ESCMID), 2022 (20)	Did not Specify	a. The panel suggests preoperative testing of asymptomatic patients 48-72 hours prior to elective surgery requiring anesthesia to reduce exposure of HCWs in settings where there is a high transmission rate and/or low vaccination coverage rate and/or access to PPE is limited b. Preoperative testing of patients prior to elective surgery requiring anesthesia might be considered in settings with a low transmission rate, high vaccination coverage, and proper access to PPE, to identify asymptomatic patients with SARSCoV-2 who might be at increased risk of poor outcomes after surgery, independent of their vaccination status	a. conditional recommendation, QoE: very low b. good practice statement
D. Asymptomatic Individuals Who Will Undergo Elective Non-Surgical Procedures			
1) European Society of Clinical Microbiology and Infectious Diseases (ESCMID), 2022 (20)	Did not Specify	a. The panel advises careful assessment of the local infrastructure, logistics, organizational structure (availability and sufficient capacity of testing laboratories), staffing, and procedure-related risks before implementing testing of all patients prior to scheduled nonsurgical procedures b. The panel discourages universal testing of patients prior to scheduled nonsurgical non-aerosol-generating procedures when vaccination coverage is high and/or during a period of low community transmission and when other IPC measures are in place and rigorously controlled c. The panel suggests considering testing asymptomatic patients before nonsurgical aerosol-generating procedures in settings with high community transmission and/or when other IPC measures cannot be rigorously implemented and controlled	a. good practice statement b. conditional recommendation, QoE: very low c. conditional recommendation, QoE: very low d. conditional recommendation, QoE: very low)

		d. The panel suggests that when recurrent ambulatory care is delivered to vulnerable patients, testing might be considered to support prevention of and/or control transmission	
E. Asymptomatic Students In Educational Settings Or Employees In A Work Place Setting			
1) Infectious Disease of Society of America (IDSA) (12)	Antigen test	"Among students in educational settings or employees in workplaces for whom SARS-CoV-2 testing is desired, the IDSA panel suggests neither for nor against two consecutive Ag tests over no testing for the diagnosis of SARS-CoV-2 infection "	Evidence gap
2) World Health Organization (WHO), 2021 (19)	Did not Specify	"Testing of asymptomatic individuals with NAAT or Ag-RDTs is currently recommended only for specific groups including contacts of confirmed or probable COVID-19 cases and **frequently exposed groups such as health care workers and long-term care facility workers**."	Not mentioned

Table 49. SARS-CoV-2 transmission scenarios and their suggested implications for subnational expansion of SARS-CoV-2 testing (Adapted from WHO [18])

Transmission Scenario	Testing Strategy Guidance And Key Actions
No cases	Test all individuals meeting the case definition and, as capacities allow, asymptomatic contacts of confirmed or probable cases, to allow for identification of new clusters or importation of new cases. Test patients with unexpected clinical presentation or an increase in hospital admissions in a specific demographic group that could be COVID-19. Strengthen or sustain capacity and expertise at the national public health laboratory. Establish a laboratory contingency plan including mapping of national testing resources and capacities and identify potential sources of infection (e.g. imported cases, zoonotic spillover events). Prepare for the possibility of increasing transmission and plan for surge SARS-CoV-2 testing capacity, including through the revision of SOPs and simulation exercises. Test all or a subset of samples from SARI/ARI/ILI surveillance for SARS-CoV-2.
Sporadic cases	Test all individuals meeting the case definition and, as capacities allow, asymptomatic contacts of confirmed or probable cases. Establish a laboratory contingency plan including mapping of national testing resources and capacities and identify potential sources of infection (e.g. imported cases, zoonotic spillover events). Test all or a subset of samples from SARI/ARI/ILI surveillance for SARS-CoV-2.
Clusters of cases	Test all individuals meeting the case definition and, as capacities allow, asymptomatic contacts of confirmed or probable cases. Activate laboratory contingency plan in localized areas. Test all or a subset of samples from SARI/ARI/ILI surveillance for SARS-CoV-2.
Community transmission (CT1 to CT4)	Test all individuals meeting the case definition and, as capacities allow, asymptomatic contacts of confirmed or probable cases. Activate laboratory contingency plan. Consider expansion of testing capacity through the following: • Activate localized surge capacity. • Expand localized testing facilities. • Increase accessibility of testing facilities. • Expand testing product options, including expanding the use of approved point of care NAAT and Ag-RDTs. • Introduce mobile testing facilities. • Introduce mobile sampling facilities. • Deploy laboratory staff from other fields, including veterinary and academic laboratories, to backstop COVID-19 laboratory staff. Test all or a subset of samples from SARI/ARI/ILI surveillance for SARS-CoV-2.

SARI, severe acute respiratory syndrome; ARI, acute respiratory infection; ILI, influenza like illness; SOP, standard operating procedure; NAAT, nucleic acid amplification test; Ag-RDT, antigen-detecting rapid diagnostic test.

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4.9 Screening for Latent TB

RECOMMENDATIONS

1. **Among asymptomatic, apparently healthy adults, we suggest against screening for latent TB.** ***(Weak recommendation, very low certainty of evidence)***

   Considerations: A weak recommendation against screening for latent TB among asymptomatic apparently healthy adults was based on the perceived lack of cost-effectiveness of screening in this population (general population). The panel further reasoned that screening the general population could be inaccessible and could be costly.

2. **Among asymptomatic, apparently healthy adults, who are at high risk for TB infection (i.e., close contacts*), we suggest screening for latent TB using TST or IGRA.** ***(Weak recommendation, very low certainty of evidence)***

   * *According to the US Centers for Disease Control, close contacts are defined as individuals with at least 4 hours of contact per week including those living in the same household or frequent visitors to the house, or contacts at work or school. Alternatively, close contacts as defined by the Philippine Department of Health National TB Control Program Manual of Procedures, are persons who shared an enclosed space, such as a social gathering place, workplace or facility, for extended periods within the day with the index person with TB during the three months before commencement of the current treatment episode.*

   Considerations: A weak recommendation for LTBI screening among high-risk individuals particularly close contacts was based on the higher probability of TB transmission among close and household contacts. Definition of close contacts was based on the US CDC and the Philippines Department of Health National TB Control Program Manual of Operations. Risk classification (as close contact) of an individual and subsequent need for LTBI screening should be based on physician assessment and recommendation.

4.9.1 Burden of Latent TB infection

WHO defined Latent Tuberculosis infection (LTBI) as “a state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically manifest active TB” [1]. Importance is given to preventive management and government-led control strategies for this disease because people with LTBI can progress to active TB or undergo reactivation, and subsequently, transmission to others [2]. Pharmacological treatment regimens for latent TB infection use isoniazid (INH), rifapentine (RPT), and/or rifampin (RIF) as recommended by the Department of Health National TB Control Program’s Manual of Procedures.

As one of the countries in the world with the highest burden and increasing annual average percentage of LTBI by 0.9% and crude prevalence of 37.1% as of 2021, continuous review of current guidelines and its implementation is warranted for this disease [3].

4.9.2 Benefits and Harms of Screening for Latent TB infection

There was no direct evidence found on the benefit of screening for LTBI in terms of incidence of TB, TB-related mortality and/or morbidity, and other preventive outcome.

A 2000 modelling cohort study investigates the benefits of screening population groups with unknown tuberculin status and providing preventive therapy for persons

with positive tuberculin skin test results were calculated with a Markov model for hypothetical 30-year-old persons [6]. Outcome estimates are reported as Number Needed to Screen (NNS).

Overall, the modeling study showed beneficial results for recent household contacts where the number needed to screen (NNS) to identify 1 person with latent *M. tuberculosis* infection is 2 to 4; to prevent 1 tuberculosis case is 10 to 126; and to prevent 1 tuberculosis death is 2 675 to 39 743, assuming all persons found to have positive tuberculin test results initiate preventive therapy. However, in the general population with no risk factors for tuberculosis, it has a relatively low number of cases per cohort and high NNS (1,669-6,837) to prevent cases and deaths (132,690-606,797).

Table 50. Benefits of screening for LTBI using the Markov method modelling study for hypothetical 30-year-old persons

Outcome	Subgroup	Number Needed to Screen (NNS)	Interpretation	Certainty of Evidence
LTBI Identification	Recent Contacts	2 - 4	Benefit	Very Low
	General Population	10 -126	Benefit	Very Low
Prevention of Death due to TB	Recent Contacts	1,669 - 6,837	Benefit	Very Low
	General Population	132,690-606,797	Benefit	Very Low

4.9.3 Benefits and Harms of Early Intervention

Benefits

For isoniazid (INH) only treatment, one RCT (n=27,380) found a reduced risk for progression to active TB at 5 years for 24 weeks isoniazid compared with placebo [RR: 0.35 (95%CI, 0.24 to 0.52) NNT:112] [7].

A network meta-analysis of 53 studies showed the efficacy of current regimens as compared with placebo or no treatment in the prevention of Active TB: INH regimen of 6 months or longer [OR: 0.65 (95% credible interval [CrI]:0.50 to 0.83)] vs placebo; Rifampicin-Isoniazid (RIF-INH) combination therapy of 3-4months [OR: 0.53 (95%CrI:0.36 to 0.78)] vs placebo; weekly Rifapentine-Isoniazid (RPT-INH) regimen [OR: 0.36 (95%CrI:0.18 to 0.73)] vs. no treatment [8].

Harms

No direct studies were found regarding the safety of screening for LTBI on the incidence of TB, TB-related mortality and/or morbidity, and other preventive outcomes. Instead, we investigated studies on the safety of interventions among those with LTBI based on USPSTF 2022 Latent TB evidence synthesis.

INH vs Placebo/No Treatment: A single trial for the INH only vs. Placebo examining the development of INH-related hepatotoxicity showed RR 3.45 (95%Ci 1.49 to 7.99) for 12 weeks treatment, RR 4.59 (95%Ci 2.03 to 10.39, number needed to harm [NNH]: 279) for CDC-recommended regimen of 24 weeks treatment, and RR 6.21 (95%Ci

2.79 to 13.79) for 52 weeks treatment showing a positive correlation of treatment duration and hepatotoxicity risk [7]. Sensitivity analysis for this trial and three additional RCTs (total N=35,161) showed RR 5.04 (95%Ci 5.5 to 10.15) [9-11]. Increased risk of developing GI stress was noted, RR 1.33 (95%Ci 1.01 to 1.75) [7]. Mortality rate due to hepatotoxicity were noted to be 0.03%, 0.00%, and 0.01% for the 12-, 24-, and 52-week INH treatment groups, respectively [7]. No mortality was noted in the placebo group. Overall mortality rate from hepatitis associated with INH was 0.14 deaths per 1,000 persons receiving INH [RR 2.35 (95% CI: 0.12 to 45.46; NNH:6,947)].

A network meta-analysis of 53 studies showed the safety outcomes of current regimens as compared with placebo or no treatment in the development of hepatotoxicity [8]. Positive correlation for the duration of INH treatment and development of hepatotoxicity were noted: INH regimen of 6 months [OR: 1.10 (95%CrI:0.40 to 3.17)] vs placebo; INH regimen of 9 months [OR: 1.70 (95%CrI:0.35 to 8.05)]; INH regimen of 12 to 72 months [OR: 2.72 (95%CrI:0.96 to 7.44)].

RIF vs INH: USPSTF meta-analysis of three studies comparing RIF with INH (N=7,339) found an increased risk of hepatotoxicity for INH group vs RIF [RR 4.22 (95%Ci 2.21 to 8.06)] [12-14]. One of the studies reported a lower risk in GI adverse events among patients treated with NIH vs RIF [RR 0.34 (95%Ci 0.03 to 3.23)] [12].

RPT + INH vs INH only: One RCT which determined the hepatotoxicity by severity grade showed decreased risk for RPT+INH vs INH only [RR 0.90 (95%CI 0.75 to 1.08)] in developing Grade 3 or 4 hepatotoxicity [7]. Other RCT which reported AST and ALT elevation of 3 times greater than upper limit of normal also showed decreased risk for RPT+INH vs INH only [RR 0.46 (95%CI 0.18 to 1.17)] [15]. The same RCT reported on GI adverse events which showed increased risk for RPT+INH vs INH only [RR 1.74 (95%CI 0.99 to 3.05)]. GI adverse events included abdominal pain, diarrhea, nausea, and vomiting [15].

RIF + INH vs RPT + INH: One RCT (N=52) which only determined hepatotoxicity for the safety outcome measured the elevation of ALT or AST (defined as above the normal range). Elevation of ALT or AST was reported for 4 (16%) participants in RIF + INH vs. 3 (11%) in RPT + INH [16].

RPT + INH (3HP) vs RPT + INH ($2H_2P_2$): One RCT (N=3,738) was conducted on different treatment regimens for RPT+INH: directly observed once-weekly INH up to 900 mg and RPT up to 900 mg for 12 weeks (the 3HP regimen) and directly observed twice-weekly INH up to 600 mg and RPT up to 600 mg for 8 weeks (the 2H2P2 regimen). Hepatotoxicity was defined as AST or ALT elevated more than 3 times the upper limit of normal along with accompanying symptoms or AST or ALT elevated more than 5 times the upper limit of normal without symptoms by which the 3HP group showed no significant difference in risk for hepatoxicity vs $2H_2P_2$ [RR 0.88 (95% CI, 0.42 to 1.84)] [17]. Rate of GI adverse events is higher in 3HP group vs $2H_2P_2$ [RR 1.69 (95% CI, 1.26 to 2.27)]. Hypersensitivity or allergy events were less common for 3HP vs $2H_2P_2$ [RR 0.67 (95% CI, 0.46 to 0.98)].

Other regimens vs placebo: RPT + INH combination therapy [OR: 0.52 (95%CrI:0.13 to 2.15)] vs placebo; RIF therapy of 3-4 months [OR: 0.14

(95%CrI:0.02 to 0.81)] vs. no treatment; INH + RIF of 3-4 months [OR: 0.72 (95%CrI:0.21 to 2.37)] [8].

Table 51. Benefits and Harm of LTBI Interventions

Outcomes	No. of Studies	RR (95% CI)	Net Benefit	Certainty of Evidence
Progression to active TB	9 RCTs (n=12,198)	INH for 6 months vs. Placebo: 0.65 (0.50 to 0.83)	Benefit	Low
	2 RCTs (n=631)	RIF-INH for 3-4months vs Placebo: 0.53 (0.36 to 0.78)	Benefit	Low
	2 RCTs (n=162)	Weekly RPT+INH vs No Treatment: 0.36 (0.18 to 0.73)	Benefit	Low
Hepatotoxicity	2 RCTs (n=1026)	INH for 6 months vs. No Treatment: 1.10 (0.40 to 3.17)	Inconclusive	Low
	3 RCTs (n=7,339)	INH vs RIF 4.22 (2.21 to 8.06)	Harm	Low
	2 RCTs (n=7994)	RPT + INH vs INH only: Range: 0.46-0.90	Favors RPT + INH	Low
GI adverse events	1 RCT (n=13,995)	INH for 6 months vs. Placebo: 1.33 (1.01 to 1.75)	Harm	Low
	3 RCTs (n=7,339)	INH vs RIF: 0.34 (0.03 to 3.23)	Inconclusive	Low
	1 RCT (n=3,986)	RPT + INH vs INH only: 1.74 (0.99 to 3.05)	Inconclusive	Low
Mortality due to hepatotoxicity	1 RCT (n=13,995)	INH: 0.03% 12 weeks (OR: 2.17) 0.00% for 24 weeks 0.01% for 52 weeks (OR: 4.18) No mortality for placebo group	Harm	Low

4.9.4 Diagnostic Accuracy of Screening and Confirmatory Tests

LTBI is a clinical diagnosis established by demonstrating prior TB infection and excluding active TB disease [2]. To demonstrate prior TB infection, available tests include the tuberculin skin test (TST) and interferon-gamma release assay (IGRA). These tests measure immune sensitization (type IV or delayed-type hypersensitivity) to mycobacterial protein antigens that might occur following exposure to mycobacteria. Recent WHO recommendations states that either TST or IGRA can be used to test for LTBI [1].

The USPSTF found 113 publications (N=69,009 participants) with 101 studies for determining accuracy and reliability [4]. Studies selected evaluate screening for LTBI with TST using Mantoux method and/or IGRAs in asymptomatic patients in a primary care setting. Pooled estimates for the Sensitivity and Specificity were measured for the TST using the Mantoux method at 5-mm, 10mm, and 15mm induration; and for

three IGRA tests (QuantiFERON-TB Gold in Tube, QuantiFERON Gold Plus, and T-SPOT). Thirty-two studies are included for TST and its various induration threshold. The rest of the studies reported is for three IGRA tests.

Since there were no direct diagnostic test for LTBI, confirmatory tests for sensitivity were determined from studies of persons with bacteriologic-confirmed, active TB who had not yet received treatment (or who had received no more than a few weeks of treatment) while the confirmatory tests for specificity relied on studies of healthy subjects known to be at low risk for TB and free of TB exposure.

Pooled estimates of TST shows moderate accuracy for the 5mm [Sn=0.80 (95%CI:0.74 to 0.87) Sp=0.95 (95%CI: 0.94 to 0.97)] and 10mm induration threshold [Sn=0.81 (95%CI:0.76 to 0.87) Sp=0.98 (95%CI: 0.97 to 0.99)]. Lower sensitivity was found for the 15mm induration threshold [Sn=0.60 (95%CI:0.46 to 0.74) Sp=0.99 (95%CI: 0.98 to 0.99)].

IGRA shows an overall better accuracy with the TSPOT.TB [Sn=0.90 (95%CI:0.87 to 0.92) Sp=0.95 (95%CI: 0.91 to 0.97)], QFT-GIT [Sn=0.81 (95%CI:0.79 to 0.84) Sp=0.99 (95%CI: 0.98 to 0.99)], and QFT-Plus [Sn=0.89 (95%CI:0.84 to 0.94) Sp=0.98 (95%CI: 0.95 to 0.99)].

Overall, TST and IGRA shows moderate sensitivity and high specificity for screening of LTBI.

Comparison of IGRA vs TST

A 2022 meta-analysis examined 458 head-to-head studies (n=204,464) on the positive rates of IGRA vs TST [5]. In the general population or healthy controls, positivity rate of IGRA is lower than TST [OR 0.54 (95%CI 0.43 to 0.66) I^2: 96]. For recent contacts, IGRA also performed lower than TST [OR 0.63 (95%CI 0.54 to 0.73) I^2: 96]. Subgroup analysis in immunocompetent BCG-vaccinated individuals, IGRA positive rate in high-TB burden areas (>200 cases per 100,000) was slightly lower than TST positive rate [OR 0.70 (95%CI 0.38 to 1.31) I^2: 91]. IGRA positive rate was equal to that of TST in the elderly (OR 0.98 [0.66 to 1.46]).

Table 52. Diagnostic Accuracy (Sensitivity and Specificity) of TST and IGRA versus Clinical Diagnosis in Latent Tuberculosis Screening
Population: Asymptomatic, apparently healthy adults
Condition: Latent tuberculosis
Index Test: TST and IGRA
Gold Standard: Clinical Diagnosis
Prevalence: 37.12% (Ding C, et al)

TEST	BASIS (No. and Type of Studies, Total Participants)	PARAMETER (95% CI)	Estimate of Effect per 1,000 Tested		CERTAINTY OF EVIDENCE
			# Diagnosed (Range)	# Missed (Range)	
TST 5mm threshold	12 (n=1,323)	Sensitivity: 0.80 (0.74 to 0.87)	297 (275 to 323)	74 (48 to 96)	Moderate
	3 (n=5,149)	Specificity: 0.95 (0.94, 0.97)	597 (591 to 610)	32 (19 to 38)	High
TST 10mm threshold	15 (n=1,427)	Sensitivity: 0.81 (0.76 to 0.87)	301 (282 to 323)	70 (48 to 89)	Moderate
	8 (n=9,604)	Specificity: 0.98 (0.97, 0.99),	616 (610 to 623)	13 (6 to 19)	High
TST 15mm threshold	9 (n=1,004)	Sensitivity: 0.60 (0.46 to 0.74)	223 (171 to 275)	148 (96 to 200)	Moderate
	10 (n=9,563)	Specificity: 0.99 (0.98 to 0.99)	623 (616 to 623)	6 (6 to 13)	High
IGRA; T-SPOT.TB	37 (n=5,367)	Sensitivity: 0.90 (0.87 to 0.92)	334 (323 to 342)	37 (229 to 48)	Moderate
	2 (n=1,664)	Specificity 0.95 (0.91 to 0.97)	597 (572 to 610)	32 (19 to 57)	High
IGRA; QFT-GIT	48 (n=7,055)	Sensitivity: 0.81 (0.79 to 0.84	301 (293 to 312)	70 (59 to 78)	Moderate
	3 (n=2,090)	Specificity: 0.99 (0.98 to 0.99)	623 (610 to 616)	6 (13 to 19)	High
IGRA; QFT-Plus	11 (n=939)	Sensitivity: 0.89 (0.84 to 0.94)	330 (312 to 349)	41 (22 to 59)	Moderate
	1 (n=211)	Specificity: 0.98 (0.95 to 0.99)	616 (597 to 610)	13 (19 to 32)	High

Table 53. Comparison of positive rates of IGRA vs TST in LTBI Screening

Subgroup	No. of Studies, No. of participants	OR (95% CI)	Interpretation	Certainty of Evidence
General Population or Healthy controls	66 Cohort Studies (n=53,799)	Overall: 0.54 (0.43 to 0.66)	Favors TST	Very Low
		General Population: 0.80 (0.56 to 1.13)	Inconclusive	Very Low
		Healthy Control: 0.46 (0.34 to 0.60)	Favors TST	Very Low
Recent Contacts	112 Cohort Studies (n=40,016)	Overall: 0.63 (0.54 to 0.73)	Favors TST	Very Low
		Close Contacts: 0.73 (0.61 to 0.88)	Favors TST	Very Low
		Close and Casual contacts: 0.50 (0.39 to 0.64)	Favors TST	Very Low
High Burden Areas	15 Cohort Studies (n=5,574)	Overall: 0.75 (0.60 to 0.94)	Favors TST	Very Low
		TB burden: 101–200 per 100, 000: 0.82 (0.66 to 1.03)	Inconclusive	Very Low
		TB burden: ≥200 per 100,000: 0.70 (0.38 to 1.31)	Inconclusive	Very Low
BCG vaccinated individuals	11 Cohort Studies (n=3,121)	TB burden: 101–200 per 100,000: 0.82 (0.66 to 1.03)	Inconclusive	Very Low
	4 Cohort Studies (n=2,753)	TB burden: ≥200 per 100, 000: 0.75 (0.60 to 0.94)	Inconclusive	Very Low
Elderly	16 Cohort Studies (n=3,319)	0.98 (0.66 to 1.46)	Inconclusive	Very Low

4.9.5 Other Considerations

A systematic review on economic evaluation for LTBI screening strategies determined various economic outcomes: cost per life years gained (27%), cost per quality-adjusted life year (QALY) gained (27%), cost per TB case prevented (36%), and cost per close contact case (10%) which showed an overall positive economic benefit for LTBI screening [18]. However, the systematic review mostly included studies from high-income countries which showed that IGRA is more cost-effective than TST. For applicability, the economic evaluation study from a non-high-income country in this review is from Brazil which found that TST was more cost-effective [19]. In a recent 2022 Malaysian study, change in Quality-adjusted life year of TST vs IGRA:

QuantiFERON is -0.01 where IGRA dominated TST in incremental cost-effectiveness ratio (ICER) outcomes [20].

A 2022 study from Zambia suggests that patient preferences in TB detection is heterogenous and different for each patient. Strategies that incorporate features including same-day results, financial incentives, and greater privacy may increase the likelihood of overcoming barriers to TB care engagement [21].

For the acceptability and feasibility of TB screening, a 2013 WHO systematic review showed significant variation in participation in TB screening according to region and by setting (urban/rural), with screening uptake lower among urbanites (82% vs. 91% p=.04). Also noted was screening in Southeast Asia had higher mean participation than in Africa or the Western Pacific regions (91% vs. 84% p=.04) [22].

An equity study from Myanmar involving highly subsidized TB care through social franchising of TB services to private sector helped reach the poor with quality services, while partly protecting them from high health care expenditure [23].

Table 54. Costs of the available LTBI screening tests in the Philippines

Parameter	Screening Intervention		Confirmatory Test
Unit cost of screening intervention in Philippine Peso (PHP)	TST	IGRA	Clinical Diagnosis
	200-300 [a]	5,000 [b] 7,500-10,000 [a]	200 (Public OPD visit) [a] 500-1000 (Private consult)[a]

a: Informal survey among Manila Hospitals and Clinics
b: Non-Profit NGO price

4.9.6 Recommendations from Other Groups

Group or Agency	Recommendation	Strength of Recommendation/ Certainty/Quality of Evidence
ATS/IDSA/CDC, 2017 [25]	Recommends screening for LTBI to identify persons who may benefit from treatment before progression to active TB infection using IGRA over TST.	Strong recommendation, moderate-quality evidence
NTCA/CDC, 2020 [26]	Recommended continuation of preplacement baseline LTBI testing using either IGRA or TST and symptom evaluation for all healthcare personnel with no prior documented history of LTBI or TB disease.	Strong recommendation
WHO, 2018 [27]	The WHO recommends systematic testing and treatment for: ● All persons living with HIV ● Patients initiating anti-TNF treatment ● Patients receiving dialysis ● Patients preparing for an organ or hematological transplant ● Patients with silicosis	

	● Persons residing in correctional facilities in countries with high TB incidence ● Healthcare workers in countries with high TB incidence ● Immigrants in countries with high TB incidence ● Asymptomatic individuals of all ages in countries with a low TB incidence who are household contacts of persons with active TB. The WHO recommends either a tuberculin skin test (TST) or interferon-gamma release assay (IGRA) to test for LTBI.	
NICE, 2019 [28]	Recommends TST testing in adults and children ages 2 to 65 who are close contacts of a person with pulmonary or laryngeal TB. Children younger than 2 years and adults who are immunocompromised should be assessed for risk before being tested. Persons from underserved groups, including persons experiencing homelessness, persons who misuse substances, persons residing in correctional facilities, and vulnerable migrants, who are younger than 65 years should be offered IGRA testing.	
USPSTF 2023 [29]	The USPSTF recommends screening for LTBI at increased risk. Populations at increased risk for LTBI based on increased prevalence of active disease and increased risk of exposure include persons who were born in, or are former residents of, countries with high tuberculosis prevalence and persons who live in or have lived in, high-risk congregate settings (e.g. homeless shelters or correctional facilities). Clinicians can consult their local state health departments for more information about populations at increased risk in their community since local demographic patterns may vary across the US.	Grade B Recommendation

Philippine Department of Health National TB Control Program Manual of Procedures [30]	All health facilities shall offer LTBI treatment to the following eligible high-risk groups even without Tuberculin Skin Test: 1. Persons living with HIV 2. Children less than 5 years old who are household contacts of bacteriologically confirmed TB case 3. Household contacts of a bacteriologically confirmed-TB case who are more than 5 years old AND with any of the following other risk factors for tuberculosis: DM, smoker, immunocompromised, malnourished, with two or more active TB. In addition, isoniazid preventive therapy may also be given to the following groups once active TB is ruled out AND there is a positive tuberculin skin test: 1. Children less than 5 years old who are household contacts of a clinically diagnosed TB case 2. Household contacts of a bacteriologically confirmed-TB case who are more than 5 years old AND with no other TB risk factors as enumerated above 3. Close contacts of bacteriologically confirmed TB (outside the household) 4. Other risk groups (ongoing dialysis, for organ/hematologic transplant, initiating anti-TNF treatment, silicosis)	Not Stated

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4.10 Screening for Intestinal Parasitism

RECOMMENDATION

Among asymptomatic, apparently healthy children and adults, we suggest against routine screening for intestinal parasitism. ***(Weak recommendation, very low certainty of evidence)***

Considerations: The panel gave a weak recommendation against routine screening for intestinal parasitism due to low certainty of evidence on the benefits of screening. In addition, the panel justified that mass deworming is an effective intervention with good outcomes. The panel further suggested that children and adults at high-risk for intestinal parasitism be screened even in the absence of symptoms.

4.10.1 Burden of Intestinal Parasitism

Intestinal parasitism caused by soil-transmitted helminths (STHs) such as *Ascaris lumbricoides, Trichuris trichiura,* and hookworms*,* are part of neglected tropical diseases that can cause morbidity and face challenges with its control and elimination. The national prevalence survey of STHs conducted from 2013-2015 among school-age children found an overall prevalence of 28.4% [1]. A study by Delos Trinos, et al published in 2021 showed the prevalence of 23.8% for *Ascaris lumbricoides*, 32.0% for *Trichuris trichiura*, and 7.3% for hookworm locally [2]. Parasitic infection particularly in children with moderate and high intensity infection/high worm burden has been associated with malnutrition and anemia. Locally, public health measures to control and eliminate infection uses preventive chemotherapy as its main strategy.

4.10.2 Benefits and Harms of Screening Tests

The systematic search did not find any studies which directly determined the benefits and harms of early screening on intestinal parasitism-related morbidity or mortality. There are also no noted studies that detailed early screening tests and reduction of incidence. Search showed studies that described interventions such as mass drug administration/preventive chemotherapy, community-based health education, ensuring proper water access, sanitation, and hygiene, that can affect prevalence of infection.

Special population – Food handlers:

A local study by Esparar et al [3] was done in 2004 to determine the prevalence of intestinal parasites among food handlers in a tertiary hospital. Direct fecal smear and formalin ether concentration technique (FECT) were used. The results showed that using 2 sample FECT they were able to detect at least one intestinal parasite/organism in 42.4% of the 59 food handlers examined. This contrasted with direct fecal smear which detected at least one organism in only 22.1% of the food handlers. The authors recommended to use a test with higher detection rate such as FECT in screening for stool samples in food handlers on top of emphasizing the importance of hygiene practices and periodic health examination.

A meta-analysis by Yimam et al [4] done in 2020, showed an intestinal parasite prevalence of 33.6% among food handlers which was similar to the Ethiopian average prevalence of 33.35%. The study also investigated interventions or practices that may correlate to decreased risk for infection among food handlers. The study found that food preparation training [OR 0.71 (0.53, 0.94)] and washing hands after toilet use [OR 0.46 (0.23, 0.94)] showed significant correlation. Health check-up (defined as periodic health check-up with associated stool examination) was not noted to be statistically significant [OR 0.70 (0.47, 1.04)]. The authors noted that confounding factors like poor socioeconomic status, low sanitary conditions, and inconsistent adherence to sanitary practices could explain the relatively lower protective effect of hygiene practices.

Studies on the prevalence of intestinal parasites and associated risk factors [5-9] were done after the publication of the meta-analysis by Yimam et al. Prevalence varied from as low as 11.1% in a Nigerian study by Bojuwoje et al [5] in 2020 to as high as 44.9% in an Ethiopian study by Tsegaye et al [9] in 2023.

For risk factors that can affect the prevalence of intestinal parasitic infection, the multivariable regression analysis in the study by Yeshanew et al [6] in 2021 noted the following factors to be protective: 1) hand wash practice decreased the possibility to be infected by 0.778% (AOR 0.2220 (0.0560,0.8830), $p \leq 0.0330$); 2) food handling and preparation training have decreased the chance of getting intestinal parasitic infections by 97.9% (AOR 0.0210 (0.0010, 0.3080), $p \leq 0.0050$); 3) medical checkup (but no note if medical checkup included stool examination) decreased the probability of infection by 95.9% (AOR 0.0410 (0.0040, 0.4340), $p \leq 0.0080$).

The multivariable regression analysis in the study by Feleke et al [8] in 2023 showed that poor hygiene practices like hand washing without soap after toilet use were more likely to be infected with intestinal parasites (AOR 20.7, 95 CI: 2.03–4.20). The study by Tsegaye et al [9] in 2023 also noted poor hand washing practices to increase the likelihood of infection: inconsistent hand washing with soap and water after visiting toilet (AOR 6.25, 95 CI: 2.05–19.02), and inconsistent hand washing with soap and water before meal (AOR 12.49, 95 CI: 4.9–31.7). The study also noted that participants who did not have periodic medical checkup were more likely to have intestinal parasitic infections (AOR 3.42, 95 CI: 1.29–9.06) but the study also did not define if the medical checkup included stool examination.

4.10.3 Benefits and Harms of Early Intervention

Treatment for intestinal parasitism entails a course of anthelmintics: albendazole 400mg single dose or mebendazole 500mg single dose or mebendazole 100mg twice daily for 3 days for ascariasis or hookworm infection; albendazole 400mg daily for 3 days or mebendazole 500mg single dose or mebendazole 100mg twice daily for 3 days for trichuriasis; pyrantel pamoate 11mg/kg dose (up to 1 gram) daily for three days for hookworm infection.

The 2020 Cochrane review [26] showed that anthelmintics are effective against *A. lumbricoides* infection with anthelmintics showing 93% cure vs placebo, with single dose albendazole showing cure in 93% of individuals vs single dose mebendazole

showing cure in 98% showing both are equally effective against ascariasis. The review also did not report serious adverse events to the drugs.

Treatment with anthelmintics have been shown to greatly decrease worm burden in infected individuals as illustrated by the finding of the 2017 systematic review by Marocco et al [27] which showed a decrease in 85% prevalence of moderate and heavy intensity infections (infections which are associated with more morbidity) in the population with preventive chemotherapy over the course of a year. These findings of decreased prevalence or decreased worm burden after implementing preventive chemotherapy are also seen in the systematic reviews by Tanjong Ghogomu et al [28] and by Clarke et al [29]. Additionally, the study by Tanjong Ghogomu [28] showed that deworming did not have a large effect on the prevalence of anemia.

Table 55. Summary of findings of systematic reviews for the treatment of intestinal parasitism

Intervention	Number of studies	Effect (CI 95%)	Side effects	Interpretation	Certainty of evidence
2020 Cochrane review: Parasitologic cure against ascariasis					
Any anthelminthic vs placebo	8	RR: 6.29 (3.91-10.12)	No serious adverse events; nausea, vomiting, abdominal pain, diarrhea, headache	Analysis favors taking an anthelminthic in providing parasitologic cure against ascariasis vs placebo	Low
Albendazole vs mebendazole	6	RR: 1.01 (1.00-1.02)	No serious adverse events; nausea, vomiting, abdominal pain, diarrhea, headache	Albendazole and mebendazole are equally effective in providing parasitologic cure against ascariasis	Low
Tanjong Ghogomu et al 2017: Deworming and effect on prevalence of infection					
Mass deworming on roundworm infection	2	RR: 0.29 (0.14-0.62)	N/A	Mass deworming has an effect in decreasing infection prevalence	Low
Mass deworming on hookworm infection	2	RR: 0.32 (0.18-0.59)	N/A		Low
Mass deworming and effect on anemia prevalence	3	RR: 0.82 (0.60-1.11)	N/A	Mass deworming has no statistically significant effect in decreasing anemia prevalence	Very Low
Clarke et al 2017: community vs targeted deworming and effect on prevalence					

Community vs targeted deworming (Ascaris)	56	OR: 16.4 (2.1 – 125.8)	N/A	Analysis favor community/ mass vs targeted/ school-based deworming	Low
Community vs targeted deworming (hookworm)	56	OR: 4.6 (1.8-11.6)	N/A		Low
Community vs targeted deworming (Trichuris)	56	OR: 2.1 (0.30-14.8)	N/A	No significant difference	Low

Special population – Food handlers:

The systematic search did not find any studies that determined the benefits of early intervention on food handlers.

4.10.4 Diagnostic Accuracy of Screening Tests

Locally available parasitological tests for the diagnosis of soil-transmitted helminths (direct fecal smear/ fecalysis, Kato-Katz smear, and FECT) did not demonstrate a high level of sensitivity.

The 2014 systematic review by Nikolay et al showed a pooled sensitivity of 52.1%, 62.8%, and 42.8% for *Ascaris lumbricoides, Trichuris trichiura,* and hookworm respectively for fecalysis. The same study showed pooled sensitivity for Kato-Katz of 63.8% for *Ascaris lumbricoides*, 82.2% for *Trichuris trichiura*, and 59.5% for hookworms. For FECT, sensitivity was shown to be at 56.9% for *Ascaris lumbricoides*, 81.2% for *Trichuris trichiura*, and 53.0% for hookworms.

Observational studies done after the publication of the systematic review also showed similar results. Meta-analysis was done on these observational studies published after 2014. Fecalysis showed sensitivity of 52% for any soil-transmitted helminth infection. FECT was shown to have a sensitivity of 68% for any soil-transmitted helminth infection. For Kato-Katz, sensitivity was noted to be 58% for *Ascaris lumbricoides,* 67% for *Trichuris trichiura*, and 62% for hookworms.

Table 56. Summary of findings of systematic review by Nikolay et al

Test	Number of studies (Population)	Sn (CI)	Estimates per 1000 tested		Certainty of evidence
			Correctly diagnosed	Missed	
Fecalysis (ascariasis)	7 (1465)	0.521 (0.466-0.577)	124 (111 to 137)	114 (101 to 127)	Moderate
Fecalysis (trichuriasis)	7 (1465)	0.628 (0.569-0.689)	201 (182 to 220)	119 (100 to 138)	Moderate
Fecalysis (hookworm)	7 (1465)	0.428 (0.383-0.484)	31 (28 to 35)	42 (38 to 45)	Moderate
Kato-Katz (ascariasis)	20 (8571)	0.638 (0.591-0.686)	152 (141 to 163)	86 (75 to 97)	Moderate
Kato-Katz (trichuriasis)	20 (8571)	0.822 (0.801-0.845)	263 (256 to 270)	57 (50 to 64)	Moderate

Kato-Katz (hookworm)	20 (8571)	0.595 (0.569-0.622)	43 (42 to 45)	30 (28 to 31)	Moderate
FECT (ascariasis)	7 (1557)	0.569 (0.511-0.635)	135 (122 to 151)	103 (87 to 116)	Moderate
FECT (trichuriasis)	7 (1557)	0.812 (0.730-0.892)	260 (234 to 285)	60 (35 to 86)	Moderate
FECT (hookworm)	7 (1557)	0.530 (0.486-0.575)	39 (35 to 42)	34 (31 to 38)	Moderate

Table 57. Summary of findings of cross-sectional studies of diagnostic accuracy (meta-analysis done)

Test	Number of studies (Population)	Sn (CI)	Estimates per 1000 tested		Certainty of evidence
			Correctly diagnosed	Missed	
Fecalysis	2 (700)	0.52 (95% CI: 0.47 to 0.57)	148 (133 to 162)	136 (122 to 151)	Low
Kato-Katz (ascariasis)	5 (6014)	0.58 (95% CI: 0.50 to 0.66)	138 (119 to 157)	100 (81 to 119)	Low
Kato-Katz (trichuriasis)	5 (6014)	0.67 (95% CI: 0.49 to 0.81)	214 (157 to 259)	106 (61 to 163)	Very Low
Kato-Katz (hookworm)	6 (6206)	0.62 (95% CI: 0.34 to 0.85)	45 (25 to 62)	28 (11 to 48)	Very Low
FECT	3 (710)	0.68 (95% CI: 0.43 to 0.85)	192 (122 to 241)	92 (43 to 162)	Very Low

4.10.5 Resource Implication

Cost

Currently the cost of routine fecalysis in a DOH retained hospital is at Php 40, while it costs around Php 100 in a private laboratory. Kato-katz technique test is priced at Php 100 while a DFS is Php 210 at RITM. Kato-Katz costs Php 300, cellulose tape test cost Php 300 and FECT cost Php 400 at UP-Manila College of Public Health.

Mebendazole 500mg tablets cost Php 105 per tablet in a private pharmacy. Its 50mg/mL oral suspension preparation costs Php 157 per 10mL bottle. Mebendazole 500mg tablets cost Php 1.75 per tablet while its 100mg/5mL oral suspension costs Php 14 per 60mL bottle as per DOH procurement price. Albendazole 400mg tablet is priced at Php 1.04 per tablet as per DOH procurement price.

Cost effectiveness

In a study by Muennig et al [10] in 1999, they compared the cost and benefits of no preventive intervention (watchful waiting) with those of universal screening or presumptive treatment with 400 mg albendazole per day for 5 days among immigrants to US coming from Asia, Middle East, sub–Saharan Africa, Eastern Europe, and Latin America and Caribbean. They were able to show that compared to watchful waiting, presumptive treatment of all immigrants at risk for parasitosis would avert at least 870

DALYs, prevent at least 33 deaths and 374 hospitalizations and save at least USD 4.5 million per year and would only cost USD4,630 per DALY averted. As compared with watchful waiting, screening would cost USD 159,236 per DALY averted. Hence doing presumptive treatment for all immigrants at risk for parasitosis will save lives and money while universal screening with treatment of persons with positive stool examinations can also save lives but is less cost effective than presumptive treatment.

In a study done by Garcia [11], in the Philippines, an economic model showed that a targeted annual treatment strategy will cost around USD0.97 per person compared to mass and annual treatment strategy which will cost around USD1.83 per person. In terms of DALYs averted, a targeted annual treatment strategy can avert about 0.03 DALYs averted per person treated, while a mass and annual treatment strategy can avert 0.04 DALYs averted per person treated. In a study by Mationg et al [12], that was conducted in 40 schools in the province of Laguna, they were able to show the need for sustainable deworming in tandem with other measures such as the provision of health education can cost only around Php 58.65 (USD1.15) per student in addition to the already in place cost of Php 58.17 per student for mass drug administration.

4.10.6 Patient's Values and Preference, Equity, Acceptability, and Feasibility

Orish et al [13] conducted a study in Ghana to know physicians' perception and diagnosis of intestinal parasitic infections among patients with gastrointestinal symptoms. They were able to find that the majority of physicians (57.6%) do not suspect intestinal parasitic infections among their patients with GI symptoms and that most (73.9%) will also not be requesting for stool investigation among their patients even with symptoms. Most physicians (75%) however consider intestinal parasitic infection as a burden in Ghana. The authors concluded that the consideration of intestinal parasitic infection as a diagnosis among patients with GI symptoms and request for stool investigations was low among physicians in this study.

In a study by Feleke et al [14], done in Ethiopia, they were able to enroll 4436 study participants who are household contacts of a patient diagnosed positive for parasitic infection in the district health facility. They were able to get a 98% response rate among household contacts who are willing to submit stool samples for testing. The prevalence of intestinal parasitic infection among family members of a known parasitic case was 86.14%. Locally, Lorenzo et al [15] did a community perception study about mass-drug administration for soil-transmitted helminthiasis and schistosomiasis in selected schools in Northern Samar and Sorsogon. Their results showed that participants held mostly correct biomedical notions of the infections and expressed willingness to participate in mass drug administration programs. However, reservations remained due to reported lack of information dissemination, lack of confidence in the drug used, and widespread fear of adverse side effects.

4.10.7 Recommendations from Other Groups

The US CDC recommends screening for soil-transmitted helminth infections for asymptomatic refugees who have contraindications to presumptive treatment at the time of arrival. Screening is done with two or more separate stool ova and parasite tests done by concentration technique; samples are collected 12 to 24 hours apart.

The 1975 Philippine Code on Sanitation states that: “No person shall be employed in any food establishment without a health certificate issued by the local health authority. This certificate shall be issued only after the required physical and medical examinations are performed and immunizations are administered at prescribed intervals.” The 1995 Implementing Rules and Regulations of Chapter III – Food Establishments – of the Code on Sanitation further expounds on this by saying that: “The health certificate shall be renewed at least every year or as often as required by local ordinance.”

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5. Research Implications/Gaps

Many research questions from the identified clinical questions in this CPG were not answered directly due to paucity in literature. Therefore, indirect evidence based on the screening cascade were presented.

No direct evidence was found on the benefits and harms of screening for syphilis, asymptomatic bacteriuria, Hepatitis A, Hepatitis C, HIV, COVID-19, LTBI, and intestinal parasitism, among asymptomatic, apparently healthy population.

There is a lack of local data on the cost-effectiveness of screening for syphilis, asymptomatic bacteriuria, and COVID-19, in asymptomatic, apparently healthy population. Generating these data is necessary as it will inform proper resource allocation, especially in a low-income country like the Philippines.

No studies were found regarding the patients' values and preference, equity, acceptability, and feasibility of screening for syphilis, chlamydia and gonorrhea, asymptomatic bacteriuria, and hepatitis A in the general population. Social science research could help determine the facilitators and barriers that could affect the implementation of this guideline.

There is a need for economic analysis of the recommendations as much of the available data come from high-income countries.

Filling in the research gaps can provide answers to the identified clinical questions which can influence the recommendations for updating this guideline.

6. Dissemination and Implementation

In the active phase of dissemination and implementation, the aim is to share widely the practice guideline towards its practical application in healthcare setting. This will be done in a targeted communication efforts such as disseminating copies to Philippine Health Insurance Corporation (PHIC) and health maintenance organizations (HMOs). Copies will also be provided to agencies that handle key populations identified in the document (such as but not limited to: DOH, Philippine National AIDS Council, National Coordinating Committee for TB, Department of Labor and Employment, National Youth Council, Department of Education, Commission on Higher Education). Efforts are focused on supporting primary care providers in adopting the guideline through training sessions and provision of educational resources. The DOH planned to develop a simplified version of this CPG and make 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. This guideline will also be presented in lectures and scientific conferences.

Continuous monitoring and evaluation will also be implemented to gauge the impact of the guideline on clinical practices, and to allow the guideline developers to make necessary adjustments to enhance its effectiveness. All strong recommendations in this guideline can be used for monitoring and auditing practices in different institutions. This can be converted to key performance indicators and can also be used in creating clinical pathways. Feedback will be continuously gathered through surveys, questionnaires, focus group discussions and feedback forms thru online platforms and attendees of conferences or workshops where the guideline is presented and implemented.

7. 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. The availability of screening tests recommended in this guideline would likely vary at the regional, provincial, or even municipal/city level. 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.

Resource Implication
As a low-middle-income country, our limited resources need to be allocated and used efficiently. The cost of the screening tests and interventions being used for infectious diseases was one important consideration discussed in the panel meetings; it should be a key gatekeeping mechanism to ensure that all payments made by the government (through PhilHealth) are cost-effective.

8. Updating of the Guidelines

The recommendations herein shall hold until such time that new evidence on screening and diagnosing the diseases tackled in this guideline emerges and contingencies dictate updating this Philippine Guidelines on Periodic Health Examination. The CPGs will be updated every 3-5 years or earlier if new significant evidence becomes available.

9. Appendices

9.1 Screening for Syphilis

Appendix 1. Search Strategy

We did not find studies on the effectiveness and safety of screening program for syphilis among healthy apparently symptomatic population. Studies comparing the incidence of syphilis between the use of screening tests and without screening tests were also not available. The only available studies were among the high-risk population: HIV-positive males, males who have sex with males, pregnant women. To determine the benefit of screening of syphilis in the high-risk population, studies reviewing the accuracy, benefits, and harms of the screening tests were collected. There were 2918 studies from Pubmed when the keywords “syphilis” and “screening” were used. Upon using the filter for randomized controlled trials, 24 studies were identified, retrieved, and reviewed. Twenty studies were excluded since it did not cover the benefits and harms of syphilis screening, hence, 4 studies were included in the review.

Appendix 2. Characteristics of Included Studies

Study ID Title Author	**Study Design**	**Country**	**Total number of patients Included**	**Population**	**Intervention**	**Control**	**Outcome**
Syphilis Laboratory guidelines: Performance Characteristics of Nontreponemal Antibody Tests (Tuddenham et. al., 2020)	Systematic Review	USA	6848 participants from 11 pooled studies are referred to in this paper	Serum from different clinics	VDRL RPR	Darkfield microscopy	Newly diagnosed syphilis cases
Performance of Treponemal tests for the Diagnosis of Syphilis (Park et. al., 2020).	Cross sectional study	USA	959 participants	Serum from 4 clinics (1 was a STI clinic)	FTA—ABS Centaur CIA Bioplex MBIA INNO-LIA LIASON CIA TPPA Trep-Sure EIA	Syphilis was diagnosed when 4 or more of the 7 tests becomes positive	Newly diagnosed syphilis cases
Routinized syphilis screening among men living with human immunodeficiency virus: A stepped wedge cluster randomized controlled trial (Burchell et al., 2022)	Randomized Control trial	Canada	3892 men followed over 7471 person-years	HIV positive males who have sex with males	Syphilis screening with HIV viral load (Routine with HIV-viral load)	Syphilis screening only based on risk (Standard)	Number of screened individuals Newly diagnosed syphilis cases
Synthesized prevention and control of one decade for mother-to-child transmission of	Cross sectional study	Shenzhen, China	2 441 237 pregnant women	Pregnant women	Syphilis screening	-	Screening rate Number of cases of

syphilis and determinants associated with congenital syphilis and adverse pregnancy outcomes in Shenzhen, South China. Eur J Clin Microbiol Infect Dis 2014;33:2183–98. (Qin et al., 2014)							congenital syphilis Incidence rate of vrse pregnancy outcomes including stillbirth and fetal loss
(Wan et. al., 2020)	Cohort study	Jiangxi, China	4210 pregnant women	Pregnant women	Treatment Adequate treatment First trimester treatment	No Treatment Inadequate treatment Third trimester treatment	Stillbirth Preterm birth Low birth weight Congenital syphilis

Appendix 3. GRADE Evidence Profile

Question: Should **VDRL** be used to diagnose Syphilis in high risk adolescents and adults?

Sensitivity	0.81 (95% CI: 0.76 to 0.86)
Specificity	1.00 (95% CI: 0.92 to 1.00)

Prevalences	7.5%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of7.5%	
True positives (patients with Syphilis)	6 studies 3703 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	none	61 (57 to 64)	⊕⊕⊕⊕ High
False negatives (patients incorrectly classified as not having Syphilis)								14 (11 to 18)	
True negatives (patients without Syphilis)	6 studies 3703 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	none	925 (849 to 925)	⊕⊕⊕⊕ High
False positives (patients incorrectly classified as having Syphilis)								0 (0 to 76)	

Question: Should **RPR** be used to diagnose Syphilis in high risk adolescents and adults?

