Progress towards triple elimination of mother-to-child transmission of HIV, hepatitis B and syphilis in Pacific Island Countries and Territories: a systematic review

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Summary

The diverse geographic, demographic, and societal factors in the Pacific Island Countries and Territories (PICTs) have contributed to unique epidemiological patterns of HIV, syphilis, and hepatitis B. Transmission can be during pregnancy, at the time of birth or via breastfeeding for HIV, and can have long-term adverse outcomes. Given the similarities in prevention of mother-to-child transmission of these infections, coordinated interventions for triple elimination are used. This systematic review has evaluated the peer-reviewed literature, grey literature, and global databases to assess the availability of data to report against elimination targets in the WHO Regional Framework for the Triple Elimination of Mother-to-Child Transmission of HIV, Hepatitis B and Syphilis in Asia and the Pacific 2018–2030. The secondary objective is to report on progress towards these targets. The findings show that none of the PICTs are on track to achieve triple elimination by 2030. Amongst the limited publicly available indicator data, there is suboptimal coverage for most indicators. It is important that there is an increase in availability of and access to antenatal care, testing, and treatment for pregnant women. Increased efforts are needed to collect data on key indicators and integrate reporting into existing systems to avoid extra burden.

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Keywords: Elimination of mother-to-child transmission; EMTCT; HIV; Hepatitis B; Syphilis; Pacific Island Countries and Territories; Systematic review

Background

Human immunodeficiency virus (HIV), hepatitis B virus (HBV) and syphilis can be transmitted from pregnant mothers to their children during pregnancy, labour, and breastfeeding (for HIV); these infections can also cause adverse pregnancy and longer-term outcomes. Without interventions, the HIV transmission rate from mother-to-child ranges from 15% to 45%, and infants born to mothers living with HIV have an increased risk of death in the first few months of life.[1] Between 70% and 90% of infants born to mothers positive for hepatitis B surface antigen (HBsAg) and

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Research in context

Evidence before this study

The Pacific Island Countries and Territories (PICTs) reportedly have high rates of syphilis, moderate to high rates of hepatitis B, and low rates of HIV except for Papua New Guinea. There are significant opportunities through coordinated interventions to prevent mother-to-child transmission of all three infections. It remains unclear how PICTs are progressing towards the goal of triple elimination of HIV, hepatitis B and syphilis. Previous summaries tend to report combined estimates or exclude the smaller PICTs in global reports.

Added value of this study

To our knowledge, this is the first systematic review of indicators related to elimination of mother-to-child transmission of HIV, hepatitis B and syphilis the PICTs. The review specifically focuses on epidemiological indicators and the process and impact indicators outlined in the WHO Regional Framework for the Triple Elimination of Mother-to-Child Transmission of HIV, Hepatitis B and Syphilis in Asia and the Pacific 2018–2030.

Implications of all the available evidence

This review found due to lack of data availability and suboptimal coverage, none of the PICTs are on track to achieve triple elimination by 2030. Pregnant women and children remain at risk for adverse effects of HIV, hepatitis B, and syphilis. It is crucial that PICTs increase the focus on prevention, detection and treatment to improve health outcomes. It is also critical that information on EMTCT indicators are collected and used to inform public health decision making.

hepatitis B e antigen (HBeAg) become chronically infected with HBV if no interventions are used.[2,3] Similarly, syphilis during pregnancy can lead to fetal loss, stillbirth, prematurity, low birth weight, neonatal and infant death, and congenital disease among newborns.[4] The social, psychological, and economic consequences for families with a child infected with these conditions are significant.

Transmission of HIV, hepatitis B and syphilis from mother to child is preventable using similar interventions. These interventions are broadly categorised as (1) early antenatal testing (and retesting, in settings of high prevalence) for HIV, hepatitis B and syphilis; (2) timely treatment and management during pregnancy and beyond; and (3) infant hepatitis B vaccination, including timely administration of the hepatitis B birth dose with, or without, passive immunisation with hepatitis B immunoglobulin (HBIG). However, these programs are often implemented as single-program silos.[5]

The World Health Organization (WHO) Western Pacific Region is comprised of 37-Member States and areas, including the 22 Pacific Island Countries and Territories (PICTs). The PICTs are marked by expansive geography, small populations, diverse cultures, and range from lower to upper-middle income economies. There are few reports describing sexually transmissible infections (STIs) and blood borne virus (BBV) epidemiology and response (prevention and management) in PICTs, with data commonly reported alongside those from much more populous Asian countries of the region. Available data suggest that the PICTs have among the highest global prevalence of syphilis,[6] intermediate to high hepatitis B prevalence,[7] and low HIV prevalence with the exception of Papua New Guinea. Papua New Guinea had a generalised HIV epidemic until 2004 and now is considered to have a concentrated epidemic, with HIV infection predominantly in key populations, including men who have sex with men and sex workers.[8–10]

In 2017, all countries in the WHO Western Pacific Region endorsed the WHO Regional Framework for the Triple Elimination of Mother-to-Child Transmission of HIV, Hepatitis B and Syphilis in Asia and the Pacific 2018–2030 (the "Regional EMTCT Framework").[5] The Regional EMTCT Framework is largely aligned with other global frameworks[11–13] and proposes an integrated and coordinated approach towards reaching the goal of triple elimination. Process and impact targets in the Regional EMTCT Framework are listed in Table 1.

It remains unclear how PICTs are progressing towards the goal of triple elimination. This study aims to assess availability of data required to report on indicators in the Regional EMTCT Framework. The secondary purpose is to describe progress towards these targets and describe the epidemiology of HIV, hepatitis B, and syphilis infection in pregnant women and children.

