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Genital tract infections, the vaginal microbiome and gestational age at birth among pregnant women in South Africa: a cohort study protocol

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2023-081562
Article Type:	Protocol
Date Submitted by the Author:	31-Oct-2023
Complete List of Authors:	Gigi, Ranjana ; University of Bern, Institute of Social and Preventive Medicine; Foundation for Professional Development, Research Unit Mdingi, Mandisa ; Foundation for Professional Development, Research Unit Jung, Hyunsul; University of Pretoria, Medical Microbiology Claassen-Weitz, Shantelle; University of Cape Town, Department of Pathology Bütikofer, Lukas; University of Bern, CTU Bern, Department of Clinical Research Klausner, Jeffrey D.; University of Southern California, Department of Population and Public Health Sciences, Keck School of Medicine Muzny, Christina; University of Alabama at Birmingham, Medicine/ID Taylor, Christopher; Louisiana State University Health Sciences Center, Department of Microbiology, Immunology, and Parasitology van de Wijgert, Janneke H.H.M.; University Medical Centre Utrecht, Julius Center for Health Sciences and Primary Care Peters, Remco; Foundation for Professional Development, Research Unit; University of Pretoria, Department of Medical Microbiology Low, Nicola; University of Bern, Institute of Social and Preventive Medicine
Keywords:	EPIDEMIOLOGIC STUDIES, Sexually Transmitted Disease, Diagnostic microbiology < INFECTIOUS DISEASES, Maternal medicine < OBSTETRICS, Follow-Up Studies

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Genital tract infections, the vaginal microbiome and gestational age at birth among pregnant women in South Africa: a cohort study protocol

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Word counts: Abstract, 294; main text, 3736; 2 figures, 1 supplemental online file

Keywords

Pregnancy complications, premature birth, reproductive tract infections, sexually transmitted infections, microbiota, South Africa

Abstract

Introduction Preterm birth complications are the most common cause of death in children under 5 years. The presence of multiple microorganisms and genital tract inflammation could be the common mechanism driving early onset of labour. South Africa has high levels of preterm birth, genital tract infections and HIV infection among pregnant women. We plan to investigate associations between the presence of multiple lower genital tract microorganisms in pregnancy and gestational age at birth.

Methods and analysis This cohort study enrolls around 600 pregnant women at one public health care facility in East London, South Africa. Eligible women are ≥ 18 years and at < 27 weeks of gestation, confirmed by ultrasound. At enrolment and 30-34 weeks of pregnancy, participants receive on-site tests for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, with treatment if test results are positive. At these visits, additional vaginal specimens are taken for: PCR detection and quantification of *Trichomonas vaginalis*, *Candida* species, *Mycoplasma genitalium*, *M. hominis*, *Ureaplasma urealyticum* and *U. parvum*; microscopy and Nugent scoring; and for 16S ribosomal ribonucleic acid gene sequencing and quantification. Pregnancy outcomes are collected from a post-natal visit and birth registers. The primary outcome is gestational age at birth. Statistical analyses will explore associations between specific microorganisms and gestational age at birth. To explore the association with the quantity of microorganisms, we will construct an index of microorganism load and use mixed effects regression models and classification and regression tree analysis to examine which combinations of microorganisms contribute to earlier gestational age at birth.

Ethics and dissemination This protocol has approvals from the University of Cape Town Research Ethics Committee and the Canton of Bern Ethics Committee. Results from this study will be uploaded to preprint servers, submitted to open access peer-reviewed journals and presented at regional and international conferences.

Registration to be registered on clinicaltrials.gov

Article summary, strengths and limitations of the study

- This cohort study takes a holistic approach, investigating both the presence and quantity of multiple lower genital tract microorganisms, including vaginal microbiota, in pregnancy and their associations with gestational age at birth.
- The study is set in a location where the prevalence of genital tract infections and adverse pregnancy outcomes are high, uses ultrasound scans to assess gestational age at enrolment accurately, and state-of-the-art molecular diagnostic methods.
- The study setting is limited to one research site, which may affect the generalisability of the findings.
- The use of gestational age at birth as a continuous outcome, instead of preterm birth as a dichotomous outcome, might limit comparability with other studies, but we will also examine the binary outcome preterm birth in secondary analyses.

Introduction

Preterm birth complications are the most common cause of death in children under 5 years.¹ Close to one million infants die every year because they are born preterm (before 37 completed weeks of gestation), mainly from infectious, respiratory and neurological complications, and those that survive can experience long-term morbidity.^{1, 2} South Africa has a high incidence of preterm birth at around 10%,³ around 30% of women have one or more curable sexually transmitted infections during pregnancy^{4, 5} and about 30% of pregnant women are living with HIV.⁶

Microbial colonisation or infection during pregnancy, in the lower or upper genital tract, have been reported to predispose to preterm birth, as do anatomical, biochemical, endocrinological, immunological, nutritional, environmental and psychosocial factors.^{7, 8} The presence of microorganisms may contribute to early onset of labour directly, through presumed ascension from the lower to the upper genital tract, or indirectly, through a pathway of inflammatory response, or a combination of both.^{7, 9} Inflammation may be the common pathway, even if infection has not reached the amniotic cavity.¹⁰

Much of the research reporting on the role of sexually transmitted infections in pregnancy and preterm birth has focused on single infections, such as *Chlamydia trachomatis*,¹¹ *Neisseria gonorrhoeae*,¹² and *Trichomonas vaginalis*.¹³ *Mycoplasma genitalium* is the most recently recognised sexually transmitted infection and, whilst an association with preterm birth has been reported, there are few studies with prospective data collection.¹⁴ Bacterial vaginosis is the most common vaginal microbiota dysbiosis and is associated with adverse pregnancy outcomes, either alone, or in combination with other sexually transmitted infections.¹⁵⁻¹⁷ Associations with adverse birth outcomes have also been observed for other genital mycoplasmas, *M. hominis*, *Ureaplasma urealyticum* and *U. parvum*.¹⁸ For individual sexually transmitted infections, bacterial vaginosis and colonisation by other genital mycoplasmas, summary odds ratios for the association with adverse birth outcomes in meta-analyses of univariable data are generally around 1.3 to 2.0.^{11-14, 16, 18} *Candida* spp. have not been found to be associated with preterm birth, but an association with more inflammatory, symptomatic yeast infection cannot be ruled out.¹⁹ Most studies about these

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3 microorganisms do not present analyses that examine the role of co-occurrence or control
4 for confounding factors, so the presence or strength of the causal association cannot be
5 assessed.²⁰ It is also important to include women living with HIV, amongst whom there are
6
7 fewer studies about associations between genital tract infections and adverse birth
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9 outcomes than amongst women without HIV infection.^{21, 22}
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13 The importance of the quantity of different microorganisms as a driver of preterm birth has
14 not been extensively studied,²³⁻²⁵ but might be as, or more, relevant than their presence.²³
15 Together with inflammation or immune activation in the genital tract during pregnancy,
16 organism load could be an important driver of the early onset of labour and preterm birth.^{8,}
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^{23, 24, 26, 27} This calls for a holistic approach to research studies, which combines information about the presence of different microorganisms, the quantified load and the microbiome, sociodemographic factors and HIV amongst women living with infection, most of whom are receiving antiretroviral therapy. The overall aim of this study is to investigate associations between the presence of lower genital tract microorganisms in pregnancy and preterm birth and other adverse pregnancy outcomes. This will be achieved through three objectives to explore: (1) the association between the presence of specific lower genital tract microorganisms and gestational age at birth (primary outcome), as well as secondary adverse pregnancy outcomes; (2) the association between quantified load of vaginal and sexually transmitted microorganisms and gestational age at birth (primary outcome) as well as secondary adverse pregnancy outcomes; and (3) the combinations of microorganisms that are most strongly associated with earlier gestational age at birth.

Methods and analysis

STUDY DESIGN AND SETTING

This prospective closed cohort study follows women enrolled during pregnancy until after they give birth (Figure 1). The study is conducted at the antenatal clinic of one primary health care facility in Buffalo City Metropolitan Municipality, Eastern Cape Province, South Africa. This cohort study is part of a larger project, called Philani Ndiphile (meaning 'be healthy and I will be healthy' in isiXhosa), which includes a randomised implementation-

effectiveness trial of screening strategies for sexually transmitted infections in pregnancy²⁸ and a case-control study about persistent *C. trachomatis* infection.

PARTICIPANTS

Inclusion criteria: Pregnant women aged 18 years or older, who live in Buffalo City Metropolitan Municipality, intend to deliver in the same municipality and provide written informed consent to take part in the study. The eligible gestational age at enrolment, confirmed by ultrasound, was below 20 weeks at the start of the study in March 2021 and was increased to 27 weeks in September 2021 to increase enrolment and to align with another trial.²⁹

Exclusion criteria: Participation in any other research study or inability to understand and speak a local language (English, Afrikaans, or isiXhosa).

Figure 1 Study visits and specimen collection

Abbreviations: CT, *Chlamydia trachomatis*; NG, *Neisseria gonorrhoeae*

ENROLMENT

A trained study field worker approaches all pregnant women attending an antenatal care visit at the clinic and individually informs them about the study. If a potential participant shows interest in the study, the study field worker checks for eligibility. The date of the last menstrual period is used initially to estimate gestational age. If all eligibility criteria are met, a study field worker obtains written informed consent from the participant.

STUDY PROCEDURES AND VISITS

At the enrolment visit, study field workers administer a questionnaire to record socio-demographic, behavioural and clinical information in an online Research Electronic Data Capture software (REDCap)³⁰ database. The study nurse examines the woman, according to the South African government standard of care.³¹ As an additional procedure, a study nurse with training in obstetric ultrasound performs an abdominal ultrasound to estimate the gestational age. If this is later than the eligibility criterion, the participant is excluded from any further study activity. A study nurse collects vaginal samples (Figure 1) for on-site

1
2
3 testing for *C. trachomatis* and *N. gonorrhoeae* using the Xpert CT/NG assay on the Gene
4 Xpert platform (Cepheid, Sunnyvale, CA, USA) and for further off-site laboratory testing (see
5 'Specimen collection and analysis').
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9 If the test result for *C. trachomatis* or *N. gonorrhoeae* is positive, the woman receives
10 immediate antibiotic treatment if still on site or is contacted by telephone and asked to
11 return to the clinic for treatment. Antibiotic treatments are first-line regimens according to
12 South African guidelines: for *C. trachomatis*, 1g oral azithromycin and for *N. gonorrhoeae*,
13 500mg intramuscular ceftriaxone (250mg until South African treatment guidelines for
14 sexually transmitted infections changed in December 2022).³² Women with vaginal
15 discharge syndrome but with negative Xpert test results for *C. trachomatis* and *N.*
16 *gonorrhoeae* receive empirical treatment for trichomoniasis with metronidazole 400 mg
17 twice a day for 7 days. The study nurse gives advice to women with *C. trachomatis* or *N.*
18 *gonorrhoeae* on safe disclosure of her diagnosis to her partner(s) and gives her a notification
19 slip(s) to request her partner(s) to attend a clinic for treatment.
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30 A follow-up visit at 30-34 weeks (third trimester visit) is scheduled at which clinical and
31 obstetric information, as well as the same vaginal specimens, are collected and treatment
32 given, if indicated.
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36 A post-natal visit is scheduled for 3-6 days after giving birth, according to the South African
37 government standard.³¹ A study nurse collects information about the birth outcome and
38 perinatal period through a questionnaire with the mother, a patient-held medical record of
39 the baby (the Road to Health card) and/or the birth register from the public birth clinics
40 within the study area. If the participant does not attend the post-natal visit, study staff
41 telephone her to ask her to return to the clinic. If the participant is not able to return to the
42 clinic, the study physician collects the information by telephone or from the birth register.
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50 51 **OUTCOMES**

52 The primary outcome is gestational age at birth, measured in days, based on the ultrasound
53 assessment at the enrolment visit. Secondary outcomes are preterm birth (<37 completed
54 weeks of gestation), low birth weight (birth weight <2500g), miscarriage (dead foetus
55 delivered before 28 completed weeks of pregnancy or with birth weight below 1000g) and
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3 stillbirth (dead foetus delivered at or after 28 completed weeks of pregnancy or with birth
4 weight above 1000g).^{33, 34} We chose gestational age at birth as the primary outcome
5 because, whilst the cut-off of 37 weeks is the standard definition of preterm birth,
6 dichotomisation of a continuous variable results in a loss of statistical power.³⁵
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10 11 12 **SPECIMEN COLLECTION AND ANALYSIS**

13 14 15 **DATA SOURCES AND VARIABLES**

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17 The source data are case report forms recording questionnaire data for the enrolment, third
18 trimester and post-natal visits and forms for laboratory and specimen results, which are
19 stored in REDCap, a secure web-based database³⁰ (online supplemental file), hosted by the
20 Foundation for Professional Development, Pretoria, South Africa.
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25 26 27 **SPECIMEN COLLECTION**

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29 At the enrolment and the third trimester visits, a study nurse collects two vaginal smears
30 using inoculation loops and air-dries them on glass slides. She then collects vaginal
31 specimens by inserting swabs into the vagina up to a mark at 4 cm and rotating around the
32 vaginal wall. Five swabs are collected in the following order: one Cepheid GeneXpert Xpert
33 Vaginal/Endocervical Swab in a tube with Xpert Swab Transport Reagent (Cepheid,
34 Sunnyvale, CA, USA); two Qiagen digene Female Swabs in a single tube with digene
35 Specimen Transport Medium (Qiagen, Hilden, Germany); and two dry FLOQswabs (COPAN,
36 Brescia, Italy) each in a separate sterile tube (Figure 1).
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45 46 47 **TRANSPORT AND STORAGE OF SPECIMENS**

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49 Vaginal smear glass slides are stored and transported in plastic slide carriers at room
50 temperature. All vaginal swabs are initially stored at the clinic in a refrigerator (2-8°C with
51 daily temperature checks). All vaginal swabs, except the Xpert swab, which is tested on-site,
52 are transported on ice packs once a week by overnight road courier, to the laboratory at the
53 Department of Medical Microbiology, University of Pretoria, where they are also stored in a
54 refrigerator until DNA extraction.
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MICROBIOLOGICAL ANALYSES

The Xpert vaginal swabs are tested on-site using the Xpert CT/NG assay (Cepheid, Sunnyvale, CA, USA) to detect *C. trachomatis* and *N. gonorrhoeae*, as per manufacturer's instructions. At the University of Pretoria, air-dried vaginal smears are heat-fixed and Gram-stained.³⁶ Two qualified people record the Nugent scores (0-3: normal; 4-6: intermediate; 7-10: bacterial vaginosis) and the presence of yeasts.³⁷ In case of discrepancies a third person assesses the slide and consensus is reached by discussion. At the University of Pretoria, one vaginal FLOQswab is used for PCRs. The genomic DNA is extracted using the High Pure PCR Template Preparation Kit (Roche Diagnostics GmbH, Mannheim, Germany) as per manufacturer's instructions. Real-time PCR assays are then performed using the LightCycler 480 Probes Master Kit (Roche Diagnostics GmbH, Mannheim, Germany) on the LightCycler 480 II instrument (Roche Diagnostics GmbH, Mannheim, Germany). Previously published primer and hydrolysis probe sequences and cycling conditions are used for detection and quantification of *M. genitalium*,³⁸ *M. hominis*,³⁹ *U. parvum*,⁴⁰ *U. Urealyticum*,⁴⁰ *T. vaginalis*⁴¹ and *Candida* spp.^{42, 43} The load for each assayed microorganism detected in vaginal swab specimens by real-time PCR or GeneXpert is obtained from the cycle threshold value.

VAGINAL MICROBIOME LABORATORY ANALYSES

The vaginal swabs stored in Qiagen digene Specimen Transport Medium will be used for DNA extraction and subsequent 16S ribosomal ribonucleic acid (rRNA) amplicon sequencing targeting the V3-V4 hypervariable regions for vaginal microbiota analyses at the Division of Medical Microbiology, University of Cape Town.

A commercial DNA extraction kit will be used and a bead-beating step included.⁴⁴ A DNA isolation control will be prepared from an unused vaginal swab specimen during this process. Two PCR rounds will be conducted to prepare amplicon libraries.⁴⁵ The aim of the first PCR round is to amplify 16S rRNA gene V3-V4 regions, using the 319F 5'-ACTCCTACGGGAGGCAGCAG-3' forward primer and 806R 5'-GGACTACHVGGGTWTCTAAT-3' reverse primer. The aim of the second PCR round is to barcode the V3-V4 amplicons by a dual-index approach, permitting multiplexing of up to 384 samples (including controls). Amplicon concentrations for all sample libraries are measured and normalised to form a mixed loading library. The libraries will be sequenced on an Illumina MiSeq instrument

(Illumina, San Diego, CA, USA), 2x300bp. To quantify the number of 16S rDNA copies per swab, a quantitative PCR using the same forward and reverse primers as described above will be used. Samples from enrolment and third trimester visits from the same woman will be processed in the same run.

VAGINAL MICROBIOTA BIOINFORMATICS

Raw sequencing reads will be processed using an established bioinformatics pipeline.⁴⁶ Taxonomic assignment of amplicon sequence variants (ASVs) will be done in DADA2⁴⁷ with SILVA⁴⁸ as the reference database. Vaginal microbiome composition data will be visualised in heatmaps and diagrams. For each vaginal sample, we will calculate diversity measures (alpha diversity), relative abundances and estimated concentrations of key vaginal bacteria and bacterial groups, as described.⁴⁶ We will use the entire sequencing dataset to design vaginal microbiota types by hierarchical clustering, and each sample will be assigned to one vaginal microbiota type.

SAMPLE SIZE CALCULATION

The sample size has been calculated for objective 1, with a univariable comparison between the presence of a genital tract microorganism in the mother and gestational age at birth. Figure 2 shows that, for any vaginal or sexually transmitted microorganism, or vaginal microbiota type that has a prevalence of 10% or more among all enrolled women, about 500-600 patients provides adequate power (80%) to detect a one-week difference (with standard deviation 2) in mean gestational age between the two groups using Student's t-test. Specifying an alpha of 0.83% allows for multiple hypothesis testing (6 hypotheses, using a Bonferroni correction). We enrol around 600 women and aim to have complete follow-up and outcome data on at least 550 women.

Figure 2 Sample size requirements at different levels of exposure prevalence with power of 80% and alpha 0.83% based on Student's t-test.

Legend: panel A, standard deviation 1.5; panel B, standard deviation 2.0. The curves for % exposed are symmetrical around a prevalence of 50%, i.e., curve for 10% exposed is same as that for 90% exposed.

STUDY TIMELINE

Enrolment began on 28 March 2021, with an estimated date for reaching the target sample size in August 2023. Follow-up of all participants until the post-natal visit is expected to be completed by March 2024.

STATISTICAL ANALYSIS

This description gives an overview of the statistical methods for each objective. A detailed statistical analysis plan will be published separately and made publicly available.

We will describe the numbers of women enrolled and available at each follow-up visit in a flow chart. We will present descriptive tables of socio-demographic, behavioural and clinical characteristics and compare women with complete follow-up with those lost to follow-up.

OBJECTIVE 1) ASSOCIATION BETWEEN SPECIFIED EXPOSURES AND PREGNANCY OUTCOMES

1a. We will examine a primary set of microorganisms as exposures, detected at either enrolment or at the third trimester visit: *M. genitalium*, *M. hominis*, *U. urealyticum*, *U. parvum*, *T. vaginalis* and *Candida* spp. are the microorganisms for which women did not receive diagnostic tests and treatment during study visits. We will use the mean and standard deviation for the continuous outcome (gestational age) and absolute and relative frequencies for the binary outcomes (all secondary outcomes). Gestational age at birth for each exposure will be compared using Student's t-test and a mean difference with 95% confidence intervals (continuous outcome) and Fisher's exact test and a risk difference with 95% confidence intervals (binary outcomes).

To control for confounding, multivariable regression models will be fitted to all outcomes with a set of pre-specified potential confounders (age, educational level, alcohol consumption, HIV infection, prior preterm birth) for all organisms. For analyses of *M. genitalium*, *T. vaginalis*, and *Candida* spp., we will also control for bacterial vaginosis (Nugent score 7-10). The other genital mycoplasmas can be identified from 16S rRNA amplicon sequencing in women with vaginal dysbiosis, so are sometimes considered part of bacterial vaginosis. For these organisms, we will conduct descriptive analyses, stratifying by the presence of bacterial vaginosis. For continuous confounders a linear relationship will be

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3 assumed by default but transformations (e.g., log) or more flexible approaches (e.g., splines
4 or fractional polynomials) will be considered if there is evidence for non-linearity. For the
5 continuous outcome we will use linear mixed effects regression models (including data from
6 either visit and the participant as random effect) and report the result as mean difference
7 with 95% confidence intervals. For the binary outcome we will use logistic mixed-effects
8 regression and report the result as odds ratios with 95% confidence intervals.
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15 1b. Comparisons for associations with timing of detection, other microorganism exposures
16 and birth outcomes will be considered secondary analyses. Associations between vaginal
17 microbiota composition and pregnancy outcomes will be assessed. We will use
18 compositional multivariable analysis methods to identify bacterial taxa that are differentially
19 abundant between binary pregnancy outcome groups at the level of individual taxon
20 relative abundances. We will use mixed effects models (with the individual participant as
21 the random effect and including data from both visits) to assess associations between
22 continuous and binary pregnancy outcome and the following fixed effects derived from the
23 vaginal microbiota data: alpha diversity, vaginal microbiota types and absolute abundances
24 of predefined bacterial groups.⁴⁶ These models will be adjusted for confounding as
25 described in the previous paragraph.
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36 OBJECTIVE 2) ASSOCIATION BETWEEN QUANTIFIED MICROORGANISM LOAD AND PREGNANCY 37 OUTCOMES 38

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40 We will investigate the hypothesis that the quantity of microorganisms with inflammatory
41 potential is associated with gestational age at birth. For this, we will analyse the vaginal
42 microbiota data jointly with sexually transmitted infections and *Candida* spp. diagnostic test
43 results during pregnancy (these will be considered as additional covariates in the above-
44 mentioned regression models). We will develop a 'vaginal inflammation index', based on
45 quantification of the vaginal microbiota and their inflammatory potential⁴⁹ and of yeasts.
46 This vaginal inflammation index will also be analysed as a fixed effect in mixed effects
47 models with pregnancy outcomes as the outcomes; these models will not include any of the
48 infection parameters that were used to design the index.
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OBJECTIVE 3) CLASSIFICATION AND REGRESSION TREE ANALYSIS FOR THE PRIMARY OUTCOME

We will conduct exploratory analyses to examine the combination of microorganisms that best predicts earlier gestational age at birth using classification and regression tree analysis.⁵⁰ This method belongs to the family of decision tree machine learning algorithms and allow for nonparametric analyses of a large number of binary, categorical or continuous predictors. They are typically easy to interpret and can detect predictors with small marginal effects when there are strong interaction effects. We will make use of the predictive potential for gestational age at birth of all sexually transmitted and genital tract microorganisms, including individual bacterial taxa or bacterial groups identified by 16S rRNA gene amplicon sequencing (as binary or continuous variables) and confounding variables identified in objective 1. We will present variable importance scores and curves of marginal effects to show how prediction of the outcome changes at different levels of the exposure of each variable in the model. To avoid overfitting, we will consider bootstrap aggregating via random forests.⁵¹

DATA MANAGEMENT AND CONFIDENTIALITY

DATA MANAGEMENT

Each potential participant screened for eligibility is assigned a unique participant identification number, which does not include any personal identifying information. Personal identification numbers are used to link records, specimens and laboratory test results of the participants. Data are stored in a REDCap database,³⁰ which is only accessible to authorised project staff. Paper records are kept in lockable fire-resistant filing cabinets. Laboratory records and journals are kept at the University of Pretoria and University of Cape Town. Forms with personal identifying information are kept separately from demographic, clinical and other data. The data manager maintains a separate, access-controlled, database that links the personal identification number with identifying information. Data quality checks are conducted by study staff onsite and data administrators at the office of the Foundation for Professional Development. All study data are stored securely at the offices of the Foundation for Professional Development in East London for up to five years after the completion of the study or as required by the institutional review board.

CONFIDENTIALITY

The research team is trained to adhere to guidelines on the Protection of Human Research Participants and Good Clinical Practice and fully protects the confidentiality of participants. Besides the measures described under data management, interviews are conducted in a private setting. In reports and publications, data will not be presented in a way where it could be linked to individual participants.

PATIENT AND PUBLIC INVOLVEMENT

There was no involvement of patients or the public in the development of the research questions or the study methods. The research findings will be shared through open access publications and in dissemination meetings with local stakeholders, healthcare providers and communities.

Discussion

This project is important because of its holistic approach, which considers associations between different genital tract infections, their quantity and the vaginal microbiota on earlier gestational age at birth. Many studies in this field have focused on only one or two microorganisms and few studies involve women in sub-Saharan Africa. Strengths of this study include the study setting, where the prevalence of both genital tract infections and adverse pregnancy outcomes is high, the use of ultrasound scans at enrolment for accurate assessment of gestational age and the use of state-of-the-art molecular diagnostic tests and 16S rRNA sequencing. The residual DNA from samples collected in this study will be available for future studies, including joint analyses with other studies of the influence of vaginal microbiota on adverse pregnancy outcomes.

There are limitations to the study design. First, this study involves participants from one clinic, which might limit the generalisability of the findings. Second, using gestational age at delivery as a continuous outcome instead of preterm birth as a dichotomous outcome, might limit comparability with other studies. We will, however, examine the binary outcome preterm birth in secondary analyses. Third, the vaginal samples are taken in a fixed

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3 sequence at each visit, which might reduce the microorganism load of later samples. Fourth,
4 the development of the vaginal inflammation index will use information about the
5 inflammatory potential of microorganisms,⁴⁹ rather than direct concentrations of
6 inflammatory markers.
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11 This study has the potential to generate new evidence about the role of different
12 microorganisms in earlier gestational age at birth through analyses of the presence and
13 quantity of individual and combinations of microorganisms, relative abundance of bacterial
14 genera and microbiota on gestational age at birth. This study will generate new hypotheses,
15 which can be investigated in future studies.
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20 21 22 **Ethics and dissemination**

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26 This protocol and the informed consent forms are approved by the University of Cape Town,
27 Research Ethics Committee (Reference: 676/2019), which includes activities at the
28 University of Southern California, University of Alabama at Birmingham and Louisiana State
29 University. Authorisation to analyse de-identified data at the University of Bern has been
30 granted by the Canton of Bern Ethics Committee (Reference: 2021-01209). Results from this
31 study will be submitted to regional and international conferences and to open access peer-
32 reviewed journals and preprint servers.
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40 41 **Data statement**

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45 The research team will prepare datasets used in analyses, in accordance with data sharing
46 requirements of open access journals in which manuscripts are published and in compliance
47 with local Protection of Personal Information Act requirements. These data files will be
48 archived with codebooks as .csv documents or R data sets and stored in REDCap. The final
49 data files will not contain any personal identifying information of participants.
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56 57 **Author contributions**

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3 RG, NL, JW, and RP conceived and designed the study. JK supported the study through
4 design of the parent study of the Philani Ndiphile project. RG, NL, JW, RP, HJ, CT, CM, SC and
5 LB contributed to the data analysis plan. RG, NL, RP, MM and HJ were involved with the
6 implementation and management of the study. RG and MM managed the data acquisition.
7
8 RG, NL, JW, RP drafted the manuscript and all authors revised it. NL, JW, RP and JK
9 supervised the study. All authors read and approved the final manuscript.
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15 16 **Funding statement**

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19 This work is supported by an MD-PhD scholarship from the Swiss National Science
20 Foundation (grant number 191225), the Swiss National Science Foundation (grant number
21 197831) and the US National Institutes of Health (grant number R01AI149339).
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26 27 **Competing interests statement**

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29
30 LB, SC, RG, HJ, JK, NL, MM, RP, CT, JW: no competing interests to declare.
31

32
33 CM has received research grant funding to her institution by Gilead Inc., Abbott Molecular,
34 Visby, and Lupin Pharmaceuticals. She is a consultant to BioNTech, Cepheid, and BioFire
35 Diagnostics. She has received honoraria for educational presentations and review activities
36 from Scynexis, Visby, Abbott, Elsevier, UpToDate, and DynaMed Plus.
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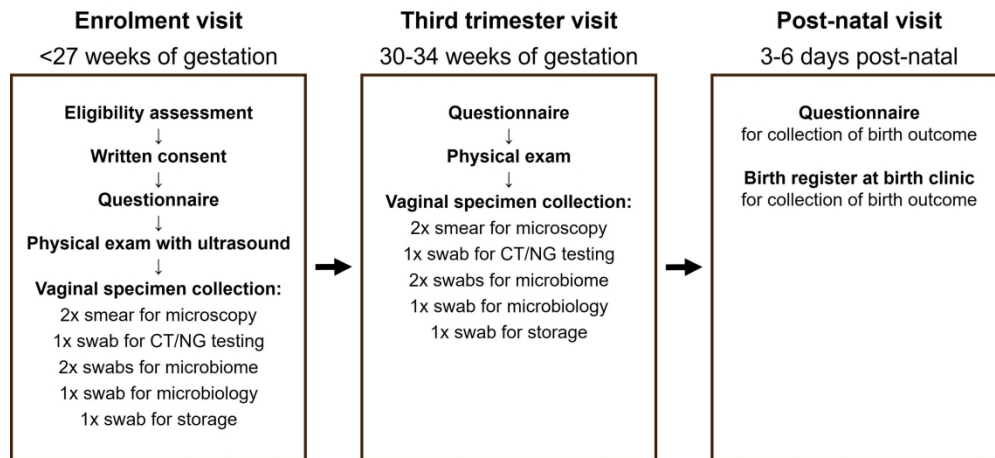


Figure 1 Study visits and specimen collection
 Abbreviations: CT, Chlamydia trachomatis; NG, Neisseria gonorrhoeae.

272x125mm (300 x 300 DPI)

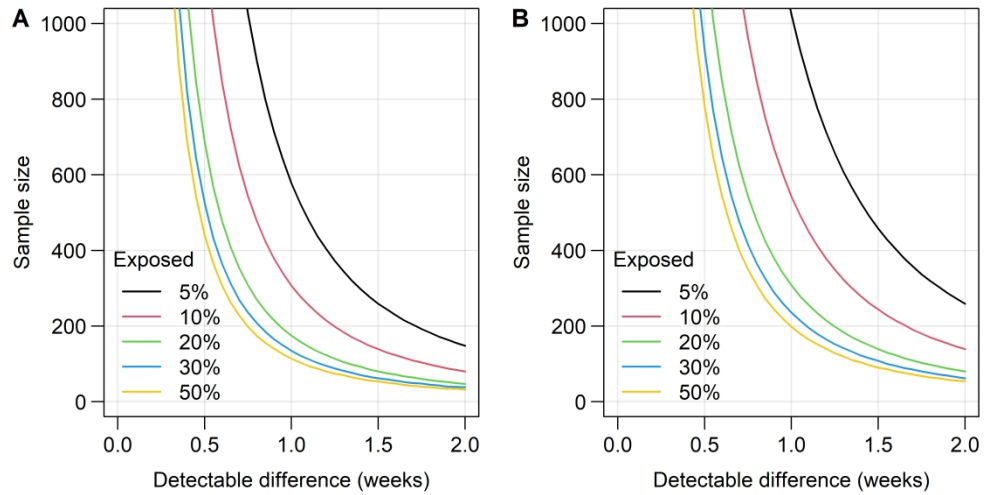


Figure 2 Sample size requirements at different levels of exposure prevalence with power of 80% and alpha 0.83% based on Student's t-test.

Legend: panel A, standard deviation 1.5; panel B, standard deviation 2.0. The curves for % exposed are symmetrical around a prevalence of 50%, i.e., curve for 10% exposed is same as that for 90% exposed.

516x258mm (236 x 236 DPI)

Supplemental online file – study questionnaire

Genital tract infections, the vaginal microbiome and gestational age at birth among pregnant women in South Africa: a cohort study protocol

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1 S...ee...g a... ..e...
2
3

4
5 Record ID
6 _____
7

8
9 **Site Information**

10 Today's Date
11
12
13 _____
14

15 Study Staff Name
16
17
18 _____
19

20 Start Time
21
22
23 _____
24

25 Please select Study Site Name

- 26
27
28 Grey Gateway
29 Duncan Village CHC
30 Nontyatyambo CHC
31 Gompo
32 Ndevana
33
34

35
36 **Introduction to the Study:**
37
38
39

40 Note to RA:

41 In this section you will be introducing the study to the participant. Please make sure to execute the following steps:

42
43
44 1. Introduce the study

45
46 Proceed
47

48 Does the participant show interest in the study

- 49
50 Yes the participant shows interest
51 No the participant is not interested in the study
52

53 END

54 The participant is not interested in the study. Thank them for their time.
55
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g S ee g

Note to RA:

The participant seems to show interest in the study. We need to determine their eligibility status. You will ask a series of questions to determine this. Please select "Proceed" to continue.

Proceed

Is the participant currently living in BCM?

Yes

No

Is the participant 18 years or older?

Yes

No

Please specify the participant's date of birth

Calculated age

Is this the participant's first ANC visit?

Yes

No

Is the participant within the first 26 weeks of her pregnancy?

Yes

No

Is the participant within the first 20 weeks of her pregnancy?

Yes

No

Gestational weeks

_____ (if unknown, enter 99)

Is the participant intending to deliver the baby at one of our collaborating MOUs?

Yes

No

Is the participant currently involved in any other ANC/HIV research trial?

Yes

No

1 Calculated Eligibility Outcome

2
3
4
5 (1 = Eligible, 0 = Not Eligible)

6
7 END

8 The participant is not eligible for our research study

9
10 This will be the end of their participation. Please thank them for their time.

11
12 ELIGIBLE

13 The participant is eligible for our research study. Please select "Proceed" to start with the consenting process.

14
15 Proceed

16
17
18
19
20
21 Consenting Process:

22
23
24
25 NOTE TO RA:

26 You will now start with the consenting process. Please make sure to do the following:

- 27
28
29 1. Read the consent form with the participant
30 2. Read in a language they prefer
31 3. Allow for questions
32 4. If willing to consent, sign all documents
33 5. Hand a signed copy (without PIN) to the patient

34
35 Proceed

36
37 Did the participant provide a signed consent to participate in the research study?

- 38
39 Yes
40 No

41
42
43 Consent refusals

44
45
46
47
48 Reasons for refusal

- 49
50 They have no time
51 Scared
52 In a different study
53 Other

54
55 If "Other", please specify

56
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1 Refusal date
2
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6 END
7 Thank the participant for their time
8
9

10
11
12 **Provided Consent**

13
14 Consent date
15
16
17
18

19
20
21 **Participant PIN**

22 CONSENTED
23 The participant has agreed to provide consent. You will now allocate a study PIN to the participant. Please use the
24 next available PIN on the hard copy enrollment log
25

26 Proceed
27

28
29 Participant PIN
30
31
32

33
34 Participant PIN Verification
35
36
37
38

39 Pin match
40
41
42
43

44 PIN valid
45
46
47
48

49 ERROR
50 The PINs you entered did not match up
51

52
53 You have entered the following PINs
54

55 first pin: [participant_pin]
56 second pin: [participant_pin_verify]
57

58 ERROR
59 The PIN you entered is invalid for [site_name]
60

You have entered the following PINs

first pin: [participant_pin] For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>
second pin: [participant_pin_verify]
06-10-2023 11:48

1 Sa□□□g /□□□□□□□□□□

2
3 You have completed the Screening and Enrollment process. Please make sure to check if all relevant fields have been
4 selected and the information captured is accurate.

5
6 Once this is done, please select the "complete" option below and then select "Save & Exit".

7
8 Once you have done this you will be directed to the baseline Data.

9
10
11
12 Notes

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16 Additional Notes

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For peer review only

1 a e e a a

2
3
4 Staff name

5 _____

6
7
8 Today's Date

9 _____

10
11 Start Time

12 _____

13
14
15
16 Sociodemographics

17
18 NOTE TO RA:

19 You are about to start the Socio-demographics section. Please make sure to ask the questions as they appear on
20 your tablet.

