


BMJ Open Challenges and outcomes of implementing a national syphilis follow-up system for the elimination of congenital syphilis in Cambodia: a mixed-methods study

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ABSTRACT

Objectives We aimed to describe the challenges and outcomes of implementing a national syphilis follow-up system to improve syphilis management in maternal and child health (MCH) services in Cambodia.

Design Operational study; quantitative cohort data and cross sectional qualitative data.

Setting Public health facilities at national level and in four provinces with high syphilis prevalence in Cambodia.

Participants Pregnant women screened for syphilis; MCH health care providers and managers.

Methods We conducted an operational research using syphilis screening and treatment data collected from a national follow-up system (cohort data) and reported in the health management information system (HMIS) between 2019 and 2020. We also conducted indepth interviews with 16 pregnant women and focus group discussions with 37 healthcare providers and managers. Descriptive statistics and thematic content analysis were used.

Outcome measures Syphilis testing and treatment results and perceptions regarding these services.

Results A total of 470 pregnant women who tested positive in rapid syphilis testing were recorded in the national syphilis follow-up system in 2019–2020. Of these, 71% (332 of 470) received a rapid plasma reagin (RPR) test and 95% (n=315) tested positive; 78% (246 of 315) received any syphilis treatment and only 28% (88 of 315) were treated adequately with benzathine penicillin G (BPG). Data from four provinces with high syphilis prevalence (more closely monitored) showed higher testing and treatment rates than at the national level. HMIS aggregated data reported a higher number of pregnant women screened and treated for syphilis than the follow-up system during the same period. Barriers

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study provides quantitative data analysis of syphilis screening and treatment at the national level and in selected high prevalence provinces, combined with perceptions of service users and providers.
- ⇒ Along the implementation of this operational research, results were shared at national and local levels and contributed to changes to guidelines and operating procedures regarding rapid plasma reagin testing location and syphilis treatment regimens.
- ⇒ Among the limitations, errors in recording and reporting cannot be excluded in this 'routine' cohort data collection despite efforts to improve the quality of data collection.
- ⇒ Missing data on the treatment of partners of syphilis-positive pregnant women treatment and on syphilis-exposed infant follow-up limit our analysis of the coverage of syphilis testing and treatment along the cascade.

to syphilis testing and treatment included late antenatal care, long distance to RPR testing and treatment, partners' lack of support to reach the health facility, BPG stockout and poor adherence to oral treatment in the absence of BPG. Providers and managers reported a lack of communication across services, insufficient skills to treat infants and absence of clear guidance regarding the revised follow-up system. Study findings contributed to changes in operating procedures nationwide to facilitate access to syphilis testing and adequate treatment and a systematic follow-up of pregnant women and exposed infants.

Conclusions Study results contributed to informing improvements to syphilis management in MCH services in Cambodia.

INTRODUCTION

Syphilis in pregnancy is a major public health problem.¹ Untreated maternal syphilis

contributes to serious neonatal complications, such as fetal loss, stillbirth, and premature and low birthweight infants, and infants with clinical evidence of syphilis are at higher risk of ill health.² Moreover, congenital syphilis is the second leading cause of preventable stillbirth worldwide. Global estimates showed that approximately 66% of adverse outcomes occurred in antenatal care (ANC) attendees who were not tested or were not treated for syphilis.³ Congenital syphilis is therefore preventable, and the elimination of mother-to-child transmission (MTCT) of syphilis can be achieved through implementation of effective early screening and treatment strategies in pregnant women.⁴ The global community has committed to eliminating mother-to-child transmission (EMTCT) of HIV and syphilis. In 2017, the WHO launched the second edition of the *Global Guidance on Criteria and Processes for Validation: Elimination of Mother-to-Child Transmission of HIV and Syphilis*, highlighting key indicators as well as criteria and targets for EMTCT of HIV and syphilis, which was again updated in 2021.⁵