Method

Several data sources were accessed to extract information on epidemiological indicators and the process and impact indicators included in the Regional EMTCT Framework (see Table 2). These sources included:

1. Peer reviewed literature.
2. Online data repositories.
3. Grey literature.

1. Systematic review of peer-reviewed literature

The PRISMA guidelines to conduct a systematic review were used to collect data on a range of EMTCT

	Impact target	Process target
Reproductive, maternal, newborn and child health		• ANC coverage (at least one visit) ≥95% • Proportion of births attended by skilled health personnel ≥95%
HIV	• ≤50 new paediatric infections per 100,000 live births. • Mother-to-child transmission rate of <5% (breastfeeding populations) or <2% (non-breastfeeding populations)	• HIV testing coverage of pregnant women ≥95% • Antiretroviral therapy coverage of HIV-positive pregnant women ≥95%
Hepatitis B	• ≤0.1% prevalence of the hepatitis B surface antigen among children (≤100 cases/100,000 live births)	• Hepatitis B birth-dose vaccine coverage ≥95% • Hepatitis B third-dose vaccine coverage ≥95% • HBsAg testing coverage of pregnant women ≥95%
Syphilis	• ≤50 congenital syphilis cases per 100,000 live births	• Syphilis testing coverage of pregnant women ≥95% • Treatment of syphilis-seropositive pregnant women ≥95%

Table 1: **Disease-specific elimination impact and process targets from the Regional Framework for triple elimination of mother-to-child transmission of HIV, hepatitis B and syphilis in Asia and the Pacific, 2018–2030.[5]**

indicators from studies published between 1 January 2010 and 10 December 2020. Electronic biographic databases searched included Ovid Medline, Ovid Emcare, and Global Health. The search strategy is described in Supplementary Table S1.

The following inclusion criteria were applied: (1) English language; (2) cross-sectional/prevalence, cohort, randomised control trials, or case–control study design; (3) conducted in a PICT; and (4) reported on an EMTCT-related indicator. Exclusion criteria included (1) non-English language, (2) review article, (3) study conducted outside a PICT, (4) sample from populations not specifically including pregnant women or children, and (5) studies only looking at

	Epidemiological data			Process indicators												Impact indicators			
	HBsAg among pregnant women	HIV positivity among pregnant women	Syphilis positivity among pregnant women	Antenatal care coverage at least once (ANC1)	Antenatal care coverage at least four times (ANC4)	Proportion of births attended by skilled health personnel	Antenatal HIV screening	Antenatal hepatitis B screening	Antenatal syphilis screening	Antenatal HIV treatment coverage	Antenatal syphilis treatment coverage	Stillbirth rate	Hepatitis B birth dose coverage (timely)	Hepatitis B birth dose coverage (ever)	Hepatitis B third dose coverage	Paediatric HIV infections per 100,000 live births	Mother-to-child transmission rate of HIV	HBsAg positivity among children	Congenital syphilis cases per 100,000 live births
American Samoa														●*	●				●
Cook Islands	●		●						●		●●	●	●●	●	●●			●●	●
Federated States of Micronesia			●						●●		●●	●	●	●*	●●			●	●●
Fiji	●		●		●	●			●●		●	●	●	●**	●●			●●	●●
French Polynesia													●	●	●			●	
Guam	●			●	●		●	●	●				●						●
Kiribati			●●	●	●	●			●●		●●	●	●		●			●●	
Marshall Islands			●●		●	●			●		●●	●	●	●*	●●			●	
Nauru			●						●		●●	●	●		●			●	●
New Caledonia		●	●																
Niue						●						●	●		●			●●	
Northern Mariana Islands														●*	●				●
Palau			●	●	●	●			●		●	●	●	●*	●●			●	
Papua New Guinea		●●	●●●	●	●●	●●●	●●		●●	●●	●●	●	●●	●	●●		●●	●●	
Pitcairn Island																			
Samoa			●●	●●	●	●●			●●		●●	●●	●		●			●	
Solomon Islands	●		●	●	●	●			●		●	●	●		●			●	
Tokelau													●	●	●			●	
Tonga			●●	●	●	●			●●		●●	●	●		●			●	●●
Tuvalu			●●			●			●●		●●	●	●		●			●	●
Vanuatu			●●	●	●	●			●		●	●	●		●			●	
Wallis and Futuna														●	●			●	

● literature review
● database review
● grey literature

*BD within 3 days of birth
**reports BD within 2 days

Table 2: **Sources of data available for Pacific Island Countries and Territories on the indicators in the Regional Framework for triple elimination of mother-to-child transmission of HIV, hepatitis B and syphilis in Asia and the Pacific, 2018–2030.**

high risk populations, such as HIV-infected pregnant women.

Data were extracted to a Microsoft Excel worksheet by one author while a second author verified the data. Data for each study included: design, year published, year of study, country, province (if relevant), setting population, sample size, indicator descriptor and the estimate. For studies with multiple indicators, data for each indicator were included.

The quality of peer-reviewed literature was assessed by one author using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools). Literature was assessed according to 14 criteria and given an overall quality rating of good, fair or poor; studies rated as "poor" were excluded.

