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Point-of-care testing and treatment of sexually transmitted infections to improve birth outcomes in high-burden, low-income settings

Submission date
22/06/2016

Recruitment status
No longer recruiting

Registration date
10/07/2016

Overall study status
Completed

Last Edited
11/08/2025

Condition category
Pregnancy and Childbirth

[X] Prospectively registered
[X] Protocol
[X] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Previous studies have shown that sexually transmitted infections (STIs) such as chlamydia, gonorrhoea, trichomonas and bacterial vaginosis can increase the risk of low birth weight, preterm birth and other adverse birth outcomes if these infections are not diagnosed and treated in pregnancy. Evidence for the potential impact of antenatal (during pregnancy) STI screening and treatment is conflicting however. This has led to different screening guidelines being adopted in different countries worldwide. The aim of this study is to measure the effectiveness, requirements to implement, cost-effectiveness and acceptability of antenatal point-of-care testing and immediate treatment of sexually transmitted infections to improve birth outcomes in high-burden, low-income settings.

Who can participate?
Pregnant women aged 16 and above, attending their first antenatal clinic visit when they are up to 26 weeks pregnant

What does the study involve?
Participating health care clinics are randomly allocated to one of two groups. The clinics in the groups undertake the two study conditions in a random order, with 4-6 months in between (during which individual participants are followed up). In the first condition, women being seen by clinics are asked to provide swabs from their genitals to test for STIs (chlamydia, gonorrhoea, trichomonas and bacterial vaginosis) when they enrol in the study (before 26 weeks of pregnancy), one month later, and when they are 34-36 weeks pregnant. If an STI is identified then they receive the treatment for it immediately. In the second condition, women being seen by clinics undergo standard management of STIs, which involves having a urine sample tested for STIs 34-36 weeks into their pregnancy. If an STI is found, the research team provides appropriate treatment after they have had their baby. Women in both groups continue to receive standard antenatal care during their pregnancy, involving scans, HIV and syphilis screening and malaria testing. For all women, 72 hours after they have given birth, the amount of women how deliver

prematurely or have children with a low birth weight are recorded. Participants are also interviewed to provide their views on the point-of-care testing and the cost effectiveness of the program is assessed.

What are the possible benefits and risks of participating?
Participants benefit from the opportunity to be tested and treated for STI's during pregnancy. Women are given light refreshments at each clinic visit and provided with a small gift to recognise their contribution, such as a study T-shirt. At the 36-week antenatal clinic visit women are given a voucher to present to their local hospital to cover costs associated with health facility birth, a mobile phone scratch card (to enable women to notify the team that they have given birth), and a child health book. At the first visit after having their baby women are given a Baby Bundle containing items such as sanitary pads, baby nappies and soap to recognise their time and valuable contribution to the study. Risks of participating are expected to be minimal, but some women may experience some slight embarrassment or discomfort while collecting the vaginal swabs, or feel slightly uncomfortable by the questions asked about sexual health.

Where is the study run from?
The study is run from Papua New Guinea Institute of Medical Research and takes place in antenatal clinics in participating regions (Papua New Guinea)

When is the study starting and how long is it expected to run for?
January 2016 to March 2022

Who is funding the study?
1. DfID/MRC/Wellcome Trust Joint Global Health Trials Grant, grant number: MR/N006089/1 (UK)
2. National Health and Medical Research Council, Australia Project Grant (Australia)
3. Swiss National Science Foundation Grant (Switzerland)

Who is the main contact?
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Additional identifiers

Protocol serial number
MR/N006089/1 / GNT1084429 / IZ07Z0160909/1 / Protocol version 0.3

Study information

Scientific Title
Cluster randomized crossover trial to evaluate point-of-care testing and treatment of sexually transmitted infections to improve birth outcomes in high-burden, low-income settings

Acronym
WANTAIM

Study objectives
Point-of-care testing and treatment of curable sexually transmitted infections in pregnancy will reduce preterm birth and low birth weight compared with standard antenatal care.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Institutional Review Board, Papua New Guinea Institute of Medical Research (IRB), 12/05/2017, ref: IRB 1608
2. Health Research Ethics Committee, University of New South Wales, Australia (UNSW HREC), 18/05/2017, ref: HC16708
3. Medical Research Advisory Committee, National Department of Health, Papua New Guinea (MRAC), 04/10/2016, ref: MRAC 16.24
4. Research Ethics Committee, London School of Hygiene and Tropical Medicine, UK (LSHTM REC), 04/05/2017, ref: REC 12009

Study design
Cluster randomised crossover trial

Primary study design
Interventional

Study type(s)
Prevention

Health condition(s) or problem(s) studied
1. Preterm birth
2. Low birth weight

Interventions
The unit of randomisation is a primary health care clinic and its catchment communities. Ten geographically distinct clusters will be assigned in a 1:1 ratio to control and intervention arms. Each participating cluster will be randomised to participate in either the intervention or the control arm of the trial in the first phase of the study, and following a short washout period of 4-6 months (during which all individual participant follow-up will be completed and staff will receive intensive training in preparation for the transition to the next trial phase), the groups will then crossover to participate in the alternative trial arm in the second phase of the study.