Sensitivity	0.84 (95% CI: 0.80 to 0.87)
Specificity	1.00 (95% CI: 0.99 to 1.00)

Prevalences	7.5%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of7.5%	
True positives (patients with Syphilis)	4 studies 3143 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	none	63 (60 to 65)	⊕⊕⊕⊕ High
False negatives (patients incorrectly classified as not having Syphilis)								12 (10 to 15)	
True negatives (patients without Syphilis)	4 studies 3143 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	none	923 (919 to 925)	⊕⊕⊕⊕ High
False positives (patients incorrectly classified as having Syphilis)								2 (0 to 6)	

Question: Should **TPPA** be used to diagnose Syphilis in high risk adolescents and adults?

Sensitivity	0.95 (95% CI: 0.92 to 0.98)
Specificity	1.00 (95% CI: 0.99 to 1.00)

Prevalences	2%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of2%	
True positives (patients with Syphilis)	1 studies 959 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	19 (18 to 20)	⊕⊕⊕◯ Moderate
False negatives (patients incorrectly classified as not having Syphilis)								1 (0 to 2)	
True negatives (patients without Syphilis)	1 studies 959 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	980 (970 to 980)	⊕⊕⊕◯ Moderate
False positives (patients incorrectly classified as having Syphilis)								0 (0 to 10)	

Explanations

a. Only 1 study included

Question: Should **FTA-ABS** be used to diagnose syphilis in high risk adolescents and adults?

Sensitivity	0.91 (95% CI: 0.87 to 0.94)

Prevalences	2%		

Specificity	0.98 (95% CI: 0.96 to 0.99)

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of2%	
True positives (patients with syphilis)	1 studies 959 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	18 (17 to 19)	⊕⊕⊕◯ Moderate
False negatives (patients incorrectly classified as not having syphilis)								2 (1 to 3)	
True negatives (patients without syphilis)	1 studies 959 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	960 (942 to 971)	⊕⊕⊕◯ Moderate
False positives (patients incorrectly classified as having syphilis)								20 (9 to 38)	

Explanations

a. Only 1 study included

Question: Should **Centaur-EIA** be used to diagnose syphilis in high risk adolescents and adults?

Sensitivity	0.97 (95% CI: 0.95 to 0.99)
Specificity	0.95 (95% CI: 0.93 to 0.97)

Prevalences	2%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of2%	
True positives (patients with syphilis)	1 studies 959 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	19 (19 to 20)	⊕⊕⊕◯ Moderate
False negatives (patients incorrectly classified as not having syphilis)								1 (0 to 1)	
True negatives (patients without syphilis)	1 studies 959 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	936 (911 to 954)	⊕⊕⊕◯ Moderate
False positives (patients incorrectly classified as having syphilis)								44 (26 to 69)	

Explanations

a. Only 1 study included

Question: Should **Trep-Sure EIA** be used to diagnose syphilis in high risk adolescents and adults?

Sensitivity	0.98 (95% CI: 0.96 to 1.00)
Specificity	0.83 (95% CI: 0.78 to 0.86)

Prevalences	2%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of2%	
True positives (patients with syphilis)	1 studies 959 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	20 (19 to 20)	⊕⊕⊕◯ Moderate
False negatives (patients incorrectly classified as not having syphilis)								0 (0 to 1)	
True negatives (patients without syphilis)	1 studies 959 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	809 (768 to 844)	⊕⊕⊕◯ Moderate
False positives (patients incorrectly classified as having syphilis)								171 (136 to 212)	

Explanations

a. Only 1 study included

Question: Should **LIASON CIA** be used to diagnose syphilis in high risk adolescents and adults?

Sensitivity	0.97 (95% CI: 0.94 to 0.99)
Specificity	0.94 (95% CI: 0.92 to 0.96)

Prevalences	2%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of2%	
True positives (patients with syphilis)	1 studies 959 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	19 (19 to 20)	⊕⊕⊕◯ Moderate
False negatives (patients incorrectly classified as not having syphilis)								1 (0 to 1)	
True negatives (patients without syphilis)	1 studies 959 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	926 (900 to 946)	⊕⊕⊕◯ Moderate

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of2%	
False positives (patients incorrectly classified as having syphilis)								54 (34 to 80)	

Explanations
a. Only 1 study included

Question: Should **Bioplex MBIA** be used to diagnose syphilis in high risk adolescents and adults?

Sensitivity	0.97 (95% CI: 0.94 to 0.99)
Specificity	0.97 (95% CI: 0.94 to 0.98)

Prevalences	2%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of2%	
True positives (patients with syphilis)	1 studies 959 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	19 (19 to 20)	⊕⊕⊕◯ Moderate
False negatives (patients incorrectly classified as not having syphilis)								1 (0 to 1)	
True negatives (patients without syphilis)	1 studies 959 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	948 (925 to 962)	⊕⊕⊕◯ Moderate
False positives (patients incorrectly classified as having syphilis)								32 (18 to 55)	

Explanations
a. Only 1 study included

Question: Should **INNO-LIA** be used to diagnose syphilis in high risk adolescents and adults?

Sensitivity	0.97 (95% CI: 0.94 to 0.99)
Specificity	0.98 (95% CI: 0.97 to 0.99)

Prevalences	2%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of2%	
True positives		cross-sectional	not serious	not serious	not serious	not serious		19 (19 to 20)	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of2%	
(patients with syphilis)	1 studies 959 patients	(cohort type accuracy study)					publication bias strongly suspected[a]		⊕⊕⊕◯ Moderate
False negatives (patients incorrectly classified as not having syphilis)								1 (0 to 1)	
True negatives (patients without syphilis)	1 studies 959 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	965 (949 to 975)	⊕⊕⊕◯ Moderate
False positives (patients incorrectly classified as having syphilis)								15 (5 to 31)	

Explanations

a. Only 1 study included

Author(s): Dr. Christopher G. Manalo, MD, MSc (cand), Dr. Erika A. Crisostomo, MD
Question: Routinized syphilis screening compared to usual syphilis testing practice for non-pregnant adolescents and adults with risk factors (HIV-positive men)
Setting: Outpatient clinics
Bibliography: Burchell AN, Tan DHS, Grewal R, MacPherson PA, Walmsley S, Rachlis A, Andany N, Mishra S, Gardner SL, Raboud J, Fisman D, Cooper C, Gough K, Maxwell J, Rourke SB, Rousseau R, Mazzulli T, Salit IE, Allen VG. Routinized Syphilis Screening Among Men Living With Human Immunodeficiency Virus: A Stepped Wedge Cluster Randomized Controlled Trial. Clin Infect Dis. 2022 Mar 9;74(5):846-853. doi: 10.1093/cid/ciab582. PMID: 34175944; PMCID: PMC8906680.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	routinized syphilis screening	usual syphilis testing practice	Relative (95% CI)	Absolute (95% CI)		
Syphilis Case Detection (Primary, Secondary, Early Latent, Latent of Unknown Duration)												
1	randomised trials	not serious	not serious	not serious	serious[a]	none	The annualized proportion of men with newly detected early syphilis as well as new latent cases and cases of unknown duration was OR 1.44 (95% CI 0.90 to 2.31) with corresponding time-adjusted to account for SW-CRCT design.				⊕⊕⊕◯ Moderate	CRITICAL

CI: confidence interval

Explanations

a. Wide confidence interval

Author(s): Dr. Christopher G. Manalo, MD, MSc (cand), Dr. Erika A. Crisostomo, MD
Question: Syphilis screening compared to no screening for asymptomatic pregnant women
Setting: Shenzhen, China
Bibliography: [1] Qin J-B, Feng T-J, Yang T-B, Hong F-C, Lan L-N, Zhang C-L, et al. Synthesized prevention and control of one decade for mother-to-child transmission of syphilis and determinants associated with congenital syphilis and adverse pregnancy outcomes in Shenzhen, South China. Eur J Clin Microbiol Infect Dis 2014;33:2183–98. https://doi.org/10.1007/s10096-014-2186-8.

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Number of Syphilis Tests (follow-up: 10 years)									
1	observational studies	not serious	not serious	not serious	not serious	none	the screening uptake for syphilis among pregnant women increased from 89.8% to 97.2%	⊕⊕◯◯ Low	CRITICAL
Newly diagnosed Congenital Syphilis (follow-up: 10 years)									
1	observational studies	not serious	not serious	not serious	not serious	none	incidence of congenital syphilis decreased from109.3 cases to 9.4 cases per 100 000 livebirths	⊕⊕◯◯ Low	CRITICAL

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Adverse pregnancy outcomes (follow-up: 10 years)									
1	observational studies	not serious	not serious	not serious	not serious	none	the incidence of adverse pregnancy outcomes such as premature birth and low birth weight decreased from 42.7% to 19.2%, and the incidence of stillbirth and fetal loss decreased from 19.0% to 3.3%	⨁⨁◯◯ Low	CRITICAL

Author(s): Dr. Christopher G. Manalo, MD, MSc (cand), Dr. Erika A. Crisostomo, MD
Question: Treatment compared to no treatment for maternal syphilis
Setting: Jiangxi, China
Bibliography: Wan Z, Zhang H, Xu H, Hu Y, Tan C, Tao Y. Maternal syphilis treatment and pregnancy outcomes: a retrospective study in Jiangxi Province, China. BMC Pregnancy Childbirth [Internet]. 2020;20(1):648. Available from: http://dx.doi.org/10.1186/s12884-020-03314-y

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	treatment	no treatment	Relative (95% CI)	Absolute (95% CI)		
Stillbirth												
1	observational studies	not serious	not serious	not serious	not serious	none	32/2846 (1.1%)	25/1364 (1.8%)	**OR 1.74** (1.01 to 3.00)	**13 more per 1,000** (from 0 fewer to 35 more)	⨁⨁◯◯ Low	CRITICAL
Preterm birth												
1	observational studies	not serious	not serious	not serious	not serious	none	238/2846 (8.4%)	143/1364 (10.5%)	**OR 1.70** (1.02 to 1.59)	**61 more per 1,000** (from 2 more to 52 more)	⨁⨁◯◯ Low	CRITICAL
Low Birth Weight												
1	observational studies	not serious	not serious	not serious	not serious	none	161/2846 (5.7%)	107/1364 (7.8%)	**OR 1.44** (1.11 to 1.86)	**31 more per 1,000** (from 8 more to 58 more)	⨁⨁◯◯ Low	CRITICAL

CI: confidence interval; **OR:** odds ratio

Author(s): Dr. Christopher G. Manalo, MD, MSc (cand), Dr. Erika A. Crisostomo, MD
Question: Adequate treatment compared to inadequate treatement for maternal syphilis
Setting: Jiangxi, China
Bibliography: Wan Z, Zhang H, Xu H, Hu Y, Tan C, Tao Y. Maternal syphilis treatment and pregnancy outcomes: a retrospective study in Jiangxi Province, China. BMC Pregnancy Childbirth [Internet]. 2020;20(1):648. Available from: http://dx.doi.org/10.1186/s12884-020-03314-y

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	adequate treatment	inadequate treatement	Relative (95% CI)	Absolute (95% CI)		
Stillbirth												
1	observational studies	not serious	not serious	not serious	not serious	none	8/1547 (0.5%)	24/1299 (1.8%)	**OR 3.68** (1.62 to 8.34)	**46 more per 1,000** (from 11 more to 117 more)	⨁⨁◯◯ Low	CRITICAL
Preterm Birth												
1	observational studies	not serious	not serious	not serious	not serious	none	86/1547 (5.6%)	152/1299 (11.7%)	**OR 2.26** (1.71 to 3.00)	**113 more per 1,000** (from 68 more to 167 more)	⨁⨁◯◯ Low	CRITICAL
Low Birth Weight												
1	observational studies	not serious	not serious	not serious	not serious	none	58/1547 (3.7%)	103/1299 (7.9%)	**OR 2.23** (1.59 to 3.14)	**82 more per 1,000** (from 41 more to 134 more)	⨁⨁◯◯ Low	CRITICAL

Neonatal Congenital Syphilis

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	adequate treatment	inadequate treatement	Relative (95% CI)	Absolute (95% CI)		
1	observational studies	not serious	not serious	not serious	not serious	none	11/1547 (0.7%)	34/1299 (2.6%)	**OR 3.63** (1.80 to 7.31)	**63 more per 1,000** (from 20 more to 138 more)	⨁⨁◯◯ Low	CRITICAL

CI: confidence interval; **OR:** odds ratio

Author(s): Dr. Christopher G. Manalo, MD, MSc (cand), Dr. Erika A. Crisostomo, MD
Question: First trimester treatment compared to third trimester treatment for maternal syphilis
Setting: Jiangxi, China
Bibliography: Wan Z, Zhang H, Xu H, Hu Y, Tan C, Tao Y. Maternal syphilis treatment and pregnancy outcomes: a retrospective study in Jiangxi Province, China. BMC Pregnancy Childbirth [Internet]. 2020;20(1):648. Available from: http://dx.doi.org/10.1186/s12884-020-03314-y

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	first trimester treatment	third trimester treatment	Relative (95% CI)	Absolute (95% CI)		
Stillbirth												
1	observational studies	not serious	not serious	not serious	not serious	none	3/682 (0.4%)	23/1234 (1.9%)	**OR 4.48** (1.31 to 15.30)	**60 more per 1,000** (from 6 more to 207 more)	⨁⨁◯◯ Low	CRITICAL
Preterm Birth												
1	observational studies	not serious	not serious	not serious	not serious	none	40/682 (5.9%)	150/1234 (12.2%)	**OR 2.34** (1.61 to 3.40)	**123 more per 1,000** (from 61 more to 198 more)	⨁⨁◯◯ Low	CRITICAL
Low Birth Weight												
1	observational studies	not serious	not serious	not serious	not serious	none	20/682 (2.9%)	104/1234 (8.4%)	**OR 3.25** (1.97 to 5.37)	**146 more per 1,000** (from 69 more to 246 more)	⨁⨁◯◯ Low	CRITICAL
Neonatal Congenital Syphilis												
1	observational studies	not serious	not serious	not serious	not serious	none	0/682 (0.0%)	34/1234 (2.8%)	**OR 2.26** (1.11 to 4.60)	**33 more per 1,000** (from 3 more to 88 more)	⨁⨁◯◯ Low	CRITICAL

CI: confidence interval; **OR:** odds ratio

Appendix 4. Evidence-to-Decision Framework Responses

Evidence to Decision Framework

Should screening for latent syphilis be routinely done among asymptomatic, apparently healthy adolescents and adults?

Population: Filipino adults

Intervention: Screening

Comparator: No screening

Outcomes: Incidence of syphilis, syphilis-related morbidity, syphilis-related mortality, adverse events of screening, stigma reduction

PHEx
PHILIPPINE PERIODIC HEALTH EXAMINATION

BURDEN OF SYPHILIS AS A PRIORITY PROBLEM

8 Responses

ACCURACY OF SCREENING TEST

8 Responses

BENEFITS OF SCREENING

8 Responses

HARMS OF SCREENING

8 Responses

CERTAINTY OF EVIDENCE

8 Responses

BALANCE OF BENEFITS AND HARMS

7 Responses

VALUES AND PREFERENCES

8 Responses

RESOURCE REQUIREMENTS

8 Responses

CERTAINTY OF EVIDENCE FOR RESOURCE REQUIREMENTS

8 Responses

Evidence to Decision Framework

Should screening for latent syphilis be routinely done among asymptomatic, apparently healthy adolescents and adults?

Population: Filipino adults

Intervention: Screening

Comparator: No screening

Outcomes: Incidence of syphilis, syphilis-related morbidity, syphilis-related mortality, adverse events of screening, stigma reduction

PHEx
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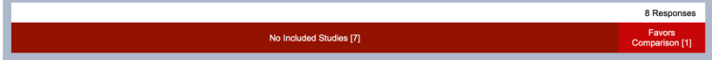
COST-EFFECTIVENESS

8 Responses



IMPACT ON HEALTH EQUITY

6 Responses

ACCEPTABILITY

6 Responses

FEASIBILITY

6 Responses

RECOMMENDATION

8 Responses

STRENGTH OF RECOMMENDATION

8 Responses

CONSENSUS PANEL COMMENTS

FOR SCREENING:

Cost-effectiveness and targeted screening for population at risk and symptomatic individuals [4]

The tests are widely available and affordable

Large benefits over moderate harms

There might be potential benefit in screening high-risk pregnant women to prevent congenital syphilis and HIV positive adults specially men having sex with men. Several studies have shown that HIV positive men having sex with men are also infected with syphilis.

Lack of evidence doesn't necessarily mean that there is no substantial benefit in screening healthy asymptomatic adolescents and adults especially if they have high risk of contracting sexually transmitted diseases like syphilis.

AGAINST SCREENING:

Low evidence [3]

No available data to support that there is substantial benefit in screening healthy asymptomatic adolescents and adults.

Not enough studies considering cost of testing

9.2 Screening for Chlamydia and Gonorrhea

Appendix 1. Search Strategy

Updated search strategy (using meta search strategy keywords):

1	'Chlamydia OR Chlamydia trichomonas OR chlamydia infection'
2	Gonorrhea OR gonococcal infection OR Neisseria gonorrhea'
3	'STI OR STD OR sexually transmitted disease OR sexually transmitted infection'
4	'HIV OR AIDS or human immunodeficiency virus
5	#3 NOT #4
6	#1 OR #2 OR #5
7	screening OR mass testing OR early detection OR early test
8	#6 AND #7 Filters: Randomized controlled trials, systematic review, from 2021-2022

Appendix 2. Characteristics of Included Study (Systematic Review)

Review Year Journal	Review aim	Search strategy	PICO	Data Analysis
Pillay, et al (11)	To conduct a systematic review on the benefits and harms of screening compared with no screening or alternative screening approaches for *Chlamydia trachomatis* and *Neisseria gonorrhea* in non-pregnant sexually active individuals as guidance for the recommendation by the Canadian Task Force on Preventive Health Care	**Databases:** five databases (Ovid Medline, Ovid Embase, Wiley Cochrane library, CINAHL via EBSCOhost, and OVID osycINFO), trial registries, conference proceedings, and reference list **Language restrictions:** English and French literature **Strategy:** presented in protocol **Last date of search:** January 24, 2020 **Exclusion criteria:** individuals with symptoms of STI, seeking care for an STI; point-of-care tests	**Population:** non-pregnant, sexually active individuals of any age not seeking for care for STI symptoms **Intervention:** any screening method for chlamydial or gonococcal infection including testing and management for people who tested positive **Outcome:** infection transmission, complications of infection **Study design:** RCTs, non-randomized controlled trials, restrospective and prospective controlled cohort studies **Preprints:** not included *full list available in supplemental document	**Risk of bias:** Individual assessment presented with criteria for grading explained in supplementary document **Publication bias:** funnel plot and Ugger's test **Subgroup analysis:** not done but explained in methodology **Sensitivity analysis:** yes **Statistical analysis:** when appropriate, sing the DerSimonian Laird random effects model using Review Manager ver 5.4

Appendix 3. Critical Appraisal using AMSTAR Tool

AMSTAR Items	Pillay (2021)
Date of last search	January 2020
Rating of overall confidence in the results of the review[§]	**HIGH**
1. Research questions, inclusion criteria include PICO components	Y
2.* Protocol registered before commencement of the review	Y
3. Selection of study designs to be included were explained	Y
4.* Adequacy of literature search	Y
5. Study selection done by at least 2 reviewers	Y
6. Data extraction done by at least 2 reviewers	Y
7.* Justification for excluding individual studies	Y
8. Described included studies in adequate detail	Y
9.* ROB from individual studies being included in the review	Y
10. Reported sources of funding for studies included	N
11.* Appropriateness of meta-analytical methods	Y
12. Potential impact of ROB in individual studies	Y
13.* Consideration of ROB when interpreting review results	Y
14. Sufficient explanation of heterogeneity	Y
15.* Assessment of presence and likely impact of publication bias	Y
16. Reported potential COI sources, funding they received	Y

NOTES:
[§] AMSTAR-2 rating for overall confidence.
*Multiple non-critical weaknesses may diminish confidence in the review and it may be appropriate to move the overall appraisal down from moderate to low confidence.

- **High** - No or 1 non-critical weakness: the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest
- **Moderate** - More than 1 non-critical weakness*: the systematic review has more than one weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review
- **Low** - 1 critical flaw with or without non-critical weaknesses: the review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest
- **Critically low** - More than 1 critical flaw with or without non-critical weaknesses: the review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies

Appendix 4. Characteristics of Included Studies (Primary Studies)

Author, year **Country**	**Design; sample size, recruitment area**	**Rates of testing outside of study and % positive (IG and control group [CG])**	**Population**	**Baseline CT positivity of IG and CG;**	**Screening approach; CT vs CT & NG; Location, test and person testing; Re-testing; Co-interventions** **Screening rates in intervention group (IG)**	**Outcome Assessment** **Incidence of PID in CG** **Follow-up Durations**
Andersen 2011 Aarhus, Denmark	RCT N = 15459 women, 14980 men	IG: 9% women, 1.5% men CG: 9.4% women, 1.4% men	Men and women aged 21-24 years old *no info about sexual history	IG: 1175 women tested (29.4%) 7.1% (84/1175) 1033 men tested (20.7%) 5.8% (60/1033)	IG: Received invitation for testing by mail, Home sample collection 4000 women, 5000 men Further divided into two groups A: received testing kit together with invitation (2000 women, 2500 men) B: needed to reply first being mailed back the test kit (2000 women, 2500 men) 29% CG: 11,459 women, 9980 men Usual care Follow-up for 9 years	**PID, ectopic pregnancy, infertility, epididymitis** Using Danish health registry (mostly clinical diagnosis) and records of doxycycline prescription ICD codes for those admitted, Follow-up after 1 year for PID and epididymitis PID: 23/4000 vs 74/11459 HR 1.12 (0.70-1.79) EP 27/4000 vs 75/11459 HR 0.97 (0.63-1.51) Infertility: 129/4000 vs 322/11459 HR 0.87 (0.71-1.07) Epididymitis: 16/5000 vs 40/9980 HR 1.25 (0.70-2.24) No difference for participating vs non-participating subjects in the intervention group for all outcomes
Hocking 2018 Australia (rural towns) 3%	Cluster RCT Re-testing encouraged (10-15months after negative test, 6weeks to 6 months after positive test) N= 63,388	CG: 17.1%	Men and women 16-29 years old who are sexually active	IG: 5%	IG: Intervention package (education package for staff, CT testing for patients, reminders and feedback system) Self-collected urine samples or vaginal swabs tested via NAAT n= 30,527 24.3% at least once (16.4% one test, 5% had two, 2.8% 3 or more)	**Clinic PID**: cumulative incidence in clinics for women 16-33 with at least one clinic visit during intervention period. **Hospital PID**: ICD codes for all 15-34 yr olds living in each cluster. Incidence in **Clinic epididymitis:** cumulative incidence among men aged 16-29 years

Author, year Country	Design; sample size, recruitment area	Rates of testing outside of study and % positive (IG and control group [CG])	Population	Baseline CT positivity of IG and CG;	Screening approach; CT vs CT & NG; Location, test and person testing; Re-testing; Co-interventions Screening rates in intervention group (IG)	Outcome Assessment Incidence of PID in CG Follow-up Durations
					CG: Usual practice n= 32811	who attended clinics during the intervention period **Chlamydia prevalence:** proportion of men and women aged 16-29 with positive CT test before randomization and after trial. 3.4% vs 3.4% (adjusted RD 0.9 95%CI 0.5to1.6)
Scholes 1996 Wahington, USA	RCT 1 screen offered to selected females N= 2607		Women 18-34years old (81% ≤24 yrs) Group Health Cooperative members assessed to have risk factors for CT Exclusion: married, never had sexual intercourse, pregnant, undergone hysterectomy, with regular use of antibiotics	IG 7%	Randomization 1:2: Screening group Two cervical samples: swab test for ELISA, and cytobrush for chlaymydial cell culture (n=1009) 645 (64%) tested for CT- 44/645 (7%) positive Control group Usual care group, no screening (n=1598) Follow-up after 12months	**Incidence of PID** Questionnaire whether there was urogenital infections, diagnosed with PID, and other health-related events and behaviors Medical database indicating diagnosis of PID or cervicitis; in-patient hospital records, laboratory records for those with positive test, pharmacy records Follow-up (76%) Considered only with PID if with a clinical diagnpsis of PID upon review of medical records
Oakeshott, 2010 London, UK	RCT N= 2529 Common rooms, lecture theaters, student bars at	IG: 269 (10%) CG: 258 (15%)	16-27 years old (mean age 21) sexually-active females	IG: 5.4% of screened group (68/1259)	Questionnaire on sexual health Self-taken vaginal swabs Random allocation AFTER sample collection: IG:	incidence of clinical pelvic inflammarory disease follow-up after 12 months – Any report by participants or their providers about signs and symptoms or dx, looked to

Author, year Country	Design; sample size, recruitment area	Rates of testing outside of study and % positive (IG and control group [CG])	Population	Baseline CT positivity of IG and CG;	Screening approach; CT vs CT & NG; Location, test and person testing; Re-testing; Co-interventions Screening rates in intervention group (IG)	Outcome Assessment Incidence of PID in CG Follow-up Durations
	universities and colleges in London		Exclusion: no sexual history, tested for CT 3 months prior, pregnant	CG: 5.9% of control positive when samples were tested 1 year after (75/1270)	immediate testing and treatment for CT infection (n= 1259) 100% CG: storage and analysis after one year (control group, deferred screening) (n= 1270)	medical records in general practitioners, hospitals, family planning clinics, and genitourinary medicine clinics. Used criteria for all cases, but medical records sometimes incomplete
Clark 2002 US (army recruits)	CCT 1 screen N= 28,074	NR	F 17-39 yrs; 88% ≤25yrs Who entered full-time military duty	9.1%	First catch urine sample tested with NAAT Screened group 7053 - 643 (+): 7 PID, 1 ectopic pregnancy, 0 infertility - 6140 (-): 43 PID, 27 ectopic pregnancy, 2 infertility 100% Unscreened group 21,021' Follow-up for 3 years or until leaving military service with mean follow 1.5 years	**PID, ectopic pregnancy, infertility:** Hospital data PID: 50 Vs 175 Ectopic pregnancy: 28 vs 70 Infertility 2 vs 9

Appendix 5. Risk of Bias Assessment

	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Bias

	Random sequence generation	Allocation concealment	Evidence of contamination?	Awareness of PID status?	>10-20%		Adjustment for clustering?
Andersen 2011 (RCT)	Low	Low	Low	Unclear	Low	Low	Information bias (assessment of cases based on ICD 10 codes or prescription of doxycycline)
Clark 2001 (CCT)	High	Unclear	Low	Unclear	Low	Low	Low
Hocking 2019 (Cluster RCT)	Low	Low	Low	Unclear	Low	Low	Low
Oakeshott 2010 (RCT)	Low	Low	Low	Low	Low	Low	Low
Scholes 1996 (RCT)	Unclear	Unclear	Low	Unclear	Unclear	Low	Low

Appendix 6. GRADE Evidence Profile

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Screening benefit	placebo	Relative (95% CI)	Absolute (95% CI)		
PID - Universal Screening												
2	randomised trials	not serious	serious[a]	serious[b]	serious[c]	none	373/93046 (0.4%)	399/105042 (0.4%)	**RR 1.05** (0.66 to 1.66)	**0 fewer per 1,000** (from 1 fewer to 3 more)	⨁◯◯◯ Very low	
PID - Universal screening- high risk												
1	randomised trials	serious[d]	not serious	not serious	not serious	publication bias strongly suspected[e]	9/1009 (0.9%)	33/1598 (2.1%)	**RR 0.43** (0.21 to 0.90)	**12 fewer per 1,000** (from 16 fewer to 2 fewer)	⨁⨁◯◯ Low	
PID - Acceptors of screening												
2	randomised trials	serious[f]	not serious	not serious	serious[g]	none	65/8244 (0.8%)	198/22207 (0.9%)	**RR 0.81** (0.61 to 1.07)	**2 fewer per 1,000** (from 3 fewer to 1 more)	⨁⨁◯◯ Low	
Infertility - Universal												
1	randomised trials	not serious	not serious	serious[b]	not serious	publication bias strongly suspected[e]	129/4000 (3.2%)	322/11459 (2.8%)	**RR 1.15** (0.94 to 1.40)	**4 more per 1,000** (from 2 fewer to 11 more)	⨁⨁◯◯ Low	
Infertility - acceptors of screening												
1	randomised trials	serious[f]	not serious	not serious	serious[c]	publication bias strongly suspected[e]	2/7053 (0.0%)	9/21021 (0.0%)	**RR 0.66** (0.14 to 3.06)	**0 fewer per 1,000** (from 0 fewer to 1 more)	⨁◯◯◯ Very low	
Ectopic Pregnancy - Universal screening												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Screening benefit	placebo	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	not serious	not serious	serious[b]	serious[c]	publication bias strongly suspected[e]	27/4000 (0.7%)	75/11459 (0.7%)	**RR 1.03** (0.67 to 1.60)	**0 fewer per 1,000** (from 2 fewer to 4 more)	⨁◯◯◯ Very low	
Ectopic Pregnancy - Acceptors of screening												
1	randomised trials	serious[f]	not serious	not serious	not serious	publication bias strongly suspected[e]	28/7053 (0.4%)	70/21021 (0.3%)	**RR 1.19** (0.77 to 1.85)	**1 more per 1,000** (from 1 fewer to 3 more)	⨁⨁◯◯ Low	
Epididymitis												
2	randomised trials	not serious	not serious	serious[b]	not serious	none	122/46168 (0.3%)	146/48697 (0.3%)	**RR 0.91** (0.72 to 1.17)	**0 fewer per 1,000** (from 1 fewer to 1 more)	⨁⨁⨁◯ Moderate	

CI: confidence interval; **RR:** risk ratio

Explanations

a. different trends among studies
b. measurement of cases in Andersen solely relies on ICD codes or prescription of doxycycline
c. wide confidence interval
d. unclear RoB for selection, performance, attrition and detection bias
e. based only on single study
f. Clark has high risk of bias for randomization and allocation concealment
g. wide confidence interval (maybe beneficial to no effect)

Harms of CT Screening (Adopted from Pillay et al.,)

Included studies: Hocking 2018 (RCT; serious AEs), Campbell 2006, Gottlieb 2011, Kangas 2006, Gotz 2005, Fielder 2013, Low 2003, Waller 2013 (observational studies)

Outcome	Certainty assessment							Findings	Certainty
	№ of studies & Participants	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration		
Serious Adverse Events from Treatment	1 N=37,543 tested with 4,574 having CT	RCT	serious	Not serious	Not serious	very serious	Not serious	One RCT (Hocking) reported methods of passive surveillance of adverse events from screening and treatment and reported no events.	⊕⊖⊖⊖ VERY LOW
Anxiety-Generalized	2 N=2,139	Observational	serious	Not serious	Not serious	Not serious	Not serious	Two studies of CT screening (Campbell and Gottlieb) measured general anxiety related to screening (testing and receiving results) using validated scales (Hospital Anxiety and Depression Scale [HADS; range 0-21] and Brief Symptom Inventory [BSI]; range 0-5 using mean of items for anxiety]). Campbell et al. found that anxiety levels in general-risk participants were not positive for CT were lower during testing (n=397) than before (n=218) receiving the invitation (change in HADS score -0.66 [95% CI -1.23 to -0.09]). Anxiety levels reduced over time (p=0.005). High-risk female patients (n=1,742) had low levels of anxiety during their testing visit, although there was slightly more anxiety for those who were later found to be CT positive than negative (BSI scores 1.52 vs. 1.42, respectively, p=0.08) (Gottlieb). For those with negative CT results and followed up after 4-6 weeks (n=280), receiving results appeared to raise their anxiety symptoms slightly (mean BSI score increased by 0.074; p value for difference from baseline NR) but not beyond a level considered “a little bit” (BSI score of 2).	⊕⊕⊖⊖ LOW

Outcome	Certainty assessment							Findings	Certainty
	№ of studies & Participants	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration		
Anxiety – Sexual Aspects of Life	2 N=1,937	Observational	-	-	serious	-	-	One study of high-risk females measured anxiety about their sexual aspects of life using the anxiety subscale of the Multidimensional Sexual Self-Concept Questionnaire (MSQ; 5 items with mean scores 1-5 and 1= strongly disagree) (Gottlieb). During the testing process, those who were later found to be CT negative (n=1,593) or positive (n=149) had mean scores that indicated either low or no anxiety (CT negative 1.32 vs CT positive 1.47, p=0.04), although scores for those with a CT infection were slightly higher. Scores for the CT negative females who responded to follow-up 4-6 weeks later (n=280) indicated that anxiety increased a small amount but was still very low (0.09 unit increase, p<0.05) after receiving test results. Of 195 CT-negative respondents who were mostly (78%) seeking screening due to risk factors, few agreed (strongly or somewhat) that they did not feel sexually attractive (7% females and 10% males) right after receiving their results (Kangas).	⨁⨁⊖⊖ LOW (High-risk) ⨁⊖⊖⊖ VERY LOW (General population)
Anxiety about Infertility	2 N=450	Observational	serious	serious	serious	Not serious	Not serious	Two studies asked CT-negative people whether they had anxiety about becoming infertile upon receiving their results (Gotz, Kangas). In one study, only 5.4% of 275 respondents agreed to some extent that the results gave them this anxiety (Gotz). In a high-risk sample, between 20-40% of 175 CT-negative respondents felt nervous about their or their partner's chances of getting pregnant, thought it may be a problem for them or their partner to become pregnant, and/or considered their chances of becoming pregnant different from before (Kangas). Results were similar between sexes. The study reporting more symptoms reported a high (92%) level of knowledge about CT causing infertility, it is unlikely they knew the absolute risk of infertility from a CT infection.	⨁⊖⊖⊖ VERY LOW

Outcome	Certainty assessment							Findings	Certainty
	№ of studies & Participants	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration		
Anxiety – other single item questions	3 N=2,307	Observational	serious	Not serious	serious	Not serious	Not serious	From asking females, when undergoing their screening test, single questions related to anxiety about testing or CT, two studies indicate that some participants without a CT infection will have concerns about having CT (33% of 1,593)(Gottieb) or feel some anxiety about the testing (n=290; mean 2.0 ± 0.9; 2=somewhat disagree, 3=somewhat agree)(Fielder). Without knowledge of their test results, more infected than non-infected women reported having concerns about CT (46% vs. 33%, p=0.03; n=1,742) or that they thought about CT a lot (20% vs. 10%, p=0.02) (Gottlieb). Coming from a high-risk sample, these findings may better reflect anxiety related to one's high-risk status rather than from the testing process itself. Two studies reported on this outcome from follow-up 1-2 months after people received a negative test result (Gottlieb, Gotz). One study with high-risk patients found that concerns about CT for females (n=280) remained and may have increased (40% vs 33%, p=0.07) after the test process (Gottlieb). The other study of general-risk participants found that 12% (n=275) had some worry about their results although the results were not separated by sex (Gotz).	⊕⊖⊖⊖ VERY LOW
Shame/Stigma Symptoms	4 N=2,542	Observational	Not serious	Not serious	Not serious	Not serious	Not serious	(Self-esteem) Using the Rosenburg Self Esteem Scale to indicate possible stigmatization, Campbell et al. found no difference in self-esteem between those responding before (n=218) versus after receiving (n=397) an invitation for screening in a general-risk population. Using the same scale in a high-risk sample, Gottlieb et al. did not find low levels of self-esteem (24 on 0-30 point scale; <15 considered low) at the testing visit (n=1593), and these results did not change at 1-month follow-up after receiving negative results (n=280).	⊕⊕⊖⊖ LOW

Outcome	Certainty assessment							Findings	Certainty
	№ of studies & Participants	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration		
								(Symptoms) Two other studies relied on single questions about specific symptoms experienced during the CT screening offer or after receiving negative results. In one study (n=71), 13% and 6% of females and males, respectively, agreed that they felt stigmatized by the offer by their general practitioner of a CT test (Kangas). Of those whom were seeking testing in the same practice due to high-risk behaviours (n=206), 18% of males and 14% of females without a CT infection agreed that they felt stigmatized telling their friends about the test. The other study found that 30% of participants (n=275) did not agree that their social environment would approve of their testing for CT (Gotz). Both studies reported that, upon receiving results, few individuals had feelings of shame (0.8%)(Gotz) or being dirty (1.5% (Gotz); 0% males and 7% females of n=195 (Kangas)).	
Embarrassment	4 N=1,353	Observational	serious	Not serious	serious	Not serious	Not serious	Two studies (n=399) indicate that undergoing a screening test in an outreach setting using either self-collected swabs (1.7 ±0.8 on 4-point Likert, Fielder) or urine samples (7% Low) may not be embarrassing for most 18-21 year olds. The screening in Low et al. was accompanied by an interactive educational intervention about STIs and screening developed as a “non-stigmatizing” intervention. Findings in primary care, also using urine or self-collected swabs, generally agree with this: 17% and 12% of CT positive (n=805) and negative (n=67) patients, respectively, stated that they would feel embarrassed undergoing future screening (Walker). In another study of screening high-risk populations in primary care (n=82), upon receiving their test results few of those without a CT infection felt embarrassed about the results (3%)(Kangas).	⊕⊖⊖⊖ VERY LOW
Relationship Break-up	2 N=445	Observational	Not serious	Not serious	serious	Not serious	Not serious	In one study with high-risk participants, one female (n=122) and no male (n=73) reported a break-up with a partner as a result of their negative CT test result (Kangas). Another study asking a high-risk sample of females without CT about break-up with a main partner within the past 30 days,	⊕⊕⊖⊖ LOW (High-risk)

Outcome	Certainty assessment							Findings	Certainty
	№ of studies & Participants	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other consideration		
								both at baseline and at 4-6 week followup, found a similar number (11% of 250) of break-ups in both time periods (Gottlieb).	⊕⊖⊖⊖ VERY LOW (General population)
Relationship Distress	2 N=1,000	Observational	Not serious	serious	serious	Not serious	Not serious	Very few (≤5% of 195) high-risk individuals of both sexes in one study reported that their partner was upset or disappointed about their screening (Kangas). In the other study, several (25% of 805) general-risk females without CT felt concerned about their partner's reaction to having another test in the future (Walker).	⊕⊖⊖⊖ VERY LOW

Abbreviations: AE: adverse event; CT: *Chlamydia trachomatis*; N: sample size; NR: not reported; RCT: randomized controlled trial; ROB: risk of bias

Explanations:

Serious Adverse Events from Treatment: Serious concerns about **ROB** from lack of active harms surveillance. Very serious concerns about **imprecision** due to small sample for this very rare event.

Anxiety-Generalized: Some concern about **ROB** from inadequate length of follow-up for this outcome.

Anxiety –Sexual Aspects of Life: Some concerns about **indirectness** due to Kangas study being largely symptomatic even though only 20% seeking testing due to this, and for indirectness to general-risk population.

Anxiety about Infertility: Some concern about **ROB** due to selection bias in Gotz. Serious concerns about **unexplained inconsistency** between magnitudes of effects. Serious concerns about **indirectness** due to symptomatic population in Kangas and lack of informed responses.

Anxiety – other single item questions: Serious concerns about **ROB** from selection bias and poor attribution to screening. Serious **indirectness** for men and general-risk populations.

Shame/Stigma Symptoms: Some concern about **ROB** from Gotz but no impact on overall conclusions. Some concern about **indirectness** from use of self-esteem for stigma and about population (20% seeking care for symptoms) in Kangas.

Embarrassment: Some concern about **ROB** from selection bias. Some concern about **indirectness** from outreach setting for two studies and population in Kangas.

Relationship Break-up: Some concerns about **indirectness** to general-risk population in Kangas and othe high-risk population.

Relationship Distress: Serious concerns about **inconsistency** in magnitude of effects. Some concerns about **indirectness** from use of anticipated reactions in Walker.

Appendix 7. Forest Plots

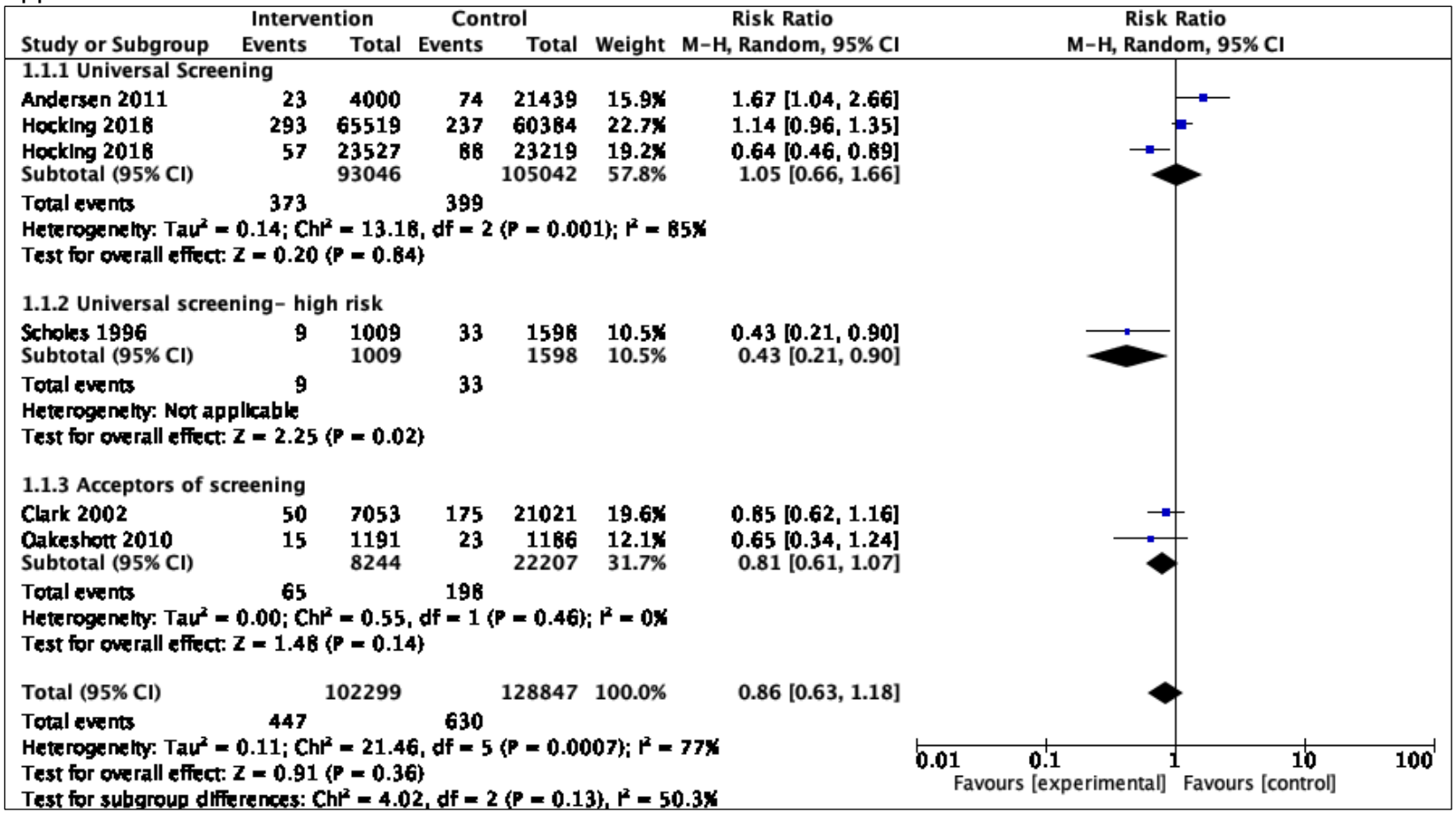


Figure 1. Risk for developing pelvic inflammatory disease

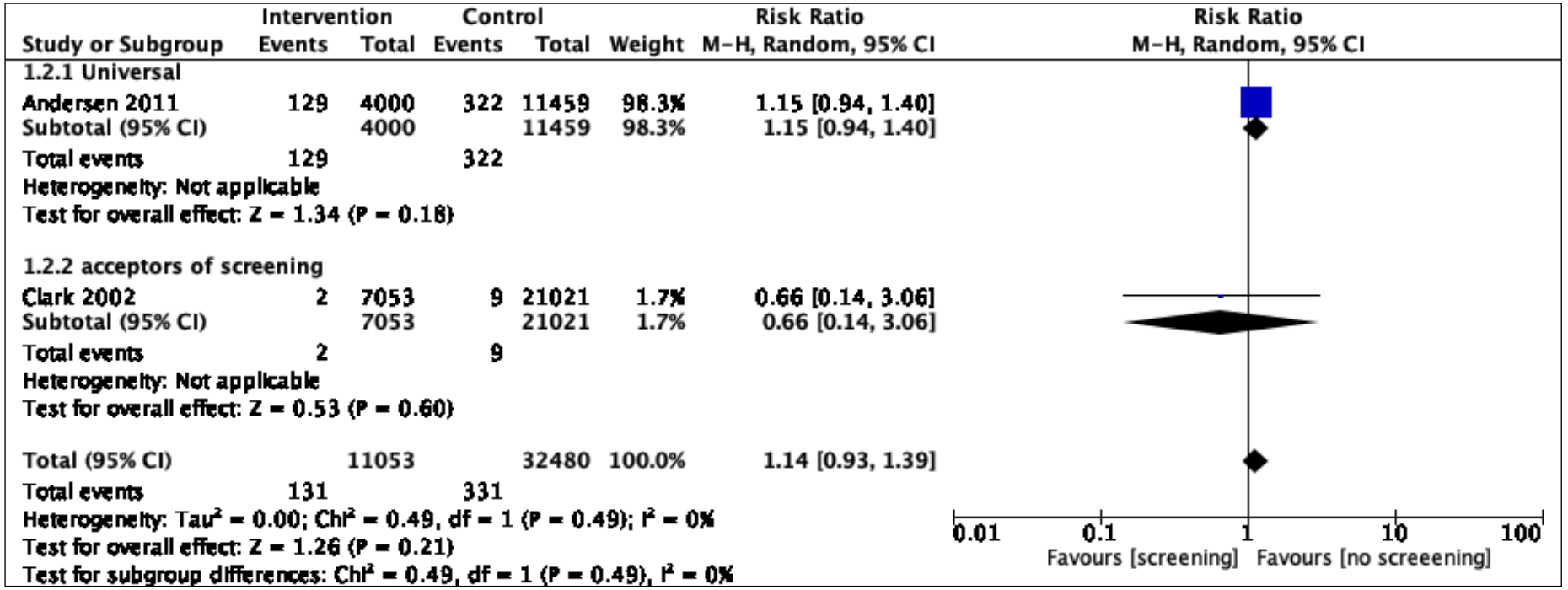


Figure 2. Risk for infertility

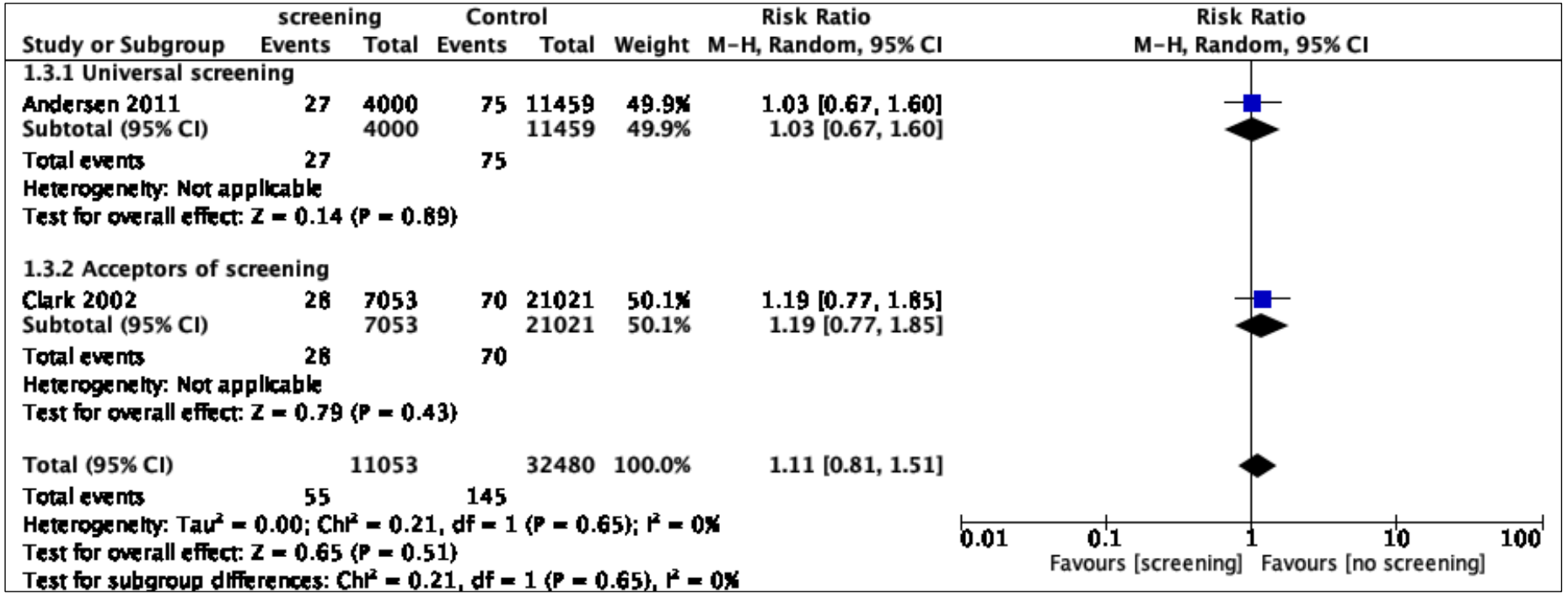


Figure 3. Risk for ectopic pregnancy

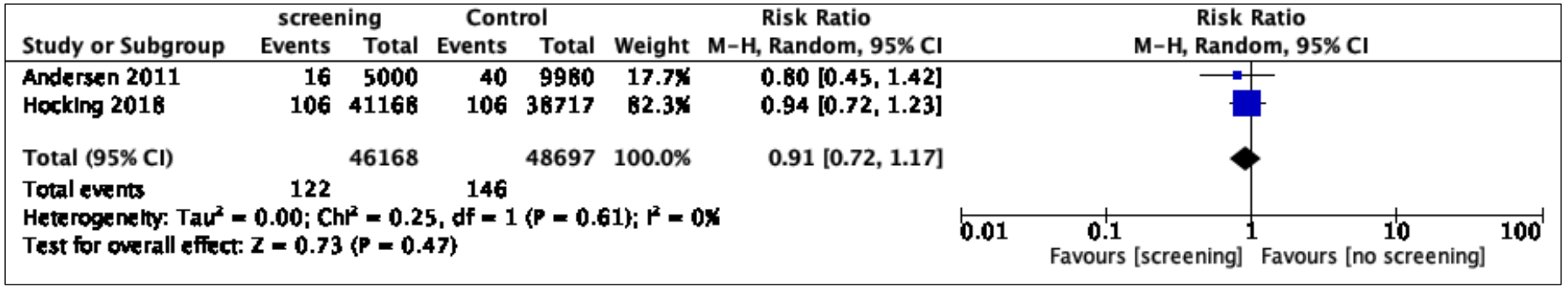


Figure 4. Risk for epididymitis

Appendix 8. Evidence-to-Decision Framework Responses

Evidence to Decision Framework

Should screening for gonorrhea and chlamydia be routinely done among asymptomatic, healthy adolescent and adult?