The Ministry of Health of Cambodia has committed to achieving elimination of EMTCT of HIV and syphilis targets by 2025, and in 2018 endorsed and launched the implementation of the National Road Map for Elimination of Mother-to-Child Transmission of HIV and Syphilis.⁶ In Cambodia, national routine data reports from 2017 showed that, among women attending ANC, 63% were screened using rapid syphilis testing. Among the 0.064% who tested positive, 71% received a rapid plasma reagin (RPR) test and 71% (n=75) were confirmed positive for syphilis. Ultimately, of those who tested positive, 97% received treatment (any drug regimen).⁷ However, the data collection was not systematic nor exhaustive, did not include private hospitals and missed which specific treatment was used. Since 2008, the national HIV programme had implemented a follow-up system for HIV-infected mothers and their HIV-exposed infants,^{8,9} but such follow-up had not been developed for syphilis-infected mothers and their syphilis-exposed infants. Following the launch of the National Road Map for EMTCT of HIV and Syphilis in Cambodia in 2018, the Ministry of Health and its partners developed a systematic monitoring and follow-up mechanism to document and track maternal and neonatal syphilis, with reporting integrated into the regular national health management information system (HMIS). The implementation of this follow-up system has not been evaluated to date. In addition, there is a gap in knowledge regarding the perceptions of access to and provision of syphilis testing, diagnosis and treatment in ANC, both from users' and healthcare providers' perspectives. We aimed to describe the main challenges and outcomes of implementing a national syphilis follow-up system between 2019 and 2020 in order to improve syphilis management in antenatal, delivery and postnatal care in Cambodia.

METHODS

Study design

An operational study, using quantitative data collected through a follow-up system (cohort data)

and cross-sectional qualitative data was conducted in Cambodia between 2019 and 2020.

Study setting and context

Implementation of prevention of MTCT of HIV and congenital syphilis in Cambodia

In Cambodia, prevention of MTCT (PMTCT) of HIV and congenital syphilis is implemented by maternal and child health (MCH) and HIV/sexually transmitted disease (STD) programmes. In the early 2000s, under the leadership of the MCH programme, with the support of the HIV/STD programme and development partners, a technical working group was established and national guidelines on PMTCT were developed and have been updated regularly. The PMTCT/Linked Response approach, linking HIV/STD and other health services, in particular MCH services, was launched in 2007, using standard operating procedures,¹⁰ and was jointly scaled up nationwide between 2008 and 2013 by MCH and HIV/STD programmes.^{8,9} This included a follow-up system for HIV-infected mothers and their exposed children. Active identification and follow-up of all HIV-positive cases was implemented and scaled up as part of the Integrated Active Case Management (IACM) nationwide,¹¹ which was then replaced by an initiative called 'Boosted IACM' throughout 2016–2019. However, the follow-up of syphilis-infected mothers and their exposed infants was not included in the Boosted IACM approach; thus, there was no mechanism in place to track syphilis-infected mothers and their exposed infants.

Since 2010, diagnosis and treatment of syphilis in pregnant women and their infants have been integrated into ANC (at all levels of care), in family health clinics (operating at the provincial level and more broadly involved in sexually transmitted infection control) and in paediatric AIDS care services (operating at the district and provincial levels) in Cambodia. Although point-of-care finger prick testing had been included in national ANC guidelines in 2013, the integration of syphilis prevention and management was not yet fully addressed and effective. A dual HIV/syphilis test was introduced in 2017, and elimination of congenital syphilis was included in Cambodia's national road map for implementing EMTCT developed by the national MCH and HIV programmes in collaboration with development partners and approved by the Ministry of Health in 2018. The road map also outlines and suggests coordination mechanisms and tools to support the follow-up.^{6,12}

Quantitative component

Study population and sampling

The study population included pregnant women who tested positive in a rapid syphilis test during ANC and their exposed newborns who were registered in the syphilis follow-up system nationwide between 1 January 2019 and 31 December 2020. Pregnant women and newborns from four selected provinces (Banteay Meanchey, Battambang, Phnom Penh and Siem Reap) showing the highest

number of syphilis cases nationwide were more closely monitored. The study included all subsequent cases registered in the follow-up system; no sampling was required.

Data collection

Individual follow-up or cohort data from all pregnant women with a positive rapid syphilis test and their exposed newborns were collected nationwide through the syphilis follow-up system, including in the four selected provinces. A standard tracking tool and forms were used by PMTCT coordinators at the operational district and provincial levels to collect follow-up information of syphilis-infected mothers and their exposed infants up to 24 months. The collected information was sent to the national programmes team via electronic email every month. National HMIS aggregated (or cross-sectional) data were also collected as a source of comparison for the follow-up cohort data.

Data analysis

Cohort data indicators included (1) the number and percentage of pregnant women tested/confirmed by RPR among those who tested positive in rapid syphilis tests, (2) the number and percentage of positive cases among pregnant women tested with RPR, (3) the number and percentage of pregnant women treated among those confirmed positive with RPR, and (4) the type of treatment received among those treated. National HMIS data were collected for 2019–2020 using similar indicators. Descriptive statistics were generated and p value calculated with 95% CI using STATA/MP V.15.0.