21
22 Please select "Proceed" to continue.

23
24 Proceed

25
26
27 Sociodemographics

28
29 How would you describe yourself in terms of race?

- 30
31
- 32 African
 - 33 Coloured
 - 34 Mixed Race
 - 35 White
 - 36 Indian
 - 37 No answer

38
39 What level of education did you complete?

- 40
41
- 42 Less than Gr. 10
 - 43 Gr.10 or 11
 - 44 Gr.12
 - 45 Diploma
 - 46 Degree
 - 47 Refused to answer
- 48
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1 Which best describes the type of house in which you live? Please choose one answer only:
2

- 3 House or brick structure on a separate stand or yard or on a farm
4 Traditional dwelling/hut/structure made of traditional materials
5 Flat
6 Town/cluster/semi-detached house (simplex, duplex or triplex)
7 Unit in retirement village
8 Dwelling/house/flat/room in backyard
9 Informal dwelling/shack IN the backyard of a formal house
10 Informal dwelling/shack NOT in backyard e.g. in an informal/squatter settlement or on farm
11 Room/flatlet not in backyard but on a shared property e.g granny flat
12 Caravan/tent
13 Worker's hostel
14 Other
-

16 If other, please specify.
17
18
19
20
21

22 What is the main material of your house walls? Please choose one answer only:
23

- 24 Bricks & plaster/finished
25 Bare brick/cement block
26 Corrugated iron/zinc
27 Wood
28 Plastic
29 Cardboard
30 Mixture of mud and cement
31 Wattle and daub
32 Mud
33 Other
-

35 If other, please specify
36
37
38
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40

41 What is the main material of your house roof? Please choose one answer only:
42

- 43 Tiles
44 Corrugated iron/zinc
45 Thatching
46 Asbestos
47 Plastic
48 Cardboard
49 Other
-

51 If other, please specify
52
53
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1 What is your current relationship status?
2

- 3 Married
4 Steady partner
5 Steady partner and Casual Partner(s)
6 Casual Partner(s)
7 No relationship
8

9 Do you live together with your partner?
10

- 11 Yes
12 No
13

14 Are you currently employed?
15

- 16 Employed
17 Self employed
18 Not employed
19

20 What is your monthly personal income?
21

- 22 None
23 < 1000 ZAR per month
24 1001 - 5000 ZAR per month
25 5001 - 10 000 ZAR per month
26 >10 000 ZAR per month
27

28 What is your household's main source of income?
29

- 30 Personal income from employment \ self employment
31 Income from partner
32 Grants
33 Other
34

35 Have you been outside of the Eastern Cape or country in the past 6 months?
36

- 37 Yes
38 No
39

40 Which provinces or country have you been to in the last 6 months?
41

42 Note to RA: please select all that apply
43

- 44 Free State
45 Gauteng
46 Kwazulu-Natal
47 Limpopo
48 Mpumalanga
49 Northern Cape
50 North West
51 Western Cape
52 Outside South Africa
53

54 Has your partner/husband been outside of the Eastern Cape or country in the past 6 months?
55

- 56 Yes
57 No
58
59
60

1 Which provinces or country has your partner/husband been to in the last 6 months?
2

3 Note to RA: Please select all that apply
4

- 5 Free State
6 Gauteng
7 Kwazulu-Natal
8 Limpopo
9 Mpumalanga
10 Northern Cape
11 North West
12 Western Cape
13 Other country
-

15 What is the main source of drinking water for your household? Please choose one answer only:
16

- 17 Piped (tap) water in dwelling
18 Piped (tap) water on site or in yard
19 Neighbour's tap
20 Public or communal tap (either free or paid)
21 Borehole on site
22 Borehole off site/communal
23 Rain water tank
24 Water carrier/tanker
25 Flowing water/stream/river
26 Stagnant water/dam/pool
27 Well
28 Spring
29 Bottled water
30 Other
-

31 If other, please specify
32
33
34
35
36

37 What type of toilet does your household use? Please choose one answer only:
38

- 39 Flush toilet (connected to sewage)
40 Flush toilet (with septic tank)
41 Chemical toilet
42 Pit latrine with ventilation pipe
43 Pit latrine without ventilation pipe
44 Bucket toilet
45 No facility/bush/field
46 Other
47
-

48 If other, please specify
49
50
51
52
53
54
55
56
57
58
59
60

1 What is the main source of energy for cooking in your household? Please choose one answer only:
2

- 3 Electricity from mains
4 Electricity from generator
5 Gas
6 Paraffin
7 Wood
8 Coal
9 Animal dung
10 Solar energy
11 Other
12

13 If other, please specify
14
15
16
17
18
19

20 Does your household have any of the following items in good working order? Read each item
21 and indicate the presence of each
22

	Yes	No
23 Television	<input type="radio"/>	<input type="radio"/>
24 Gas or Electric stove	<input type="radio"/>	<input type="radio"/>
25 Fridge/freezer	<input type="radio"/>	<input type="radio"/>
26 Private motor vehicle in running 27 condition	<input type="radio"/>	<input type="radio"/>
28 Bicycle	<input type="radio"/>	<input type="radio"/>
29 Bed	<input type="radio"/>	<input type="radio"/>
30 Sofa or sofa set	<input type="radio"/>	<input type="radio"/>
31 Kitchen sink	<input type="radio"/>	<input type="radio"/>

32 Do you think that you will need to borrow money to pay for healthcare during your pregnancy?
33
34

- 35 Yes
36 No
37

38 How much money did you spend coming to the clinic today (including transport costs, snacks while waiting etc.) ?
39
40
41

42 _____
43 ([RANDS])
44
45

46 Did you lose any money from your job because of coming to the clinic today?
47
48

- 49 Yes
50 No
51

52 If yes, how much money did you lose?
53
54
55

56 _____
57 ([RANDS])
58
59

60 How much time did you spend travelling to the clinic today (Hours)?
61

62 _____
63 ([HOURS])

1 How much time did you spend travelling to the clinic today (Minutes)?

2
3
4
5 _____
6 ([MINUTES])

7 Time spent travelling in minutes.

8
9
10 _____
11
12 How much time do you normally spend waiting and seeing the doctor or nurse in a clinic such as this one (Hours)?

13
14
15 _____
16 ([HOURS])

17
18 How much time do you normally spend waiting and seeing the doctor or nurse in a clinic such as this one?

19
20
21 _____
22 ([MINUTES])

23
24 How much time do you normally spend waiting and seeing the doctor or nurse in a clinic such as this one in minutes?

25
26
27 _____
28 ([MINUTES])

29
30
31 Are you planning to wait for your results today?
32 (New question added @13/09/2022)

- 33
34 Yes
35 No

36
37 What is your main reason why you are not intending to wait today?
38 (New question added @13/09/2022)

- 39
40 Have to get to work
41 Have to get back to my kids/family
42 Want to go to the shop
43 Transport availability
44 Lack of privacy
45 Hungry
46 No space to wait
47 Not feeling well
48 Boring
49 Other

50
51 If "Other" , please specify.

52 (New question added @13/09/2022)

53
54
55
56
57
58 What would make you change your mind?

59 (New question added @13/09/2022)

1 Do you do any of the following activities in a lake / stream?
2

3 Note to RA: Please select multiple that apply
4

- 5 Play
6 Bath
7 Wash blankets
8 Do laundry
9 Fish
10 Collect water
11 Crossing
12 None
13
14

15 Behavioural Questionnaire 16 17 18 19

20
21 NOTE TO RA:

22 You just completed all questions related to socio-demographics. You are about to start with the Behavioral
23 Questionnaire.

24 Please select "Proceed":
25

- 26 Proceed
27

28
29 When was the last time you had sex?

- 30 In the past week
31 In the past month
32 More than a month ago
33

34
35 Did you use a condom the last time you had sex?

- 36 Yes
37 No
38

39
40 Do you use a lubricant?
41

- 42 Yes
43 No
44

45 Can you please elaborate on the type of lubricant that you use?
46
47
48
49

50 What do you use to clean your vagina?
51

- 52 Water only
53 Soap and water
54 Other household products
55 Other
56

57 Please specify what other things you used on your vagina.
58
59
60

1 Do you do any vaginal douching?

- 2
3 Yes
4 No
5

6 Please specify
7
8
9
10
11

12 Do you do any form of vaginal cleansing?

- 13
14 Yes
15 No
16

17 Please specify
18
19
20
21
22
23

24 Do you use anything to clean inside your vagina?

- 25
26 Yes
27 No
28

29 Do you insert anything in your vagina for tightening?

- 30
31 Yes
32 No
33

34 Please specify
35
36
37
38
39

40 In the past 6 months, how many sexual partners did you have?

- 41
42 One
43 More than one
44

45 In the past 6 months, have you engaged in any of the following?
46 (Select ALL that apply)
47

- 48 Vaginal sex
49 Oral sex
50 Anal sex
51

52 Have you recently agreed to sex even though you did not feel like to?

- 53
54 Yes
55 No
56
57
58
59
60

1 Note to RA: Discuss with participant counselling options

- 2
3 Yes
4 Participant doesn't need counselling
5

6 Please specify
7
8
9
10
11

12 In the past 6 months, have you been forced to have sex with anyone?

- 13
14 Yes
15 No
16

17
18 Note to RA: Discuss with participant counselling options

- 19
20 Yes
21 Participant doesn't need counselling
22

23 Please specify
24
25
26
27
28

29 In the past 6 months, have you received any benefits (money or goods) for sex?

- 30
31 Yes
32 No
33

34 Do you suspect your steady partner to have any other sex partners?

- 35
36 Yes
37 No
38 Unsure
39

40 When did your last menstrual period start?

41 Note to RA: Please ask participant to give the most accurate date.
42
43
44
45 _____
46

47 Just before I became pregnant.
48

49 NOTE: Please tick the statement that most applies to you:

- 50
51 I wanted to have a baby
52 I had mixed feelings about having a baby
53 I did not want to have a baby
54

55 How many times have you been pregnant before your current pregnancy?
56
57 _____
58
59 _____
60

How many live children have you delivered?

1 Of the live births that you had, how many were normal vaginal delivery?
2
3
4 _____
5

6 Of the live births that you had, how many were "emergency cesarean"?
7
8
9 _____
10

11 Of the live births that you had, how many were "elective cesarean"?
12
13
14
15 _____
16

17 Live birth Match
18
19
20 _____
21

22 Note to RA: The numbers you have entered do not match. Please check again.
23

24 How many of your live birth's were premature?
25
26
27 _____
28

29 How many of your live birth's were full term?
30
31
32 _____
33

34 Delivery timing calc
35
36
37 _____
38
39

40 Note: The numbers you have captured do not add up
41

42 Have you ever had an ectopic pregnancy?
43

- 44 Yes
- 45 No
- 46

47 Have you ever had a miscarriage?
48

- 49 Yes
- 50 No
- 51

52 Have you ever had a stillbirth?
53

- 54 Yes
- 55 No
- 56
- 57
- 58
- 59
- 60

1 Do you smoke cigarettes?
2

- 3 Yes
4 No
5

6 Have you used any of the following since you found out you were pregnant? (select multiple)
7 (Select ALL that apply.)
8

- 9 Alcohol
10 Tik
11 Dagga
12 Grandpa
13 Other
14 None
15

16 Please specify
17
18
19
20
21

22 Do you know your current HIV status?
23

- 24 HIV negative (tested today by clinical staff)
25 HIV positive on ART
26 HIV positive, not on ART
27 Don't know (never tested)
28 Don't know (no yet tested today)
29

30 Was the participant newly diagnosed within the past week?
31

- 32 Yes
33 No
34

35 Can we test you for HIV today?
36

- 37 Yes
38 No
39

40 Unknown HIV Status:
41

42 Note to RA/ Nurse: HIV test needs to be conducted
43

- 44 Proceed to test
45

46 HIV rapid test result:
47

- 48 Positive
49 Negative
50

51 HIV confirmatory test
52

- 53 Positive
54 Negative
55

56 Elisa blood barcode
57
58
59
60

1 Have you ever been treated for an STI in the last year?

- 2
3 Yes, I had discharge
4 Yes, I had ulcers
5 Yes, I had genital warts
6 Yes, no symptoms but notified by partner
7 No

8
9 Does the participant have pre-existing diabetes?

- 10
11 Yes
12 No

13
14 Are you on treatment for your diabetes?

- 15
16 Yes
17 No

18
19 Does the participant have pre-existing hypertension?

- 20
21 Yes
22 No

23
24 Are you currently on medication for your hypertension?

- 25
26 Yes
27 No

28
29 Does the participant have pre-existing thyroid disease?

- 30
31 Yes
32 No

33
34 Is the participant taking medication for her thyroid disease?

- 35
36 Yes
37 No

38
39 Do you know your partner's HIV status?

- 40
41 Yes, HIV positive on ART
42 Yes, HIV positive but not on ART
43 Yes, HIV negative
44 No

45
46 You have completed the baseline questionnaire. Please make sure to log out of your REDCap account.

47
48 Once you have done this you can hand the process over to the nurse who will conduct the clinical history.

49
50
51
52
53
54
55
56
57
58
59
60

□□ T□S

Additional notes

For peer review only

P a a

Staff Name

Today's Date

Start time

You are about to administer the questions associated with the physical exam.

Please select "Proceed" to continue.

Proceed

Clinical History

Do you currently have any of the following symptoms?

RA: Please select all that apply

- Abnormal vaginal discharge
- Pain during urination
- Lower abdominal pain
- Pain related to intercourse
- Vaginal bleeding related to intercourse
- Genital itchiness
- Any skin abnormalities
- None

How many days ago did your abnormal vaginal discharge start?

How many days ago did the pain during urination start?

Provide further details

Have you received treatment for these symptoms?

- Yes
- No

1 Where did you get the treatment from?
2

- 3 Over the counter
4 Healthcare facility
5 Traditional healer
6

7 Please provide further details
8
9
10
11
12

13 If you were told you had an STI would you disclose to your partner(s)?
14

- 15 Yes, to steady partner
16 Yes, to casual partner(s)
17 Yes, to all steady and casual partner(s)
18 No
19

20 Co-Morbidities
21

22
23 You are about to start asking questions related to co-morbidities.
24

25 Please select "Proceed" to continue.
26

- 27 Proceed
28

29 Did the participant screen positive for any TB symptoms?
30

- 31 Yes
32 No
33

34 The participant shows signs of TB. A specimen needs to be collected for further testing. Please select below to
35 specify whether a specimen was collected successfully.
36

- 37 Yes
38 No
39

40 Instruction: Please record the specimen tracking number below
41

42 _____
43
44

45 Are you on cotrimoxazole prophylaxes?
46

- 47 Yes, on cotrimoxazole
48 Yes, started today
49 No
50

51 Did the participant start antiretroviral therapy today?
52

- 53 Yes
54 No
55

56 Specify reason for not starting
57
58
59
60

1 Was blood taken today for the participant's CD4 count?
2

- 3 Yes
4 No
5

6 Please record barcode for blood tube for CD4 count testing?
7
8
9
10 _____
11

12 Is the participant's most recent CD4 count within the last 12 months available?
13

- 14 Yes
15 No
16

17 What was the date of the CD4 specimen collection?
18
19
20 _____
21

22 What was the participant's most recent CD4 count?
23
24
25 _____
26 (if no number listed, enter 9999)
27

28 Was blood taken today for the participant's viral load?
29

- 30 Yes
31 No
32

33 Please record barcode for blood tube for viral load testing?
34
35
36 _____
37

38 Is the participant's most recent viral load within the past 12 months available?
39

- 40 Yes
41 No
42

43 What was the date of the viral load specimen collection?
44
45
46 _____
47

48 What was the participant's most recent viral load?
49
50
51 _____
52 (if no number listed, enter 0000)
53

54 Was blood taken today for the participant's viral load?
55

- 56 Yes
57 No
58
59

60 Please record the barcode for viral load testing?

1 Is the participant's most recent viral load available?
2

- 3 Yes
4 No
5

6 What was the date of the viral load specimen collection?
7
8
9
10 _____
11

12 What was the participant's most recent viral load?
13
14
15 _____
16

17 Which regimen for ART were you started on today?
18

- 19 TLD
20 TEE
21 AZT/3TC/LPV
22 Other
23

24 Which regimen for ART were you on so far?
25

- 26 TLD
27 TEE
28 AZT/3TC/LPV
29 Other
30

31 Has the regimen for ART been changed today?
32

- 33 Yes
34 No
35

36 To which regimen for ART has it been changed today?
37

- 38 TLD
39 TEE
40 AZT/3TC/LPV
41 Other
42

43 Please select "Proceed" to collect blood for viral load testing.
44

- 45 Proceed
46

47 Did you successfully collect blood for viral load testing?
48

- 49 Yes
50 No
51

52 Please capture the barcode associated with the blood tube used for testing viral load.
53
54
55
56 _____
57
58
59
60

1 Was a CD4 count test done?

- 2
3 Yes
4 Yes, but no result available
5 Not done
6

7 Please specify last known CD4-cell count.
8
9
10 _____
11

12 Was blood taken today for the participant's CD4 count ?

- 13
14 Yes
15 No
16

17 Please record the barcode for CD4 testing?
18
19 _____
20
21

22 Is the participant's most recent CD4 available?

- 23
24 Yes
25 No
26

27 What was the date of the CD4 specimen collection?
28
29 _____
30
31

32 What was the participant's most recent CD4 Count?
33
34 _____
35
36

37 Has a syphilis test been done for the participant?
38

- 39 Yes
40 No
41
42

43 Instruction: Please conduct a rapid test for syphilis.
44

45 Specify if the participant agreed to testing / you managed to execute the test.
46

- 47 Yes
48 No
49

50 Which syphilis test have you used?
51

- 52 Alere Syphilis TP (provided by FPD)
53 HIV/Syphilis Duo (provided by FPD)
54 No rapid test used only NHLS bloods for RPR
55 Other please specify
56

57 Please specify
58
59
60

1 Syphilis result

- 2
3 Positive
4 Negative
5 Indeterminate
6

7 Titer value 1:

8
9
10 _____
11

12 Please collect blood for further syphilis testing and specify if the blood was collected successfully.

- 13
14 Yes
15 No
16

17
18 Treatment given

- 19
20 Benzathine penicillin, 2.4 mU
21 Out of stock
22

23 Please contact the study clinician and specify treatment given to participant

24
25
26
27
28
29 Please capture the barcode below.

30
31
32 _____
33

34 Participant weight in kilograms

35
36
37 _____
38

39 Participant height in cm

40
41
42 _____
43

44 Participant systolic blood pressure

45
46
47 _____
48

49 Participant diastolic blood pressure

50
51
52 _____
53

54
55 How was Hemoglobin measured?

- 56
57 Hb meter at the clinic
58 Hb at NHLS
59

60 Please capture Hb result

1 Please capture the barcode for Hb
2
3
4 _____
5

6 Participant MUAC in cm
7
8
9 _____

10 (1 Decimal Place)
11

12 Please collect participant's urine for later testing.
13
14

15
16
17
18 **Ultrasound Results**
19
20
21
22
23
24

25
26 You are about to start capturing information pertaining to the ultrasound results.
27

28 Please select "Proceed" to continue.

29 Proceed
30

31
32 Ultra-sound scan date
33
34
35 _____
36

37 Was the pregnancy confirmed?
38

- 39 Yes, intra-uterine
40 Yes, extra-uterine
41 No
42

43 NOTE: Please refer immediately
44

45
46 NOTE
47 Due to the status of the pregnancy, the participant is no longer eligible to continue with the study. This is the end of
48 their involvement in the study. Please thank them for their time. Also do the following:
49

- 50
51 - Save and Exit the form
52
53 - Complete a Study Note confirming termination of study participation
54

55 Please specify the number of foetus
56
57
58 _____
59
60

1 You are about to capture the gestational age of the foetuses. Please select "Proceed" and then capture the number
2 of weeks followed by days.
3

4 Proceed

6 Gestational age in weeks

10 _____

12 Gestational age in days

15 _____

17 Calc: Gestational age in days

20 _____

22 EDD based on ultra-sound

25 _____

27 Calc: Days to EDD

30 _____

32 Calc assist for EDD

34 The number of days must be equal to 280.

37 _____

39 Note to Nurse:

41 You did not enter either gestational age or EDD correctly.

44 Calc: Eligibility

45 _____

47 END

48 The participant is not eligible for our research study

50 This will be the end of their participation. Please thank them for their time.

52 STI Clinical Examination (To be done By Nurse)

55 You are about to capture information related to STI clinical examination.

56 Please select "Proceed" to continue

58 Proceed

1 During your examination, were there any signs of abnormal vaginal discharge?
2

- 3 Yes
4 No
5

6 During your examination, were there any signs of inguinal lymphadenopathy?
7

- 8 Yes
9 No
10

11 Are these bubo?
12

- 13 Yes
14 No
15

16
17 Note to RA: Please contact study clinician and specify treatment given to participant
18
19
20
21
22

23 During your examination, were there any signs of lower abdominal pain?
24

- 25 Yes
26 No
27

28 During your examination, were there any signs of scratch marks?
29

- 30 Yes
31 No
32

33 During your examination, were there any signs of skin conditions?
34

- 35 Yes
36 No
37

38 Please specify the nature of the skin conditions
39
40
41
42
43
44

45 During your examination, were there any other observations that need to be noted?
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

□□□□e □□□□□□□□ □e□□ □e□□□□□□

You are about to capture the results from the dipstick testing

Please select "Proceed" to continue

Proceed

Blood - Hemoglobin

- Negative
- Ca. 10
- Ca. 50
- Ca. 250/300

Blood - Erythrocytes

- Negative
- Ca. 5 -10
- Ca. 50
- Ca. 250/300

Urobilinogen

- Normal
- 2
- 4
- 8
- 12

Bilirubin

- Negative
- 1 plus
- 2 plus
- 3 plus
- Not available

Protein

- Negative
- 30
- 100
- 500

Nitrate

- Negative
- Positive

For peer review only

1 Keton

- 2
3 Negative
4 1 plus
5 2 plus
6 3 plus
7 Not available
8

9 Glucose

- 10
11 Negative
12 Normal
13 50
14 150
15 500
16 ≥ 1000
17

18 pH

- 19
20 5
21 6
22 7
23 8
24 9
25 Not available
26

27 SG

- 28
29 1.000
30 1.005
31 1.010
32 1.015
33 1.020
34 1.025
35 1.030
36 Not available
37

38 Leucocytes

- 39
40 Negative
41 25
42 75
43 500
44

45 NOTE

46 The participant's clinical gestational age is more than 20 weeks. They are not eligible to proceed with the study
47 activities.

48
49 Please do the following:

- 50
51 1. Explain the reason for study termination
52 2. Complete the study electronic termination tool
53 3. Complete the study termination document and place in file

54 End
55
56
57
58
59
60

1
2
3 T S
4
5
6

7 Additional Notes
8
9
10
11
12

13 You have completed capturing the information from the clinical exam. Please make sure to check that you have
14 completed all the fields.
15

16 Please select "Complete" then "Save and Exit".
17

18 You will now proceed to collecting study specimens and randomization
19
20
21
22
23
24
25
26
27
28
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30
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56
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59
60

For peer review only

Site name a Ra a

Staff Name

Today's Date

Start time

Specimen Collection

NOTE
You will now start with the process of specimen collection. You will need to collect several specimens from the participant. These specimens need to be collected in the order in which they are presented here. The outcome of the randomization will have an impact on whether these specimens will be tested immediately or whether they will need to be prepared for storage.

The following specimens will need to be collected:

- 1. Vaginal loop to be used to prepare two slides
- 2. Vaginal swab to be used for STI testing
- 3. Vaginal swab to be used for profiling
- 4. Vaginal swab to be used for microbiome
- 5. Vaginal swab to be used for cytokine

Done

NOTE
You will now start with the process of specimen collection. You will need to collect several specimens from the participant. These specimens need to be collected in the order in which they are presented here.

The following specimens will need to be collected:

- 1. 1 x Vaginal loop to be used to prepare two slides
- 2. 1 x Vaginal swab to be used for STI testing
- 3. 1 x Vaginal swab to be used for profiling
- 4. 2 x Vaginal swab to be used for microbiome
- 5. 1 x Vaginal swab to be used for cytokine

Done

Vaginal Smear

Please specify the vaginal pH

(if not available, enter 99)

1 Please select which pH strips are used to measure vaginal pH

- 2
3 CardinalHealth pH Indicator Strips (range 3.6-6.1)
4 pH Indicator Strips pH 0-14
5 Natureland vaginal pH test (range 3.5-6.5)
6

7 You will need to use a single loop to collect vaginal smear on two glass slides for microscopy

- 8
9 Done
10

11 Confirm the PIN associated with the first vaginal slide that will be used for Nugent score

- 12
13 [participant_pin]-S1
14

15 Confirm the PIN associated with the second vaginal slide that will be used for yeast microscopy

- 16
17 [participant_pin]-S2
18
19

20 Vaginal Swabs

21
22 NOTE

23 You will now collect four vaginal swabs. They will be used as follows:

- 24
25 1. STI testing (test for arms 1 and 2, store for arm 3)
26 2. Profiling (stored)
27 3. Microbiome (stored)
28 4, Cytokine
29

- 30 Done
31

32 NOTE

33 You will now collect four vaginal swabs. They will be used as follows:

- 34
35 1. STI testing
36 2. Profiling (stored)
37 3. Microbiome (stored)
38 4, Cytokine
39

- 40 Done
41

42 Please confirm the PIN associated with the urine for Schistosomiasis testing.
43 (2022/10/21 - Stopped collecting the urine specimen)

- 44
45 [participant_pin] - UD1
46

47 Please confirm the PIN associated with the vaginal swab that will be used for STI testing.

- 48
49 [participant_pin] - BV1
50

51 Please confirm the PIN associated with the vaginal swab that will be used for profiling.

- 52
53 [participant_pin] - BV2
54

55 Please confirm the PIN associated with the vaginal swab that will be used for microbiome.

- 56
57 [participant_pin] - BV3
58
59
60

Please confirm the PIN associated with the vaginal swab that will be used for cytokines.

[participant_pin] - BV4

NOTE

You have finished the collection of the vaginal swabs. Please ensure specimens have been prepared for storage and shipment. The vaginal swab that is collected for STI testing should be kept aside following the outcome of the randomization. If the participant is in arm 1 or 2 the specimen should be used for immediate testing. If however, the participant is randomized to arm 3, you can store the specimen.

Please select "Proceed" to start the process of randomization

Done

Randomization

Arm 1

Arm 2

Arm 3

Activities Associated with "[randomization]"

NOTE

The participant has been randomized to "[randomization]". You will now need to do the following:

1. Prepare the STI swab for testing using the GeneXpert

Done

NOTE:

The participant has been randomized to "[randomization]". You will now need to do the following:

1. Prepare the STI swab for testing using the GeneXpert

2. Screen for symptoms

3. Provide treatment and partner referral if positive

Done

NOTE:

The participant has been randomized to "[randomization]". You will now need to do the following:

1. Screen for symptoms

2. Provide treatment and partner referral if positive

Done

NOTE

You will now need to do the following:

1. Prepare the STI swab for testing using the GeneXpert

Done

STI Results

	Positive	Negative
CT	<input type="radio"/>	<input type="radio"/>

1 NG

2 TV

3

4

5 NOTE: See Calculation:

6

7 The result from the STI test?

8

9

10

11 (0 = Negative, 1 = Positive, 2 = No result)

12

13 Date the result was obtained

14

15

16 _____

17

18 Did the participant wait for her STI results?
(New question added @ 03/11/2022)

21 Yes

22 No

23

24 Symptomatic Screening Outcome Following Negative Test

25

27 The result from the GeneXpert was negative.

28

29 Was the participant reporting STI symptoms or showed symptoms during the clinical assessment?

30

31 Yes

32 No

33

34 Does the participant report any medication allergies?

35

36 Yes

37 No

38

39 Please contact study clinician before giving any treatment. Please specify discussed medication allergies and
40 treatment plan with study clinician

41

42

43

44

45

46 The following treatment has been provided

47

- 48 Azithromycin 1g stat dose
- 49 Azithromycin 2g stat dose
- 50 Ceftriaxone 250mg IM injection
- 51 Ceftriaxone 1g IM injection
- 52 Metronidazole 400mg bd x 1 week
- 53 Metronidazole 2g stat dose
- 54 Clotrimazole pessary and/or cream
- 55 Trimethoprim/sulfamethoxazole 400/80 mg 2 tbl. bds for 5 days (bactrim)
- 56 Ceftriaxone 500mg IM injection
- 57

58 Date treatment given

59

60 _____

1 What made you change your mind about waiting for the results?
2 (New question added @13/09/2022)
3
4
5
6
7

8 Partner notification provided
9

- 10 Yes, 1
11 Yes, multiple
12 No
13

14 Please explain why the partner notification note was not provided?
15
16
17
18
19

20
21 **ELIGIBLE**

22 The participant is eligible for our nested chlamydia case-control study. Please select "Proceed" to start with the
23 consenting process.

- 24 Proceed
25

26
27 Did the participant provide a signed consent to participate in the chlamydia case control study?
28

- 29 Yes
30 No
31

32 Reasons for refusal
33

- 34 They have no time
35 Scared
36 In a different study
37 Other
38

39 If "Other", please specify
40
41
42
43
44

45 Consent or refusal date
46
47
48
49
50

51
52 **NOTES**
53

54 Participant successfully enrolled
55
56

57 Additional notes
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You are done with all activities associated with "[randomization]". Please hand the tablet over to the RA to capture the remaining schedule dates.

You are done with all activities. Please hand the tablet over to the RA to capture the remaining schedule dates.

For peer review only

Scheduling of Dates Associated with [randomization]

Scheduling of Dates Associated with [randomization].

NOTE

You are about to schedule dates associated with [randomization] participants.

Please select "Proceed".

Proceed

Scheduling of Dates Associated

NOTE:

You are about to schedule dates associated with microbiome participants.

Please select "proceed"

Proceed

Scheduling Dates for 3-Week ToC

NOTE: The participant tested positive and therefore we need to schedule a date, exactly 3-weeks from today to conduct a test-of-cure.

Calculator Assist

The number here must be equal to 21

Scheduling the 3-week ToC

NOTE:

Please schedule a date, 3 weeks from today treatment given. Please use the calculator assistance to ensure that you schedule a date exactly 21 days from today.

ERROR

The field does not equal to 21, please change it

Have you handed the TOC date to the participant?

Yes

No

Scheduling Dates Associated with ToC Reminder

Schedule date for REMINDER of 3-week ToC visit

1 Calculator Assist for scheduling ToC reminder date

2
3 The reminder phone call will be made 18 days following the treatment date. The number of days need to equal to 18.

4
5
6
7
8 **ERROR**

9 You did not enter the date correctly. The number should equal to 18. Please redo the date.

11 Scheduling Dates Associated with 3-Week ToC Missed Visit Date

12
13
14 **NOTE:**

15 You have successfully scheduled the reminder date.

16
17 Please select "proceed" to schedule the missed visit date for the 3 week ToC visit.

18
19 Proceed

21 Schedule the date for the MISSED VISIT of the ToC visit.

22
23 This date should be 3 weeks after the date on which the participant received their test result.

24
25
26
27
28 Calculator Assist for scheduling 3-week ToC Missed Visit

29
30 The participant's time period allowed for attending a ToC will start 35 days after they received their result and will
31 close 35 days after the date they received their result.

32
33 The number here must show 35

34
35
36
37
38 **ERROR**

39 You did not enter the date correctly. The number should equal to 35. Please redo the date.

40
41 **NOTE:**

42 You have successfully scheduled the 3-week ToC close date

43
44 Please select "proceed" to start scheduling the next visit dates

45
46 Proceed

48 Dates Associated with reminder for the 28 Week call

49
50
51 **NOTE:**

52 You are about to schedule dates for the call reminder at 28 weeks.

53
54 Please select "Proceed".

55
56 Proceed

58 **Note:**

59 Schedule the date for the 28 week call. We will contact each participant to ask the date for their 30 weeks clinic visit
60 is.

1 Calculation assist for scheduling the 32-week reminder date.

3 This number must equal to 196

8 Days to call reminder

13 ERROR
14 The number you have entered does not match 196. Please select a different date so that the number equals to 196.

17 CONGRATULATIONS

18 You have finished scheduling all dates.

23 NOTES

25 Notes box

For peer review only

□□ □□e□□□e□□ □e□□□□□□

Staff

Date

Time

You are about to capture results of specimens collected during the baseline visit.

Please select "Proceed" to continue

Proceed

Hb results received

Yes

No

Please capture Hb result

Please capture the barcode for Hb

Please capture the results of the sputum for TB testing

MTB Negative

MTB Positive Rifampicin Susceptible

MTB Positive Rifampicin Resistant

Not suitable

Specimen missing

Invalid

Not applicable

Please contact participant

Please recollect specimen on participant next visit

CD4 count results received?

Yes

Clotted blood

Missing

Please recollect blood or collect outcome from ART clinic

Please record the barcode for CD4 count testing

1 Please capture the result of the blood tube collected for CD4 count testing

6 Date sample for CD4 count was taken

12 Viral load results received?

- 13 Yes
- 14 Clotted blood
- 15 Missing

18 Please recollect blood or collect outcome from ART clinic

20 Please capture the result of the blood tube collected for viral load testing

26 Date sample for viral load was taken

31 Please record barcode for viral load testing

36 Please capture the result of the syphilis testing

- 37 RPR Negative
- 38 RPR Positive
- 39 RPR Indeterminate
- 40 Not received

43 Please contact participant

52 Notes

57 Notes

Pre-e Re

Staff

Date

Time

You are about to capture results of specimens collected during the baseline visit.

Please select "Proceed" to continue

Proceed

Please capture the result for the Nugent score testing

- Slide reading not satisfactory
- Slide reading was satisfactory

Please capture the result for the Nugent score testing

Please specify if yeast was present

- Yes
- No

Please capture the result for the yeast infection testing

- Slide reading not satisfactory
- Slide reading was satisfactory

Please capture the result for the Yeast Infection testing

Please specify if candida was present

- Yes
- No

1 Please capture the result for the schistosomiasis

- 2
- 3 Positive
- 4 Negative
- 5 Indeterminate
- 6

7 Please specify the result for the schistosomiasis

- 8
- 9 Trace
- 10 1+
- 11 2+
- 12 3+
- 13 4+
- 14

15

16

17

18

19 _____

20

21 Note:

22 Please notify the study clinician

23

24

25

26 Notes

27

28

29

30 Notes

31

32

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Participant Reminders

Staff Name

Today's Date

Time

Opening date for Week 30-34

Closing date for Week 30-34

NOTE:

You are about to call a participant to remind them of a specific visit. Please make sure to do the following:

1. Obtain all relevant contact numbers for the participant on their record
2. Ensure that you have checked what the exact date is when the participant is expected to present
3. Make sure to give the participant a brief description of what will be done at the visit.
4. You will make up to 3 attempts to get hold of the participant.