Population: Filipino adults

Intervention: Screening

Comparator: No screening

Outcomes: Incidence of gonorrhea or chlamydia infection, infection-related morbidity and mortality, adverse events, stigma reduction

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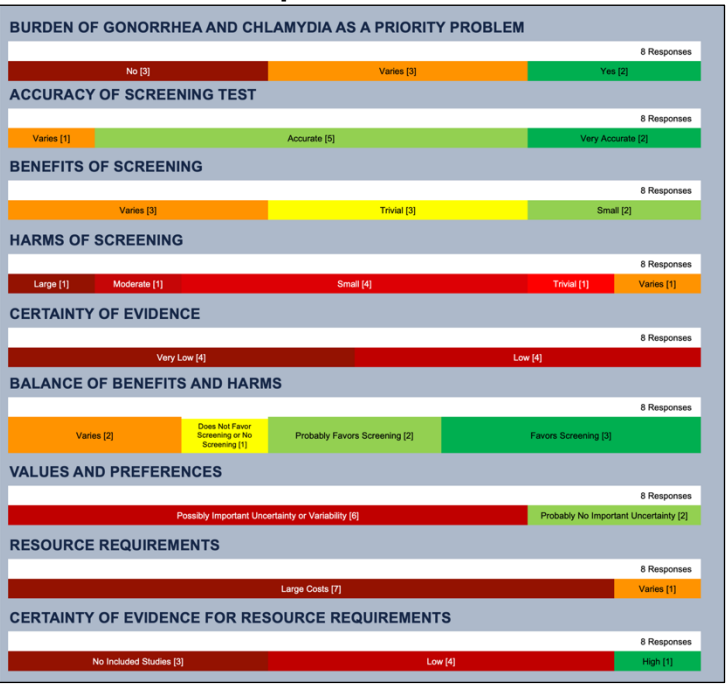


Evidence to Decision Framework

Should screening for gonorrhea and chlamydia be routinely done among asymptomatic, healthy adolescent and adult?

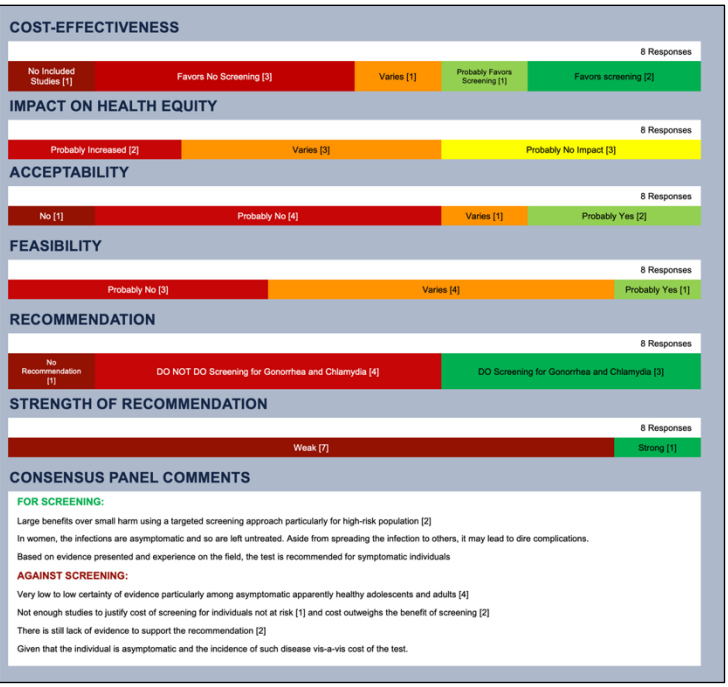
Population: Filipino adults

Intervention: Screening

Comparator: No screening

Outcomes: Incidence of gonorrhea or chlamydia infection, infection-related morbidity and mortality, adverse events, stigma reduction

PHEx PHILIPPINE PERIODIC HEALTH EXAMINATION



9.3 Screening for Asymptomatic Bacteriuria

Appendix 1. Search Strategy

Table 1. Search for local and international clinical practice guidelines for possible adaptation.

AS OF SEPTEMBER 17, 2022		
Clinical Practice Guideline	**Date Published**	**Directness with Research Question (Yes or No)**
US Preventive Services Task Force (USPSTF)	2019	Yes
Infectious Diseases Society of America (IDSA)	2019	No
Philippine Society for Microbiology and Infectious Diseases, Inc. (PSMID)	2015	No
Canadian Task Force on Preventive Health Care	2018	Yes
National Institute for Health Care and Excellence (NICE)	2018	No
European Association of Urology	2017	No
American Academy of Family Physicians	2020	Yes* **Used USPSTF recommendations and evidence as reference*

Table 2. Search strategy via PubMed until September 19, 2022 to search for new studies

AS OF SEPTEMBER 19, 2022: PUBMED		
SEARCH	**QUERY**	**RESULTS**
#1	"Urinary Tract Infection"[Mesh]	49,928
#2	"Urinalysis"[Mesh]	9,115
#3	culture	2,138,146
#4	#2 OR #3	2,146,189
#5	#1 AND #4	7,411
#6	"Mass Screening"[Mesh]	142,004
#7	#5 AND #6	157

Table 3. Search strategy via Cochrane Library until September 20, 2022 to search for new studies

SEPTEMBER 20, 2022: COCHRANE LIBRARY	
SEARCH TERMS	**RESULTS**
Asymptomatic bacteriuria, Screening	3 Cochrane Reviews 40 Trials

Appendix 2. Characteristics of Included Studies, adapted from USPSTF 2019 & Canadian Task Force on Preventive Health Care 2018 Clinical Practice Guidelines

Appendix 3. Quality Assessment of Included Studies, adapted from USPSTF 2019 & Canadian Task Force on Preventive Health Care 2018 Clinical Practice Guidelines

Appendix 4. Forest Plots

Appendix 5. GRADE Evidence Profile

Screening using urinalysis or urine culture compared to no screening for urinary tract infection among asymptomatic, healthy adults

Certainty assessment							Summary of findings	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)	Impact
							With no screening / With screening using urinalysis or urine culture	
Incidence of Urinary Tract Infection								
217 (2 RCTs)	serious[a,b]	not serious	very serious[c]	serious[d]	none	⨁◯◯◯ Very low	1 RCT (n=124) reported 7.9% and 16.4% incidence symptomatic UTI at 6 months follow-up (RR 0.48, 95% CI 0.18 to 1.33), p=0.15 among patients with ASB treated with antimicrobials versus patients not given treatment. 1 RCT (n=93) reported microbiologic reinfection, relapse and persistence rates of 15.6% and 75.9% (RR 0.21, 95% CI 0.11 to 0.38) among treatment and control groups, respectively at 0-3 months follow-up. Rates were 45% and 75.9% respectively (RR 0.60, 95% CI 0.43, 0.84) at 4-6 months follow-up.	
Adverse Events								
217 (2 RCTs)	serious[a,b]	not serious	very serious[c]	serious[e]	none	⨁◯◯◯ Very low	2/127 patients (1.6%) in the treatment group reported adverse reactions to antibiotic therapy (ofloxacin). One had vertigo and the other had upper gastrointestinal symptoms wherein both patients eventually withdrew from the study.	
Antimicrobial Resistance								

93 (1 RCT)	serious[a,b]	not serious	very serious[c]	serious[e]	none	⨁◯◯◯ Very low	At 3 months follow-up, urine cultures of patients who had relapse, reinfection or persistence and were given antimicrobial treatment had resistance to antibiotics (ofloxacin) in 16/29 (55.2%) of isolates, versus only 1/22 (4.5%) ofloxacin resistance among isolates from patients not previously treated with antibiotics.

CI: confidence interval

Explanations

a. Lacked reporting on method of randomization and allocation of participants and methods of outcome assessment
b. Lacked details on patients' baseline characteristics and if there was significant difference between intervention and control groups at baseline
c. No direct evidence was found comparing screening versus no screening of ASB. Instead, included RCTs assessed the outcomes between treatment with antimicrobials versus no treatment among patients who screened positive for ASB.
d. Downgraded for small sample size and a wide confidence interval
e. Downgraded for small sample size

Screening using urinalysis or urine culture compared to no screening for urinary tract infection among pregnant women

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Screening for ASB using urinalysis or urine culture**	**No screening**	**Relative (95% CI)**	**Absolute (95% CI)**		
Pyelonephritis												
3 n=5659	observational studies	very serious[a]	not serious	not serious	not serious	strong association	10/2008 (0.5%)	67/3651 (1.8%)	**RR 0.28** (0.15 to 0.54)	**13 fewer per 1,000** (from 16 fewer to 8 fewer)	⨁◯◯◯ Very low	CRITICAL
Premature rupture of membranes												

1 (n=372)	observational studies	serious[b]	not serious	not serious	serious[c]	none	6/186 (3.2%)	7/186 (3.8%)	**RR 0.86** (0.29 to 2.50)	**5 fewer per 1,000** (from 27 fewer to 56 more)	⊕◯◯◯ Very low	CRITICAL

Low birth weight

1 (n=372)	observational studies	serious[b]	not serious	not serious	serious[c]	none	1/186 (0.5%)	5/186 (2.7%)	**RR 0.20** (0.02 to 1.70)	**22 fewer per 1,000** (from 26 fewer to 19 more)	⊕◯◯◯ Very low	CRITICAL

Preterm Delivery

2 (n=722)	observational studies	serious[d]	not serious	not serious	serious[c]	none	33/347 (9.5%)	23/375 (6.1%)	**RR 1.57** (0.78 to 3.13)	**35 more per 1,000** (from 13 fewer to 131 more)	⊕◯◯◯ Very low	CRITICAL

CI: confidence interval; **RR:** risk ratio

Explanations

a. Poor quality studies based on the Newcastle-Ottawa Assessment Scale, as adapted from the Canadian Task Force on Preventive Health Care 2018 Guidelines. There were noted issues on ascertainment of exposure, comparability of cohorts and adequacy of follow-up.

b. High risk of bias based on Newcastle-Ottawa Assessment Scale, as adapted from the Canadian Task Force on Preventive Health Care 2018 Guidelines. Issues were comparability of cohorts and adequacy of follow-up.

c. Downgraded for small sample size and wide confidence interval.

d. High risk of bias based on Newcastle-Ottawa Assessment Scale, as adapted from the Canadian Task Force on Preventive Health Care 2018 Guidelines. Issues were comparability of cohorts and ascertainment of exposure.

Appendix 6. Evidence-to-Decision Framework Responses

Evidence to Decision Framework

Should urinalysis or urine culture be done annually for screening for urinary tract infection among asymptomatic, apparently healthy adults?

Population: Filipino adults

Intervention: Screening

Comparator: No screening

Outcomes: Rational use of antibiotics, antimicrobial resistance, incidence of urinary tract infection in the pregnant, fetal outcomes in the pregnant

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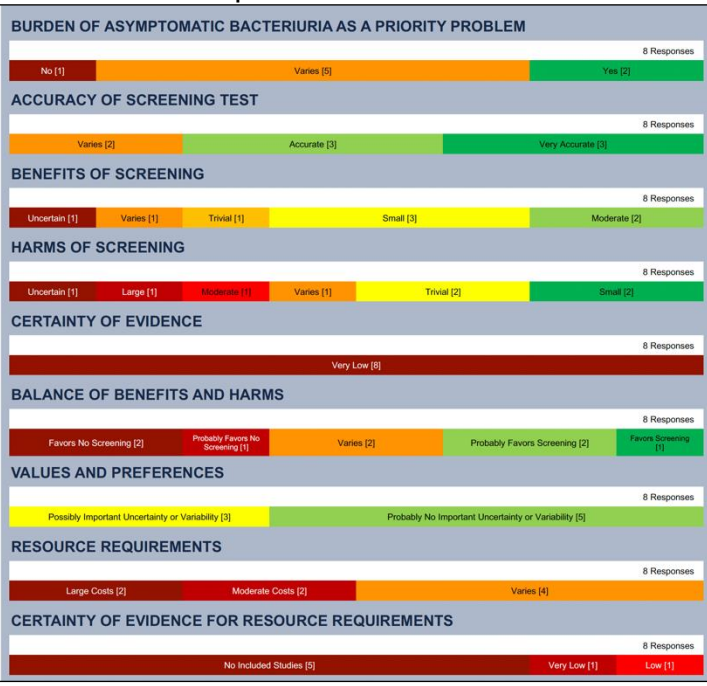

Evidence to Decision Framework

Should urinalysis or urine culture be done annually for screening for urinary tract infection among asymptomatic, apparently healthy adults?

Population: Filipino adults

Intervention: Screening

Comparator: No screening

Outcomes: Rational use of antibiotics, antimicrobial resistance, incidence of urinary tract infection in the pregnant, fetal outcomes in the pregnant

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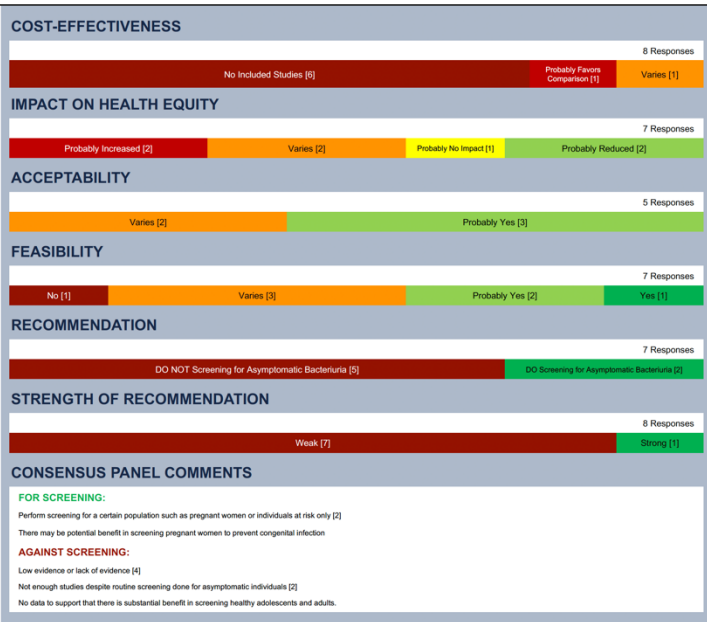
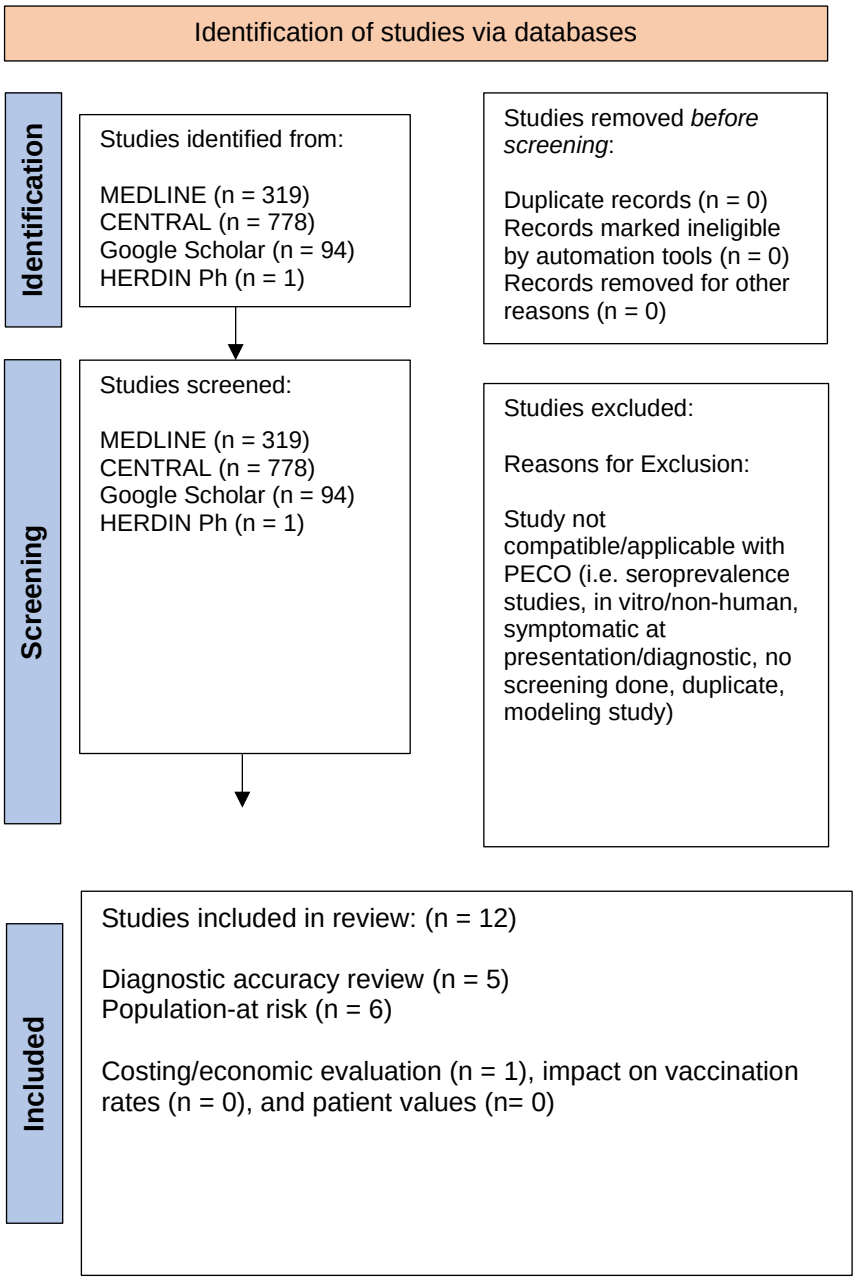


9.4 Screening for Hepatitis A

Appendix 1. Search Strategy

DATABASE	SEARCH STRATEGY / SEARCH TERMS	DATE AND TIME OF SEARCH	RESULTS	
			Yield	Eligible
Medline	("hepatitis a"[MeSH Major Topic] OR "hepatitis a antibodies"[MeSH Major Topic]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields]) Search Filter: 10 years	January 31, 2023 2:00 PM	319 (9 assessed)	2
CENTRAL	("hepatitis a"[MeSH Major Topic] OR "hepatitis a antibodies"[MeSH Major Topic]) AND ("diagnosis"[Subheading] OR "diagnosis"[All Fields] OR "screening"[All Fields] OR "mass screening"[MeSH Terms] OR ("mass"[All Fields] AND "screening"[All Fields]) OR "mass screening"[All Fields])	January 31, 2023 11:00AM	778 (16 assessed)	1
Google Scholar	“Hepatitis A Screening” “Hepatitis A Routine Screening” “Hepatitis A Antibody Test Routine Screening”	January 31, 2023 4:00 PM	94 (5 assessed)	0
HERDIN Ph	“Hepatitis A Screening” “Hepatitis A Routine Screening” “Hepatitis A Antibody Test Routine Screening”	January 31, 2023 4:00 PM	1	0

Appendix 2. PRISMA Diagram


Identification of studies via databases
Identification
Studies identified from:
MEDLINE (n = 319)
CENTRAL (n = 778)
Google Scholar (n = 94)
HERDIN Ph (n = 1)
Studies removed *before screening*:
Duplicate records (n = 0)
Records marked ineligible by automation tools (n = 0)
Records removed for other reasons (n = 0)
Screening
Studies screened:
MEDLINE (n = 319)
CENTRAL (n = 778)
Google Scholar (n = 94)
HERDIN Ph (n = 1)
Studies excluded:
Reasons for Exclusion:
Study not compatible/applicable with PECO (i.e. seroprevalence studies, in vitro/non-human, symptomatic at presentation/diagnostic, no screening done, duplicate, modeling study)
Included
Studies included in review: (n = 12)
Diagnostic accuracy review (n = 5)
Population-at risk (n = 6)
Costing/economic evaluation (n = 1), impact on vaccination rates (n = 0), and patient values (n= 0)

Appendix 3. Characteristics of Included Studies

Title/Author	Study design	Country	Number of patients	Population	Screening Test	Comparison	Outcomes
Diagnostic Accuracy							
Use of conventional and IgM-specific radioimmunoassays for anti-hepatitis A antibody in an outbreak of hepatitis A Storch et al 1982 [13]	Prospective cohort study (Diagnostic accuracy)	USA	150	Students during a university-wide outbreak	IgM-specific Hepatitis A antibody	Persons with Hepatitis A Vs. Persons with no Hepatitis A	Sensitivity, Specificity, Positive Predictive Value
Improving the accuracy of clinical interpretation of serological testing for the diagnosis of acute hepatitis A infection Rycroft et al, 2022 [14]	Retrospective cohort study (Quality Assurance study)	UK	84 (positive results)	Clinically diagnosed patients in a UK hospital	Anti-HAV IgM antibody	Positive and negative IgM results according to titer levels Low level positive: 1.20-4.00	Positive predictive value

Accuracy of rapid test for diagnosis of hepatitis A with different infection rate settings and with predictive modeling Ribiero et al, 2019 [15]	Retrospective cohort study (Diagnostic accuracy)	Brazil	384	Patients with symptoms of acute hepatitis; blood donors	Anti-HAV IgG and IgM Rapid test	Reference EIA assay	Sensitivity, Specificity, Positive Predictive Value
New, ultrasensitive enzyme immunoassay for detecting vaccine- and disease-induced hepatitis A virus-specific immunoglobulin G in saliva Ochnio et al 1997 [16]	Retrospective cohort study (Diagnostic accuracy)	Canada	1,250	Immune and susceptible individuals, unvaccinated travelers	Anti-HAV IgG test using saliva samples	Reference EIA assay using serum and plasma	Sensitivity, Specificity
Screening / Testing Among Individuals at Risk							
Routine testing for IgG antibodies against hepatitis A virus in Israel Samuels 2005 [17]	Cross-sectional survey	Israel	1,017	Patients undergoing general health screening or ongoing follow-up for chronic (non-Hepatitis A) illness	Anti-HAV IgG antibodies	N/A	Recall of past hepatitis, receipt of post-exposure prophylaxis (ISG), or receipt of active immunization Number of seronegative patients sent for active immunization

Prevalence of hepatitis A antibodies in food handlers in Italy Angelillio et al 1996 [18]	Cross-sectional survey	Italy	294	Food handlers	Anti-HAV IgG antibodies	N/A	Seroprevalence
. Food-borne hepatitis A: recommendations for control Carl 1983 [19]	Cross-sectional survey	USA	1000	Food handlers in 20 documented outbreaks	N/A	N/A	Secondary attack rate
The risk of hepatitis A infection among healthcare workers: a review of reported outbreaks and sero-epidemiologic studies Chodick et al 2006	Systematic review	Multiple countries	11,244 (23 reports)	Healthcare workers	Anti-HAV IgG antibodies	Controls	Prevalence of HAV, Secondary attack rates
Screening travelers for hepatitis A antibodies		USA	527				Prevalence of HAV, cost

Lee & Blodget 2000	Cost-comparison study			Travelers who denied having previous Hepatitis A vaccination	Anti-HAV IgG antibodies	Prevaccination screening versus none	
Increased risk for hepatitis A among female day nursery workers in Belgium Jacques et al 1994	Prospective cohort study	Belgium	973	Daycare/nursery workers	Anti-HAV IgG antibodies	Blood donors	Prevalence

ISG – Immunoseroglobulin; EIA – enzyme immunoassays

Title/Author	Study design	Country	Number of participants/subjects	Population	Screening Test	Comparator	Outcomes
An economic assessment of pre-vaccination screening for hepatitis A and B Jacobs et al 2003	Cost Analysis (Comparison) Study - Modeling	USA	1,000 adults (hypothetical cohort)	Hypothetical cohorts: first-year college students, military recruits, travelers to endemic countries, patients with STDs	(1) Screen and defer vaccination until results are known (2) Screen and vaccinate	(3) Vaccinate without screening	Cost-effectiveness

Appendix 4. GRADE Evidence Profile

Should screening for Hepatitis A be routinely done among asymptomatic, apparently healthy adults?

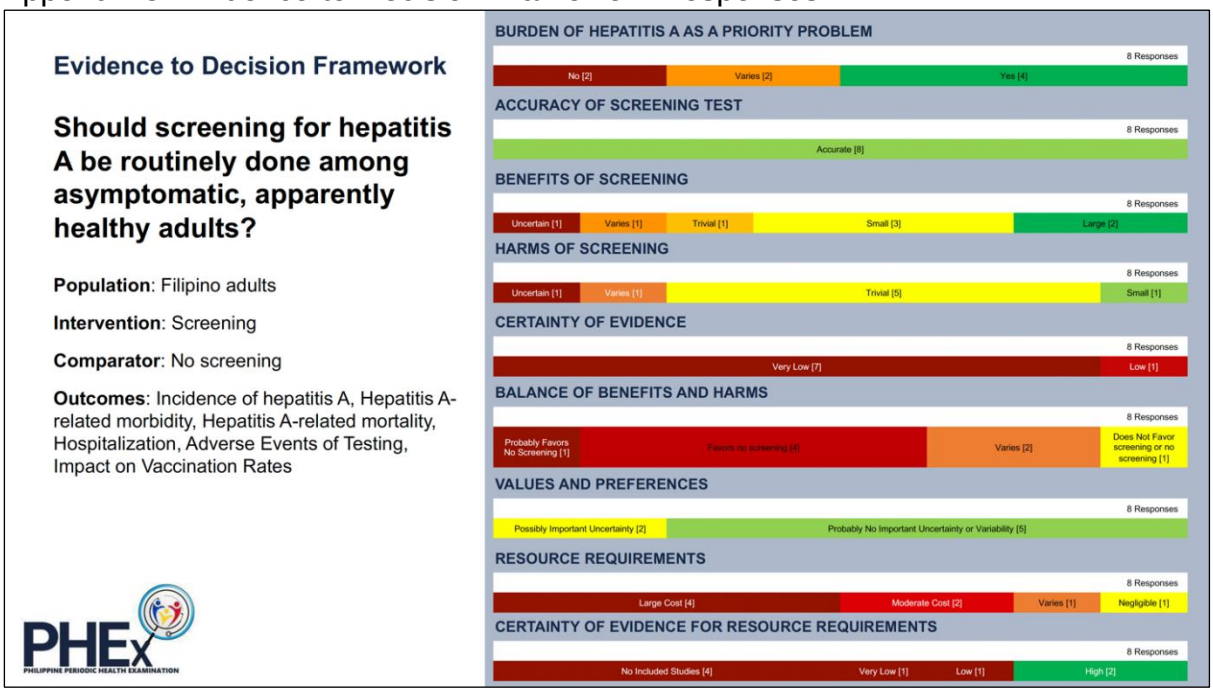
Certainty assessment							Summary of findings	
Participants (studies)	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)	
							With Hepatitis A	Without Hepatitis A
Diagnostic Accuracy of Anti-HAV IgM antibody tests using conventional assays								
234 (2 observational studies)	serious[a,b]	not serious	serious	not serious	none	⊕⊕◯◯ Low	A 1982 study demonstrated 100% sensitivity (7/7), 99% specificity (149/150), and a positive predictive value of 88% (7/8) during an epidemiologic outbreak investigation in a university. Another study reported a 100% positive predictive value for titer levels 4.0 and above.	
Diagnostic Accuracy of Rapid Anti-HAV antibody tests versus conventional assays								
384 (1 observational study)	serious[a,b]	not serious	serious	not serious	none	⊕⊕◯◯ Low	Anti-HAV IgM rapid tests had good sensitivity (87%, 95%CI 0.78-0.91) and specificity (80%, 0.72-0.86) compared to EIA among those suspected of Hepatitis A. Among serum samples involved in outbreak investigations, Anti-HAV IgM has good sensitivity at 81% (95%CI 68.6-90.12) and excellent specificity at 100% (92-100), while Anti-HAV IgM has good sensitivity at	

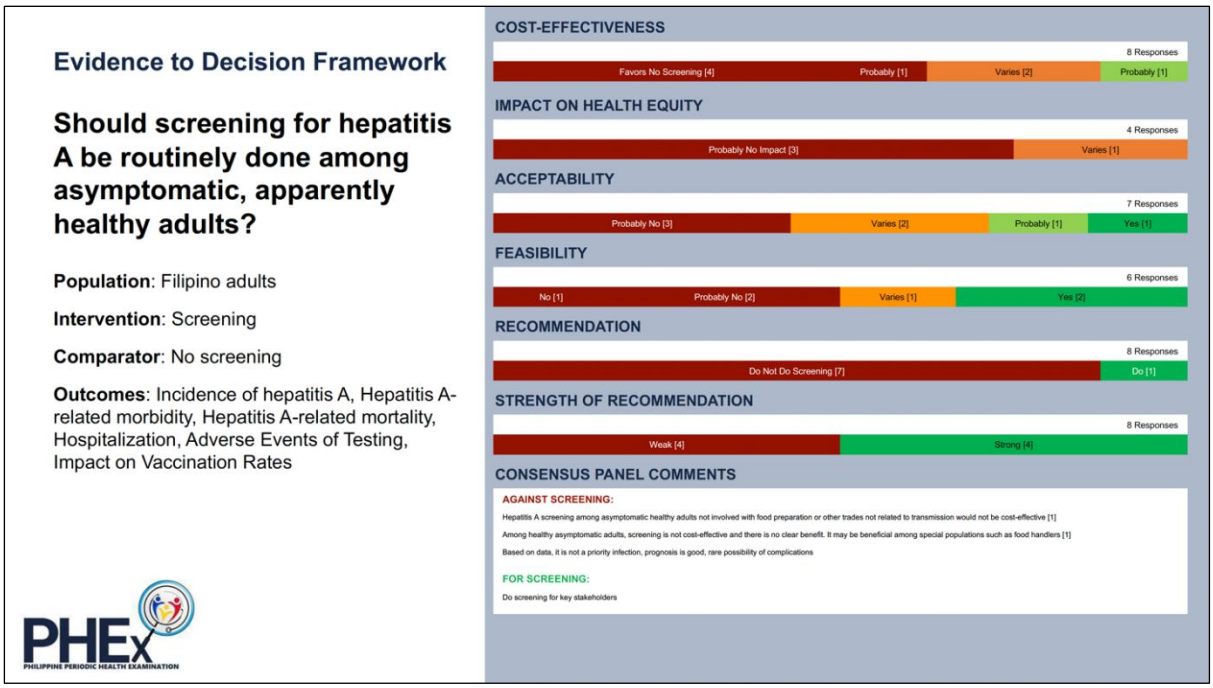
							79% (95%CI 66.98-87.89) but poor specificity at 22% (95%CI 9.82-38.21). Anti-HAV IgG, rapid tests among blood donors, have poor sensitivity at 49% (95%CI 36.6-61.93) but excellent specificity and positive predictive value at 100%.

Diagnostic Accuracy of anti-IgG antibody tests using saliva versus serum

1,250 (1 observational study)	serious[a,b]	not serious	serious	not serious	none	⊕⊕◯◯ Low	Samples collected from oral fluid or saliva showed excellent diagnostic accuracy specific for IgG, with sensitivity of 99% (95%CI 98.4 to 99.9) and specificity of 98% (95%CI 97.7 to 99.4). However, this method requires an extremely sensitive assay since antibody concentrations in oral fluid were estimated to be 800-1000-fold lower than those in serum and plasma.

Appendix 5. Evidence-to-Decision Framework Responses





9.5 Screening for Hepatitis C

Appendix 1. Search Strategy

There were three available clinical practice guidelines (Table 5) on screening and treatment for Hepatitis C based on electronic search of literature (MEDLINE through Pubmed) and one from other sources (Google search for Philippine guidelines) retrieved from an initial search done last October 31, 2022. (4) Canadian Task Force on Preventive Health Care - Recommendations on hepatitis C screening for adults. The relevant studies from the evidence reviews of these guidelines which address our PICO questions were extracted and reviewed (adolopment).

Table 1. Clinical Practice Guidelines on Hepatitis C

Clinical Practice Guidelines	Date Published	Directness with Research Question (Yes or No)
US Preventive Services Task Force (USPSTF)	2020	Yes
Hepatology Society of the Philippines - Consensus Statements on the Diagnosis and Treatment of Hepatitis C	2018	Yes
American Association for Study of Liver Diseases – Infectious Disease Society of America - Hepatitis C Guidance: AASLD-IDSA Recommendations for Testing, Managing and Treating Adults infected with Hepatitis C virus	2015	Yes
Recommendations on hepatitis C screening for adults Canadian Task Force on Preventive Health Care	2017	Yes

Furthermore, Pubmed was also searched using the following search terms: “hepatitis C”, “screening”, “diagnostic accuracy” and “systematic review” last February 16, 2023. Additionally, the following MESH search terms in the last MEDLINE search done last March 11, 2023:“hepatitis C”, “men who have sex with men”, “commercial sex workers”, “IV drug users”, “blood donors”, “prevalence” and “outcomes.”

Appendix 2. Characteristics of Included Studies

Table 2. Association of SVR vs No SVR after HCV anti-viral treatment on Mortality

Primary study author and Year	Population (Study setting)	Intervention	Outcome: Mortality	Hazard Ratio (95% CI)
Yoshida 2002 [51]	2,889 (Japan)	Interferon	SVR: 7/817 Non-SVR: 49/1,613	HR 0.32 (0.12-0.86)
Imazeki 2003 [52]	459 (Japan)	Interferon	SVR: 4/116 Non-SVR: 29/239	HR 0.35 (0.09-1.36)
Kasahara 2004 [53]	295 (Japan)	Interferon	SVR: 7/738 Non-SVR: 94/1,930	HR 0.24 (0.08-0.68)
Yu 2006 [54]	1,619 (Taiwan)	Interferon	SVR: 16/715 Non-SVR: 6/342	HR 0.28 (0.08-1.02)
Arase 2007 [55]	500 (Japan)	Interferon	SVR: 9/140 Non-SVR: 44/369	HR 0.39 (0.16-0.93)
Backus 2011 [56]	16,864 (US)	Interferon	SVR: 7,434 Non-SVR: 9,430	HR 0.66 (0.57-0.76)
Innes 2011 [57]	1,215 (Scotland)	Interferon	SVR: 13/560 Non-SVR: 75/655	HR 0.22 (0.09-0.58)
Maruoka 2012 [58]	721 (Japan)	Interferon	SVR: 10/221 Non-SVR: 74/356	HR 0.20 (0.08-0.54)
Cozen 2013 [59]	358 (US)	Interferon	SVR: 6/69 Non-SVR: 14/71	HR 0.50 (0.12-2.10)

Singal 2013 [60]	242 (US)	Interferon	SVR: 2/83 Non-SVR: 40/159	HR 0.11 (0.03-0.47)
Dierperink 2014 [61]	536 (US)	Interferon	SVR: 19/222 Non-SVR: 81/314	HR 0.47 (0.26-0.85)
Butt 2017 [62]	6,973 (US)	DAA	SVR: 6,371 Non-SVR: ?/599	HR 0.57 (0.33-0.99)
Carrat 2019 [63]	9,895 (France)	DAA	SVR: 129/3,286 Non-SVR: 89/146	HR 1.36 (0.15-12.35)

Table 3. Association of SVR vs No SVR after HCV anti-viral treatment on Hepatocellular Carcinoma

Primary study author and Year	Population (Study setting)	Intervention	Outcome: Hepatocellular Carcinoma	Hazard Ratio (95% CI)
Imai 1999 [64]	419 (Japan)	Interferon	SVR: 2/151 Non-SVR: 34/268	0.06 (0.01-0.48)
Kasahara 1998 [65]	1,022 (Japan)	Interferon	SVR: 5/313 Non-SVR: 41/405	0.19 (0.06-0.58)
Ikeda 1990 [66]	1,643 (Japan)	Interferon	SVR: 6/606 Non-SVR: 21/585	0.33 (0.12-0.96)
Yoshida 1999 [67]	2,890 (Japan)	Interferon	SVR: 10/789 Non-SVR: 76/1,568	0.32 (0.14-0.70)
Tanaka 2000 [68]	738 (Japan)	Interferon	SVR: 2/175 Non-SVR: 16/419	0.29 (0.07-1.28)
Okanoue 2002 [69]	1,370 (Japan)	Interferon	SVR: 41/426 Non-SVR: 110/358	0.13 (0.06-0.27)
Izumi 2005 [70]	495 (Japan)	Interferon	SVR: 3/155 Non-SVR: 28/340	0.36 (0.04-0.83)
Yu 2006 [54]	1,619 (Taiwan)	Interferon	SVR: 12/715 Non-SVR: 39/342	0.24 (0.11-0.52)
Arase 2007 [55]	500 (Japan)	Interferon	SVR: 2/140 Non-SVR: 26/360	0.19 (0.08-0.96)
Kurokawa 2009 [71]	403 (Japan)	Interferon	SVR: 5/139 Non-SVR: 16/264	0.28 (0.08-0.96)
Asahina 2010 [72]	2,166 (Japan)	Interferon	SVR: 22/686 Non-SVR: 146/1356	0.38 (0.18-0.83)
Tateyama 2011 [73]	707 (Japan)	Interferon	SVR: 5/139 Non-SVR: 84/234	0.14 (0.04-0.52)
Maruoka 2012 [58]	721 (Japan)	Interferon	SVR: 2/221 Non-SVR: 34/356	0.12 (0.03-0.41)
Osaki 2012 [74]	328 (Japan)	Interferon	SVR: 1/185 Non-SVR: 22/197	0.12 (0.01-0.94)
Dohmen 2013 [75]	474 (Japan)	Interferon	SVR: 285 Non-SVR: 189	0.39 (0.32-0.48)
Dieperink 2014 [61]	536 (US)	Interferon	SVR: 9/222 Non-SVR: 29/314	0.41 (0.18-0.96)
El-Serag 2014 [76]	22,411 (US)	Not reported	SVR: 7577 Non-SVR: 8767	0.30 (0.23-0.38
Lee 2017 [77]	1,176 (South Korea)	Interferon	SVR: 3/306 Non-SVR: 9/183	0.09 (0.02-0.40)
Iannou 2018 [78]	62,354 (US)	Mixed	SVR: 642/28,655 Non-SVR: 2,629/23,211	0.32 (0.28 – 0.37)
Carrat 2019 [63]	9,895 (Japan)	DAA	SVR: 258/3286 Non-SVR 32/146	0.22 (0.03-1.76)

Appendix 3. GRADE Evidence Profile

Table 4. GRADE Evidence Profile of Diagnostic Accuracy of anti-HCV in healthy adults

Sensitivity	0.99 (95% CI: 0.98 to 1.00)
Specificity	1.00 (95% CI: 1.00 to 1.00)

Prevalences	0.7%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of0.7%	
True positives (patients with Hepatitis C)	5 studies 15943 patients	cross-sectional (cohort type accuracy study)	serious[a]	serious[b]	not serious	not serious	none	7 (7 to 7)	⊕⊕◯◯ Low
False negatives (patients incorrectly classified as not having Hepatitis C)								0 (0 to 0)	
True negatives (patients without Hepatitis C)	5 studies 15943 patients	cross-sectional (cohort type accuracy study)	serious[a]	serious[b]	not serious	not serious	none	993 (993 to 993)	⊕⊕◯◯ Low
False positives (patients incorrectly classified as having Hepatitis C)								0 (0 to 0)	

Explanations

a. non-randomized study designs
b. different/variable units of analysis

Table 5. GRADE Evidence Profile of Diagnostic Accuracy of anti-HCV in blood donors

Sensitivity	0.77 (95% CI: 0.70 to 0.83)
Specificity	0.99 (95% CI: 0.99 to 1.00)

Prevalences	11.5%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of11.5%	
True positives (patients with hepatitis C)	1 studies 2400 patients	cross-sectional (cohort type accuracy study)	serious	serious	not serious	not serious	none	89 (81 to 95)	⊕⊕◯◯ Low
False negatives (patients incorrectly classified as not having hepatitis C)								26 (20 to 34)	
True negatives (patients without hepatitis C)	1 studies 2400 patients	cross-sectional (cohort type accuracy study)	serious	serious	not serious	not serious	none	876 (876 to 885)	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of11.5%	
False positives (patients incorrectly classified as having hepatitis C)								9 (0 to 9)	⊕⊕◯◯ Low

Explanations

a. non-randomized study designs
b. baseline patient characteristics not fully described

Table 6. GRADE Evidence Profile of SVR versus no SVR in all-cause mortality and hepatocellular carcinoma

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SVR	no SVR	Relative (95% CI)	Absolute (95% CI)		
All cause mortality												
13	observational studies	serious[a]	serious[b]	not serious	not serious	none	20772/36986 (56.2%)	16214/36986 (43.8%)	**HR 0.40** (0.28 to 0.56)	**232 fewer per 1,000** (from 289 fewer to 162 fewer)	⨁◯◯◯ Very low	CRITICAL
Hepatocellular carcinoma												
20	observational studies	serious[a]	serious[b,c]	not serious	not serious	none	45171/85053 (53.1%)	39882/85053 (46.9%)	**HR 0.29** (0.23 to 0.38)	**301 fewer per 1,000** (from 333 fewer to 255 fewer)	⨁◯◯◯ Very low	CRITICAL

Explanations

a. non-randomized controlled study design
b. variable treatment regimens (interferon and DAA)
c. variable degree of baseline cirrhosis, some not reported or unclear

Table 7. GRADE Evidence Profile of Adverse Events of DAA versus Placebo

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SVR	no SVR	Relative (95% CI)	Absolute (95% CI)		
4	randomised trials	not serious	serious[a]	not serious	not serious	none	1277/1798 (71.0%)	327/503 (65.0%)	**RR 1.12** (1.02 to 1.24)	**78 more per 1,000** (from 13 more to 156 more)	⨁⨁⨁◯ Moderate	CRITICAL

CI: confidence interval; **HR:** hazard Ratio; **RR:** risk ratio

Explanations

a. wide discrepancies in sample sizes

Appendix 4. Evidence-to-Decision Framework Responses

Evidence to Decision Framework

Should screening for hepatitis C be routinely done among asymptomatic, apparently healthy adults?

Population: Filipino adults

Intervention: Screening

Comparator: No screening

Outcomes: Incidence of hepatitis C, Hepatitis C-related morbidity, Hepatitis C-related mortality, Incidence of Liver Cancer, Adverse Events of Testing, Impact on Vaccination Rates

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BURDEN OF HEPATITIS C AS A PRIORITY PROBLEM

8 Responses

ACCURACY OF SCREENING TEST

8 Responses

BENEFITS OF SCREENING

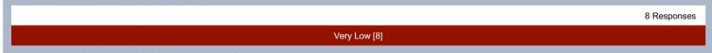
8 Responses

HARMS OF SCREENING

8 Responses

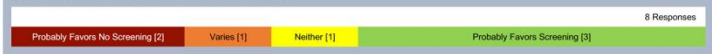
CERTAINTY OF EVIDENCE

8 Responses



BALANCE OF BENEFITS AND HARMS

8 Responses



VALUES AND PREFERENCES

8 Responses

RESOURCE REQUIREMENTS

8 Responses

CERTAINTY OF EVIDENCE FOR RESOURCE REQUIREMENTS

8 Responses

Evidence to Decision Framework

Should screening for hepatitis C be routinely done among asymptomatic, apparently healthy adults?