2. Online data repositories

Available data from 2010 onwards were extracted from the WHO's Global Health Observatory (GHO) data repository,[14] UNICEF's Maternal and Newborn Health Coverage Database,[15] UNAIDS, WHO and UNICEF HIV and AIDS data hub for Asia and the Pacific,[16] and the WHO vaccine-preventable diseases monitoring system.[17] Data sources from the 2018 Baseline Report for Triple Elimination of Mother-to-Child Transmission of HIV, Hepatitis B and Syphilis in Asia and the Pacific were reviewed to identify additional sources with none identified.[18] Data from the most recent year prior to 2020 were used due to possible impacts of health seeking behaviour and reporting during the coronavirus disease pandemic (COVID-19). Data were available only for WHO Member States; data for territories or areas are not reported separately in these global databases. The Pitcairn Islands does not have a routine immunisation programme, and therefore immunisation data are not available.[19]

3. Grey literature

Targeted internet searches were conducted to identify publicly available government reports published since 2010, such as demographic and health surveys, annual health information system reports and UNAIDS Global AIDS Progress reports. Unpublished data from national surveillance systems and situation analyses were not included. Data were excluded from the analysis if inconsistent information was included in the same report, as this suggested poor quality data.

Additionally, data published in a WHO Regional overview of hepatitis B were included.[19]

Data extraction and collation

Quantitative outcomes were extracted from all data sources where available. Data included Regional EMTCT Framework process and impact indicators and relevant epidemiological indicators. The standard error and 95% confidence interval were calculated for each of the data points extracted through the literature review when possible. Where there were multiple years of data for a given indicator for the same country or territory, the most recent data were used. Due to the low HIV incidence in all PICTs except Papua New Guinea, methodology for reporting on HIV indicators was often inconsistent. As such, these indicators are not included in the analysis except for Papua New Guinea.

Maps were created for the prevalence of hepatitis B and syphilis among pregnant women, and hepatitis B among children; maps were developed using R version 4.1.0[20] using shapefiles from the Pacific Community.[21] Maps were not created for HIV due to the lack of data and low number of cases in most PICTs.

Process indicators were presented in a heat map (Fig. 1). Coverage was categorised as low (0–79.9%), medium (80–94.9%), and high (≥95%) using cut-offs for eligible persons or study populations. The cut-off was based on the 95% targets set in the Regional EMTCT Framework. There is no target for stillbirth rate in the Regional EMTCT Framework and therefore this indicator was not categorised. Due to the small number of reports that included impact indicator data other than HBsAg levels in children, these were described in text only.

Results

Description of data sources

Peer reviewed literature

A total of 296 unique reports were screened and after initial exclusions, 60 full-text reports were assessed for eligibility; 44 were excluded and 16 were included in the systematic review component of data extraction (Fig. 2).[22–37] Two reports included for analysis described the same study.[22,23] Included studies are described in Supplementary Table S2 and all data points presented in Supplementary Table S3. Most (n = 13) of the included studies were rated "good" in the quality assessment rating; with the criterion for sample size justification having the poorest performance across the studies (Supplementary Fig. S1).

Online data repositories

Online data repositories had data available for 11 indicators from 14 countries (see Table 2 and Supplementary Table S3).

Grey literature

Demographic and Health Surveys and Global AIDS Monitoring Reports could be identified for 15 PICTs and 13 indicators were covered (refer to Table 2 and Supplementary Table S3).

Process indicator targets

ANC coverage (at least one visit) ≥95%

Antenatal care (ANC) coverage is defined within the Regional EMTCT Framework as a visit to a healthcare

	Antenatal care coverage at least once (ANC1)	Antenatal care coverage at least four times (ANC4)	Proportion of births attended by skilled health personnel	Antenatal HIV screening	Antenatal hepatit is B screening	Antenatal syphilis screening	Antenatal HIV treatment coverage	Antenatal syphilis treatment coverage	Stillbirth rate (per 1000 total births)	Hepatitis B birth dose coverage (timely)	Hepatitis B birth dose coverage (ever)	Hepatitis B third dose coverage
American Samoa											96.70	82.00
Cook Islands						100.00			5.18	>99.5	98.01	98.00
Federated States of Micronesia						94.50		70.00	11.7	70.00	53.50	84.00
Fiji		94.00	100.00			100.00		77.97	8.58	77.00	98.18	99.00
French Polynesia										87.61	91.25	97.83
Guam	88.99	73.26		68.88	98.08	93.53				100.00		
Kiribati	89.00	67.00	92.00			23.40		100.00	14.32	99.00		94.00
Marshall Islands		67.80	92.00			96.60		100.00	10.86	87.00	86.70	82.00
Nauru						61.80		61.80	13.12	>99.5		96.00
New Caledonia												
Niue			100.00						9.37	>99.5		>99.5
Northern Mariana Islands											97.50	62.10
Palau	90.00	81.00	100.00			100.00		100.00	7.71	>99.5	96.60	98.00
Papua New Guinea	76.00	55.00	53.00	19.30		25.60	81.40	79.60	16.09	21.00	95.54	40.00
Pitcairn Islands												
Samoa	93.00	73.00	83.00			89.40		100.00	8.75	78.00		68.00
Solomon Islands	89.00	69.00	86.00			4.90		100.00	10.06	66.00		94.00
Tokelau										76.84	94.74	100.00
Tonga	98.00	89.00	98.00			95.70		100.00	7.7	99.00		99.00
Tuvalu			100.00			100.00		100.00	11.87	98.00		92.00
Vanuatu	76.00	52.00	89.00			82.10		100.00	11.1	82.00		90.00
Wallis and Futuna											97.00	96.02

≥95%
80%-94.9%
<80%

Fig. 1: Heat map of available process indicators.