Qualitative component

Study population and sampling

The qualitative component was conducted in the four selected (high syphilis prevalence) provinces (see study population in the Quantitative component). Pregnant women who tested positive in a rapid syphilis test in ANC and subsequently confirmed with an RPR test were included in the study for an indepth interview (IDI). Health service providers working in ANC, maternity hospitals and family health clinics and the managers/coordinators at the operational district and provincial level in each of the four provinces and at the national level were included for a focus group discussion (FGD). We used purposive and convenient sampling to identify and recruit pregnant women who tested positive in a rapid syphilis test in ANC (four per province) and healthcare providers and managers (one FGD per province and one FGD at the national level) (online supplemental table 1).

Recruitment process and data collection

Women who met the inclusion criteria and healthcare providers involved in the syphilis programme at the provincial level were initially invited to participate in the IDIs and FGDs, respectively, by the Provincial AIDS and STD Program (PASP) teams, on behalf of the MCH and HIV programmes. The research team and the PASP officers then followed up by telephone to arrange the meeting

date and time. National-level providers or managers were directly invited by the HIV and MCH programmes. Sixteen IDIs with women and five FGDs with healthcare providers and managers (including 37 participants) were conducted in four provinces and at the national level (online supplemental table 1).

Data collection and management

IDIs and FGDs were held face to face at the National Maternal and Child Health Center, municipal health department in Phnom Penh, and provincial health department, provincial hospital and referral hospital in each of the provinces, except for three IDIs (two in Battambang and one in Siem Reap provinces) which were held by phone due to the long distance between the participant's house and the referral hospital, especially during the COVID-19 pandemic travel restrictions. One interviewer led the IDI process, took notes and recorded it. One facilitator and one note taker conducted the FGDs. Four interviewers (with public health or medical/paramedical background) were trained prior to data collection, first, on basic knowledge related to syphilis follow-up based on the national road map on elimination of HIV under technical guidance officers from the HIV and MCH programme (1-day training). This was followed by a one-afternoon session on qualitative data collection processes and IDI and FGD checklists.

Data analysis

Audio-recorded interviews were transcribed in Khmer, then translated to English. Data were imported and analysed in Microsoft Excel. Thematic content analysis was performed using both deductive and inductive approaches. Data were coded into themes/subthemes as described by Braun and Clarke.^{13 14} Content analysis was employed to identify the main themes related to existing programmes and systems, for example, reported challenges and recommendations and further information on the integration strategy of the syphilis with MCH and HIV programme. Emerging themes from the data were also included.

Ethical issues

All participants were thoroughly informed about the study aims, content, benefits, risks and confidentiality issues, including their right to withdraw consent at any time without having to provide a reason for withdrawal or having to fear negative consequences. Written informed consent was sought from interviewees participating in IDIs and FGDs, except for three pregnant women who were interviewed by phone who gave a verbal consent.

Patient and public involvement

A wide range of public health stakeholders (MCH, HIV/STD programmes staff, managers at the national level and from the districts where the research took place, international and national organisations) were involved in the design, implementation, analysis and dissemination of

Table 1 National syphilis follow-up cohort data, 2019–2020

Variables	Total, 2019–2020		2019		2020		P value*
	n	%	n	%	n	%	
Pregnant women with a positive rapid syphilis test	470		206		264		
Received RPR test							
Yes	332	70.6	149	72.3	183	69.3	0.477
No	138	29.4	57	27.7	81	30.7	
RPR result							
Positive	315	94.9	140	94.0	175	95.6	0.55
Negative	6	1.8	4	2.7	2	1.1	
Unknown/not recorded	11	3.3	5	3.4	6	3.3	
Treatment							
Benzathine penicillin G	88	27.9	66	47.1	22	12.6	<0.001
Erythromycin/cefixime	158	50.2	48	34.3	110	62.9	
Unknown/no treatment	69	22.0	26	18.5	43	24.6	

*P value calculated using proportions between years 2019 and 2020.
RPR, rapid plasma reagin.

the research, which led to improved syphilis screening and treatment guidelines in Cambodia.

Patients were not included in the study design phase. After providing informed consent, women having experienced syphilis screening and treatment were able to express their perceptions of the healthcare services (qualitative component).