Please select "Proceed"

Proceed

The presentation dates are below:

TOC

Date: [baseline_arm_1][toc_3week]

WEEK 28 CALLING

Date: [baseline_arm_1][sched_28w_rem]

WEEK-32

30-34 Week Open Date: [week_28_arm_1][calling_wk30_34_open_date]

30-34 Week Close Date: [week_28_arm_1][calling_wk30_34_close_date]

30-34 Week Actual Date: [week_28_arm_1][week32_visit_date]

POST-NATAL VISIT

Visit open date: [predelivery_checki_arm_1][pd_remind_date_schedpd]

Visit close date: [predelivery_checki_arm_1][pd_close_date_schedpd]

Date of Delivery: [predelivery_checki_arm_1][pd_remind_date_delivery]

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>

6-WEEK IMMUNIZATION VISIT

1 Actual Date: [predelivery_checki_arm_1][sixw_im_schedpd]
2

3
4 Please select the calling attempt

- 5 First Attempt
6 Second Attempt
7 Third Attempt
8
9

10
11
12
13 Details of Calling Attempt 1
14
15
16

17
18 Outcome of the attempt

- 19 Successful - Participant
20 Successful - Family member
21 Unsuccessful - Voicemail
22 Unsuccessful - Invalid
23

24
25 Date of the attempt
26
27
28 _____
29
30

31
32 Details of Calling Attempt 2
33
34
35

36
37 Outcome of the attempt

- 38 Successful - Participant
39 Successful - Family member
40 Unsuccessful - Voicemail
41 Unsuccessful - Invalid
42

43
44 Date of the attempt
45
46
47 _____
48
49

50
51
52
53 Details of Calling Attempt 3

54
55 Outcome of the attempt

- 56 Successful - Participant
57 Successful - Family member
58 Unsuccessful - Voicemail
59 Unsuccessful - Invalid
60

Date of the attempt

1
2
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Calling notes

For peer review only

700 000000 0000000000e0

Staff Name

Today's date

Start time

NOTE

Did the participant present within the specified dates presented below:

Start: [baseline_arm_1][toc_reminder_date]

Actual: [baseline_arm_1][toc_3week]

End: [baseline_arm_1][arm1_toc_close_date]

- Yes
- No

The participant did not have a positive baseline STI result and therefore a ToC visit is not applicable. Activities associated with this visit will need to be captured under the "Ad-Hoc" tool

Note
You are about to start activities associated with the Test-of-Cure visit for participants in arm 1. The following activities are associated with this visit:

1. Collect 1 Loop with 2 slides
2. Collect 3 vaginal Swabs
 - Test of Cure Test
 - Profiling (Storage)
 - Microbiome (Storage)
3. Running the Test-of-Cure
4. Collect Clinical History, Adherence and Disclosure data

Please select "Proceed"

- Proceed

Specimen Collection_ToC

NOTE

Please collect one vaginal loop and prepare 2 slides. Please remember to do the following:

1. Pack slides individually in their own package
2. Record the PIN on the outside of package
3. Complete the lab CRF with the matching PINs and test instructions

Select "Proceed" to confirm the PINs associated with the slides.

- Proceed

1 Did you manage to collect the vaginal loop?
2

- 3 Yes
4 No
5

6 Date of vaginal loop specimen collection
7
8
9
10 _____
11

12 Please confirm the pin for the first vaginal swab that will be used for Nugent score

- 13 [baseline_arm_1][participant_pin]-TL1
14

15
16 Please confirm the pin for the second vaginal swab that will be used for yeast microscopy

- 17 [baseline_arm_1][participant_pin]-TL2
18
19

20 NOTE:

21 You are about the start with the process of collecting the following 3 vaginal swabs:

- 22
23 1. Swab to be used to conduct ToC (Immediately)
24 2. Swab for profiling
25 3. Swab to be used for microbiome
26

27 Please select "Proceed"

- 28 Proceed
29
30

31 Please specify the vaginal pH
32
33
34 _____
35

36 Please confirm the PIN associated with the vaginal swab that will be used for STI testing.

- 37 [baseline_arm_1][participant_pin] - TCV1
38
39

40 Did you manage to collect the vaginal swab for profiling

- 41 Yes
42 No
43
44

45 Please confirm the PIN associated with the vaginal swab that will be used for profiling.

46 This must be stored

- 47 [baseline_arm_1][participant_pin] - TCV2
48
49

50
51 Did you manage to collect the vaginal swab for microbiome testing?

- 52 Yes
53 No
54
55

56
57 Please confirm the PIN associated with the vaginal swab that will be used for microbiome.

58 This must be stored

- 59 [baseline_arm_1][participant_pin] - TCV3
60

1 Date of specimen collection for vaginal swabs
2
3
4
5

6 NOTE
7 You have collected all specimens associated with this visit. Once you select the "Proceed" option below you will be
8 directed to the start of the clinical history questionnaire. The completion of the questionnaire might take some time
9 so it would be a good idea to start running the vaginal swab to conduct the Test of Cure in line with the below
10 baseline results.
11
12
13

14 NG: [baseline_arm_1][sti_result_ng]

15
16 TV: [baseline_arm_1][sti_result_tv]

17
18 CT: [baseline_arm_1][sti_result_ct]

19
20 Proceed
21
22

23 24 Clinical History Review 25 26 27 28 29 30

31
32 You are done trying to collect specimens. Because you were not able to collect a Vaginal Swab for STI testing you
33 will not be able to run a test. Please proceed to completing the clinical history.
34

35 Proceed
36

37 Do you currently have any of the following symptoms?

38 Multiple selection

- 39
40 Abnormal vaginal discharge
41 Pain during urination
42 Lower abdominal pain
43 None
44

45 When did these symptoms start for abnormal vaginal discharge?

- 46
47 After previous visit
48 Persistent since previous visit
49 Recurrent since previous visit
50

51 When did these symptoms start for pain during urination?

- 52
53 After previous visit
54 Persistent since previous visit
55 Recurrent since previous visit
56
57
58
59
60

1 □□□e□e□□e
2
3
4

5 NOTE

6 The following questions pertain to adherence to the STI medication.

7
8 Select Proceed

9
10 Proceed

11
12 Did you finish the whole course of treatment?

- 13
14 Yes
15 No
16

17
18 How many days did you take treatment for?

19 _____
20
21

22
23 Did you throw up within 2 hours after taking any of the STI treatment?

- 24
25 Yes
26 No
27

28 Did you take any other non-chronic treatment at the time?

- 29
30 Yes
31 No
32

33 What type of treatment were you taking ?
34
35
36
37
38

39 NOTE

40 You are done with questions related to Adherence. You are about to start asking questions associated with
41 Disclosure.

42
43 Please select "Proceed"

44
45 Proceed
46
47

48 Disclosure
49
50
51

52
53 Did you have sex in the past month?

- 54
55 Yes
56 No
57
58
59
60

1 How many different male partners did you have sexual intercourse with in the past month ?

- 2
3 1
4 2
5 More than 2 partners
6

7 Please specify how many partners?
8
9
10 _____
11 _____

12 What type of sex did you have with partner 1 (Husband/ Steady partner)?

- 13
14 Vaginal
15 Anal
16 Oral
17

18 Did you use a condom the last time you had sex with this partner?

- 19
20
21 Yes
22 No
23

24 Did you notify him of your STI result?

- 25
26 Yes I gave him the notification slip
27 Yes I told him
28 No
29

30 What was his reaction when you told him of your STI infection?

- 31
32 Supportive
33 Angry
34 Violent
35 Disengaged
36

37 How did disclosure affect your relationship?

- 38
39 Continued as before
40 Started using a condom
41 He engaged with other partners
42 He refused sex
43 Relationship ended
44

45 Did he take the treatment?

- 46
47 Yes
48 No
49 Don't know
50

51 Where did he seek treatment?

- 52
53 Private
54 Public
55 Traditional
56
57
58
59
60

1 Why did you not notify this partner?
2

- 3 I didn't feel it was necessary
4 I am embarrassed
5 I'm afraid he gets angry
6 I'm afraid he gets violent
7 I'm afraid he will end the relationship
8

9 What type of sex did you have with partner 2?
10

- 11 Vaginal
12 Anal
13 Oral
14

15 Did you use a condom the last time you had sex with this partner?
16

- 17 Yes
18 No
19

20 Did you notify him of your STI result?
21

- 22 Yes I gave him the notification slip
23 Yes I told him
24 No
25

26 What was his reaction when you told him of your STI infection?
27

- 28 Supportive
29 Angry
30 Violant
31 Disengaged
32

33 How did disclosure affect your relationship?
34

- 35 Continued as before
36 Started using a condom
37 He engaged with other partners
38 He refused sex
39 Relationship ended
40

41 Did he take the treatment?
42

- 43 Yes
44 No
45 Don't know
46

47 Where did he seek treatment?
48

- 49 Private
50 Public
51 Traditional
52
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1 Why did you not notify your partner?
2

- 3 I didn't feel it was necessary
4 I am embarrassed
5 I'm afraid he gets angry
6 I'm afraid he gets violent
7 I'm afraid he will end the relationship
8

9 Did you tell anyone else of your STI infection?
10

- 11 Yes
12 No
13

14 Who did you tell?
15 (Select multiple)
16

- 17 Family member
18 Friend
19 Healthcare worker
20 Other
21

22 NOTE:

23 You have completed the ToC questionnaire. Please select "Proceed" to capture the outcome of the STI test.
24

- 25 Proceed
26
27

28 ToC Outcome
29

	Positive	Negative	Did not test
30 CT	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
31 NG	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
32 TV	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

33 NOTE: See calculation
34

35 The result from the STI result

(1 = Positive, 0 = Negative)

36 Does the participant show any symptoms of an STI?
37

- 38 Yes
39 No
40

41 Please contact the study clinician and discuss treatment.
42
43
44
45
46
47
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1 The participant tested/screened positive for an STI. Please specify the treatment that has been provided.

- 2
3 Azithromycin 1g stat dose
4 Azithromycin 2g stat dose
5 Ceftriaxone 250mg IM injection
6 Ceftriaxone 1g IM injection
7 Metronidazole 400mg bd x 1 week
8 Metronidazole 2g stat dose
9 Clotrimazole pessary and/or cream
10 Ceftriaxone 500mg IM injection

11
12 Date treatment given
13
14
15 _____
16

17 Please specify if a partner notification has been given to the patient.

- 18
19 Yes
20 No
21

22 **NOTE**

23 The patient did not test positive or show any signs of an infection

24 Select "Proceed" to conclude visit

- 25
26
27 Proceed
28
29

30 **Notes**
31
32
33
34

35 Additional notes
36
37
38
39
40

41 You have completed the ToC Visit Activities. Please make sure to check if all relevant fields have been selected and
42 the information captured is accurate.

43
44 Once this is done, please select the "Complete" option below and then select "Save & Exit".
45
46
47
48
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700 00e000e00_0e0000

You are about to capture the results of the first loop used for Nugent scoring.

Please select "Proceed" to continue

Proceed

Was the reading satisfactory for the Nugent score?

Yes
 No

Please specify the Nugent score

Please specify if candida was present

Yes
 No

Additional comments

You are about to capture the results of the second loop used for smear microscopy.

Please select "Proceed" to continue

Proceed

Was the reading satisfactory?

Yes
 No

Please specify the Nugent score

1 Please specify if candida was present

- 3 Yes
- 4 No

6 Additional comments

For peer review only

2
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Scheduling the Dates Associated with the 32 Week Gestational Visit

Scheduling the Dates Associated with the 32 Week Gestational Visit

The pregnancy (in days) is currently:

NOTE

You are about the start scheduling dates associated with the 32-week visit. You will need to schedule the following associated dates:

1. Week 32 date - Actual visit
2. Week 32 reminder date
3. Week 30 date - Visit window opens
4. Week 35 date - Visit window closes

Select "Proceed" to start scheduling

Proceed

Schedule the date for the 32 week gestational age, visit

Note to RA: please make sure that this date does not fall on Friday, weekend, and public holidays.

Calculate assist for 32-week visit

The number here must be between 210 and 244.

Days Difference (the difference between 32 weeks & Gestational age)

Match

The date you have entered does not meet the 93 day criteria. Does the intended or original date fall on a Friday weekend or public holiday?

- Yes
 No

ERROR

The numbers you have entered does not match. Please select a different date so that the numbers match.

Dates Associated with reminder for the 32 Week Gestational Age Visit

1
2
3 a a e 32 ge a a age

NOTE:

4 You have successfully scheduled the 32-week date.

5
6
7 We will need to contact the participant at least 3 days before the scheduled visit to remind them.

8
9 Select "Proceed" to schedule the reminder date for the 32 week visit.

10
11 Proceed

12
13 Note:
14 Schedule the date for the 32 week reminder. We will contact each participant starting 3 days prior to their 32-week
15 gestation date. That means the date scheduled here should be 3 days earlier then the scheduled date for the
16 32-week visit. If the date falls on a weekend choose the closest week date.

17
18
19
20
21 Calculation assist for scheduling the 32-week reminder date.

22
23 This number must be between 1 and 4.

ERROR

24
25
26
27
28 The date that you have entered is invalid. Please select a different date so that the number is less than or equal to 3.

NOTE:

29
30
31 You have successfully scheduled the 32-week reminder date.

32
33
34
35 Select "Proceed" to schedule the 32 week open visit date.

36
37 Proceed

38
39 Schedule the date for the 32 weeks opening visit date.

40
41 Note: Participants will have from 30 weeks of gestation to present for their 32-week visit date.

42
43
44
45
46 Calculation Assist for scheduling the 32-Week opening visit date.

47
48 This number must equal to 210

ERROR

49
50
51
52
53 The number you have entered does not match 210. Please select a different date so that the number equals 210.

NOTE:

54
55
56
57 You have successfully scheduled the 32-week opening date.

58
59
60 Select "Proceed" to schedule the 32 weeks missed visit date.

Proceed

1 Schedule the date for the 32 weeks missed visit date.

2
3 Note: Participants will have until 34 weeks of gestation to present for their 32-week visit date after which the visit will
4 be closed out.
5
6
7 _____
8

9 Calculation Assist for scheduling the 32-Week missed visit date.

10
11 This number must equal to 244
12
13
14 _____
15

16 ERROR
17 The number you have entered does not match 244. Please select a different date so that the number equals to 244.
18
19

20
21
22
23 **Estimated Delivery Date**
24

25 You are about the schedule the Estimated Delivery Date.

26
27 Please select "proceed"

28
29 Proceed
30

31 Estimated Delivery Date
32
33
34 _____
35

36 Days difference between estimated date of delivery and gestational age
37
38
39 _____
40

41 Calculation Assist for scheduling the Estimated Date for Delivery date.

42
43 This number must equal to [edod_calc]
44
45
46 _____
47

48 Match
49
50 _____
51

52 ERROR
53 The number you have entered does not match. Please select a different date so that the numbers match
54

55 You have completed all the scheduling dates.

56
57 Please check that all dates entered comply with the "calculation assistance".
58
59
60

1 You are about the schedule dates associated with the following events:
2
3

4 1. Pre-birth check-inn

5
6 Proceed
7
8

9
10
11
12 Check-In Calling at 37 Weeks
13
14
15

16 Proceed to the check-in calling date

17
18 Proceed
19

20
21 Check-in calling date
22
23
24 _____
25

26 Calculation Assist for check-in calling date

27 This number must equal to 259

28
29
30
31 _____
32

33 NOTE

34 The date you have entered is incorrect. Please make sure that the numbers correspond.
35

36 CONGRATULATIONS

37
38 You have finished scheduling all dates.
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

32 ee

Staff name

Today's date

Start time

Did the participant present within the dates presented below:

30-34 Week Start Date: [week_28_arm_1][sched_32w_open_date]

30-34 Week Actual Date: [week_28_arm_1][week32_visit_date]

30-34 Week Closing Date: [week_28_arm_1][sched_32w_mv_date]

- Yes
- No

Open ad-hoc visit to capture relevant information

Specimen Collection_32-Week

NOTE

You will now start with the process of specimen collection. You will need to collect several specimens from the participant. These specimens need to be collected in the order in which they are presented here.

The following specimens will need to be collected:

1. 1 x Vaginal loop to be used to prepare two slides
2. 1 x Vaginal swab to be used for STI testing (Arm 2 and Microbiome (Empilweni): immediate testing; Arm 1 and 3: Storage)
3. 1 x Vaginal swab to be used for profiling
4. 2 x Vaginal swab to be used for microbiome
5. 1 x Vaginal swab to be used for cytokine

- Proceed

Vaginal Smear

Please specify the vaginal pH

(if not available, enter 99)

1 Please select which pH strips are used to measure vaginal pH

- 2
3 CardinalHealth pH Indicator Strips (range 3.6-6.1)
4 pH Indicator Strips pH 0-14
5 Natureland vaginal pH test (range 3.5-6.5)
6

7 You will need to use a single loop to collect vaginal smear on two glass slides for microscopy
8 (if not available, enter 99)

- 9
10 Done
11

12 Confirm PIN associated with the first Vaginal Loop to be used to test for Nugent score

- 13
14 [baseline_arm_1][participant_pin] - WL1
15

16 Confirm PIN associated with the second Vaginal Loop to be used to test for Yeast microscopy

- 17
18 [baseline_arm_1][participant_pin] - WL2
19
20

21 Vaginal Swabs

22
23 **NOTE**

24 You will now collect four vaginal swabs. They will be used as follows:

- 25
26 1. STI testing (Arm 2 and Microbiome (Empilweni): immediate testing; Arm 1 and 3: Storage)
27 2. Profiling (stored)
28 3. Microbiome (stored)
29 4. Cytokine (stored)
30

- 31 Done
32

33 Confirm PIN associated with the vaginal swab to be used to test for STI

- 34
35 [baseline_arm_1][participant_pin] - WV1
36

37 Please confirm PIN associated with the vaginal swab to be used for Profiling

- 38
39 [baseline_arm_1][participant_pin] - WV2
40
41

42 Please confirm PIN associated with the vaginal swab to be used for microbiome

- 43
44 [baseline_arm_1][participant_pin] - WV3
45

46 Please confirm the PIN associated with the vaginal swab that will be used for cytokines.

- 47
48 [baseline_arm_1][participant_pin] - WV4
49

50 **NOTE**

51 The participant is in arm 2 and therefore an immediate STI test is conducted at the 32-week visit. Please prepare the
52 swab for testing before you continue to the questionnaires.
53

- 54 Proceed
55

56 **NOTE**

57 You are done with all specimen collection and will now proceed to administering the clinical history.

58 Please select "Proceed"

- 59
60 Proceed

██████████a ██████████ Re██████e

Have you been to the clinic since the last visit with us?

- Yes
- No

What was the purpose of your visit?

- ANC Visit
- HIV/ART
- STI Treatment
- Other

Summary notes from visit

Have you used any of the following since the first study visit?
Select multiple

- Alcohol
- Tik
- Dagga
- Grandpa
- Other
- None

Please specify other drugs used?

Do you currently have any of the following symptoms?

RA: Please select all that apply

- Abnormal vaginal discharge
- Pain during urination
- Lower abdominal pain
- Pain related to intercourse
- Vaginal bleeding related to intercourse
- Genital itchiness
- Any skin abnormalities
- None

When did these symptoms start for abnormal vaginal discharge?

- After previous visit
- Persistent since previous visit
- Recurrent since previous visit

1 When did these symptoms start for pain during urination?
2

- 3 After previous visit
4 Persistent since previous visit
5 Recurrent since previous visit
6

7 When did these symptoms start for the lower abdominal pain?
8

- 9 After previous visit
10 Persistent since previous visit
11 Recurrent since previous visit
12

13 When did these symptoms start for the pain related to intercourse?
14

- 15 After previous visit
16 Persistent since previous visit
17 Recurrent since previous visit
18

19 When did these symptoms start for vaginal bleeding related to intercourse?
20

- 21 After previous visit
22 Persistent since previous visit
23 Recurrent since previous visit
24

25 When did these symptoms start for genital itchiness?
26

- 27 After previous visit
28 Persistent since previous visit
29 Recurrent since previous visit
30

31 Please specify any skin abnormalities
32
33
34
35
36
37

38 Baseline Treatment Date:

39 [baseline_arm_1][sti_treatment_date]
40

41 TOC Treatment Date:

42 [toc_arm_1_arm_1][toc_sti_treatment_date]
43

44 Did the participant receive any STI treatment at their last study visit?
45

- 46 Yes
47 No
48

49 Are you planning to wait for your results today?
50 (New question added @13/09/2022)
51

- 52 Yes
53 No
54
55
56
57
58
59
60

1 What is your main reason why you are not intending to wait today?

2 (New question added @13/09/2022)

- 3
- 4 Have to get to work
- 5 Have to get back to my kids/family
- 6 Want to go to the shop
- 7 Transport availability
- 8 Lack of privacy
- 9 Hungry
- 10 No space to wait
- 11 Not feeling well
- 12 Boring
- 13 Other

14

15 If "Other", please specify.

16 (New question added @13/09/2022)

17

18

19

20

21

22 What would make you change your mind?

23 (New question added @13/09/2022)

24

25

26

27

28

29 You are done with questions associated with clinical history review. You will now start with questions associated with Adherence.

- 30
- 31
- 32 Proceed
- 33
- 34

35 Adherence

36

37

38

39 Did you finish the whole course of STI treatment

- 40
- 41 Yes
- 42 No
- 43

44

45 How many days did you take treatment for?

46

47 _____

48

49

50 Did you throw up within 2 hours after taking any of the STI treatment

- 51
- 52 Yes
- 53 No
- 54

55 Did you take any other non-chronic treatment at the time

- 56
- 57 Yes
- 58 No
- 59

60 What type of treatment

1 You are done with questions associated with the adherence. You are about to start asking questions associated with
2 disclosure.

3
4 Proceed

5
6
7
8
9
10 Disclosure

11
12 Did you notify your partner of your STI result?

- 13 Yes I gave him the notification slip
14 Yes I told him
15 No

16
17
18 What was his reaction when you told him of your STI infection

- 19 Supportive
20 Angry
21 Violent
22 Disengaged

23
24
25 How did disclosure affect your relationship?

- 26 Continued as before
27 Started using a condom
28 He engaged with other partners
29 He refused sex
30 Relationship ended

31
32
33 Did he take treatment?

- 34 Yes
35 No
36 I don't know

37
38
39 Where did he seek treatment

- 40 Private
41 Public
42 Traditional

43
44
45 Why did you not notify your partner?

- 46 I didn't feel it was necessary
47 I am embarrassed
48 I'm afraid he gets angry
49 I'm afraid he gets violent
50 I'm afraid he will end the relationship

51
52
53 Did you tell anyone else of your STI infection?

- 54 Yes
55 No
56
57
58
59
60

1 Who did you tell?
2

- 3 Family member
4 Friend
5 HCW
6 Other
7
8

9
10
11
12 Behavioral Questionnaire

13 NOTE TO RA:

14 You just completed all questions related to Disclosure. You are about to start with the Behavioral Questionnaire.

15 Please select "Proceed":

- 16
17
18 Proceed
19

20
21 Did you have sex since the last visit?

- 22 Yes
23 No
24

25
26 How many different male partners did you have sexual intercourse with in the past month?

- 27 1
28 2
29 more than 2
30

31
32 Were any of these new partners than the ones from the last visit

- 33 Yes
34 No
35

36
37 What type of sex did you have with partner 1 (Husband/ Steady partner)?

- 38 Vaginal
39 Anal
40 Oral
41
42

43 Did you use a condom the last time you had sex with partner 1 (Husband/ Steady partner)?

- 44 Yes
45 No
46
47

48
49 What type of sex did you have with partner 2?

- 50 Vaginal
51 Anal
52 Oral
53

54
55 Did you use a condom the last time you had sex with partner 2?

- 56 Yes
57 No
58
59
60

1 What type of sex did you have with the rest of the partners?
2

- 3 Vaginal
4 Anal
5 Oral
6

7 Did you use a condom the last time you had sex with one of them?
8

- 9 Yes
10 No
11

12 Where are you planning to deliver?
13

- 14 Frere
15 CMH
16 Nontyantambo
17 Empilweni
18 Bisho
19 Other
20

21 Please specify
22
23
24
25
26
27

28 You are done with the questions associated with Behavioral Questionnaire. You will now start asking questions
29 associated with the Physical Examination.

- 30 Proceed
31
32

33 Physical Examination 34 35 36 37

38 Weight of mother
39
40
41 _____
42

43 Systolic blood pressure
44
45 _____
46
47

48 Diastolic blood pressure
49
50
51 _____
52

53 How was Hemoglobin measured?
54

- 55 Hb meter at the clinic
56 Hb at NHLS
57

58 Please capture Hb result"
59
60

1 Please capture the barcode for Hb
2
3
4 _____
5

6 Fundal height
7
8
9 _____
10

11 Progression of pregnancy

- 13 Progressing normal
14 Abnormality detected
15

16 Provide further details of abnormality
17
18
19
20
21
22

23 During your examination, were there any signs of abnormal vaginal discharge?
24

- 25 Yes
26 No
27

28 During your examination, were there any signs of inguinal lymphadenopathy?
29

- 30 Yes
31 No
32

33 Are these bubo?
34

- 35 Yes
36 No
37

38 Note to RA: Please contact the study clinician and specify treatment given to the participant
39
40
41
42
43
44

45 During your examination, were there any signs of lower abdominal pain?
46

- 47 Yes
48 No
49

50 During your examination, were there any signs of scratch marks?
51

- 52 Yes
53 No
54

55 During your examination, were there any signs of skin conditions?
56

- 57 Yes
58 No
59

60 Please specify the nature of the skin conditions

1 During your examination, were there any other observations that need to be noted?
2
3
4
5
6

7 You have completed the questions associated with the Physical Examination. You will now start capturing the results
8 from the rapid tests.
9

10 Proceed
11
12

13 Rapid Test Results 14 15 16 17

18 Do you know your current HIV status?
19

- 20 HIV negative (tested today by clinical staff)
21 HIV positive on ART
22 HIV positive, not on ART
23 Don't know (never tested)
24 Don't know (no yet tested today)
25

26 Was the participant newly diagnosed with HIV today
27

- 28 Yes
29 No
30

31 Please conduct an HIV Rapid test and capture the result below
32

- 33 Positive
34 Negative
35

36 Please conduct a confirmatory HIV Rapid test and capture the result below
37

- 38 Positive
39 Negative
40

41 Did you collect a tube of blood for CD4 count?
42

- 43 Yes
44 No
45

46 Please record barcode for blood tube for CD4 count testing?
47
48
49
50
51

52 Is the participant's most recent CD4 count since Baseline available?
53

- 54 Yes
55 No
56

57 What was the date of the CD4 specimen collection?
58
59
60

1 What was the participant's most recent CD4 count?

2
3
4
5 _____
6 (if no number listed, enter 9999)
7

8 Did you collect a tube of blood for viral load?

- 9 Yes
10 No
11

12 Please record barcode for blood tube for viral load testing?

13 _____
14
15
16

17 Is the participant's most recent viral load since Baseline available?

- 18 Yes
19 No
20
21
22

23 What was the date of the viral load specimen collection?

24 _____
25
26
27

28 What was the participant's most recent viral load?

29
30
31 _____
32 (if no number listed, enter 0000)
33

34 Which regimen for ART were you started on today?

- 35 TLD
36 TEE
37 AZT/3TC/LPV
38 Other
39
40

41 Which regimen for ART were you on so far?

- 42 TLD
43 TEE
44 AZT/3TC/LPV
45 Other
46
47

48 Has the regimen for ART been changed today?

- 49 Yes
50 No
51
52

53 To which regimen for ART has it been changed today?

- 54 TLD
55 TEE
56 AZT/3TC/LPV
57 Other
58
59
60

1 Has a syphilis test been done for the participant?
2

- 3 Yes
4 No
5

6 Which syphilis test have you used?
7

- 8 Alere Syphilis TP (provided by FPD)
9 HIV/Syphilis Duo (provided by FPD)
10 No rapid test used only NHLS bloods for RPR
11 Other please specify
12

13 Please specify
14
15
16
17
18
19

20 Syphilis result.

- 21 Positive
22 Negative
23 Indeterminate
24

25 Titer value 1:
26
27
28

29 _____
30 (If RPR is non-reactive, enter 0)
31

32 Blood needs to be collected for further syphilis testing. Please confirm if blood was collected.
33

- 34 Yes
35 No
36

37 Collect blood for RPR and capture barcode PIN below
38
39
40 _____
41

42 Treatment given
43

- 44 Benzathine penicillin 2.4 MU IM weekly x3
45 Out of stock
46

47 Please contact study clinician and specify treatment given
48
49
50
51
52

53 Please collect participant's urine for testing
54
55
56
57
58
59
60

□□□□e □□□□□□□□ □e□□ □e□□□□□□

You are about to capture the results from the dipstick testing

Please select "Proceed" to continue

- Proceed

Blood - Hemoglobin

- Negative
- Ca. 10
- Ca. 50
- Ca. 250/300

Blood - Erythrocytes

- Negative
- Ca. 5 -10
- Ca. 50
- Ca. 250/300

Urobilinogen

- Normal
- 2
- 4
- 8
- 12

Bilirubin

- Negative
- 1 plus
- 2 plus
- 3 plus
- Not available

Protein

- Negative
- 30
- 100
- 500

Nitrate

- Negative
- Positive

For peer review only

1 Keton

- 2
3 Negative
4 1 plus
5 2 plus
6 3 plus
7 Not available

8
9 Glucose

- 10
11 Negative
12 Normal
13 50
14 150
15 500
16 ≥ 1000

17
18 pH

- 19
20 5
21 6
22 7
23 8
24 9
25 Not available

26
27 SG

- 28
29 1.000
30 1.005
31 1.010
32 1.015
33 1.020
34 1.025
35 1.030
36 Not available

37
38 Leucocytes

- 39
40 Negative
41 25
42 75
43 500

44
45
46
47
48
49 STI Results and Screening
50
51
52
53
54
55
56
57
58
59
60

The participant is in arm 2 or for Empilweni and therefore you are about to capture results for the STI testing.

Proceed

STI Test Outcome

The previous STI results of the participants are:

Baseline

NG:[baseline_arm_1][sti_result_ng]

CT:[baseline_arm_1][sti_result_ct]

TV:[baseline_arm_1][sti_result_tv]

TOC

NG:[toc_arm_1_arm_1][toc_ng]

CT:[toc_arm_1_arm_1][toc_ct]

TV:[toc_arm_1_arm_1][toc_tv]

Negative

Positive

CT

NG

TV

STI Calculation _ w32

Date the result was obtained.

Did the participant wait for her STI results?

(New question added @ 03/11/2022)

Yes

No

Was the participant reporting STI symptoms or showed symptoms during the clinical assessment?

Yes

No

Does the participant report any medication allergies?

Yes

No

1 Please contact the study clinician before giving any treatment. Please specify discussed medication allergies and
2 treatment plan with the study clinician
3
4
5
6
7

8 The following treatment has been provided
9

- 10 Azithromycin 1g stat dose
11 Azithromycin 2g stat dose
12 Ceftriaxone 250mg IM injection
13 Ceftriaxone 1g IM injection
14 Metronidazole 400mg bd x 1 week
15 Metronidazole 2g stat dose
16 Clotrimazole pessary and/or cream
17 Trimethoprim/sulfamethoxazole 400/80 mg 2 tbl. bds for 5 days (bactrim)
18 Ceftriaxone 500mg IM injection
19

20 Date treatment given
21
22
23 _____
24

25 What made you change your mind about waiting for the results?
26 (New question added @13/09/2022)
27
28
29
30
31

32 Partner notification provided
33

- 34 Yes, 1
35 Yes, multiple
36 No
37

38 Please explain why the partner notification note was not provided?
39
40
41
42
43
44

45 You have completed capturing the information from the 32 week exam. Please make sure to check that you have
46 completed all the fields.
47

48 Please select "Complete" then "Save and Exit".
49
50

51 Notes
52
53
54

55 Additional notes
56
57
58
59
60

32 e e e

You are about to capture the results of specimens collected during the 32-week visit

Please select "Proceed" to continue

Proceed

Hb Results received

Yes

No

Please capture the Hb result

Please capture the barcode for Hb

Please specify whether the reading was satisfactory for the loop used for Nugent score

Yes

No

Please capture the score for the loop used for Nugent scoring

Please specify if candida was present for the loop used for Nugent scoring

Yes

No

Please specify whether the reading was satisfactory for the loop used for yeast microscopy

Yes

No

Please capture the nugent score for the loop used for yeast microscopy

1 Please specify if candida was present for the loop used for yeast microscopy

- 2
3 Yes
4 No
5

6 Please capture the results for the blood used for Syphilis testing

- 7
8 RPR Negative
9 RPR Positive
10 RPR Indeterminate
11

12
13
14
15
16 _____
17 Please capture the result for viral load testing

18
19
20
21 _____
22 Is the participant's most recent viral load available?

- 23
24 Yes
25 No
26

27
28 What was the date of the viral load specimen collection?

29
30
31 _____
32 What was the participant's most recent viral load?

33
34
35
36
37 _____
38
39
40
41
42 _____
43
44

45 Notes

46
47
48
49
50 Notes

Participant Registration Re-enrollment_2

Staff Name

Today's Date

Time

The presentation dates are below:

TOC

Date: [baseline_arm_1][toc_3week]

WEEK 28 CALLING

Date: [baseline_arm_1][sched_28w_rem]

WEEK-32

30-34 Week Actual Date: [week_28_arm_1][week32_visit_date]

Call In Check

Week 37 Call In Check: [week_28_arm_1][cic_date]

POST-NATAL VISIT

Visit open date: [predelivery_checki_arm_1][pd_remind_date_schedpd]

Visit close date: [predelivery_checki_arm_1][pd_close_date_schedpd]

Date of Delivery: [predelivery_checki_arm_1][pd_remind_date_delivery]

6-WEEK IMMUNIZATION VISIT

Actual Date: [predelivery_checki_arm_1][sixw_im_schedpd]

NOTE:

You are about to call a participant to remind them of a specific visit. Please make sure to do the following:

1. Obtain all relevant contact numbers for the participant on their record
2. Ensure that you have checked what the exact date is when the participant is expected to present
3. Make sure to give the participant a brief description of what will be done at the visit.
4. You will make up to 3 attempts to get hold of the participant.

Please select "Proceed"

Proceed

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>

Please select the calling attempt

- First Attempt
- Second Attempt
- Third Attempt

Details of Calling Attempt 1

Outcome of the attempt

- Successful - Participant
- Successful - Family member
- Unsuccessful - Voicemail
- Unsuccessful - Invalid

Date of the attempt

Did she deliver?

- Yes
- No

Capture delivery Date

NOTE: instruct to come to the site.

Details of Calling Attempt 2

Outcome of the attempt

- Successful - Participant
- Successful - Family member
- Unsuccessful - Voicemail
- Unsuccessful - Invalid

Date of the attempt

1 Did she deliver?
2

- 3 Yes
4 No
5

6 Capture delivery Date
7

8 NOTE: instruct to come to the site.
9

10 _____
11

12
13
14 **Details of Calling Attempt 3**
15
16
17

18
19 Outcome of the attempt

- 20 Successful - Participant
21 Successful - Family member
22 Unsuccessful - Voicemail
23 Unsuccessful - Invalid
24

25
26 Date of the attempt
27

28 _____
29

30
31 Did she deliver?
32

- 33 Yes
34 No
35

36 Capture delivery Date
37

38 NOTE: instruct to come to the site.
39

40 _____
41

42
43
44 **Notes**
45

46
47 Calling notes
48
49
50
51
52
53
54
55
56
57
58
59
60

1 S...e...e ...a...g ... 38 ...ee...

2
3
4
5 NOTE FW: Please make sure that you call the participant once per week.

6
7 Proceed

8
9
10 Did you schedule the 38 weeks call

11 Yes
12 No

13
14
15 Please select the calling attempt

16 First Attempt
17 Second Attempt
18 Third Attempt

19
20
21
22 Details of Calling Attempt 1

23
24
25
26 Outcome of the attempt

27 Successful - Participant
28 Successful - Family member
29 Unsuccessful - Voicemail
30 Unsuccessful - Invalid

31
32
33 Date of the attempt

34 _____
35
36
37

38
39 Did she deliver?