Intervention arm: Women will provide genital specimens for point-of-care STI testing (chlamydia, gonorrhoea, trichomonas and bacterial vaginosis), and be provided with immediate treatment as indicated by their test results, at enrolment (preferably before 20 weeks gestation), one month after trial enrolment, at 34-36 weeks antenatal follow-up.
Point-of-care testing will be conducted using the Cepheid GeneXpert platform (chlamydia, gonorrhoea, trichomonas) and the Gryphus Diagnostics BVBlue Test (bacterial vaginosis).

Control arm: The management of suspected STIs among women in the control arm of the trial will be carried out in accordance with WHO-endorsed PNG national syndromic management guidelines that are based on clinical symptoms alone without laboratory confirmation. Urine specimens collected for routine urine glucose and protein testing in the control arm of the trial will be retained at enrolment, after one month and at 34-36 weeks. These specimens will be tested in an off-site laboratory for chlamydia, gonorrhoea and trichomonas. If positive, the research team will provide appropriate antibiotic treatment at the postnatal visit.

Women attending antenatal clinics in both the control and intervention arms of the trial will receive standard antenatal care in accordance with PNG national guidelines. This includes routine screening for HIV infection and syphilis.

Women in both trial arms will receive additional antenatal and postnatal care in accordance with study-specific procedures:

Additional antenatal care:
1. An obstetric ultrasound scan for pregnancy dating purposes at enrolment (first antenatal clinic visit)
2. Collection/testing of urine and/or vaginal specimens for sexually transmitted infections
3. Additional testing of fingerprick blood specimens for malaria infection

Additional postnatal care:
A postnatal follow-up visit conducted by a trained member of the clinical research team within 72 hours of birth. This will be carried out either at the health facility or in the community following birth. The visit will include the collection of information required for the trial (e.g. birth weight) and be an opportunity to provide additional care for both mother and newborn infant that would not be available as part of routine standard practice (e.g. provision of birth dose vaccinations)

Period of follow-up:
Women will be enrolled at 26 weeks gestation or less, return for a minimum of three antenatal clinic visits (as per WHO and PNG national clinical management guidelines), and complete trial participation at the end of the postnatal visit conducted within 72 hours of birth. The total period of trial participation and follow-up will therefore be approximately 20 weeks per participant.

A sub-set of women and their newborns will be asked to continue trial participation up to 6 weeks postnatally in order to collect additional secondary outcome data. The total period of trial participation and follow-up will be 26 weeks for those who agree to extended postnatal follow-up.

Intervention Type
Other

Primary outcome(s)
Proportion of women and their newborns who experience preterm birth and/or low birth weight, measured within 72 hours in both trial arms.
1. Preterm birth:
The classification of infants as preterm or low birth weight relies on accurate assessment of gestational age. Following best practice, an obstetric ultrasound examination will be carried out by a trained member of the research team to estimate gestational age, as used earlier by our team (Study 3). Findings will be compared with self-reported date of last menstrual period, and pregnancies re-dated according to recommended procedures. The proportion of women experiencing a preterm birth (< 37 weeks gestation) in each trial phase will be calculated by comparing the estimated gestational age (measured at enrolment) with the date and time of birth (measured at the postnatal visit).
2. Low birth weight:
Calibrated, medical grade infant weighing scales accurate to within 10g will be used, two weight readings taken 5-10 minutes apart, and the date and time of each recording noted. The time between the second measurement and estimated time of birth will be used to indicate delay between birth and weight measurement in each case. The mean of the two weight measurements will be used to calculate the proportion of low birth weight newborns (< 2500g) in each trial arm. The inclusion of birth weight data in the primary outcome will be censored at 72 hours of birth: weight measurements after 72 hours but within 1 week of birth will be categorised as ‘late birth weights’ and will not be included with primary outcome data but will be analysed separately.

Key secondary outcome(s))
1. Mean birth weight: calculated within 72 hours of birth in the intervention and control arms of the trial from primary outcome data
2. Premature rupture of membranes: interviews with women during antenatal visits, in labour and/or during the postnatal assessment will be used to establish the timing of rupture of