RESULTS

Quantitative component

Syphilis screening and treatment among pregnant women

Cohort data

National cohort data reported by PMTCT coordinators using the syphilis follow-up system show a total of 470 pregnant women who tested positive in a rapid syphilis test were recorded in the follow-up system between January 2019 and December 2020 (table 1). The mean age of the women was 27 years (SD=6.7) and the median age was 27 (IQR=21–32), ranging from 15 to 44 (data not shown). Of those who tested positive in the rapid syphilis test, 70.6% (332 of 470) received an RPR test, and of these 94.9% (315 of 332) showed a positive result. Among women confirmed positive by RPR, 78.1% (246 of 315) received any syphilis treatment. However, only 27.9% (88 of 315) of women were treated adequately with benzathine penicillin G (BPG), while 50% (158 of 315) were treated with other drugs (erythromycin or cefixime) and 22% (n=69) received no or unknown treatment. RPR testing rates were similar in 2019 and 2020; however, the use of BPG in 2020 was significantly lower (12.6%) compared with 2019 (47.1%) (table 1). There were either no data or unreliable data on partners' treatment recorded in the follow-up system.

Overall, the highest numbers of pregnant women who tested positive in a rapid syphilis test were in the four provinces included in this operational research (namely Siem

Reap, Phnom Penh, Battambang and Banteay Meanchey) and also in the province of Takeo. These four provinces accounted for 52.3% (246 of 470) of the total pregnant women with a positive rapid syphilis test followed up nationwide in 2019–2020 and received a closer follow-up.

Of the 246 women followed up in the four provinces of the study, 80.1% (197 of 246) got RPR test, of which 95.4% showed a positive result (table 2). Among women confirmed positive by RPR, a total of 87.1% (169 of 194) received any treatment. However, only 24.7% (48 of 194) were treated with BPG, while 62.4% (121 of 194) were treated with other drugs (erythromycin or cefixime) and 13% (n=25) received no or unknown treatment.

Overall, data from the four targeted provinces over 2019 and 2020 showed a (non-significant) higher rapid syphilis testing rate in 2020 compared with 2019. However, in line with national-level data, the use of BPG was significantly lower (6.2% vs 52.6%, $p<0.001$) in 2020 versus in 2019 (table 2).

Data per province (table 3, figure 1) showed significant differences in RPR testing rates, with higher rates (>87.0%) in Battambang and Banteay Meanchey and lower rates in Phnom Penh (78.7%) and Siem Reap (64.7%). The use of BPG ranged between 8.2% (Phnom Penh) and 42.0% in the province of Battambang.

Cross-sectional: aggregated data

National aggregated (or cross-sectional) HMIS data on syphilis screening programme for 2019–2020 showed that among 824675 pregnant women who received at least one ANC visit, 70.5% were tested with a rapid syphilis test, of which 1172 (0.2%) tested positive (online supplemental table 2A). A total of 809 (69%) of these women received an RPR test, and of these ultimately 83.1% (n=672) were confirmed positive for syphilis and 653 (97.2%) were treated, more than two times in terms of number than what was reported in the follow-up system. Aggregated

Table 2 Syphilis follow-up cohort data in 2019–2020 in the four target provinces (Banteay Meanchey, Battambang, Phnom Penh and Siem Reap)

Variables	Total, 2019–2020		2019		2020		P value*
	n	%	n	%	n	%	
Pregnant women with a positive rapid syphilis test	246		110		136		
Received RPR test							
Yes	197	80.1	84	76.4	113	83.1	0.189
No	49	19.9	26	23.6	23	16.9	
RPR result							
Positive	194	95.4	81	96.4	113	100.0	0.129
Negative	2	2.0	2	1.2	0	0.0	
Unknown/not recorded	1	2.5	1	2.4	0	0.0	
Treatment							
Benzathine penicillin G	48	24.7	41	50.6	7	6.2	<0.001
Erythromycin/cefixime	121	62.4	35	43.2	86	76.1	
Unknown/no treatment	25	12.9	5	6.3	20	17.7	

*P value calculated using proportions between years 2019 and 2020.
RPR, rapid plasma reagin.

data from the four target provinces showed higher syphilis testing rates and as expected higher syphilis prevalence in ANC than the overall national data (online supplemental table 2B). Although to a lesser extent than at the national level, a higher number of women tested and treated were reported in HMIS data than in the follow-up system.

Follow-up and outcomes among syphilis-exposed infants

We could not report on infant treatment and mother and infant follow-up after birth to assess the outcomes of syphilis-infected pregnant women and their infants due to the incomplete programme data of the follow-up tool. Aggregated data showed that between 70% and 80% of partners of women who got any syphilis treatment were also treated (online supplemental table 2A,B).