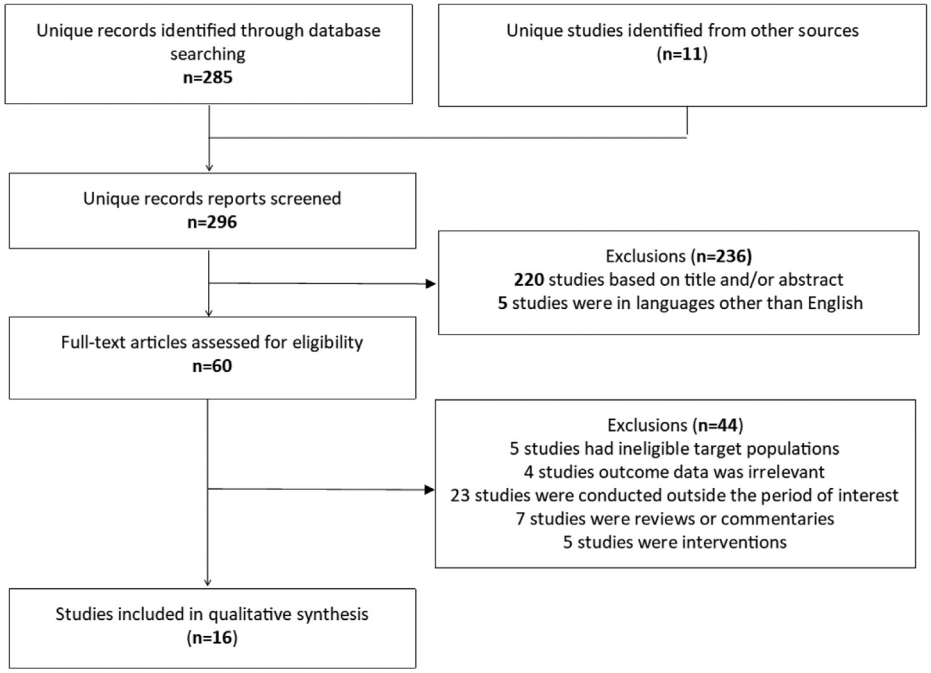

Fig. 2: Flow chart of the systematic review process.

professional during pregnancy and there are indicators for one antenatal care visit (ANC1) and four (ANC4) visits. Since 2016, WHO has recommended a minimum of eight contacts during the antenatal period[38] but this information is not yet regularly reported in global databases.

Of the eight PICTs with data for ANC1, two (Papua New Guinea and Vanuatu) had low ANC1 coverage (defined as <80.0%), five (Guam, Kiribati, Palau, Samoa, and Solomon Islands) had medium ANC1 coverage (80–94.9%) and one (Tonga) met the ANC1 coverage target of 95% or higher. ANC4 data were available for ten PICTs. Coverage ranged from 52% in Vanuatu to 94% in Fiji. Seven PICTs (Guam, Kiribati, Marshall Islands, Papua New Guinea, Samoa, Solomon Islands and Vanuatu) had low ANC4 coverage, three (Fiji, Palau, and Tonga) had medium ANC4 coverage and no PICTs reported ANC4 coverage over 95%.

Proportion of births attended by skilled health personnel ≥95%

Coverage estimates for skilled attendants at birth, Sustainable Development Goal indicator 3.1.2, were available for 11 PICTs, among which one country (Papua New Guinea) had low coverage, five (Kiribati, Marshall Islands, Samoa, Solomon Islands, Vanuatu) had medium coverage and five (Fiji, Niue, Palau, Tonga, and Tuvalu) countries were meeting the skilled attendants at birth coverage target (≥95%).

HIV testing coverage of pregnant women (pregnant women with known HIV status) ≥95%

WHO recommends antenatal screening for HIV, hepatitis B, and syphilis at least once and as early as possible in the pregnancy.[39] Two reports included data on the proportion of pregnant women who were tested for HIV during pregnancy; coverage was reported as 19% in Papua New Guinea and 69% in Guam.

Antiretroviral therapy (ART) coverage of HIV-positive pregnant women ≥95%

ART treatment coverage among HIV-infected pregnant women in Papua New Guinea was estimated between 54% in 2007–2011[29] and 81.4% in 2019.[40] Additionally, Fiji reported providing treatment to all 13 identified HIV-infected pregnant women.[41]

HBsAg testing coverage of pregnant women ≥95%

One report included data on the proportion of pregnant women who were tested for hepatitis B during pregnancy, with an estimate of 98% in Guam.[22,23]

Hepatitis B birth-dose vaccine coverage ≥95%

Seventeen reports included data on timely hepatitis B birth dose coverage (defined as within 24 h of birth); coverage ranged from 21% in Papua New Guinea to 100% in Guam among infants born to mothers with hepatitis B[22,23] and over 98% in the Cook Islands, Kiribati, Nauru, Niue, Palau, Tonga and Tuvalu.[42] Rates of first dose coverage (over 24 h after birth) were also available for eleven PICTs; for example, hepatitis B birth dose was administered to 53.5% of infants within 3 days of birth in the Federated States of Micronesia.[25] However, dosage after 24 h of birth is not considered as meeting the indicator requirements.

Hepatitis B third-dose vaccine coverage ≥95%

Nineteen reports included data on coverage of the hepatitis B third dose (defined as the third dose of a hepatitis B vaccine course including in countries with a four-dose schedule); coverage ranged from 40% in Papua New Guinea[43] to over 99% in Fiji,[14] Niue,[43] Tokelau,[37] and Tonga.[43] Additional estimates were available for infant hepatitis vaccination coverage from a WHO regional publication (Supplemental Table S4).

Syphilis testing coverage of pregnant women ≥95%

Fourteen reports included data on the proportion of pregnant women who were tested for syphilis during pregnancy. Four PICTs (Kiribati, Nauru, Papua New Guinea, Solomon Islands) reported low coverage, four (Federated States of Micronesia, Guam, Samoa, Vanuatu) reported medium coverage and six (Cook Islands, Fiji, Marshall Islands, Palau, Tonga, Tuvalu) reported high coverage.

