A cluster-randomised trial of a continuous quality improvement intervention to support antenatal screening for the triple elimination of syphilis, HIV and hepatitis B in Indonesia: protocol for the MENJAGA ("Protection") study

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Abstract

Introduction

Prevention of mother-to-child-transmission (PMTCT) of syphilis, human immunodeficiency virus (HIV) and hepatitis B (HBV) is a key priority for the Indonesian government. Despite national guidelines, screening for these diseases among pregnant women remains relatively low in Indonesia. Continuous Quality Improvement (CQI) – an approach involving the iterative development and testing of data-driven interventions to achieve improvement - has been effectively used to strengthen the quality of public health care in a range of low- and middle-income countries (LMIC) but there are very few examples from PMTCT programs. This protocol describes a study to evaluate the effectiveness, cost-effectiveness and implementation process of a CQI intervention designed to promote antenatal screening for syphilis, HIV and HBV in primary health care centres (PHCs) in Indonesia (also known as Pusat Kesehatan Masyarakat or "*Puskesmas*").

Methods and analysis

The study will be conducted as a two-arm, parallel cluster randomised control trial in 40 Puskesmas in two sites in West Java province (Bandung city and Bogor district). *Puskesmas* randomised to the intervention arm (n=10 per district) will receive targeted and enhanced support in line with the CQI approach. Puskesmas randomised to the control arm (n=10 per district) will continue to provide syphilis, HIV and HBV testing as per the current standard of care. The primary outcome (proportion of pregnant women tested for syphilis, HIV and HBV in the first trimester) will be evaluated at pre-baseline, baseline, and endline. Secondary clinical outcomes include the proportion of women tested for syphilis, HIV and HBV during their first antenatal care visit and during pregnancy, as well as the proportion of pregnant women that tested positive and commenced treatment. A process evaluation will be undertaken to explore implementation, acceptability and reach of the CQI intervention. An economic

evaluation will measure the total cost and cost-effectiveness of the intervention compared with standard of care.

Trial registration

The trial has been registered with ClinicalTrials.gov (NCT06058286) and the ISRCTN registry https://doi.org/10.1186/ISRCTN11251878.

Introduction

Triple elimination of syphilis, human immunodeficiency virus (HIV) infection and hepatitis B (HBV) is a major global health challenge (1, 2). A recent meta-analysis reported a global pooled prevalence for syphilis, HIV and HBV among pregnant women of 2.9% (95% CI, 2.4-3.4%), 0.8% (0.7-0.9%) and 4.8% (3.8-5.8%) respectively, with higher prevalence among low and middle-income countries (LMICs) (3). Transmission of these diseases can occur during pregnancy, at the time of birth, or via breastfeeding for HIV and can have long-term adverse outcomes for mothers and their newborns, including syphilis related early foetal deaths (2) and syphilis and HIV related preterm births and low birth weight (4). Transmission to newborns is essentially preventable through early diagnosis and treatment in pregnancy (5). The relatively low cost and simplicity of point-of-care testing for syphilis, HIV and HBV combined with the immediacy of results has the potential to greatly benefit resource-constrained settings by allowing rapid initiation of treatment (6).

Although several countries in the Southeast Asia WHO region, such as Thailand, Malaysia, the Maldives, and Sri Lanka, have achieved the elimination of mother-to-child-transmission of syphilis and HIV (7), Indonesia still has a long way to go (8). In 2022, screening rates for the three diseases were well below the Indonesian government's target of full coverage, with 57.7% of pregnant women tested for HIV, 65.0% tested for HBV, and only 24.5% tested for syphilis, and a positivity rate of 0.3% for HIV, 1.6% for HBV, and 0.5% for syphilis (9). These low testing rates occur despite approximately 98% of pregnant women attending antenatal care (ANC) at least once during pregnancy and 86% attending at least four times (9), the existence of government-subsidised ANC services, and national guidelines to support antenatal screening. Furthermore, the Ministry of Health (MoH) recommends testing during the first trimester for prompt management during pregnancy (8), however data on first-trimester testing is lacking.

