Protektem Pikinini Blo Yu Trial: Protocol for a field trial to assess the effectiveness of treating-all pregnant women with hepatitis B infection with tenofovir prophylaxis in Vanuatu, 2024-2025

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BACKGROUND

Hepatitis B infection is a major public health concern in the Pacific island nation of Vanuatu, where approximately 9% of the general population are estimated to be living with chronic hepatitis B [1]. Most new infections are due to mother-to-child transmission.

Hepatitis B vaccination is available in Vanuatu, but coverage rates for birth dose and third dose are suboptimal, leaving many children at risk of infection. While treatment with tenofovir disoproxil fumarate (TDF) is available, there is limited capacity to measure hepatitis B viral load and no hepatitis B e antigen testing available - tests that are required by National guidelines and, until March 2024, were recommended globally to determine eligibility for TDF prophylaxis during pregnancy.

In March 2024, the WHO guidelines [2] were updated to recommend TDF prophylaxis for pregnant women living with hepatitis B in a universal peripartum antiviral prophylaxis approach when additional testing is not available. However, these recommendations are preliminary and based on a pragmatic approach, and low-certainty evidence.

This field trial will provide important evidence to these preliminary recommendations through evaluating the effectiveness, acceptability, cost-effectiveness, and safety of a prophylaxis for all approach to TDF prophylaxis for pregnant women with reactive hepatitis B surface antigen (HBsAg) tests.

METHODS

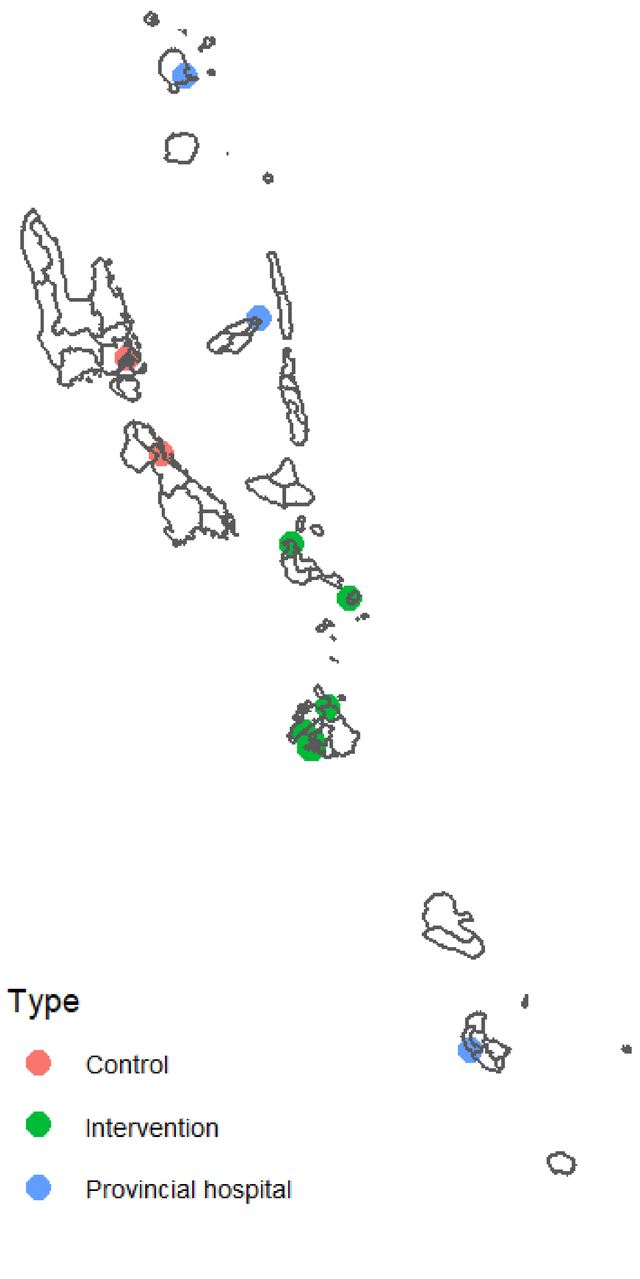
This study is a prospective, single-arm field trial, assessing the effectiveness of using universal peripartum antiviral prophylaxis compared to a real-world external control group.

Participants will be consenting pregnant women with reactive HBsAg results who will receive oral TDF prophylaxis from the second trimester of pregnancy to 14 weeks after giving birth, when their infant should receive their final pentavalent vaccine. The real-world external control group will be all consenting pregnant women with reactive HBsAg results at two provincial hospitals who will receive routine care. Both groups will be encouraged to have their infants fully immunised with hepatitis B birth dose and three doses of pentavalent vaccine.

A sample size of at least 60 mother-infant pairs in the control arm and 72 mother-infant pairs in the intervention arm are required, accounting for a 20% loss-to-follow up rate and TDF compliance rate of 80% in the intervention arm.

For both groups, infants will be followed up at six to 12 months after birth and tested for HBsAg. The primary outcome of interest will be HBsAg status of the infants. Additionally, cost-effectiveness will be assessed and a qualitative analysis of the feasibility and acceptability of midwife delivered care will be conducted.

FIGURE 1. PARTICIPATING CLINICS



DISCUSSION

The outcome of this field study will provide critical evidence to inform global and national recommendations for prophylaxis during pregnancy.

The results will address a critical evidence gap in the clinical management of pregnant women living with hepatitis B, particularly in settings with limited access to laboratory testing.

REFERENCES

1. WHO Collaborating Centre for Viral Hepatitis, AHSM. International Scoping Visit Report: Vanuatu. 2019. p. 1–39.
2. World Health Organization. Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection [Internet]. Geneva: World Health Organization; 2024. Available from: https://iris.who.int/bitstream/handle/10665/376353/9789240090903-eng.pdf?sequence=1

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