Treatment of syphilis-seropositive pregnant women ≥95%

Twelve reports included data on the proportion of pregnant women who tested positive for syphilis who received treatment during pregnancy; coverage ranged from 62% to 100%, with eight (Kiribati, Marshall Islands, Palau, Samoa, Solomon Islands, Tonga, Tuvalu, Vanuatu) PICTs reporting high coverage of over 95% (Supplemental Table S3).

Impact indicator targets

≤50 new paediatric HIV infections per 100,000 live births

No data were identified for rate of new paediatric HIV infections. However, one study reported the number of paediatric HIV infections; in Papua New Guinea there were 484 paediatric HIV infections reported in 2017, however the rate per 100,000 live births was not presented.[29]

Mother-to-child HIV transmission rate of <5% (breastfeeding populations) or <2% (non-breastfeeding populations)

One study reported data on the mother-to-child HIV transmission rate; in Papua New Guinea 38% of infants born to HIV-infected mothers were HIV-infected by 18 months.[29] Based on the 2020 Global AIDS Monitoring Country Report for Papua New Guinea, mother-to-child transmission rate of HIV was 22%.[40] In Fiji, two of the thirteen infants (15.4%) born to HIV

positive mothers in 2015 were HIV positive.[41] Based on the grey literature, fewer than ten children born to mothers living with HIV the Republic of the Marshall Islands (two tested negative and the third is untested, as of time of report[44]), Samoa (seven cases of mother-to-child transmission (MTCT) were reported and two HIV free[45]), Solomon Islands (three negative and two reported as presumptive positive[46]), and Vanuatu (one child not tested[47]).

≤0.1% prevalence of the hepatitis B surface antigen (HBsAg) among children (≤100 cases/100,000 live births)

HBsAg estimates varied between sources but there are estimates available for 17 PICTs in different aged cohorts (from under 11 years), which ranged from 0% prevalence in several countries/territories to 8.48% in Vanuatu in 2015 for children <5 years.[14]

Additional data were available from American Samoa based on a representative hepatitis B serosurveys for children aged 5 years. Based on data from the WHO Regional publication, estimates ranged from 0% to 3.3%.[19] (Fig. 3, Supplemental Tables S3 and S4).

≤50 congenital syphilis cases per 100,000 live births

Case rates of congenital syphilis were reported from nine countries and included zero cases in American Samoa,[48] Cook Islands,[49] Nauru,[50] Northern Mariana Islands,[48] Tonga[51] and Tuvalu.[14] In 2013, there were several cases reported in Federated States of Micronesia, which brought the rate to 419 per 100,000 live births that year[14] compared to zero cases in 2017.[52] In Fiji[14] and Guam,[48] the rate was 87.9 and 59.4 per 100,000 live births, respectively. In the Marshall Islands, there were two cases reported in 2015.[53]

Epidemiological data description

HIV-prevalence among pregnant women

The majority of PICTs report zero new cases of HIV among pregnant women annually, with many reporting fewer than 50 cases among the entire population. Papua New Guinea identified a range of 0.8–1.6% of pregnant women who were HIV positive.[28,31,40] Kiribati and Nauru have reported one case each,[50,54] and New Caledonia reported no HIV-positive women in a sample of 3353 pregnant women in 2008–2011.[34]

Hepatitis B-prevalence among pregnant women

HBsAg positivity data among pregnant women were available for four countries; with positivity ranging from 2% in pregnant women in Guam[22,23] and Fiji[27] to 13.8% in Honiara, Solomon Islands[33] (Fig. 4 and Supplemental Table S3).

Syphilis positivity among pregnant women

Syphilis positivity among pregnant women attending antenatal care was available for 14 PICTs and ranged from 0% in the Cook Islands and Tonga to 10.4% in Tuvalu[49,51,55] (Fig. 5 and Supplemental Table S3).

Discussion

No PICT collects and reports sufficient data to report on all indicators and many available indicator estimates are below the required levels. Therefore, it is unlikely that any will be ready to apply for validation of elimination

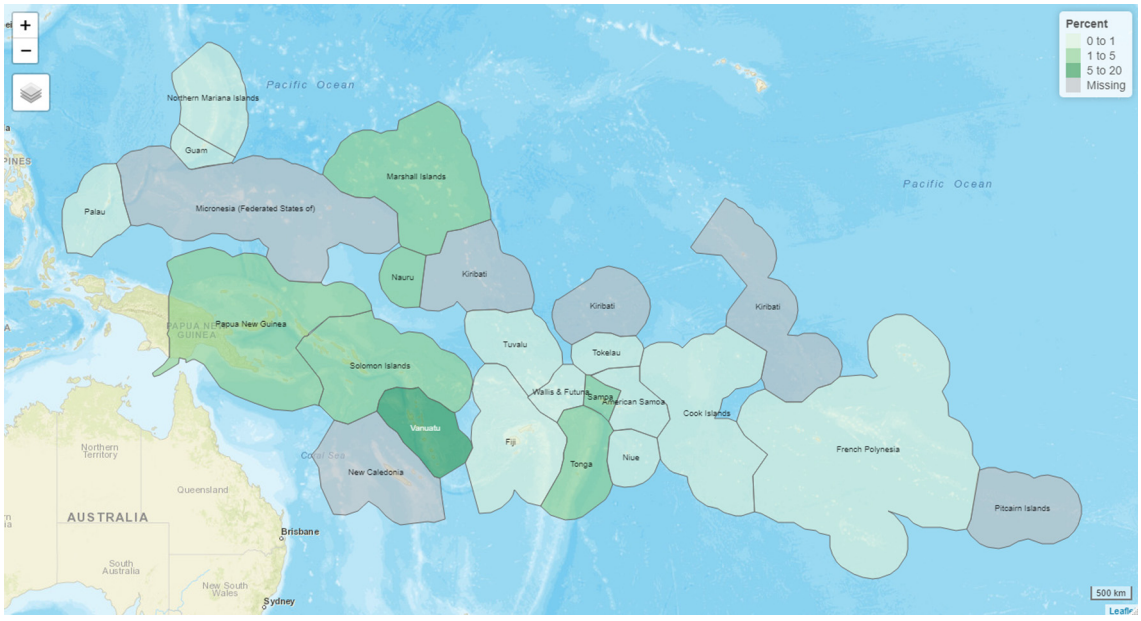

Fig. 3: Prevalence of HBsAg among children.