Studies, including our own, highlight several barriers preventing the effective implementation of syphilis, HIV and HBV testing in ANC services in Indonesia (10–13). These barriers include inadequate supply-chain management (10), high staff turnover, difficulty in engaging private providers (10,13), complexity of the recording and reporting system (10–12), and stigma (10,12). Low-cost, scalable solutions to support the scale-up of testing and treatment for syphilis, HIV and HBV are urgently needed. A 2018 systematic review of 670 studies evaluating interventions to improve the quality of care in LMICs reported that multi-faceted Continuous Quality Improvement (CQI) interventions hold promise in terms of sustained care improvements, noting, however, that few rigorous evaluations have been undertaken

(14). The CQI approach is designed to improve healthcare provider capacity and adherence to clinical guidelines. Key features of the CQI approach include systematic, local data-guided activities, designing interventions (or changes to clinic processes) tailored to the local contexts, and iterative development and testing of interventions (7).

To date, only a few studies have evaluated CQI interventions in the context of ANC screening and treatment for HIV (15–17). These studies, all addressing the quality of HIV testing and treatment in public health care facilities in Africa, show improvements in screening and treatment resulting from a range of actions at the clinic level, including maximising the use of existing resources through staff redeployment, reducing duplication of activities, 'bundling' interventions to maximise the time available during patient visits, linking maternal antenatal patient records to infant cards, sharing information among staff and pregnant women about referral pathways and data review meetings. In Indonesia, two studies have used CQI to improve the quality of ANC (18,19) but none focus on the triple elimination of syphilis, HIV and HBV. To our knowledge, this is the first cluster-randomised trial, with integrated process and economic evaluations, to assess the impact of a multi-faceted CQI intervention designed to improve antenatal testing of syphilis, HIV and HBV in Indonesia. This intervention has the potential to contribute significantly to improved maternal and child health in Indonesia while also strengthening the underlying health system.

Methods and analysis

This protocol has been prepared following the SPIRIT (Standard Protocol Items for Randomised Trials) statement – see Supplement 1 for the complete checklist (20).

Design

This is a two-arm, parallel cluster-randomised control trial evaluating the effectiveness, cost-effectiveness and implementation of a multi-faceted CQI intervention. A cluster is defined as a primary health care (PHC) facility known as a Pusat Kesehatan Masyarakat ("*Puskesmas*") and its linked network of village and/or private midwives.

Preparation and co-design

Stakeholder involvement

In preparation for the trial, situational analyses and stakeholder meetings were conducted between June and September in 2022 in two districts to gather qualitative and quantitative information related to practices and barriers to triple elimination. Discussions with the district health and *Puskesmas* officials were conducted to gather routinely available data on coverage of testing and its barriers. This information was then presented in a stakeholder meeting at the end of 2022 with staff from the Provincial Health Office (PHO) and District Health Offices (DHO) to gather feedback and facilitate the co-design of the intervention and implementation strategy.

During this initial phase, there were anecdotal reports from field officers that due to the MENJAGA stakeholder meetings and ongoing discussions with the DHOs and midwife's association, some *Puskesmas* may have started to implement changes to address barriers to triple elimination in the districts. Therefore, in order to try to capture any potential unintended impacts of the study preparation on the main trial outcome measures, we decided to collect additional de-identified routinely available data to describe testing coverage of syphilis, HIV and HBV from before the stakeholder meetings and trial preparation had commenced (i.e. from 2022). We named this our "pre-baseline" data collection.

In the preparation phase, it also became clear that treatment for HIV was only available in one or two referral *Puskesmas* in each district. It was therefore decided that these "treatment facilities" should be handled differently in the main trial and that they would not be included in the randomisation but would be purposively selected for the intervention and analysed separately from the main study sample.

Assessment of routinely available data

In December 2023, we visited all participating *Puskesmas* (see 'Setting and population') to gain an understanding of how routine testing and treatment data is being recorded and reported. We aimed to assess the validity of anonymised routine data for primary outcome data collection, by comparing data from *Puskesmas* registers to the "Pink book". The Pink book is a patient-held maternal and child health care record in which health care providers document ANC interactions, including testing for syphilis, HIV and HBV. This assessment was conducted on a sub-sample of ~10% women from all participating *Puskesmas* during the baseline and endline data collection.