Qualitative component

Barriers to syphilis screening and treatment among pregnant women

Users' perspectives

Long distances between the home and healthcare facilities, especially the referral hospital (where RPR and syphilis treatment take place), affected the utilisation of health services for syphilis testing and treatment among pregnant women (table 4).

There is a pregnant woman living near my house who is syphilis positive too, but she can't come because her husband lives far away and her parents are old. (Pregnant woman (PW2) from Siem Reap)

Table 3 Syphilis follow-up cohort data, per province, in 2019–2020 in the four target provinces

Variables	Banteay Meanchey		Battambang		Phnom Penh		Siem Reap		P value*
	n	%	n	%	n	%	n	%	
Pregnant women with a positive rapid syphilis test	46		55		94		51		
Received RPR test									
Yes	40	87.0	50	90.9	74	78.7	33	64.7	0.005
No	6	13.0	5	9.1	20	21.3	18	35.3	
RPR result									
Positive	40	100	50	100	73	98.7	31	93.9	0.033
Negative	0	0.0	0	0.00	0	0.0	2	6.1	
Unknown/not recorded	0	0.0	0	0.00	1	1.4	0	0.0	
Treatment									
Benzathine penicillin G	9	22.5	21	42.0	6	8.2	12	38.7	0.001
Erythromycin/cefixime	29	72.5	24	48.0	49	67.1	19	61.3	
Unknown/no treatment	2	5.0	5	10.0	18	24.7	0	0.0	

*P value calculated using proportions between the four provinces.
RPR, rapid plasma reagin.

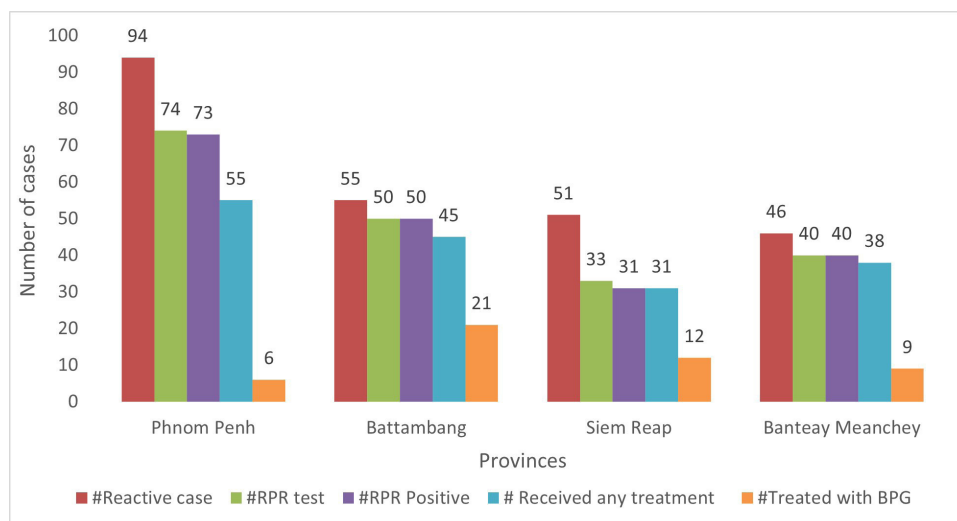


Figure 1 Cascade of syphilis screening and treatment in four provinces: cohort data, 2019–2020. BPG, benzathine penicillin G; RPR, rapid plasma reagin.

Lack of rapid syphilis tests at health facilities was also reported by women as a barrier (table 4).

Some pregnant women only found out about their syphilis-positive status at the time they delivered at the referral hospital after having had only one ANC visit.

Women reported that their partners were an important barrier to syphilis RPR testing and treatment. In many cases, husbands/partners refused to accompany pregnant women to the referral hospital so they could not get the RPR testing and the treatment.