membranes and whether this occurred prior to the onset of labour. The timing of membrane rupture will be calculated using client-held health books and study records. The proportion of women in each trial arm who experience membrane rupture prior to the onset of labour will then be calculated.
3. Curable STIs diagnosed and treated: the number of women with chlamydia, gonorrhoea or trichomonas (or a combination of these infections) at their first antenatal visit in the control arm will be determined by Xpert™ testing of stored urine specimens. The proportion of those correctly diagnosed and appropriately treated will then be calculated and compared to the proportion diagnosed and treated in the intervention arm.
4. Cost-effectiveness: incremental cost-effectiveness ratios (ICERs) will be calculated for three outcomes (preterm birth, low birth weight and STIs diagnosed and treated) using cost data sourced from health facilities, and health service clients. Long term outcomes will also be modelled as cost per life year saved and cost per DALY averted
5. Health system implementation requirements: quantitative client and health staff CRF data, and qualitative semi-structured interview (SSI) findings, will be used to identify health system implementation challenges and benefits. These are likely to include patient-flow and turnaround-time; work-flow and staff time; training and supervision needs; procedures for finance, payment and health information; community engagement; and shifts in client-provider relationships.
6. Acceptability of antenatal point-of-care STI testing and treatment: client and health staff CRF data will provide quantitative measures of acceptability and will be supplemented by qualitative information from semi-structured interviews with trial participants and health providers. Quantitative data collected at enrolment, antenatal follow-up and the 72 hour postnatal visit will be used to calculate the proportion of participants who would be willing to utilise the intervention again, and who would recommend the intervention to others. Qualitative data from semi-structured interviews will undergo thematic analysis and be used to draw conclusions about acceptability from client and health provider perspectives.
7. Eye infection or moderate/severe clinical pneumonia: the numerator is the number of cases of eye infection and moderate/severe pneumonia occurring within 4-6 weeks of birth. The denominator is the number of live births.
8. Mother to child transmission of C. trachomatis or N. gonorrhoeae: the numerator is the number of neonates / infants with positive eye (C. trachomatis or N. gonorrhoeae) or nasopharyngeal (C. trachomatis) swabs within 4-6 weeks of birth. The denominator is the number of mothers with either infection detected at the final antenatal follow-up visit (34-36 weeks).
9. Diagnostic test accuracy of Xpert™ compared with laboratory-based PCR: sensitivity, specificity, positive and negative predictive value (with 95% confidence intervals) of Xpert™ CT /NG for the detection of neonatal and infant C. trachomatis or N. gonorrhoeae infection using eye and nasopharyngeal swabs collected within 4-6 weeks of birth compared with laboratory-based PCR

Completion date
30/03/2022

Eligibility

Key inclusion criteria
1. Aged 16 years or over at time of enrolment visit
2. Attending first antenatal clinic visit
3. Estimated gestational age 26 weeks or below based on obstetric ultrasound examination at first antenatal clinic visit
4. Able to complete study informed consent procedures; to understand why the study is being

carried out, and the potential risks and benefits associated with study participation
5. Willing to undergo a clinical assessment including ultrasound examination; to provide urine or self-collected vaginal swabs for STI testing; and to comply with study follow-up procedures, including a postnatal visit within 72 hours of birth for the measurement of primary outcome data
6. Live within approximately one hour drive of participating study clinic
7. Able to provide reliable contact details to facilitate future community tracing and postnatal follow-up

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Key exclusion criteria
1. Severe, symptomatic anaemia identified during the enrolment visit that requires hospitalisation (Hb <6 g/dl accompanied by symptoms requiring urgent treatment)
2. Permanent disability, that prevents or impedes study participation and/or comprehension (such that it is not possible to obtain informed consent to participate)

Date of first enrolment
01/09/2016

Date of final enrolment
30/12/2020

Locations

Countries of recruitment
Papua New Guinea

Study participating centre
Papua New Guinea Institute of Medical Research
Highlands Hwy
Goroka
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EHP441

Sponsor information

Organisation
Papua New Guinea Institute of Medical Research

ROR
https://ror.org/01x6n0t15

Funder(s)

Funder type
Charity

Funder Name
DFID/MRC/Wellcome Trust Joint Global Health Trials (JGHT) Grant: MR/N006089/1

Funder Name
National Health and Medical Research Council (NHMRC) Australia Project Grant: 1084429

Alternative Name(s)
National Health and Medical Research Council, Australian Government, NHMRC National Health and Medical Research Council, NHMRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Australia

Funder Name
Schweizerischer Nationalfonds zur Förderung der Wissenschaftlichen Forschung

Alternative Name(s)
Schweizerischer Nationalfonds, Swiss National Science Foundation, Fonds National Suisse de la Recherche Scientifique, Fondo Nazionale Svizzero per la Ricerca Scientifica, Fonds National Suisse, Fondo Nazionale Svizzero, Schweizerische Nationalfonds, The Swiss National Science Foundation (SNSF), SNF, SNSF, FNS

Funding Body Type
Private sector organisation

Funding Body Subtype

Trusts, charities, foundations (both public and private)

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		14/04/2024	17/04/2024	Yes	No
Results article	Health economics using cross-sectional data	27/11/2024	11/08/2025	Yes	No
Protocol article	protocol	20/11/2019	10/02/2020	Yes	No
Protocol article	Protocol for an economic evaluation alongside a cluster-randomised trial	12/08/2021	11/08/2025	Yes	No
Participant information sheet	version V05	06/06/2016	11/07/2016	No	Yes
Statistical Analysis Plan	version 9	29/10/2022	17/02/2023	No	No