Data validation involved an exit survey with consenting pregnant women to directly obtain information on testing and treatment for syphilis, HIV, and HBV recorded in their ANC Pink book. Based on our situational analyses, this book is considered to be the most reliable and complete source of data on testing. Data from the Pink book was compared to aggregate and individual data recorded at the *Puskesmas*, which consists of several data sources for ANC including mother's card and ANC registers (ANC cohort and ANC e-cohort), as well as data sources for triple elimination (SIHA, SIHEPI, and triple elimination registers) (Table 1). Based on results of the data validation exercise which showed discrepancies between aggregate and individual level data on testing, it was decided that the primary and secondary outcomes of this study would be measured using individual-level data recorded at registers of participating *Puskesmas* (Table 1).

Table 1. Data sources for syphilis, HIV and HBV tests and treatment

Data Source	Description	Person in Charge of Filling Out
Pink Book	Patient-held maternal and child health book, consisting of information related to pregnancy and child health, considered the gold standard as it contains comprehensive information across healthcare providers.	Completed by both health care providers (midwives, obstetrician/gynaecologist, physician) and mothers.
Mother's Card	Considered a shortened version of the Pink Book: a card kept at some *Puskesmas* which contains information on each pregnant woman including history of pregnancy, ANC, delivery, and postpartum.	Healthcare providers at *Puskesmas* (midwives, physicians)
ANC Cohort	A paper-based register containing information on pregnant women within a certain healthcare facility/provider (i.e., village midwives, *Puskesmas*) with information related to pregnancy, ANC, and delivery.	Village midwives (rural areas), midwives' coordinator at *Puskesmas* (urban areas)
ANC e-Cohort	An electronic version of ANC Cohort containing information on pregnant women within *Puskesmas* catchment area.	Midwives' coordinator at *Puskesmas*
SIHA	An electronic surveillance system for HIV and STIs, including syphilis, includes all target populations, including pregnant women.	Disease Control Unit (i.e., HIV/STI program officials) at *Puskesmas*
SIHEPI	An electronic surveillance system for Hepatitis, including HBV, covers all target populations, including pregnant women.	Disease Control Unit (i.e., HIV/STI program officials) at *Puskesmas*
Triple Elimination register	A paper-based register kept at the *Puskesmas* to record testing of pregnant women for syphilis, HIV and HBV	Disease Control Unit (i.e., HIV/STI program officials) at *Puskesmas*

Control

Puskesmas randomised to the control arm will continue to provide ANC services and syphilis, HIV and HBV testing as per the existing standard of care, with supervision from district-level programmers in the Family Unit and the Disease Control Unit of the DHO.

Intervention

Over approximately six months, intervention facilities will receive targeted and enhanced support in line with the CQI approach to promote implementation of the national guidelines and sustained provision of testing for HIV, syphilis, and HBV for all pregnant women in their first trimester and facilitate effective linkage to care for positive cases. The study intervention will comprise four core sets of activities: 1) recruiting and training of district-level CQI coaches; 2) recruiting and training facility-

level CQI advocates; 3) quarterly CQI meetings at the district level; and 4) monthly CQI meetings and/or monitoring at the *Puskesmas* level.

Recruiting and training CQI coaches: In each district, we will recruit three persons (e.g., syphilis, HIV or HBV programmer, a maternal and children health programmer from the DHO, and representatives from the Indonesian Midwives Association) who will lead implementation of the intervention at the district level. They will act as CQI coaches and be responsible for recruiting, training, and supporting CQI advocates at participating facilities, conducting CQI meetings, and monitoring and evaluating the progress of the CQI intervention. CQI coaches will receive training from an independent CQI expert from Indonesia and will be supported by two field officers from the research team who will help facilitate and coordinate CQI meetings with the facilities and provide general support and advice to the coaches. The training of CQI coaches will be delivered by the independent CQI expert, that includes guidance on CQI practices and on testing and treatment for syphilis, HIV and HBV.