Population: Filipino adults

Intervention: Screening

Comparator: No screening

Outcomes: Incidence of hepatitis C, Hepatitis C-related morbidity, Hepatitis C-related mortality, Incidence of Liver Cancer, Adverse Events of Testing, Impact on Vaccination Rates

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COST-EFFECTIVENESS

8 Responses

IMPACT ON HEALTH EQUITY

8 Responses

ACCEPTABILITY

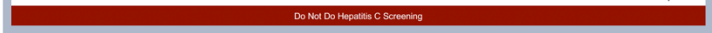
8 Responses

FEASIBILITY

6 Responses

RECOMMENDATION

8 Responses



STRENGTH OF RECOMMENDATION

8 Responses

CONSENSUS PANEL COMMENTS

AGAINST SCREENING:	FOR SCREENING:
Probably not cost-effective to screen	It is more cost-effective to screen Hepatitis C in those who belong to high-risk groups.
Not for the general population who are asymptomatic and at low risk	Screen for high-risk groups

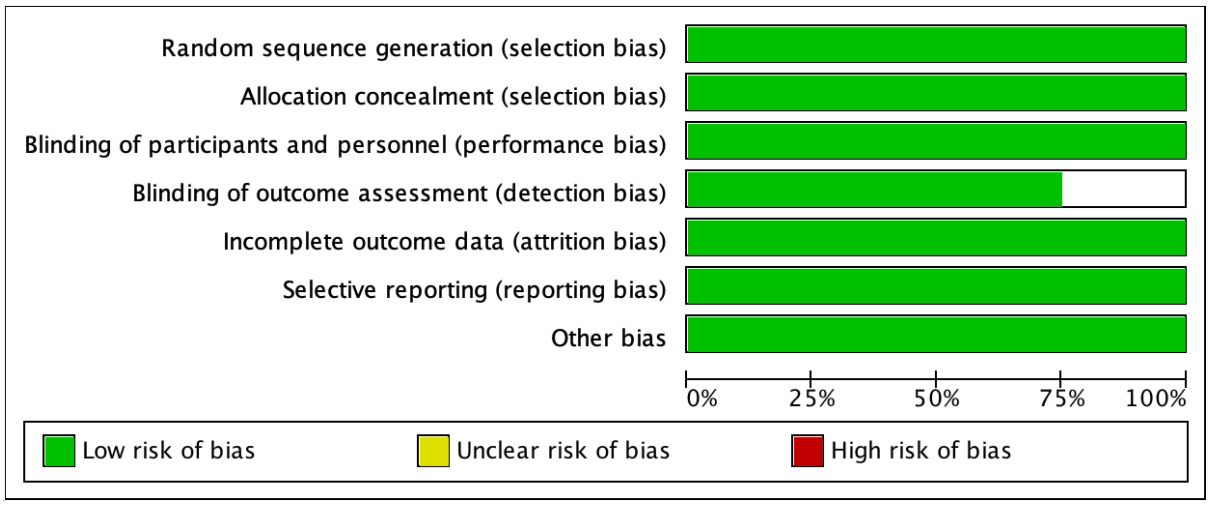
9.6 Screening for HIV

Appendix 1. Search Strategy

Search number	Query	Filters	Results
30	#14AND#23AND#27	Randomized Controlled trial	30
29	#14AND#23AND#27	2019-2023	560
28	#14AND#23AND#27	English	4,891
27	#24or#25or#26		331,150
26	blood donor		120, 199
25	screening[MeSH Terms]		170, 383
24	Mass screening		186, 640
23	#15or#16or#17or#17or18or#19or#20or#21or#22		199, 699
22	HIV seronegativity[MeSH Terms]		3, 897
21	HIV seropositivity[MeSH Terms]		23, 934
20	HIV serodiagnosis[MeSH Terms]		6, 747
19	Acquired immunodeficiency syndrome[MeSH Terms]		78, 302
18	HIV antigens[MeSH Terms]		15, 908
17	HIV testing[MeSH Terms]		7, 547
16	HIV antibodies[MeSH Terms]		11, 886
15	HIV[MeSH Terms]		106, 895
14	#1or#2or#3or#4or#5or#6or#7or#8or#9or#10or#11or#12or#13		8, 237, 339
13	diagnosis[MeSH Subheading]		4,100, 548
12	diagnosis, differential[MeSH Terms]		467, 259
11	diagnostic services[MeSH Terms]		188, 126
10	diagnostic imaging[MeSH Terms]		2, 894, 873
9	diagnostic errors[MeSH Terms]		122, 288
8	diagnostic equipment[MeSH Terms]		38, 853
7	diagnostic[Title/Abstract]		867, 740
6	diagnosis[Title/Abstract]		1, 860, 543
5	diagnoses[Title/Abstract]		160, 831
4	diagnosed[Title/Abstract]		708, 423
3	diagnose[Title/Abstract]		93, 804
2	sensitivity and specificity[MeSH Terms]		644, 736
1	sensitiv*[Title/Abstract]		1, 628, 301

Search number	Query	Filters	Results
11	(((HIV) AND (AIDS)) AND (((Rapid Diagnostic Test) AND (Rapid Test)) AND (Western Blot))) AND (Meta-analysis[Title/Abstract])		1
10	Meta-analysis[Title/Abstract]		228, 298
9	((HIV) AND (AIDS)) AND (((Rapid Diagnostic Test) AND (Rapid Test)) AND (Western Blot))		85
8	((Rapid Diagnostic Test) AND (Rapid Test)) AND (Western Blot)		315
7	Western blot		389, 730
6	Rapid Diagnostic Test) or (Rapid Test)		18, 082
5	Rapid Test		111, 314
4	Rapid Diagnostic Test		26, 569
3	HIV or AIDS		179, 787
2	AIDS		300, 512
1	"hiv"[MeSH Terms] OR "hiv"[All Fields]		4008, 745

Appendix 2. Risk of Bias Assessment



Appendix 3. Locally Available Diagnostic Test Kits

Comparison between Rapid Diagnostic Tests and Western Blot in the Rapid HIV Diagnostic Algorithm for the Philippines

Parameter	Rapid Diagnostic Tests			Western Blot
	SD Bioline HIV Ag-Ab cassette	Alere Determine HIV 1/2	Geenius HIV ½ Confirmatory Assay Kit	
Sensitivity	100%	99.9%	100%	100%
Specificity	99.87%	99.6%	100%	100%
Turn Around time	10-20 minutes	20-30 mins	20-30 mins	7-21 days

Reference: https://doh.gov.ph/sites/default/files/publications/IB_rHIVda.pdf

Appendix 4. Characteristics of Included Studies

Study Name Author Year	Country	No. of Patients/Duration of follow-up	Populations	Intervention	Outcomes	Adverse Events
SMART 2008	*Not stated	N=477 Median 4 years exposure of ART	Age ≥13y.o HIV + CD4 cell count Good health at the time of study entry Greater than 350 cells/mm3 within 45 days of study entry	A. Immediate ART >350 cells/mm3 B. Deferred ART: <250 cells/mm3	Primary Composite Outcome (Opportunistic Disease or Death): Early (6/249) vs Deferred (21/228); HR 4.19 (95% CI, 1.69 to 10.39, p-value 0.002) All-cause mortality: Early(5/249) vs. Deferred (15/228); HR 3.5 (95% CI, 1.3 to 9.6, p-value 0.02) AIDS-related events (Fatal/Non-fatal): Early(4/249) vs Late(11/228); HR 3.26 (95% CI, 1.04-10.25; p-value 0.04) Tuberculosis: Early (1/249) vs. Deferred (3/228) Bacterial Infection: Early(2/249) vs. Deferred (0/228)	Grade 4 event; Early (18/249) vs Deferred (25/228); HR 1.6 (95% CI, 0.9-3.0)
HPTN 052 Cohen 2011 supplement	Botswana Brazil India Kenya Malawi South Africa Thailand US Zimbabwe	N=1,763 Median 5.5 years	Sero-discordant couples where one person is HIV-infceted and the other is not. No history of ART CD4 > 350 to <550 cells/mm3 and no previous long-term ART	A. Immediate ART: CD4 > 350 to <550 cells/mm3 B. Delayed ART: CD4 < 250 cells/mm^3	Primary event (pulmonary TB, severe bacterial infection, a WHO clinical stage 4 event, or death): Early (40/886) vs Delayed (65/877); HR 0.59; 95% CI, 0.40-0.88; p-value 0.01). All-cause mortality: Early(10/886) vs Delayed(13/877); HR, 0.77(95% CI, 0.34 to 1.76; p-value0.27) AIDS-related event: Early(53/886) vs Deferred(76/877) Tuberculosis (see supplement): Early(17/886) vs Deferred (33/875) Serious bacterial infection: Early(19/886) vs Deferred (13/875)	Grade 3 or 4: Early (127/886) vs Deferred(119/877) Cardiac/vascular disease (supplement): Early(7/886) vs. Deferred(9/877) Metabolism and Nutrition Disorder: Early(48/886) vs. Deferred(32/877)
HPTN 052 Cohen 2016	Botswana Brazil India Kenya Malawi South Africa Thailand US Zimbabwe	N=1763 Median 1.7 years	Age ≥18y.o HIV serology positive Sero-discordant couples where one person is HIV-infected and the other is not. No history of ART CD4 > 350 to <550 cells/mm3 and no previous long-term ART	A. Immediate ART: CD4 > 350 to <550 cells/mm3 B. Delayed ART: CD4 < 250 cells/mm^3	Any HIV transmission: Early(19/901) vs Deferred (59/888); HR, 0.31 (95% CI, 0.19 to 0.53) Linked HIV transmission: Early 0.3% (3/901) vs Deferred 4.8% (43/888); HR, 0.07 (95% CI, 0.02 to 0.22)	NA
TEMPRANO ANRS 12136 Study Group	Ivory coast	N=2,056 Median 30 months	Age ≥18y.o HIV-1 or Dual infection with HIV-1 HIV-2 CD4 counts <800/mm3 and no criteria for starting ART according to the m ost recent WHO guidelines	A. Early ART B. Early ART plus IPT C. Deferred ART D. Deferred ART plus Isoniazid preventive therapy (IPT)	A&B: Early ART versus C&D: Deferred ART Primary composite (AIDS, non-AIDS defining Cancer, non-AIDS defining invasive bacterial disease, or death from any cause at 30 months): Early(64/1033) vs. Deferred(111/1023), HR 0.56; 95% CI, 0.41-0.76) All-cause mortality: Early (21/1033) vs. Deferred(26/1023) HR,0.80 (95% CI, 0.45-1.40) AIDS-related event: Early(33/1033) vs. Deferred(65/1023), HR 0.50; 95% CI, 0.32 to 0.79) Tuberculosis: Early(28/1033) vs. Deferred (55/1023), HR 0.50 (95% CI, 0.32 to 0.79) Bacterial Infection: Early(14/1033) vs. Deferred (36/1033), HR 0.39 (95% CI 0.21 to 0.71)	A&B: Early ART versus C&D: Deferred ART Grade 3 or 4: Early(75/1033) vs. (90/1023)

INSIGHT START 2015	Africa Europe Israel North and South America Mexico Australia	N=4685 Median 4.5 years	Age ≥18y.o HIV infection documented by plasma HIV RNA viral load, rapid HIV tests or any licensed ELISA test Perceived life expectancy of at least 6 months Two CD4+ cell counts greater than 500 cells/mm(3) at least 2 weeks apart within 60 days before randomization	A.Early ART B.Deferred ART Defer ART until the CD4+ count declines to <350 cells/mm3 or AIDS develops	Early vs Deferred ART Primary composite endpoints(AIDS, serious non-AIDS-related event or death from any cause): Early (42/2326) vs. Deferred (96/2359); HR 0.43(95% CI, 0.30 to 0.62, p-value <0.001) All-cause mortality: Early (12/2326) vs. Deferred(21/2359) HR,0.58 (95% CI, 0.28 to 1.17, p-value 0.13) AIDS-related event: Early(14/2326) vs. Deferred(50/2359), HR 0.28; 95% CI,0.15 to 0.50, p-value <0.001) Tuberculosis: Early(6/2326) vs. Deferred (20/2359), HR 0.29 (95% CI, 0.12 to 0.73, p-value 0.008) Bacterial Infection: Early(14/1033) vs. Deferred (36/1033), HR 0.52 (95% CI 0.20 to 0.70, p-value 0.002)	Grade 4 events, Early (73/2326) vs. Deferred (73/2359), HR 1.01(95% CI, 0.73 to1.39, p-value 0.97) Most common grade 4 events, unscheduled hospitalization, or death from any cause : Infection with unspecified pathogen: Early (64/2326) vs. Deferred (65/2359), HR 0.99 (0.70-1.40, p-value 0.96)

Appendix 5. GRADE Evidence Profile

Author(s): Christopher G. Manalo, MD, MSc (cand)

Question: Should HIV Rapid Diagnostic Test be used to diagnose HIV in asymptomatic, apparently healthy adolescents and adults?

Setting: Outpatient and community setting

Bibliography: Huang X, Liu X, Chen J, Bao Y, Hou J, Lu X, Xia W, Xia H, Song A, Liu Z, Su B, Chen H, Chen Y and Wu H (2018) Evaluation of Blood-Based Antibody Rapid Testing for HIV Early Therapy: A Meta- Analysis of the Evidence. Front. Immunol. 9:1458. doi: 10.3389/fimmu.2018.01458

Sensitivity	1.00 (95% CI: 0.99 to 1.00)
Specificity	1.00 (95% CI: 0.99 to 1.00)

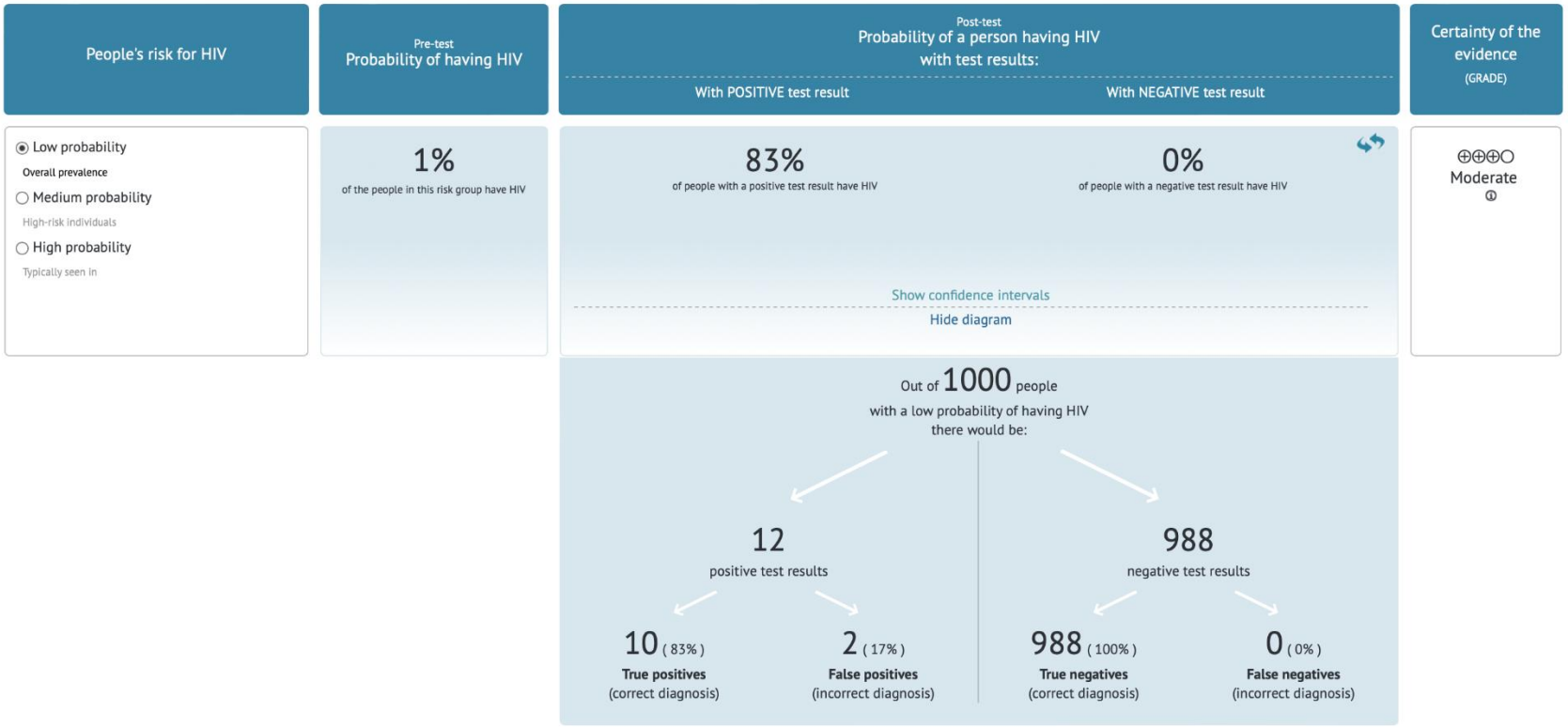
Prevalences	1%	15%	

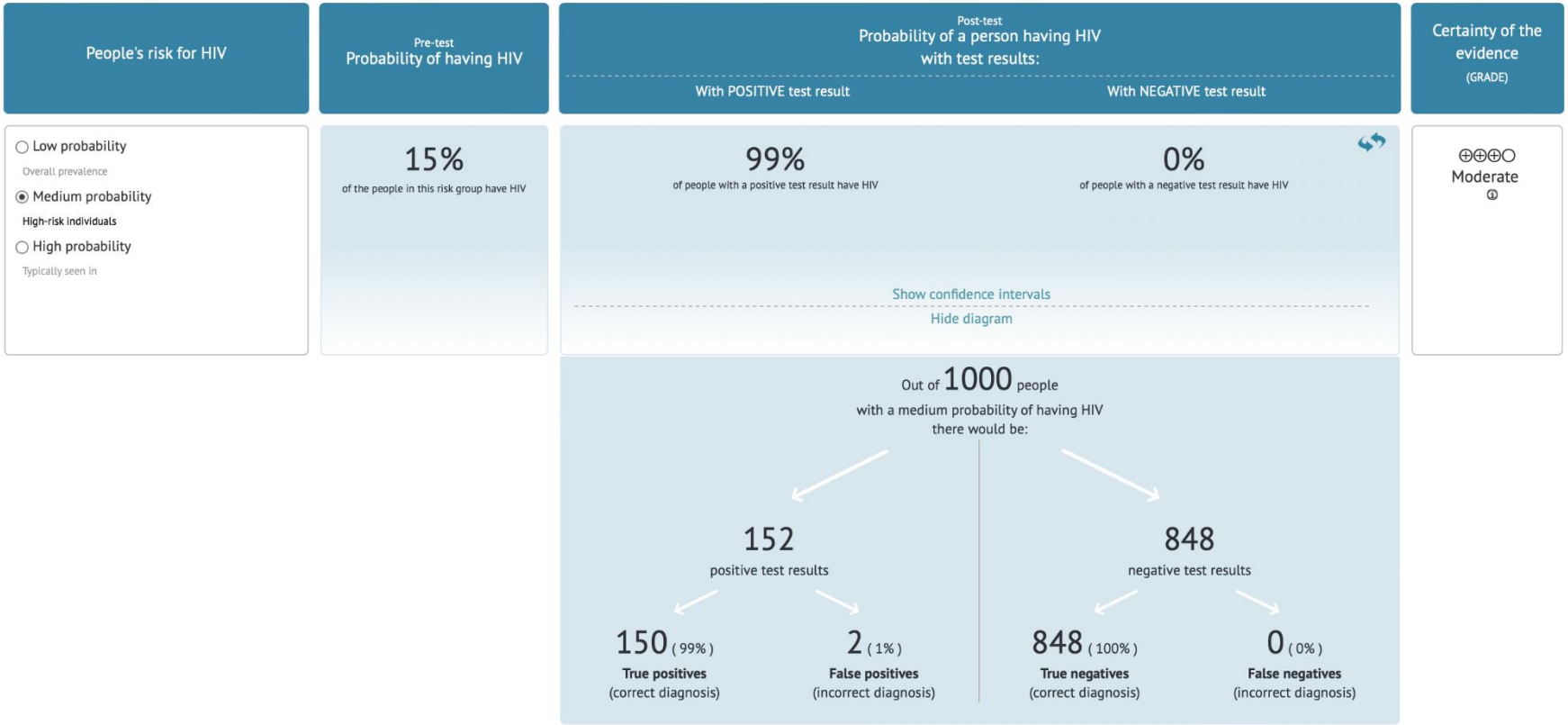
Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested		Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of1%	pre-test probability of15%	
True positives (patients with HIV)	20 studies 27,343 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious[a]	not serious	none	10 (10 to 10)	150 (149 to 150)	⊕⊕⊕◯ Moderate
False negatives (patients incorrectly classified as not having HIV)								0 (0 to 0)	0 (0 to 1)	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested		Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of1%	pre-test probability of15%	
True negatives (patients without HIV)	20 studies 27,343 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious[a]	not serious	none	988 (984 to 989)	848 (845 to 849)	⊕⊕⊕◯ Moderate
False positives (patients incorrectly classified as having HIV)								2 (1 to 6)	2 (1 to 5)	

Explanations

a. Substantial heterogeneity observed


People's risk for HIV
Pre-test
Probability of having HIV
Post-test
Probability of a person having HIV
with test results:
With POSITIVE test result
With NEGATIVE test result
Certainty of the evidence
(GRADE)
Low probability
Overall prevalence
Medium probability
High-risk individuals
High probability
Typically seen in
1%
of the people in this risk group have HIV
83%
of people with a positive test result have HIV
0%
of people with a negative test result have HIV
Moderate
Show confidence intervals
Hide diagram
Out of 1000 people
with a low probability of having HIV
there would be:
12
positive test results
988
negative test results
10 (83%)
True positives
(correct diagnosis)
2 (17%)
False positives
(incorrect diagnosis)
988 (100%)
True negatives
(correct diagnosis)
0 (0%)
False negatives
(incorrect diagnosis)



Author(s): Christopher G. Manalo, MD, MSc (cand)

Question: HIV screening compared to no screening for asymptomatic, apparently healthy adolescents and adults

Setting: Outpatient and community setting

Bibliography:

[1] Marks G, Crepaz N, Senterfitt JW, Janssen RS. Meta-analysis of high-risk sexual behavior in persons aware and unaware they are infected with HIV in the United States: implications for HIV prevention programs. J Acquir Immune Defic Syndr. 2005 Aug 1;39(4):446-53. doi: 10.1097/01.qai.0000151079.33935.79. PMID: 16010168.

[2] Marks G, Crepaz N, Janssen RS. Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. AIDS. 2006 Jun 26;20(10):1447-50. doi: 10.1097/01.aids.0000233579.79714.8d. PMID: 16791020.

Certainty assessment							Impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
Prevalence of high-risk sexual behavior, in particular, UAV									
11	observational studies (cross-sectional & cohort studies)	serious[a]	not serious	serious[b]	not serious	none	The analysis, which integrated all 11 independent study findings, indicated that the prevalence of unprotected anal and vaginal intercourse (UAV) with any partner was lower by 68% (95% CI 59% to 76%) in HIV-positive individuals aware of their serostatus when compared with HIV-positive individuals unaware of their serostatus after adjusting data from primary studies to focus on UAV with partners who were not yet HIV-positive.	⨁◯◯◯ Very low	CRITICAL
New outcome									
1	Modelling study	serious[c]	not serious	serious[b]	not serious	none	Conservative estimates showed that out of 32,000 cases (about 80% of 40,000 new HIV infections transmitted through sexual intercourse) about 17,280 sexual transmission could be from individuals unaware of their serostatus translating to a transmission rate of 6.9% compared to a transmission rate of only 2.0% from individuals aware of their serostatus. The transmission rate could be 3.5 times higher in unaware individuals.	⨁◯◯◯ Very low	CRITICAL

CI: confidence interval

Explanations

a. Recall bias suspected
b. Included HIV-positive individuals
c. Use of empirical data

Author(s): Christopher G. Manalo, MD, MSc (cand)
Question: Early compared to deferred treatment for HIV

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	early	deferred treatment	Relative (95% CI)	Absolute (95% CI)		
Primary Composite Outcomes												
4	randomised trials	not serious	not serious	not serious	not serious	none	151/4494 (3.4%)	287/4487 (6.4%)	**RR 0.53** (0.44 to 0.64)	**30 fewer per 1,000** (from 36 fewer to 23 fewer)	⨁⨁⨁⨁ High	CRITICAL

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	early	deferred treatment	Relative (95% CI)	Absolute (95% CI)		
All-cause Mortality												
4	randomised trials	not serious	serious[a]	not serious	not serious	none	48/4494 (1.1%)	160/4487 (3.6%)	**RR 0.39** (0.19 to 0.80)	**22 fewer per 1,000** (from 29 fewer to 7 fewer)	⨁⨁⨁◯ Moderate	CRITICAL
AIDS-related Events												
4	randomised trials	not serious	serious[a]	not serious	not serious	none	104/4494 (2.3%)	202/4487 (4.5%)	**RR 0.47** (0.31 to 0.71)	**24 fewer per 1,000** (from 31 fewer to 13 fewer)	⨁⨁⨁◯ Moderate	CRITICAL
Incidence of tuberculosis												
4	randomised trials	not serious	not serious	not serious	not serious	none	52/4494 (1.2%)	111/4487 (2.5%)	**RR 0.47** (0.34 to 0.65)	**13 fewer per 1,000** (from 16 fewer to 9 fewer)	⨁⨁⨁⨁ High	CRITICAL
Incidence of Bacterial Infections												
4	randomised trials	not serious	serious[a]	not serious	serious[b]	none	49/4494 (1.1%)	85/4487 (1.9%)	**RR 0.67** (0.30 to 1.57)	**6 fewer per 1,000** (from 13 fewer to 11 more)	⨁⨁◯◯ Low	CRITICAL
Certainty assessment							**№ of patients**		**Effect**		**Certainty**	**Importance**
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**early**	**deferred treatment**	**Relative (95% CI)**	**Absolute (95% CI)**		
SERIOUS ADVERSE EVENTS (Grade 3 or 4 Adverse Events)												
4	randomised trials	not serious	not serious	not serious	serious[b]	none	298/4494 (6.6%)	307/4487 (6.8%)	**RR 0.94** (0.80 to 1.11)	**4 fewer per 1,000** (from 14 fewer to 8 more)	⨁⨁⨁◯ Moderate	CRITICAL

CI: confidence interval; **RR:** risk ratio

Explanations

a. Significant statistical heterogeneity
b. Wide confidence interval

Appendix 6. Forest Plots

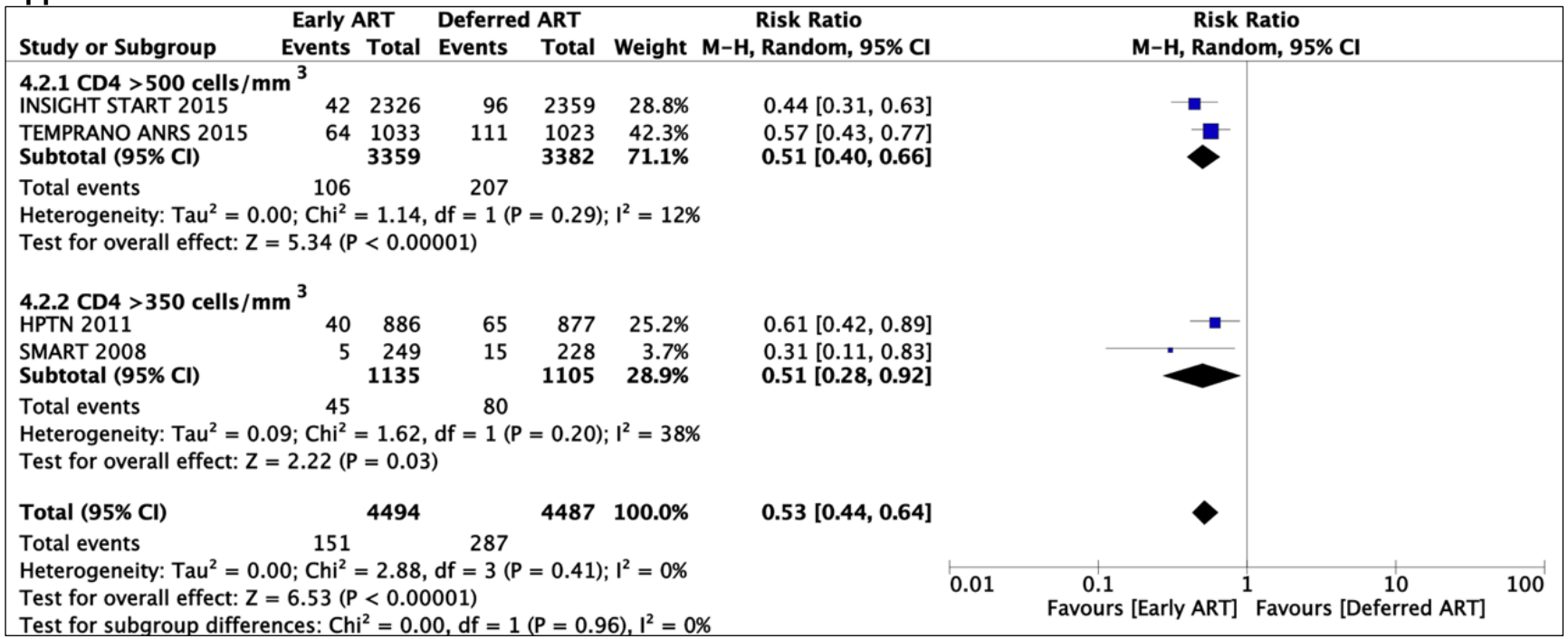


FIGURE 1. Primary Composite Outcome For Early versus Deferred (or Delayed) ART Initiation

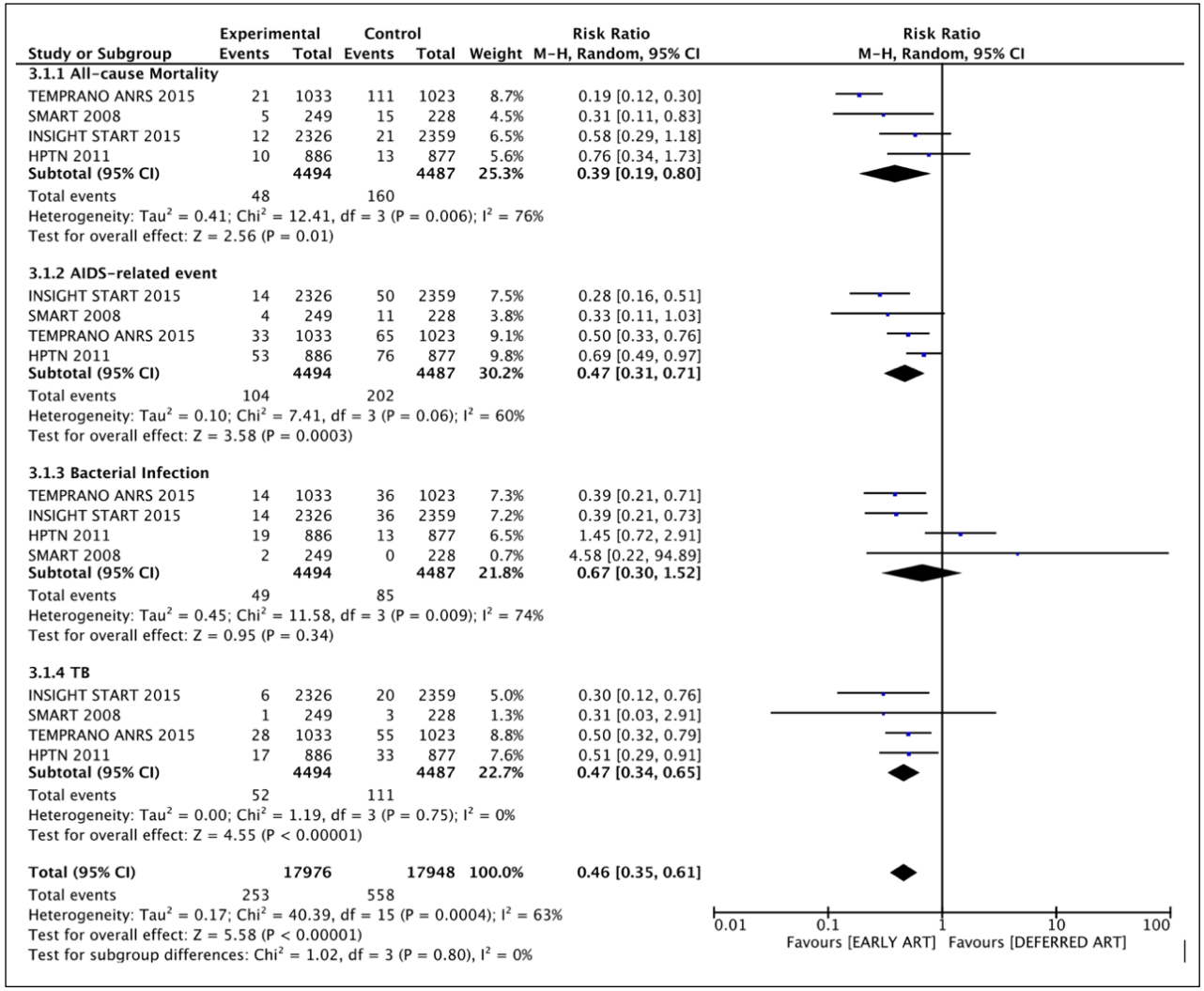


FIGURE 2. Other Critical Outcomes For Early versus Deferred (or Delayed) ART Initiation

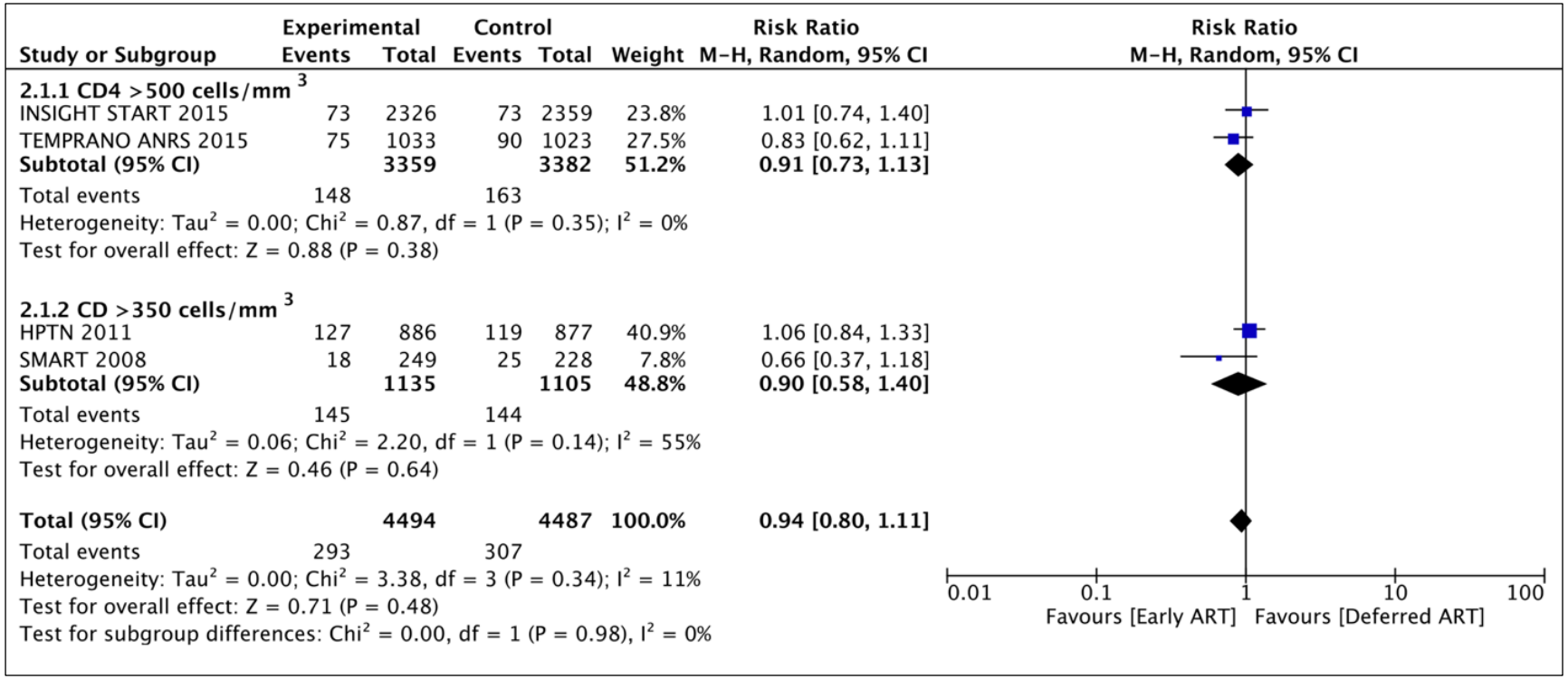


FIGURE 3. Serious Adverse Events For Early versus Deferred (or Delayed) ART Initiation

Appendix 7. Evidence-to-Decision Framework Responses

Evidence to Decision Framework

Should screening for HIV be routinely done among asymptomatic, apparently healthy adolescents and adults?

Population: Filipino adolescents and adults

Intervention: Screening

Comparator: No screening

Outcomes: All-cause mortality, AIDS-related events, Incidence of tuberculosis, Incidence of bacterial/opportunistic infections, HIV transmission, Adverse Events of Testing, Adverse Events of Treatment

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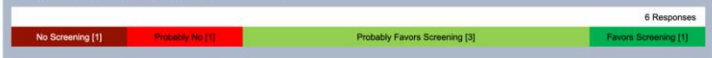
ACCURACY OF SCREENING TEST

BENEFITS OF SCREENING

HARMS OF SCREENING

CERTAINTY OF EVIDENCE

BALANCE OF BENEFITS AND HARMS



VALUES AND PREFERENCES

RESOURCE REQUIREMENTS

CERTAINTY OF EVIDENCE FOR RESOURCE REQUIREMENTS

Evidence to Decision Framework

Should screening for HIV be routinely done among asymptomatic, apparently healthy adolescents and adults?

Population: Filipino adolescents and adults

Intervention: Screening

Comparator: No screening

Outcomes: All-cause mortality, AIDS-related events, Incidence of tuberculosis, Incidence of bacterial/opportunistic infections, HIV transmission, Adverse Events of Testing, Adverse Events of Treatment

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PHILIPPINE PERIODIC HEALTH EXAMINATION

COST-EFFECTIVENESS

IMPACT ON HEALTH EQUITY

ACCEPTABILITY

FEASIBILITY

RECOMMENDATION

STRENGTH OF RECOMMENDATION

CONSENSUS PANEL COMMENTS

AGAINST SCREENING:	FOR SCREENING:
No research showing good result in screening asymptomatic apparently healthy individuals	Depending on the risk
There is low evidence to support testing in asymptomatic, apparently healthy adolescents and adults.	Screening for high-risk population
Since HIV transmission is well-known, testing no or low-risk individuals would not be cost effective nor beneficial	Do screening in targeted populations

9.7 Screening for Dental Infections

Appendix 1. Search Strategy

DATABASE	SEARCH STRATEGY	DATE AND TIME OF SEARCH	RESULTS	
			Yield	Eligible
PubMed (Dental screening)	(("dental screening"[All Fields] OR "dental care"[All Fields] OR "oral health screening"[All Fields] OR "dental recall interval"[All Fields] OR "dental recall"[All Fields] OR "oral health review"[All Fields]) AND ("adults"[All Fields] OR "asymptomatic"[All Fields] OR "primary care"[All Fields]) AND ("metaanalysis"[Publication Type] OR "randomized controlled trial"[Publication Type] OR "systematic review"[Publication Type])	3/21/2023 4:00 AM	15	3
PubMed (Routine prophylaxis)	(("dental caries"[All Fields] OR "dental infection"[All Fields] OR "periodontal disease"[All Fields] OR "gingivitis"[All Fields]) AND ("dental screening"[All Fields] OR "dental care"[All Fields] OR "oral health prophylaxis"[All Fields])) AND (randomizedcontrolledtrial[Filter])	4/8/2023 1:30 PM	233	3
Wiley Online Library (Dental Screening")	("dental care" [Title] OR "recall interval" [Title]) AND ("Dentistry" [Filter] AND "Journals" [Filter] AND "1990 – 2023" [Filter])	3/21/2023 5:30 AM	480	1
Wiley Online Library (Routine prophylaxis)	("routine dental care" OR "dental prophylaxis") AND ("periodontal disease" OR "dental caries") AND ("randomised clinical trial")	4/8/2023 4:00 PM	68	0
Cochrane Oral Health's Trials Register (Dental Screening")	("routine check up" OR "dental screening" OR "oral health screening" OR "dental recall" OR "dental recall interval" OR "oral health review") AND ("adult" OR "asymptomatic" OR "primary care")	3/21/2023 10:28 AM	17	4
Cochrane Oral Health's Trials Register (Routine prophylaxis)	("routine dental care" OR "dental prophylaxis") AND ("periodontal disease" OR "dental caries" OR "periodontal health)	4/8/2020 4:35 PM	189	1
Cochrane Central Register of Controlled Clinical Trials (CENTRAL)	("dental screening"):ti,ab,kw OR ("dental recall"):ti,ab,kw AND ("dental caries"):ti,ab,kw	3/21/2023 10: 35 AM	49	1
US National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov)	"dental caries" OR "periodontal disease" [condition or disease]; "Dental recall" OR "asymptomatic" [other terms]	3/21/2023 10: 43 AM	14	0
World Health Organization International	"dental recall" OR "dental caries" OR "dental health check"	3/21/2023 11:30 AM	69	0

ClinicalTrials Registry Platform				
HERDIN	"dental caries" OR "periodontal disease" AND "dental recall" OR "dental screening"	3/21/2023 7:00 pm	94	0
Science Direct	("dental caries" OR "periodontal disease") AND ("dental recall" OR "dental screening")	3/21/2023 7:15 pm	289	3

Appendix 2. PRISMA Flow Diagrams

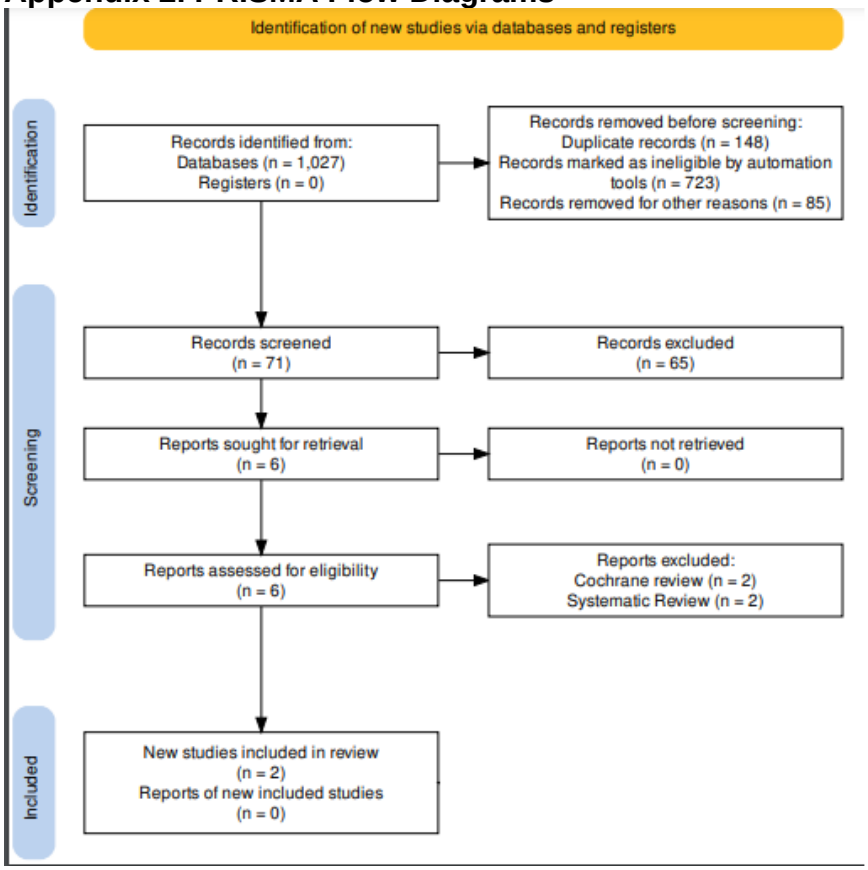


Figure 1. PRISMA for Dental Screening

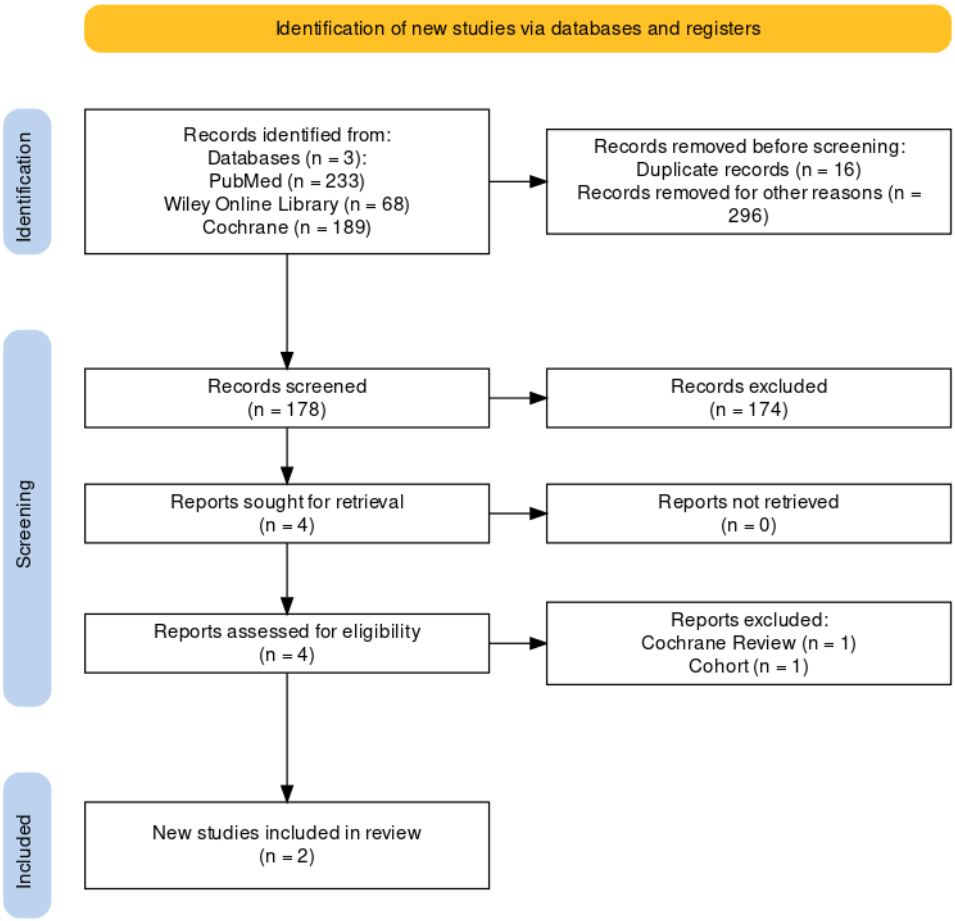


Figure 2. PRISMA for Routine Prophylaxis

Appendix 3. Characteristics of Included Studies

Dental Screening

Study	N	Population	Intervention	Control	Outcome	Setting
Wang, et al.	49	18 years old and above patients seeking dental consult	24 months interval	12 months interval	Extent of Dental Caries and periodontal disease	Dental Clinic, Toronto
Clarkson, et al.	2372	Patients seeking dental consult	24 months interval	6 months interval	Extent of Dental Caries and periodontal disease	Multi-center (dental clinics) across UK
			Risk-based approach	6 months interval		
			Risk-based approach	24 months interval		

Routine Prophylaxis

Study	N	Population	Intervention	Control	Outcome	Setting
Jones, et al. RCT	307	18 to 60 years patients regularly seeking consult	6 monthly PI	No PI	periodontal disease (gingivitis, calculus, plaque formation)	Family Dental Clinic, Northwest England
			12 monthly PI			

Ramsay, et al. Cluster* RCT *for oral health advise	2372	18 years and above patients seeking dental consult	6 monthly PI 12 monthly PI	No PI	Gingivitis, calculus	General Dental Clinics, Scotland and NE England

Appendix 4. GRADE Evidence Profile

Wang, et al.

Summary of findings:

Screening for dental infection every 24 months compared to screening for dental infection every 12 months for apparently healthy adults

Patient or population: apparently healthy adults
Setting: Out Patient
Intervention: screening for dental infection every 24 months
Comparison: screening for dental infection every 12 months

Outcomes	Anticipated absolute effects* (95% CI) Risk with screening for dental infection every 12 months	Anticipated absolute effects* (95% CI) Risk with screening for dental infection every 24 months	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Dental caries assessed with: DMFS	The mean dental caries was **11.9**	MD **1.8 higher** (2.09 lower to 5.69 higher)	-	49 (1 RCT)	⨁⨁◯◯ Low[a]	a,b

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: 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 certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. There is high risk of detection bias as there was only one examiner who identified dental caries upon follow-up. Selection bias is suggested as there is no clear explanation to how randomization and allocation concealment was performed.
b. There is low certainty of evidence that there is an important difference in caries experience among adults assigned to either a 24-month or a 12-month dental follow-up or recall.

Clarkson, et al.

Summary of findings:

Risk based dental screening for infection compared to dental screening for infection every 6 months for apparently healthy adults

Patient or population: apparently healthy adults
Setting: Out Patient
Intervention: risk based dental screening for infection
Comparison: dental screening for infection every 6 months

Outcomes	Anticipated absolute effects* (95% CI) Risk with dental screening for infection every 6 months	Anticipated absolute effects* (95% CI) Risk with risk based dental screening for infection	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments

Dental caries assessed with: ICDAS	The mean dental caries was **14.7**	MD **0.15 higher** (0.77 lower to 1.07 higher)	-	1486 (1 RCT)	⨁⨁⨁◯ Moderate[a,b]	c,d
Gingival bleeding	The mean gingival bleeding was **34.5**	MD **0.47 higher** (1.76 lower to 2.7 higher)	-	1473 (1 RCT)	⨁⨁⨁◯ Moderate[a]	a,e

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: 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 certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Screening for dental infection every 6 months compared to screening for dental infection every 24 months for apparently healthy adults

Patient or population: apparently healthy adults
Setting: Out Patient
Intervention: screening for dental infection every 6 months
Comparison: screening for dental infection every 24 months

Outcomes	Anticipated absolute effects* (95% CI) Risk with screening for dental infection every 24 months	Risk with screening for dental infection every 6 months	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Dental Caries assessed with: ICDAS	The mean dental Caries was **14.1**	MD **0.6 higher** (1.32 lower to 2.5 higher)	-	273 (1 RCT)	⨁⨁◯◯ Low[a,b]	a,b
Gingival bleeding	The mean gingival bleeding was **34.4**	MD **1.2 higher** (3.8 lower to 6.2 higher)	-	271 (1 RCT)	⨁⨁◯◯ Low[a]	a,c

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: 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 certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. The 24 month recall demonstrated a bigger proportion of carries although GRADE was downgraded for imprecision with a wide CI and small sample size.
b. There is low-certainty evidence that there is probably little to no difference between 24-month and 6-month recall intervals for the outcome of number of tooth surfaces with any caries.
c. There is low-certainty evidence that there is probably little to no difference between 24-month and 6-month recall intervals for the total amount of gingival bleeding.

Risk based dental screening compared to screening for dental infection very 24 months for apparently healthy adults

Patient or population: apparently healthy adults
Setting: Out Patient
Intervention: risk based dental screening
Comparison: screening for dental infection very 24 months

Outcomes	Anticipated absolute effects* (95% CI) Risk with screening for dental infection very 24 months	Anticipated absolute effects* (95% CI) Risk with risk based dental screening	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Dental Caries assessed with: ICDAS	The mean dental Caries was **14.1**	MD **1.4 lower** (3.49 lower to 0.69 higher)	-	281 (1 RCT)	⨁⨁◯◯ Low[a,b]	a,b
Gingival Bleeding	The mean gingival Bleeding was **34.4**	MD **1.2 lower** (5.7 lower to 3.3 higher)	-	295 (1 RCT)	⨁⨁◯◯ Low[c,d]	c,d

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: 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 certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. There is low-certainty evidence that there is probably little to no difference between risk-based and 24- month recall intervals for the outcome of number of tooth surfaces with any caries.
b. GRADE level was brought down by one due to imprecision with a wide CI and small sample size. Effect is large indicating higher proportions of dental caries with longer recall interval at 24 months.
c. There is low-certainty evidence that there is probably little to no difference between risk-based and 24- month recall intervals for the outcome of gingival bleeding.
d. GRADE level was brought down by one due to imprecision with wide CI and small sample size.