Table 4 Users' and providers' perspectives of syphilis services (key findings, IDI and FGD)

Key issues	Challenges		Explanation (reasons)	Key quotes
	Users (IDI)	Providers (FGD)		
Testing difficulties	<ul style="list-style-type: none"> ▶ When test kits run out, PW screening and treatment were moved to the next day. ▶ Spend much time waiting for the result after being tested. ▶ Partners refused to support PW, for example, to take the test because they wonder why they have syphilis. 	<ul style="list-style-type: none"> ▶ Lack of testing kits and medicine. ▶ Difficult to confirm and follow-up PW and partner. ▶ Challenges to test infants at maternity wards (stockout of kits and double tasks). 	<ul style="list-style-type: none"> ▶ When the titre was not available on site for both PW and syphilis-exposed infants, they were referred to other sites and had to pay test fees. ▶ Still need more efforts to encourage PW (and partners) to take syphilis test, and if positive get treatment and follow up. 	<p>"Sometimes when they [health staff] are out of test kits, we [PW] must go back home without getting tested." (IDI2, Siem Reap)</p>
Referral system (RPR test and syphilis treatment)	<ul style="list-style-type: none"> ▶ PW did not comply with referral due to long distances to health facilities, spending long time at the health facility and did not understand the provider's advice. 	<ul style="list-style-type: none"> ▶ Patient did not return when referred to district hospital. ▶ Stockouts of benzathine penicillin G. 	<ul style="list-style-type: none"> ▶ Lack of recording system in the register book. ▶ Problems related to the reporting system mentioned in most sites. 	<p>"The referral system or following-up cases outside the hospitals have issues." (FGD, MCH, Siem Reap)</p>
Follow-up and treatment issues	<ul style="list-style-type: none"> ▶ PW faced financial problems, distance from health services and (oral) medication side effects. 	<ul style="list-style-type: none"> ▶ PW and partners are lost to follow-up. ▶ PW seeking service late leads to challenges to providing treatment. ▶ Paediatric staff lacked drugs or skills to properly treat infants. 	<ul style="list-style-type: none"> ▶ Side effects of (oral) medication prevent PW from coming to their next appointment. ▶ No contact information or sometimes the patient changes health service location. ▶ For example, penicillin G had to be retrieved from other hospitals or searched for. ▶ Paediatric staff not fully aware of treatment guidelines. 	<p>"(...) The only problem is when we transfer the PW with Syphilis out to other hospitals, and we do not hear back from PW at all.... We do not know where the mother goes to give birth and get treatment...." (FGD, provincial level)</p>
Follow-up system issues		<ul style="list-style-type: none"> ▶ Lack of communication. ▶ The mechanism to follow-up PW was not clear and well understood by the staff. 	<ul style="list-style-type: none"> ▶ Challenges to access PW and their child's health record in logbook and referral letter from one health facility to another. Besides, many patients had never received any feedback information. 	<p>"The follow-up system is not clear because it depends on the patients themselves and depends on a health center that refers to the patient. And I think that this system does not work well because there is not clear communication." (FGD, Banteay Meanchey)</p>

FGD, focus group discussion; IDI, indepth interview; PW, pregnant women; RPR, rapid plasma reagin.

They [doctor] told me to call my husband to go to referral hospital to receive treatment together, but my husband didn't agree to go, so I didn't go too. (PW2 from Battambang)

Regarding treatment, one woman reported that she found it difficult to take the oral treatment due to the large size of the pills or because she had digestion problems after swallowing it during the pregnancy. In one case, a woman reported that the doctor asked her to stop taking the treatment until the delivery of the baby. After receiving the first dose of treatment, some pregnant women never returned for their next appointment. Other barriers that surfaced during the interviews included long waiting times, financial problems and health providers not telling women to follow up on their baby's health.

Nope, she [doctor] didn't tell me. (Pregnant woman #2,1 from Battambang).

Providers' and managers' perspectives

In addition to similar barriers presented by the users, issues related to the referral system were mentioned (table 4).

The referral system or following-up cases outside the hospitals have issues. (FGD, MCH, Siem Reap)

(...) The only problem is when we transfer the PW with Syphilis out to other hospitals, and we do not hear back from PW at all... We do not know where the mother goes to give birth and get treatment... (FGD, provincial level)

Challenges with follow-up and reporting system, and the logbook in particular, also emerged from the interviews with health providers across all study sites. Common problems with the logbook included the complicated and tedious filling process and the limited capacity to fill in the information into a record book/logbook, which according to them stemmed from insufficient training on how to use the book.

Most information was recorded with incomplete information. The recording book was well designed, but the staff needed to figure out how to gather information to fill in that book, which led to some confusion in service provision and data recording. A key challenge identified by health staff in ensuring adequate follow-up with a pregnant woman who received a positive syphilis test was when her partner was negative. Managing the sensitivities around this issue was critical to avoid any violence within the couple. Sometimes health providers felt they had to lie to couples in this circumstance and would treat both the woman and her partner regardless of their result. Lastly, providers also explained that some patients affected by syphilis also faced some behavioural problems or mental illnesses. In these cases, communication could be complicated and would lead to late appointments, refusal of treatment or even ceasing any follow-up.