Recruiting and training CQI advocates: The CQI coaches will assist *Puskesmas* to select two CQI advocates at each participating intervention facility. The advocates are midwives working in ANC clinics and *Puskesmas* staff responsible for the HIV/syphilis/HBV program. Advocates will ideally be senior staff members (e.g., head or coordinator of HIV/syphilis/HBV program or head of *Puskesmas*), acting as a focal point for the intervention and recognised by colleagues as having this CQI role. In addition to the CQI advocates, we will also invite the head of each intervention facility to be actively involved in the CQI training. Training will cover CQI approaches and guidelines on syphilis, HIV and HBV testing and treatment. Following a train-the-trainer model, coaches will be involved in the training of the CQI advocates to help them address any gaps in knowledge/competencies around HIV/syphilis/HBV testing and treatment. The CQI coaches will provide 'light touch' top-up training in CQI methods as needed throughout the implementation period. Advocates will also receive training to promote engagement of all staff at their facility. *Puskesmas*-based CQI advocates (with the support of coaches) will work with other facility staff to identify and implement simple, workable solutions to address gaps they have identified at their facilities. Facility staff will be responsible for driving the development and testing of these solutions (also referred to as 'change ideas' in the CQI literature), using the existing resources that they feel are best suited to the local context. In some facilities, this may include strategies to expand access to rapid diagnostic tests if it becomes the priority area for improvement.

District-level CQI meetings: These meetings are conducted quarterly by the CQI coaches to share learnings, help facility-level CQI advocates with troubleshooting, and provide refresher training on CQI methods.

Facility-level CQI meetings and/or monitoring: The CQI advocates will conduct routine meetings in their facility to plan, monitor and evaluate implementation of their change ideas. Advocates will be supported by field officers, to facilitate monthly CQI meetings, particularly during the early stages of implementing their change ideas. CQI coaches will conduct monthly routine monitoring visits to the *Puskesmas* to assess progress and provide feedback.

Setting and population

The trial will be conducted in two districts in West Java province (Bandung and Bogor). These sites were selected in consultation with the MoH to ensure diversity in geographic settings (encompassing rural, urban, and remote areas), testing coverage for syphilis, HIV and HBV, and facility size.

Facility eligibility criteria

Facilities will be considered eligible for the study if they meet the following criteria: 1) at least 320 first ANC visits or registrations in 2021; 2) recorded 30% or less coverage of HIV testing amongst pregnant women based on 2021 data; 3) expected to provide ANC services and syphilis/HIV/HBV testing for the duration of the study; 4) not currently engaged in another quality improvement intervention or other health-related research (based on data and information from district health officials); and 5) willing to participate in the study and provide consent (given by the facility manager or other staff in charge).

Facility recruitment and randomisation

From the list of eligible facilities, 20 *Puskesmas* will be randomly selected from each district. The head of the *Puskesmas* will be approached to discuss the trial, and to obtain agreement for their *Puskesmas* to take part in the trial including acceptance of randomisation assignment into either study arm. If they do not agree, then they will be replaced by another facility selected randomly from the remaining eligible facilities. In each district the *Puskesmas* will be randomly assigned to either the control or intervention group with a 1:1 allocation. The randomisation process will ensure balance in facility characteristics including number of ANC visits per year, percentage of women tested for HIV in 2022, and *Puskesmas* accreditation and autonomy status i.e., level of independence and autonomy in financial management. *Puskesmas* with special autonomy have more independence for financial management, including for procurement and hiring additional doctors, nurses, or other health officials, whereas *Puskesmas* without this status rely more on support from the DHO. The proportion of women tested for HIV 2022 will be used as the basis for our sample size calculation since it is the most complete data available at the commencement of the study for the three diseases.

As mentioned above, the “HIV treatment” puskesmas from each district will not be included in the main study sample (see section on Stakeholder involvement).

Masking (blinding)

Because of the nature of the intervention, district health officials and healthcare providers will be aware of allocation. Enumerators collecting outcome data and women interviewed for the process evaluation will be masked to allocation.

Sample size calculation

The trial has been designed to detect a 20% relative difference in the proportion of women tested for syphilis, HIV and HBV attending ANC in the intervention arm compared to those in the control arm in each district. This difference is based on: 1) the proportion of women tested for HIV in each district’s *Puskesmas* in 2021 (i.e. 32%

in Bandung, and 27% in Bogor); and 2) a pragmatic decision regarding time and resources available for data collection. Considerable variability was observed in the data obtained from DHO reports on testing coverage across *Puskesmas* within each district. In order to focus on clusters with the greatest need for change, we targeted facilities where <30% of pregnant women were tested for HIV in 2021.