Routine Prophylaxis (Jones, et al and Ramsay, et al)

Summary of findings:

No PI compared to 6 monthly PI in Periodontal Disease Prevention

Patient or population: Periodontal Disease Prevention
Setting: Out Patient
Intervention: no PI
Comparison: 6 monthly PI

Outcomes	Anticipated absolute effects* (95% CI) Risk with 6 monthly PI	Anticipated absolute effects* (95% CI) Risk with no PI	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
Gingivitis	The mean gingivitis ranged from **37.9- 39.3**	MD **0.24 lower** (3.16 lower to 2.68 higher)	-	1087 (2 RCTs)	⨁⨁◯◯ Low[a,b]	a,b
Plaque	The mean plaque was **0.39**	MD **0.04 higher** (0.13 lower to 0.05 higher)	-	207 (1 RCT)	⨁⨁◯◯ Low[a,b]	a,b
Calculus	The mean calculus ranged from **0.71- 31.3**	MD **0.29 lower** (0.56 lower to 0.02 lower)	-	1086 (2 RCTs)	⨁⨁◯◯ Low[a,b]	a,b

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: 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 certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Summary of findings:

No PI compared to 12 monthly PI in Periodontal Disease Prevention

Patient or population: Periodontal Disease Prevention
Setting: Out Patient
Intervention: no PI
Comparison: 12 monthly PI

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with 12 monthly PI	**Risk with no PI**				
Gingivitis	The mean gingivitis ranged from **38.2 - 38.8**	MD **1.09 lower** (4.08 lower to 1.91 higher)	-	1091 (2 RCTs)	⨁⨁◯◯ Low[a,b]	[a,b]
Calculus	The mean calculus ranged from **0.89- 0.34**	MD **0.09 lower** (4.08 lower to 1.91 higher)	-	1089 (1 RCT)	⨁⨁◯◯ Low[a,b]	[a,b]
Plaque	The mean plaque was **0.44**	MD **0** (0.1 lower to 0.09 higher)	-	200 (1 RCT)	⨁⨁◯◯ Low[a,b]	[a,b]

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **MD:** mean difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: 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 certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Appendix 5. Economic Evaluation Studies

Source: Clarkson, J., Pitts, N., Fee, P. et al. Examining the effectiveness of different dental recall strategies on maintenance of optimum oral health: the INTERVAL dental recalls randomised controlled trial. Br Dent J 230, 236–243 (2021). https://doi.org/10.1038/s41415-021-2612-0

Table 1. Comparison 1: 24-month recall versus 12-month recall at 2 years follow-up

Outcome	Subgroup	24-month recall	12-month recall	Effect estimate
Cost (health-system perspective costs and resource use): total time used by each participant (minutes)	3 to 5 years old (primary teeth)	mean 42 (SD 34.7); 31 participants	mean 52 (SD 30.2); 27 participants	MD −10.00 (95% CI −26.70 to 6.70)
	16 to 20 years old (permanent teeth)	mean 62.5 (SD 53.8); 61 participants	mean 86.2 (SD 58.8); 66 participants	MD −23.70 (95% CI −43.28 to −4.12)

CI = confidence interval; MD = mean difference; SD = standard deviation

Table 2. Comparison 2: Risk-based recall versus 6-month recall at 4 years follow-up

Outcome	Risk-based recall	6-month recall	Effect estimate
Cost (patient perspective costs): GBP per patient	mean 197.33 (SD 155.1); 966 participants	mean 206.82 (SD 149.89); 978 participants	MD −9.49 (95% CI −23.05 to 4.07); P = 0.17
Cost (healthcare system perspective costs and resource use): GBP per patient	mean 123.37 (SD 185.66); 1001 participants	mean 109.6 (SD 164.09); 1009 participants	MD 13.77 (95% CI −1.56 to 29.11); P = 0.08
Prevalence of root caries	147 out of 663 participants	154 out of 643 participants	RR 0.93 (95% CI 0.76 to 1.13); P = 0.45
Patient satisfaction with actual care received: 1 to 7 scale where a higher score is a better outcome	mean 5.3 (SD 0.6136); 798 participants	mean 5.27 (SD 0.6136); 809 participants	MD 0.03 (95% CI −0.03 to 0.09); P = 0.33

Appendix 6. Forest Plots

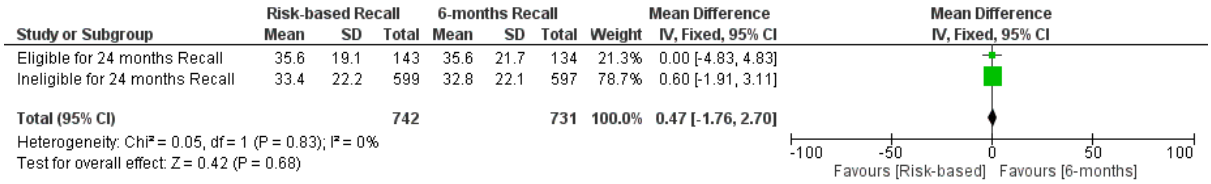


Figure 1. Forest Plot on the comparison between Recall Intervals on Gingival Bleed (1 RCT).

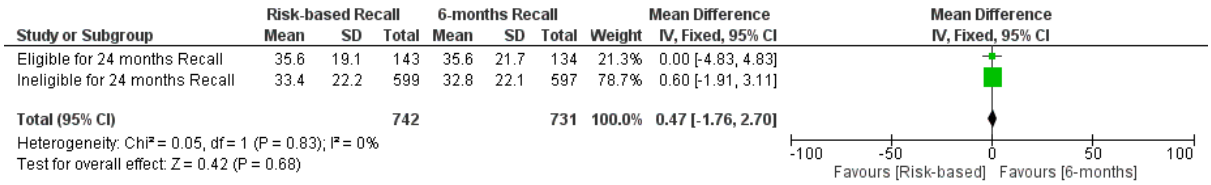


Figure 2. Forest Plot on the comparison between Recall Intervals on Dental Caries (1 RCT).

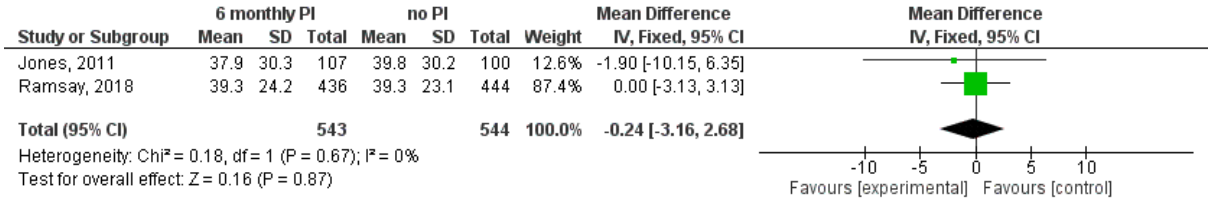


Figure 3. Forest Plot on the comparison between 6 monthly PI vs no PI for Gingivitis (2 RCTs).

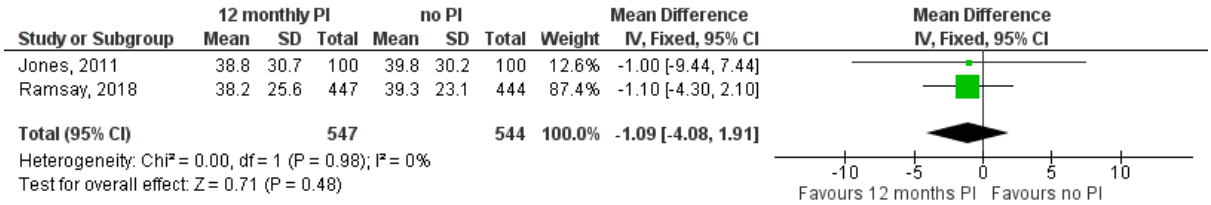


Figure 4. Forest Plot on the comparison between 12 monthly PI vs no PI for Gingivitis (2 RCTs).

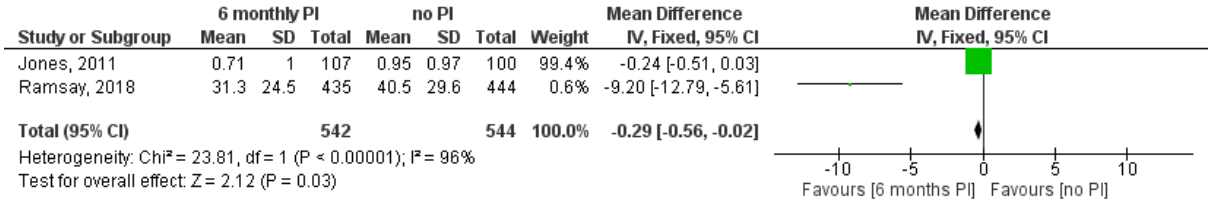


Figure 5. Forest Plot on the comparison between 6 monthly PI vs no PI for Calculus (2 RCTs).

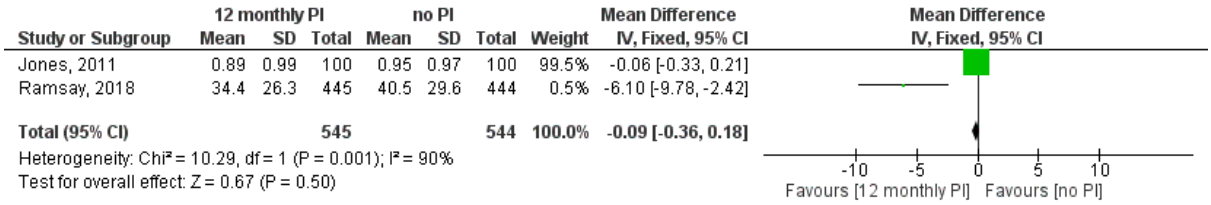
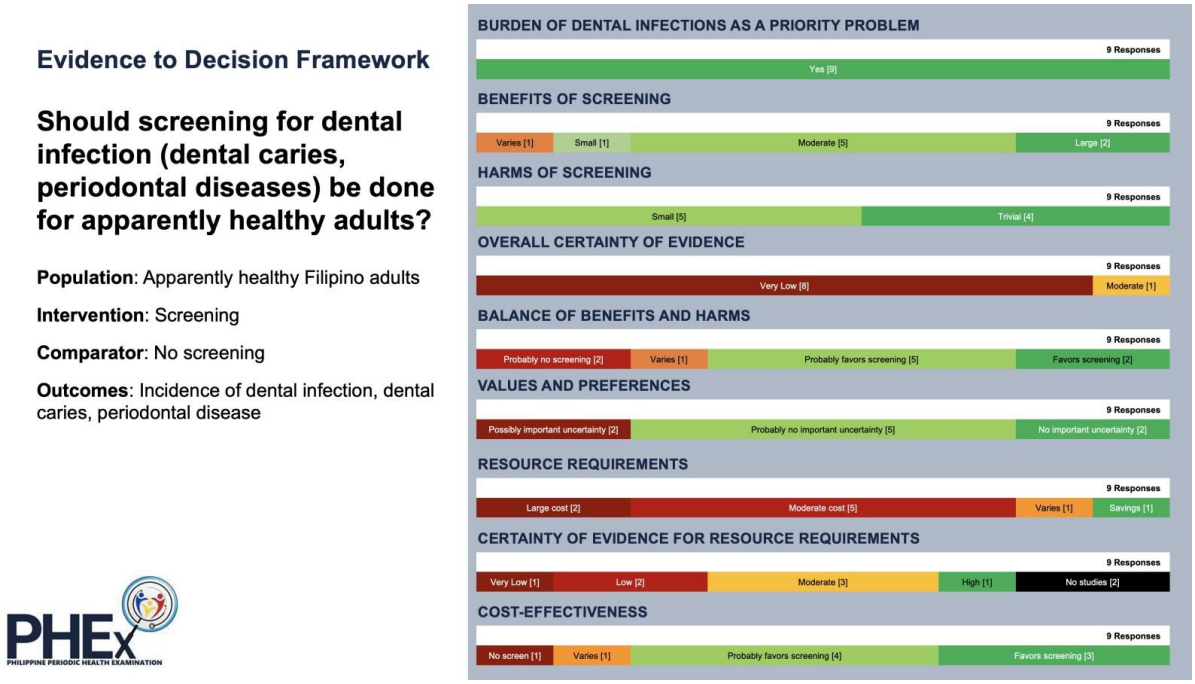


Figure 6. Forest Plot on the comparison between 12 monthly PI vs no PI for Calculus (2 RCTs).

Appendix 7. Evidence-to-Decision Framework Responses



Evidence to Decision Framework

Should screening for dental infection (dental caries, periodontal diseases) be done for apparently healthy adults?

Population: Apparently healthy Filipino adults

Intervention: Screening

Comparator: No screening

Outcomes: Incidence of dental infection, dental caries, periodontal disease

PHEx
PHILIPPINE PERIODIC HEALTH EXAMINATION

IMPACT ON HEALTH EQUITY

ACCEPTABILITY

FEASIBILITY

RECOMMENDATION

STRENGTH OF RECOMMENDATION

CONSENSUS PANEL COMMENTS

NO RECOMMENDATION:	FOR DENTAL SCREENING:
No sufficient evidence to cite	Risk-based screening Dental problems are most often neglected. They are mostly non-lethal but they can lead to serious illnesses which can lead to death. They also affect the quality-of-life of patients as well as their work. Given the opportunity people may be more than willing to have their teeth checked. Based on experience that oral care is important but often overlooked Screening allows for both prevention and early intervention in dental infections and caries. Prevention of dental infection that may debilitate an individual.

9.8 Screening for COVID-19

Appendix 1. Search Strategy

A comprehensive and systematic search of local and internal databases was done on 09 March 2023 to 19 March 2023 from database inception until 09 March 2023 through MEDLINE, Cochrane CENTRAL, and MedRxiv using the combined MeSH and keywords search on Covid-19, rapid antigen test, RT-PCR, screening and asymptomatic. A filter was placed to include only clinical trials, RCTs and meta-analysis. Only studies with the outcome of interest were included. The references of included studies were also hand searched to identify additional studies that may not have appeared in the database search.

PubMed by MEDLINE (as of 09 March 2023)

#	Query	Results
1	(coronavirus OR "corona virus" OR coronavirinae OR coronaviridae OR betacoronavirus OR covid19 OR "covid 19" OR nCoV OR "CoV 2" OR CoV2 OR sarscov2 OR 2019nCoV OR "novel CoV" OR "wuhan virus") OR ((wuhan OR hubei OR huanan) AND ("severe acute respiratory" OR pneumonia) AND (outbreak)) OR "Coronavirus"[Mesh] OR "Coronavirus Infections"[Mesh] OR "COVID-19" [Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2" [Supplementary Concept] OR "Betacoronavirus"[Mesh]	365,472
2	(reverse transcription polymerase chain reaction test) OR (RT-PCR)	290,986
3	(rapid antigen testing) OR (Antigen Test)	172,850
4	#2 OR #3	458,183
5	#1 AND #4	15,208
6	screen OR screening	5,841,807
7	#5 AND #6	8,158
8	asymptomatic OR "no symptoms" OR "no symptom" OR symptomless	201,636
9	#7 AND #8	1,222
10	#7 AND #8 Filters: Clinical Study, Clinical Trial, Observational Study, Meta-analysis, Systematic Reviews, Randomized Controlled Trial, Humans	112

Cochrane (as of 09 March 2023)

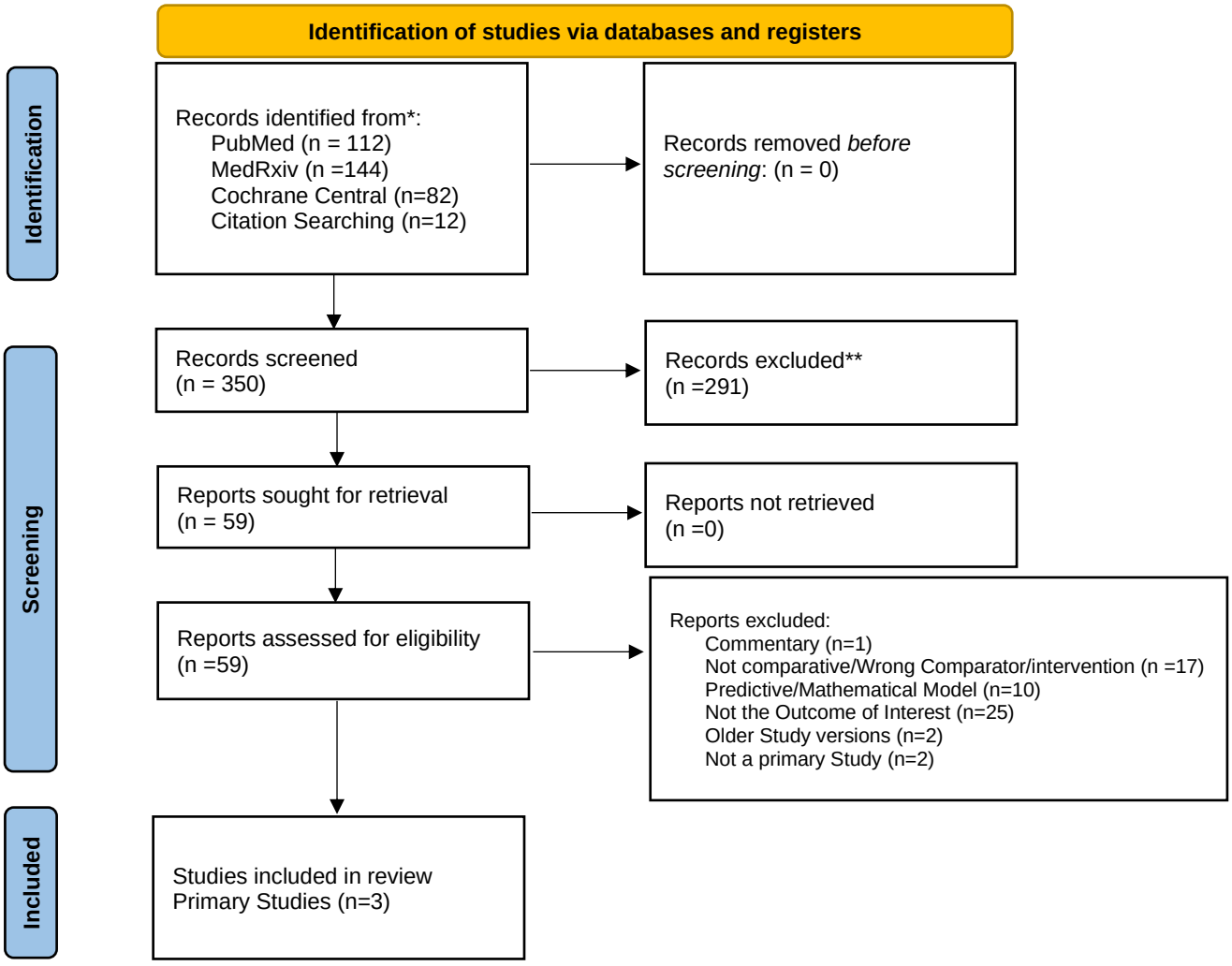
#	Query	Results
#1	COVID-19 OR COVID19 OR 2019 nCoV Infection OR Novel Coronavirus Disease OR Severe Acute Respiratory Syndrome Coronavirus 2 Infection OR SARS-CoV-2	15000
#2	(reverse transcription polymerase chain reaction test) OR (RT-PCR)	3583
#3	(rapid antigen testing) OR (Antigen Test)	4834
#4	#2 OR #3	8227
#5	#1 AND #4	1465
#6	screen OR screening	81840

#7	#5 AND #6	305
#8	(asymptomatic) OR ("no symptoms") OR "no symptom" OR symptomless	15826
#9	#7 AND #8	82

MedRxiv (as of 19 March 2023)

#	Query	Results
#1	"((COVID-19) OR (SARS-COV-2) OR (nCov)) AND ((RT-PCR) OR (rapid antigen test)) AND (screening) AND (asymptomatic)"	144

Appendix 2. PRISMA Flow Diagram



Appendix 3. Characteristics of Included Studies

Author, Year	Study design	Setting	Number of patients	Population	Intervention Group(s)	Control	Outcomes
Green et al, 2022	Before and After Study	Liverpool, UK	3 Dec 2020 to 31 Jul 2021 n=668,243	Asymptomatic people age ≥5 years living or working in the City of Liverpool	Covid-SMART "community testing" using a SARS-CoV-2 rapid antigen lateral flow test (LFT) performed at a testing centre or via a universal access home test kit.	Synthetic controls: non-adjacent set of neighborhoods with aggregate trends in covid-19 hospital admissions similar to Liverpool	• Uptake of asymptomatic lateral flow testing • Positivity rates • Repeat Lateral Flow testing: variation • Home lateral flow testing • Impact of LCR community asymptomatic testing on Covid-19 hospital admissions
Di Lorenzo et al, 2022	Cohort Study (Interim Analysis)	Oncology Unit at the "Andrea Tortora" Hospital	As of 1 Oct 2021 N=76	Asymptomatic for COVID-19 cancer patients who had received any anticancer systemic therapy within 3 months since the day they tested positive for SARS-CoV-2 on RT-PCR	Institutional screening program-screened for SARS-CoV-2 using RT-PCR nasal swab	Those diagnosed outside the institutional screening for any reason	• Need for O2 therapy Admission to the intensive care unit • Hospital Admission • Death
Aranaz-Andrés JM, 2022	Cross-Sectional Study (dIagnosis study)	Italy Ramón y Cajal Hospital	N=34 541 sample	Asymptomatic hospitalized patients during hospital outbreaks	Panbio COVID-19 AG" RADT (Abbott) (Index test)	TaqPath COVID-19 test RT-PCR (reference standard)	Sensitivity and Specificity

Appendix 4. GRADE Evidence Profile

Author(s): Anna Maria Vida P. Garcia
Question: Screening test compared to no screening test for Asymptomatic, Apparently Healthy Individuals
Setting: Outpatient
Bibliography:

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	screening test	no screening test	Relative (95% CI)	Absolute (95% CI)		
Hospital Admission (Rapid Antigen Test)												
1	observational studies	serious[a]	not serious	not serious	not serious	none	Dec 3, 2020 – Jan 2, 2021 (testing region vs non-testing control areas) • 32% (95% CI:-39% to -22%, p-value<0.001) reduction in hospital admissions. • 32% reduction is the equivalent of 391 fewer admissions				⊕◯◯◯ Very low	
Hospital Admission (RT-PCR)												
1	observational studies	serious[b]	not serious	serious[c]	serious[d]	none			**OR 31.5** (3.1 to 317.8)	**32 fewer per 1,000** (from 318 fewer to 3 fewer)	⊕◯◯◯ Very low	
Need of Oxygen Therapy (RT-PCR)												
1	observational studies	serious[b]	not serious	serious[c]	serious[d]	none			**OR 16.2** (2.2 to 117.1)	**16 fewer per 1,000** (from 117 fewer to 2 fewer)	⊕◯◯◯ Very low	
Need for ICU Admission (RT-PCR)												
1	observational studies	serious[b]	not serious	serious[c]	serious[d]	none			**OR 23.0** (2.4 to 223.8)	**23 fewer per 1,000** (from 224 fewer to 2 fewer)	⊕◯◯◯ Very low	

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	screening test	no screening test	Relative (95% CI)	Absolute (95% CI)		
Mortality (RT-PCR)												
1	observational studies	serious[b]	not serious	serious[c]	serious[d]	none			**OR 8.8** (1.2 to 65.5)	**9 fewer per 1,000** (from 66 fewer to 1 fewer)	⊕◯◯◯ Very low	

CI: confidence interval; **OR:** odds ratio

Explanations

a. possibility of presence of spill-over effects
b. selection bias, unplanned analysis, small sample size
c. Cancer patients, Not outppatient setting
d. wide confidence interval

Should Rapid antigen Test be used to screen for COVID-19 in Asymptomatic, Apparently Healthy Individuals?
Patient or population: Asymptomatic, Apparently Healthy Individuals
Setting:
Pooled sensitivity:0.63 (95% CI: 0.56 to 0.69)|**Pooled specificity**:1.00 (95% CI: 1.00 to 1.00)

Test result	Number of results per 1,000 patients tested (95% CI)			Number of participants (studies)	Certainty of the Evidence (GRADE)
	Prevalence1% Typically seen in	**Prevalence5%** Typically seen in	**Prevalence10%** Typically seen in		
True positives	**6** (6 to 7)	**32** (28 to 34)	**63** (56 to 69)	4553 (59)	⊕⊕⊕◯ **Moderate**[a,b,c]
False negatives	**4** (3 to 4)	**18** (16 to 22)	**37** (31 to 44)		
True negatives	**990** (990 to 990)	**950** (950 to 950)	**900** (900 to 900)	97541 (59)	⊕⊕⊕⊕ **High**[a,c]
False positives	**0** (0 to 0)	**0** (0 to 0)	**0** (0 to 0)		

CI: confidence interval

Explanations

a. Although some of the included studies were judged to have a high or unclear risk of bias in one or more domains, a sensitivity analysis excluding studies with a high risk of bias did not show a difference in the effect estimate. For this reason, we did not downgrade for the risk of bias.
b. There is serious unexplained inconsistency in the results despite partial explanation of having different types of tests in different studies.
c. There is some indirectness

Should RAgT be used to screen for COVID-19 in Asymptomatic, Apparently Healthy Individuals?
Patient or population: Asymptomatic, Apparently Healthy Individuals (With or Without Known Exposure)
Setting:
New test: [comparator test] |**Cut-off value**:
Pooled sensitivity:0.75 (95% CI: 0.55 to 0.95)|**Pooled specificity**:0.99 (95% CI: 0.99 to 1.00)

Should SARS-CoV-2 RAgT be used to diagnose COVID-19 in asymptomatic individuals?

Bottom panel | Explanations

Source of data: ○ from single study ◉ pooled across studies ○ range from studies

Sensitivity	0.55 (95% CI: 0.48 to 0.62)
Specificity	0.99 (95% CI: 0.99 to 1.00)

Effect per	1,000		
Prevalences	1%	5%	10%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	pre-test probability of 1%	pre-test probability of 5%	pre-test probability of 10%	
True positives (patients with COVID-19)	50 studies 40956 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	not serious	none	5 (5 to 6)	27 (24 to 31)	55 (48 to 62)	⨁⨁⨁◯ Moderate
False negatives (patients incorrectly classified as not having COVID-19)								5 (4 to 5)	23 (19 to 26)	45 (38 to 52)	
True negatives (patients without COVID-19)	50 studies 40956 patients	cross-sectional (cohort type accuracy study)	serious [a]	not serious	not serious	not serious	none	985 (984 to 986)	945 (944 to 946)	896 (895 to 896)	⨁⨁⨁◯ Moderate
False positives (patients incorrectly classified as having COVID-19)								5 (4 to 6)	5 (4 to 6)	4 (4 to 5)	

Should SARS-CoV-2 RAgT be used to diagnose COVID-19 in asymptomatic individuals?

Bottom panel | Explanations

Probabilities | Positives / Negatives | Sensitivity / Specificity | Correctly Diagnosed | Plain Language Summary

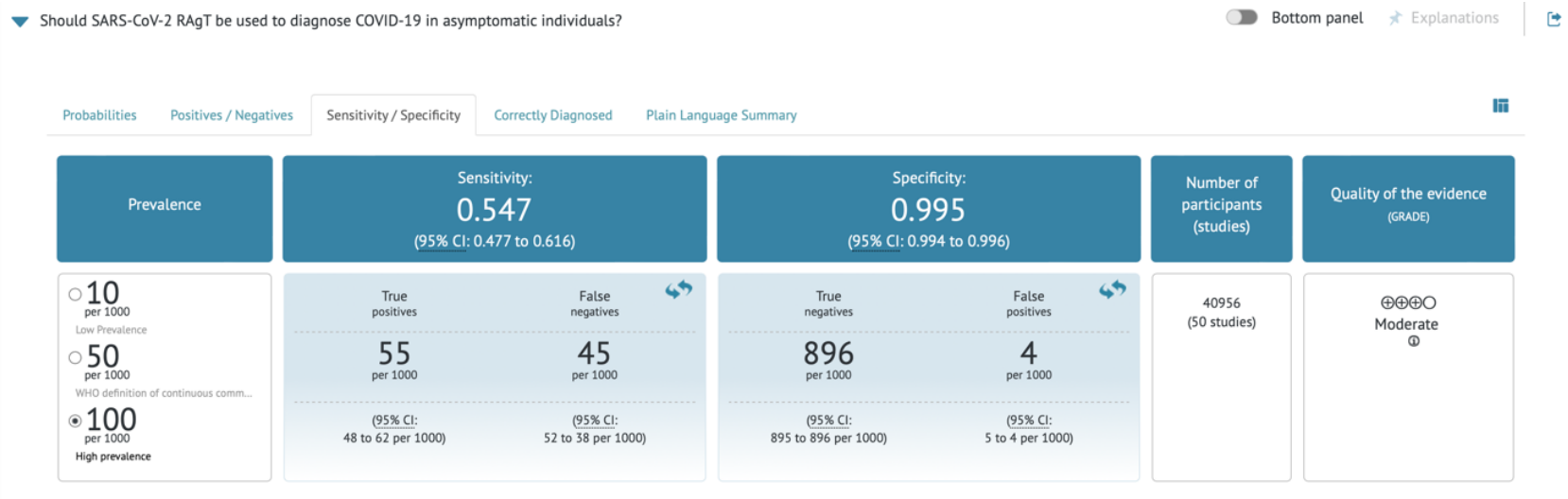
Prevalence	Sensitivity: 0.547 (95% CI: 0.477 to 0.616)		Specificity: 0.995 (95% CI: 0.994 to 0.996)		Number of participants (studies)	Quality of the evidence (GRADE)
	True positives	False negatives	True negatives	False positives		
◉ 10 per 1000 Low Prevalence	5 per 1000	5 per 1000	985 per 1000	5 per 1000	40956 (50 studies)	⊕⊕⊕◯ Moderate ⓘ
	(95% CI: 5 to 6 per 1000)	(95% CI: 5 to 4 per 1000)	(95% CI: 984 to 986 per 1000)	(95% CI: 6 to 4 per 1000)		
○ 50 per 1000 WHO definition of continuous comm...						
○ 100 per 1000 High prevalence						

Should SARS-CoV-2 RAgT be used to diagnose COVID-19 in asymptomatic individuals?

Bottom panel | Explanations

Probabilities | Positives / Negatives | Sensitivity / Specificity | Correctly Diagnosed | Plain Language Summary

Prevalence	Sensitivity: 0.547 (95% CI: 0.477 to 0.616)		Specificity: 0.995 (95% CI: 0.994 to 0.996)		Number of participants (studies)	Quality of the evidence (GRADE)
	True positives	False negatives	True negatives	False positives		
○ 10 per 1000 Low Prevalence	27 per 1000	23 per 1000	945 per 1000	5 per 1000	40956 (50 studies)	⊕⊕⊕◯ Moderate ⓘ
	(95% CI: 24 to 31 per 1000)	(95% CI: 26 to 19 per 1000)	(95% CI: 944 to 946 per 1000)	(95% CI: 6 to 4 per 1000)		
◉ 50 per 1000 WHO definition of continuous community transmission						
○ 100 per 1000 High prevalence						



Should RT-PCR be used to screen for COVID-19 in Asymptomatic, Apparently Healthy Individuals?
Patient or population: Asymptomatic, Apparently Healthy Individuals
Setting:
New test: [comparator test] |**Cut-off value**:
Pooled sensitivity:0.75 (95% CI: 0.55 to 0.95)|**Pooled specificity**:0.99 (95% CI: 0.99 to 1.00)

Test result	Number of results per 1,000 patients tested (95% CI)			Number of participants (studies)	Certainty of the Evidence (GRADE)
	Prevalence10% Typically seen in	**Prevalence25%** Typically seen in	**Prevalence50%** Typically seen in		
True positives	**75** (55 to 95)	**188** (138 to 238)	**375** (275 to 475)	385 (6)	⊕◯◯◯ **Very low**[a,b,c]
False negatives	**25** (5 to 45)	**62** (12 to 112)	**125** (25 to 225)		
True negatives	**891** (891 to 900)	**742** (742 to 750)	**495** (495 to 500)	2 (457)	⊕◯◯◯ **Very low**[a,b,c]
False positives	**9** (0 to 9)	**8** (0 to 8)	**5** (0 to 5)		

CI: confidence interval

Explanations

a. Reference standard considered to be nasopharyngeal specimen RT-PCR
b. Studies report test accuracy results but do not report on patient-important outcomes based on these results.
c. A small number of patients included.

Should RT-PCR be used to screen for COVID-19 in Asymptomatic, Apparently Healthy Individuals?
Patient or population: Asymptomatic, Apparently Healthy Individuals
Setting:
New test: [comparator test] |**Cut-off value**:
Pooled sensitivity:0.75 (95% CI: 0.55 to 0.95)|**Pooled specificity**:0.99 (95% CI: 0.99 to 1.00)

Should SARS-CoV-2 RT-PCR be used to diagnose COVID-19 in asymptomatic individuals??

Bottom panel | Explanations

Source of data: ○ from single study ◉ pooled across studies ○ range from studies

Sensitivity	0.75 (95% CI: 0.55 to 0.95)
Specificity	0.99 (95% CI: 0.99 to 1.00)

Effect per	1,000		
Prevalences	10%	25%	50%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Other considerations	pre-test probability of 10%	pre-test probability of 25%	pre-test probability of 50%	
True positives (patients with COVID-19)	6 studies 385 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	serious [b]	none	75 (55 to 95)	188 (138 to 238)	375 (275 to 475)	⨁⨁◯◯ Low
False negatives (patients incorrectly classified as not having COVID-19)								25 (5 to 45)	62 (12 to 112)	125 (25 to 225)	
True negatives (patients without COVID-19)	2 studies 457 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	serious [b]	none	891 (891 to 900)	742 (742 to 750)	495 (495 to 500)	⨁⨁◯◯ Low
False positives (patients incorrectly classified as having COVID-19)								9 (0 to 9)	8 (0 to 8)	5 (0 to 5)	

Should SARS-CoV-2 RT-PCR be used to diagnose COVID-19 in asymptomatic individuals??

Bottom panel | Explanations

Probabilities | Positives / Negatives | Sensitivity / Specificity | Correctly Diagnosed | Plain Language Summary

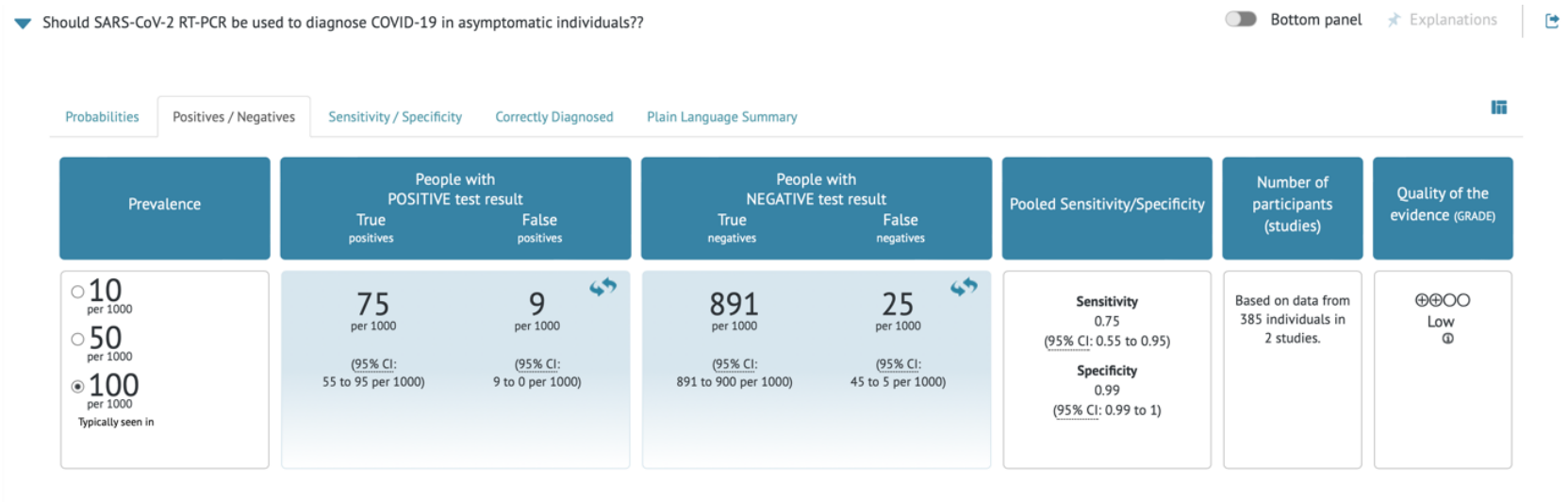
Prevalence	People with POSITIVE test result: True positives	People with POSITIVE test result: False positives	People with NEGATIVE test result: True negatives	People with NEGATIVE test result: False negatives	Pooled Sensitivity/Specificity	Number of participants (studies)	Quality of the evidence (GRADE)
◉ 10 per 1000 ○ 50 per 1000 ○ 100 per 1000 Typically seen in	8 per 1000 (95% CI: 6 to 10 per 1000)	10 per 1000 (95% CI: 10 to 0 per 1000)	980 per 1000 (95% CI: 980 to 990 per 1000)	2 per 1000 (95% CI: 4 to 0 per 1000)	**Sensitivity** 0.75 (95% CI: 0.55 to 0.95) **Specificity** 0.99 (95% CI: 0.99 to 1)	Based on data from 385 individuals in 2 studies.	⊕⊕◯◯ Low ⓘ

Should SARS-CoV-2 RT-PCR be used to diagnose COVID-19 in asymptomatic individuals??

Bottom panel | Explanations

Probabilities | Positives / Negatives | Sensitivity / Specificity | Correctly Diagnosed | Plain Language Summary

Prevalence	People with POSITIVE test result: True positives	People with POSITIVE test result: False positives	People with NEGATIVE test result: True negatives	People with NEGATIVE test result: False negatives	Pooled Sensitivity/Specificity	Number of participants (studies)	Quality of the evidence (GRADE)
○ 10 per 1000 ◉ 50 per 1000 ○ 100 per 1000 Typically seen in	38 per 1000 (95% CI: 28 to 48 per 1000)	9 per 1000 (95% CI: 9 to 0 per 1000)	941 per 1000 (95% CI: 941 to 950 per 1000)	12 per 1000 (95% CI: 22 to 2 per 1000)	**Sensitivity** 0.75 (95% CI: 0.55 to 0.95) **Specificity** 0.99 (95% CI: 0.99 to 1)	Based on data from 385 individuals in 2 studies.	⊕⊕◯◯ Low ⓘ


Should SARS-CoV-2 RT-PCR be used to diagnose COVID-19 in asymptomatic individuals??
Bottom panel
Explanations
Probabilities
Positives / Negatives
Sensitivity / Specificity
Correctly Diagnosed
Plain Language Summary
Prevalence
People with POSITIVE test result
True positives
False positives
People with NEGATIVE test result
True negatives
False negatives
Pooled Sensitivity/Specificity
Number of participants (studies)
Quality of the evidence (GRADE)
10 per 1000
50 per 1000
100 per 1000
Typically seen in
75 per 1000
(95% CI: 55 to 95 per 1000)
9 per 1000
(95% CI: 9 to 0 per 1000)
891 per 1000
(95% CI: 891 to 900 per 1000)
25 per 1000
(95% CI: 45 to 5 per 1000)
Sensitivity
0.75
(95% CI: 0.55 to 0.95)
Specificity
0.99
(95% CI: 0.99 to 1)
Based on data from 385 individuals in 2 studies.
⊕⊕◯◯
Low
①

Appendix 5. Evidence-to-Decision Framework Responses

Evidence to Decision Framework

Should COVID-19 screening test be done among asymptomatic apparently healthy adults?

Population: Asymptomatic apparently healthy Filipino adults

Intervention: Screening

Comparator: No screening

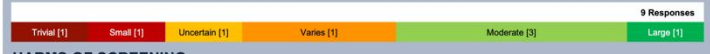
Outcomes: COVID-19 related-mortality and morbidity, hospitalization, incidence of COVID, outbreak, adverse event of testing, stigma of testing, prevention of transmission, quarantine and isolation rates, early initiation of treatment

PHEx
PHILIPPINE PERIODIC HEALTH EXAMINATION

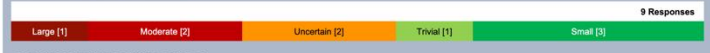
BURDEN OF COVID-19 AS A PRIORITY PROBLEM

ACCURACY OF SCREENING TEST

BENEFITS OF SCREENING



HARMS OF SCREENING



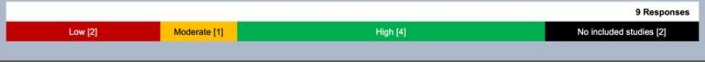
CERTAINTY OF EVIDENCE

BALANCE OF BENEFITS AND HARMS

VALUES AND PREFERENCES

RESOURCE REQUIREMENTS

CERTAINTY OF EVIDENCE FOR RESOURCE REQUIREMENTS



Evidence to Decision Framework

Should COVID-19 screening test be done among asymptomatic apparently healthy adults?

Population: Asymptomatic apparently healthy Filipino adults

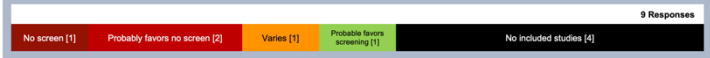
Intervention: Screening

Comparator: No screening

Outcomes: COVID-19 related-mortality and morbidity, hospitalization, incidence of COVID, outbreak, adverse event of testing, stigma of testing, prevention of transmission, quarantine and isolation rates, early initiation of treatment

PHEx
PHILIPPINE PERIODIC HEALTH EXAMINATION

COST-EFFECTIVENESS

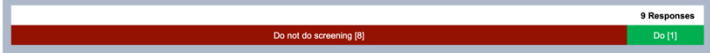


IMPACT ON HEALTH EQUITY

ACCEPTABILITY

FEASIBILITY

RECOMMENDATION



STRENGTH OF RECOMMENDATION

CONSENSUS PANEL COMMENTS

AGAINST SCREENING:

Harm (cost) outweighs benefit

Low evidence to support testing in asymptomatic healthy adults. Targeted testing (high-risk close contacts) may be more practical and cost-effective. Yield of testing may also depend on current COVID-19 numbers in the country.

Studies and experience; Exposure (or suspected exposure) should be the main consideration; Screen for symptomatic and close contacts

If we test everyone, it would be against the risk and time-based testing of COVID-19, against IATF resolution 163A and DOLE, DOH protocols

FOR SCREENING:

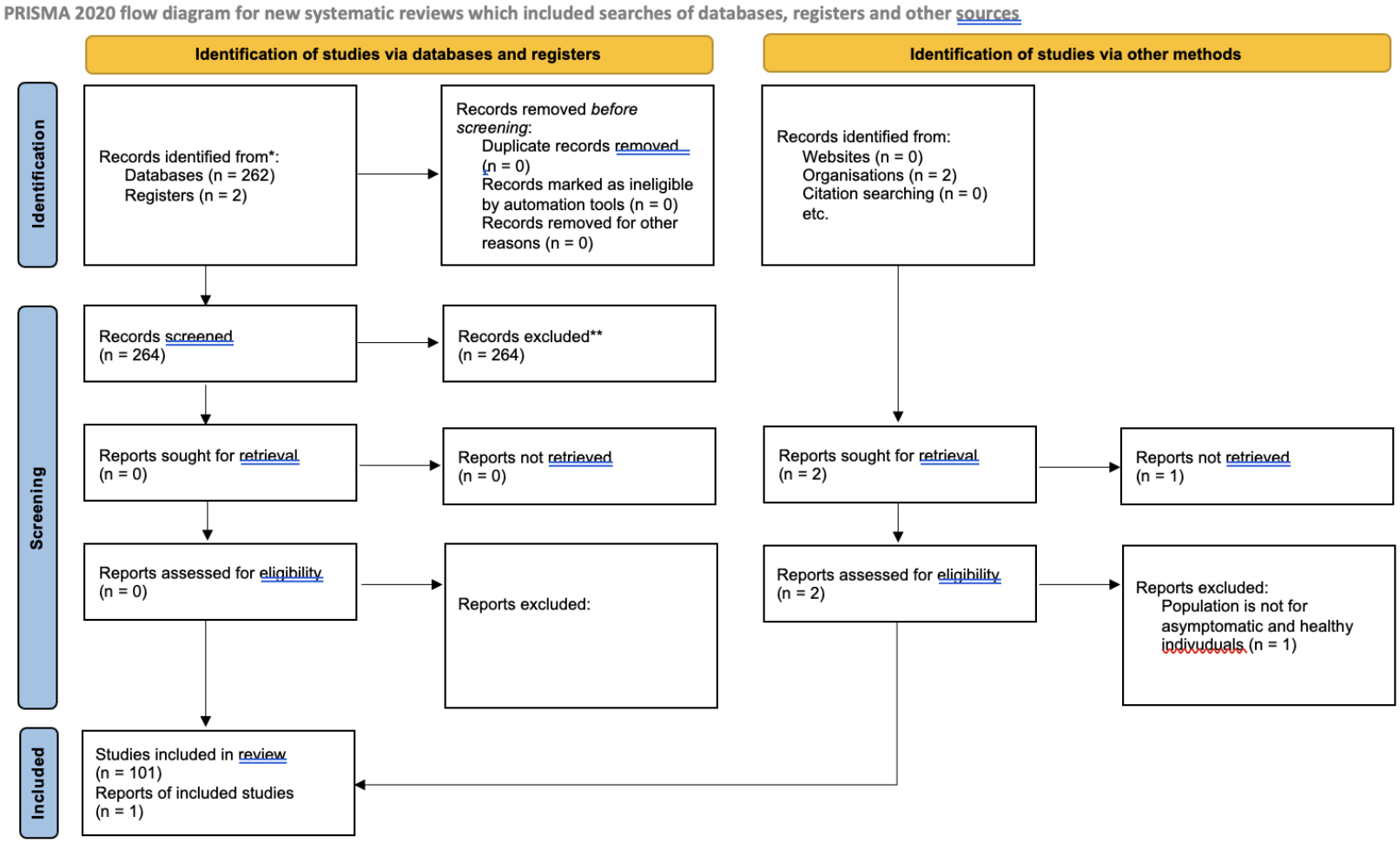
At the moment, we have no full knowledge of the virus hence screening will be of help.

9.9 Screening for Latent TB

Appendix 1. Search Strategy (as of 12 March 2023)

DATABASE	#	SEARCH STRATEGY / SEARCH TERMS	DATE AND TIME OF SEARCH	RESULTS	
				Yield	Eligible
USPSTF	1	All infectious disease guidelines	January 25, 2023 10:00PM	21	1
Canadian Task Force on Preventive Health	1	all published guidelines	January 25, 2023 10:00PM	22	0
	2	All archived guidelines		1	
	3	#1 and #2		23	0
National Institute for Health and Care Excellence	1	Tuberculosis	January 25, 2023 10:00PM	1	0
Cochrane	1	(tuberculosis):ti,ab,kw with Cochrane Library publication date Between Jul 2022 and Feb 2023 (Word variations have been searched)	February 01, 2023 10:00PM	2	0
PUBMED	1	tuberculosis (2022-2023)	February 01, 2023 10:00PM	2	0
	2	tuberculosis and Screening (2022-2023)		636,262	
	3	Latent tuberculosis		46, 323	
	4	#2 and #3		1,282	
	5	IGRA		14	
	6	PPD OR TST		16	
	7	#4 and #6		93	
	8	#4 and #5		74	
	9	#4 and (#5 OR #6)		141	
HERDIN	1	Tuberculosis AND Screening	February 21, 2023 10:00PM	74	0

Appendix 2. PRISMA Flow Diagram



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

Appendix 3. GRADE Evidence Profile

Question: Should TST be used to screen for Latent TB Infection in asymptomatic apparently healthy individuals?

Sensitivity	0.80 (95% CI: 0.74 to 0.87)
Specificity	0.95 (95% CI: 0.94 to 0.97)

Prevalences	37.12%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 37.12%	
True positives (patients with Latent TB Infection)	12 studies 1323 patients	cohort & case-control type studies	serious[a]	not serious[a]	not serious	not serious	none	297 (275 to 323)	⊕⊕⊕◯ Moderate
False negatives (patients incorrectly classified as not having Latent TB Infection)								74 (48 to 96)	
True negatives (patients without Latent TB Infection)	3 studies 5149 patients	cohort & case-control type studies	not serious	not serious	not serious	not serious	none	597 (591 to 610)	⊕⊕⊕⊕ High
False positives (patients								32 (19 to 38)	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 37.12%	
incorrectly classified as having Latent TB Infection)									

Explanations

a. Variable quality in the quality, timing, and/or presence of reporting of testing.

Question: Should TST (10mm) be used to screen for Latent TB Infection in asypmtomatic aparently healthy individuals?

Sensitivity	0.81 (95% CI: 0.76 to 0.87)
Specificity	0.98 (95% CI: 0.97 to 0.99)

Prevalences	37.12 %

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of37.12%	
True positives (patients with Latent TB Infection)	15 studies 1427 patients	cohort & case-control type studies	serious[a]	not serious[a]	not serious	not serious	none	301 (282 to 323)	⨁⨁⨁◯ Moderate
False negatives								70 (48 to 89)	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of37.12%	
(patients incorrectly classified as not having Latent TB Infection)									
True negatives (patients without Latent TB Infection)	8 studies 9604 patients	cohort & case-control type studies	not serious	not serious	not serious	not serious	none	616 (610 to 623)	⨁⨁⨁⨁ High
False positives (patients incorrectly classified as having Latent TB Infection)								13 (6 to 19)	

Explanations

a. Variable quality in the quality, timing, and/or presence of reporting of testing.

Question: Should TST (15mm) be used to screen for Latent TB Infection in asypmtomatic aparently healthy individuals?

Sensitivity	0.60 (95% CI: 0.46 to 0.74)
Specificity	0.99 (95% CI: 0.98 to 0.99)

Prevalences	37.12 %

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of37.12%	
True positives (patients with Latent TB Infection)	9 studies 1004 patients	cohort & case-control type studies	serious[a]	not serious[a]	not serious	not serious	none	223 (171 to 275)	⊕⊕⊕◯ Moderate
False negatives (patients incorrectly classified as not having Latent TB Infection)								148 (96 to 200)	
True negatives (patients without Latent TB Infection)	10 studies 9563 patients	cohort & case-control type studies	not serious	not serious	not serious	not serious	none	623 (616 to 623)	⊕⊕⊕⊕ High
False positives (patients incorrectly classified as having Latent TB Infection)								6 (6 to 13)	

Explanations

a. Variable quality in the quality, timing, and/or presence of reporting of testing.

Question: Should IGRA T-SPOT.TB be used to screen for Latent TB Infection in asypmtomatic aparently healthy individuals?

Sensitivity	0.90 (95% CI: 0.87 to 0.92)
Specificity	0.95 (95% CI: 0.91 to 0.97)

Prevalences	37.12 %

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of37.12%	
True positives (patients with Latent TB Infection)	37 studies 5367 patients	cohort & case-control type studies	serious[a]	not serious[a]	not serious	not serious	none	334 (323 to 342)	⨁⨁⨁◯ Moderate
False negatives (patients incorrectly classified as not having Latent TB Infection)								37 (29 to 48)	
True negatives (patients without Latent TB Infection)	2 studies 1664 patients	cohort & case-control type studies	not serious	not serious	not serious	not serious	none	597 (572 to 610)	⨁⨁⨁⨁ High
False positives (patients incorrectly classified as having Latent TB Infection)								32 (19 to 57)	

Explanations

a. Variable quality in the quality, timing, and/or presence of reporting of testing.