40 Yes
41 No

42
43
44 Details of Calling Attempt 2

45
46
47
48
49 Outcome of the attempt

50 Successful - Participant
51 Successful - Family member
52 Unsuccessful - Voicemail
53 Unsuccessful - Invalid

54
55
56 Date of the attempt

57 _____
58
59
60

1 Did she deliver?
2

- 3 Yes
4 No
5
6

7 Details of Calling Attempt 3
8
9
10
11
12
13

14 Outcome of the attempt
15

- 16 Successful - Participant
17 Successful - Family member
18 Unsuccessful - Voicemail
19 Unsuccessful - Invalid
20

21 Date of the attempt
22
23
24
25 _____
26

27 Did she deliver?
28

- 29 Yes
30 No
31
32

33
34 Schedule calling for 39 weeks
35

36 NOTE FW: Please make sure that you call the participant once per week.
37

- 38 Proceed
39

40 Did you schedule the 39 weeks call
41

- 42 Yes
43 No
44

45 Please select the calling attempt
46

- 47 First Attempt
48 Second Attempt
49 Third Attempt
50
51
52
53
54
55
56
57
58
59
60

1 e a a g e 1
2
3
4

5 Outcome of the attempt

- 6 Successful - Participant
- 7 Successful - Family member
- 8 Unsuccessful - Voicemail
- 9 Unsuccessful - Invalid

10 Date of the attempt

11 _____

12 Did she deliver?

- 13 Yes
- 14 No

15 Capture delivery Date

16 NOTE: instruct to come to the site.

17 _____

18 Details of Calling Attempt 2

19 Outcome of the attempt

- 20 Successful - Participant
- 21 Successful - Family member
- 22 Unsuccessful - Voicemail
- 23 Unsuccessful - Invalid

24 Date of the attempt

25 _____

26 Did she deliver?

- 27 Yes
- 28 No

29 Details of Calling Attempt 3

30 Outcome of the attempt

- 31 Successful - Participant
- 32 Successful - Family member
- 33 Unsuccessful - Voicemail
- 34 Unsuccessful - Invalid

35 Date of the attempt

36 _____

1 Did she deliver?

- 2
- 3 Yes
- 4 No
- 5

6 Calling notes

13 Schedule calling for 40 weeks

15 NOTE FW: Please make sure that you call the participant once per week.

- 16
- 17 Proceed
- 18

19 Please select the calling attempt

- 20
- 21 First Attempt
- 22 Second Attempt
- 23 Third Attempt
- 24

25 Did you schedule a call for 40 weeks

- 26
- 27 Yes
- 28 No
- 29
- 30

31 Details of Calling Attempt 1

36 Outcome of the attempt

- 37 Successful - Participant
- 38 Successful - Family member
- 39 Unsuccessful - Voicemail
- 40 Unsuccessful - Invalid
- 41

43 Date of the attempt

46 _____

48 Did she deliver?

- 49
- 50 Yes
- 51 No
- 52

53 Capture delivery Date

55 NOTE: instruct to come to the site.

58 _____

1 **☐ e☐a☐☐☐ ☐☐☐ a☐☐☐☐g ☐☐☐e☐☐☐ 2**

2
3 Outcome of the attempt

- 4 Successful - Participant
5 Successful - Family member
6 Unsuccessful - Voicemail
7 Unsuccessful - Invalid
8

9
10 Date of the attempt

11
12
13 _____
14

15 Did she deliver?

- 16 Yes
17 No
18
19

20
21 **Details of Calling Attempt 3**

22
23 Outcome of the attempt

- 24 Successful - Participant
25 Successful - Family member
26 Unsuccessful - Voicemail
27 Unsuccessful - Invalid
28

29
30 Date of the attempt

31
32
33 _____
34

35 Calling notes

36
37
38
39
40

41 Did she deliver?

- 42 Yes
43 No
44
45

46
47 **Schedule calling for 41 weeks**

48 NOTE FW: Please make sure that you call the participant once per week.

- 49 Proceed
50

51
52 Please select the calling attempt

- 53 First Attempt
54 Second Attempt
55 Third Attempt
56
57
58
59
60

1 Did you schedule a call for 41 weeks

- 2
3 Yes
4 No
5
6

7 **Details of Calling Attempt 1**

8
9 Outcome of the attempt

- 10 Successful - Participant
11 Successful - Family member
12 Unsuccessful - Voicemail
13 Unsuccessful - Invalid
14

15
16 Date of the attempt

17
18
19 _____
20
21

22 **Details of Calling Attempt 2**

23
24 Outcome of the attempt

- 25 Successful - Participant
26 Successful - Family member
27 Unsuccessful - Voicemail
28 Unsuccessful - Invalid
29

30
31 Date of the attempt

32
33
34 _____
35

36 Did she deliver?

- 37 Yes
38 No
39
40

41
42 **Details of Calling Attempt 3**

43
44 Outcome of the attempt

- 45 Successful - Participant
46 Successful - Family member
47 Unsuccessful - Voicemail
48 Unsuccessful - Invalid
49

50
51 Date of the attempt

52
53
54 _____
55

56 Calling notes

57
58
59
60

1 Did she deliver?
2

- 3 Yes
4 No
5

6 Capture delivery Date
7

8 NOTE: instruct to come to the site.
9
10
11 _____
12
13

14 Schedule calling for 41 weeks (293 days) 15

16 NOTE FW: Please make sure that you call the participant once per week.
17

- 18 Proceed
19

20 Did you schedule a call for 41 weeks
21

- 22 Yes
23 No
24

25 Please select the calling attempt
26

- 27 First Attempt
28 Second Attempt
29 Third Attempt
30
31

32 Details of Calling Attempt 1 33

34 Outcome of the attempt
35

- 36 Successful - Participant
37 Successful - Family member
38 Unsuccessful - Voicemail
39 Unsuccessful - Invalid
40

41 Calling notes
42
43
44
45
46

47 Did she deliver?
48

- 49 Yes
50 No
51

52 Capture delivery Date
53

54 NOTE: instruct to come to the site.
55
56
57 _____
58
59
60

1 Scheduling page 42 week 296 page

2
3 NOTE FW: Please make sure that you call the participant once per week.

4
5 Proceed

6
7 Please select the calling attempt

- 8
9 First Attempt
10 Second Attempt
11 Third Attempt

12
13 Did you schedule a call for 42 weeks

- 14
15 Yes
16 No

17
18
19 **Details of Calling Attempt 1**

20 Outcome of the attempt

- 21
22 Successful - Participant
23 Successful - Family member
24 Unsuccessful - Voicemail
25 Unsuccessful - Invalid

26
27
28 Date of the attempt

29
30
31 _____

32
33 Did she deliver?

- 34
35 Yes
36 No

37
38
39 **Details of Calling Attempt 2**

40
41
42
43
44
45
46 Outcome of the attempt

- 47
48 Successful - Participant
49 Successful - Family member
50 Unsuccessful - Voicemail
51 Unsuccessful - Invalid

52
53 Date of the attempt

54
55
56 _____

1 Did she deliver?
2

- 3 Yes
4 No
5
6

7 **Details of Calling Attempt 3**
8
9
10

11 Outcome of the attempt

- 12
13 Successful - Participant
14 Successful - Family member
15 Unsuccessful - Voicemail
16 Unsuccessful - Invalid
17

18 Date of the attempt
19
20
21
22 _____
23

24 **Outcome of the call**
25
26
27
28

29 Did the participant deliver?
30

- 31 Yes
32 No
33

34 Calling notes
35
36
37
38
39

40 Did she deliver?
41

- 42 Yes
43 No
44

45 Capture delivery Date
46

47 NOTE: instruct to come to the site.
48
49
50
51 _____
52
53
54
55
56
57
58
59
60

Scheduling_P... e... e... e... g... a... e...

You are about the schedule dates associated with the following events:

- 1. Post-Delivery Appointment
- 2. 6-Weeks Immunization Appointment

Proceed

Post-Delivery Study Visit

You will now schedule dates associated with the post-delivery study visit.

The following dates are associated with this visit:

- 1. Calling reminder date / Visit opening date
- 2. Visit closing date

Select "Proceed" to continue

Proceed

Please capture the date of delivery

Please schedule the date for the post-delivery reminder call.

Please note that the Delivery date is [pd_remind_date_delivery]. The reminder call will happen 1 day following delivery.

Calculation Assist for Post Delivery reminder call

This number must equal to: 1

Match

NOTE

The date you have entered is incorrect. Please make sure that the numbers correspond.

1 The post-delivery closing date.
2
3
4
5

6 Calculation Assist for Post Delivery closing date
7

8 The participant will have 14 days post-delivery to present at the clinic. The delivery date was
9 [pd_remind_date_delivery]. This number must therefore equal to: 14
10
11
12
13

14 Match
15
16
17
18
19
20

21 **NOTE**

22 The date you have entered is incorrect. Please make sure that the numbers correspond.
23
24
25

26 Facility delivered

- Frere
- CMH
- Nontyantambo
- Empilweni
- Bisho
- Other

27
28
29
30
31
32
33 Please specify the facility of delivery
34
35
36
37
38

39
40
41 **6-Week Immunization Visit**
42
43
44
45

46 **NOTE:**

47 In this section you will schedule all dates associated with the 6-Week Immunization Study Visit. These dates will
48 include:
49

- 50 1. Calling reminder date for 6-Weeks Immunization visit
- 51 2. Scheduled date of 6-Weeks Immunization visit
- 52 3. Closing date for attending the 6-Weeks Immunization visit

53 Select Proceed to continue

54
55 Proceed
56
57

58 Please schedule the date for the 6-weeks immunization reminder
59
60

1 Calculation Assist for 6-weeks immunization reminder. We will call all patients 5 weeks (35 days) following their
2 delivery date. The updated delivery date for the participant was [calling_delivery_date_37weeks].
3

4 This number must therefore equal to: 35 and 40
5
6
7 _____
8

9 Match
10
11
12 _____
13

16 NOTE
17 The date you have entered is incorrect. Please make sure that the numbers correspond.
18
19
20

22 Please schedule the date for the 6-weeks immunization visit. This visit is scheduled to take place 6 weeks (42 days)
23 following delivery. The updated delivery date is [calling_delivery_date_37weeks]
24
25
26 _____
27

28 Calculation Assist for 6-weeks immunization visit
29

30 This number must equal to: 42
31
32
33 _____
34

35 Match
36
37
38 _____
39

40 NOTE
41 The date you have entered is incorrect. Please make sure that the numbers correspond.
42

43 Please schedule the date for the 6-weeks immunization visit closing date.
44
45
46 _____
47

48 Calculation Assist for 6-Weeks Immunization visit Close Date. Mothers will have up to 8 weeks post delivery to attend
49 this visit. This means 56 days following the delivery.
50

51 This number must equal to: 56
52
53
54 _____
55

56 Match
57
58
59 _____
60

1
2
3
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7
8
9
10
11
12
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14
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60

NOTE

The date you have entered is incorrect. Please make sure that the numbers correspond.

CONGRATULATIONS

You have finished scheduling all dates.

For peer review only

Reg e a a

Participant PIN

[baseline_arm_1][participant_pin]

Staff name

Today's date

Start time

You are about to capture data retrieved from the birth registry. Please select "Proceed" to start

Proceed

Delivery Details

Delivery site

- Frere
- CMH
- Nontyantyambo
- Empilweni
- Bisho
- Other

Please specify name of delivery facility

Clinic file number

Delivery date

Calculated gestational age

(Added @22/03/2023)

1 Please specify the number of babies during pregnancy

- 2
3 1
4 2
5 3
6

7 Outcome type for baby 1

- 8
9 Live birth
10 Still birth
11 Early Neonatal Death
12

13 Outcome type for baby 2

- 14
15 Live birth
16 Still birth
17 Early Neonatal Death
18

19 Outcome type for baby 3

- 20
21 Live birth
22 Still birth
23 Early Neonatal Death
24

25 Type of delivery for baby 1

- 26
27 Born before arrival
28 Normal Vaginal Delivery
29 Assisted Vaginal Delivery
30 Elective Cesarean Section
31 Emergency Cesarean Section
32

33 Type of delivery for baby 2

- 34
35 Born before arrival
36 Normal Vaginal Delivery
37 Assisted Vaginal Delivery
38 Elective Cesarean Section
39 Emergency Cesarean Section
40

41 Type of delivery for baby 3

- 42
43 Born before arrival
44 Normal Vaginal Delivery
45 Assisted Vaginal Delivery
46 Elective Cesarean Section
47 Emergency Cesarean Section
48

49 Please specify reason

50

51

52

53

54

55

56 Please specify reason

57

58

59

60

1 Please specify reason
2
3
4
5
6

7 Gender - Baby 1
8

- 9 Female
10 Male
11

12 Gender - Baby 2
13

- 14 Female
15 Male
16

17 Gender - Baby 3
18

- 19 Female
20 Male
21
22

23 **Complications in labor/Delivery**
24

	Yes	No
25 Induction of labour	<input type="radio"/>	<input type="radio"/>
26 Antepartum haemorrhage	<input type="radio"/>	<input type="radio"/>
27 Post Partum haemorrhage	<input type="radio"/>	<input type="radio"/>
28 Severe pre-eclampsia	<input type="radio"/>	<input type="radio"/>
29 Eclampsia	<input type="radio"/>	<input type="radio"/>
30 Prolonged rupture of membranes	<input type="radio"/>	<input type="radio"/>
31 Ruptured uterus	<input type="radio"/>	<input type="radio"/>
32 Sepsis	<input type="radio"/>	<input type="radio"/>
33 Obstructed or prolonged labour	<input type="radio"/>	<input type="radio"/>
34 Retained Placenta	<input type="radio"/>	<input type="radio"/>
35 Manual removal of placenta	<input type="radio"/>	<input type="radio"/>

36 Maternal outcome
37

- 38 Live
39 Death
40
41

42 APGAR score at 5 minutes for baby 1
43

44 _____
45
46

47 APGAR score at 5 minutes for baby 2
48

49 _____
50
51

52 APGAR score at 5 minutes for baby 3
53

54 _____
55
56

1 Birth weight for baby 1 in grams
2
3
4 _____
5

6 Birth weight for baby 2 in grams
7
8
9 _____
10

11 Birth weight for baby 3 in grams
12
13
14 _____
15

16
17 Did you breastfeed your baby/ies within 1 hour of giving birth?
18

- 19 Yes
20 No
21

22 Infant feeding
23 (New question added @15/11/2022)
24

- 25 Exclusive Breast Feeding (EBF)
26 Exclusive Formula Feeding (EFF)
27

28 Any birth defects to note for baby 1
29

- 30 Yes
31 No
32

33 Any birth defects to note for baby 2
34

- 35 Yes
36 No
37

38 Any birth defects to note for baby 3
39

- 40 Yes
41 No
42

43 Please specify
44
45
46
47
48
49

50 Remarks outcome
51
52
53
54
55

56 Maternal outcome
57
58
59
60

1 You have completed the Birth register. Please make sure to check if all relevant fields have been selected and the
2 information captured is accurate.
3

4 Once this is done, please select the "Complete" option below and then select "Save & Exit".
5
6
7
8
9
10
11
12
13
14
15
16
17
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46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

Post-natal visit

Staff name

Today's date

Start time

Post-Natal Visit

The participant was scheduled to present within the two dates below. Please specify if the participant presented within this timeframe.

Visit open date: [predelivery_checki_arm_1][pd_remind_date_delivery]

Visit close date: [predelivery_checki_arm_1][pd_close_date_schedpd]

- Yes
No

You are about to administer the questions associated with the post natal visit.

Please select "Proceed"

- Proceed?

Clinical History Review

Have you been to the clinic since the last visit with us?

- Yes
No

What was the purpose of your visit?

- ANC Visit
HIV/ART
STI Treatment
Other

Summary notes from the visit

1 Were there any abnormalities/complications since your last study visit regarding your pregnancy and delivery or did
2 you receive any non-chronic treatment?
3

- 4 Yes
5 No
6

7 Please specify
8
9
10
11
12

13 Have you used any of the following since the first study visit?
14 Select multiple
15

- 16 Alcohol
17 Tik
18 Dagga
19 Grandpa
20 Other
21 None
22

23 Please specify other drugs used?
24
25
26
27
28

29 The Baseline STI results of the participants are:

30 NG: [baseline_arm_1][sti_result_ng]

31 CT: [baseline_arm_1][sti_result_ct]

32 TV: [baseline_arm_1][sti_result_tv]
33
34
35

36 The TOC STI results of the participants are:

37 NG: [toc_arm_1_arm_1][toc_ng]

38 CT: [toc_arm_1_arm_1][toc_ct]

39 TV: [toc_arm_1_arm_1][toc_tv]
40
41
42
43
44

45 The Week 32 STI results of the participants are:

46 CT: [3034_weeks_arm_1][w32_ct_res]

47 NG: [3034_weeks_arm_1][w32_ng_res]

48 TV: [3034_weeks_arm_1][w32_tv_res]
49
50
51
52
53

54 Did the participant receive any STI treatment at their last study visit?

- 55 Yes
56 No
57
58
59
60

1 **Disclosure**

2
3 You are done with questions associated with the clinical history review. You will now start with questions associated
4 with Adherence.

5 Proceed

7
8 Did you finish the whole course of STI treatment?

9
10 Yes

11 No

12
13 How many days did you take treatment for?

14
15
16 _____

17
18 Did you throw up within 2 hours after taking any of the STI treatment?

19
20 Yes

21 No

22
23 Did you take any other non-chronic treatment at the time?

24
25 Yes

26 No

27
28
29 What type of treatment

30
31
32
33
34
35 **Disclosure**

36
37 You are done with questions associated with the adherence. You are about to start asking questions associated with
38 disclosure.

39
40 Proceed

41
42 Did you notify your partner of your STI result?

43
44 Yes I gave him the notification slip

45 Yes I told him

46 No

47
48 What was his reaction when you told him of your STI infection

49
50 Supportive

51 Angry

52 Violent

53 Disengaged

54

55

56

57

58

59

60

1 How did disclosure affect your relationship?
2

- 3 Continued as before
4 Started using a condom
5 He engaged with other partners
6 He refused sex
7 Relationship ended
8

9 Did he take treatment?
10

- 11 Yes
12 No
13 I don't know
14

15 Where did he seek treatment?
16

- 17 Private
18 Public
19 Traditional
20

21 Why did you not notify your partner?
22

- 23 I didn't feel it was necessary
24 I am embarrassed
25 I'm afraid he gets angry
26 I'm afraid he gets violent
27 I'm afraid he will end the relationship
28

29 Did you tell anyone else of your STI infection?
30

- 31 Yes
32 No
33

34 Did you tell anyone else of your STI infection?
35

- 36 Yes
37 No
38

39 Who did you tell?
40

- 41 Family member
42 Friend
43 HCW
44 Other
45
46
47

48 Delivery Details of Infant
49
50
51

52 Facility delivered
53

- 54 Frere
55 CMH
56 Nontyantambo
57 Empilweni
58 Bisho
59 Other
60

Please specify facility of delivery

1 Date of delivery
2
3
4
5

6 Calculated gestational age
7

8 (Added @22/03/2023)
9

10 Please specify the number of babies during pregnancy
11

- 12
13 1
14 2
15 3
-

16 Outcome type for baby 1
17

- 18 Live birth
19 Still birth
20 Early Neonatal Death
21
-

22 Outcome type for baby 2
23

- 24 Live birth
25 Still birth
26 Early Neonatal Death
27
-

28 Outcome type for baby 3
29

- 30 Live birth
31 Still birth
32 Early Neonatal Death
33
-

34 Type of delivery for baby 1
35

- 36 Born before arrival
37 Normal Vaginal Delivery
38 Assisted Vaginal Delivery
39 Elective Cesarean Section
40 Emergency Cesarean Section
41
-

42 Type of delivery for baby 2
43

- 44 Born before arrival
45 Normal Vaginal Delivery
46 Assisted Vaginal Delivery
47 Elective Cesarean Section
48 Emergency Cesarean Section
49
-

50 Type of delivery for baby 3
51

- 52 Born before arrival
53 Normal Vaginal Delivery
54 Assisted Vaginal Delivery
55 Elective Cesarean Section
56 Emergency Cesarean Section
57
-

58 Please specify reason
59
60

1 Please specify reason
2
3
4
5
6

7 Please specify reason
8
9
10
11
12

13 Gender - Baby 1
14

- 15 Female
- 16 Male

18 Gender - Baby 2
19

- 20 Female
- 21 Male

22 Gender - Baby 3
23

- 24 Female
- 25 Male

26 Maternal outcome
27

- 28 Live
- 29 Death

30 Specify
31
32
33
34
35
36
37
38
39

40 APGAR score at 5 minutes for baby 1
41

42 Note to RA: Check on Road to Health
43
44
45

46 _____
(if no number listed, enter 99)
47

48 APGAR score at 5 minutes for baby 2
49

50 Note to RA: Check on Road to Health
51
52

53 _____
(if no number listed, enter 99)
54

55 APGAR score at 5 minutes for baby 3
56

57 Note to RA: Check on Road to Health
58
59

60 _____
(if no number listed, enter 99)

1 Birth weight in grams for baby 1
2

3 Note to RA: Check on Road to Health
4
5
6 _____
7

8 Birth weight in grams for baby 2
9

10 Note to RA: Check on Road to Health
11
12
13 _____
14

15 Birth Weight in grams for baby 3
16

17 Note to RA: Check on Road to Health
18
19
20 _____
21

22 Newborn problems
23

24 Note to RA: Check on Road to Health
25

- 26 Birth defects
27 Hypoxic brain injury
28 Convulsions /fits
29 Jaundice
30 None
31

32 Please Specify
33
34
35
36
37

38 Was the baby exposed to HIV?
39 (Added @29/03/2023)
40

- 41 Yes
42 No
43

44 Was Nevirapine given to the baby/babies
45

- 46 Yes
47 No
48

49 Was birth PCR done for the baby/babies
50

- 51 Yes
52 No
53

54 NOTE: If not taken by birth facility please take blood for PCR.
55

56 PCR Barcode for the baby/baby 1
57
58
59 _____
60

1 NOTE: If not taken by birth facility please take blood for PCR.
2

3 PCR Barcode for the baby/baby 2
4
5
6 _____
7

8 NOTE: If not taken by birth facility please take blood for PCR.
9

10 PCR Barcode for the baby/baby 3
11
12
13 _____
14

15 Result of birth PCR for baby 1
16

- 17 Positive
18 Negative
19 Indeterminate
20 Not yet available
21

22 Result of birth PCR for baby 2
23

- 24 Positive
25 Negative
26 Indeterminate
27 Not yet available
28

29 Result of birth PCR for baby 3
30

- 31 Positive
32 Negative
33 Indeterminate
34 Not yet available
35

36 Call clinician and make a note about this.
37
38
39
40
41
42

43 Was eye ointment given to the baby 1
44

- 45 Yes
46 No
47 Don't know
48

49 Was eye ointment given to the baby 2
50

- 51 Yes
52 No
53 Don't know
54

55 Was eye ointment given to the baby 3
56

- 57 Yes
58 No
59 Don't know
60

Please specify to how many babies and which one

1 Was the baby/babies admitted to hospital following delivery

- 2
3 Yes
4 No
5

6 Please specify the details about the reason for admission, number of babies admitted and which babies

7
8
9
10
11
12 Does baby 1 have any of the following symptoms?

- 13
14 Cough
15 Runny nose
16 Eye discharge
17 Sneezing
18 None
19

20 Does baby 2 have any of the following symptoms?

- 21
22 Cough
23 Runny nose
24 Eye discharge
25 Sneezing
26 None
27

28 Does baby 3 have any of the following symptoms

- 29
30 Cough
31 Runny nose
32 Eye discharge
33 Sneezing
34 None
35

36 Is the baby/babies receiving any treatment at the moment

- 37
38 Yes
39 No
40

41 Please specify

42 Feeding methods

- 43
44
45
46
47
48 Breastfeeding
49 Formula feeding
50 Mixed
51
52
53
54
55
56
57
58
59
60

1 e
2 a
3 e
4 e
5

6 Is the baby present with the biological mother

- 7 Yes
8 No
9

10 Please specify
11
12
13
14
15

16
17 Are you currently taking any treatment

- 18 Yes
19 No
20
21

22 Please specify
23
24
25
26
27

28 Have you had sexual intercourse since delivery of your baby?

- 29 Yes
30 No
31
32

33 Do you have any of the following symptoms?

- 34 Discharge
35 Pain when urinating
36 None
37
38

39 Please specify
40
41
42
43
44

45 You have completed all the questions associated with this visit. You will now start with the process of specimen collection. You will need to collect the following specimens:

46 From the mother you will need to collect 3 vaginal swabs:

- 47 - Vaginal Swab 1 for STI testing (Storage)
48 - Vaginal Swab 2 for Microbiome (Storage)
49 - Vaginal Swab 3 for Profiling (Storage)
50
51
52
53
54

55 From the baby you need to collect:

- 56 - Nasopharyngeal swab
57
58 - Conjunctival
59
60

Select "Proceed" to capture the information associated with these specimens

Proceed

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>

1 Please confirm the barcode for the vaginal swab collected for STI testing

2
3 [baseline_arm_1][participant_pin]-PNV1

4
5 Please confirm the barcode for the vaginal swab collected for Microbiome

6
7 [baseline_arm_1][participant_pin]-PNV3

8
9
10 Please confirm the Barcode for the Vaginal Swab collected for Profiling

11
12 [baseline_arm_1][participant_pin]-PNV2

13
14 Please confirm the Barcode for the Nasopharyngeal swab (right nose) baby 1

15
16 [baseline_arm_1][participant_pin]-PNB1N1

17
18 Please confirm the Barcode for the Nasopharyngeal swab (left nose) baby 1

19
20 [baseline_arm_1][participant_pin]-PNB1N2

21
22 Please confirm the barcode for the Nasopharyngeal swab (right nose) baby 2

23
24 [baseline_arm_1][participant_pin]-PNB2N1

25
26 Please confirm the barcode for the Nasopharyngeal swab (left nose) baby 2

27
28 [baseline_arm_1][participant_pin]-PNB2N2

29
30 Please confirm the barcode for the Nasopharyngeal swab (right nose) baby 3

31
32 [baseline_arm_1][participant_pin]-PNB3N1

33
34 Please confirm the barcode for the Nasopharyngeal swab (left nose) baby 3

35
36 [baseline_arm_1][participant_pin]-PNB3N2

37
38 Please confirm the Barcode for the Nasopharyngeal swab for STI testing baby 1

39
40 [baseline_arm_1][participant_pin]-PNB1N1

41
42 Please confirm the barcode for the Conjunctival swab (right eye) baby 1

43
44 [baseline_arm_1][participant_pin]-PNB1C1

45
46 Please confirm the barcode for the Conjunctival swab (left eye) baby 1

47
48 [baseline_arm_1][participant_pin]-PNB1C2

49
50 Please confirm the barcode for the Conjunctival swab (right eye) baby 2

51
52 [baseline_arm_1][participant_pin]-PNB2C1

53
54 Please confirm the barcode for the Conjunctival swab (left eye) baby 2

55
56 [baseline_arm_1][participant_pin]-PNB2C2

1 Please confirm the barcode for the Conjunctival swab (right eye) baby 3

2
3 [baseline_arm_1][participant_pin]-PNB3C1

4
5 Please confirm the barcode for the Conjunctival swab (left eye) baby 3

6
7 [baseline_arm_1][participant_pin]-PNB3C2

8
9 Please specify the vaginal pH

10
11 _____

12
13
14 Please select which pH strips are used to measure vaginal pH

15
16 CardinalHealth pH Indicator Strips (range 3.6-6.1)

17 pH Indicator Strips pH 0-14

18 Natureland vaginal pH test (range 3.5-6.5)

19
20 Did you give the participant the study voucher?

21
22 Yes

23 No

24
25
26 You have completed capturing the Post-Natal information. Please make sure to check that you have completed all the fields.

27
28
29 Please give the participant 6 weeks immunization visit date as per schedule.

30
31 Please select "Complete" then "Save and Exit".

32
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36 Notes

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40 Additional notes

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Postnatal STI Re...

Date

Staff name

You are about to capture the results of the specimens collected during the post natal visit

Please select "Proceed" to continue

Proceed

Receive Date

Test date (Mother)

STI results from the mother

	Positive	Negative
CT	<input type="radio"/>	<input type="radio"/>
NG	<input type="radio"/>	<input type="radio"/>
TV	<input type="radio"/>	<input type="radio"/>

STI result, mother_ calc

Test date (Baby)

STI Results from Baby 1

	Positive	Negative
CT (Right Nose)	<input type="radio"/>	<input type="radio"/>
NG (Right Nose)	<input type="radio"/>	<input type="radio"/>
TV (Right Nose)	<input type="radio"/>	<input type="radio"/>
CT (Left Nose)	<input type="radio"/>	<input type="radio"/>
NG (Left Nose)	<input type="radio"/>	<input type="radio"/>
TV (Left Nose)	<input type="radio"/>	<input type="radio"/>

1	CT (Right Eye)	<input type="radio"/>	<input type="radio"/>
2	NG (Right Eye)	<input type="radio"/>	<input type="radio"/>
3			
4	TV (Right Eye)	<input type="radio"/>	<input type="radio"/>
5	CT (Left Eye)	<input type="radio"/>	<input type="radio"/>
6	NG (Left Eye)	<input type="radio"/>	<input type="radio"/>
7			
8	TV (Left Eye)	<input type="radio"/>	<input type="radio"/>
9			

STI Results from Baby 2

	Positive	Negative
12		
13	<input type="radio"/>	<input type="radio"/>
14	<input type="radio"/>	<input type="radio"/>
15		
16	<input type="radio"/>	<input type="radio"/>
17	<input type="radio"/>	<input type="radio"/>
18	<input type="radio"/>	<input type="radio"/>
19	<input type="radio"/>	<input type="radio"/>
20	<input type="radio"/>	<input type="radio"/>
21	<input type="radio"/>	<input type="radio"/>
22	<input type="radio"/>	<input type="radio"/>
23	<input type="radio"/>	<input type="radio"/>
24	<input type="radio"/>	<input type="radio"/>
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26	<input type="radio"/>	<input type="radio"/>
27	<input type="radio"/>	<input type="radio"/>
28	<input type="radio"/>	<input type="radio"/>
29	<input type="radio"/>	<input type="radio"/>

STI Results from Baby 3

	Positive	Negative
32		
33	<input type="radio"/>	<input type="radio"/>
34	<input type="radio"/>	<input type="radio"/>
35	<input type="radio"/>	<input type="radio"/>
36	<input type="radio"/>	<input type="radio"/>
37	<input type="radio"/>	<input type="radio"/>
38	<input type="radio"/>	<input type="radio"/>
39	<input type="radio"/>	<input type="radio"/>
40	<input type="radio"/>	<input type="radio"/>
41	<input type="radio"/>	<input type="radio"/>
42	<input type="radio"/>	<input type="radio"/>
43	<input type="radio"/>	<input type="radio"/>
44	<input type="radio"/>	<input type="radio"/>
45	<input type="radio"/>	<input type="radio"/>
46	<input type="radio"/>	<input type="radio"/>
47	<input type="radio"/>	<input type="radio"/>
48	<input type="radio"/>	<input type="radio"/>
49	<input type="radio"/>	<input type="radio"/>

Result of birth PCR for baby 1

- Positive
 Negative
 Indeterminate
 Not yet available

1 Result of birth PCR for baby 2

- 2
- 3 Positive
- 4 Negative
- 5 Indeterminate
- 6 Not yet available
- 7

8 Result of birth PCR for baby 3

- 9
- 10 Positive
- 11 Negative
- 12 Indeterminate
- 13 Not yet available
- 14
- 15

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17 Notes

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22 Notes

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peer review only

6 weeks / a

Staff name

Today's date

Time

Did the mother present within the specified dates below:

Start Date: [predelivery_checki_arm_1][sixweek_remind_schedpd]

Actual Date: [predelivery_checki_arm_1][sixw_im_schedpd]

End Date: [predelivery_checki_arm_1][sixw_im_close_schedpd]

- Yes
- No

You are about to administer the questions associated with 6-weeks immunization visit.

Please select "Proceed"

- Proceed

How many babies were delivered?

- 1
- 2
- 3

Was baby 1 admitted to hospital since the last study visit

- Yes
- No

Was baby 2 admitted to hospital following delivery

- Yes
- No

Was baby 3 admitted to hospital following delivery

- Yes
- No

Please specify

1 Does baby 1 have any of the following symptoms?
2

- 3 Cough
4 Runny nose
5 Eye discharge
6 Sneezing
7 None
8

9 Does baby 2 have any of the following symptoms?
10

- 11 Cough
12 Runny nose
13 Eye discharge
14 Sneezing
15 None
16

17 Does baby 3 have any of the following symptoms?
18

- 19 Cough
20 Runny nose
21 Eye discharge
22 Sneezing
23 None
24

25 Are any of the babies receiving any treatment at the moment
26
27
28
29
30

31 Feeding methods
32

- 33 Breastfeeding
34 Formula feeding
35 Mixed
36

37 Have you or the baby been to the clinic since the last visit with us?
38

- 39 Yes
40 No
41

42 What was the purpose of your visit?
43

- 44 ANC Visit
45 HIV/ART
46 STI Treatment
47 Other
48
49

50 Summary notes from the visit
51
52
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1 Do you know your current HIV status?
2

- 3 HIV negative (tested today by clinical staff)
4 HIV positive on ART
5 Known HIV positive, not on ART
6 Newly diagnosed HIV positive (tested today by clinical staff)
7 Don't know (never tested)
8 Don't know (no yet tested today)
9

10 Please conduct a HIV Rapid test and capture the result below
11

- 12 Positive
13 Negative
14

15 Please conduct a confirmatory HIV Rapid test and capture the result below
16

- 17 Positive
18 Negative
19

20 HIV PCR result of baby 1
21

- 22 Positive
23 Negative
24 No result
25

26 Please record barcode for blood and HIV PCR
27

28 _____
29
30
31

32 HIV PCR result of baby 2
33

- 34 Positive
35 Negative
36 No result
37

38 Please record barcode for blood and HIV PCR
39

40 _____
41
42

43 HIV PCR result of baby 3
44

- 45 Positive
46 Negative
47 No result
48

49 Please record barcode for blood and HIV PCR
50

51 _____
52
53

54 NOTE

55 You have collected all specimens associated with this visit. Once you select the "Proceed" option below you will be
56

57 CT: [post_natal_arm_1][sti_result_ct]
58

59 NG: [post_natal_arm_1][sti_result_ng]
60

TV: [post_natal_arm_1][sti_result_tv]

Proceed

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>

1 STI result, mother_calc
2
3
4
5

6 Does the participant report any medication allergies?
7

- 8 Yes
9 No
10
-

11 Please contact the study clinician before giving any treatment. Please specify discussed medication allergies and
12 treatment plan with the study clinician
13
14
15
16
17

18 The following treatment has been provided
19

- 20 Azithromycin 1g stat dose
21 Azithromycin 2g stat dose
22 Ceftriaxone 250mg IM injection
23 Ceftriaxone 1g IM injection
24 Metronidazole 400mg bd x 1 week
25 Metronidazole 2g stat dose
26 Clotrimazole pessary and/or cream
27 Trimethoprim/sulfamethoxazole 400/80 mg 2 tbl. bds for 5 days (bactrim)
28
-

29 Date treatment given
30
31
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33

34 Partner notification provided
35

- 36 Yes, 1
37 Yes, multiple
38 No
39
-

40 Please explain why the partner notification note was not provided?
41
42
43
44
45
46

47 The mother tested positive for an STI at the Post Natal visit. You need to collect a Nasal Pharyngeal swab for baby 1.
48 Did you manage to collect this specimen?
49

- 50 Yes
51 No
52
-

53 Please confirm the PIN for the Nasal Pharyngeal swab for baby 1.
54

- 55 [baseline_arm_1][participant_pin]-NPB1
56
57
58
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1 The mother tested positive for an STI at the Post Natal visit. You need to collect a Nasal Pharyngeal swab for baby 2.
2 Did you manage to collect this specimen?
3

- 4 Yes
5 No
6

7 Please confirm the PIN for the Nasal Pharyngeal swab for baby 2 .
8

9 [baseline_arm_1][participant_pin]-NPB2
10

11
12 The mother tested positive for an STI at the Post Natal visit. You need to collect a Nasal Pharyngeal swab for baby 3.
13 Did you manage to collect this specimen?

- 14 Yes
15 No
16

17
18 Please confirm the PIN for the Nasal Pharyngeal swab for baby 3.
19

20 [baseline_arm_1][participant_pin]-NPB3
21

22 You have completed capturing the Post-Natal information. Please make sure to check that you have completed all
23 the fields.
24

25 Please select "Unverified" then "Save and Exit".
26
27

28 Notes

29 Additional notes
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Staff Name

Today's date

Start time

Was there an adverse birth outcome?

- Yes
- No

Was there a serious adverse event

- Yes
- No

Early loss of baby

What type of early loss?

- Miscarriage
- Ectopic
- Termination of pregnancy
- Still Born

Date

Ectopic pregnancy

Date of surgery

Termination pregnancy

Date

Reviewed by site PI

- Yes
- No

Date Reviewed

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Review Notes

Name of Reviewer

Remco Peters

You have completed capturing the adverse outcomes information. Please make sure to check that you have completed all the fields.

Please select "Complete" then "Save and Exit".