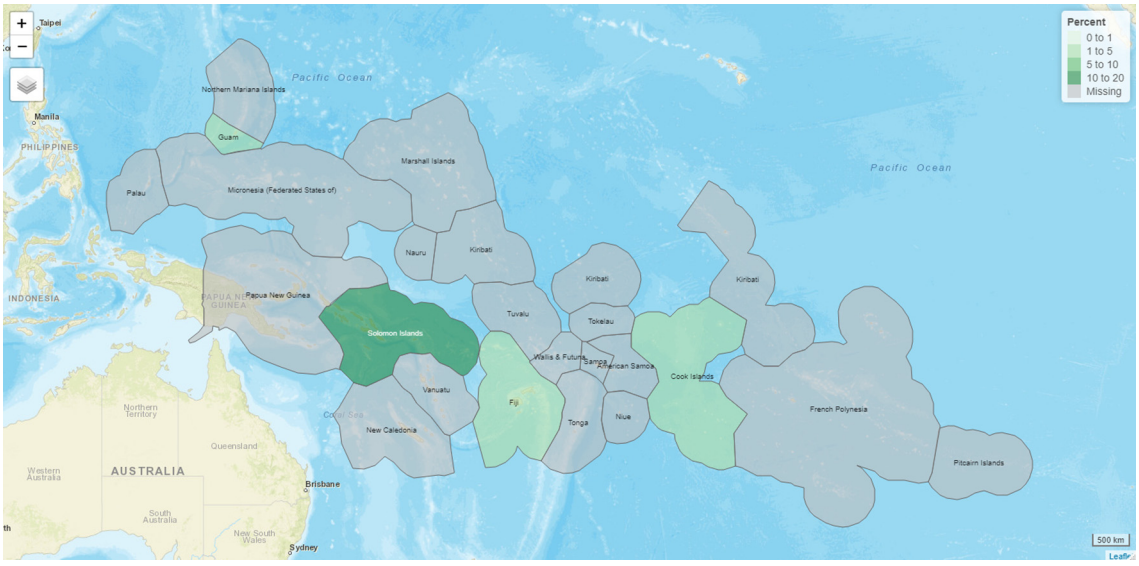

Fig. 4: Prevalence of HBsAg among ANC women.

even if such validation was warranted. The lack of available data on indicators means it is difficult to understand the extent of the problem, likely leading to under investment or erroneous resource allocation. Furthermore, without an understanding of how the coverage of these indicators is changing, programmatic changes will not be reflexive or timely. The collection of data is required to identify whether targets are being achieved. In PICTs where data were available, many were not reaching the required targets outlined in the Regional EMTCT Framework. This review highlights the need for additional investment to improve access to and availability of services to ensure that pregnant women and their children have the best care possible to prevent transmission of HIV, hepatitis B, and syphilis.

WHO guidance on the validation of elimination of HIV and syphilis requires countries to achieve and maintain (for over 1 year) impact targets including a population HIV case rate of ≤50 per 100,000 live births, a HIV MTCT rate of <5% in breastfeeding countries or <2% in non-breastfeeding countries, and a case rate of congenital syphilis of ≤50 per 100,000 live births.[56]

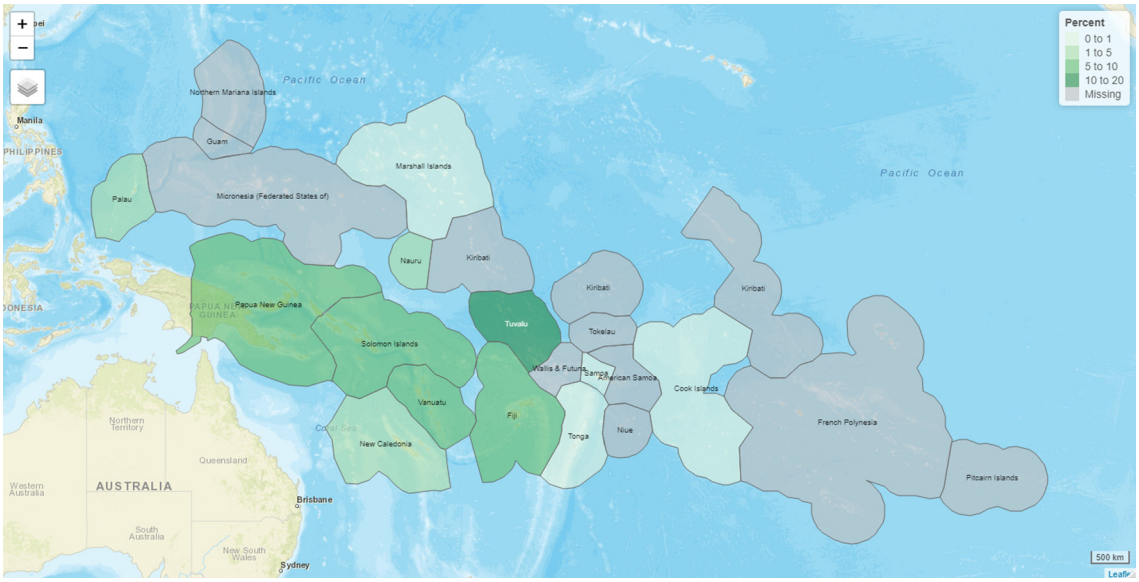

Fig. 5: Prevalence of syphilis among ANC women.