Question: Should IGRA; QFT-GIT be used to screen for Latent TB Infection in asymptomatic apparently healthy individuals?

Sensitivity	0.81 (95% CI: 0.79 to 0.84)
Specificity	0.99 (95% CI: 0.98 to 0.97)

Prevalences	37.12 %

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of37.12%	
True positives (patients with Latent TB Infection)	48 studies 7055 patients	cohort & case-control type studies	serious[a]	not serious[a]	not serious	not serious	none	301 (293 to 312)	⨁⨁⨁◯ Moderate
False negatives (patients incorrectly classified as not having Latent TB Infection)								70 (59 to 78)	
True negatives (patients without Latent TB Infection)	3 studies 2090 patients	cohort & case-control type studies	not serious	not serious	not serious	not serious	none	623 (610 to 616)	⨁⨁⨁⨁ High
False positives (patients incorrectly								6 (13 to 19)	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of37.12%	
classified as having Latent TB Infection)									

Explanations

a. Variable quality in the quality, timing, and/or presence of reporting of testing.

Question: Should IGRA; QFT-Plus be used to screen for Latent TB Infection in asymptomatic apparently healthy individuals?

Sensitivity	0.89 (95% CI: 0.84 to 0.94)
Specificity	0.98 (95% CI: 0.95 to 0.97)

Prevalences	37.12 %

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of37.12%	
True positives (patients with Latent TB Infection)	11 studies 939 patients	cohort & case-control	serious[a]	not serious[a]	not serious	not serious	none	330 (312 to 349)	⊕⊕⊕◯ Moderate

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of37.12%	
False negatives (patients incorrectly classified as not having Latent TB Infection)		type studies						41 (22 to 59)	
True negatives (patients without Latent TB Infection)	1 studies 211 patients	cohort & case-control type studies	not serious	not serious	not serious	not serious	none	616 (597 to 610)	⊕⊕⊕⊕ High
False positives (patients incorrectly classified as having Latent TB Infection)								13 (19 to 32)	

Explanations

a. Variable quality in the quality, timing, and/or presence of reporting of testing.

Question: IGRA compared to TST for detecting latent TB infection

Setting:

Bibliography:

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IGRA	TST	Relative (95% CI)	Absolute (95% CI)		
General Population												
66	observational studies	not serious	serious[a]	not serious	serious[b]	none	10006/53799 (18.6%)	16623/53799 (30.9%)	**RR 0.54** (0.43 to 0.66)	**142 fewer per 1,000** (from 176 fewer to 105 fewer)	⨁◯◯◯ Very low	
Recent Contacts												
112	observational studies	not serious	serious[a]	not serious	serious[b]	none	13654/40016 (34.1%)	17887/40016 (44.7%)	**RR 0.63** (0.54 to 0.73)	**165 fewer per 1,000** (from 206 fewer to 121 fewer)	⨁◯◯◯ Very low	
High Burden Areas												

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IGRA	TST	Relative (95% CI)	Absolute (95% CI)		
15	observational studies	not serious	serious[a]	not serious	serious[b]	none	2842/5574 (51.0%)	3142/5574 (56.4%)	**RR 0.75** (0.60 to 0.94)	**141 fewer per 1,000** (from 225 fewer to 34 fewer)	⨁◯◯◯ Very low	

CI: confidence interval; **RR:** risk ratio

Explanations
a. High heterogeneity between studies
b. Wide confidence interval

Question: Current regimens compared to no treatment for Latent TB infection
Setting:
Bibliography:

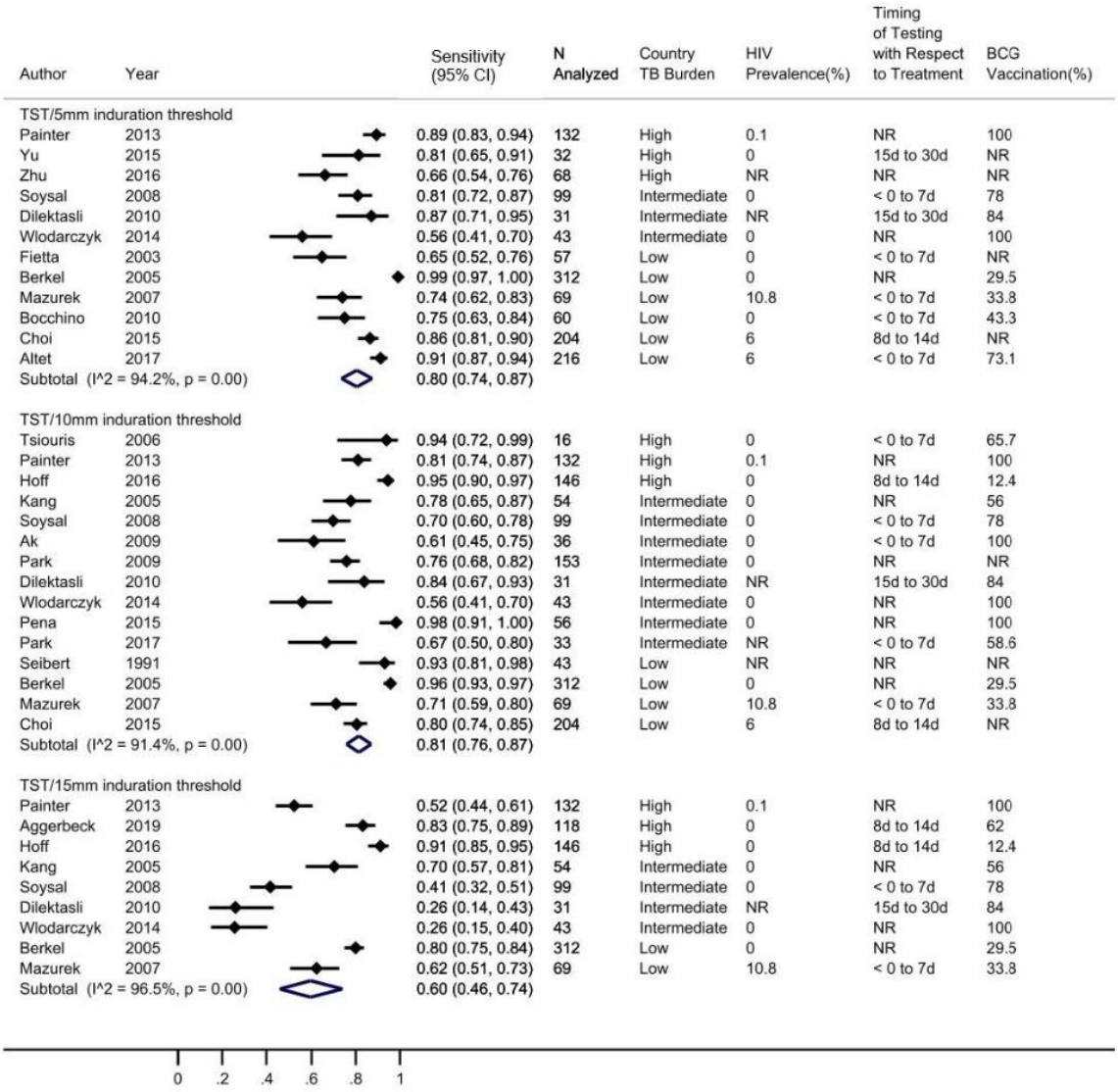
Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	current regimens	no treatment	Relative (95% CI)	Absolute (95% CI)		
Progression to Active TB												
61	randomised trials	not serious	serious[a]	not serious	serious[b]	none			**RR 0.65** (0.50 to 0.83)	**1 fewer per 1,000** (from 1 fewer to 1 fewer)	⊕⊕◯◯ Low	
Hepatotoxicity												
61	randomised trials	not serious	serious[a]	not serious	serious[b]	none			**RR 1.10** (0.40 to 3.17)	**1 fewer per 1,000** (from 3 fewer to 0 fewer)	⊕⊕◯◯ Low	
GI Adverse Events												
1	randomised trials	not serious	not serious	not serious	very serious[b]	none			**RR 1.33** (1.01 to 1.75)	**1 fewer per 1,000** (from 2 fewer to 1 fewer)	⊕⊕◯◯ Low	

CI: confidence interval; **RR:** risk ratio

Explanations
a. High heterogeneity among studies
b. Wide confidence interval

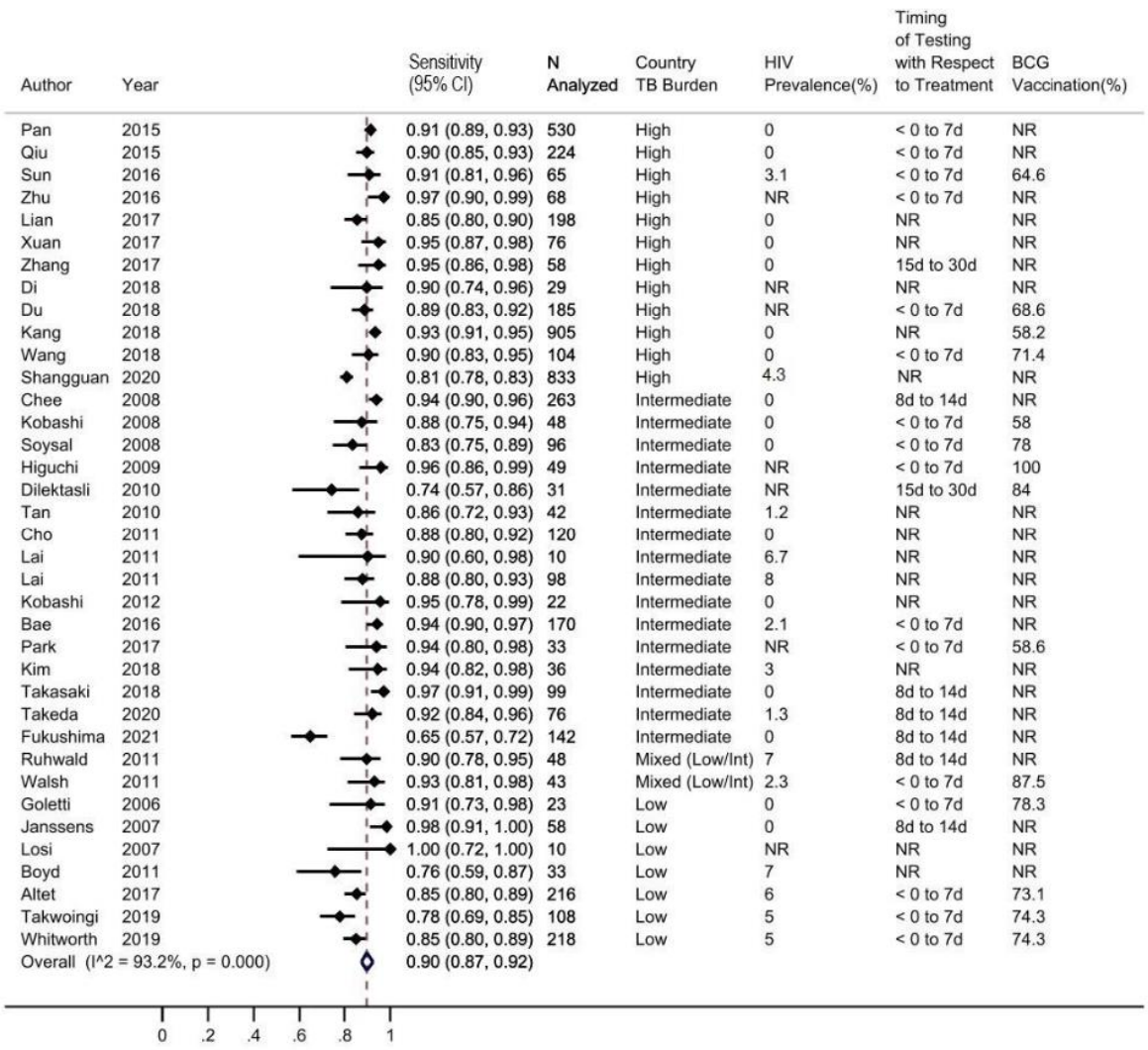
Appendix 4. Forest Plots

Figure 3. Individual Study and Pooled Estimates of Sensitivity for Various Thresholds of the TST for TB Infection



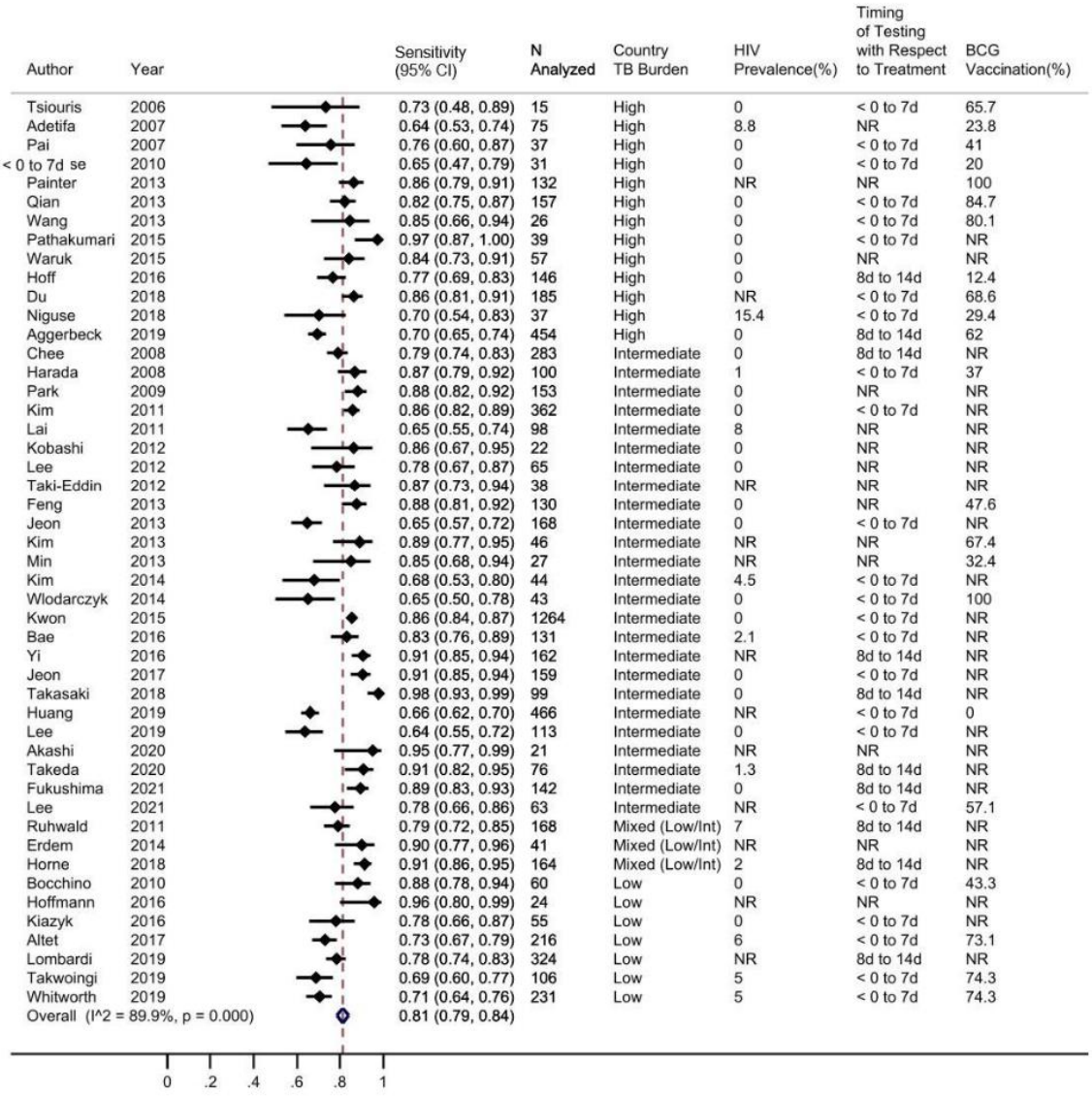
Abbreviations: BCG=Bacille Calmett-Guérin; CI=confidence interval; HIV=human immunodeficiency virus; I^2=the proportion of variation in study estimates due to heterogeneity; N=number; NR=not reported; TST=tuberculin skin test; TB=tuberculosis.

Figure 4. Individual Study and Pooled Estimates of Sensitivity for the T-SPOT.*TB* Test for TB Infection



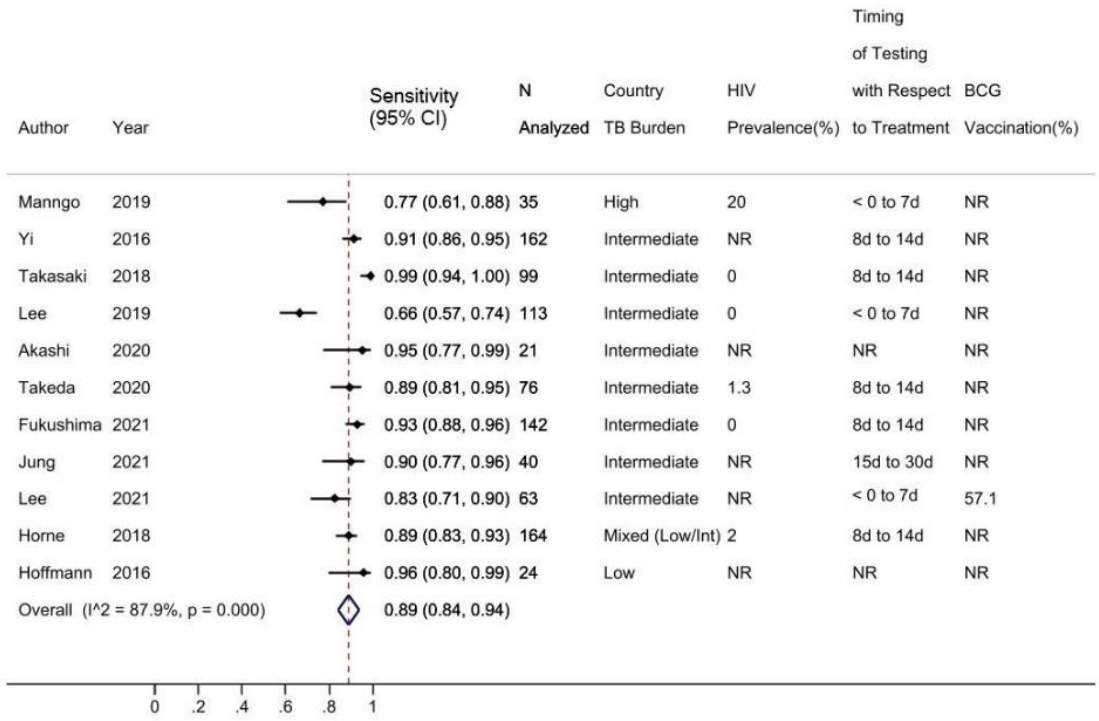
Abbreviations: BCG=Bacille Calmett-Guérin; CI=confidence interval; HIV=human immunodeficiency virus; I^2=the proportion of variation in study estimates due to heterogeneity; Int=Intermediate; N=number; NR=not reported; TB=tuberculosis.

Figure 5. Individual Study and Pooled Estimates of Sensitivity for the QFT-GIT Test for TB Infection



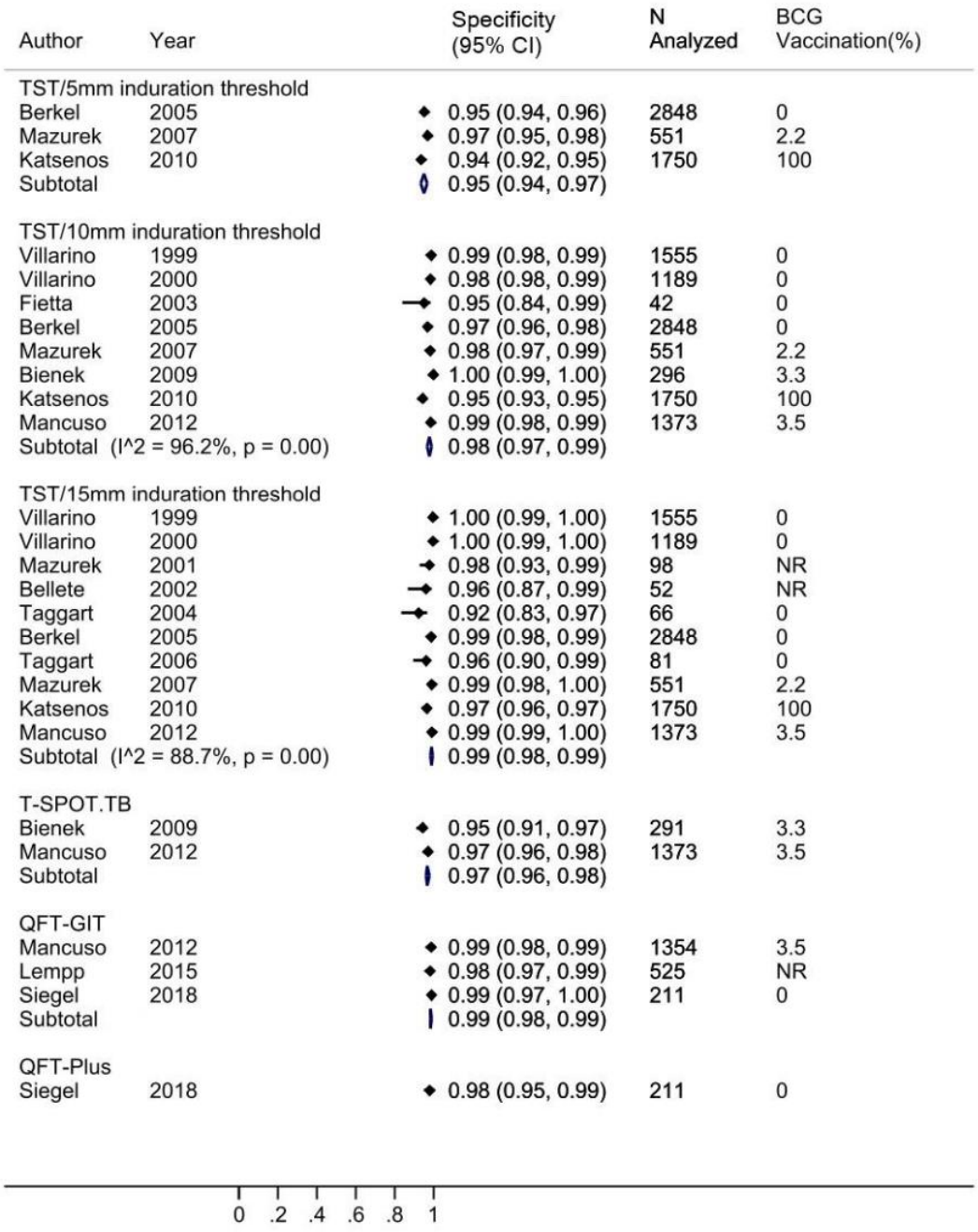
Abbreviations: BCG=Bacille Calmett-Guérin; CI=confidence interval; HIV=human immunodeficiency virus; I^2=the proportion of variation in study estimates due to heterogeneity; N=number; NR=not reported; TB=tuberculosis.

Figure 6. Individual Study and Pooled Estimates of Sensitivity for the QFT-Gold Plus Test for TB Infection



Abbreviations: BCG=Bacille Calmett-Guérin; CI=confidence interval; HIV=human immunodeficiency virus; I^2=the proportion of variation in study estimates due to heterogeneity; N=number; NR=not reported; TB=tuberculosis.

Figure 7. Individual Study and Pooled Estimates of Specificity for Various Thresholds of the TST and IGRA Tests for TB Infection



Abbreviations: BCG=Bacille Calmett-Guérin; CI=confidence interval; I^2=the proportion of variation in study estimates due to heterogeneity; N=number; NR=not reported; QFT-GIT=QuantiFERON-TB Gold-In-Tube® test (3rd-generation test); QFT-Plus=QuantiFERON-TB Gold Plus® test (4th generation test); T-SPOT.*TB*=Commercial ELISpot Assay; TST=tuberculin skin test.

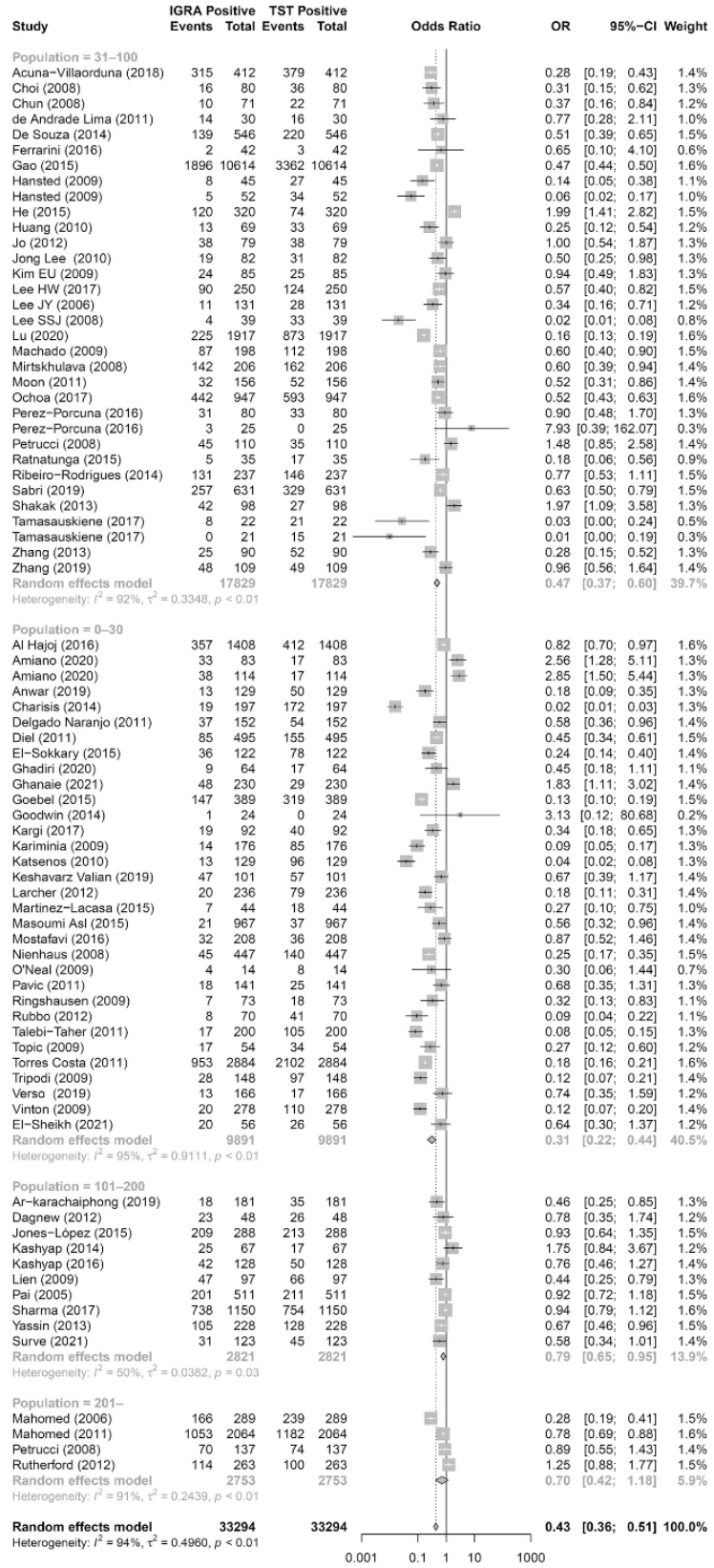


Figure 1: Forest plot of IGRA vs TST in immunocompetent individuals

Appendix 5. Evidence-to-Decision Framework Responses

Evidence to Decision Framework

Should screening for latent TB be done among asymptomatic, apparently healthy adults?

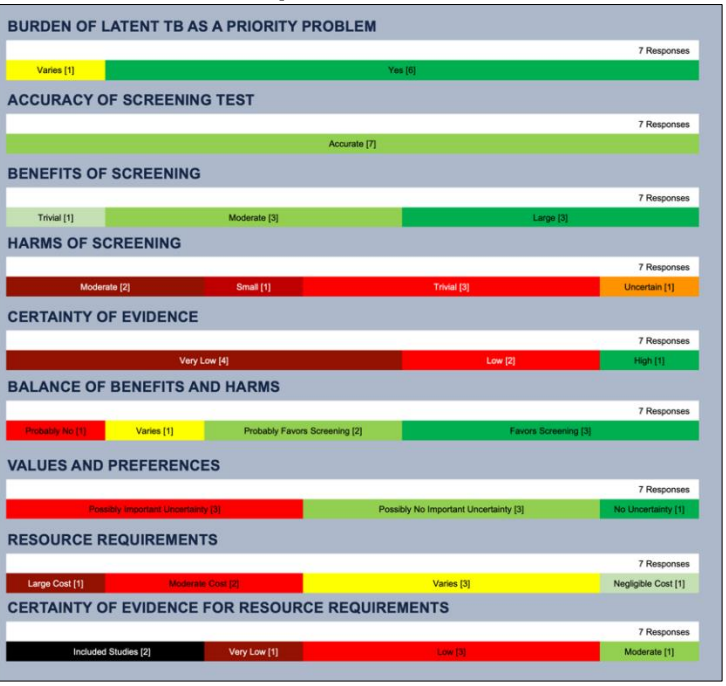
Population: Filipino adults

Intervention: Screening

Comparator: No screening

Outcomes: Need for early initiation of treatment, TB-related mortality, Prevention of transmission, TB prevention and control, TB-related morbidity, Incidence of TB

PHEx
PHILIPPINE PERIODIC HEALTH EXAMINATION



Evidence to Decision Framework

Should screening for latent TB be done among asymptomatic, apparently healthy adults?

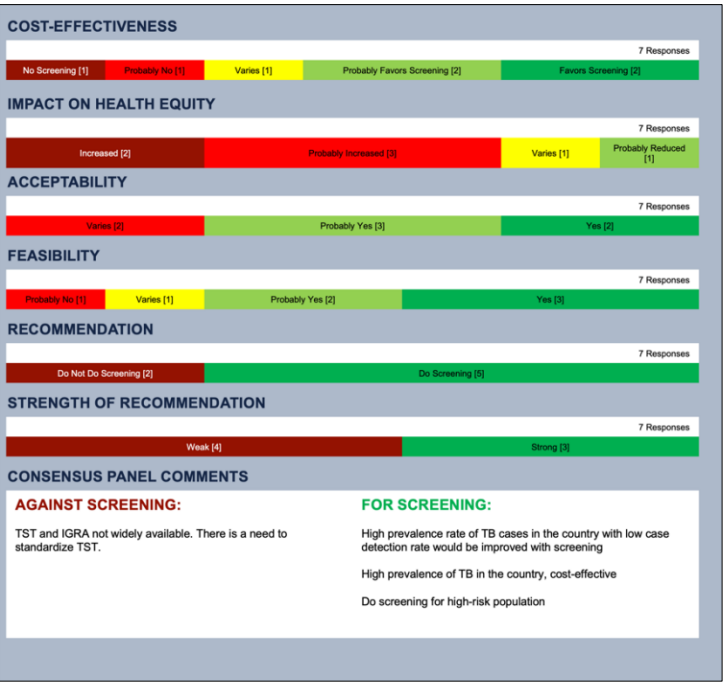
Population: Filipino adults

Intervention: Screening

Comparator: No screening

Outcomes: Need for early initiation of treatment, TB-related mortality, Prevention of transmission, TB prevention and control, TB-related morbidity, Incidence of TB

PHEx
PHILIPPINE PERIODIC HEALTH EXAMINATION



CONSENSUS PANEL COMMENTS

AGAINST SCREENING:

TST and IGRA not widely available. There is a need to standardize TST.

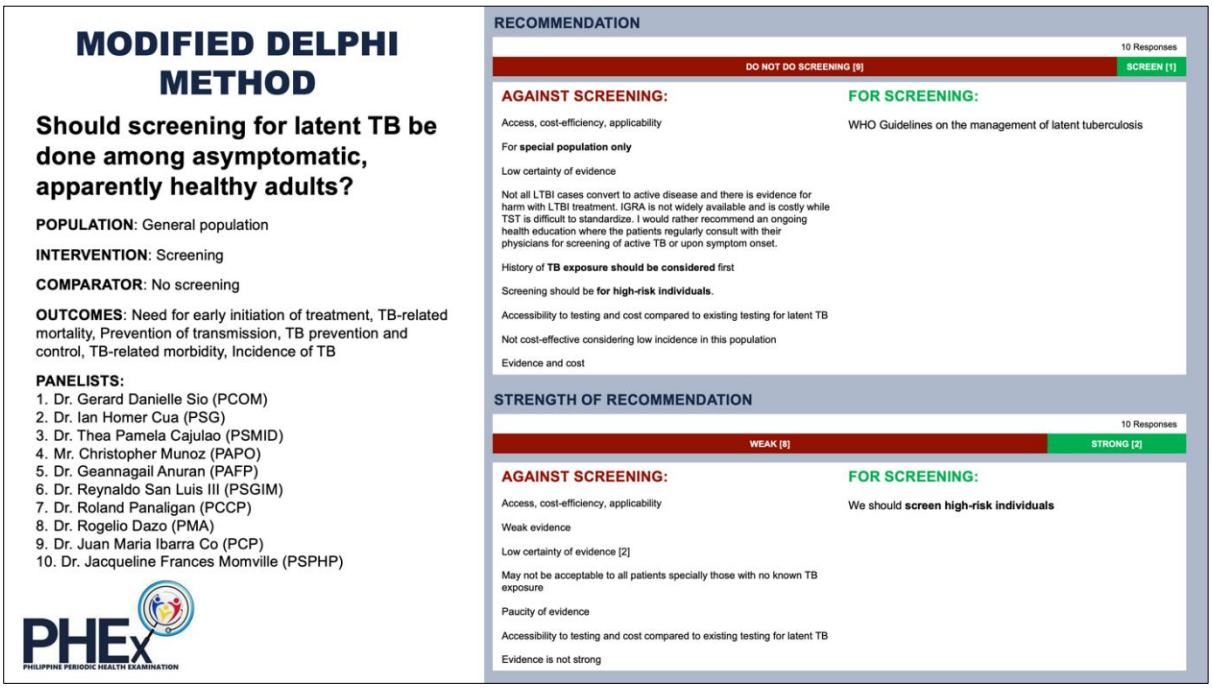
FOR SCREENING:

High prevalence rate of TB cases in the country with low case detection rate would be improved with screening

High prevalence of TB in the country, cost-effective

Do screening for high-risk population

Appendix 6. Modified Delphi Voting Results for LTBI Screening among asymptomatic, apparently healthy adults (general population)



MODIFIED DELPHI METHOD

Should screening for latent TB be done among asymptomatic, apparently healthy adults?

POPULATION: General population

INTERVENTION: Screening

COMPARATOR: No screening

OUTCOMES: Need for early initiation of treatment, TB-related mortality, Prevention of transmission, TB prevention and control, TB-related morbidity, Incidence of TB

PANELISTS:
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RECOMMENDATION

10 Responses

DO NOT DO SCREENING [9] | SCREEN [1]

AGAINST SCREENING:

Access, cost-efficiency, applicability

For **special population only**

Low certainty of evidence

Not all LTBI cases convert to active disease and there is evidence for harm with LTBI treatment. IGRA is not widely available and is costly while TST is difficult to standardize. I would rather recommend an ongoing health education where the patients regularly consult with their physicians for screening of active TB or upon symptom onset.

History of **TB exposure should be considered** first

Screening should be **for high-risk individuals**.

Accessibility to testing and cost compared to existing testing for latent TB

Not cost-effective considering low incidence in this population

Evidence and cost

FOR SCREENING:

WHO Guidelines on the management of latent tuberculosis

STRENGTH OF RECOMMENDATION

10 Responses

WEAK [8] | STRONG [2]

AGAINST SCREENING:

Access, cost-efficiency, applicability

Weak evidence

Low certainty of evidence [2]

May not be acceptable to all patients specially those with no known TB exposure

Paucity of evidence

Accessibility to testing and cost compared to existing testing for latent TB

Evidence is not strong

FOR SCREENING:

We should **screen high-risk individuals**

9.10 Screening for Intestinal Parasitism

Appendix 1. Search Strategy

Systematic search was conducted using Pubmed database from February to March 2023 for studies investigating screening for intestinal parasitism among asymptomatic, apparently healthy individuals. Database was searched using the following search terms: “intestinal parasites”, “soil-transmitted helminth”, “helminthiasis”, “screening”. Search was further refined using the following search parameters:
(intestinal parasites OR soil-transmitted helminth OR Helminthiasis OR Helminths OR Ascariasis) AND (screening) AND (reduced incidence OR reduced morbidity OR reduced mortality)

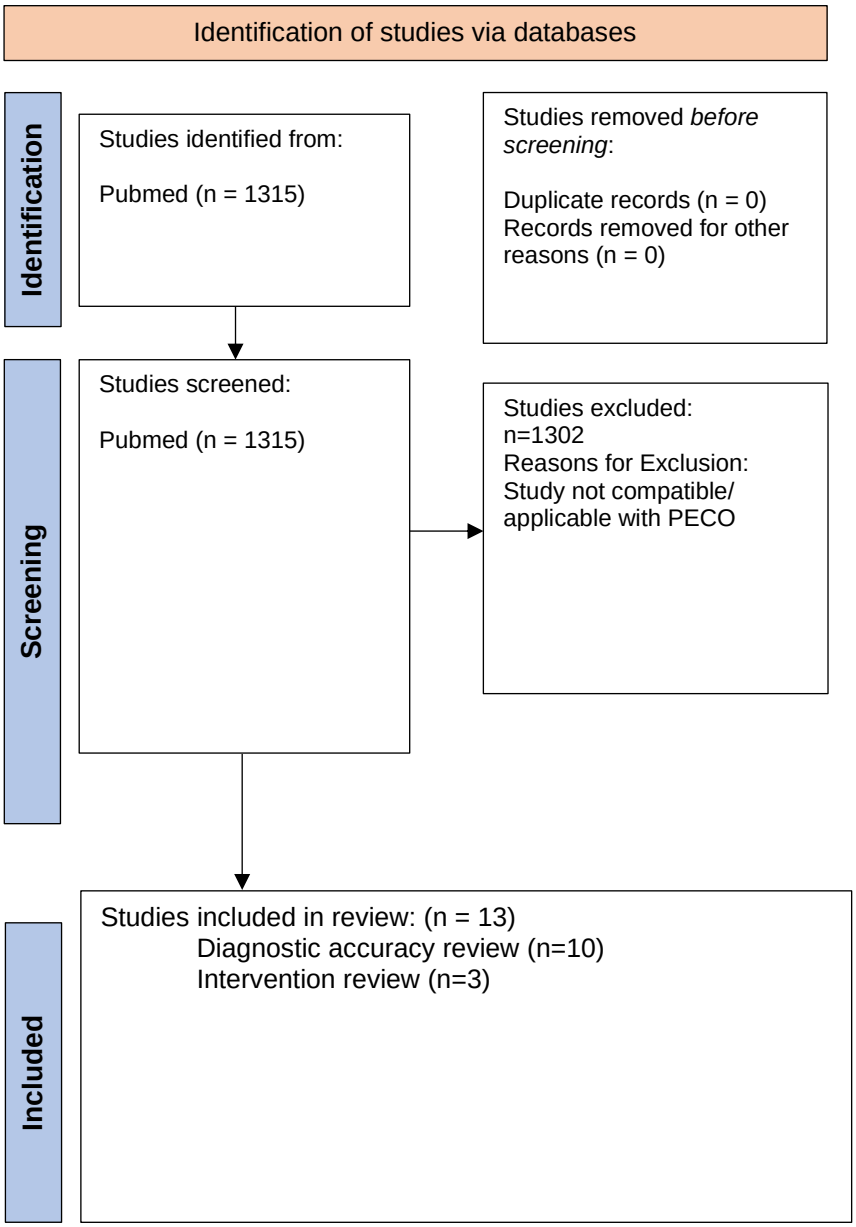
RCT, meta-analysis, systematic review, and human filter were put in place. Results of search showed studies that described interventions such as mass drug administration, community based health education, ensuring proper water access, sanitation, and hygiene, rather than use of screening tests.

Search parameters were modified into the following:
(intestinal parasites OR soil-transmitted helminth OR Helminthiasis OR Helminths OR Ascariasis) AND (diagnostic techniques and procedures OR Kato* OR concentration* OR direct* OR wet* OR parasite egg count) AND (sensitivity and specificity OR accuracy)
Meta-analysis, systematic review, and human filter were put in place. – 30 results

To broaden the search, search was done again with the abovementioned search terms and the last 10 years and human filter put in place. -1260 (100 assessed)

Systematic search was also conducted using Pubmed regarding treatment for individuals with intestinal parasitism. The following search terms were used:
(intestinal parasites OR soil-transmitted helminth OR Helminthiasis OR Helminths or Ascariasis) AND (early treatment OR albendazole OR mebendazole OR pyrantel pamoate OR anthelminthic OR deworming) AND (reduced incidence OR reduced morbidity OR reduced mortality)
The meta analysis and systematic review filter were put in place – 25 results

Appendix 2. PRISMA Flow Diagram



Appendix 3. Characteristics of Included Studies

Title/ Author	Study design	Country	Number of participants	Population	Screening Test	Outcomes
Diagnostic accuracy						
Sensitivity of diagnostic tests for human soil-transmitted helminth infections: a meta-analysis in the absence of a true gold standard Nikolay et al 2014 (10)	Systematic review	Multiple countries	20 studies	General population	Fecalysis, Kato-Katz, FECT	Sensitivity fecalysis: sensitivity 52.1% (46.6-57.7%) for Ascaris lumbricoides, 62.8% (56.9-68.9%) for Trichuris trichiura, 42.8% (38.3-48.4%) for hookworm; 1 slide Kato-Katz (KK): sensitivity 63.8% (59.1-68.6%) for Ascaris lumbricoides, 82.2% (80.1-84.5%) for Trichuris trichiura, 59.5% (56.9-62.2%) for hookworm; FECT: 56.9% (51.1-63.5%) for Ascaris lumbricoides, 81.2% (73.0-89.2%) for Trichuris trichiura, 53.0% (48.6-57.5%) for hookworm
Diagnostic sensitivity of direct wet mount microscopy for soil-transmitted helminth infections in Jimma Town, Ethiopia Dana et al 2020 (11)	Cross sectional study	Ethiopia	600	School children	Fecalysis, Kato-Katz	Sensitivity direct microscopy/ fecalysis: Any STH 51.0% (46.2-55.9)
Evaluating the performance of diagnostic methods for soil transmitted helminths in the Amhara National Regional State, Northwest Ethiopia Fenta et al 2020 (12)	Cross sectional study	Ethiopia	520	School children	Kato-Katz, FECT	Sensitivity KK sensitivity: Any STH 55.2% (48.5–61.7), Ascaris lumbricoides 50.0% (35.2–64.8), Trichuris trichiura 75.0% (31.0–95.4) , hookworm 55.7% (48.3–62.8) FECT sensitivity: Any STH 57.9% (51.0–64.5), Ascaris lumbricoides 32.5% (20.1–48.0), Trichuris trichiura 75.0% (31.0–95.4), hookworm 64.2% (56.9–70.9)

Comparison among FLOTAC, Kato-Katz and formalin ether concentration techniques for diagnosis of intestinal parasitic infections in school children in an Egyptian rural setting Allam et al 2021 (13)	Cross sectional study	Egypt	90	School children	Kato-Katz, FECT	Sensitivity KK sensitivity: Any STH 100% (93-100), FECT sensitivity 48% (34-62)
Diagnostic performance of a single and duplicate Kato-Katz, Mini-FLOTAC, FECPAKG2 and qPCR for the detection and quantification of soil-transmitted helminths in three endemic countries Cools et al 2019 (14)	Cross sectional study	Ethiopia, Lao PDR, Tanzania	1521	School children	Kato-Katz	Sensitivity KK sensitivity: Ascaris lumbricoides 71.9% (68.0- 75.6), Trichuris trichiura, 88.1% (86.0- 90.2), hookworm 72.6% (69.2; 76.0)
Comparison of direct wet mount, Kato-Katz and formol ether sedimentation technique for the diagnosis of hookworm infection in Debre Elias Woreda, Northwest Ethiopia Aschale et al 2021 (15)	Cross sectional study	Ethiopia	192	General population	Fecalysis, Kato-Katz, FECT	Sensitivity Direct wet mount/ fecalysis sensitivity: hookworm 61.4% (53.6- 68.9) KK sensitivity: hookworm 97.4% (93.9- 99.1) FECT sensitivity: hookworm 85.6% (79.4- 90.5)
Intestinal Parasite Infections and Accuracy of Direct Thin and Thick Smear, Formol-Ether Sedimentation, Centrifugal Flotation, and Mini-FLOTAC Techniques	Cross sectional study	Egypt	100	General population	Fecalysis, Kato-Katz, FECT	Sensitivity Fecalysis Sensitivity for helminths73.9% (CI 0.76-0.98), Kato-Katz Sensitivity for helminths 87% (CI 0.93-1.0),

Among Patients with Gastrointestinal Tract Disorders from the Greater Cairo Region, Egypt Hussein et al 2017 (16)						FECT sensitivity for helminths 91.3% (CI 0.89-1.0)
Diagnostic Accuracy and Cost-Effectiveness of Alternative Methods for Detection of Soil-Transmitted Helminths in a Post-Treatment Setting in Western Kenya Assefa et al 2014 (17)	Cross sectional study	Kenya	525	School children	Kato-Katz	Sensitivity KK sensitivity Any STH 52.0% (38.5–65.9), Ascaris lumbricoides 53.3% (33.9–74.2), Trichuris trichiura 52.9% (37.7–72.5), hookworm 52.6% (37.8–67.1)
The increased sensitivity of qPCR in comparison to Kato-Katz is required for the accurate assessment of the prevalence of soil-transmitted helminth infection in settings that have received multiple rounds of mass drug administration Dunn et al 2020 (18)	Cross sectional study	Myanmar	648	General population	Kato-Katz	Sensitivity KK sensitivity Ascaris lumbricoides 45.45%, Trichuris trichiura 52.30%, hookworm 25.30%
Comparison of multi-parallel qPCR and double-slide Kato-Katz for detection of soil-transmitted helminth infection among children in rural Bangladesh Benjamin-Chung et al 2020	Cross sectional study	Bangladesh	2800	School children	Kato-Katz	Sensitivity KK sensitivity Ascaris lumbricoides 49% (34- 64), Trichuris trichiura 52% (33- 71), hookworm 32% (22- 41)

(19)						

Title/ Author	Study design	Country	Number of participants	Population	Intervention	Outcomes
Anthelmintic drugs for treating ascariasis (Cochrane database systematic review) Conterno et al 2020 (20)	Systematic review	Multiple countries	20 studies	General population	Albendazole, mebendazole, ivermectin	Parasitological cure
Deworming in non-pregnant adolescent girls and adult women: a systematic review and meta-analysis Tanjong Ghogomu et al 2018 (21)	Systematic review	Multiple countries	4 studies	Adolescent and adult non-pregnant women	Deworming vs non-deworming	Prevalence of roundworm, hookworm infection, prevalence of anemia, iron-deficiency
Differential effect of mass deworming and targeted deworming for soil-transmitted helminth control in children: a systematic review and meta-analysis Clarke et al 2017 (22)	Systematic review	Multiple countries	56 studies	School children	Community wide vs children only deworming	Prevalence of ascariasis, trichuriasis, hookworm infection

Appendix 4. GRADE Evidence Profile

Question: Should fecalysis be used to screen for ascariasis in the general population?