In 2021, 43 facilities out of 80 met this threshold in Bandung with a mean testing rate of 17% and an intra-cluster correlation coefficient (ICC) of 0.08 while in Bogor 56 facilities out of 101 met this threshold with a mean testing rate of 11% and an ICC of 0.09. We estimate that 20 clusters (facilities), randomised 10v10, and at least 50 women (numbers of records extracted) per cluster will have 84% power to detect an increase from 20% to 40% in Bandung and 85% power to detect an increase from 15% to 35% in Bogor (a 20% relative increase in the proportion of women tested in the intervention arm compared to the control arm in each district).

Population and sampling

Based on the intervention timeline, we will randomly sample data on pregnant women recorded in *Puskesmas* ANC registers (i.e., ANC cohort or e-cohort) during 2022 (pre-baseline), 2023 (baseline) and 2024 (endline). For each year, data from 50 pregnant women over a two-month period will be extracted and analysed.

Outcome evaluation

Primary and secondary outcome evaluation

The primary outcome is defined as the proportion of women attending ANC in a cluster who are tested for syphilis, HIV and HBV during the first trimester (<13 weeks into pregnancy). Secondary outcomes include the proportion of pregnant women tested for syphilis, HIV and HBV during the first visit; the proportion of pregnant women tested for syphilis, HIV and HBV during pregnancy; the proportion of women who tested positive during their pregnancy who commenced treatment; stock-outs of rapid diagnostic tests and treatment (where relevant) for syphilis, HIV, and HBV in the past two months, acceptability of the intervention, total intervention cost and cost-effectiveness.

Data collection for primary outcome

Routinely available data for the primary outcome and secondary outcomes will be extracted by research staff from various data sources at participating *Puskesmas a*nd their network (Table 1). These data sources include the Mother's Card (i.e., a shortened version of the Pink Book kept at some *Puskesmas* as an ANC record), as well as different registers at *Puskesmas* i.e., ANC Cohort and ANC e-Cohort, syphilis and HIV reporting and surveillance system (SIHA), HBV reporting system (SIHEPI) and the *Puskesmas* triple elimination register. The ANC Cohort is a manual form filled out by village midwives or *Puskesmas* midwives, while the ANC e-Cohort is the electronic version generally filled out by midwives' coordinator at the *Puskesmas.* These registers contain information on antenatal care, delivery and postnatal care, including data in triple elimination for pregnant women in the catchment area of

Puskesmas. SIHA is an online surveillance system for HIV and sexually transmitted infections (STIs) including syphilis and generally filled out by the HIV/syphilis program officers at the *Puskesmas*. The various data sources are explained in more detail in Table 1.

Similar to the preparation and co-design phase, we will undertake data validation on a subsample of pregnant women at endline. We will conduct exit surveys with consenting pregnant women to directly obtain information on testing and treatment for syphilis, HIV and HBV recorded in their ANC Pink Book. Data from the Pink Book will be compared to individual data recorded in the *Puskesmas* register during the data collection process. During the exit survey, we will also collect qualitative information for the process evaluation (e.g., women's experience, satisfaction and acceptance related to ANC services and ANC screening for syphilis, HIV and HBV, and perceived barriers related to testing) and treatment costs (see sections below on Context and Process Evaluation and on Economic Evaluation).

Statistical analysis

The primary analysis will be based on the intention-to-treat principle. Primary and secondary outcomes will be evaluated at endline. The primary endpoint will be compared between intervention and control clusters using logistic regression, fitted using generalised estimating equations, and robust standard errors. Effect sizes will be summarised as odds ratios with 95% confidence intervals and relative differences in the proportions of women tested between the control and intervention groups. As well as combining the testing data and service characteristic data we will explore patient, staff, and facility level characteristics associated with the uptake of testing/treatment and uptake of the CQI intervention.