Notes

Additional notes

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Staff Name

Today's Date _____

Start time _____

Presentation Outcome

Presentation outcome.

Did the participant present at the study site for this visit?

- Yes
- No

Activities Associated with ToC for Arm 1

You are about to facilitate activities associated with the 4-week ToC. You will need to execute the following:

1. Collect Specimens
2. Run a STI test
3. Conduct clinical history and behavioral questionnaire
4. Symptom screening if negative test
5. Treatment and partner referral if positive test

Proceed

Activities Associated with 32 Week Visit

You are about to facilitate activities associated with the 32 week visit. You will need to execute the following:

1. Collect Specimens
2. Run a STI test
3. Conduct clinical history and behavioral questionnaire
4. Symptom screening if negative test
5. Treatment and partner referral if positive test

Proceed

You are about to facilitate activities associated with the 32 week visit. You will need to execute the following:

1. Collect Specimens
2. Conduct clinical history and behavioral questionnaire
3. Symptom screening
4. Treatment and partner referral if positive screening

Proceed

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5 You are about to facilitate activities associated with the the 1st post natal visit. You will need to execute the
6 following:

- 8 1. Determine the presentation date (Only proceed when its 14 days after the delivery date)
- 9 2. Collect pregnancy and birth outcomes data (Discharge Summary and/or Road to Health Card)
- 10 3. Conduct mother and child clinical examination and history questionnaire
- 11 4. Specimen collection for mother and child

13 Proceed

16 Pregnancy and Birth Outcome Data

18 You are about to start with the pregnancy and birth outcome data capturing.

20 You can use the discharge summary and road to health as your data sources.

22 Select "Proceed" below to display the pregnancy and birth outcome details

23 Proceed

26 Delivery date

30 Mother and Baby Clinical Examination and History

31 You are done capturing the pregnancy and birth outcome data.

33 The next step is to capture the mother and baby clinical examination and history details.

35 Select "Proceed" below to display the questionnaire.

37 Proceed

40 Scheduling the 6 week Immunization Date

42 Schedule a 6 week immunization.

44 Use the below date assist to schedule the 6 week
45 immunization date.

47 The below field must be equal to 42.

49 Use the date field above to ensure that the current field is equal to 42.

1 Proceed

2
3 You will need to collect a single vaginal loop that will be used to prepare two slides. Once collected you will need to
4 prepare the slides for storage.

5 Proceed

6
7
8 Date of collection of vaginal loops

9
10
11 _____

12
13
14

15 Confirm the pin associated with the first vaginal loop that will be used for

16 [baseline_arm_1][participant_pin]-FL1

17
18
19 Confirm the PIN associated with the second vaginal loop that will be used for

20 [baseline_arm_1][participant_pin]-FL2

21 22 23 24 Storage of Loops

25
26 You have collected both slides. Before commencing with the rest of the specimens, please make sure to do the
27 following:

- 28
29 1. Slides are individually packed in their own package
30 2. Record PIN on outside of package
31 3. Complete the lab CRF with matching PINs and test instructions

32
33 Proceed

34 35 36 Vaginal Swab Collection

37
38 You will now collect 3 vaginal swabs. They will be used as follows:

- 39 1. STI testing (1st Specimen)
40 2. Profiling (2nd Specimen)
41 3. Microbiome (3rd Specimen)

42
43 Proceed

44
45
46

47
48 Date of specimen collection for vaginal swabs

49
50
51 _____

52
53 Confirm the PIN associated with the first vaginal swab

54 [baseline_arm_1][participant_pin]-FV1



2
3 Confirm the PIN associated with the second vaginal swab

4 [baseline_arm_1][participant_pin]-FV2

6
7 Confirm the PIN associated with the third vaginal swab

8
9 [baseline_arm_1][participant_pin]-FV3

11 12 Nasopharyngeal Swab Collection

13 You are about to collect the Nasopharyngeal swab on the Baby.

14
15 Collect the specimen and confirm the PIN below.

16
17 [baseline_arm_1][participant_pin]-NS1

19 20 GeneXpert Testing for the First Specimen

21 You will now start with the testing of the first vaginal swab specimen.

22
23 Follow the below steps:

- 24 1. Ensure that the GeneXpert Machine is switched-on. Perform a quick quality check on the machine.
- 25 2. Load the specimen and run the machine.
- 26 3. Conduct Clinical History and Behavioural Questionnaire

27
28
29 Select "Start Test" when ready to run the test.

30
31 Start Test

32 33 34 Clinical History and Behavioural Questionnaire

35 You have started running the STI test.

36
37 Conduct clinical history and behavioural questionnaire. Select "Proceed" to display the questionnaire

38
39 Proceed

40
41
42 How often have you had sex since the last time we saw you?

- 43
44 0
- 45 1 to 5 times a week
- 46 More than 5 times a week

47 48 49 STI Results

	Positive	Negative
51 NG	<input type="radio"/>	<input type="radio"/>
52 TV	<input type="radio"/>	<input type="radio"/>
53 CT	<input type="radio"/>	<input type="radio"/>

1 The participant tested positive for an STI.

2
3 The next step is to administer treatment with the participant.

4
5 Select "Proceed" to display treatment options.

6
7 Proceed

8
9
10

11
12 The next step is to screen the patient for STI symptoms

13
14 Is the participant symptomatic?

15 Yes

16 No

17
18
19 The participant screened positive for at least a single STI symptom

20
21 The next step is to administer treatment with the participant.

22
23 Select "Proceed" to display treatment options.

24
25 Proceed

26 27 Treatment and Partner Notification

28
29 Select the treatment regimen you administered to the participant

30
31 Azithromycin

32 Doxycyclin

33 Ceftriaxone

34 Metronidazole

35
36 Did you administer partner notification treatment?

37
38 Yes

39 No

40 41 42 Storage Processes

43
44 You have collected all required specimens.

45 You can now prepare the specimens for storage, follow the below steps:

46 1. Ensure that each specimen has a complete Lab CRF

47 2. Pack the Lab CRFs in the specimen container

48 3. Ensure that the Lab CRF is complete and specimens are stored according to the storage requirements.

49
50 Select "Confirm" after perform the above specimen procedures.

51
52 Confirm

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Additional notes

For peer review only

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Staff member

Date

Participant ID: [baseline_arm_1][participant_pin_verify]

TERMINATION DETAILS

Date of termination

Study Time-Point

- BASELINE
- TOC
- 32 WEEKS
- POST-NATAL VISIT

Reason for termination

- End of study (study completed)
- death (participant)
- Participant refused further participation
- Participant unable to adhere to visit schedule
- Participant relocated, no follow-up planned
- Investigator decision
- unable to contact the participant
- Participant not eligible for enrollment
- Invalid ID due to duplicate screening/enrollment
- Other
- Early study closure
- End of study (adverse outcome)

Specify refusal reason/ Investigator reason

Other, Specify

General Comments

For peer review only



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Staff name

Please capture date of visit

Please summarize the purpose of the visit

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Safety Protocol

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Today's date

Time

Staff

Safety Protocol Issue

- Social Harm
- Protocol Violation
- Unanticipated Problem

Date Reported

Notes

For peer review only

STI a a a a a a g

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Staff Member Name

Date

SECTION B: QUALITY ASSURANCE

Forms Received from the Field

- BQ Consent form
- Study Note
- Proof of Reimbursement
- Enrolment Log
- Expert Baseline: CT/NG
- Expert Baseline: TV
- Expert Postnatal: CT/NG
- Expert Postnatal: TV
- NHLS: CD4 Count
- NHLS: Syphilis Test
- NHLS: Viral Load
- NHLS: Baby HIV PCR
- OTHER
(Select all that you received)

Other - Specify the other form(s) received

QUALITY ASSURANCE: Phase 2A

Get all the participant's enrolment source documents and perform a comprehensive QC on all the source documents. After the QC is done, mark each document as "checked, properly completed" if you have no query opened on the source document.

IN CASES WHERE A QUERY IS OPENED. PLEASE CONTACT THE RESPONSIBLE DATA COLLECTOR IMMEDIATELY

Please note that you also accept receipt of all source documents by checking them below.

	Checked, Properly Completed	Not completed, Returned to the RA
Consent Form	<input type="radio"/>	<input type="radio"/>
Study Note	<input type="radio"/>	<input type="radio"/>
Proof of Reimbursement	<input type="radio"/>	<input type="radio"/>
Enrolment Log	<input type="radio"/>	<input type="radio"/>
Expert Baseline: CT/NG	<input type="radio"/>	<input type="radio"/>

1	Expert Baseline: TV	<input type="radio"/>	<input type="radio"/>
2	Expert Postnatal: CT/NG	<input type="radio"/>	<input type="radio"/>
3			
4	Expert Postnatal: TV	<input type="radio"/>	<input type="radio"/>
5	NHLS: CD4 Count	<input type="radio"/>	<input type="radio"/>
6	NHLS: Syphilis Test	<input type="radio"/>	<input type="radio"/>
7			
8	NHLS: Viral Load	<input type="radio"/>	<input type="radio"/>
9	NHLS: Baby HIV PCR	<input type="radio"/>	<input type="radio"/>
10			
11	[forms_received_oth]	<input type="radio"/>	<input type="radio"/>

13
14 Skip

17 Electronic Data QC

19 You are supposed to go through each electronic data tool and ensure the following:

- 22 1. Each Tracking Field has a data point.
- 23 2. The data is consistent
- 24 3. The data is verified with source documents

28 After doing the above inspection. You marked the forms as complete and locked the form.

31 Once all the forms are checked and properly completed.

	Checked and Completed Properly	Query Opened
33 1, Baseline: Screening and	<input type="radio"/>	<input type="radio"/>
34 Enrolment		
35		
36 2, Baseline: Baseline data	<input type="radio"/>	<input type="radio"/>
37 3, STI: Physical Exam	<input type="radio"/>	<input type="radio"/>
38 4, STI: Specimen and	<input type="radio"/>	<input type="radio"/>
39 Randomization		
40		
41 5, STI: Scheduling	<input type="radio"/>	<input type="radio"/>
42 6, STI: TOC Visit Activities	<input type="radio"/>	<input type="radio"/>
43 7, STI: Calling Reminder_2	<input type="radio"/>	<input type="radio"/>
44 8,STI: Scheduling post Delivery	<input type="radio"/>	<input type="radio"/>
45 activities		
46		
47 9, Birth Register data	<input type="radio"/>	<input type="radio"/>
48 10, Post Natal Visit Activities	<input type="radio"/>	<input type="radio"/>
49 11, 6 week Immunization Visit	<input type="radio"/>	<input type="radio"/>
50 Activities		
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Date of QC

COMMENTS

Comments

SAVING INSTRUCTION

MARK THIS FORM AS COMPLET ONCE VERIFIED AND LOCK IT.

SELECT SAVE AND EXIT FORM.

Proceed to QC other source documents.

For peer review only

Scheduling 2

Scheduling of Dates Associated with [randomization].

NOTE

You are about to schedule dates associated with [randomization] participants.

Please select "Proceed".

Proceed

Scheduling of Dates Associated

NOTE:

You are about to schedule dates associated with microbiome participants.

Please select "proceed"

Proceed

Scheduling Dates for 3-Week ToC

NOTE: The participant tested positive and therefore we need to schedule a date, exactly 3-weeks from today to conduct a test-of-cure.

Scheduling the 3-week ToC

NOTE:

Please schedule a date, 3 weeks from today treatment given. Please use the calculator assistance to ensure that you schedule a date exactly 21 days from today.

Calculator Assist

The number here must be equal to 21

ERROR

The field does not equal to 21, please change it

Have you handed the TOC date to the participant?

Yes

No

Scheduling Dates Associated with ToC Reminder

1 Schedule date for REMINDER of 3-week ToC visit
2
3
4 _____
5

6 Calculator Assist for scheduling ToC reminder date
7

8 The reminder phone call will be made 18 days following the treatment date. The number of days need to equal to 18.
9
10
11 _____
12

13 ERROR

14 You did not enter the date correctly. The number should equal to 18. Please redo the date.
15
16

17
18
19 Scheduling Dates Associated with 3-Week ToC Missed Visit Date
20
21
22

23
24
25 NOTE:

26 You have successfully scheduled the reminder date.

27
28 Please select "proceed" to schedule the missed visit date for the 3 week ToC visit.

29
30 Proceed
31

32 Schedule the date for the MISSED VISIT of the ToC visit.
33

34 This date should be 3 weeks after the date on which the participant received their test result.
35
36 _____
37
38

39 Calculator Assist for scheduling 3-week ToC Missed Visit
40

41 The participant's time period allowed for attending a ToC will start 3 weeks after they received their result and will
42 close 3 weeks after the date they received their result.
43

44 The number here must show 35
45
46
47
48
49
50
51 _____
52

53 ERROR

54 You did not enter the date correctly. The number should equal to 35. Please redo the date.
55

56 NOTE:

57 You have successfully scheduled the 3-week ToC close date

58
59 Please select "proceed" to start scheduling the next visit dates

60 Proceed

1 Dates Associated with reminder for the 28 Week call

2
3
4
5
6 NOTE:
7 You are about to schedule dates for the call reminder at 28 weeks.

8 Please select "Proceed".

9
10 Proceed

11
12
13 Note:
14 Schedule the date for the 28 week call. We will contact each participant to ask the date for their 30 weeks clinic visit
15 is.

16
17
18
19
20 Calculation assist for scheduling the 32-week reminder date.

21 This number must equal to 196

22
23
24
25
26
27 Days to call reminder

28
29
30
31
32 ERROR

33 The number you have entered does not match 196. Please select a different date so that the number equals to 196.

34
35 Scheduling the Dates Associated with the 32 Week Gestational Visit

36
37
38
39 NOTE
40 You are about the start scheduling dates associated with the 32 week visit. You will need to schedule the following
41 associated dates:

- 42
43 1. Week 32 date
44 2. Week 32 reminder date
45 3. Week 32 missed visit date

46
47 Select "Proceed" to start scheduling

48
49 Proceed

50
51 Schedule the date for the 32 week gestational age, visit

52
53
54 Note to RA: please make sure that this date does not fall on Friday, weekend, and public holidays.

55
56
57
58
59 Days Difference (the difference between 32 weeks & Gestational age)

1 Calculate assist for 32 week visit

2
3 The number here must equal to [gest_week_calc]

4
5
6
7
8 _____

10 Match

11 _____

13 The date you have entered does not meet the 93 day criteria. Does the intended or original date fall on a Friday weekend or public holiday?

- 14
15
16 Yes
17 No

18
19
20 **ERROR**

21 The numbers you have entered does not match. Please select a different date so that the numbers match.

22
23 Dates Associated with reminder for the 32 Week Gestational Age Visit

24
25
26
27 **NOTE:**

28 You have successfully scheduled the 32 week date.

29
30 We will need to contact the participant at least 7 days before the scheduled visit to remind them.

31
32 Select "Proceed" to schedule the reminder date for the 32 week visit.

33
34 Proceed

35
36 **Note:**
37 Schedule the date for the 32 week reminder. We will contact each participant starting 7 days prior to their 32-week gestation date. That means the date scheduled here should be 7 days earlier then the scheduled date for the 32-week visit.

38
39
40
41
42 _____

44 Calculation assist for scheduling the 32-week reminder date.

45
46 This number must equal to 7

47
48
49 _____

51 **ERROR**

52 The number you have entered does not match 7. Please select a different date so that the number equals to 7

1
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3
4 **Proceed** to schedule the 32 week missed visit date.
5
6
7

8 **NOTE:**
9 You have successfully scheduled the 32 week reminder date.
10
11

12 Select "Proceed" to schedule the 32 week missed visit date.
13
14

15
16 Proceed
17

18 Schedule the date for the 32 week missed visit date.
19

20 Note: Participants will have 3 weeks (21 days) to present for their 32 week visit date after which the visit will be
21 closed out.
22
23

24 _____
25
26 Calculation Assist for scheduling the 32-Week missed visit date.
27

28 This number must equal to 21
29
30

31 _____
32
33 **ERROR**
34 The number you have entered does not match 21. Please select a different date so that the number equals to 21
35
36

37
38
39
40 **Estimated Delivery Date**
41
42
43
44

45 You are about to schedule the Estimated Delivery Date.
46

47 Please select "proceed"
48

49 Proceed
50

51 **Estimated Delivery Date**
52
53

54 _____
55
56 Days difference between estimated date of delivery and gestational age
57
58

59 _____
60

1 Calculation Assist for scheduling the Estimated Date for Delivery date.

3 This number must equal to [edod_calc]

8 Match

12 ERROR

13 The number you have entered does not match. Please select a different date so that the numbers match

15 You have completed all the scheduling dates.

17 Please check that all dates entered comply with the "calculation assistance". Once this has been done you can select "Complete" and "Save & Exit"

22 NOTES

24 Notes box

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Name

Time

For peer review only

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Please specify the updated delivery date

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BMJ Open

Genital tract infections, the vaginal microbiome and gestational age at birth among pregnant women in South Africa: a cohort study protocol

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2023-081562.R1
Article Type:	Protocol
Date Submitted by the Author:	28-Nov-2023
Complete List of Authors:	Gigi, Ranjana ; University of Bern, Institute of Social and Preventive Medicine; Foundation for Professional Development, Research Unit Mdingi, Mandisa ; Foundation for Professional Development, Research Unit Jung, Hyunsul; University of Pretoria, Medical Microbiology Claassen-Weitz, Shantelle; University of Cape Town, Department of Pathology Bütikofer, Lukas; University of Bern, CTU Bern, Department of Clinical Research Klausner, Jeffrey D.; University of Southern California, Department of Population and Public Health Sciences, Keck School of Medicine Muzny, Christina; University of Alabama at Birmingham, Division of Infectious Diseases Taylor, Christopher; Louisiana State University Health Sciences Center, Department of Microbiology, Immunology, and Parasitology van de Wiggert, Janneke H.H.M.; Utrecht University, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht Peters, Remco; Foundation for Professional Development, Research Unit; University of Pretoria, Department of Medical Microbiology Low, Nicola; University of Bern, Institute of Social and Preventive Medicine
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Obstetrics and gynaecology, Infectious diseases, HIV/AIDS
Keywords:	EPIDEMIOLOGIC STUDIES, Sexually Transmitted Disease, Diagnostic microbiology < INFECTIOUS DISEASES, Maternal medicine < OBSTETRICS, Follow-Up Studies

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Manuscripts

Genital tract infections, the vaginal microbiome and gestational age at birth among pregnant women in South Africa: a cohort study protocol

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Word counts: Abstract, 294; main text, 3736; 2 figures, 1 supplemental online file

Keywords

Pregnancy complications, premature birth, reproductive tract infections, sexually transmitted infections, microbiota, South Africa

Abstract

Introduction Preterm birth complications are the most common cause of death in children under 5 years. The presence of multiple microorganisms and genital tract inflammation could be the common mechanism driving early onset of labour. South Africa has high levels of preterm birth, genital tract infections and HIV infection among pregnant women. We plan to investigate associations between the presence of multiple lower genital tract microorganisms in pregnancy and gestational age at birth.

Methods and analysis This cohort study enrolls around 600 pregnant women at one public health care facility in East London, South Africa. Eligible women are ≥ 18 years and at < 27 weeks of gestation, confirmed by ultrasound. At enrolment and 30-34 weeks of pregnancy, participants receive on-site tests for *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, with treatment if test results are positive. At these visits, additional vaginal specimens are taken for: PCR detection and quantification of *Trichomonas vaginalis*, *Candida* species, *Mycoplasma genitalium*, *M. hominis*, *Ureaplasma urealyticum* and *U. parvum*; microscopy and Nugent scoring; and for 16S ribosomal ribonucleic acid gene sequencing and quantification. Pregnancy outcomes are collected from a post-natal visit and birth registers. The primary outcome is gestational age at birth. Statistical analyses will explore associations between specific microorganisms and gestational age at birth. To explore the association with the quantity of microorganisms, we will construct an index of microorganism load and use mixed effects regression models and classification and regression tree analysis to examine which combinations of microorganisms contribute to earlier gestational age at birth.

Ethics and dissemination This protocol has approvals from the University of Cape Town Research Ethics Committee and the Canton of Bern Ethics Committee. Results from this study will be uploaded to preprint servers, submitted to open access peer-reviewed journals and presented at regional and international conferences.

Registration ClinicalTrials.gov Identifier: NCT06131749

Article summary, strengths and limitations of the study

- This cohort study takes a holistic approach, investigating both the presence and quantity of multiple lower genital tract microorganisms, including vaginal microbiota, in pregnancy and their associations with gestational age at birth.
- The study is set in a location where the prevalence of genital tract infections and adverse pregnancy outcomes are high, uses ultrasound scans to assess gestational age at enrolment accurately, and state-of-the-art molecular diagnostic methods.
- The study setting is limited to one research site, which may affect the generalisability of the findings.
- The use of gestational age at birth as a continuous outcome, instead of preterm birth as a dichotomous outcome, might limit comparability with other studies, but we will also examine the binary outcome preterm birth in secondary analyses.

Introduction

Preterm birth complications are the most common cause of death in children under 5 years.¹ Close to one million infants die every year because they are born preterm (before 37 completed weeks of gestation), mainly from infectious, respiratory and neurological complications, and those that survive can experience long-term morbidity.[1], [2] South Africa has a high incidence of preterm birth at around 10%.[3] around 30% of women have one or more curable sexually transmitted infections during pregnancy [4], [5] and about 30% of pregnant women are living with HIV. [6]

Microbial colonisation or infection during pregnancy, in the lower or upper genital tract, have been reported to predispose to preterm birth, as do anatomical, biochemical, endocrinological, immunological, nutritional, environmental and psychosocial factors.[7], [8] The presence of microorganisms may contribute to early onset of labour directly, through presumed ascension from the lower to the upper genital tract, or indirectly, through a pathway of inflammatory response, or a combination of both.[7], [9] Inflammation may be the common pathway, even if infection has not reached the amniotic cavity. [10]

Much of the research reporting on the role of sexually transmitted infections in pregnancy and preterm birth has focused on single infections, such as *Chlamydia trachomatis*, [11] *Neisseria gonorrhoeae*, [12] and *Trichomonas vaginalis*. [13] *Mycoplasma genitalium* is the most recently recognised sexually transmitted infection and, whilst an association with preterm birth has been reported, there are few studies with prospective data collection. [14] Bacterial vaginosis is the most common vaginal microbiota dysbiosis and is associated with adverse pregnancy outcomes, either alone, or in combination with other sexually transmitted infections. [15-17] Associations with adverse birth outcomes have also been observed for other genital mycoplasmas, *M. hominis*, *Ureaplasma urealyticum* and *U. parvum*. [18] For individual sexually transmitted infections, bacterial vaginosis and colonisation by other genital mycoplasmas, summary odds ratios for the association with adverse birth outcomes in meta-analyses of univariable data are generally around 1.3 to 2.0. [11-14, 16, 18] *Candida* spp. have not been found to be associated with preterm birth, but an association with more inflammatory, symptomatic yeast infection cannot be ruled out. [19] Most studies about these microorganisms do not present analyses that examine the role of co-occurrence or control for confounding factors, so the presence or strength of the causal association cannot be assessed. [20] It is also important to include women living with HIV, amongst whom there are fewer studies about associations between genital tract infections and adverse birth outcomes than amongst women without HIV infection. [21-22]

The importance of the quantity of different microorganisms as a driver of preterm birth has not been extensively studied, [23-25] but might be as, or more, relevant than their presence. [23] Together with inflammation or immune activation in the genital tract during pregnancy, organism load could be an important driver of the early onset of labour and preterm birth.[8,23,24,26,27] This calls for a holistic approach to research studies, which combines information about the presence of different microorganisms, the quantified load and the microbiome, sociodemographic factors and HIV amongst women living with infection, most of whom are receiving antiretroviral therapy. The overall aim of this study is to investigate associations between the presence of lower genital tract microorganisms in pregnancy and preterm birth and other adverse pregnancy outcomes. This will be achieved through three objectives to explore: (1) the association between the presence of specific lower genital tract microorganisms and gestational age at birth (primary outcome), as well as

1
2
3 secondary adverse pregnancy outcomes; (2) the association between quantified load of vaginal and
4 sexually transmitted microorganisms and gestational age at birth (primary outcome) as well as
5 secondary adverse pregnancy outcomes; and (3) the combinations of microorganisms that are most
6 strongly associated with earlier gestational age at birth.
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8
9

10 **Methods and analysis**

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14

15 **STUDY DESIGN AND SETTING**

16 This prospective closed cohort study follows women enrolled during pregnancy until after they give
17 birth (Figure 1). The study is conducted at the antenatal clinic of one primary health care facility in
18 Buffalo City Metropolitan Municipality, Eastern Cape Province, South Africa. This cohort study is part
19 of a larger project, called Philani Ndiphile (meaning 'be healthy and I will be healthy' in isiXhosa),
20 which includes a randomised implementation-effectiveness trial of screening strategies for sexually
21 transmitted infections in pregnancy [28] and a case-control study about persistent *C. trachomatis*
22 infection.
23
24
25

26 **PARTICIPANTS**

27 Inclusion criteria: Pregnant women aged 18 years or older, who live in Buffalo City Metropolitan
28 Municipality, intend to deliver in the same municipality and provide written informed consent to
29 take part in the study. The eligible gestational age at enrolment, confirmed by ultrasound, was
30 below 20 weeks at the start of the study in March 2021 and was increased to 27 weeks in September
31 2021 to increase enrolment and to align with another trial. [29]
32
33

34 Exclusion criteria: Participation in any other research study or inability to understand and speak a
35 local language (English, Afrikaans, or isiXhosa).
36
37

38 **Figure 1** Study visits and specimen collection

39 Abbreviations: CT, *Chlamydia trachomatis*; NG, *Neisseria gonorrhoeae*
40
41

42 **ENROLMENT**

43 A trained study field worker approaches all pregnant women attending an antenatal care visit at the
44 clinic and individually informs them about the study. If a potential participant shows interest in the
45 study, the study field worker checks for eligibility. The date of the last menstrual period is used
46 initially to estimate gestational age. If all eligibility criteria are met, a study field worker obtains
47 written informed consent from the participant.
48
49

50 **STUDY PROCEDURES AND VISITS**

51 At the enrolment visit, study field workers administer a questionnaire to record socio-demographic,
52 behavioural and clinical information in an online Research Electronic Data Capture software
53 (REDCap) [30] database. The study nurse examines the woman, according to the South African
54 government standard of care. [31] As an additional procedure, a study nurse with training in
55 obstetric ultrasound performs an abdominal ultrasound to estimate the gestational age. If this is
56 later than the eligibility criterion, the participant is excluded from any further study activity. A study
57 nurse collects vaginal samples (Figure 1) for on-site testing for *C. trachomatis* and *N. gonorrhoeae*
58
59
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1
2
3 using the Xpert CT/NG assay on the Gene Xpert platform (Cepheid, Sunnyvale, CA, USA) and for
4 further off-site laboratory testing (see 'Specimen collection and analysis').
5

6 If the test result for *C. trachomatis* or *N. gonorrhoeae* is positive, the woman receives immediate
7 antibiotic treatment if still on site or is contacted by telephone and asked to return to the clinic for
8 treatment. Antibiotic treatments are first-line regimens according to South African guidelines: for *C.*
9 *trachomatis*, 1g oral azithromycin and for *N. gonorrhoeae*, 500mg intramuscular ceftriaxone (250mg
10 until South African treatment guidelines for sexually transmitted infections changed in December
11 2022). [32] Women with vaginal discharge syndrome but with negative Xpert test results for *C.*
12 *trachomatis* and *N. gonorrhoeae* receive empirical treatment for trichomoniasis with metronidazole
13 400 mg twice a day for 7 days. The study nurse gives advice to women with *C. trachomatis* or *N.*
14 *gonorrhoeae* on safe disclosure of her diagnosis to her partner(s) and gives her a notification slip(s)
15 to request her partner(s) to attend a clinic for treatment.
16
17
18

19 A follow-up visit at 30-34 weeks (third trimester visit) is scheduled at which clinical and obstetric
20 information, as well as the same vaginal specimens, are collected and treatment given, if indicated.
21

22 A post-natal visit is scheduled for 3-6 days after giving birth, according to the South African
23 government standard. [31] A study nurse collects information about the birth outcome and perinatal
24 period through a questionnaire with the mother, a patient-held medical record of the baby (the
25 Road to Health card) and/or the birth register from the public birth clinics within the study area. If
26 the participant does not attend the post-natal visit, study staff telephone her to ask her to return to
27 the clinic. If the participant is not able to return to the clinic, the study physician collects the
28 information by telephone or from the birth register.
29
30
31

32 **OUTCOMES**

33 The primary outcome is gestational age at birth, measured in days, based on the ultrasound
34 assessment at the enrolment visit. Secondary outcomes are preterm birth (<37 completed weeks of
35 gestation), low birth weight (birth weight <2500g), miscarriage (dead foetus delivered before 28
36 completed weeks of pregnancy or with birth weight below 1000g) and stillbirth (dead foetus
37 delivered at or after 28 completed weeks of pregnancy or with birth weight above 1000g). [33,34]
38 We chose gestational age at birth as the primary outcome because, whilst the cut-off of 37 weeks is
39 the standard definition of preterm birth, dichotomisation of a continuous variable results in a loss of
40 statistical power. [35]
41
42
43
44

45 **SPECIMEN COLLECTION AND ANALYSIS**

46 **DATA SOURCES AND VARIABLES**

47 The source data are case report forms recording questionnaire data for the enrolment, third
48 trimester and post-natal visits and forms for laboratory and specimen results, which are stored in
49 REDCap, a secure web-based database [30] (online supplemental file), hosted by the Foundation for
50 Professional Development, Pretoria, South Africa.
51
52
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54

55 **SPECIMEN COLLECTION**

56 At the enrolment and the third trimester visits, a study nurse collects two vaginal smears using
57 inoculation loops and air-dries them on glass slides. She then collects vaginal specimens by inserting
58 swabs into the vagina up to a mark at 4 cm and rotating around the vaginal wall. Five swabs are
59 collected in the following order: one Cepheid GeneXpert Xpert Vaginal/Endocervical Swab in a tube
60

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3 with Xpert Swab Transport Reagent (Cepheid, Sunnyvale, CA, USA); two Qiagen digene Female
4 Swabs in a single tube with digene Specimen Transport Medium (Qiagen, Hilden, Germany); and two
5 dry FLOQswabs (COPAN, Brescia, Italy) each in a separate sterile tube (Figure 1).
6
7

8 TRANSPORT AND STORAGE OF SPECIMENS

9 Vaginal smear glass slides are stored and transported in plastic slide carriers at room temperature.
10 All vaginal swabs are initially stored at the clinic in a refrigerator (2-8°C with daily temperature
11 checks). All vaginal swabs, except the Xpert swab, which is tested on-site, are transported on ice
12 packs once a week by overnight road courier, to the laboratory at the Department of Medical
13 Microbiology, University of Pretoria, where they are also stored in a refrigerator until DNA
14 extraction.
15
16

17 MICROBIOLOGICAL ANALYSES

18 The Xpert vaginal swabs are tested on-site using the Xpert CT/NG assay (Cepheid, Sunnyvale, CA,
19 USA) to detect *C. trachomatis* and *N. gonorrhoeae*, as per manufacturer's instructions. At the
20 University of Pretoria, air-dried vaginal smears are heat-fixed and Gram-stained. [36] Two qualified
21 people record the Nugent scores (0-3: normal; 4-6: intermediate; 7-10: bacterial vaginosis) and the
22 presence of yeasts. [37] In case of discrepancies a third person assesses the slide and consensus is
23 reached by discussion. At the University of Pretoria, one vaginal FLOQswab is used for PCRs. The
24 genomic DNA is extracted using the High Pure PCR Template Preparation Kit (Roche Diagnostics
25 GmbH, Mannheim, Germany) as per manufacturer's instructions. Real-time PCR assays are then
26 performed using the LightCycler 480 Probes Master Kit (Roche Diagnostics GmbH, Mannheim,
27 Germany) on the LightCycler 480 II instrument (Roche Diagnostics GmbH, Mannheim, Germany).
28 Previously published primer and hydrolysis probe sequences and cycling conditions are used for
29 detection and quantification of *M. genitalium*, [38] *M. hominis*, [39] *U. parvum*, [40] *U. Urealyticum*,
30 [40] *T. vaginalis* [41] and *Candida* spp. [42,43] The load for each assayed microorganism detected in
31 vaginal swab specimens by real-time PCR or GeneXpert is obtained from the cycle threshold value.
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38 VAGINAL MICROBIOME LABORATORY ANALYSES

39 The vaginal swabs stored in Qiagen digene Specimen Transport Medium will be used for DNA
40 extraction and subsequent 16S ribosomal ribonucleic acid (rRNA) amplicon sequencing targeting the
41 V3-V4 hypervariable regions for vaginal microbiota analyses at the Division of Medical Microbiology,
42 University of Cape Town.
43

44 A commercial DNA extraction kit will be used and a bead-beating step included. [44] A DNA isolation
45 control will be prepared from an unused vaginal swab specimen during this process. Two PCR rounds
46 will be conducted to prepare amplicon libraries.[45] The aim of the first PCR round is to amplify 16S
47 rRNA gene V3-V4 regions, using the 319F 5'-ACTCCTACGGGAGGCAGCAG-3' forward primer and 806R
48 5'-GGACTACHVGGGTWTCTAAT-3' reverse primer. The aim of the second PCR round is to barcode the
49 V3-V4 amplicons by a dual-index approach, permitting multiplexing of up to 384 samples (including
50 controls). Amplicon concentrations for all sample libraries are measured and normalised to form a
51 mixed loading library. The libraries will be sequenced on an Illumina MiSeq instrument (Illumina, San
52 Diego, CA, USA), 2x300bp. To quantify the number of 16S rDNA copies per swab, a quantitative PCR
53 using the same forward and reverse primers as described above will be used. Samples from
54 enrolment and third trimester visits from the same woman will be processed in the same run.
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VAGINAL MICROBIOTA BIOINFORMATICS

Raw sequencing reads will be processed using an established bioinformatics pipeline.[46] Taxonomic assignment of amplicon sequence variants (ASVs) will be done in DADA2[47] with SILVA[48] as the reference database. Vaginal microbiome composition data will be visualised in heatmaps and diagrams. For each vaginal sample, we will calculate diversity measures (alpha diversity), relative abundances and estimated concentrations of key vaginal bacteria and bacterial groups, as described. [46] We will use the entire sequencing dataset to design vaginal microbiota types by hierarchical clustering, and each sample will be assigned to one vaginal microbiota type.

SAMPLE SIZE CALCULATION

The sample size has been calculated for objective 1, with a univariable comparison between the presence of a genital tract microorganism in the mother and gestational age at birth. Figure 2 shows that, for any vaginal or sexually transmitted microorganism, or vaginal microbiota type that has a prevalence of 10% or more among all enrolled women, about 500-600 patients provides adequate power (80%) to detect a one-week difference (with standard deviation 2) in mean gestational age between the two groups using Student's t-test. Specifying an alpha of 0.83% allows for multiple hypothesis testing (6 hypotheses, using a Bonferroni correction). We enrol around 600 women and aim to have complete follow-up and outcome data on at least 550 women.

Figure 2 Sample size requirements at different levels of exposure prevalence with power of 80% and alpha 0.83% based on Student's t-test.

Legend: panel A, standard deviation 1.5; panel B, standard deviation 2.0. The curves for % exposed are symmetrical around a prevalence of 50%, i.e., curve for 10% exposed is same as that for 90% exposed.

STUDY TIMELINE

Enrolment began on 28 March 2021, with an estimated date for reaching the target sample size in August 2023. Follow-up of all participants until the post-natal visit is expected to be completed by March 2024.

STATISTICAL ANALYSIS

This description gives an overview of the statistical methods for each objective. A detailed statistical analysis plan will be published separately and made publicly available.

We will describe the numbers of women enrolled and available at each follow-up visit in a flow chart. We will present descriptive tables of socio-demographic, behavioural and clinical characteristics and compare women with complete follow-up with those lost to follow-up.