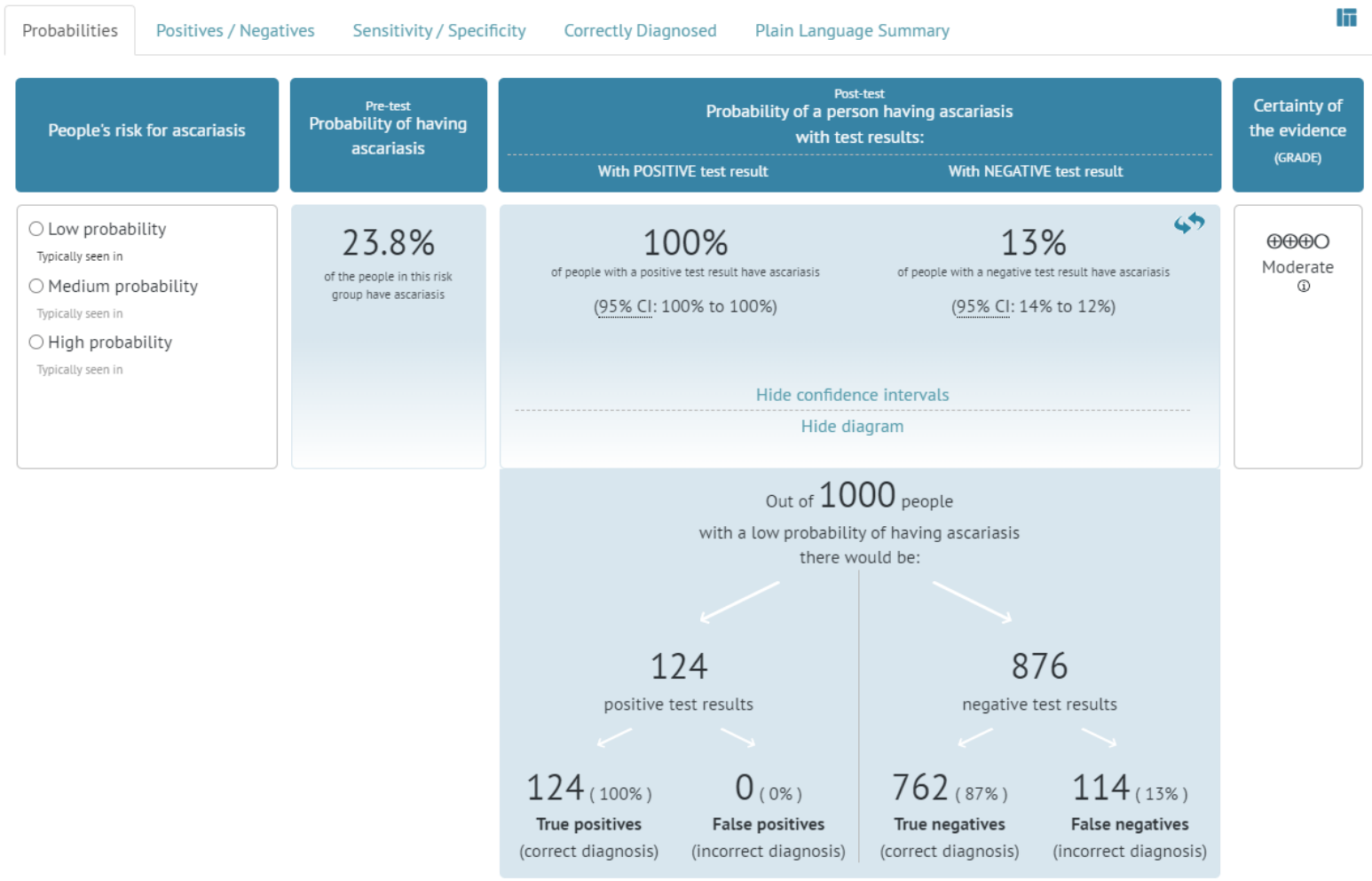
Sensitivity	0.52 (95% CI: 0.47 to 0.58)
Specificity	1.00 (95% CI: 1.00 to 1.00)

Prevalences	23.8%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of23.8%	
True positives (patients with ascariasis)	7 studies 1465 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	124 (111 to 137)	⨁⨁⨁◯ Moderate
False negatives (patients incorrectly classified as not having ascariasis)								114 (101 to 127)	
True negatives (patients without ascariasis)	7 studies 1465 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	762 (762 to 762)	⨁⨁⨁◯ Moderate
False positives (patients incorrectly classified as having ascariasis)								0 (0 to 0)	

Explanations

a. studies do not directly answer primary question


Probabilities
Positives / Negatives
Sensitivity / Specificity
Correctly Diagnosed
Plain Language Summary
People's risk for ascariasis
Pre-test
Probability of having ascariasis
Post-test
Probability of a person having ascariasis with test results:
With POSITIVE test result
With NEGATIVE test result
Certainty of the evidence
(GRADE)
Low probability
Typically seen in
Medium probability
Typically seen in
High probability
Typically seen in
23.8%
of the people in this risk group have ascariasis
100%
of people with a positive test result have ascariasis
(95% CI: 100% to 100%)
13%
of people with a negative test result have ascariasis
(95% CI: 14% to 12%)
Hide confidence intervals
Hide diagram
⊕⊕⊕○
Moderate
Out of 1000 people
with a low probability of having ascariasis
there would be:
124
positive test results
876
negative test results
124 (100%)
True positives
(correct diagnosis)
0 (0%)
False positives
(incorrect diagnosis)
762 (87%)
True negatives
(correct diagnosis)
114 (13%)
False negatives
(incorrect diagnosis)

Question: Should fecalysis be used to screen for trichuriasis in the general population?

Sensitivity	0.63 (95% CI: 0.57 to 0.69)
Specificity	1.00 (95% CI: 1.00 to 1.00)

Prevalences	32%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of32%	
True positives (patients with trichuriasis)	7 studies 1465 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	201 (182 to 220)	⨁⨁⨁◯ Moderate
False negatives (patients incorrectly classified as not having trichuriasis)								119 (100 to 138)	
True negatives (patients without trichuriasis)	7 studies 1465 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	680 (680 to 680)	⨁⨁⨁◯ Moderate
False positives (patients incorrectly classified as having trichuriasis)								0 (0 to 0)	

Explanations

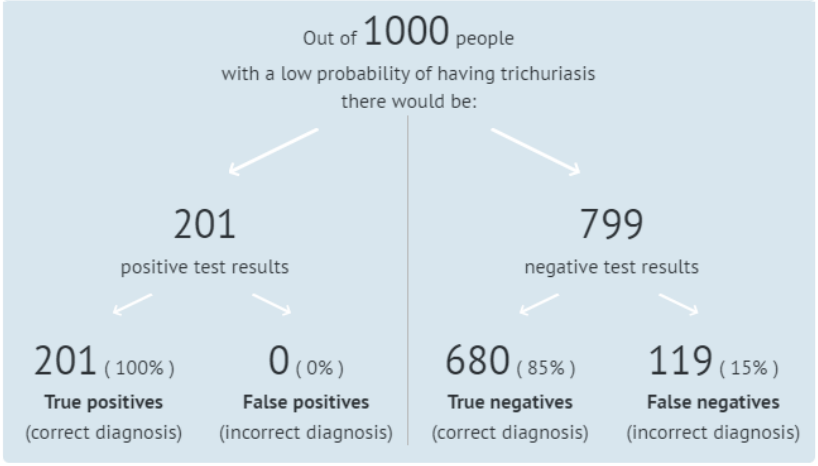
a. studies do not directly answer primary question

Probabilities | Positives / Negatives | Sensitivity / Specificity | Correctly Diagnosed | Plain Language Summary

People's risk for trichuriasis	Pre-test Probability of having trichuriasis	Post-test Probability of a person having trichuriasis with test results: With POSITIVE test result	Post-test Probability of a person having trichuriasis with test results: With NEGATIVE test result	Certainty of the evidence (GRADE)
○ Low probability Typically seen in ○ Medium probability Typically seen in ○ High probability Typically seen in	32% of the people in this risk group have trichuriasis	100% of people with a positive test result have trichuriasis (95% CI: 100% to 100%)	15% of people with a negative test result have trichuriasis (95% CI: 17% to 13%)	⊕⊕⊕○ Moderate

Hide confidence intervals

Hide diagram



Question: Should fecalysis be used to screen for hookworm infection in the general population?

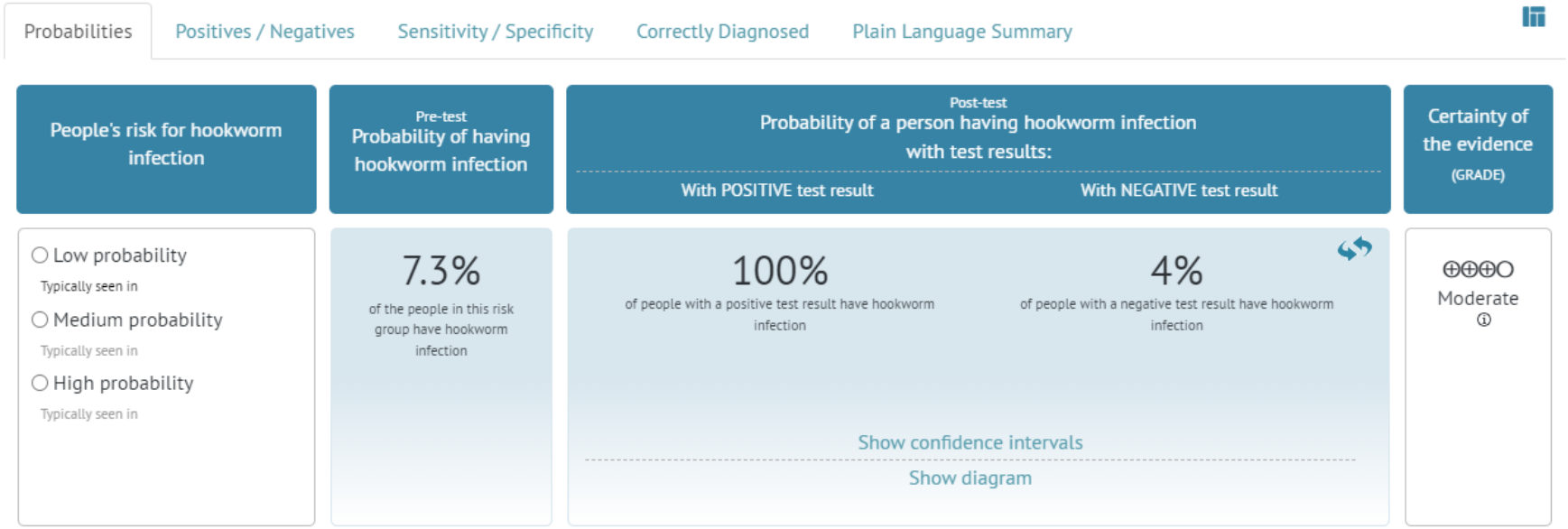
Sensitivity	0.43 (95% CI: 0.38 to 0.48)
Specificity	1.00 (95% CI: 1.00 to 1.00)

Prevalences	7.3%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of7.3%	
True positives (patients with hookworm infection)	7 studies 1465 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	31 (28 to 35)	⨁⨁⨁◯ Moderate
False negatives (patients incorrectly classified as not having hookworm infection)								42 (38 to 45)	
True negatives (patients without hookworm infection)	7 studies 1465 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	927 (927 to 927)	⨁⨁⨁◯ Moderate
False positives (patients incorrectly classified as having hookworm infection)								0 (0 to 0)	

Explanations

a. studies do not directly answer primary question



Question: Should Kato-Katz be used to screen for ascariasis in the general population?

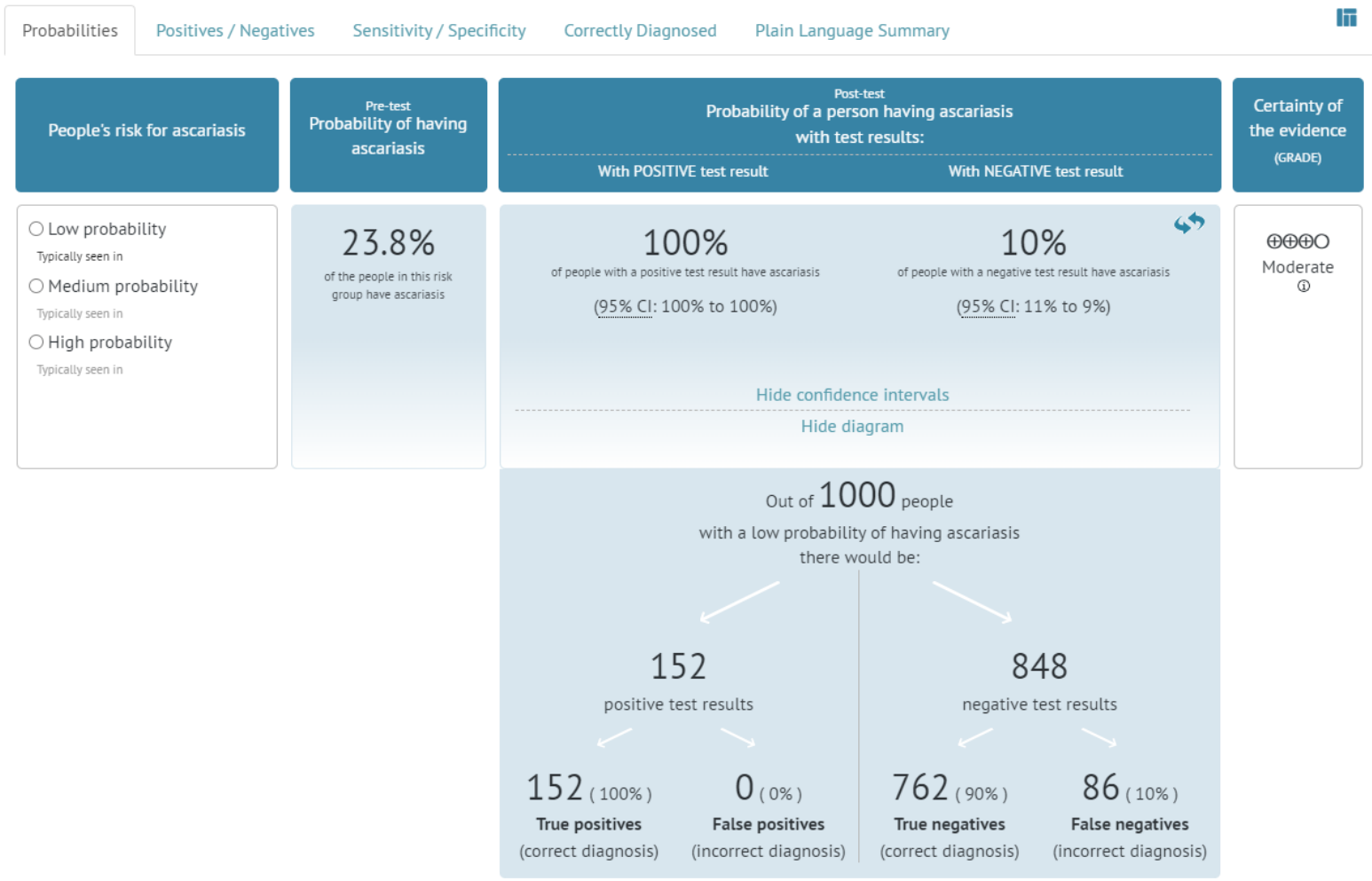
Sensitivity	0.64 (95% CI: 0.59 to 0.69)
Specificity	1.00 (95% CI: 1.00 to 1.00)

Prevalences	23.8%	0%	0%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of23.8%	pre-test probability of0%	pre-test probability of0%	
True positives (patients with ascariasis)	20 studies 8571 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	152 (141 to 163)	0 (0 to 0)	0 (0 to 0)	⨁⨁⨁◯ Moderate
False negatives (patients incorrectly classified as not having ascariasis)								86 (75 to 97)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without ascariasis)	20 studies 8571 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	762 (762 to 762)	1000 (1000 to 1000)	1000 (1000 to 1000)	⨁⨁⨁◯ Moderate
False positives (patients incorrectly classified as having ascariasis)								0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	

Explanations

a. studies do not directly answer primary question


Probabilities
Positives / Negatives
Sensitivity / Specificity
Correctly Diagnosed
Plain Language Summary
People's risk for ascariasis
Pre-test
Probability of having ascariasis
Post-test
Probability of a person having ascariasis with test results:
With POSITIVE test result
With NEGATIVE test result
Certainty of the evidence
(GRADE)
Low probability
Typically seen in
Medium probability
Typically seen in
High probability
Typically seen in
23.8%
of the people in this risk group have ascariasis
100%
of people with a positive test result have ascariasis
(95% CI: 100% to 100%)
10%
of people with a negative test result have ascariasis
(95% CI: 11% to 9%)
Hide confidence intervals
Hide diagram
⊕⊕⊕○
Moderate
Out of 1000 people
with a low probability of having ascariasis
there would be:
152
positive test results
848
negative test results
152 (100%)
True positives
(correct diagnosis)
0 (0%)
False positives
(incorrect diagnosis)
762 (90%)
True negatives
(correct diagnosis)
86 (10%)
False negatives
(incorrect diagnosis)

Question: Should Kato-Katz be used to screen for trichuriasis in the general population?

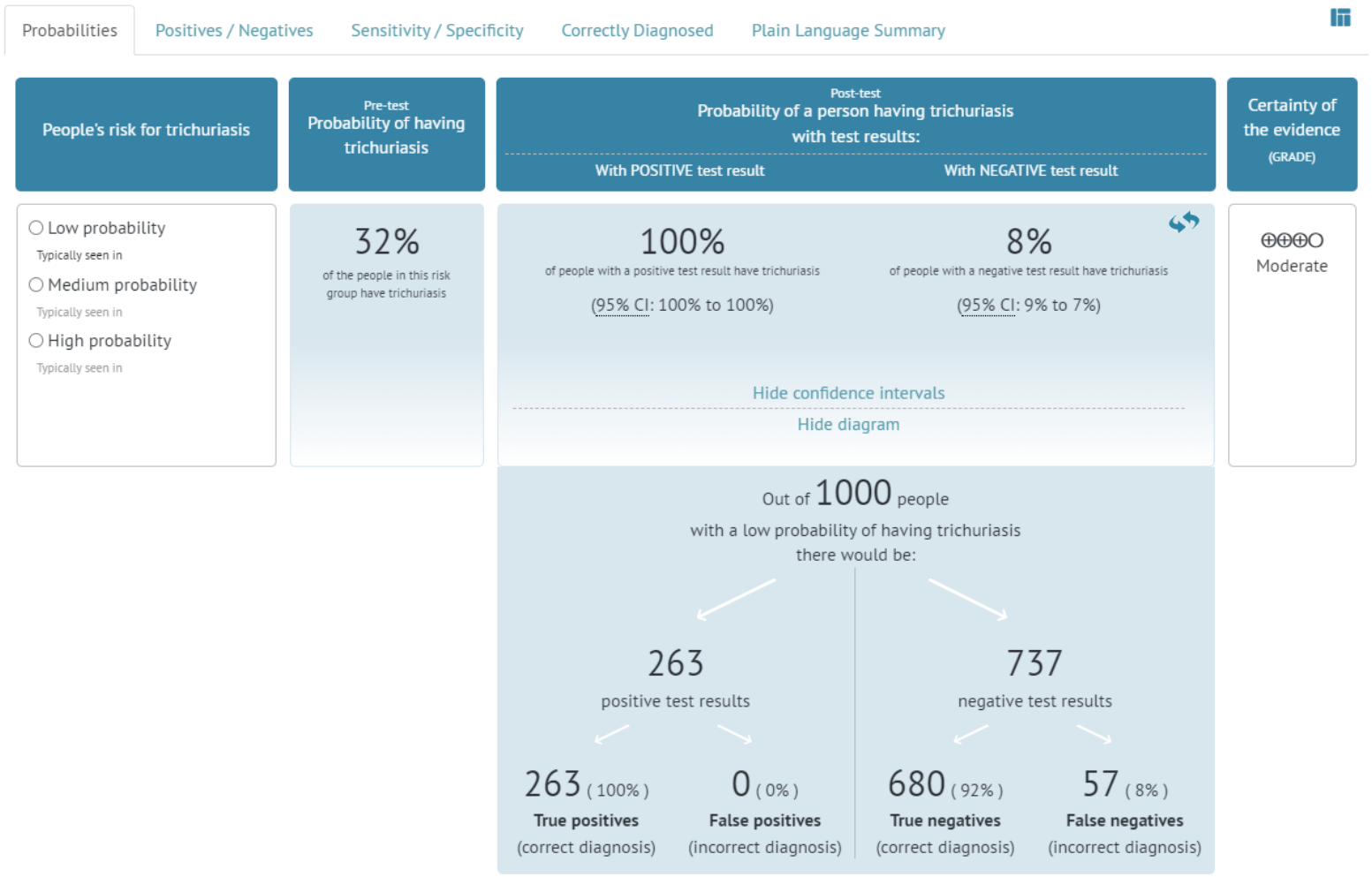
Sensitivity	0.82 (95% CI: 0.80 to 0.84)
Specificity	1.00 (95% CI: 1.00 to 1.00)

Prevalences	32%	0%	0%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of32%	pre-test probability of0%	pre-test probability of0%	
True positives (patients with trichuriasis)	20 studies 8571 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	263 (256 to 270)	0 (0 to 0)	0 (0 to 0)	⨁⨁⨁◯ Moderate
False negatives (patients incorrectly classified as not having trichuriasis)								57 (50 to 64)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without trichuriasis)	20 studies 8571 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	680 (680 to 680)	1000 (1000 to 1000)	1000 (1000 to 1000)	⨁⨁⨁◯ Moderate
False positives (patients incorrectly classified as having trichuriasis)								0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	

Explanations

a. studies do not directly answer primary question


Probabilities
Positives / Negatives
Sensitivity / Specificity
Correctly Diagnosed
Plain Language Summary
People's risk for trichuriasis
Pre-test
Probability of having trichuriasis
Post-test
Probability of a person having trichuriasis with test results:
With POSITIVE test result
With NEGATIVE test result
Certainty of the evidence (GRADE)
Low probability
Typically seen in
Medium probability
Typically seen in
High probability
Typically seen in
32%
of the people in this risk group have trichuriasis
100%
of people with a positive test result have trichuriasis
(95% CI: 100% to 100%)
8%
of people with a negative test result have trichuriasis
(95% CI: 9% to 7%)
⊕⊕⊕○
Moderate
Hide confidence intervals
Hide diagram
Out of 1000 people
with a low probability of having trichuriasis
there would be:
263
positive test results
737
negative test results
263 (100%)
True positives
(correct diagnosis)
0 (0%)
False positives
(incorrect diagnosis)
680 (92%)
True negatives
(correct diagnosis)
57 (8%)
False negatives
(incorrect diagnosis)

Question: Should Kato-Katz be used to screen for hookworm infection in the general population?

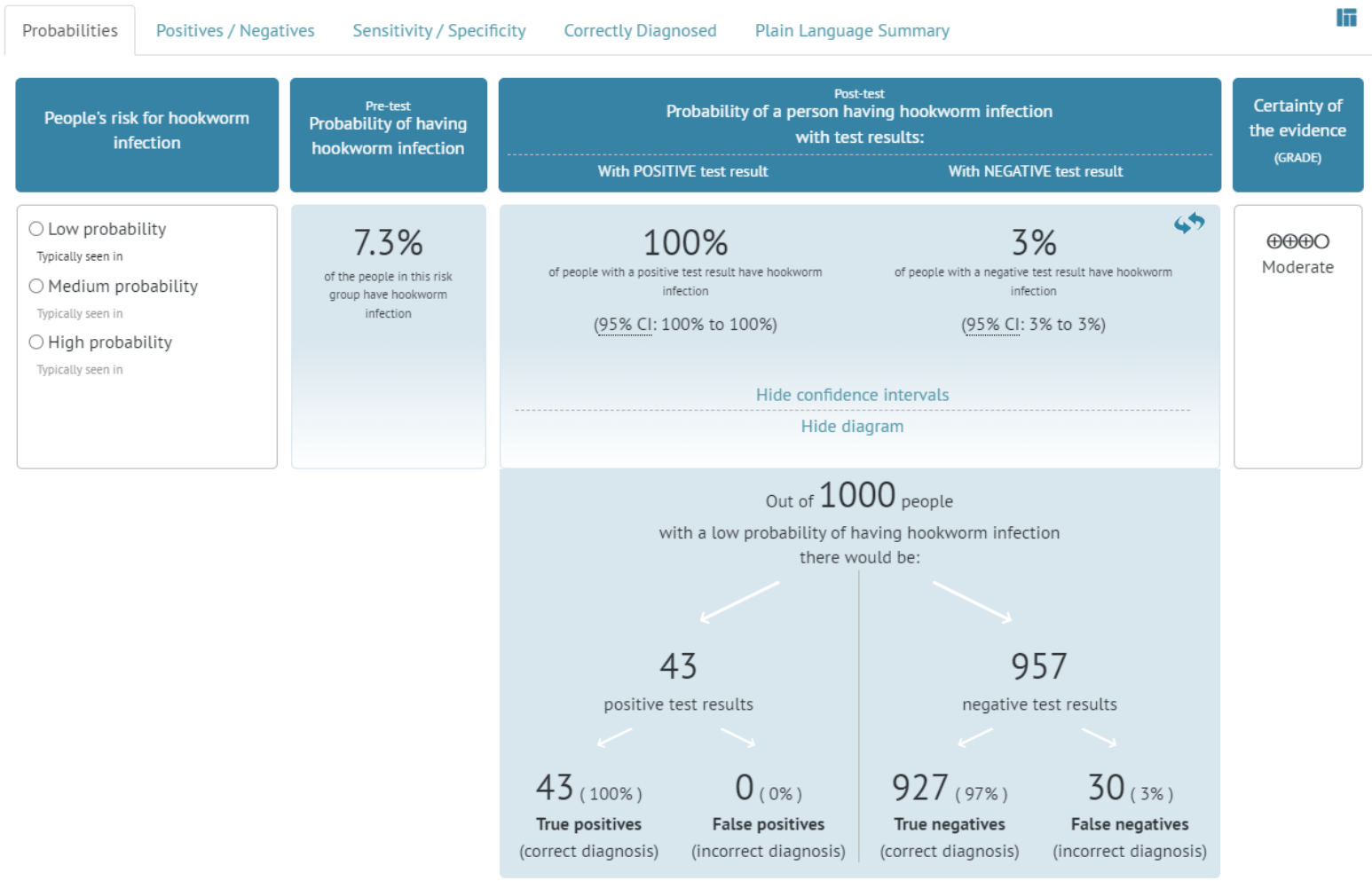
Sensitivity	0.59 (95% CI: 0.57 to 0.62)
Specificity	1.00 (95% CI: 1.00 to 1.00)

Prevalences	7.3%	0%	0%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of7.3%	pre-test probability of0%	pre-test probability of0%	
True positives (patients with hookworm infection)	20 studies 8571 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	43 (42 to 45)	0 (0 to 0)	0 (0 to 0)	⨁⨁⨁◯ Moderate
False negatives (patients incorrectly classified as not having hookworm infection)								30 (28 to 31)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without hookworm infection)	20 studies 8571 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	927 (927 to 927)	1000 (1000 to 1000)	1000 (1000 to 1000)	⨁⨁⨁◯ Moderate
False positives (patients incorrectly classified as having hookworm infection)								0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	

Explanations

a. studies do not directly answer primary question


Probabilities
Positives / Negatives
Sensitivity / Specificity
Correctly Diagnosed
Plain Language Summary
People's risk for hookworm infection
Pre-test
Probability of having hookworm infection
Post-test
Probability of a person having hookworm infection with test results:
With POSITIVE test result
With NEGATIVE test result
Certainty of the evidence
(GRADE)
Low probability
Typically seen in
Medium probability
Typically seen in
High probability
Typically seen in
7.3%
of the people in this risk group have hookworm infection
100%
of people with a positive test result have hookworm infection
(95% CI: 100% to 100%)
3%
of people with a negative test result have hookworm infection
(95% CI: 3% to 3%)
Hide confidence intervals
Hide diagram
⊕⊕⊕○
Moderate
Out of 1000 people
with a low probability of having hookworm infection
there would be:
43
positive test results
957
negative test results
43 (100%)
True positives
(correct diagnosis)
0 (0%)
False positives
(incorrect diagnosis)
927 (97%)
True negatives
(correct diagnosis)
30 (3%)
False negatives
(incorrect diagnosis)

Question: Should FECT be used to screen for ascariasis in the general population?

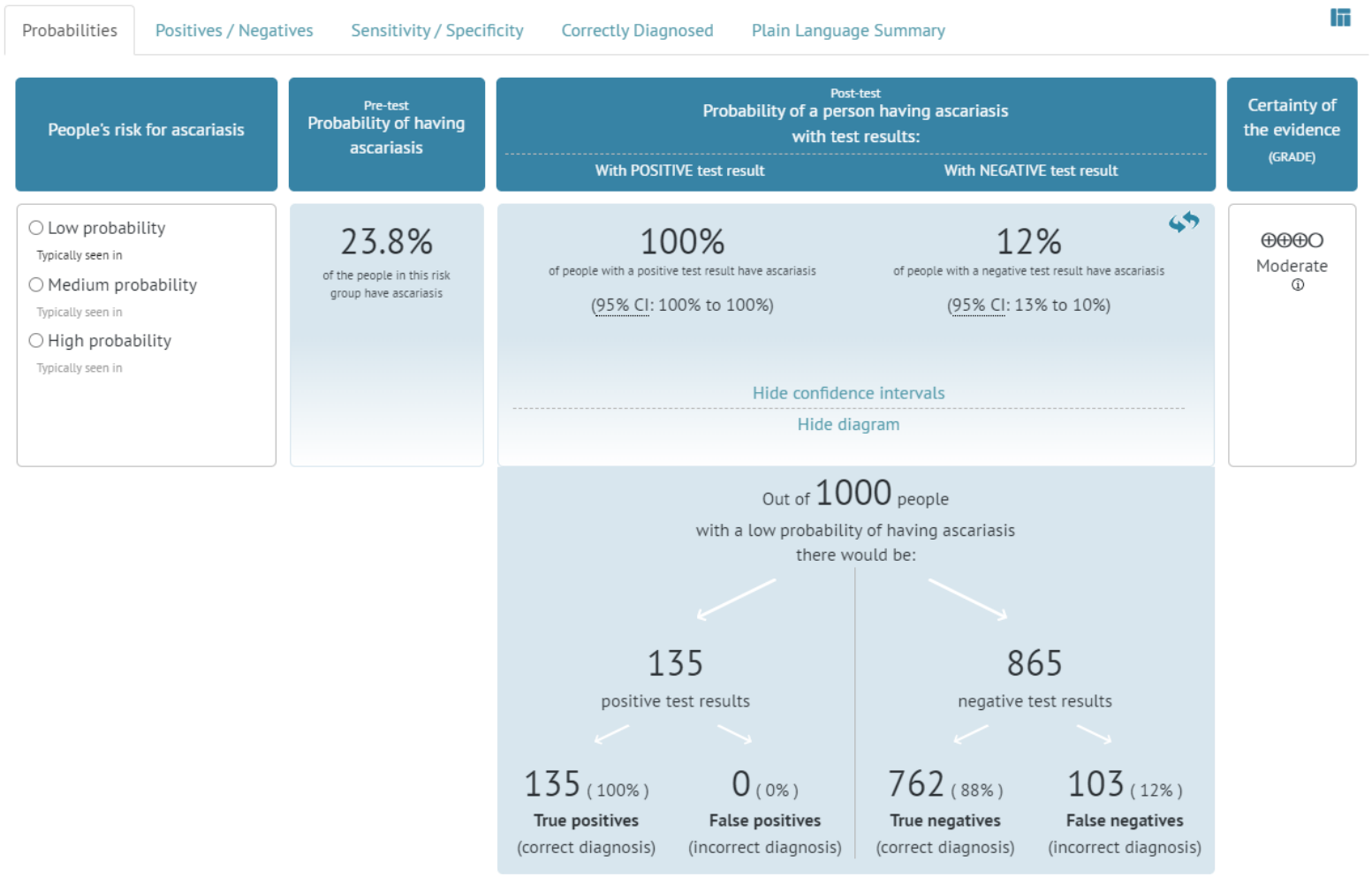
Sensitivity	0.57 (95% CI: 0.51 to 0.64)
Specificity	1.00 (95% CI: 1.00 to 1.00)

Prevalences	23.8%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of23.8%	
True positives (patients with ascariasis)	7 studies 1557 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	135 (122 to 151)	⨁⨁⨁◯ Moderate
False negatives (patients incorrectly classified as not having ascariasis)								103 (87 to 116)	
True negatives (patients without ascariasis)	7 studies 1557 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	762 (762 to 762)	⨁⨁⨁◯ Moderate
False positives (patients incorrectly classified as having ascariasis)								0 (0 to 0)	

Explanations

a. studies do not directly answer primary question


Probabilities
Positives / Negatives
Sensitivity / Specificity
Correctly Diagnosed
Plain Language Summary
People's risk for ascariasis
Pre-test
Probability of having ascariasis
Post-test
Probability of a person having ascariasis with test results:
With POSITIVE test result
With NEGATIVE test result
Certainty of the evidence
(GRADE)
Low probability
Typically seen in
Medium probability
Typically seen in
High probability
Typically seen in
23.8%
of the people in this risk group have ascariasis
100%
of people with a positive test result have ascariasis
(95% CI: 100% to 100%)
12%
of people with a negative test result have ascariasis
(95% CI: 13% to 10%)
Moderate
Hide confidence intervals
Hide diagram
Out of 1000 people
with a low probability of having ascariasis
there would be:
135
positive test results
865
negative test results
135 (100%)
True positives
(correct diagnosis)
0 (0%)
False positives
(incorrect diagnosis)
762 (88%)
True negatives
(correct diagnosis)
103 (12%)
False negatives
(incorrect diagnosis)

Question: Should FECT be used to screen for trichuriasis in the general population?

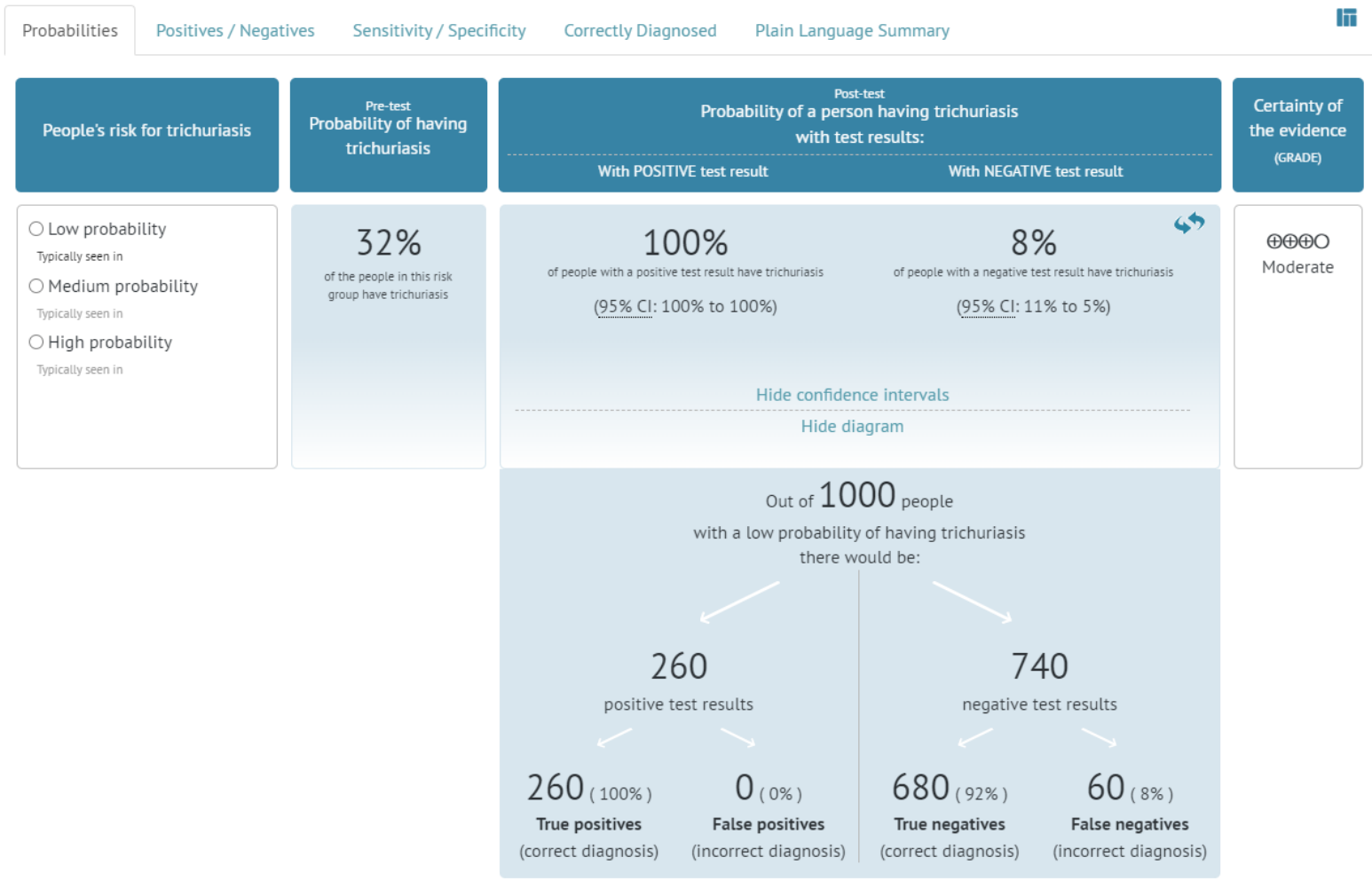
Sensitivity	0.81 (95% CI: 0.73 to 0.89)
Specificity	1.00 (95% CI: 1.00 to 1.00)

Prevalences	32%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of32%	
True positives (patients with trichuriasis)	7 studies 1557 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	260 (234 to 285)	⨁⨁⨁◯ Moderate
False negatives (patients incorrectly classified as not having trichuriasis)								60 (35 to 86)	
True negatives (patients without trichuriasis)	7 studies 1557 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	not serious	not serious	none	680 (680 to 680)	⨁⨁⨁◯ Moderate
False positives (patients incorrectly classified as having trichuriasis)								0 (0 to 0)	

Explanations

a. studies do not directly answer primary question


Probabilities
Positives / Negatives
Sensitivity / Specificity
Correctly Diagnosed
Plain Language Summary
People's risk for trichuriasis
Pre-test
Probability of having trichuriasis
Post-test
Probability of a person having trichuriasis with test results:
With POSITIVE test result
With NEGATIVE test result
Certainty of the evidence (GRADE)
Low probability
Typically seen in
Medium probability
Typically seen in
High probability
Typically seen in
32%
of the people in this risk group have trichuriasis
100%
of people with a positive test result have trichuriasis
(95% CI: 100% to 100%)
8%
of people with a negative test result have trichuriasis
(95% CI: 11% to 5%)
Hide confidence intervals
Hide diagram
⊕⊕⊕○
Moderate
Out of 1000 people
with a low probability of having trichuriasis
there would be:
260
positive test results
740
negative test results
260 (100%)
True positives
(correct diagnosis)
0 (0%)
False positives
(incorrect diagnosis)
680 (92%)
True negatives
(correct diagnosis)
60 (8%)
False negatives
(incorrect diagnosis)

Question: Should FECT be used to screen for hookworm infection in the general population?

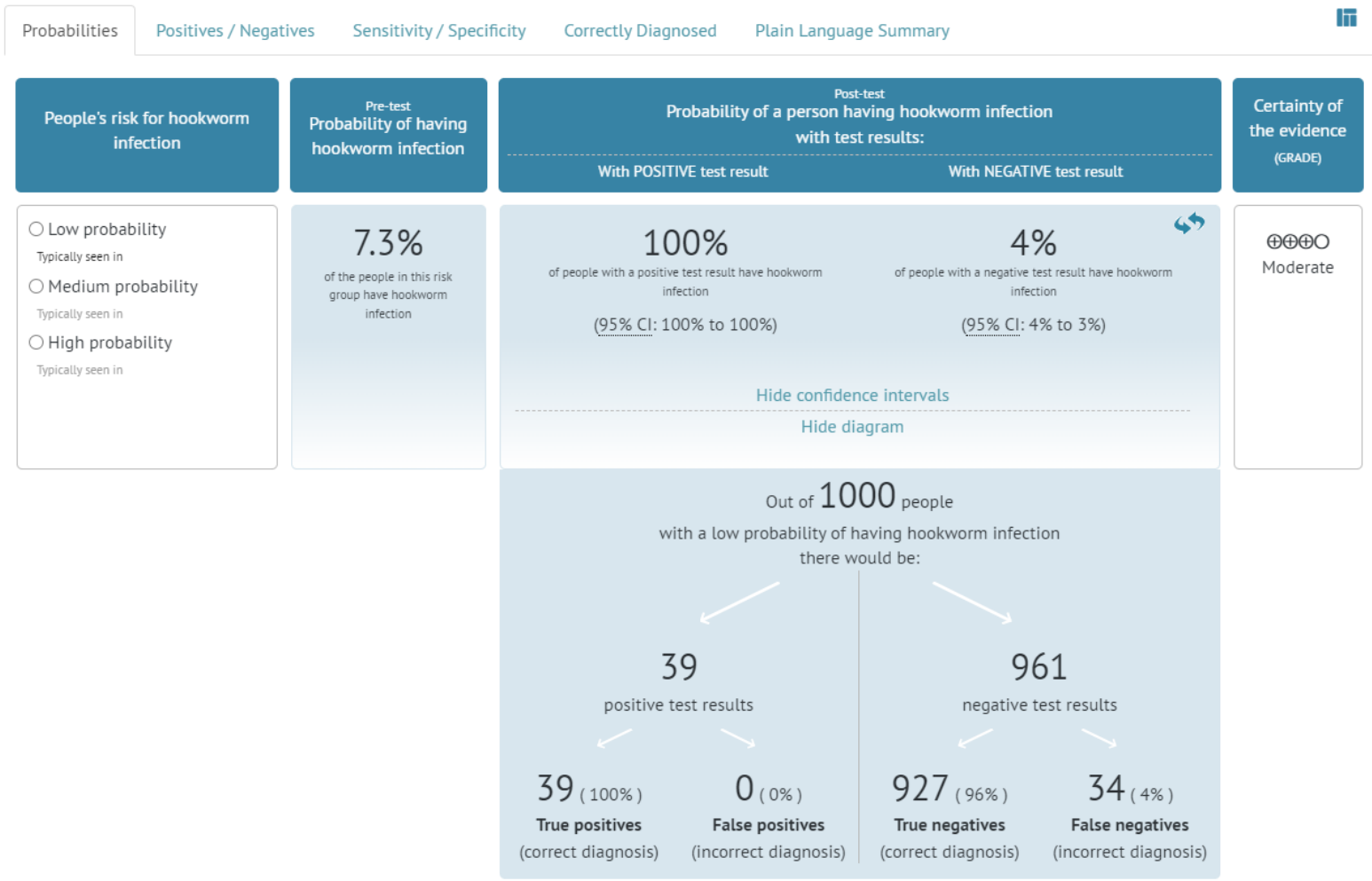
Sensitivity	0.53 (95% CI: 0.49 to 0.57)
Specificity	1.00 (95% CI: 1.00 to 1.00)

Prevalences	7.3%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of7.3%	
True positives (patients with hookworm infection)	7 studies 1557 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	39 (35 to 42)	⨁⨁⨁◯ Moderate
False negatives (patients incorrectly classified as not having hookworm infection)								34 (31 to 38)	
True negatives (patients without hookworm infection)	7 studies 1557 patients	cross-sectional (cohort type accuracy study)	not serious	serious [a]	not serious	not serious	none	927 (927 to 927)	⨁⨁⨁◯ Moderate
False positives (patients incorrectly classified as having hookworm infection)								0 (0 to 0)	

Explanations

a. studies do not directly answer primary question


Probabilities
Positives / Negatives
Sensitivity / Specificity
Correctly Diagnosed
Plain Language Summary
People's risk for hookworm infection
Pre-test
Probability of having hookworm infection
Post-test
Probability of a person having hookworm infection with test results:
With POSITIVE test result
With NEGATIVE test result
Certainty of the evidence (GRADE)
Low probability
Typically seen in
Medium probability
Typically seen in
High probability
Typically seen in
7.3%
of the people in this risk group have hookworm infection
100%
of people with a positive test result have hookworm infection
(95% CI: 100% to 100%)
4%
of people with a negative test result have hookworm infection
(95% CI: 4% to 3%)
Hide confidence intervals
Hide diagram
⊕⊕⊕○
Moderate
Out of 1000 people
with a low probability of having hookworm infection
there would be:
39
positive test results
961
negative test results
39 (100%)
True positives
(correct diagnosis)
0 (0%)
False positives
(incorrect diagnosis)
927 (96%)
True negatives
(correct diagnosis)
34 (4%)
False negatives
(incorrect diagnosis)

Question: Should fecalysis be used to screen for soil-transmitted helminth infection in the general population?

Sensitivity	0.52 (95% CI: 0.47 to 0.57)
Specificity	0.97 (95% CI: 0.94 to 0.99)

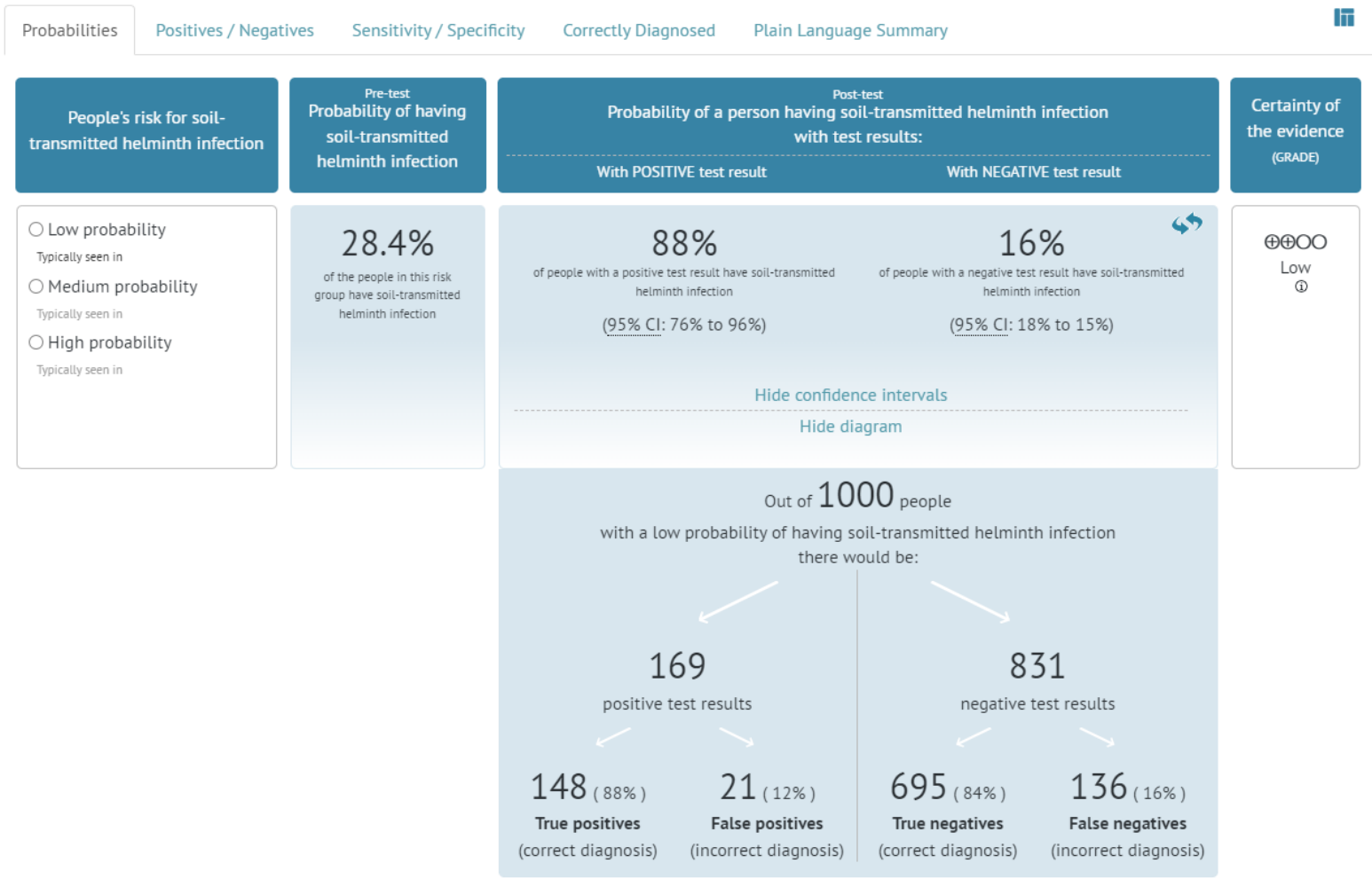
Prevalences	28.4%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of28.4%	
True positives (patients with soil-transmitted helminth infection)	2 studies 700 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	serious[b]	not serious	none	148 (133 to 162)	⨁⨁◯◯ Low
False negatives (patients incorrectly classified as not having soil-transmitted helminth infection)								136 (122 to 151)	
True negatives (patients without soil-transmitted helminth infection)	2 studies 700 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	serious[b]	not serious	none	695 (673 to 709)	⨁⨁◯◯ Low
False positives (patients incorrectly classified as having soil-transmitted helminth infection)								21 (7 to 43)	

Explanations

a. studies do not directly answer primary question

b. wide discrepancy in sample sizes


Probabilities
Positives / Negatives
Sensitivity / Specificity
Correctly Diagnosed
Plain Language Summary
People's risk for soil-transmitted helminth infection
Pre-test
Probability of having soil-transmitted helminth infection
Post-test
Probability of a person having soil-transmitted helminth infection with test results:
With POSITIVE test result
With NEGATIVE test result
Certainty of the evidence (GRADE)
Low probability
Typically seen in
Medium probability
Typically seen in
High probability
Typically seen in
28.4%
of the people in this risk group have soil-transmitted helminth infection
88%
of people with a positive test result have soil-transmitted helminth infection
(95% CI: 76% to 96%)
16%
of people with a negative test result have soil-transmitted helminth infection
(95% CI: 18% to 15%)
Hide confidence intervals
Hide diagram
⊕⊕OO
Low
Out of 1000 people
with a low probability of having soil-transmitted helminth infection
there would be:
169
positive test results
831
negative test results
148 (88%)
True positives
(correct diagnosis)
21 (12%)
False positives
(incorrect diagnosis)
695 (84%)
True negatives
(correct diagnosis)
136 (16%)
False negatives
(incorrect diagnosis)

Question: Should Kato-Katz be used to screen for ascariasis in the general population?