Context and process evaluation

Guided by a theory of change model, we will map the key mechanisms through which the intervention is expected to have an impact and collect both quantitative and qualitative primary data to assess implementation and the role of contextual factors. This will be achieved through different complementary approaches. A health facility survey using a structured questionnaire will be conducted at the beginning, midway and end of intervention implementation (all participating *Puskesmas*). The survey will explore facility capacity in terms of availability of resources to support the PMTCT program, opening hours for ANC and triple elimination testing, as well as occurrences of stock outs of rapid diagnostic tests (including dual tests) for syphilis, HIV and HBV, and treatment (where relevant) in the preceeding 2 months. It will also explore changes in the recording and reporting of triple elimination, existence of other interventions underway to improve triple elimination at the facility and district level, and awareness among staff of CQI activities taking place outside their facility (control *Puskesmas* only). Throughout the study, monthly field notes will also be maintained by field officers in consultation with the research team, in which relevant contextual information will be recorded including any significant events that may impact ANC testing and treatment or the CQI intervention.

In-depth interviews will be conducted with staff at the *Puskesmas* and district level. At the *Puskesmas*, we will interview staff in eight intervention *Puskesmas* and four control *Puskesmas* that will be selected purposively based on clinic testing rates for syphilis, HIV and HBV. Up to 5 staff from each of these 12 *Puskesmas* will be purposively sampled (a mixture of doctors, midwives, nurses, and lay health workers) and invited to take part in a semi-structured interview at the end of the trial. The aim of these interviews is to explore acceptability of screening for syphilis, HIV and HBV, access and understanding of PMTCT guidelines, cascades of care, referral processes and any changes in policy during the study period. Staff from intervention *Puskesmas* will also be asked about uptake of the intervention (or not) including any implementation challenges while those in the control *Puskesmas* will be asked additional questions about potential spillover effects from the intervention *Puskesmas*.

At the district level, three CQI coaches per district and up to two representatives from the DHO will be invited to take part in an interview to explore their experience and perceptions of the impact of the CQI intervention, and issues around sustainability and scale-up of the intervention. Finally, we will conduct in-depth interviews with a purposively selected sample of up to 20 pregnant women at different stages of pregnancy to explore challenges and experiences with screening for syphilis, HIV, and HBV. In addition, questions related to challenges and experiences in screening for syphilis, HIV, and HBV will also be included in the exit survey of pregnant women (see section on Assessment of routinely available data). The number of interviews is an estimate only; thematic saturation and available project resources will help determine the final number.

All interviews will be digitally recorded, transcribed verbatim, and translated from Bahasa to English. Translated texts will be independently coded using NVivo software. Coded segments will be thematically analysed. WHO's framework on the Building Blocks of Health Systems (21) will be used to guide analysis of the in-depth interviews data to ensure system-wide factors impacting implementation and uptake of the intervention are captured along with patient and facility-level factors.

Determinants of antenatal screening

We will conduct multi-level logistic regression models to understand factors associated with the uptake of antenatal screening for syphilis, HIV, and HBV. Data from participants in both the intervention and control groups will be included in this analysis. Sociodemographic variables will be categorized into individual-level factors (e.g., age, education level, employment status, insurance type, receipt of the CQI intervention) and household-level factors (e.g., household wealth, location, and size). The outcome measure will be whether the participant underwent antenatal screening. Identifying the factors that influence the decision to undertake antenatal screening will help inform the design of future interventions and health programs aimed at increasing screening uptake and improving access to care and treatment.

Table 2: Data collection and sources for primary and secondary outcomes

Outcome	Data	Description of data source	Interval/data collection
Primary	Denominator: Number of pregnant women attending ANC across *Puskesmas* network	ANC register at *Puskesmas* and private/village midwives, ANC Cohort of village midwives and *Puskesmas*, and/or Pink Book	Over a period of 2 months at pre-baseline, baseline and endline
	Numerator: Number of women in the *Puskesmas* network who are tested for syphilis, HIV and HBV, in the first trimester (<13 weeks) of pregnancy	ANC register of *Puskesmas* and private/village midwives, ANC Cohort, Pink Book, SIHA and SIHEPI	
Secondary (testing)	Denominator: Number of pregnant women attending ANC across *Puskesmas* network	ANC register at *Puskesmas* and private/village midwives, ANC Cohort of village midwives and *Puskesmas*, and/or Pink Book	
	Numerator 1: Number of women in the *Puskesmas* network who are tested for syphilis, HIV and HBV, during the pregnancy	ANC register of *Puskesmas* and private/village midwives, ANC cohort, Pink Book, SIHA and SIHEPI	
	Numerator 2: Number of women in the *Puskesmas* network who are tested for syphilis, HIV and HBV, at their first visit		
	Numerator 3: Number of women in the *Puskesmas* network who are tested for syphilis, HIV or HBV, in the first trimester (<13 weeks) of pregnancy		
	Numerator 4: Number of women in the *Puskesmas* network who are tested for syphilis, HIV, or HBV, during the pregnancy		
	Numerator 5: Number of women in the *Puskesmas* network who are tested for syphilis, HIV, or HBV, at their first visit		