Achieving these targets is difficult for countries with very low maternal HIV and syphilis prevalence and small populations and can lead to high estimates despite low absolute numbers.[57] However, it is in the guidance notes that national or regional validation committees in countries with small populations and small numbers of HIV- and/or syphilis-positive pregnant women per year may use alternative strategies to assess the MTCT rate and population case rates. For example, in-depth review of each maternal case and infant outcomes should be conducted and summarized in a standardized line-listing or case summary format and data pooled from the prior 4 years to provide more stable estimates of the MTCT and case rates.[56] To our knowledge, there is no documentation that details how PICTs conduct in-depth review of maternal cases and deaths of HIV, syphilis or hepatitis B and it is recommended that all countries consider developing a program to case manage maternal cases as well as infant incomes.

The most important strategy to prevent MTCT transmission of hepatitis B is to deliver the first dose of monovalent hepatitis B vaccine as soon as possible after birth, preferably within 24 h, followed by at least two subsequent doses.[2,58] In 2016, Wiesen et al.[59] estimated that in the past 25 years hepatitis B immunization programmes in the Western Pacific Region have averted 7,167,128 deaths that would otherwise have occurred in the lifetime of children born between 1990 and 2014. As of 2017, ten PICTs have reached the 95% coverage target for timely birth dose (Supplemental Table S4).[19] This review has highlighted the low coverage in several countries; interruptions to health service delivery including reduced access to antenatal care and skilled birth attendants due to the COVID pandemic may have further impacted immunisation uptake.[60]

Barriers identified in PICTs for timely delivery of hepatitis B birth dose include access to appropriately stored vaccine,[59,61] high rates of home births unattended by a skilled provider,[62,63] low rates of parental understanding of the importance of hepatitis B birth dose,[59,63] lack of community outreach,[59] vaccine stock outs[59,64] and the need for better vaccine forecasting to avoid wastage[64] as program implementation challenges. There is evidence that monovalent hepatitis B vaccine is relatively heat stable, making it suitable for storage outside cold chain for up to a month.[65] A pilot study in the Solomon Islands showed increase of timely hepatitis B birth dose when stored out of the cold chain[64] and additional modelling suggests taking vaccine out of cold chain is likely to increase coverage and be cost effective.[66] Novel vaccine delivery devices, such as prefilled auto-disable devices and microarray patches, and delivery mechanisms such as drones, have also been a cost effective method to address barriers to coverage.[66,67] These findings are important to consider in PICTs as programmatic implementation challenges will be similar given geographical isolation of health facilities in many settings and high rates of reported vaccine stock outs.

There is evidence that tenofovir improves HBV deoxyribonucleic acid (DNA) suppression at the time of birth[68] and, in 2020, WHO released guidelines on the use of tenofovir for the prevention of MTCT of hepatitis B.[69] Antiviral treatment can reduce maternal viral load and further reduce the risk of MTCT when used in women with high HBV DNA (defined as >200,000 IU/ml) in addition to a timely birth dose of HBV vaccine and HBIG, when available (noting that it is not available in many PICT). Sustained high vaccination coverage, inclusive of timely HBV birth dose, in all sub-national units is therefore of paramount importance to the hepatitis B elimination response in PICTs, with antiviral treatment during pregnancy providing additional protection in women with high viral load.[69] Introduction of antiviral treatment to PICTs with established high hepatitis B vaccination coverage and capacity to scale up monitoring and treatment should be considered. Most PICTs do not currently have the capacity to conduct HBV viral load testing and expansion of testing capacity using existing GeneXpert machines or other emerging HBV viral load testing platforms should be explored. Availability of GeneXpert machines has expanded due to investments made during the COVID-19 pandemic but there will need to be plans in place to ensure they are maintained, cartridges are routinely available, and personnel are trained (personal communication). In the absence of HBV DNA testing, the WHO guidelines recommend use of HBeAg to identify women eligible for antivirals,[69] although access to HBeAg testing is also limited in a number of PICTs.

Nine PICTs (American Samoa, the Commonwealth of the Northern Mariana Islands, the Cook Islands, French Polynesia, Guam, Niue, Palau, Tokelau, and Tonga) have been verified by WHO as having met the regional target of reducing the prevalence of hepatitis B among children 5 years of age to ≤1%. Based on available information, the Marshall Islands was also under review for verification as of 2019.[19] The verification process for the 2030 prevalence goal of 0.1% prevalence among ≤5 year olds has been updated and offers options for countries with small populations, such as conducting a survey to validate elimination.[70] Whilst recommended, surveys can be costly and difficult to achieve and increasingly additional approaches are included in guidance documents that offer alternative approaches, such as measurement of MTCT rate through follow up of HBV exposed infants.[70]

The reported prevalence of syphilis among pregnant women identified in this review was generally lower than in the 2016 WHO global and regional estimates of STIs,[6,71] which reported the highest prevalence in Oceania (5.2%). Oceania also had the highest prevalence of chlamydia (16.4% for women, 13.1% for men),

gonorrhoea (9.3% for women, 8.1% for men), and trichomoniasis (24.3% for women, 2.4% for men).[6] However, the reported prevalence rates used in the WHO global estimates were only from New Caledonia, Papua New Guinea, and Solomon Islands which have notably higher rates of STIs than many other PICTs.[31,72–75] The low coverage of HIV testing in the Solomon Islands is reportedly due to frequent stock outs of HIV testing kits[46] and Papua New Guinea also reports shortages of HIV test kits.[76] Test kit stockouts were also reported for chlamydia testing in Samoa.[45] Low levels of testing among pregnant women have obvious consequences for ongoing MTCT. Many PICTs are starting to use dual HIV and syphilis point-of-care (POC) tests, and expanded use of these could strengthen testing, particularly in areas where lab access is limited. Additionally, there may be an opportunity to invest in multiplex-POCs that combine testing for HIV, hepatitis B and syphilis in one test, which has been shown to reduce MTCT in other resource limited areas.[77]