Barriers to follow-up of exposed infants

The follow-up and treatment of syphilis-exposed infants were important issues raised by health providers at the provincial and national levels. The stockout of BPG, which leads to use of other drug regimens, has implications not only for the mothers (eg, side effects, as mentioned above), but most importantly for syphilis-exposed infants, who need to be treated systematically according to guidelines. However, providers reported not being able to treat infants in most cases for a range of different reasons. First, most sites were out of stock of drugs (BPG and penicillin G) for infants. Penicillin G had to be retrieved from other hospitals or was difficult to find or buy. Sometimes the mother left (early) the referral hospital because she lives far away. Providers also reported that they had a shortage of RPR test kits and could not compare a newborn's RPR titre with the mother's. Health staff at the provincial level mentioned difficulties in drawing blood from infants (hard to find the infant's blood vessels). Even if the test was available, performing the (quantitative) RPR test titre at the maternity in referral hospitals was reported as an additional task (to follow both the mother and the infant).

...I think if I can just do the blood test, and follow-up on their [mothers] treatment [...]. But if I have to take care of the infants as well, I think that would be a bit hard. (NMCH Phnom Penh)

On the other hand, the paediatric ward staff at some referral hospitals reported that they lacked skills to properly treat infants; they reported not being well aware of proper treatment guidelines for syphilis-exposed infants, a lack of staff capacity building through refresher training and a lack of communication at national and subnational levels. Even though such treatments can be done at the referral hospital, some staff felt that children should be referred to higher level hospitals, such as the National Pediatric Hospital. Besides the difficulties with follow-up and treatment of syphilis-exposed infants, staff in some provinces reported difficulties with filling out the follow-up sheet.

DISCUSSION

Despite the HIV and MCH programme efforts to jointly implement the National Road Map for EMTCT of HIV and Congenital Syphilis by 2025, many pregnant women and children remained without a final diagnosis and appropriate treatment for syphilis in Cambodia in 2019–2020. Among the pregnant women who were positive in a rapid syphilis test and recorded in the syphilis follow-up system, 70% and 80% received an RPR test at the national level and four closely supervised targeted provinces, respectively. This is in line with previous studies and global results.¹⁵ A small pilot research study conducted in Vietnam among 3000 pregnant women, without operational challenges of nationwide implementation, reported much higher screening coverages

(>95%) for HIV, Hepatitis B virus and syphilis.¹⁶ A close look at the data from each of the four targeted provinces shows a wide range of RPR screening rates, from 65% in Siem Reap to 87% and 91% in Battambang and Banteay Meanchey, respectively, illustrating that despite receiving a similar refresher training and being more closely supervised, some provinces performed better than others. Phnom Penh encountered the additional challenges of referrals between urban facilities.

The proportions of pregnant women receiving any syphilis treatment at the national level and four targeted provinces (80% and 88%, respectively) were below the 2025 target of 95% coverage, yet better than in many countries.¹⁵ Three of the four targeted provinces had any treatment rates at 90% or above, except for Phnom Penh (75%). Nevertheless, not even one-third of women who tested positive with RPR received an adequate BPG treatment, which was even lower in 2020 than in 2019. Two studies documenting syphilis screening and treatment in Hunan Province, China, showed a similar syphilis treatment rate of 83% in 2016 and an overall treatment rate of 86% between 2015 and 2018.^{17,18} However, the proportion of women treated adequately with BPG in that study was much higher (84%) than in our study.¹⁷ As highlighted in the qualitative findings by providers and managers, recurrent stockouts of RPR tests and BPG occurred from 2019 to 2020. This was mainly due to a delay in the procurement process at the national level by the national supply system through the central medical store, using the national budget. These stockouts occurred despite an earlier call for better BPG planning and management, including Cambodia.¹⁹ On the other hand, as illustrated by different BPG treatment rates between our four provinces, a lack of communication and coordination from the sites to the national levels to request and supply for an urgent need of tests and drugs also led to stockout in many settings. Some treatment sites also managed to obtain BPG drugs from other provinces where the number of cases was lower or used their own hospitals' income from service user fees to buy these items locally (in private sector). The local purchases could in turn be charged to the clients, which represented an obstacle to treatment, as mentioned by some clients during the interviews. According to the WHO and national guidelines, the use of alternative syphilis treatment regimens in the absence of BPG leads to compulsory infant treatment, which in many sites was not administrated. In addition, women reported interrupting oral treatment due to side effects (qualitative findings). This calls for preventing stockouts of RPR test and BPG in MCH settings.