OBJECTIVE 1) ASSOCIATION BETWEEN SPECIFIED EXPOSURES AND PREGNANCY OUTCOMES

1a. We will examine a primary set of microorganisms as exposures, detected at either enrolment or at the third trimester visit: *M. genitalium*, *M. hominis*, *U. urealyticum*, *U. parvum*, *T. vaginalis* and *Candida* spp. are the microorganisms for which women did not receive diagnostic tests and treatment during study visits. We will use the mean and standard deviation for the continuous outcome (gestational age) and absolute and relative frequencies for the binary outcomes (all secondary outcomes). Gestational age at birth for each exposure will be compared using Student's t-test and a mean difference with 95% confidence intervals (continuous outcome) and Fisher's exact test and a risk difference with 95% confidence intervals (binary outcomes).

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2
3 To control for confounding, multivariable regression models will be fitted to all outcomes with a set
4 of pre-specified potential confounders (age, educational level, alcohol consumption, HIV infection,
5 prior preterm birth) for all organisms. For analyses of *M. genitalium*, *T. vaginalis*, and *Candida* spp.,
6 we will also control for bacterial vaginosis (Nugent score 7-10). The other genital mycoplasmas can
7 be identified from 16S rRNA amplicon sequencing in women with vaginal dysbiosis, so are
8 sometimes considered part of bacterial vaginosis. For these organisms, we will conduct descriptive
9 analyses, stratifying by the presence of bacterial vaginosis. For continuous confounders a linear
10 relationship will be assumed by default but transformations (e.g., log) or more flexible approaches
11 (e.g., splines or fractional polynomials) will be considered if there is evidence for non-linearity. For
12 the continuous outcome we will use linear mixed effects regression models (including data from
13 either visit and the participant as random effect) and report the result as mean difference with 95%
14 confidence intervals. For the binary outcome we will use logistic mixed-effects regression and report
15 the result as odds ratios with 95% confidence intervals.

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19 1b. Comparisons for associations with timing of detection, other microorganism exposures and birth
20 outcomes will be considered secondary analyses. Associations between vaginal microbiota
21 composition and pregnancy outcomes will be assessed. We will use compositional multivariable
22 analysis methods to identify bacterial taxa that are differentially abundant between binary
23 pregnancy outcome groups at the level of individual taxon relative abundances. We will use mixed
24 effects models (with the individual participant as the random effect and including data from both
25 visits) to assess associations between continuous and binary pregnancy outcome and the following
26 fixed effects derived from the vaginal microbiota data: alpha diversity, vaginal microbiota types and
27 absolute abundances of predefined bacterial groups. [46] These models will be adjusted for
28 confounding as described in the previous paragraph.

32 33 OBJECTIVE 2) ASSOCIATION BETWEEN QUANTIFIED MICROORGANISM LOAD AND PREGNANCY 34 OUTCOMES

35 We will investigate the hypothesis that the quantity of microorganisms with inflammatory potential
36 is associated with gestational age at birth. For this, we will analyse the vaginal microbiota data
37 jointly with sexually transmitted infections and *Candida* spp. diagnostic test results during pregnancy
38 (these will be considered as additional covariates in the above-mentioned regression models). We
39 will develop a 'vaginal inflammation index', based on quantification of the vaginal microbiota and
40 their inflammatory potential [49] and of yeasts. This vaginal inflammation index will also be analysed
41 as a fixed effect in mixed effects models with pregnancy outcomes as the outcomes; these models
42 will not include any of the infection parameters that were used to design the index.

43 44 45 46 47 OBJECTIVE 3) CLASSIFICATION AND REGRESSION TREE ANALYSIS FOR THE PRIMARY OUTCOME

48 We will conduct exploratory analyses to examine the combination of microorganisms that best
49 predicts earlier gestational age at birth using classification and regression tree analysis. [50] This
50 method belongs to the family of decision tree machine learning algorithms and allow for
51 nonparametric analyses of a large number of binary, categorical or continuous predictors. They are
52 typically easy to interpret and can detect predictors with small marginal effects when there are
53 strong interaction effects. We will make use of the predictive potential for gestational age at birth of
54 all sexually transmitted and genital tract microorganisms, including individual bacterial taxa or
55 bacterial groups identified by 16S rRNA gene amplicon sequencing (as binary or continuous
56 variables) and confounding variables identified in objective 1. We will present variable importance
57 scores and curves of marginal effects to show how prediction of the outcome changes at different
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3 levels of the exposure of each variable in the model. To avoid overfitting, we will consider bootstrap
4 aggregating via random forests. [51]
5
6

7 **DATA MANAGEMENT AND CONFIDENTIALITY**

10 **DATA MANAGEMENT**

11 Each potential participant screened for eligibility is assigned a unique participant identification
12 number, which does not include any personal identifying information. Personal identification
13 numbers are used to link records, specimens and laboratory test results of the participants. Data are
14 stored in a REDCap database, [30] which is only accessible to authorised project staff. Paper records
15 are kept in lockable fire-resistant filing cabinets. Laboratory records and journals are kept at the
16 University of Pretoria and University of Cape Town. Forms with personal identifying information are
17 kept separately from demographic, clinical and other data. The data manager maintains a separate,
18 access-controlled, database that links the personal identification number with identifying
19 information. Data quality checks are conducted by study staff onsite and data administrators at the
20 office of the Foundation for Professional Development. All study data are stored securely at the
21 offices of the Foundation for Professional Development in East London for up to five years after the
22 completion of the study or as required by the institutional review board.
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27 **CONFIDENTIALITY**

28 The research team is trained to adhere to guidelines on the Protection of Human Research
29 Participants and Good Clinical Practice and fully protects the confidentiality of participants. Besides
30 the measures described under data management, interviews are conducted in a private setting. In
31 reports and publications, data will not be presented in a way where it could be linked to individual
32 participants.
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36 **PATIENT AND PUBLIC INVOLVEMENT**

37 There was no involvement of patients or the public in the development of the research questions or
38 the study methods. The research findings will be shared through open access publications and in
39 dissemination meetings with local stakeholders, healthcare providers and communities.
40
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43 **Discussion**

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46 This project is important because of its holistic approach, which considers associations between
47 different genital tract infections, their quantity and the vaginal microbiota on earlier gestational age
48 at birth. Many studies in this field have focused on only one or two microorganisms and few studies
49 involve women in sub-Saharan Africa. Strengths of this study include the study setting, where the
50 prevalence of both genital tract infections and adverse pregnancy outcomes is high, the use of
51 ultrasound scans at enrolment for accurate assessment of gestational age and the use of state-of-
52 the-art molecular diagnostic tests and 16S rRNA sequencing. The residual DNA from samples
53 collected in this study will be available for future studies, including joint analyses with other studies
54 of the influence of vaginal microbiota on adverse pregnancy outcomes.
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58 There are limitations to the study design. First, this study involves participants from one clinic, which
59 might limit the generalisability of the findings. Second, using gestational age at delivery as a
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3 continuous outcome instead of preterm birth as a dichotomous outcome, might limit comparability
4 with other studies. We will, however, examine the binary outcome preterm birth in secondary
5 analyses. Third, the vaginal samples are taken in a fixed sequence at each visit, which might reduce
6 the microorganism load of later samples. Fourth, the development of the vaginal inflammation index
7 will use information about the inflammatory potential of microorganisms, [49] rather than direct
8 concentrations of inflammatory markers.
9

10
11 This study has the potential to generate new evidence about the role of different microorganisms in
12 earlier gestational age at birth through analyses of the presence and quantity of individual and
13 combinations of microorganisms, relative abundance of bacterial genera and microbiota on
14 gestational age at birth. This study will generate new hypotheses, which can be investigated in
15 future studies.
16

17 18 19 **Ethics and dissemination**

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21
22 This protocol and the informed consent forms are approved by the University of Cape Town,
23 Research Ethics Committee (Reference: 676/2019), which includes activities at the University of
24 Southern California, University of Alabama at Birmingham and Louisiana State University.
25 Authorisation to analyse de-identified data at the University of Bern has been granted by the Canton
26 of Bern Ethics Committee (Reference: 2021-01209). Results from this study will be submitted to
27 regional and international conferences and to open access peer-reviewed journals and preprint
28 servers.
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32 33 **Data statement**

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36 The research team will prepare datasets used in analyses, in accordance with data sharing
37 requirements of open access journals in which manuscripts are published and in compliance with
38 local Protection of Personal Information Act requirements. These data files will be archived with
39 codebooks as .csv documents or R data sets and stored in REDCap. The final data files will not
40 contain any personal identifying information of participants.
41
42
43

44 45 **Author contributions**

46
47 RG, NL, JW, and RP conceived and designed the study. JK supported the study through design of the
48 parent study of the Philani Ndiphile project. RG, NL, JW, RP, HJ, CT, CM, SC and LB contributed to the
49 data analysis plan. RG, NL, RP, MM and HJ were involved with the implementation and management
50 of the study. RG and MM managed the data acquisition. RG, NL, JW, RP drafted the manuscript and
51 all authors revised it. NL, JW, RP and JK supervised the study. All authors read and approved the final
52 manuscript.
53
54

55 56 **Funding statement**

1
2
3 This work is supported by an MD-PhD scholarship from the Swiss National Science Foundation (grant
4 number 191225), the Swiss National Science Foundation (grant number 197831) and the US National
5 Institutes of Health (grant number R01AI149339).
6
7

8 **Competing interests statement**

9

10 LB, SC, RG, HJ, JK, NL, MM, RP, CT, JW: no competing interests to declare.
11

12 CM has received research grant funding to her institution by Gilead Inc., Abbott Molecular, Visby,
13 and Lupin Pharmaceuticals. She is a consultant to BioNTech, Cepheid, and BioFire Diagnostics. She
14 has received honoraria for educational presentations and review activities from Scynexis, Visby,
15 Abbott, Elsevier, UpToDate, and DynaMed Plus.
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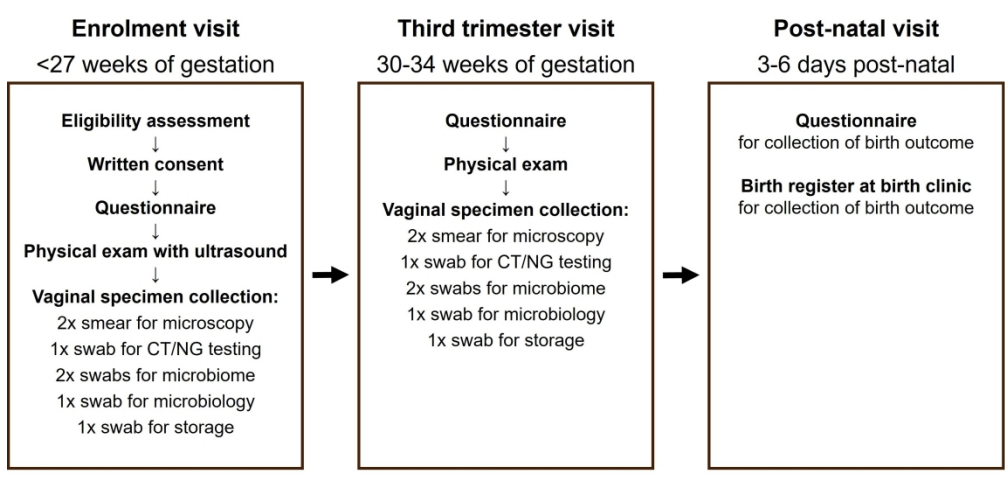


Figure 1 Study visits and specimen collection
 Abbreviations: CT, Chlamydia trachomatis; NG, Neisseria gonorrhoeae.

272x125mm (330 x 330 DPI)

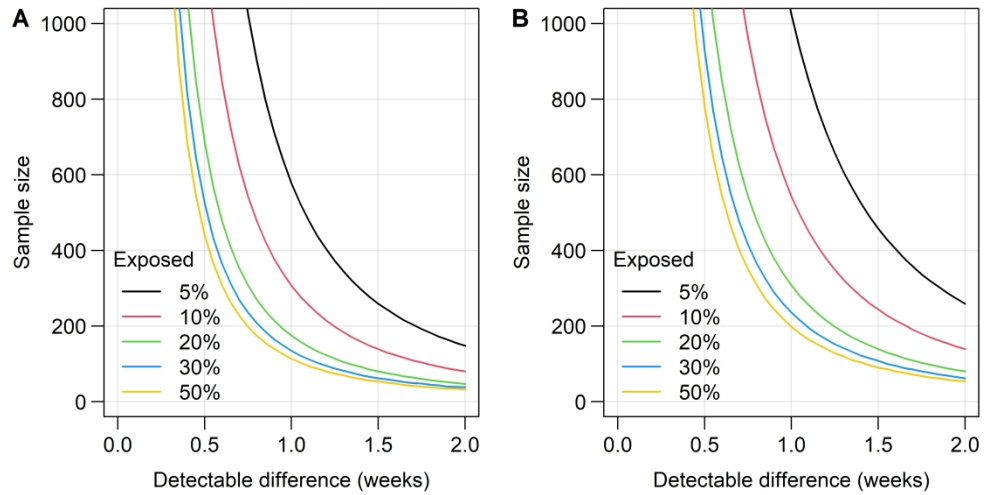


Figure 2 Sample size requirements at different levels of exposure prevalence with power of 80% and alpha 0.83% based on Student's t-test.

Legend: panel A, standard deviation 1.5; panel B, standard deviation 2.0. The curves for % exposed are symmetrical around a prevalence of 50%, i.e., curve for 10% exposed is same as that for 90% exposed.

516x258mm (236 x 236 DPI)

Supplemental online file – study questionnaire

Genital tract infections, the vaginal microbiome and gestational age at birth among pregnant women in South Africa: a cohort study protocol

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Screening and Enrolment

Record ID

Site Information

Today's Date

Study Staff Name

Start Time

Please select Study Site Name

- Grey Gateway
- Duncan Village CHC
- Nontyatyambo CHC
- Gompo
- Ndevana

Introduction to the Study:

Note to RA:

In this section you will be introducing the study to the participant. Please make sure to execute the following steps:

1. Introduce the study

- Proceed

Does the participant show interest in the study

- Yes the participant shows interest
- No the participant is not interested in the study

END

The participant is not interested in the study. Thank them for their time.

Eligibility Screening

Note to RA:

The participant seems to show interest in the study. We need to determine their eligibility status. You will ask a series of questions to determine this. Please select "Proceed" to continue.

Proceed

Is the participant currently living in BCM?

Yes

No

Is the participant 18 years or older?

Yes

No

Please specify the participant's date of birth

Calculated age

Is this the participant's first ANC visit?

Yes

No

Is the participant within the first 26 weeks of her pregnancy?

Yes

No

Is the participant within the first 20 weeks of her pregnancy?

Yes

No

Gestational weeks

_____ (if unknown, enter 99)

Is the participant intending to deliver the baby at one of our collaborating MOUs?

Yes

No

Is the participant currently involved in any other ANC/HIV research trial?

Yes

No

1 Calculated Eligibility Outcome

2
3
4
5 (1 = Eligible, 0 = Not Eligible)

6
7 END

8 The participant is not eligible for our research study

9
10 This will be the end of their participation. Please thank them for their time.

11
12
13 ELIGIBLE

14 The participant is eligible for our research study. Please select "Proceed" to start with the consenting process.

15 Proceed

16
17
18
19
20
21 **Consenting Process:**

22
23
24
25
26 NOTE TO RA:

27 You will now start with the consenting process. Please make sure to do the following:

- 28
29 1. Read the consent form with the participant
30 2. Read in a language they prefer
31 3. Allow for questions
32 4. If willing to consent, sign all documents
33 5. Hand a signed copy (without PIN) to the patient

34 Proceed

35
36
37 Did the participant provide a signed consent to participate in the research study?

- 38 Yes
39 No

40
41
42
43
44 **Consent refusals**

45
46
47
48 Reasons for refusal

- 49
50 They have no time
51 Scared
52 In a different study
53 Other

54
55 If "Other", please specify

1 Refusal date

6 END
7 Thank the participant for their time

12 **Provided Consent**

14 Consent date

21 **Participant PIN**

23 CONSENTED
24 The participant has agreed to provide consent. You will now allocate a study PIN to the participant. Please use the
25 next available PIN on the hard copy enrollment log

26 Proceed

29 Participant PIN

34 Participant PIN Verification

39 Pin match

44 PIN valid

49 ERROR
50 The PINs you entered did not match up

53 You have entered the following PINs

55 first pin: [participant_pin]
56 second pin: [participant_pin_verify]

58 ERROR
59 The PIN you entered is invalid for [site_name]

You have entered the following PINs

first pin: [participant_pin] For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>
second pin: [participant_pin_verify]
06-10-2023 11:48

1 **Saving Instruction**

2
3 You have completed the Screening and Enrollment process. Please make sure to check if all relevant fields have been
4 selected and the information captured is accurate.

5
6 Once this is done, please select the "complete" option below and then select "Save & Exit".

7
8 Once you have done this you will be directed to the baseline Data.
9

10
11
12 **Notes**

13
14
15
16 Additional Notes
17
18
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60

For peer review only

Baseline Data

Staff name

Today's Date

Start Time

Sociodemographics

NOTE TO RA:

You are about to start the Socio-demographics section. Please make sure to ask the questions as they appear on your tablet.

Please select "Proceed" to continue.

Proceed

Sociodemographics

How would you describe yourself in terms of race?

- African
- Coloured
- Mixed Race
- White
- Indian
- No answer

What level of education did you complete?

- Less than Gr. 10
- Gr.10 or 11
- Gr.12
- Diploma
- Degree
- Refused to answer

1 Which best describes the type of house in which you live? Please choose one answer only:
2

- 3 House or brick structure on a separate stand or yard or on a farm
4 Traditional dwelling/hut/structure made of traditional materials
5 Flat
6 Town/cluster/semi-detached house (simplex, duplex or triplex)
7 Unit in retirement village
8 Dwelling/house/flat/room in backyard
9 Informal dwelling/shack IN the backyard of a formal house
10 Informal dwelling/shack NOT in backyard e.g. in an informal/squatter settlement or on farm
11 Room/flatlet not in backyard but on a shared property e.g granny flat
12 Caravan/tent
13 Worker's hostel
14 Other

15
16 If other, please specify.
17
18
19
20
21

22 What is the main material of your house walls? Please choose one answer only:
23

- 24 Bricks & plaster/finished
25 Bare brick/cement block
26 Corrugated iron/zinc
27 Wood
28 Plastic
29 Cardboard
30 Mixture of mud and cement
31 Wattle and daub
32 Mud
33 Other

34
35 If other, please specify
36
37
38
39
40

41 What is the main material of your house roof? Please choose one answer only:
42

- 43 Tiles
44 Corrugated iron/zinc
45 Thatching
46 Asbestos
47 Plastic
48 Cardboard
49 Other

50
51 If other, please specify
52
53
54
55
56
57
58
59
60

1 What is your current relationship status?

- 2
3 Married
4 Steady partner
5 Steady partner and Casual Partner(s)
6 Casual Partner(s)
7 No relationship
8

9 Do you live together with your partner?

- 10
11 Yes
12 No
13

14 Are you currently employed?

- 15
16 Employed
17 Self employed
18 Not employed
19

20 What is your monthly personal income?

- 21
22 None
23 < 1000 ZAR per month
24 1001 - 5000 ZAR per month
25 5001 - 10 000 ZAR per month
26 >10 000 ZAR per month
27

28 What is your household's main source of income?

- 29
30 Personal income from employment \ self employment
31 Income from partner
32 Grants
33 Other
34

35 Have you been outside of the Eastern Cape or country in the past 6 months?

- 36
37 Yes
38 No
39

40 Which provinces or country have you been to in the last 6 months?

41 Note to RA: please select all that apply

- 42
43 Free State
44 Gauteng
45 Kwazulu-Natal
46 Limpopo
47 Mpumalanga
48 Northern Cape
49 North West
50 Western Cape
51 Outside South Africa
52
53

54 Has your partner/husband been outside of the Eastern Cape or country in the past 6 months?

- 55
56 Yes
57 No
58
59
60

1 Which provinces or country has your partner/husband been to in the last 6 months?
2

3 Note to RA: Please select all that apply
4

- 5 Free State
6 Gauteng
7 Kwazulu-Natal
8 Limpopo
9 Mpumalanga
10 Northern Cape
11 North West
12 Western Cape
13 Other country

14
15 What is the main source of drinking water for your household? Please choose one answer only:
16

- 17 Piped (tap) water in dwelling
18 Piped (tap) water on site or in yard
19 Neighbour's tap
20 Public or communal tap (either free or paid)
21 Borehole on site
22 Borehole off site/communal
23 Rain water tank
24 Water carrier/tanker
25 Flowing water/stream/river
26 Stagnant water/dam/pool
27 Well
28 Spring
29 Bottled water
30 Other

31 If other, please specify
32
33
34
35
36

37
38 What type of toilet does your household use? Please choose one answer only:
39

- 40 Flush toilet (connected to sewage)
41 Flush toilet (with septic tank)
42 Chemical toilet
43 Pit latrine with ventilation pipe
44 Pit latrine without ventilation pipe
45 Bucket toilet
46 No facility/bush/field
47 Other

48 If other, please specify
49
50
51
52
53
54
55
56
57
58
59
60

1 What is the main source of energy for cooking in your household? Please choose one answer only:

- 2
3 Electricity from mains
4 Electricity from generator
5 Gas
6 Paraffin
7 Wood
8 Coal
9 Animal dung
10 Solar energy
11 Other

12
13 If other, please specify
14
15
16
17
18
19

20 **Does your household have any of the following items in good working order? Read each item**
21 **and indicate the presence of each**

	Yes	No
23 Television	<input type="radio"/>	<input type="radio"/>
24 Gas or Electric stove	<input type="radio"/>	<input type="radio"/>
25 Fridge/freezer	<input type="radio"/>	<input type="radio"/>
26 Private motor vehicle in running condition	<input type="radio"/>	<input type="radio"/>
27 Bicycle	<input type="radio"/>	<input type="radio"/>
28 Bed	<input type="radio"/>	<input type="radio"/>
29 Sofa or sofa set	<input type="radio"/>	<input type="radio"/>
30 Kitchen sink	<input type="radio"/>	<input type="radio"/>

31
32
33
34
35
36
37 Do you think that you will need to borrow money to pay for healthcare during your pregnancy?

- 38
39 Yes
40 No
41

42
43 How much money did you spend coming to the clinic today (including transport costs, snacks while waiting etc.) ?

44
45 _____
46 ([RANDS])
47

48
49 Did you lose any money from your job because of coming to the clinic today?

- 50
51 Yes
52 No
53

54 If yes, how much money did you lose?

55
56 _____
57 ([RANDS])
58
59

60 How much time did you spend travelling to the clinic today (Hours)?

_____ ([HOURS])

1 How much time did you spend travelling to the clinic today (Minutes)?

2
3
4
5 _____
6 ([MINUTES])

7 Time spent travelling in minutes.

8
9
10 _____
11
12 How much time do you normally spend waiting and seeing the doctor or nurse in a clinic such as this one (Hours)?

13
14
15 _____
16 ([HOURS])

17
18 How much time do you normally spend waiting and seeing the doctor or nurse in a clinic such as this one?

19
20
21 _____
22 ([MINUTES])

23
24 How much time do you normally spend waiting and seeing the doctor or nurse in a clinic such as this one in minutes?

25
26
27 _____
28 ([MINUTES])

29
30 Are you planning to wait for your results today?
(New question added @13/09/2022)

- 31
32
33
34 Yes
35 No

36
37 What is your main reason why you are not intending to wait today?
(New question added @13/09/2022)

- 38
39
40 Have to get to work
41 Have to get back to my kids/family
42 Want to go to the shop
43 Transport availability
44 Lack of privacy
45 Hungry
46 No space to wait
47 Not feeling well
48 Boring
49 Other

50
51 If "Other" , please specify.

52 (New question added @13/09/2022)

53
54
55
56
57
58 What would make you change your mind?
59 (New question added @13/09/2022)

60

1 Do you do any of the following activities in a lake / stream?
2

3 Note to RA: Please select multiple that apply
4

- 5 Play
6 Bath
7 Wash blankets
8 Do laundry
9 Fish
10 Collect water
11 Crossing
12 None
13
14

15 Behavioural Questionnaire 16 17 18 19

20
21 NOTE TO RA:

22 You just completed all questions related to socio-demographics. You are about to start with the Behavioral
23 Questionnaire.

24 Please select "Proceed":
25

- 26 Proceed
27

28
29 When was the last time you had sex?

- 30 In the past week
31 In the past month
32 More than a month ago
33

34
35 Did you use a condom the last time you had sex?

- 36 Yes
37 No
38

39
40 Do you use a lubricant?

- 41 Yes
42 No
43

44
45 Can you please elaborate on the type of lubricant that you use?
46
47
48
49

50 What do you use to clean your vagina?
51

- 52 Water only
53 Soap and water
54 Other household products
55 Other
56

57 Please specify what other things you used on your vagina.
58
59
60

1 Do you do any vaginal douching?
2

- 3 Yes
4 No
5

6 Please specify
7
8
9
10
11

12 Do you do any form of vaginal cleansing?
13

- 14 Yes
15 No
16

17 Please specify
18
19
20
21
22
23

24 Do you use anything to clean inside your vagina?
25

- 26 Yes
27 No
28

29 Do you insert anything in your vagina for tightening?
30

- 31 Yes
32 No
33

34 Please specify
35
36
37
38
39

40 In the past 6 months, how many sexual partners did you have?
41

- 42 One
43 More than one
44

45 In the past 6 months, have you engaged in any of the following?
46 (Select ALL that apply)
47

- 48 Vaginal sex
49 Oral sex
50 Anal sex
51

52 Have you recently agreed to sex even though you did not feel like to?
53

- 54 Yes
55 No
56
57
58
59
60

1 Note to RA: Discuss with participant counselling options

- 2
3 Yes
4 Participant doesn't need counselling
5

6 Please specify
7
8
9
10
11

12 In the past 6 months, have you been forced to have sex with anyone?

- 14 Yes
15 No
16

18 Note to RA: Discuss with participant counselling options

- 19 Yes
20 Participant doesn't need counselling
21
22

23 Please specify
24
25
26
27
28

29 In the past 6 months, have you received any benefits (money or goods) for sex?

- 31 Yes
32 No
33

34 Do you suspect your steady partner to have any other sex partners?

- 36 Yes
37 No
38 Unsure
39

40 When did your last menstrual period start?

42 Note to RA: Please ask participant to give the most accurate date.
43
44
45 _____
46

47 Just before I became pregnant.
48

49 NOTE: Please tick the statement that most applies to you:

- 51 I wanted to have a baby
52 I had mixed feelings about having a baby
53 I did not want to have a baby
54

55 How many times have you been pregnant before your current pregnancy?
56
57 _____
58
59 _____
60

How many live children have you delivered?

1 Of the live births that you had, how many were normal vaginal delivery?
2
3
4 _____
5

6 Of the live births that you had, how many were "emergency cesarean"?
7
8
9 _____
10

11 Of the live births that you had, how many were "elective cesarean"?
12
13
14
15 _____
16

17 Live birth Match
18
19
20 _____
21

22 Note to RA: The numbers you have entered do not match. Please check again.
23

24 How many of your live birth's were premature?
25
26
27 _____
28

29 How many of your live birth's were full term?
30
31
32 _____
33

34 Delivery timing calc
35
36
37 _____
38
39

40 Note: The numbers you have captured do not add up
41

42 Have you ever had an ectopic pregnancy?
43

- 44 Yes
45 No
46

47 Have you ever had a miscarriage?
48

- 49 Yes
50 No
51

52 Have you ever had a stillbirth?
53

- 54 Yes
55 No
56
57
58
59
60

1 Do you smoke cigarettes?
2

- 3 Yes
4 No
5

6 Have you used any of the following since you found out you were pregnant? (select multiple)
7 (Select ALL that apply.)
8

- 9 Alcohol
10 Tik
11 Dagga
12 Grandpa
13 Other
14 None
15

16 Please specify
17
18
19
20
21

22 Do you know your current HIV status?
23

- 24 HIV negative (tested today by clinical staff)
25 HIV positive on ART
26 HIV positive, not on ART
27 Don't know (never tested)
28 Don't know (no yet tested today)
29

30 Was the participant newly diagnosed within the past week?
31

- 32 Yes
33 No
34

35 Can we test you for HIV today?
36

- 37 Yes
38 No
39

40 Unknown HIV Status:
41

42 Note to RA/ Nurse: HIV test needs to be conducted
43

- 44 Proceed to test
45

46 HIV rapid test result:
47

- 48 Positive
49 Negative
50

51 HIV confirmatory test
52

- 53 Positive
54 Negative
55

56 Elisa blood barcode
57
58
59
60

1 Have you ever been treated for an STI in the last year?
2

- 3 Yes, I had discharge
4 Yes, I had ulcers
5 Yes, I had genital warts
6 Yes, no symptoms but notified by partner
7 No
8

9 Does the participant have pre-existing diabetes?
10

- 11 Yes
12 No
13

14 Are you on treatment for your diabetes?
15

- 16 Yes
17 No
18

19 Does the participant have pre-existing hypertension?
20

- 21 Yes
22 No
23

24 Are you currently on medication for your hypertension?
25

- 26 Yes
27 No
28

29 Does the participant have pre-existing thyroid disease?
30

- 31 Yes
32 No
33

34 Is the participant taking medication for her thyroid disease?
35

- 36 Yes
37 No
38

39 Do you know your partner's HIV status?
40

- 41 Yes, HIV positive on ART
42 Yes, HIV positive but not on ART
43 Yes, HIV negative
44 No
45
46

47 You have completed the baseline questionnaire. Please make sure to log out of your REDCap account.
48

49 Once you have done this you can hand the process over to the nurse who will conduct the clinical history.
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
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NOTES

Additional notes

For peer review only

Physical Exam

Staff Name

Today's Date

Start time

You are about to administer the questions associated with the physical exam.

Please select "Proceed" to continue.

Proceed

Clinical History

Do you currently have any of the following symptoms?

RA: Please select all that apply

- Abnormal vaginal discharge
- Pain during urination
- Lower abdominal pain
- Pain related to intercourse
- Vaginal bleeding related to intercourse
- Genital itchiness
- Any skin abnormalities
- None

How many days ago did your abnormal vaginal discharge start?

How many days ago did the pain during urination start?

Provide further details

Have you received treatment for these symptoms?

Yes

No

1 Where did you get the treatment from?
2

- 3 Over the counter
4 Healthcare facility
5 Traditional healer
6

7 Please provide further details
8
9
10
11
12

13 If you were told you had an STI would you disclose to your partner(s)?
14

- 15 Yes, to steady partner
16 Yes, to casual partner(s)
17 Yes, to all steady and casual partner(s)
18 No
19

20 Co-Morbidities
21

22
23 You are about to start asking questions related to co-morbidities.
24

25 Please select "Proceed" to continue.
26

- 27 Proceed
28

29 Did the participant screen positive for any TB symptoms?
30

- 31 Yes
32 No
33

34 The participant shows signs of TB. A specimen needs to be collected for further testing. Please select below to
35 specify whether a specimen was collected successfully.
36

- 37 Yes
38 No
39

40 Instruction: Please record the specimen tracking number below
41

42 _____
43
44

45 Are you on cotrimoxazole prophylaxes?
46

- 47 Yes, on cotrimoxazole
48 Yes, started today
49 No
50

51 Did the participant start antiretroviral therapy today?
52

- 53 Yes
54 No
55

56 Specify reason for not starting
57
58
59
60

1 Was blood taken today for the participant's CD4 count?
2

- 3 Yes
4 No
5

6 Please record barcode for blood tube for CD4 count testing?
7
8
9
10 _____
11

12 Is the participant's most recent CD4 count within the last 12 months available?
13

- 14 Yes
15 No
16

17 What was the date of the CD4 specimen collection?
18
19
20 _____
21

22 What was the participant's most recent CD4 count?
23
24
25 _____
26 (if no number listed, enter 9999)
27

28 Was blood taken today for the participant's viral load?
29

- 30 Yes
31 No
32

33 Please record barcode for blood tube for viral load testing?
34
35
36 _____
37

38 Is the participant's most recent viral load within the past 12 months available?
39

- 40 Yes
41 No
42

43 What was the date of the viral load specimen collection?
44
45
46 _____
47

48 What was the participant's most recent viral load?
49
50
51 _____
52 (if no number listed, enter 0000)
53

54 Was blood taken today for the participant's viral load?
55

- 56 Yes
57 No
58
59

60 Please record the barcode for viral load testing?

1 Is the participant's most recent viral load available?

- 2
3 Yes
4 No
5

6 What was the date of the viral load specimen collection?

7
8
9 _____
10

11 What was the participant's most recent viral load?

12
13
14 _____
15

16
17 Which regimen for ART were you started on today?

- 18
19 TLD
20 TEE
21 AZT/3TC/LPV
22 Other
23

24 Which regimen for ART were you on so far?

- 25
26 TLD
27 TEE
28 AZT/3TC/LPV
29 Other
30

31 Has the regimen for ART been changed today?

- 32
33 Yes
34 No
35

36 To which regimen for ART has it been changed today?

- 37
38 TLD
39 TEE
40 AZT/3TC/LPV
41 Other
42

43 Please select "Proceed" to collect blood for viral load testing.

- 44
45 Proceed
46

47 Did you successfully collect blood for viral load testing?

- 48
49 Yes
50 No
51

52 Please capture the barcode associated with the blood tube used for testing viral load.

53
54
55 _____
56

57
58
59
60

1 Was a CD4 count test done?

- 2
3 Yes
4 Yes, but no result available
5 Not done
6

7 Please specify last known CD4-cell count.
8
9
10 _____
11

12 Was blood taken today for the participant's CD4 count ?

- 13
14 Yes
15 No
16

17 Please record the barcode for CD4 testing?
18
19 _____
20
21

22 Is the participant's most recent CD4 available?

- 23
24 Yes
25 No
26

27 What was the date of the CD4 specimen collection?
28
29 _____
30
31

32 What was the participant's most recent CD4 Count?
33
34 _____
35
36

37 Has a syphilis test been done for the participant?

- 38
39 Yes
40 No
41
42

43 Instruction: Please conduct a rapid test for syphilis.

44 Specify if the participant agreed to testing / you managed to execute the test.

- 45
46 Yes
47 No
48
49

50 Which syphilis test have you used?

- 51
52 Alere Syphilis TP (provided by FPD)
53 HIV/Syphilis Duo (provided by FPD)
54 No rapid test used only NHLS bloods for RPR
55 Other please specify
56

57 Please specify
58
59
60

1 Syphilis result

- 2
3 Positive
4 Negative
5 Indeterminate
6

7 Titer value 1:

8
9
10 _____
11

12 Please collect blood for further syphilis testing and specify if the blood was collected successfully.

- 13
14 Yes
15 No
16

17
18 Treatment given

- 19
20 Benzathine penicillin, 2.4 mU
21 Out of stock
22

23 Please contact the study clinician and specify treatment given to participant

24
25
26
27
28
29 Please capture the barcode below.

30
31
32 _____
33

34 Participant weight in kilograms

35
36
37 _____
38

39 Participant height in cm

40
41
42 _____
43

44 Participant systolic blood pressure

45
46
47 _____
48

49 Participant diastolic blood pressure

50
51
52 _____
53

54
55 How was Hemoglobin measured?

- 56
57 Hb meter at the clinic
58 Hb at NHLs
59

60 Please capture Hb result

1 Please capture the barcode for Hb
2
3
4 _____
5

6 Participant MUAC in cm
7
8
9 _____

10 (1 Decimal Place)
11

12 Please collect participant's urine for later testing.
13
14

15 16 17 18 **Ultrasound Results** 19 20 21 22 23 24

25
26 You are about to start capturing information pertaining to the ultrasound results.
27

28 Please select "Proceed" to continue.

29 Proceed
30

31
32 Ultra-sound scan date
33
34
35 _____
36

37 Was the pregnancy confirmed?
38

- 39 Yes, intra-uterine
40 Yes, extra-uterine
41 No
42

43 NOTE: Please refer immediately
44

45
46 NOTE
47 Due to the status of the pregnancy, the participant is no longer eligible to continue with the study. This is the end of
48 their involvement in the study. Please thank them for their time. Also do the following:
49

- 50
51 - Save and Exit the form
52
53 - Complete a Study Note confirming termination of study participation
54

55 Please specify the number of foetus
56
57
58 _____
59
60

1 You are about to capture the gestational age of the foetuses. Please select "Proceed" and then capture the number
2 of weeks followed by days.