Outcome	Data	Description of data source	Interval/data collection
Secondary (treatment)	Denominator: Number of pregnant women found to be test-positive during their pregnancy	SIHA and SIHEPI	Over a period of one year at pre-baseline, baseline, and endline
	Numerator: Number of pregnant women found to be test-positive during their pregnancy who commenced treatment		
Process evaluation	Occurrences of stock outs of rapid diagnostic tests for syphilis, HIV, HBV, and dual tests during the past two months	Health facility survey	At the beginning, midway, and end of the intervention period
	Occurrences of stockouts of treatment for syphilis, HIV and HBV during the past two months at *Puskesmas* providing treatment	Health facility survey	At midway, and end of the intervention period
	Acceptability, sustainability and challenges to intervention implementation and uptake, including changes in recording and reporting, and changes in policy during the intervention	- Health facility survey - Interviews with *Puskesmas* staff, CQI coaches, midwives, at the intervention *Puskesmas*	At the end of the intervention period
	Challenges and experiences in screening and referring pregnant women for syphilis, HIV, and HBV	- Interviews with pregnant women - Exit survey of pregnant women	
	Experiences and perceptions of the impact of the CQI intervention, sustainability and scale up of the intervention	Interviews with CQI coaches and DHO staff	
	Potential spillover effects, cascades of care, referral processes and changes in policy during the intervention period	Interviews with *Puskesmas* staff, midwives, and pregnant women in the control *Puskesmas*	
	Contextual information including any significant events that may impact ANC testing and treatment or the CQI intervention including changes in policies or procedures related to triple elimination	Field notes	Monthly, throughout the intervention period
	Factors associated with the uptake of antenatal screening for syphilis, HIV, and HBV	Exit Survey	At the end of the intervention period

Outcome	Data	Description of data source	Interval/data collection
Economic evaluation	Total treatment costs	Exit survey of pregnant women Project and MoH accounts/reports	Throughout trial
	Total program costs	Project and MoH accounts/reports	

Economic evaluation

If effectiveness is demonstrated, based on the primary outcome, we will conduct a trial-based cost-effectiveness analysis based on a six months' time horizon with additional modelling of costs and effects to help determine whether upfront investments in setting up CQI processes can be sustained and the potential for any downstream savings.

The economic evaluation will be undertaken from a health system and societal perspective. Program costs will be categorised across each phase of the intervention and include all resources used by the MoH and any implementing partner in delivering the CQI intervention (e.g., workforce requirements; training/supervision; data recording and monitoring; consumables for developing action plans and reports, team meetings). Treatment costs incurred by the health system (e.g. outreach, *Puskesmas*, hospitalisations) will be measured using project/facility/district level financial accounts and MoH reports. Patient costs, including the costs of transportation and lost productivity, will be captured for a subset of patients participating in the exit survey (see section on Assessment of routinely available data*)*. Incremental cost-effectiveness ratios (ICERs) will be reported in terms of the additional costs of implementing the CQI intervention against the additional proportion of patients tested for syphilis, HIV and/or HBV. Drawing on available evidence on the efficacy of treatment (for both mothers and their babies), we will model these outcomes to determine long-term incremental cost per Disability-Adjusted Life Years (DALY) averted, allowing for comparisons in costs and effects across different settings and ANC quality-improvement interventions. Sensitivity analyses will be conducted to assess the impact of parameter changes with the greatest uncertainty on cost-effectiveness.