Sensitivity	0.58 (95% CI: 0.50 to 0.66)
Specificity	1.00 (95% CI: 0.44 to 1.00)

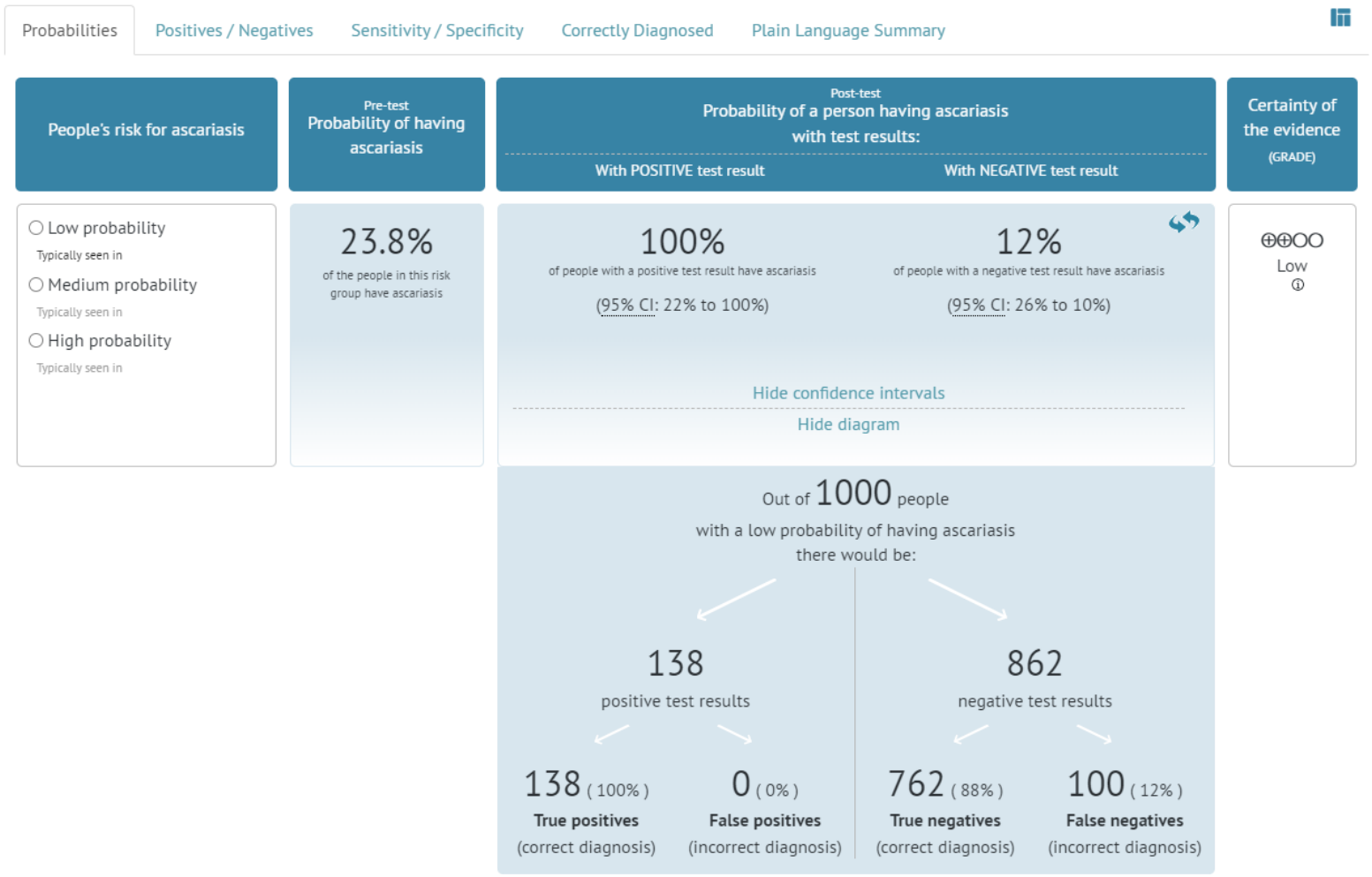
Prevalences	23.8%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of23.8%	
True positives (patients with ascariasis)	5 studies 6014 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	serious[b]	not serious	none	138 (119 to 157)	⨁⨁◯◯ Low
False negatives (patients incorrectly classified as not having ascariasis)								100 (81 to 119)	
True negatives (patients without ascariasis)	5 studies 6014 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	serious[b]	not serious	none	762 (335 to 762)	⨁⨁◯◯ Low
False positives (patients incorrectly classified as having ascariasis)								0 (0 to 427)	

Explanations

a. studies do not directly answer primary question

b. non-randomized design


Probabilities
Positives / Negatives
Sensitivity / Specificity
Correctly Diagnosed
Plain Language Summary
People's risk for ascariasis
Pre-test
Probability of having ascariasis
Post-test
Probability of a person having ascariasis with test results:
With POSITIVE test result
With NEGATIVE test result
Certainty of the evidence
(GRADE)
Low probability
Typically seen in
Medium probability
Typically seen in
High probability
Typically seen in
23.8%
of the people in this risk group have ascariasis
100%
of people with a positive test result have ascariasis
(95% CI: 22% to 100%)
12%
of people with a negative test result have ascariasis
(95% CI: 26% to 10%)
Hide confidence intervals
Hide diagram
⊕⊕◯◯
Low
Out of 1000 people
with a low probability of having ascariasis
there would be:
138
positive test results
862
negative test results
138 (100%)
True positives
(correct diagnosis)
0 (0%)
False positives
(incorrect diagnosis)
762 (88%)
True negatives
(correct diagnosis)
100 (12%)
False negatives
(incorrect diagnosis)

Question: Should Kato-Katz be used to screen for trichuriasis in the general population?

Sensitivity	0.67 (95% CI: 0.49 to 0.81)
Specificity	1.00 (95% CI: 0.93 to 1.00)

Prevalences	32%		

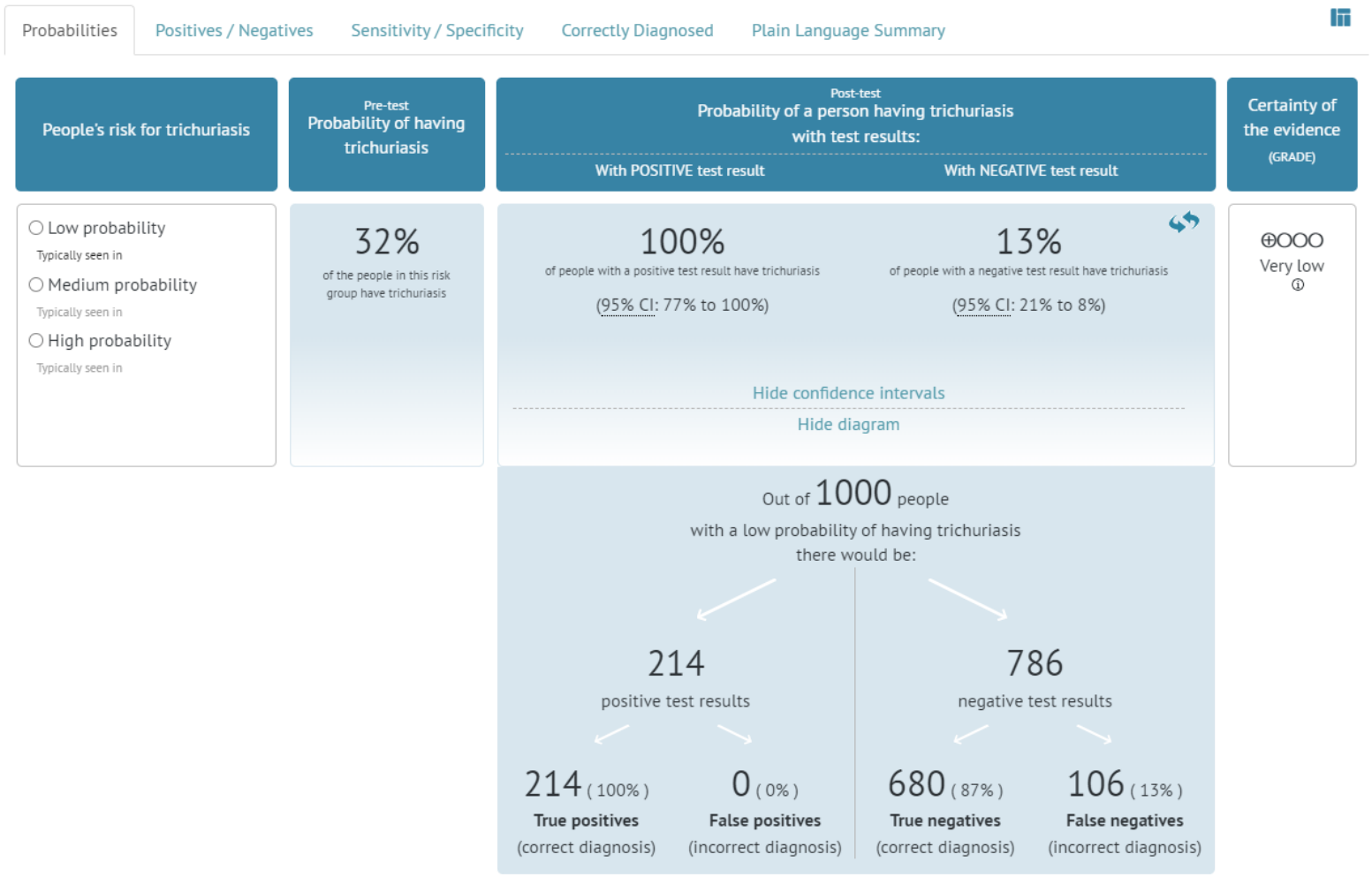
Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of32%	
True positives (patients with trichuriasis)	5 studies 6014 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	serious[b]	serious[c]	none	214 (157 to 259)	⨁◯◯◯ Very low
False negatives (patients incorrectly classified as not having trichuriasis)								106 (61 to 163)	
True negatives (patients without trichuriasis)	5 studies 6014 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	serious[b]	serious[c]	none	680 (632 to 680)	⨁◯◯◯ Very low
False positives (patients incorrectly classified as having trichuriasis)								0 (0 to 48)	

Explanations

a. studies do not directly answer primary question

b. wide discrepancy in sample size

c. wide confidence interval


Probabilities
Positives / Negatives
Sensitivity / Specificity
Correctly Diagnosed
Plain Language Summary
People's risk for trichuriasis
Pre-test
Probability of having trichuriasis
Post-test
Probability of a person having trichuriasis with test results:
With POSITIVE test result
With NEGATIVE test result
Certainty of the evidence
(GRADE)
Low probability
Typically seen in
Medium probability
Typically seen in
High probability
Typically seen in
32%
of the people in this risk group have trichuriasis
100%
of people with a positive test result have trichuriasis
(95% CI: 77% to 100%)
13%
of people with a negative test result have trichuriasis
(95% CI: 21% to 8%)
⊕OOO
Very low
Hide confidence intervals
Hide diagram
Out of 1000 people
with a low probability of having trichuriasis
there would be:
214
positive test results
786
negative test results
214 (100%)
True positives
(correct diagnosis)
0 (0%)
False positives
(incorrect diagnosis)
680 (87%)
True negatives
(correct diagnosis)
106 (13%)
False negatives
(incorrect diagnosis)

Question: Should Kato-Katz be used to screen for hookworm infection in the general population?

Sensitivity	0.62 (95% CI: 0.34 to 0.85)
Specificity	1.00 (95% CI: 0.94 to 1.00)

Prevalences	7.3%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of7.3%	
True positives (patients with hookworm infection)	6 studies 6206 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	serious[b]	serious[c]	none	45 (25 to 62)	⨁◯◯◯ Very low
False negatives (patients incorrectly classified as not having hookworm infection)								28 (11 to 48)	
True negatives (patients without hookworm infection)	6 studies 6206 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	serious[b]	serious[c]	none	927 (871 to 927)	⨁◯◯◯ Very low
False positives (patients incorrectly classified as having hookworm infection)								0 (0 to 56)	

Explanations

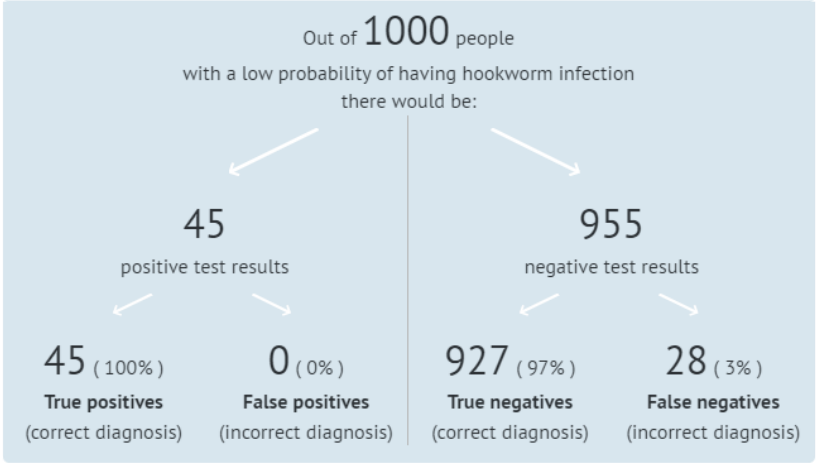
a. studies do not answer primary question
b. wide discrepancy in sample size
c. wide confidence interval

Probabilities | Positives / Negatives | Sensitivity / Specificity | Correctly Diagnosed | Plain Language Summary

People's risk for hookworm infection	Pre-test Probability of having hookworm infection	Post-test Probability of a person having hookworm infection with test results: With POSITIVE test result	Post-test Probability of a person having hookworm infection with test results: With NEGATIVE test result	Certainty of the evidence (GRADE)
○ Low probability Typically seen in ○ Medium probability Typically seen in ○ High probability Typically seen in	7.3% of the people in this risk group have hookworm infection	100% of people with a positive test result have hookworm infection (95% CI: 31% to 100%)	3% of people with a negative test result have hookworm infection (95% CI: 5% to 1%)	⊕OOO Very low

Hide confidence intervals

Hide diagram



Question: Should FECT be used to screen for soil-transmitted helminth infection in the general population?

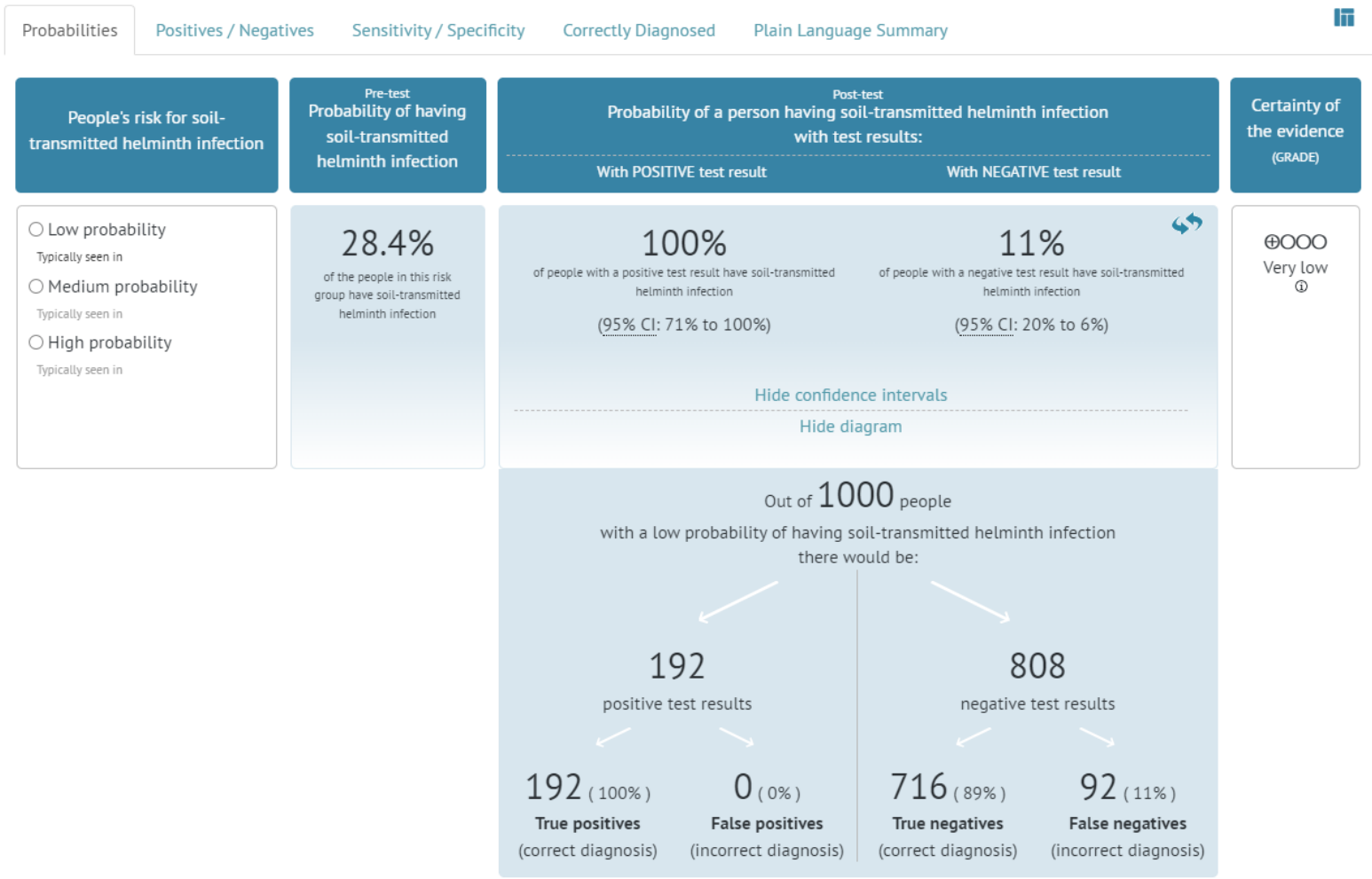
Sensitivity	0.68 (95% CI: 0.43 to 0.85)
Specificity	1.00 (95% CI: 0.93 to 1.00)

Prevalences	28.4%		

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of28.4%	
True positives (patients with soil-transmitted helminth infection)	3 studies 710 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	serious[b]	serious[c]	none	192 (122 to 241)	⨁◯◯◯ Very low
False negatives (patients incorrectly classified as not having soil-transmitted helminth infection)								92 (43 to 162)	
True negatives (patients without soil-transmitted helminth infection)	3 studies 710 patients	cross-sectional (cohort type accuracy study)	not serious	serious[a]	serious[b]	serious[c]	none	716 (666 to 716)	⨁◯◯◯ Very low
False positives (patients incorrectly classified as having soil-transmitted helminth infection)								0 (0 to 50)	

Explanations

a. studies do not answer primary question
b. wide discrepancy in sample size
c. wide confidence interval


Probabilities
Positives / Negatives
Sensitivity / Specificity
Correctly Diagnosed
Plain Language Summary
People's risk for soil-transmitted helminth infection
Pre-test
Probability of having soil-transmitted helminth infection
Post-test
Probability of a person having soil-transmitted helminth infection with test results:
With POSITIVE test result
With NEGATIVE test result
Certainty of the evidence (GRADE)
Low probability
Typically seen in
Medium probability
Typically seen in
High probability
Typically seen in
28.4%
of the people in this risk group have soil-transmitted helminth infection
100%
of people with a positive test result have soil-transmitted helminth infection
(95% CI: 71% to 100%)
11%
of people with a negative test result have soil-transmitted helminth infection
(95% CI: 20% to 6%)
⊕OOO
Very low
Hide confidence intervals
Hide diagram
Out of 1000 people
with a low probability of having soil-transmitted helminth infection
there would be:
192
positive test results
808
negative test results
192 (100%)
True positives
(correct diagnosis)
0 (0%)
False positives
(incorrect diagnosis)
716 (89%)
True negatives
(correct diagnosis)
92 (11%)
False negatives
(incorrect diagnosis)

Author(s): Yimam Y, Woreta A, Mohebali M.
Question: Regular health exam compared to no regular health exam in reducing incidence of intestinal parasitism in food handlers
Setting: Food handlers in Ethiopia
Bibliography: Yimam Y, Woreta A, Mohebali M. Intestinal parasites among food handlers of food service establishments in Ethiopia: a systematic review and meta-analysis. BMC Public Health. 2020 Dec;20(1):73.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	regular health exam	no regular health exam	Relative (95% CI)	Absolute (95% CI)		
Positive for intestinal parasite												
9	observational studies	not serious	not serious	not serious	not serious	none	327/1269 (25.8%)	425/1119 (38.0%)	**OR 0.70** (0.47 to 1.04)	**80 fewer per 1,000** (from 156 fewer to 9 more)	⨁⨁◯◯ Low	CRITICAL

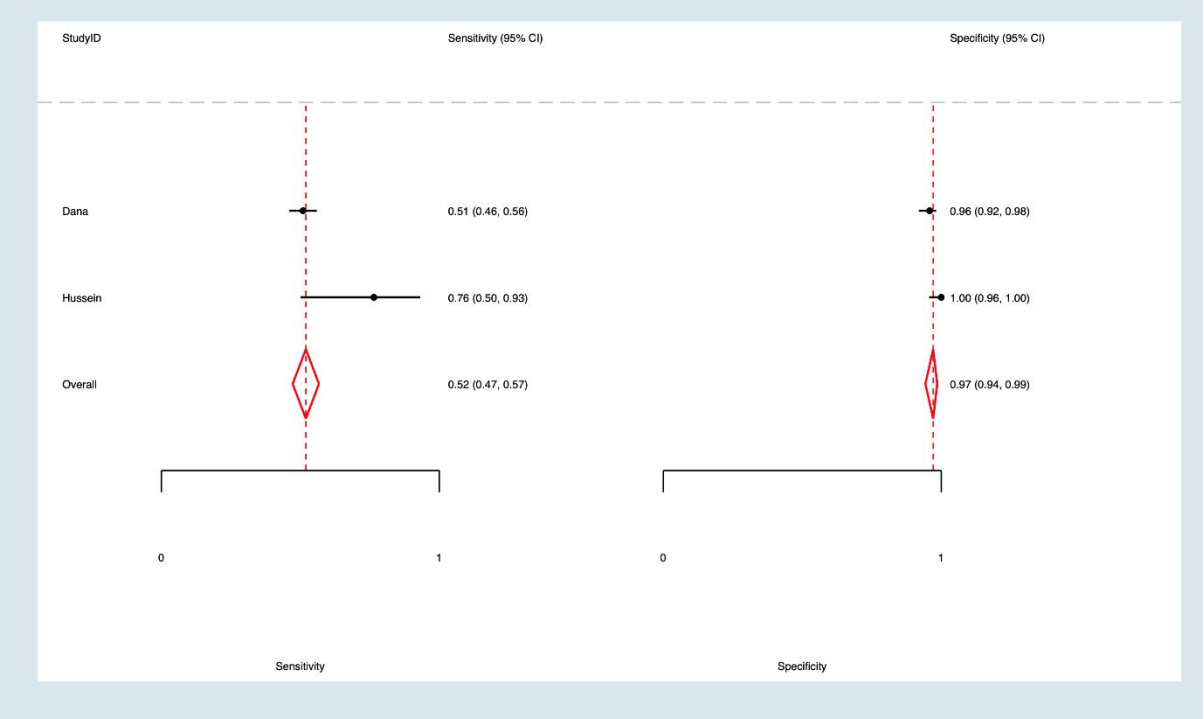
CI: confidence interval; **OR:** odds ratio

Outcomes	Plain language statements	Absolute Effect With no regular health exam	Absolute Effect With regular health exam	Relative effect (95% CI)	Certainty of the evidence GRADE
Positive for intestinal parasite	*Regular health exam may reduce risk of intestinal parasitism but it is not statistically significant*	380 per 1000	300 per 1000	OR 0.7 (0.47 to 1.04)	⨁⨁◯◯ LOW

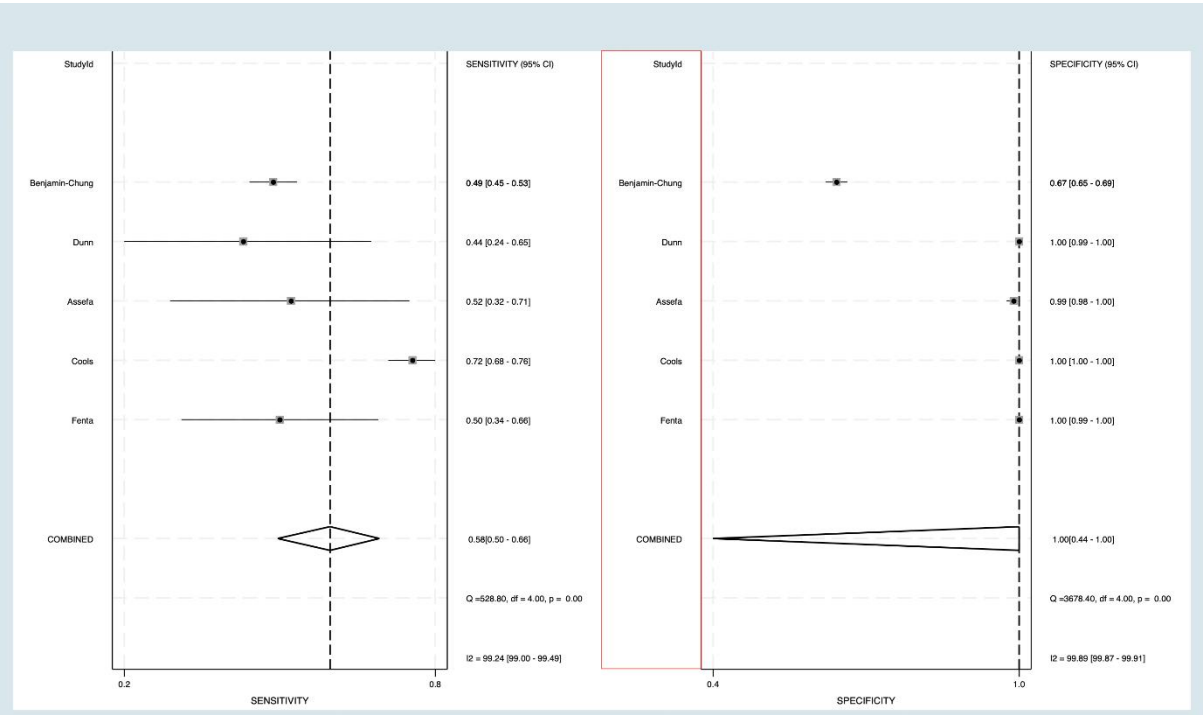
Difference: 80 fewer per 1000 patients (95% CI: 156 fewer to 9 more per 1000 patients)
Based on data from 2388 patients in 9 studies

Appendix 5. Forest Plots

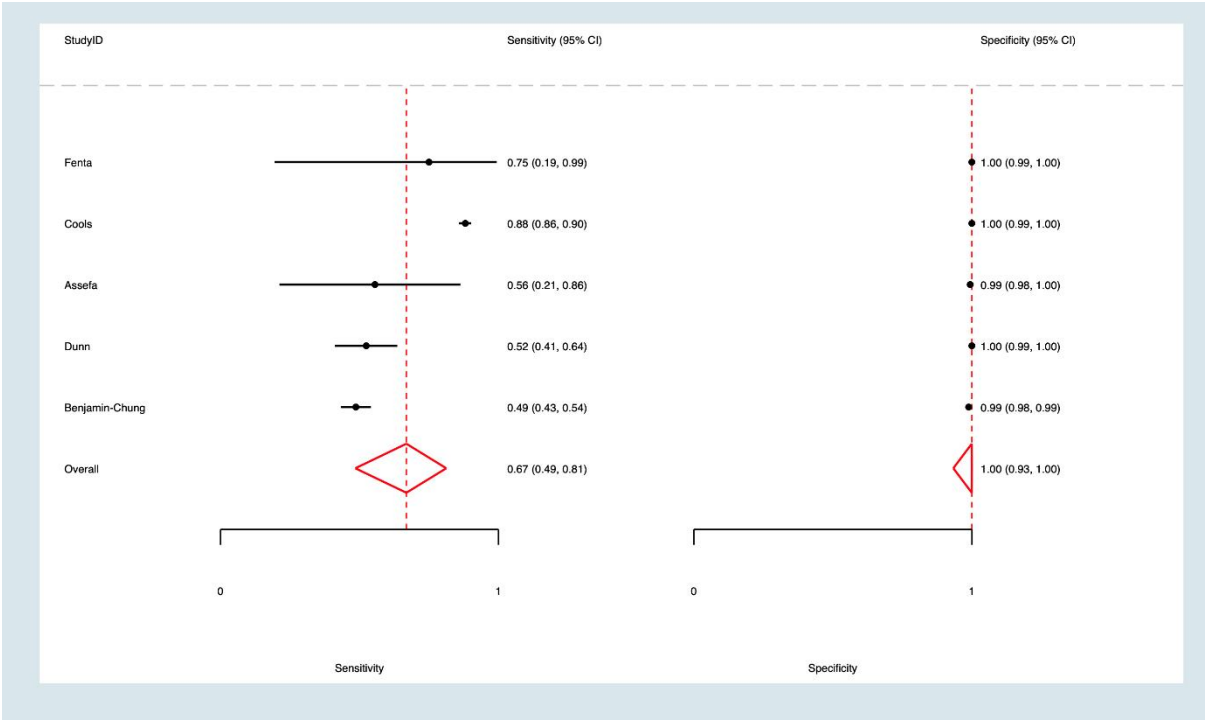
Fecalysis for any STH



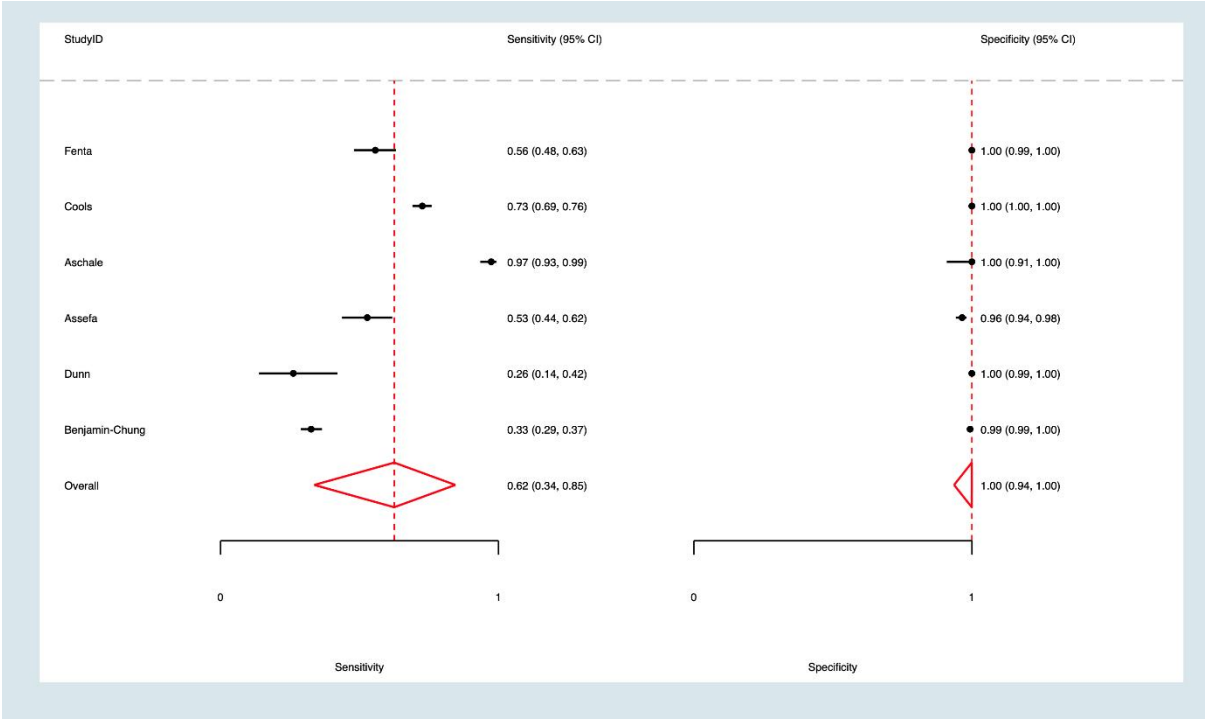
Kato-Katz for ascariasis



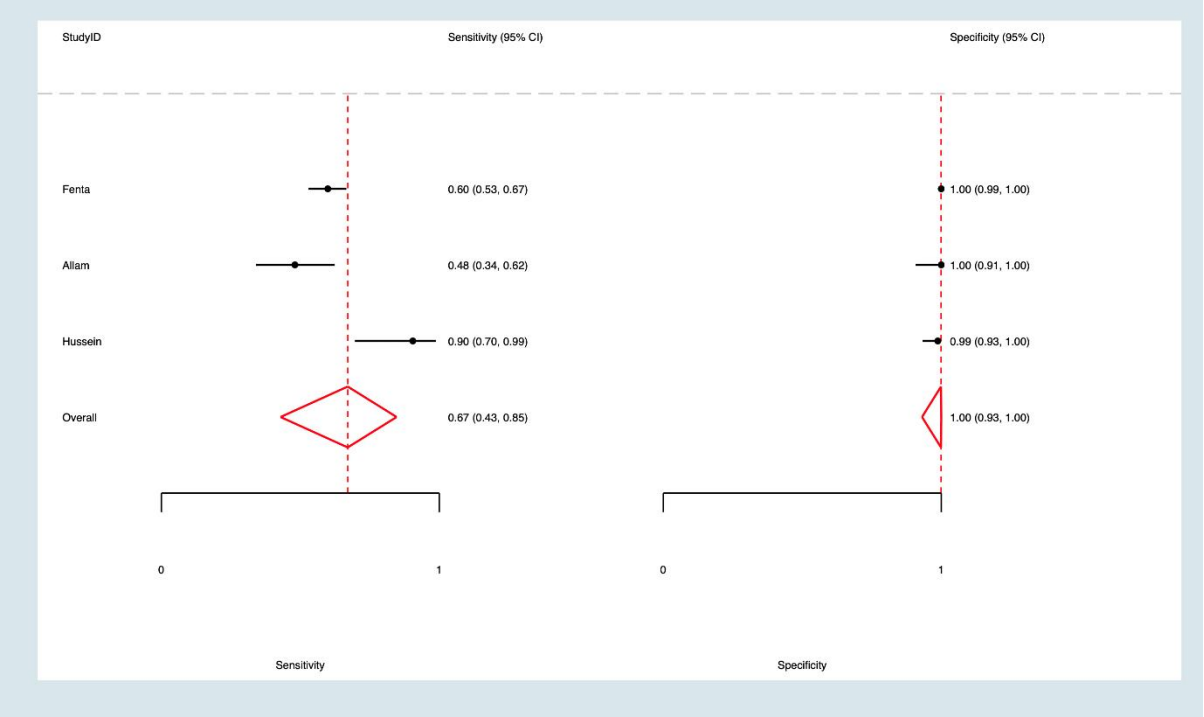
Kato-Katz for trichuriasis



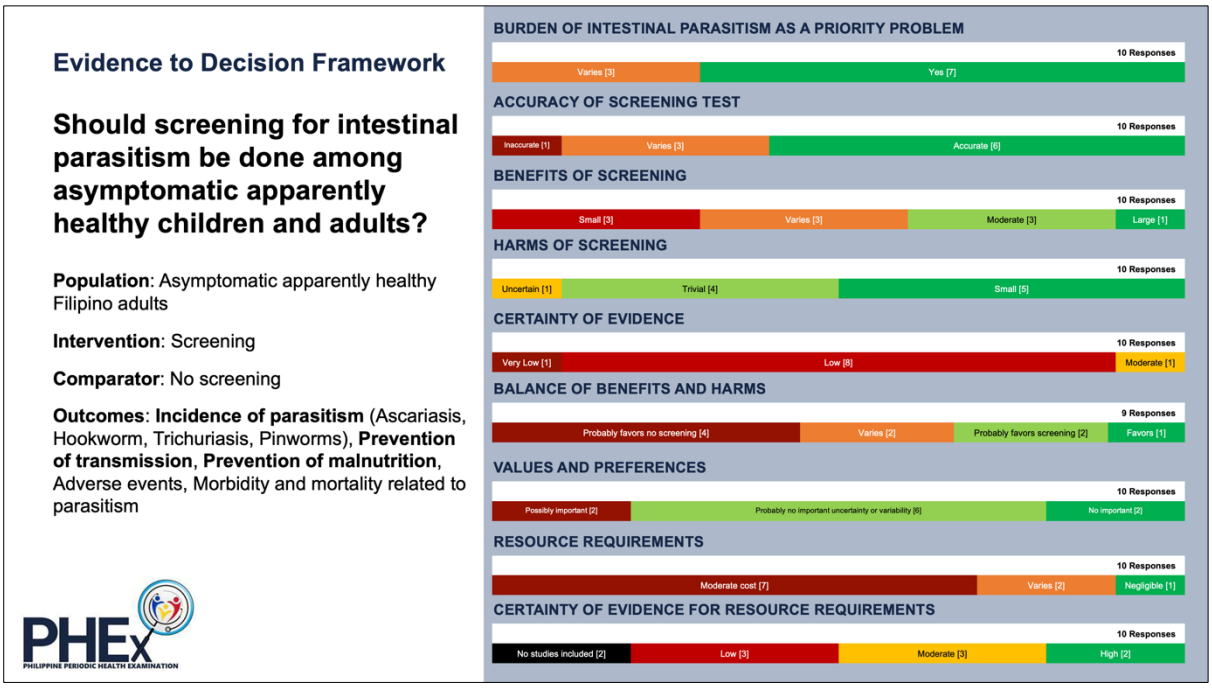
Kato-Katz for hookworm infection



FECT for any STH



Appendix 6. Evidence-to-Decision Framework Responses



Evidence to Decision Framework

Should screening for intestinal parasitism be done among asymptomatic apparently healthy children and adults?

Population: Asymptomatic apparently healthy Filipino adults

Intervention: Screening

Comparator: No screening

Outcomes: **Incidence of parasitism** (Ascariasis, Hookworm, Trichuriasis, Pinworms), **Prevention of transmission**, **Prevention of malnutrition**, Adverse events, Morbidity and mortality related to parasitism

PHEx
PHILIPPINE PERIODIC HEALTH EXAMINATION

COST-EFFECTIVENESS

IMPACT ON HEALTH EQUITY

ACCEPTABILITY

FEASIBILITY

RECOMMENDATION

STRENGTH OF RECOMMENDATION

CONSENSUS PANEL COMMENTS

AGAINST SCREENING:	FOR SCREENING:
Deworming is effective regardless of screening and screening should be done on those with high-risk for transmission such as **food handlers**.	Due to prevalence
Absence of strong evidence to support [screening]	For **food handlers**
Not cost-effective for the general population and screening might be more beneficial to certain population such as those who are symptomatic or are **food handlers**	For prevention
Screening should only be done among **food handlers.**	

PERIODIC HEALTH EXAMINATION TASK FORCE ON SCREENING FOR INFECTIOUS DISEASES 2022-2023

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Ronald M. Panaligan, MD
Mr. Christopher Muñoz
Rogelio Dazo, Jr., MD
Thea Pamela Cajulao, MD
Juan Maria Ibarra Co, MD
Gerard Danielle K. Sio, MD

Consensus Panel Meeting Facilitator: Cary Amiel Villanueva, MD
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Administrative Officer: Rhea Pablo-Anwar, RN

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COI Administrative Officer:	Ivy Cruz

SUMMARY OF COI DECLARATIONS

Name	Affiliation	Summary of Declared Conflicts of Interest	Management
Geannagail O. Anuran, MD	Philippine Academy of Family Physicians	None	A
Ian Homer Cua, MD	Philippine Society of Gastroenterology	None	A
Jacqueline Frances F. Momville, MD	Philippine Society of Public Health Physicians	None	A
Reynaldo San Luis, MD	Philippine Society of General Internal Medicine	None	A
Ronald M. Panaligan, MD	Philippine College of Chest Physicians	None	A
Mr. Christopher Muñoz	Philippine Alliance of Patient Organizations	None	A
Rogelio Dazo, Jr., MD	Philippine Medical Association	None	A
Thea Pamela Cajulao, MD	Philippine Society for Microbiology and Infectious Diseases	None	A
Juan Maria Ibarra Co, MD	Philippine College of Physicians	None	A
Gerard Danielle K. Sio, MD	Philippine College of Occupational Medicine	Non-financial COI- Occupational and Environmental Health and Safety System Consultant; Hep B CPG Consensus Panel	B

AGREE REPORTING CHECKLIST (SELF EVALUATION)

Fillable forms may be downloaded here: http://www.agreetrust.org/resource-centre/agree-reporting-checklist/

This checklist is intended to guide the reporting of clinical practice guidelines.

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
DOMAIN 1: SCOPE AND PURPOSE		
1. OBJECTIVES *Report the overall objective(s) of the guideline. The expected health benefits from the guideline are to be specific to the clinical problem or health topic.*	☒ Health intent(s) (i.e., prevention, screening, diagnosis, treatment, etc.) ☐ Expected benefit(s) or outcome(s) ☒ Target(s) (e.g., patient population, society)	p. 16
2. QUESTIONS *Report the health question(s) covered by the guideline, particularly for the key recommendations.*	☒ Target population ☒ Intervention(s) or exposure(s) ☒ Comparisons (if appropriate) ☒ Outcome(s) ☒ Health care setting or context	pp. 16-19
3. POPULATION *Describe the population (i.e., patients, public, etc.) to whom the guideline is meant to apply.*	☒ Target population, sex and age ☒ Clinical condition (if relevant) ☒ Severity/stage of disease (if relevant) ☒ Comorbidities (if relevant) ☐ Excluded populations (if relevant)	p. 19
DOMAIN 2: STAKEHOLDER INVOLVEMENT		
4. GROUP MEMBERSHIP *Report all individuals who were involved in the development process. This may include members of the steering group, the research team involved in selecting and reviewing/rating the evidence and individuals involved in formulating the final recommendations.*	☒ Name of participant ☐ Discipline/content expertise (e.g., neurosurgeon, methodologist) ☒ Institution (e.g., St. Peter's hospital) ☐ Geographical location (e.g., Seattle, WA) ☒ A description of the member's role in the guideline development group	p. 20
5. TARGET POPULATION PREFERENCES AND VIEWS *Report how the views and preferences of the target population were sought/considered and what the resulting outcomes were.*	☒ Statement of type of strategy used to capture patients'/publics' views and preferences (e.g., participation in the guideline development group, literature review of values and preferences) ☒ Methods by which preferences and views were sought (e.g., evidence from literature, surveys, focus groups) ☐ Outcomes/information gathered on patient/public information ☒ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	p. 20
6. TARGET USERS *Report the target (or intended) users of the guideline.*	☒ The intended guideline audience (e.g. specialists, family physicians, patients, clinical or institutional leaders/administrators)	p. 19

	☒ How the guideline may be used by its target audience (e.g., to inform clinical decisions, to inform policy, to inform standards of care)	
DOMAIN 3: RIGOUR OF DEVELOPMENT		
7. SEARCH METHODS *Report details of the strategy used to search for evidence.*	☒ Named electronic database(s) or evidence source(s) where the search was performed (e.g., MEDLINE, EMBASE, PsychINFO, CINAHL) ☒ Time periods searched (e.g., January 1, 2004 to March 31, 2008) ☒ Search terms used (e.g., text words, indexing terms, subheadings) ☒ Full search strategy included (e.g., possibly located in appendix)	pp. 21, 137, 147, 165, 170, 179, 185, 200, 210, 222
8. EVIDENCE SELECTION CRITERIA *Report the criteria used to select (i.e., include and exclude) the evidence. Provide rationale, where appropriate.*	☒ Target population (patient, public, etc.) characteristics ☒ Study design ☒ Comparisons (if relevant) ☒ Outcomes ☒ Language (if relevant) ☐ Context (if relevant)	pp. 137, 201, 202, 211, 223, 245
9. STRENGTHS & LIMITATIONS OF THE EVIDENCE *Describe the strengths and limitations of the evidence. Consider from the perspective of the individual studies and the body of evidence aggregated across all the studies. Tools exist that can facilitate the reporting of this concept.*	☒ Study design(s) included in body of evidence ☒ Study methodology limitations (sampling, blinding, allocation concealment, analytical methods) ☒ Appropriateness/relevance of primary and secondary outcomes considered ☒ Consistency of results across studies ☒ Direction of results across studies ☒ Magnitude of benefit versus magnitude of harm ☒ Applicability to practice context	pp. 27-31, 38-42, 46-50, 56-60, 67-70, 77-84, 91-97, 101-106, 115-121
10. FORMULATION OF RECOMMENDATIONS *Describe the methods used to formulate the recommendations and how final decisions were reached. Specify any areas of disagreement and the methods used to resolve them.*	☒ Recommendation development process (e.g., steps used in modified Delphi technique, voting procedures that were considered) ☒ Outcomes of the recommendation development process (e.g., extent to which consensus was reached using modified Delphi technique, outcome of voting procedures) ☒ How the process influenced the recommendations (e.g., results of Delphi technique influence final recommendation, alignment with recommendations and the final vote)	p. 22
11. CONSIDERATION OF BENEFITS AND HARMS	☒ Supporting data and report of benefits	pp. 27-31, 38-42, 46-

Report the health benefits, side effects, and risks that were considered when formulating the recommendations.	☒ Supporting data and report of harms/side effects/risks ☒ Reporting of the balance/trade-off between benefits and harms/side effects/risks ☒ Recommendations reflect considerations of both benefits and harms/side effects/risks	50, 56-60, 67-70, 77-84, 91-97, 101-106, 115-121
12. LINK BETWEEN RECOMMENDATIONS AND EVIDENCE *Describe the explicit link between the recommendations and the evidence on which they are based.*	☒ How the guideline development group linked and used the evidence to inform recommendations ☒ Link between each recommendation and key evidence (text description and/or reference list) ☒ Link between recommendations and evidence summaries and/or evidence tables in the results section of the guideline	pp. 25-26, 37, 46, 55, 66, 76, 89, 101, 115, 127
13. EXTERNAL REVIEW *Report the methodology used to conduct the external review.*	☒ Purpose and intent of the external review (e.g., to improve quality, gather feedback on draft recommendations, assess applicability and feasibility, disseminate evidence) ☒ Methods taken to undertake the external review (e.g., rating scale, open-ended questions) ☒ Description of the external reviewers (e.g., number, type of reviewers, affiliations) ☒ Outcomes/information gathered from the external review (e.g., summary of key findings) ☒ How the information gathered was used to inform the guideline development process and/or formation of the recommendations (e.g., guideline panel considered results of review in forming final recommendations)	p. 23
14. UPDATING PROCEDURE *Describe the procedure for updating the guideline.*	☒ A statement that the guideline will be updated ☒ Explicit time interval or explicit criteria to guide decisions about when an update will occur ☒ Methodology for the updating procedure	p. 136
DOMAIN 4: CLARITY OF PRESENTATION		
15. SPECIFIC AND UNAMBIGUOUS RECOMMENDATIONS *Describe which options are appropriate in which situations and in which population groups, as informed by the body of evidence.*	☒ A statement of the recommended action ☒ Intent or purpose of the recommended action (e.g., to improve quality of life, to decrease side effects) ☒ Relevant population (e.g., patients, public) ☒ Caveats or qualifying statements, if relevant (e.g., patients or conditions for	pp. 25-26, 37, 46, 55, 66, 76, 89, 101, 115, 127

	whom the recommendations would not apply) ☒ If there is uncertainty about the best care option(s), the uncertainty should be stated in the guideline	
16. MANAGEMENT OPTIONS *Describe the different options for managing the condition or health issue.*	☒ Description of management options ☒ Population or clinical situation most appropriate to each option	pp. 27-31, 38-42, 46-50, 56-60, 67-70, 77-84, 91-97, 101-106, 115-121
17. IDENTIFIABLE KEY RECOMMENDATIONS *Present the key recommendations so that they are easy to identify.*	☒ Recommendations in a summarized box, typed in bold, underlined, or presented as flow charts or algorithms ☒ Specific recommendations grouped together in one section	pp. 12-14
DOMAIN 5: APPLICABILITY		
18. FACILITATORS AND BARRIERS TO APPLICATION *Describe the facilitators and barriers to the guideline's application.*	☒ Types of facilitators and barriers that were considered ☒ Methods by which information regarding the facilitators and barriers to implementing recommendations were sought (e.g., feedback from key stakeholders, pilot testing of guidelines before widespread implementation) ☒ Information/description of the types of facilitators and barriers that emerged from the inquiry (e.g., practitioners have the skills to deliver the recommended care, sufficient equipment is not available to ensure all eligible members of the population receive mammography) ☒ How the information influenced the guideline development process and/or formation of the recommendations	p. 136
19. IMPLEMENTATION ADVICE/TOOLS *Provide advice and/or tools on how the recommendations can be applied in practice.*	☒ Additional materials to support the implementation of the guideline in practice. For example: o Guideline summary documents o Links to check lists, algorithms o Links to how-to manuals o Solutions linked to barrier analysis (see Item 18) o Tools to capitalize on guideline facilitators (see Item 18) o Outcome of pilot test and lessons learned	p. 135

20. RESOURCE IMPLICATIONS *Describe any potential resource implications of applying the recommendations.*	☒ Types of cost information that were considered (e.g., economic evaluations, drug acquisition costs) ☒ Methods by which the cost information was sought (e.g., a health economist was part of the guideline development panel, use of health technology assessments for specific drugs, etc.) ☒ Information/description of the cost information that emerged from the inquiry (e.g., specific drug acquisition costs per treatment course) ☒ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	p. 136
21. MONITORING/ AUDITING CRITERIA *Provide monitoring and/or auditing criteria to measure the application of guideline recommendations.*	☒ Criteria to assess guideline implementation or adherence to recommendations ☒ Criteria for assessing impact of implementing the recommendations ☒ Advice on the frequency and interval of measurement ☒ Operational definitions of how the criteria should be measured	pp. 24, 135
DOMAIN 6: EDITORIAL INDEPENDENCE		
22. FUNDING BODY *Report the funding body's influence on the content of the guideline.*	☒ The name of the funding body or source of funding (or explicit statement of no funding) ☒ A statement that the funding body did not influence the content of the guideline	p. 3
23. COMPETING INTERESTS *Provide an explicit statement that all group members have declared whether they have any competing interests.*	☒ Types of competing interests considered ☒ Methods by which potential competing interests were sought ☒ A description of the competing interests ☒ How the competing interests influenced the guideline process and development of recommendations	p. 23