3
4 Proceed

5
6 Gestational age in weeks

7
8
9 _____

10
11 Gestational age in days

12
13
14 _____

15
16 Calc: Gestational age in days

17
18
19 _____

20
21 EDD based on ultra-sound

22
23
24 _____

25
26 Calc: Days to EDD

27
28
29 _____

30
31 Calc assist for EDD

32
33 The number of days must be equal to 280.

34
35
36 _____

37
38 Note to Nurse:

39
40 You did not enter either gestational age or EDD correctly.

41
42 Calc: Eligibility

43
44 END

45
46 The participant is not eligible for our research study

47
48 This will be the end of their participation. Please thank them for their time.

49
50 STI Clinical Examination (To be done By Nurse)

51
52 You are about to capture information related to STI clinical examination.

53
54 Please select "Proceed" to continue

55
56 Proceed

1 During your examination, were there any signs of abnormal vaginal discharge?
2

- 3 Yes
4 No
5

6 During your examination, were there any signs of inguinal lymphadenopathy?
7

- 8 Yes
9 No
10

11 Are these bubo?
12

- 13 Yes
14 No
15

16
17 Note to RA: Please contact study clinician and specify treatment given to participant
18
19
20
21
22

23 During your examination, were there any signs of lower abdominal pain?
24

- 25 Yes
26 No
27

28 During your examination, were there any signs of scratch marks?
29

- 30 Yes
31 No
32

33 During your examination, were there any signs of skin conditions?
34

- 35 Yes
36 No
37

38 Please specify the nature of the skin conditions
39
40
41
42
43
44

45 During your examination, were there any other observations that need to be noted?
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Urine Dipstick test results

You are about to capture the results from the dipstick testing

Please select "Proceed" to continue

Proceed

Blood - Hemoglobin

- Negative
 Ca. 10
 Ca. 50
 Ca. 250/300

Blood - Erythrocytes

- Negative
 Ca. 5 -10
 Ca. 50
 Ca. 250/300

Urobilinogen

- Normal
 2
 4
 8
 12

Bilirubin

- Negative
 1 plus
 2 plus
 3 plus
 Not available

Protein

- Negative
 30
 100
 500

Nitrate

- Negative
 Positive

1 Keton

- 2
3 Negative
4 1 plus
5 2 plus
6 3 plus
7 Not available

8
9 Glucose

- 10
11 Negative
12 Normal
13 50
14 150
15 500
16 ≥ 1000

17
18 pH

- 19
20 5
21 6
22 7
23 8
24 9
25 Not available

26
27 SG

- 28
29 1.000
30 1.005
31 1.010
32 1.015
33 1.020
34 1.025
35 1.030
36 Not available

37
38 Leucocytes

- 39
40 Negative
41 25
42 75
43 500

44
45 NOTE

46 The participant's clinical gestational age is more than 20 weeks. They are not eligible to proceed with the study
47 activities.

48
49 Please do the following:

- 50
51 1. Explain the reason for study termination
52 2. Complete the study electronic termination tool
53 3. Complete the study termination document and place in file

54
55 End
56
57
58
59
60

1
2 **NOTES**
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7 Additional Notes
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13 You have completed capturing the information from the clinical exam. Please make sure to check that you have
14 completed all the fields.
15

16 Please select "Complete" then "Save and Exit".
17

18 You will now proceed to collecting study specimens and randomization
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For peer review only

Specimens and Randomization

Staff Name

Today's Date

Start time

Specimen Collection

NOTE
 You will now start with the process of specimen collection. You will need to collect several specimens from the participant. These specimens need to be collected in the order in which they are presented here. The outcome of the randomization will have an impact on whether these specimens will be tested immediately or whether they will need to be prepared for storage.

The following specimens will need to be collected:

1. Vaginal loop to be used to prepare two slides
2. Vaginal swab to be used for STI testing
3. Vaginal swab to be used for profiling
4. Vaginal swab to be used for microbiome
5. Vaginal swab to be used for cytokine

Done

NOTE
 You will now start with the process of specimen collection. You will need to collect several specimens from the participant. These specimens need to be collected in the order in which they are presented here.

The following specimens will need to be collected:

1. 1 x Vaginal loop to be used to prepare two slides
2. 1 x Vaginal swab to be used for STI testing
3. 1 x Vaginal swab to be used for profiling
4. 2 x Vaginal swab to be used for microbiome
5. 1 x Vaginal swab to be used for cytokine

Done

Vaginal Smear

Please specify the vaginal pH

_____ (if not available, enter 99)

1 Please select which pH strips are used to measure vaginal pH

- 2
- 3 CardinalHealth pH Indicator Strips (range 3.6-6.1)
- 4 pH Indicator Strips pH 0-14
- 5 Natureland vaginal pH test (range 3.5-6.5)
- 6

7 You will need to use a single loop to collect vaginal smear on two glass slides for microscopy

8

9 Done

10

11 Confirm the PIN associated with the first vaginal slide that will be used for Nugent score

12

13 [participant_pin]-S1

14

15 Confirm the PIN associated with the second vaginal slide that will be used for yeast microscopy

16

17 [participant_pin]-S2

18

19

20 Vaginal Swabs

21

22 NOTE

23 You will now collect four vaginal swabs. They will be used as follows:

- 24
- 25 1. STI testing (test for arms 1 and 2, store for arm 3)
 - 26 2. Profiling (stored)
 - 27 3. Microbiome (stored)
 - 28 4, Cytokine
- 29

30 Done

31

32 NOTE

33 You will now collect four vaginal swabs. They will be used as follows:

- 34
- 35 1. STI testing
 - 36 2. Profiling (stored)
 - 37 3. Microbiome (stored)
 - 38 4, Cytokine
- 39

40 Done

41

42 Please confirm the PIN associated with the urine for Schistosomiasis testing.
43 (2022/10/21 - Stopped collecting the urine specimen)

44

45 [participant_pin] - UD1

46

47 Please confirm the PIN associated with the vaginal swab that will be used for STI testing.

48

49 [participant_pin] - BV1

50

51 Please confirm the PIN associated with the vaginal swab that will be used for profiling.

52

53 [participant_pin] - BV2

54

55 Please confirm the PIN associated with the vaginal swab that will be used for microbiome.

56

57 [participant_pin] - BV3

58

59

60

Please confirm the PIN associated with the vaginal swab that will be used for cytokines.

[participant_pin] - BV4

NOTE

You have finished the collection of the vaginal swabs. Please ensure specimens have been prepared for storage and shipment. The vaginal swab that is collected for STI testing should be kept aside following the outcome of the randomization. If the participant is in arm 1 or 2 the specimen should be used for immediate testing. If however, the participant is randomized to arm 3, you can store the specimen.

Please select "Proceed" to start the process of randomization

Done

Randomization

- Arm 1
- Arm 2
- Arm 3

Activities Associated with "[randomization]"

NOTE

The participant has been randomized to "[randomization]". You will now need to do the following:

1. Prepare the STI swab for testing using the GeneXpert

Done

NOTE:

The participant has been randomized to "[randomization]". You will now need to do the following:

1. Prepare the STI swab for testing using the GeneXpert
2. Screen for symptoms
3. Provide treatment and partner referral if positive

Done

NOTE:

The participant has been randomized to "[randomization]". You will now need to do the following:

1. Screen for symptoms
2. Provide treatment and partner referral if positive

Done

NOTE

You will now need to do the following:

1. Prepare the STI swab for testing using the GeneXpert

Done

STI Results

	Positive	Negative
CT	<input type="radio"/>	<input type="radio"/>

1 NG

2 TV

3

4

5 NOTE: See Calculation:

6

7 The result from the STI test?

8

9

10

11 (0 = Negative, 1 = Positive, 2 = No result)

12

13 Date the result was obtained

14

15

16 _____

17

18 Did the participant wait for her STI results?
(New question added @ 03/11/2022)

19

20

21 Yes

22 No

23

24 Symptomatic Screening Outcome Following Negative Test

25

26

27 The result from the GeneXpert was negative.

28

29 Was the participant reporting STI symptoms or showed symptoms during the clinical assessment?

30

31 Yes

32 No

33

34 Does the participant report any medication allergies?

35

36 Yes

37 No

38

39 Please contact study clinician before giving any treatment. Please specify discussed medication allergies and treatment plan with study clinician

40

41

42

43

44

45

46 The following treatment has been provided

47

- 48 Azithromycin 1g stat dose
- 49 Azithromycin 2g stat dose
- 50 Ceftriaxone 250mg IM injection
- 51 Ceftriaxone 1g IM injection
- 52 Metronidazole 400mg bd x 1 week
- 53 Metronidazole 2g stat dose
- 54 Clotrimazole pessary and/or cream
- 55 Trimethoprim/sulfamethoxazole 400/80 mg 2 tbl. bds for 5 days (bactrim)
- 56 Ceftriaxone 500mg IM injection
- 57

58 Date treatment given

59

60 _____

1 What made you change your mind about waiting for the results?
2 (New question added @13/09/2022)
3
4
5
6
7

8 Partner notification provided
9

- 10 Yes, 1
11 Yes, multiple
12 No
13

14 Please explain why the partner notification note was not provided?
15
16
17
18
19

20 **ELIGIBLE**

21 The participant is eligible for our nested chlamydia case-control study. Please select "Proceed" to start with the
22 consenting process.
23

- 24 Proceed
25

26 Did the participant provide a signed consent to participate in the chlamydia case control study?
27

- 28 Yes
29 No
30

31 Reasons for refusal
32

- 33 They have no time
34 Scared
35 In a different study
36 Other
37

38 If "Other", please specify
39
40
41
42
43
44

45 Consent or refusal date
46
47
48
49

50
51 **NOTES**

52 Participant successfully enrolled
53
54
55
56

57 Additional notes
58
59
60

1 You are done with all activities associated with "[randomization]". Please hand the tablet over to the RA to capture
2 the remaining schedule dates.
3

4 You are done with all activities. Please hand the tablet over to the RA to capture the remaining schedule dates.
5
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Scheduling

Scheduling of Dates Associated with [randomization].

NOTE

You are about to schedule dates associated with [randomization] participants.

Please select "Proceed".

Proceed

Scheduling of Dates Associated

NOTE:

You are about to schedule dates associated with microbiome participants.

Please select "proceed"

Proceed

Scheduling Dates for 3-Week ToC

NOTE: The participant tested positive and therefore we need to schedule a date, exactly 3-weeks from today to conduct a test-of-cure.

Calculator Assist

The number here must be equal to 21

Scheduling the 3-week ToC

NOTE:

Please schedule a date, 3 weeks from today treatment given. Please use the calculator assistance to ensure that you schedule a date exactly 21 days from today.

ERROR

The field does not equal to 21, please change it

Have you handed the TOC date to the participant?

Yes

No

Scheduling Dates Associated with ToC Reminder

Schedule date for REMINDER of 3-week ToC visit

1 Calculator Assist for scheduling ToC reminder date

2
3 The reminder phone call will be made 18 days following the treatment date. The number of days need to equal to 18.

4
5
6
7
8 **ERROR**

9 You did not enter the date correctly. The number should equal to 18. Please redo the date.

11 Scheduling Dates Associated with 3-Week ToC Missed Visit Date

12
13
14 **NOTE:**

15 You have successfully scheduled the reminder date.

16
17 Please select "proceed" to schedule the missed visit date for the 3 week ToC visit.

18
19 Proceed

21 Schedule the date for the MISSED VISIT of the ToC visit.

22
23 This date should be 3 weeks after the date on which the participant received their test result.

24
25
26
27
28 Calculator Assist for scheduling 3-week ToC Missed Visit

29
30 The participant's time period allowed for attending a ToC will start 35 days after they received their result and will close 35 days after the date they received their result.

31
32
33 The number here must show 35

34
35
36
37
38 **ERROR**

39 You did not enter the date correctly. The number should equal to 35. Please redo the date.

40
41 **NOTE:**

42 You have successfully scheduled the 3-week ToC close date

43
44 Please select "proceed" to start scheduling the next visit dates

45
46 Proceed

48 Dates Associated with reminder for the 28 Week call

49
50
51 **NOTE:**

52 You are about to schedule dates for the call reminder at 28 weeks.

53
54 Please select "Proceed".

55
56 Proceed

58 **Note:**

59 Schedule the date for the 28 week call. We will contact each participant to ask the date for their 30 weeks clinic visit is.

1 Calculation assist for scheduling the 32-week reminder date.

2
3 This number must equal to 196

4
5
6 _____
7
8 Days to call reminder

9
10
11 _____
12
13
14 **ERROR**
15 The number you have entered does not match 196. Please select a different date so that the number equals to 196.

16
17 **CONGRATULATIONS**

18 You have finished scheduling all dates.

19
20
21
22
23 **NOTES**

24
25 Notes box

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BL specimens results

1
2
3
4
5 Staff _____
6
7

8 Date _____
9
10

11 Time _____
12
13

14 You are about to capture results of specimens collected during the baseline visit.

15 Please select "Proceed" to continue

16
17
18 Proceed
19

20 Hb results received

21
22 Yes

23 No
24

25 Please capture Hb result
26
27
28
29 _____
30

31 Please capture the barcode for Hb
32
33
34 _____
35

36 Please capture the results of the sputum for TB testing

37
38 MTB Negative

39 MTB Positive Rifampicin Susceptible

40 MTB Positive Rifampicin Resistant

41 Not suitable

42 Specimen missing

43 Invalid

44 Not applicable
45

46 Please contact participant
47

48 Please recollect specimen on participant next visit
49

50 CD4 count results received?

51
52 Yes

53 Clotted blood

54 Missing
55

56 Please recollect blood or collect outcome from ART clinic
57
58

59 Please record the barcode for CD4 count testing
60

1 Please capture the result of the blood tube collected for CD4 count testing

6 Date sample for CD4 count was taken

12 Viral load results received?

- 13 Yes
- 14 Clotted blood
- 15 Missing

18 Please recollect blood or collect outcome from ART clinic

20 Please capture the result of the blood tube collected for viral load testing

25 Date sample for viral load was taken

31 Please record barcode for viral load testing

36 Please capture the result of the syphilis testing

- 37 RPR Negative
- 38 RPR Positive
- 39 RPR Indeterminate
- 40 Not received

43 Please contact participant

52 **Notes**

57 Notes

UP Specimen Results

Staff _____

Date _____

Time _____

You are about to capture results of specimens collected during the baseline visit.

Please select "Proceed" to continue

Proceed

Please capture the result for the Nugent score testing

- Slide reading not satisfactory
- Slide reading was satisfactory

Please capture the result for the Nugent score testing

Please specify if yeast was present

- Yes
- No

Please capture the result for the yeast infection testing

- Slide reading not satisfactory
- Slide reading was satisfactory

Please capture the result for the Yeast Infection testing

Please specify if candida was present

- Yes
- No

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Please capture the result for the schistosomiasis

- Positive
- Negative
- Indeterminate

Please specify the result for the schistosomiasis

- Trace
- 1+
- 2+
- 3+
- 4+

Note:

Please notify the study clinician

Notes

Notes

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Calling Reminders

Staff Name

Today's Date

Time

Opening date for Week 30-34

Closing date for Week 30-34

NOTE:

You are about to call a participant to remind them of a specific visit. Please make sure to do the following:

1. Obtain all relevant contact numbers for the participant on their record
2. Ensure that you have checked what the exact date is when the participant is expected to present
3. Make sure to give the participant a brief description of what will be done at the visit.
4. You will make up to 3 attempts to get hold of the participant.

Please select "Proceed"

Proceed

The presentation dates are below:

TOC

Date: [baseline_arm_1][toc_3week]

WEEK 28 CALLING

Date: [baseline_arm_1][sched_28w_rem]

WEEK-32

30-34 Week Open Date: [week_28_arm_1][calling_wk30_34_open_date]

30-34 Week Close Date: [week_28_arm_1][calling_wk30_34_close_date]

30-34 Week Actual Date: [week_28_arm_1][week32_visit_date]

POST-NATAL VISIT

Visit open date: [predelivery_checki_arm_1][pd_remind_date_schedpd]

Visit close date: [predelivery_checki_arm_1][pd_close_date_schedpd]

Date of Delivery: [predelivery_checki_arm_1][pd_remind_date_delivery]

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6-WEEK IMMUNIZATION VISIT

1 Actual Date: [predelivery_checki_arm_1][sixw_im_schedpd]
2

3
4 Please select the calling attempt

- 5 First Attempt
6 Second Attempt
7 Third Attempt
8
9

10
11
12
13 **Details of Calling Attempt 1**
14
15
16

17
18 Outcome of the attempt

- 19 Successful - Participant
20 Successful - Family member
21 Unsuccessful - Voicemail
22 Unsuccessful - Invalid
23

24
25 Date of the attempt
26
27
28 _____
29

30
31
32 **Details of Calling Attempt 2**
33
34
35

36
37 Outcome of the attempt

- 38 Successful - Participant
39 Successful - Family member
40 Unsuccessful - Voicemail
41 Unsuccessful - Invalid
42

43
44 Date of the attempt
45
46
47 _____
48

49
50 **Details of Calling Attempt 3**
51
52
53

54 Outcome of the attempt

- 55 Successful - Participant
56 Successful - Family member
57 Unsuccessful - Voicemail
58 Unsuccessful - Invalid
59

60
Date of the attempt

1
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Notes

Calling notes

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ToC Visit Activities

Staff Name

Today's date

Start time

NOTE

Did the participant present within the specified dates presented below:

Start: [baseline_arm_1][toc_reminder_date]

Actual: [baseline_arm_1][toc_3week]

End: [baseline_arm_1][arm1_toc_close_date]

Yes

No

The participant did not have a positive baseline STI result and therefore a ToC visit is not applicable. Activities associated with this visit will need to be captured under the "Ad-Hoc" tool

Note

You are about to start activities associated with the Test-of-Cure visit for participants in arm 1. The following activities are associated with this visit:

1. Collect 1 Loop with 2 slides
2. Collect 3 vaginal Swabs
 - Test of Cure Test
 - Profiling (Storage)
 - Microbiome (Storage)
3. Running the Test-of-Cure
4. Collect Clinical History, Adherence and Disclosure data

Please select "Proceed"

Proceed

Specimen Collection_ToC

NOTE

Please collect one vaginal loop and prepare 2 slides. Please remember to do the following:

1. Pack slides individually in their own package
2. Record the PIN on the outside of package
3. Complete the lab CRF with the matching PINs and test instructions

Select "Proceed" to confirm the PINs associated with the slides.

Proceed

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1 Did you manage to collect the vaginal loop?
2

- 3 Yes
4 No
5

6 Date of vaginal loop specimen collection
7
8
9
10 _____
11

12 Please confirm the pin for the first vaginal swab that will be used for Nugent score

- 13 [baseline_arm_1][participant_pin]-TL1
14

16 Please confirm the pin for the second vaginal swab that will be used for yeast microscopy

- 17 [baseline_arm_1][participant_pin]-TL2
18
19

20 NOTE:

21 You are about the start with the process of collecting the following 3 vaginal swabs:

- 22
23 1. Swab to be used to conduct ToC (Immediately)
24 2. Swab for profiling
25 3. Swab to be used for microbiome
26

27 Please select "Proceed"

- 28 Proceed
29
30

31 Please specify the vaginal pH
32
33
34 _____
35

36 Please confirm the PIN associated with the vaginal swab that will be used for STI testing.

- 37 [baseline_arm_1][participant_pin] - TCV1
38
39

40 Did you manage to collect the vaginal swab for profiling

- 41 Yes
42 No
43
44

45 Please confirm the PIN associated with the vaginal swab that will be used for profiling.

47 This must be stored

- 48 [baseline_arm_1][participant_pin] - TCV2
49
50

51 Did you manage to collect the vaginal swab for microbiome testing?

- 52 Yes
53 No
54
55

56 Please confirm the PIN associated with the vaginal swab that will be used for microbiome.

57 This must be stored

- 58 [baseline_arm_1][participant_pin] - TCV3
59
60

1 Date of specimen collection for vaginal swabs
2
3
4
5

6 NOTE
7 You have collected all specimens associated with this visit. Once you select the "Proceed" option below you will be
8 directed to the start of the clinical history questionnaire. The completion of the questionnaire might take some time
9 so it would be a good idea to start running the vaginal swab to conduct the Test of Cure in line with the below
10 baseline results.
11
12
13

14 NG: [baseline_arm_1][sti_result_ng]

15
16 TV: [baseline_arm_1][sti_result_tv]

17
18 CT: [baseline_arm_1][sti_result_ct]

19
20 Proceed
21
22

23 24 **Clinical History Review** 25 26 27 28 29 30

31
32 You are done trying to collect specimens. Because you were not able to collect a Vaginal Swab for STI testing you
33 will not be able to run a test. Please proceed to completing the clinical history.

34 Proceed
35

36
37 Do you currently have any of the following symptoms?
38 Multiple selection

- 39 Abnormal vaginal discharge
40 Pain during urination
41 Lower abdominal pain
42 None
43

44
45 When did these symptoms start for abnormal vaginal discharge?

- 46 After previous visit
47 Persistent since previous visit
48 Recurrent since previous visit
49

50
51 When did these symptoms start for pain during urination?

- 52 After previous visit
53 Persistent since previous visit
54 Recurrent since previous visit
55
56
57
58
59
60

Adherence

NOTE

The following questions pertain to adherence to the STI medication.

Select Proceed

Proceed

Did you finish the whole course of treatment?

Yes
 No

How many days did you take treatment for?

Did you throw up within 2 hours after taking any of the STI treatment?

Yes
 No

Did you take any other non-chronic treatment at the time?

Yes
 No

What type of treatment were you taking ?

NOTE

You are done with questions related to Adherence. You are about to start asking questions associated with Disclosure.

Please select "Proceed"

Proceed

Disclosure

Did you have sex in the past month?

Yes
 No

1 How many different male partners did you have sexual intercourse with in the past month ?

- 2
3 1
4 2
5 More than 2 partners
6

7 Please specify how many partners?
8
9
10 _____
11 _____

12 What type of sex did you have with partner 1 (Husband/ Steady partner)?

- 13
14 Vaginal
15 Anal
16 Oral
17

18 Did you use a condom the last time you had sex with this partner?

- 19
20
21 Yes
22 No
23

24 Did you notify him of your STI result?

- 25
26 Yes I gave him the notification slip
27 Yes I told him
28 No
29

30 What was his reaction when you told him of your STI infection?

- 31
32 Supportive
33 Angry
34 Violent
35 Disengaged
36

37 How did disclosure affect your relationship?

- 38
39 Continued as before
40 Started using a condom
41 He engaged with other partners
42 He refused sex
43 Relationship ended
44

45 Did he take the treatment?

- 46
47 Yes
48 No
49 Don't know
50

51 Where did he seek treatment?

- 52
53 Private
54 Public
55 Traditional
56
57
58
59
60

1 Why did you not notify this partner?
2

- 3 I didn't feel it was necessary
4 I am embarrassed
5 I'm afraid he gets angry
6 I'm afraid he gets violent
7 I'm afraid he will end the relationship
8

9 What type of sex did you have with partner 2?
10

- 11 Vaginal
12 Anal
13 Oral
14

15 Did you use a condom the last time you had sex with this partner?
16

- 17 Yes
18 No
19

20 Did you notify him of your STI result?
21

- 22 Yes I gave him the notification slip
23 Yes I told him
24 No
25

26 What was his reaction when you told him of your STI infection?
27

- 28 Supportive
29 Angry
30 Violant
31 Disengaged
32

33 How did disclosure affect your relationship?
34

- 35 Continued as before
36 Started using a condom
37 He engaged with other partners
38 He refused sex
39 Relationship ended
40

41 Did he take the treatment?
42

- 43 Yes
44 No
45 Don't know
46

47 Where did he seek treatment?
48

- 49 Private
50 Public
51 Traditional
52
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60

1 Why did you not notify your partner?
2

- 3 I didn't feel it was necessary
- 4 I am embarrassed
- 5 I'm afraid he gets angry
- 6 I'm afraid he gets violent
- 7 I'm afraid he will end the relationship

8
9 Did you tell anyone else of your STI infection?
10

- 11 Yes
- 12 No

13
14 Who did you tell?
15 (Select multiple)
16

- 17 Family member
- 18 Friend
- 19 Healthcare worker
- 20 Other

21
22 NOTE:
23 You have completed the ToC questionnaire. Please select "Proceed" to capture the outcome of the STI test.
24

- 25 Proceed

26
27
28 **ToC Outcome**

	Positive	Negative	Did not test
30 CT	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
31 NG	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
32 TV	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

33
34
35
36 NOTE: See calculation

37 The result from the STI result (1 = Positive, 0 = Negative)

38
39
40 Does the participant show any symptoms of an STI?
41

- 42 Yes
- 43 No

44
45 Please contact the study clinician and discuss treatment.
46
47
48
49
50
51
52
53
54
55
56
57
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59
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1 The participant tested/screened positive for an STI. Please specify the treatment that has been provided.

- 2
3 Azithromycin 1g stat dose
4 Azithromycin 2g stat dose
5 Ceftriaxone 250mg IM injection
6 Ceftriaxone 1g IM injection
7 Metronidazole 400mg bd x 1 week
8 Metronidazole 2g stat dose
9 Clotrimazole pessary and/or cream
10 Ceftriaxone 500mg IM injection

11
12 Date treatment given
13
14
15 _____
16

17 Please specify if a partner notification has been given to the patient.

- 18
19 Yes
20 No
21

22 **NOTE**

23 The patient did not test positive or show any signs of an infection

24 Select "Proceed" to conclude visit

- 25
26
27 Proceed
28
29

30 **Notes**

31
32
33
34
35 Additional notes
36
37
38
39
40

41 You have completed the ToC Visit Activities. Please make sure to check if all relevant fields have been selected and
42 the information captured is accurate.

43
44 Once this is done, please select the "Complete" option below and then select "Save & Exit".
45
46
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60

ToC specimens_result

You are about to capture the results of the first loop used for Nugent scoring.

Please select "Proceed" to continue

Proceed

Was the reading satisfactory for the Nugent score?

Yes

No

Please specify the Nugent score

Please specify if candida was present

Yes

No

Additional comments

You are about to capture the results of the second loop used for smear microscopy.

Please select "Proceed" to continue

Proceed

Was the reading satisfactory?

Yes

No

Please specify the Nugent score

1 Please specify if candida was present

- 2
3 Yes
4 No
5

6 Additional comments
7
8
9
10
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60

For peer review only

Scheduling_Office

Scheduling the Dates Associated with the 32 Week Gestational Visit

The pregnancy (in days) is currently:

NOTE

You are about the start scheduling dates associated with the 32-week visit. You will need to schedule the following associated dates:

1. Week 32 date - Actual visit
2. Week 32 reminder date
3. Week 30 date - Visit window opens
4. Week 35 date - Visit window closes

Select "Proceed" to start scheduling

Proceed

Schedule the date for the 32 week gestational age, visit

Note to RA: please make sure that this date does not fall on Friday, weekend, and public holidays.

Calculate assist for 32-week visit

The number here must between 210 and 244.

Days Difference (the difference between 32 weeks & Gestational age)

Match

The date you have entered does not meet the 93 day criteria. Does the intended or original date fall on a Friday weekend or public holiday?

- Yes
 No
-

ERROR

The numbers you have entered does not match. Please select a different date so that the numbers match.

Dates Associated with reminder for the 32 Week Gestational Age Visit

Dates associated with the 32 weeks gestational age missed visit

NOTE:

You have successfully scheduled the 32-week date.

We will need to contact the participant at least 3 days before the scheduled visit to remind them.

Select "Proceed" to schedule the reminder date for the 32 week visit.

Proceed

Note:
Schedule the date for the 32 week reminder. We will contact each participant starting 3 days prior to their 32-week gestation date. That means the date scheduled here should be 3 days earlier than the scheduled date for the 32-week visit. If the date falls on a weekend choose the closest week date.

Calculation assist for scheduling the 32-week reminder date.

This number must be between 1 and 4.

ERROR

The date that you have entered is invalid. Please select a different date so that the number is less than or equal to 3.

NOTE:

You have successfully scheduled the 32-week reminder date.

Select "Proceed" to schedule the 32 week open visit date.

Proceed

Schedule the date for the 32 weeks opening visit date.

Note: Participants will have from 30 weeks of gestation to present for their 32-week visit date.

Calculation Assist for scheduling the 32-Week opening visit date.

This number must equal to 210

ERROR

The number you have entered does not match 210. Please select a different date so that the number equals 210.

NOTE:

You have successfully scheduled the 32-week opening date.

Select "Proceed" to schedule the 32 weeks missed visit date.

Proceed

1 Schedule the date for the 32 weeks missed visit date.
2

3 Note: Participants will have until 34 weeks of gestation to present for their 32-week visit date after which the visit will
4 be closed out.
5
6
7
8

9 Calculation Assist for scheduling the 32-Week missed visit date.
10

11 This number must equal to 244
12
13
14
15

16 ERROR

17 The number you have entered does not match 244. Please select a different date so that the number equals to 244.
18
19
20

21 22 23 **Estimated Delivery Date** 24

25 You are about the schedule the Estimated Delivery Date.
26

27 Please select "proceed"
28

29 Proceed
30

31 Estimated Delivery Date
32
33
34
35

36 Days difference between estimated date of delivery and gestational age
37
38
39
40

41 Calculation Assist for scheduling the Estimated Date for Delivery date.
42

43 This number must equal to [edod_calc]
44
45
46
47

48 Match
49
50
51

52 ERROR

53 The number you have entered does not match. Please select a different date so that the numbers match
54

55 You have completed all the scheduling dates.
56

57 Please check that all dates entered comply with the "calculation assistance".
58
59
60

1 You are about the schedule dates associated with the following events:
2
3

4 1. Pre-birth check-inn

5
6 Proceed
7
8

9
10
11 **Check-In Calling at 37 Weeks**
12
13
14
15

16 Proceed to the check-in calling date

17
18 Proceed
19

20
21 Check-in calling date
22
23
24 _____
25

26 Calculation Assist for check-in calling date

27 This number must equal to 259

28
29
30
31 _____
32

33 **NOTE**

34 The date you have entered is incorrect. Please make sure that the numbers correspond.
35

36 **CONGRATULATIONS**

37
38 You have finished scheduling all dates.
39
40
41
42
43
44
45
46
47
48
49
50
51
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60

32-Week Visit Activities

Staff name

Today's date

Start time

Did the participant present within the dates presented below:

30-34 Week Start Date: [week_28_arm_1][sched_32w_open_date]

30-34 Week Actual Date: [week_28_arm_1][week32_visit_date]

30-34 Week Closing Date: [week_28_arm_1][sched_32w_mv_date]

- Yes
- No

Open ad-hoc visit to capture relevant information

Specimen Collection_32-Week

NOTE

You will now start with the process of specimen collection. You will need to collect several specimens from the participant. These specimens need to be collected in the order in which they are presented here.

The following specimens will need to be collected:

1. 1 x Vaginal loop to be used to prepare two slides
2. 1 x Vaginal swab to be used for STI testing (Arm 2 and Microbiome (Empilweni): immediate testing; Arm 1 and 3: Storage)
3. 1 x Vaginal swab to be used for profiling
4. 2 x Vaginal swab to be used for microbiome
5. 1 x Vaginal swab to be used for cytokine

- Proceed

Vaginal Smear

Please specify the vaginal pH

(if not available, enter 99)

1 Please select which pH strips are used to measure vaginal pH

- 2
3 CardinalHealth pH Indicator Strips (range 3.6-6.1)
4 pH Indicator Strips pH 0-14
5 Natureland vaginal pH test (range 3.5-6.5)
6

7 You will need to use a single loop to collect vaginal smear on two glass slides for microscopy
8 (if not available, enter 99)

9
10 Done
11

12 Confirm PIN associated with the first Vaginal Loop to be used to test for Nugent score

13
14 [baseline_arm_1][participant_pin] - WL1
15

16 Confirm PIN associated with the second Vaginal Loop to be used to test for Yeast microscopy

17
18 [baseline_arm_1][participant_pin] - WL2
19
20

21 Vaginal Swabs
22

23 NOTE

24 You will now collect four vaginal swabs. They will be used as follows:

- 25
26 1. STI testing (Arm 2 and Microbiome (Empilweni): immediate testing; Arm 1 and 3: Storage)
27 2. Profiling (stored)
28 3. Microbiome (stored)
29 4. Cytokine (stored)
30

31 Done
32

33 Confirm PIN associated with the vaginal swab to be used to test for STI

34
35 [baseline_arm_1][participant_pin] - WV1
36

37 Please confirm PIN associated with the vaginal swab to be used for Profiling

38
39 [baseline_arm_1][participant_pin] - WV2
40
41

42 Please confirm PIN associated with the vaginal swab to be used for microbiome

43
44 [baseline_arm_1][participant_pin] - WV3
45

46 Please confirm the PIN associated with the vaginal swab that will be used for cytokines.

47
48 [baseline_arm_1][participant_pin] - WV4
49

50 NOTE

51 The participant is in arm 2 and therefore an immediate STI test is conducted at the 32-week visit. Please prepare the
52 swab for testing before you continue to the questionnaires.
53

54 Proceed
55

56 NOTE

57 You are done with all specimen collection and will now proceed to administering the clinical history.

58 Please select "Proceed"

59
60 Proceed

Clinical History Review

Have you been to the clinic since the last visit with us?

- Yes
 No

What was the purpose of your visit?

- ANC Visit
 HIV/ART
 STI Treatment
 Other

Summary notes from visit

Have you used any of the following since the first study visit?

Select multiple

- Alcohol
 Tik
 Dagga
 Grandpa
 Other
 None

Please specify other drugs used?

Do you currently have any of the following symptoms?

RA: Please select all that apply

- Abnormal vaginal discharge
 Pain during urination
 Lower abdominal pain
 Pain related to intercourse
 Vaginal bleeding related to intercourse
 Genital itchiness
 Any skin abnormalities
 None

When did these symptoms start for abnormal vaginal discharge?

- After previous visit
 Persistent since previous visit
 Recurrent since previous visit

1 When did these symptoms start for pain during urination?
2

- 3 After previous visit
4 Persistent since previous visit
5 Recurrent since previous visit
6

7 When did these symptoms start for the lower abdominal pain?
8

- 9 After previous visit
10 Persistent since previous visit
11 Recurrent since previous visit
12

13 When did these symptoms start for the pain related to intercourse?
14

- 15 After previous visit
16 Persistent since previous visit
17 Recurrent since previous visit
18

19 When did these symptoms start for vaginal bleeding related to intercourse?
20

- 21 After previous visit
22 Persistent since previous visit
23 Recurrent since previous visit
24

25 When did these symptoms start for genital itchiness?
26

- 27 After previous visit
28 Persistent since previous visit
29 Recurrent since previous visit
30

31 Please specify any skin abnormalities
32
33
34
35
36
37

38 Baseline Treatment Date:

39 [baseline_arm_1][sti_treatment_date]
40

41 TOC Treatment Date:

42 [toc_arm_1_arm_1][toc_sti_treatment_date]
43

44 Did the participant receive any STI treatment at their last study visit?
45

- 46 Yes
47 No
48

49 Are you planning to wait for your results today?
50 (New question added @13/09/2022)
51

- 52 Yes
53 No
54
55
56
57
58
59
60

1 What is your main reason why you are not intending to wait today?
2 (New question added @13/09/2022)
3

- 4 Have to get to work
5 Have to get back to my kids/family
6 Want to go to the shop
7 Transport availability
8 Lack of privacy
9 Hungry
10 No space to wait
11 Not feeling well
12 Boring
13 Other

14
15 If "Other", please specify.
16 (New question added @13/09/2022)
17
18
19
20
21

22 What would make you change your mind?
23 (New question added @13/09/2022)
24
25
26
27
28

29 You are done with questions associated with clinical history review. You will now start with questions associated with
30 Adherence.
31

- 32 Proceed
33
34

35 Adherence

36
37
38

39 Did you finish the whole course of STI treatment
40

- 41 Yes
42 No
43

44 How many days did you take treatment for?
45
46
47
48 _____
49

50 Did you throw up within 2 hours after taking any of the STI treatment
51

- 52 Yes
53 No
54

55 Did you take any other non-chronic treatment at the time
56

- 57 Yes
58 No
59

60 What type of treatment

1 You are done with questions associated with the adherence. You are about to start asking questions associated with
2 disclosure.