Many factors related to moderate to low screening and BPG administration in study settings can be drawn from our qualitative findings. First, from the service users' perspectives, barriers to accessing syphilis testing and treatment are in line with previous studies elsewhere²⁰: late ANC visits, long distance to referral hospitals where RPR testing and/or syphilis treatment are provided, partner's refusal of the test and/or lack of transportation

support to reach the facility, and limited information provided by health staff to pregnant women led to low RPR testing and treatment uptake. In addition, lost to follow-up for syphilis treatment and financial problems were also reported. Providers reported a lack of clear instructions to fill in a revised reporting system (syphilis follow-up tracking tool), poor communication and coordination across the different healthcare services involved in testing and treating pregnant women and their exposed infants, as well as insufficient skills to treat infants. As reported in previous studies, the role and dedication of the PMTCT coordinator in implementing the road map and the follow-up system might also explain differences in performance across provinces.^{21,22}

A comparison between our cohort follow-up data and the HMIS data suggests that the new follow-up system as part of the EMTCT road map implementation was still poorly used in 2019–2020. Both at the national level and in four target provinces, there was a lower (over 50%) number of pregnant women screened and treated for syphilis registered in the follow-up system than those reported in HMIS aggregated data. A more recent comparison of HMIS and follow-up system data (2021) showed less discrepancy between the two data collection sources, with a substantial increased use of the follow-up system over time. Changes that were implemented over the course of this operational research have contributed to the improvement of the follow-up system.²³

The follow-up system in 2019–2020 did not capture data on exposed infants' testing and treatment of syphilis. Low treatment administration due to lack of adequate skills and confidence in treating babies with injectable penicillin was mentioned by provincial paediatric staff and is not only reported in Cambodia.²¹ Similarly, the lack of treatment and follow-up data was related to the lack of linkages between the family health clinic providing syphilis treatment to mothers and the maternity and paediatric wards. Without such data, the overall syphilis treatment effectiveness and the outcomes of syphilis infection remain unknown. The follow-up system for syphilis cases among pregnant women and their exposed infants should have been piloted in a small number of districts with high syphilis prevalence so that issues of inadequate skills and lack of confidence of staff as well as poor linkages between related service points have been identified and addressed before scaling up nationwide. In Korea, a study conducted at the national level was able to identify 548 infants who were further examined for congenital syphilis.²⁴ A surveillance system for syphilis including pregnant women confirmed with syphilis and their exposed infants has recently been set up in South Africa and is promising.²⁵ Documenting the outcomes of syphilis infection among pregnant women and exposed infants, including stillbirths, needs to be addressed in Cambodia.³

The main strength of this type of study is that it provides quantitative data of syphilis screening and treatment at the national level and in a subset of provinces in Cambodia

with high syphilis prevalence, combined with perceptions of service users and providers to further understand these. Most importantly, alongside the implementation of this operational research, results were shared at the national and local levels and together with an EMTCT mock review conducted by independent experts, which contributed to changes to guidelines and operating procedures.²⁶ RPR testing was no longer compulsory before initiating syphilis treatment, and adequate treatment (BPG) has been made available at district referral hospitals if women cannot reach a provincial treatment centre. However, capacity building (not only on treatment but also on management of anaphylactic shock) and infrastructure readiness, as well as strengthening systematic monitoring and follow-up of cases of mothers and their exposed infants, are required to achieve the goal of eliminating congenital syphilis.

Our study is subject to a number of limitations. Errors in recording and reporting cannot be excluded in routine cohort data collection despite efforts to improve the quality of data collection. Missing data on partners of syphilis-positive pregnant women treatment and syphilis-exposed infant follow-up limited our analysis of the coverage of syphilis testing and treatment along the cascade. Given the limited sample size of the qualitative study and that some IDIs were conducted by phone (due to financial constraints and travel restrictions during the COVID-19 pandemic), saturation might not have been reached and may limit the extent of the views on barriers to access syphilis testing and treatment.

CONCLUSION AND RECOMMENDATIONS

Syphilis testing and adequate treatment remained below elimination targets in Cambodia. The study results contributed to informing improvements to syphilis management in MCH services in Cambodia.

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