Screening and treatment of pregnant women and vaccination of infants for HBV significantly reduces the risk of MTCT for all three infections. Integration of HIV and syphilis elimination care into routine services has been advocated for previously[31,57] however, laboratory integration to facilitate testing for HIV, hepatitis B, and syphilis as part of routine obstetric blood tests and integration of messaging about prevention of MTCT in routine antenatal education and counselling could also increase provision and demand for screening and treatment as well as uptake of timely hepatitis B birth dose.

There is a clear need for investment in strengthening data collection systems to ensure that the necessary indicators can be measured systematically and reported at both country and regional level. Furthermore, it would be beneficial to align EMTCT-related indicators and targets across national guidance documents, as recommended by WHO.[70] Summary national data, such as those reported here, do not reflect geographic differences in epidemiology, development, or intervention coverage between main and outer islands, or urban and rural areas. In most PICTs, government offices, health care facilities, and other services are centred on one or two "main islands". Other, "outer islands" may be a great distance away from the main island.[25] Tippins et al.[25] reported a 50% gap in hepatitis B birth dose vaccination coverage between main and outer islands. It is unclear from many reports to what extent the estimates presented are nationally representative although some specify the subnational area the estimates cover (Supplementary Table S2). While summary national estimates are important, so too is collating and reviewing district level data to identify geographic areas requiring increased focus and scale up of service provision. PICTs collate these data monthly, with annual consolidation in health information system reports. However, many reports are not online and therefore these data are not included in this review. It may be beneficial for elimination monitoring to establish a regional online system to collate and review district level data at a national and PICT level. Strategies used by one country to ensure high coverage of an indicator may have relevance for another country, and regular review of these data would facilitate opportunities to improve coverage across the region.

There are several limitations to consider. Firstly, the data used within this analysis are the latest, publicly available information and there may be additional data that are not in the published literature or reports. Another limitation is the potential for issues around congenital syphilis diagnoses, however it was not possible to verify these diagnoses from the published reports. Furthermore, the analysis does not consider the timing of screening; for example, Cha et al.[32] report that whilst 87% of pregnant women received syphilis screening, only 67% were screened within the recommended 24 weeks. The ANC indicators do not assess timing of antenatal visits and high coverage of early antenatal visits is a foundational aspect of EMTCT intervention. So, while many PICTs report relatively high ANC1, it is important to consider the possible variability in impact this has on EMTCT. Furthermore, the published literature may not report on exactly the Regional EMTCT Framework indicator. The variety in years of report is also important to note, particularly for Hepatitis B, given the variable years that vaccination programs started. There are other important indicators such as hepatitis B treatment or antiviral prophylaxis during pregnancy and early neonatal death that are not included in the Regional EMTCT Framework. Restricting the search to only English language literature may have limited data from French speaking PICTs (French Polynesia, New Caledonia, and Wallis and Futuna). Additionally, the robustness and representativeness of data in the literature varies between studies, including differences in sample sizes and calculations, sampling methodology and bias (ex. Convenience vs. random samples), participation rates among possible study participants, recall bias, as well as the national representativeness of estimates from main cities only. As such, caution is needed in the interpretation of data and comparison between PICTs, particularly given the different contexts of each PICT.

Conclusion

This study is the first systematic review of EMTCT data in the Pacific. It has highlighted the lack of available data on indicators outlined in the Regional EMTCT Framework. It has also highlighted high prevalence of syphilis and hepatitis B and low coverage for key EMTCT indicators in many PICTs and adds to the evidence around challenges and progress towards EMTCT.[14] For the

Pacific Region to reach the global elimination goals and requirements in the Regional EMTCT Framework,[5] there is a need for increased coverage and improved reliability of data. This review also highlights the importance of removing the siloed provision of prevention, treatment, and control services for HIV, hepatitis B, and syphilis. Through laboratory integration and multiplex-POC antenatal testing, provision of education and counselling, and case management of positive and high-risk women, there may be an increase in coverage estimates and a reduction in the healthcare seeking burden for pregnant women, while ultimately improving overall health outcomes for women and babies. Given the unique context of small island nations in the Pacific and globally, it may also be necessary to take a more nuanced view of relevant indicators for small island states for future global strategies, as has been done in the latest WHO guidance for country validation of viral hepatitis elimination.[70] The balance of the burden of reporting on healthcare workers and the needs for data to inform programmatic work and ability to report against global strategies needs to be considered.

Contributors

Leila Bell: Conceptualisation, visualisation, writing - original draft, writing - review & editing. Caroline van Gemert: Conceptualisation, methodology, supervision, writing - original draft, writing - review & editing. Nicole Allard: Interpretation, writing - review & editing. Anne Brink: Interpretation, writing - review & editing. Po-Lin Chan: Interpretation, writing - review & editing. Benjamin Cowie: Interpretation, writing - review & editing. Margaret Hellard: Conceptualisation, writing - review & editing. Caroline SE Homer: Interpretation, writing - review & editing. Jess Howell: Interpretation, writing - review & editing. Michelle O'Connor: Interpretation, writing - review & editing. Jane Hocking: Supervision, conceptualisation, writing - review & editing.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanwpc.2023.100740.

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