Dissemination

Results will be published in international peer-reviewed journals, policy briefs and visual reports. In addition to involving stakeholders in the co-design of the intervention and implementation strategy (see the Preparatory and Co-design section), we will also conduct meetings with key stakeholders including representatives from the MoH, PHO of West Java, DHO of Bandung and Bogor, Non-Governmental Organisation (NGOs), the Indonesian Midwives Association, and to share and discuss the study findings and refine plans for dissemination which are likely to include the aforementioned stakeholders. We will not involve any of the stakeholders in other aspects of the

research study, including the design of the trial, implementation of the protocol, data collection for outcome measurement and analysis, and interpretation of the results. The benefits and burden of the intervention will be assessed through interviews with stakeholders at the end of the intervention.

Ethics

Ethical approval has been granted by the Interventions Research Ethics Committee London School of Hygiene and Tropical Medicine (approval number: 28328) and from the Medical and Health Research Ethics Committee Universitas Gadjah Mada (approval number: KE/FK/0485/EC/2023). Written informed consent was obtained from the heads of all participating clinics, CQI advocates and coaches, staff, and women participating in interviews for the data validation and intervention evaluation. There is no individual consent process for the outcome evaluation due to the reliance on de-identified routine data for the measurement of clinical outcomes.

No money will be paid to participants, the only exception being the reimbursement of travel costs for women participating in interviews. All data collected will be de-identified to protect participant confidentiality. Electronic data will be kept on a secure server accessed only by designated staff with a password.

The trial has been registered with ClinicalTrials.gov (NCT06058286) and the ISRCTN registry https://doi.org/10.1186/ISRCTN11251878. As mentioned above, the results will be disseminated through publications in international peer-reviewed journals, presentations at conferences, and lay summaries provided to the MoH, DHO of Bandung and Bogor, National Development Planning Agency, District Development Planning Agencies of Bandung and Bogor, NGOs, UN Agencies in Indonesia, Indonesian Midwives Association, Association of Indonesia Local Health Offices (ADINKES), etc. On completion of the trial and after the publication of these results, the data can be made available on request by contacting the corresponding author of this protocol.

Discussion

This is the first trial to evaluate the effect of a CQI intervention on antenatal screening for syphilis, HIV and HBV in Indonesia. The findings of the study will be useful for program implementers seeking to achieve triple elimination of syphilis, HIV and HBV transmission from mother to child by 2030 (22). A number of elements of the study will aid generalisability and scale-up if effectiveness is demonstrated including active engagement of key community stakeholders from the MoH, PHO, DHO, health care providers, and Indonesian Midwives Association. Our integrated process and economic evaluations will provide useful information on a broad set of factors driving intervention uptake and sustainability. The use of routine facility data for measuring outcomes will aid efforts to strengthen health information and surveillance systems for ANC. Finally, the findings from this study will help improve testing for HIV, syphilis and

HBV among pregnant women and strengthen the underlying maternal and child health program in *Puskesmas*.

Strengths and study limitations

This study has several strengths. First, this is an evaluation of a low-cost sustainable CQI intervention that has the potential to improve triple elimination in Indonesia. Second, the primary outcome of testing during the first trimester provides information on adherence to national guidelines. Third, we will combine the strengths of a cluster randomized trial design with process and economic evaluations to gain a rich understanding of the effectiveness, implementation and efficiency of the CQI intervention. Fourth, the study involves relevant stakeholders in the co-design and implementation of the CQI intervention, with particular input from facility staff to promote sustainability and empowerment. Lastly (as mentioned above), if effectiveness can be proven, we plan to conduct a cost-effectiveness analysis. This can inform resource allocation decisions in ANC and primary care more broadly.

There are also limitations to our study. First, the use of routinely available data is susceptible to reporting bias by staff at the facility and district level; hence, the study will also conduct data validation on a sub-sample of data. Second, there is a possibility of spillover bias due to within-district random allocation of the CQI intervention. Third, the CQI intervention will be implemented and evaluated in two districts within one province, limiting generalisability of the findings to other districts with similar characteristics. Lastly, the intervention will be implemented over 6 months and evaluated 4 - 8 weeks after implementation; any long-term impacts of the intervention will not be captured.

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