3
4 Proceed

5
6
7
8
9
10 **Disclosure**

11
12 Did you notify your partner of your STI result?

- 13 Yes I gave him the notification slip
14 Yes I told him
15 No

16
17
18 What was his reaction when you told him of your STI infection

- 19 Supportive
20 Angry
21 Violent
22 Disengaged

23
24
25 How did disclosure affect your relationship?

- 26 Continued as before
27 Started using a condom
28 He engaged with other partners
29 He refused sex
30 Relationship ended

31
32
33 Did he take treatment?

- 34 Yes
35 No
36 I don't know

37
38
39 Where did he seek treatment

- 40 Private
41 Public
42 Traditional

43
44
45 Why did you not notify your partner?

- 46 I didn't feel it was necessary
47 I am embarrassed
48 I'm afraid he gets angry
49 I'm afraid he gets violent
50 I'm afraid he will end the relationship

51
52
53 Did you tell anyone else of your STI infection?

- 54 Yes
55 No

1 Who did you tell?
2

- 3 Family member
4 Friend
5 HCW
6 Other
7
8

9
10
11
12 **Behavioral Questionnaire**
13

14 NOTE TO RA:

15 You just completed all questions related to Disclosure. You are about to start with the Behavioral Questionnaire.

16 Please select "Proceed":
17

- 18 Proceed
19

20
21 Did you have sex since the last visit?
22

- 23 Yes
24 No
25

26 How many different male partners did you have sexual intercourse with in the past month?
27

- 28 1
29 2
30 more than 2
31

32 Were any of these new partners than the ones from the last visit
33

- 34 Yes
35 No
36

37 What type of sex did you have with partner 1 (Husband/ Steady partner)?
38

- 39 Vaginal
40 Anal
41 Oral
42

43 Did you use a condom the last time you had sex with partner 1 (Husband/ Steady partner)?
44

- 45 Yes
46 No
47

48 What type of sex did you have with partner 2?
49

- 50 Vaginal
51 Anal
52 Oral
53

54 Did you use a condom the last time you had sex with partner 2?
55

- 56 Yes
57 No
58
59
60

1 What type of sex did you have with the rest of the partners?
2

- 3 Vaginal
4 Anal
5 Oral
6

7 Did you use a condom the last time you had sex with one of them?
8

- 9 Yes
10 No
11

12 Where are you planning to deliver?
13

- 14 Frere
15 CMH
16 Nontyantambo
17 Empilweni
18 Bisho
19 Other
20

21 Please specify
22
23
24
25
26
27

28 You are done with the questions associated with Behavioral Questionnaire. You will now start asking questions
29 associated with the Physical Examination.

- 30 Proceed
31
32

33 **Physical Examination** 34 35 36 37

38 Weight of mother
39
40
41 _____
42

43 Systolic blood pressure
44
45 _____
46
47

48 Diastolic blood pressure
49
50
51 _____
52

53 How was Hemoglobin measured?
54

- 55 Hb meter at the clinic
56 Hb at NHLS
57

58 Please capture Hb result"
59
60

1 Please capture the barcode for Hb
2
3
4 _____
5

6 Fundal height
7
8
9 _____
10

11 Progression of pregnancy

- 13 Progressing normal
14 Abnormality detected
15

16 Provide further details of abnormality
17
18
19
20
21
22

23 During your examination, were there any signs of abnormal vaginal discharge?
24

- 25 Yes
26 No
27

28 During your examination, were there any signs of inguinal lymphadenopathy?
29

- 30 Yes
31 No
32

33 Are these bubo?
34

- 35 Yes
36 No
37

38 Note to RA: Please contact the study clinician and specify treatment given to the participant
39
40
41
42
43
44

45 During your examination, were there any signs of lower abdominal pain?
46

- 47 Yes
48 No
49

50 During your examination, were there any signs of scratch marks?
51

- 52 Yes
53 No
54

55 During your examination, were there any signs of skin conditions?
56

- 57 Yes
58 No
59

60 Please specify the nature of the skin conditions

1 During your examination, were there any other observations that need to be noted?
2
3
4
5
6

7 You have completed the questions associated with the Physical Examination. You will now start capturing the results
8 from the rapid tests.
9

10 Proceed
11
12

13 Rapid Test Results 14 15 16 17

18 Do you know your current HIV status?
19

- 20 HIV negative (tested today by clinical staff)
21 HIV positive on ART
22 HIV positive, not on ART
23 Don't know (never tested)
24 Don't know (no yet tested today)
25

26 Was the participant newly diagnosed with HIV today
27

- 28 Yes
29 No
30

31 Please conduct an HIV Rapid test and capture the result below
32

- 33 Positive
34 Negative
35

36 Please conduct a confirmatory HIV Rapid test and capture the result below
37

- 38 Positive
39 Negative
40

41 Did you collect a tube of blood for CD4 count?
42

- 43 Yes
44 No
45

46 Please record barcode for blood tube for CD4 count testing?
47
48
49
50 _____
51

52 Is the participant's most recent CD4 count since Baseline available?
53

- 54 Yes
55 No
56

57 What was the date of the CD4 specimen collection?
58
59
60 _____

1 What was the participant's most recent CD4 count?
2
3
4

5 _____
6 (if no number listed, enter 9999)
7

8 Did you collect a tube of blood for viral load?
9

- 10 Yes
11 No
12

13 Please record barcode for blood tube for viral load testing?
14
15
16 _____
17

18 Is the participant's most recent viral load since Baseline available?
19

- 20 Yes
21 No
22

23 What was the date of the viral load specimen collection?
24
25
26 _____
27

28 What was the participant's most recent viral load?
29
30
31 _____
32 (if no number listed, enter 0000)
33

34 Which regimen for ART were you started on today?
35

- 36 TLD
37 TEE
38 AZT/3TC/LPV
39 Other
40

41 Which regimen for ART were you on so far?
42

- 43 TLD
44 TEE
45 AZT/3TC/LPV
46 Other
47

48 Has the regimen for ART been changed today?
49

- 50 Yes
51 No
52

53 To which regimen for ART has it been changed today?
54

- 55 TLD
56 TEE
57 AZT/3TC/LPV
58 Other
59
60

1 Has a syphilis test been done for the participant?
2

- 3 Yes
4 No
5

6 Which syphilis test have you used?
7

- 8 Alere Syphilis TP (provided by FPD)
9 HIV/Syphilis Duo (provided by FPD)
10 No rapid test used only NHLS bloods for RPR
11 Other please specify
12

13 Please specify
14
15
16
17
18
19

20 Syphilis result.

- 21 Positive
22 Negative
23 Indeterminate
24

25 Titer value 1:
26
27
28

29 _____
30 (If RPR is non-reactive, enter 0)
31

32 Blood needs to be collected for further syphilis testing. Please confirm if blood was collected.
33

- 34 Yes
35 No
36

37 Collect blood for RPR and capture barcode PIN below
38
39
40 _____
41

42 Treatment given
43

- 44 Benzathine penicillin 2.4 MU IM weekly x3
45 Out of stock
46

47 Please contact study clinician and specify treatment given
48
49
50
51
52

53 Please collect participant's urine for testing
54
55
56
57
58
59
60

Urine Dipstick test results

You are about to capture the results from the dipstick testing

Please select "Proceed" to continue

Proceed

Blood - Hemoglobin

Negative

Ca. 10

Ca. 50

Ca. 250/300

Blood - Erythrocytes

Negative

Ca. 5 -10

Ca. 50

Ca. 250/300

Urobilinogen

Normal

2

4

8

12

Bilirubin

Negative

1 plus

2 plus

3 plus

Not available

Protein

Negative

30

100

500

Nitrate

Negative

Positive

1 Keton

- 2
- 3 Negative
- 4 1 plus
- 5 2 plus
- 6 3 plus
- 7 Not available

8

9 Glucose

- 10
- 11 Negative
- 12 Normal
- 13 50
- 14 150
- 15 500
- 16 ≥1000

17

18 pH

- 19
- 20 5
- 21 6
- 22 7
- 23 8
- 24 9
- 25 Not available

26

27 SG

- 28
- 29 1.000
- 30 1.005
- 31 1.010
- 32 1.015
- 33 1.020
- 34 1.025
- 35 1.030
- 36 Not available

37

38 Leucocytes

- 39
- 40 Negative
- 41 25
- 42 75
- 43 500

44

45

46

47

48 **STI Results and Screening**

49

50

51

52

53

54

55

56

57

58

59

60

The participant is in arm 2 or for Empilweni and therefore you are about to capture results for the STI testing.

Proceed

STI Test Outcome

The previous STI results of the participants are:

Baseline

NG:[baseline_arm_1][sti_result_ng]

CT:[baseline_arm_1][sti_result_ct]

TV:[baseline_arm_1][sti_result_tv]

TOC

NG:[toc_arm_1_arm_1][toc_ng]

CT:[toc_arm_1_arm_1][toc_ct]

TV:[toc_arm_1_arm_1][toc_tv]

	Negative	Positive
CT	<input type="radio"/>	<input type="radio"/>
NG	<input type="radio"/>	<input type="radio"/>
TV	<input type="radio"/>	<input type="radio"/>

STI Calculation _ w32

Date the result was obtained.

Did the participant wait for her STI results?
(New question added @ 03/11/2022)

Yes
 No

Was the participant reporting STI symptoms or showed symptoms during the clinical assessment?

Yes
 No

Does the participant report any medication allergies?

Yes
 No

1 Please contact the study clinician before giving any treatment. Please specify discussed medication allergies and
2 treatment plan with the study clinician
3
4
5
6
7

8 The following treatment has been provided
9

- 10 Azithromycin 1g stat dose
11 Azithromycin 2g stat dose
12 Ceftriaxone 250mg IM injection
13 Ceftriaxone 1g IM injection
14 Metronidazole 400mg bd x 1 week
15 Metronidazole 2g stat dose
16 Clotrimazole pessary and/or cream
17 Trimethoprim/sulfamethoxazole 400/80 mg 2 tbl. bds for 5 days (bactrim)
18 Ceftriaxone 500mg IM injection
19

20 Date treatment given
21
22
23 _____
24

25 What made you change your mind about waiting for the results?
26 (New question added @13/09/2022)
27
28
29
30
31

32 Partner notification provided
33

- 34 Yes, 1
35 Yes, multiple
36 No
37

38 Please explain why the partner notification note was not provided?
39
40
41
42
43
44

45 You have completed capturing the information from the 32 week exam. Please make sure to check that you have
46 completed all the fields.
47

48 Please select "Complete" then "Save and Exit".
49
50

51 Notes

52
53
54

55 Additional notes
56
57
58
59
60

32W specimens results

You are about to capture the results of specimens collected during the 32-week visit

Please select "Proceed" to continue

Proceed

Hb Results received

Yes

No

Please capture the Hb result

Please capture the barcode for Hb

Please specify whether the reading was satisfactory for the loop used for Nugent score

Yes

No

Please capture the score for the loop used for Nugent scoring

Please specify if candida was present for the loop used for Nugent scoring

Yes

No

Please specify whether the reading was satisfactory for the loop used for yeast microscopy

Yes

No

Please capture the nugent score for the loop used for yeast microscopy

1 Please specify if candida was present for the loop used for yeast microscopy

- 2
- 3 Yes
- 4 No
- 5

6 Please capture the results for the blood used for Syphilis testing

- 7
- 8 RPR Negative
- 9 RPR Positive
- 10 RPR Indeterminate
- 11
- 12
- 13
- 14
- 15
- 16 _____

17

18 Please capture the result for viral load testing

19 _____

20

21 _____

22

23 Is the participant's most recent viral load available?

- 24
- 25 Yes
- 26 No
- 27

28 What was the date of the viral load specimen collection?

29 _____

30

31 _____

32

33 What was the participant's most recent viral load?

34 _____

35

36 _____

37

38 _____

39

40

41 _____

42

43

44

45

46 **Notes**

47

48

49

50 Notes

51

52

53

54

55

56

57

58

59

60

Calling Reminders_2

Staff Name

Today's Date

Time

The presentation dates are below:

TOC

Date: [baseline_arm_1][toc_3week]

WEEK 28 CALLING

Date: [baseline_arm_1][sched_28w_rem]

WEEK-32

30-34 Week Actual Date: [week_28_arm_1][week32_visit_date]

Call In Check

Week 37 Call In Check: [week_28_arm_1][cic_date]

POST-NATAL VISIT

Visit open date: [predelivery_checki_arm_1][pd_remind_date_schedpd]

Visit close date: [predelivery_checki_arm_1][pd_close_date_schedpd]

Date of Delivery: [predelivery_checki_arm_1][pd_remind_date_delivery]

6-WEEK IMMUNIZATION VISIT

Actual Date: [predelivery_checki_arm_1][sixw_im_schedpd]

NOTE:

You are about to call a participant to remind them of a specific visit. Please make sure to do the following:

1. Obtain all relevant contact numbers for the participant on their record
2. Ensure that you have checked what the exact date is when the participant is expected to present
3. Make sure to give the participant a brief description of what will be done at the visit.
4. You will make up to 3 attempts to get hold of the participant.

Please select "Proceed"

Proceed

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>

Please select the calling attempt

- First Attempt
- Second Attempt
- Third Attempt

Details of Calling Attempt 1

Outcome of the attempt

- Successful - Participant
- Successful - Family member
- Unsuccessful - Voicemail
- Unsuccessful - Invalid

Date of the attempt

Did she deliver?

- Yes
- No

Capture delivery Date

NOTE: instruct to come to the site.

Details of Calling Attempt 2

Outcome of the attempt

- Successful - Participant
- Successful - Family member
- Unsuccessful - Voicemail
- Unsuccessful - Invalid

Date of the attempt

1 Did she deliver?
2

- 3 Yes
- 4 No

5
6 Capture delivery Date
7

8 NOTE: instruct to come to the site.
9

10
11
12
13
14 **Details of Calling Attempt 3**
15

16
17
18
19 Outcome of the attempt

- 20 Successful - Participant
- 21 Successful - Family member
- 22 Unsuccessful - Voicemail
- 23 Unsuccessful - Invalid

24
25
26 Date of the attempt
27

28
29
30
31 Did she deliver?
32

- 33 Yes
- 34 No

35
36 Capture delivery Date
37

38 NOTE: instruct to come to the site.
39

40
41
42
43
44
45 **Notes**
46

47 Calling notes
48
49
50
51
52
53
54
55
56
57
58
59
60

Schedule calling for 38 weeks

NOTE FW: Please make sure that you call the participant once per week.

Proceed

Did you schedule the 38 weeks call

Yes

No

Please select the calling attempt

First Attempt

Second Attempt

Third Attempt

Details of Calling Attempt 1

Outcome of the attempt

Successful - Participant

Successful - Family member

Unsuccessful - Voicemail

Unsuccessful - Invalid

Date of the attempt

Did she deliver?

Yes

No

Details of Calling Attempt 2

Outcome of the attempt

Successful - Participant

Successful - Family member

Unsuccessful - Voicemail

Unsuccessful - Invalid

Date of the attempt

1 Did she deliver?
2

- 3 Yes
4 No
5
6

7 **Details of Calling Attempt 3**
8
9
10
11
12
13

14 Outcome of the attempt
15

- 16 Successful - Participant
17 Successful - Family member
18 Unsuccessful - Voicemail
19 Unsuccessful - Invalid
20

21 Date of the attempt
22
23
24
25 _____
26

27 Did she deliver?
28

- 29 Yes
30 No
31
32

33 **Schedule calling for 39 weeks**
34

35 NOTE FW: Please make sure that you call the participant once per week.
36

- 37 Proceed
38
39

40 Did you schedule the 39 weeks call
41

- 42 Yes
43 No
44

45 Please select the calling attempt
46

- 47 First Attempt
48 Second Attempt
49 Third Attempt
50
51
52
53
54
55
56
57
58
59
60

Details of Calling Attempt 1

Outcome of the attempt

- Successful - Participant
 Successful - Family member
 Unsuccessful - Voicemail
 Unsuccessful - Invalid

Date of the attempt

Did she deliver?

- Yes
 No

Capture delivery Date

NOTE: instruct to come to the site.

Details of Calling Attempt 2

Outcome of the attempt

- Successful - Participant
 Successful - Family member
 Unsuccessful - Voicemail
 Unsuccessful - Invalid

Date of the attempt

Did she deliver?

- Yes
 No

Details of Calling Attempt 3

Outcome of the attempt

- Successful - Participant
 Successful - Family member
 Unsuccessful - Voicemail
 Unsuccessful - Invalid

Date of the attempt

1 Did she deliver?
2

- 3 Yes
4 No
5

6 Calling notes
7
8
9
10
11
12

13 Schedule calling for 40 weeks 14

15 NOTE FW: Please make sure that you call the participant once per week.
16

- 17 Proceed
18

19 Please select the calling attempt
20

- 21 First Attempt
22 Second Attempt
23 Third Attempt
24

25 Did you schedule a call for 40 weeks
26

- 27 Yes
28 No
29
30

31 Details of Calling Attempt 1 32 33 34

35 Outcome of the attempt
36

- 37 Successful - Participant
38 Successful - Family member
39 Unsuccessful - Voicemail
40 Unsuccessful - Invalid
41
42

43 Date of the attempt
44
45
46
47

48 Did she deliver?
49

- 50 Yes
51 No
52

53 Capture delivery Date
54

55 NOTE: instruct to come to the site.
56
57
58
59
60

Details of Calling Attempt 2

Outcome of the attempt

- Successful - Participant
 Successful - Family member
 Unsuccessful - Voicemail
 Unsuccessful - Invalid

Date of the attempt

Did she deliver?

- Yes
 No

Details of Calling Attempt 3

Outcome of the attempt

- Successful - Participant
 Successful - Family member
 Unsuccessful - Voicemail
 Unsuccessful - Invalid

Date of the attempt

Calling notes

Did she deliver?

- Yes
 No

Schedule calling for 41 weeks

NOTE FW: Please make sure that you call the participant once per week.

- Proceed

Please select the calling attempt

- First Attempt
 Second Attempt
 Third Attempt

1 Did you schedule a call for 41 weeks

- 2
3 Yes
4 No
5
6

7 **Details of Calling Attempt 1**

8
9 Outcome of the attempt

- 10 Successful - Participant
11 Successful - Family member
12 Unsuccessful - Voicemail
13 Unsuccessful - Invalid
14

15
16 Date of the attempt

17
18
19 _____
20
21

22 **Details of Calling Attempt 2**

23
24 Outcome of the attempt

- 25 Successful - Participant
26 Successful - Family member
27 Unsuccessful - Voicemail
28 Unsuccessful - Invalid
29

30
31 Date of the attempt

32
33
34 _____
35

36 Did she deliver?

- 37 Yes
38 No
39
40

41
42 **Details of Calling Attempt 3**

43
44 Outcome of the attempt

- 45 Successful - Participant
46 Successful - Family member
47 Unsuccessful - Voicemail
48 Unsuccessful - Invalid
49

50
51 Date of the attempt

52
53
54 _____
55

56 Calling notes

57
58
59
60

1 Did she deliver?
2

- 3 Yes
4 No
5

6 Capture delivery Date
7

8 NOTE: instruct to come to the site.
9
10
11
12
13

14 **Schedule calling for 41 weeks (293 days)** 15

16 NOTE FW: Please make sure that you call the participant once per week.
17

- 18 Proceed
19

20 Did you schedule a call for 41 weeks
21

- 22 Yes
23 No
24

25 Please select the calling attempt
26

- 27 First Attempt
28 Second Attempt
29 Third Attempt
30
31

32 **Details of Calling Attempt 1** 33

34 Outcome of the attempt
35

- 36 Successful - Participant
37 Successful - Family member
38 Unsuccessful - Voicemail
39 Unsuccessful - Invalid
40

41 Calling notes
42
43
44
45
46

47 Did she deliver?
48

- 49 Yes
50 No
51

52 Capture delivery Date
53

54 NOTE: instruct to come to the site.
55
56
57
58
59
60

Schedule calling for 42 weeks (296 days)

NOTE FW: Please make sure that you call the participant once per week.

Proceed

Please select the calling attempt

First Attempt

Second Attempt

Third Attempt

Did you schedule a call for 42 weeks

Yes

No

Details of Calling Attempt 1

Outcome of the attempt

Successful - Participant

Successful - Family member

Unsuccessful - Voicemail

Unsuccessful - Invalid

Date of the attempt

Did she deliver?

Yes

No

Details of Calling Attempt 2

Outcome of the attempt

Successful - Participant

Successful - Family member

Unsuccessful - Voicemail

Unsuccessful - Invalid

Date of the attempt

1 Did she deliver?
2

- 3 Yes
4 No
5
6

7 **Details of Calling Attempt 3**
8
9
10

11
12 Outcome of the attempt

- 13 Successful - Participant
14 Successful - Family member
15 Unsuccessful - Voicemail
16 Unsuccessful - Invalid
17

18
19 Date of the attempt
20
21
22 _____
23

24
25 **Outcome of the call**
26
27
28

29 Did the participant deliver?
30

- 31 Yes
32 No
33

34 Calling notes
35
36
37
38
39

40 Did she deliver?
41

- 42 Yes
43 No
44

45 Capture delivery Date
46

47 NOTE: instruct to come to the site.
48
49
50
51 _____
52
53
54
55
56
57
58
59
60

Scheduling_Post_Delivery_Activities using Updated EDD

You are about the schedule dates associated with the following events:

1. Post-Delivery Appointment
2. 6-Weeks Immunization Appointment

Proceed

Post-Delivery Study Visit

You will now schedule dates associated with the post-delivery study visit.

The following dates are associated with this visit:

1. Calling reminder date / Visit opening date
2. Visit closing date

Select "Proceed" to continue

Proceed

Please capture the date of delivery

Please schedule the date for the post-delivery reminder call.

Please note that the Delivery date is [pd_remind_date_delivery]. The reminder call will happen 1 day following delivery.

Calculation Assist for Post Delivery reminder call

This number must equal to: 1

Match

NOTE

The date you have entered is incorrect. Please make sure that the numbers correspond.

1 The post-delivery closing date.

6 Calculation Assist for Post Delivery closing date

8 The participant will have 14 days post-delivery to present at the clinic. The delivery date was
9 [pd_remind_date_delivery]. This number must therefore equal to: 14

14 Match

21 NOTE

23 The date you have entered is incorrect. Please make sure that the numbers correspond.

27 Facility delivered

- Frere
 CMH
 Nontyantambo
 Empilweni
 Bisho
 Other

34 Please specify the facility of delivery

42 **6-Week Immunization Visit**

46 NOTE:

47 In this section you will schedule all dates associated with the 6-Week Immunization Study Visit. These dates will
48 include:

- 50 1. Calling reminder date for 6-Weeks Immunization visit
 51 2. Scheduled date of 6-Weeks Immunization visit
 52 3. Closing date for attending the 6-Weeks Immunization visit

54 Select Proceed to continue

55 Proceed

58 Please schedule the date for the 6-weeks immunization reminder

1 Calculation Assist for 6-weeks immunization reminder. We will call all patients 5 weeks (35 days) following their
2 delivery date. The updated delivery date for the participant was [calling_delivery_date_37weeks].
3

4 This number must therefore equal to: 35 and 40
5
6
7 _____
8

9 Match
10
11
12 _____
13

16 NOTE
17 The date you have entered is incorrect. Please make sure that the numbers correspond.
18
19
20

21
22 Please schedule the date for the 6-weeks immunization visit. This visit is scheduled to take place 6 weeks (42 days)
23 following delivery. The updated delivery date is [calling_delivery_date_37weeks]
24
25
26 _____
27

28 Calculation Assist for 6-weeks immunization visit
29

30 This number must equal to: 42
31
32
33 _____
34

35 Match
36
37
38 _____
39

40 NOTE
41 The date you have entered is incorrect. Please make sure that the numbers correspond.
42

43 Please schedule the date for the 6-weeks immunization visit closing date.
44
45
46 _____
47

48 Calculation Assist for 6-Weeks Immunization visit Close Date. Mothers will have up to 8 weeks post delivery to attend
49 this visit. This means 56 days following the delivery.
50

51 This number must equal to: 56
52
53
54 _____
55

56 Match
57
58
59 _____
60

1
2
3
4
5
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7
8
9
10
11
12
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14
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NOTE

The date you have entered is incorrect. Please make sure that the numbers correspond.

CONGRATULATIONS

You have finished scheduling all dates.

For peer review only

Birth Register Data

Participant PIN

[baseline_arm_1][participant_pin]

Staff name

Today's date

Start time

You are about to capture data retrieved from the birth registry. Please select "Proceed" to start

Proceed

Delivery Details

Delivery site

- Frere
- CMH
- Nontyantyambo
- Empilweni
- Bisho
- Other

Please specify name of delivery facility

Clinic file number

Delivery date

Calculated gestational age

(Added @22/03/2023)

1 Please specify the number of babies during pregnancy

- 2
3 1
4 2
5 3
6

7 Outcome type for baby 1

- 8
9 Live birth
10 Still birth
11 Early Neonatal Death
12

13 Outcome type for baby 2

- 14
15 Live birth
16 Still birth
17 Early Neonatal Death
18

19 Outcome type for baby 3

- 20
21 Live birth
22 Still birth
23 Early Neonatal Death
24

25 Type of delivery for baby 1

- 26
27 Born before arrival
28 Normal Vaginal Delivery
29 Assisted Vaginal Delivery
30 Elective Cesarean Section
31 Emergency Cesarean Section
32

33 Type of delivery for baby 2

- 34
35 Born before arrival
36 Normal Vaginal Delivery
37 Assisted Vaginal Delivery
38 Elective Cesarean Section
39 Emergency Cesarean Section
40

41 Type of delivery for baby 3

- 42
43 Born before arrival
44 Normal Vaginal Delivery
45 Assisted Vaginal Delivery
46 Elective Cesarean Section
47 Emergency Cesarean Section
48

49 Please specify reason

50
51
52
53
54
55
56 Please specify reason
57
58
59
60

1 Please specify reason
2
3
4
5
6

7 Gender - Baby 1
8

- 9 Female
10 Male
11

12 Gender - Baby 2
13

- 14 Female
15 Male
16

17 Gender - Baby 3
18

- 19 Female
20 Male
21
22

23 **Complications in labor/Delivery**
24

	Yes	No
25 Induction of labour	<input type="radio"/>	<input type="radio"/>
26 Antepartun haemorrhage	<input type="radio"/>	<input type="radio"/>
27 Post Partum haemorrhage	<input type="radio"/>	<input type="radio"/>
28 Severe pre-eclampsia	<input type="radio"/>	<input type="radio"/>
29 Eclampsia	<input type="radio"/>	<input type="radio"/>
30 Prolonged rupture of membranes	<input type="radio"/>	<input type="radio"/>
31 Ruptured uterus	<input type="radio"/>	<input type="radio"/>
32 Sepsis	<input type="radio"/>	<input type="radio"/>
33 Obstructed or prolonged labour	<input type="radio"/>	<input type="radio"/>
34 Retained Placenta	<input type="radio"/>	<input type="radio"/>
35 Manual removal of placenta	<input type="radio"/>	<input type="radio"/>

36 Maternal outcome
37

- 38 Live
39 Death
40
41

42 APGAR score at 5 minutes for baby 1
43
44

45 _____
46
47

48 APGAR score at 5 minutes for baby 2
49
50

51 _____
52
53

54 APGAR score at 5 minutes for baby 3
55
56

57 _____
58
59
60

1 Birth weight for baby 1 in grams
2
3
4 _____
5

6 Birth weight for baby 2 in grams
7
8
9 _____
10

11 Birth weight for baby 3 in grams
12
13
14 _____
15

16
17 Did you breastfeed your baby/ies within 1 hour of giving birth?

- 18
19 Yes
20 No
21

22 Infant feeding
23 (New question added @15/11/2022)
24

- 25 Exclusive Breast Feeding (EBF)
26 Exclusive Formula Feeding (EFF)
27

28 Any birth defects to note for baby 1
29

- 30 Yes
31 No
32

33 Any birth defects to note for baby 2
34

- 35 Yes
36 No
37

38 Any birth defects to note for baby 3
39

- 40 Yes
41 No
42

43 Please specify
44
45
46
47
48
49

50 Remarks outcome
51
52
53
54
55

56 Maternal outcome
57
58
59
60

1 You have completed the Birth register. Please make sure to check if all relevant fields have been selected and the
2 information captured is accurate.
3

4 Once this is done, please select the "Complete" option below and then select "Save & Exit".
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
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53
54
55
56
57
58
59
60

For peer review only

Post-Natal Visit Activities

Staff name

Today's date

Start time

Post-Natal Visit

The participant was scheduled to present within the two dates below. Please specify if the participant presented within this timeframe.

Visit open date: [predelivery_checki_arm_1][pd_remind_date_delivery]

Visit close date: [predelivery_checki_arm_1][pd_close_date_schedpd]

- Yes
 No

You are about to administer the questions associated with the post natal visit.

Please select "Proceed"

- Proceed?

Clinical History Review

Have you been to the clinic since the last visit with us?

- Yes
 No

What was the purpose of your visit?

- ANC Visit
 HIV/ART
 STI Treatment
 Other

Summary notes from the visit

1 Were there any abnormalities/complications since your last study visit regarding your pregnancy and delivery or did
2 you receive any non-chronic treatment?
3

- 4 Yes
5 No
6

7 Please specify
8
9
10
11
12

13 Have you used any of the following since the first study visit?
14 Select multiple
15

- 16 Alcohol
17 Tik
18 Dagga
19 Grandpa
20 Other
21 None
22

23 Please specify other drugs used?
24
25
26
27
28

29 The Baseline STI results of the participants are:

30 NG: [baseline_arm_1][sti_result_ng]

31 CT: [baseline_arm_1][sti_result_ct]

32 TV: [baseline_arm_1][sti_result_tv]

33 The TOC STI results of the participants are:

34 NG: [toc_arm_1_arm_1][toc_ng]

35 CT: [toc_arm_1_arm_1][toc_ct]

36 TV: [toc_arm_1_arm_1][toc_tv]

37 The Week 32 STI results of the participants are:

38 CT: [3034_weeks_arm_1][w32_ct_res]

39 NG: [3034_weeks_arm_1][w32_ng_res]

40 TV: [3034_weeks_arm_1][w32_tv_res]

41 Did the participant receive any STI treatment at their last study visit?
42
43
44

- 45 Yes
46 No
47
48
49
50
51
52
53
54

Adherence

You are done with questions associated with the clinical history review. You will now start with questions associated with Adherence.

Proceed

Did you finish the whole course of STI treatment?

Yes

No

How many days did you take treatment for?

Did you throw up within 2 hours after taking any of the STI treatment?

Yes

No

Did you take any other non-chronic treatment at the time?

Yes

No

What type of treatment

Disclosure

You are done with questions associated with the adherence. You are about to start asking questions associated with disclosure.

Proceed

Did you notify your partner of your STI result?

Yes I gave him the notification slip

Yes I told him

No

What was his reaction when you told him of your STI infection

Supportive

Angry

Violent

Disengaged

1 How did disclosure affect your relationship?
2

- 3 Continued as before
4 Started using a condom
5 He engaged with other partners
6 He refused sex
7 Relationship ended
8

9 Did he take treatment?
10

- 11 Yes
12 No
13 I don't know
14

15 Where did he seek treatment?
16

- 17 Private
18 Public
19 Traditional
20

21 Why did you not notify your partner?
22

- 23 I didn't feel it was necessary
24 I am embarrassed
25 I'm afraid he gets angry
26 I'm afraid he gets violent
27 I'm afraid he will end the relationship
28

29 Did you tell anyone else of your STI infection?
30

- 31 Yes
32 No
33

34 Did you tell anyone else of your STI infection?
35

- 36 Yes
37 No
38

39 Who did you tell?
40

- 41 Family member
42 Friend
43 HCW
44 Other
45
46
47

48 Delivery Details of Infant

49
50
51

52 Facility delivered
53

- 54 Frere
55 CMH
56 Nontyantambo
57 Empilweni
58 Bisho
59 Other
60

Please specify facility of delivery

1 Date of delivery
2
3
4 _____
5

6 Calculated gestational age
7
8 _____
9

(Added @22/03/2023)

10 Please specify the number of babies during pregnancy
11

- 12
13 1
14 2
15 3
-

16 Outcome type for baby 1
17

- 18 Live birth
19 Still birth
20 Early Neonatal Death
21
-

22 Outcome type for baby 2
23

- 24 Live birth
25 Still birth
26 Early Neonatal Death
27
-

28 Outcome type for baby 3
29

- 30 Live birth
31 Still birth
32 Early Neonatal Death
33
-

34 Type of delivery for baby 1
35

- 36 Born before arrival
37 Normal Vaginal Delivery
38 Assisted Vaginal Delivery
39 Elective Cesarean Section
40 Emergency Cesarean Section
41
-

42 Type of delivery for baby 2
43

- 44 Born before arrival
45 Normal Vaginal Delivery
46 Assisted Vaginal Delivery
47 Elective Cesarean Section
48 Emergency Cesarean Section
49
-

50 Type of delivery for baby 3
51

- 52 Born before arrival
53 Normal Vaginal Delivery
54 Assisted Vaginal Delivery
55 Elective Cesarean Section
56 Emergency Cesarean Section
57
-

58 Please specify reason
59
60

1 Please specify reason
2
3
4
5
6

7 Please specify reason
8
9
10
11
12

13 Gender - Baby 1
14

- 15 Female
- 16 Male

17
18
19 Gender - Baby 2
20

- 21 Female
- 22 Male

23
24 Gender - Baby 3
25

- 26 Female
- 27 Male

28
29 Maternal outcome
30

- 31 Live
- 32 Death

33
34 Specify
35
36
37
38
39

40 APGAR score at 5 minutes for baby 1
41

42 Note to RA: Check on Road to Health
43
44
45

46 _____
(if no number listed, enter 99)
47

48 APGAR score at 5 minutes for baby 2
49

50 Note to RA: Check on Road to Health
51
52

53 _____
(if no number listed, enter 99)
54

55 APGAR score at 5 minutes for baby 3
56

57 Note to RA: Check on Road to Health
58
59

60 _____
(if no number listed, enter 99)

1 Birth weight in grams for baby 1

2
3 Note to RA: Check on Road to Health

4
5
6
7
8 Birth weight in grams for baby 2

9
10 Note to RA: Check on Road to Health

11
12
13
14
15 Birth Weight in grams for baby 3

16
17 Note to RA: Check on Road to Health

18
19
20
21
22 Newborn problems

23
24 Note to RA: Check on Road to Health

- 25
26 Birth defects
- 27 Hypoxic brain injury
- 28 Convulsions /fits
- 29 Jaundice
- 30 None

31
32 Please Specify

33
34
35
36
37
38 Was the baby exposed to HIV?

39 (Added @29/03/2023)

- 40
41 Yes
- 42 No

43
44 Was Nevirapine given to the baby/babies

- 45
46 Yes
- 47 No

48
49 Was birth PCR done for the baby/babies

- 50
51 Yes
- 52 No

53
54
55 NOTE: If not taken by birth facility please take blood for PCR.

56
57 PCR Barcode for the baby/baby 1

58
59
60

1 NOTE: If not taken by birth facility please take blood for PCR.
2

3 PCR Barcode for the baby/baby 2
4
5
6
7

8 NOTE: If not taken by birth facility please take blood for PCR.
9

10 PCR Barcode for the baby/baby 3
11
12
13
14

15 Result of birth PCR for baby 1
16

- 17 Positive
18 Negative
19 Indeterminate
20 Not yet available
21

22 Result of birth PCR for baby 2
23

- 24 Positive
25 Negative
26 Indeterminate
27 Not yet available
28

29 Result of birth PCR for baby 3
30

- 31 Positive
32 Negative
33 Indeterminate
34 Not yet available
35

36 Call clinician and make a note about this.
37
38
39
40
41
42

43 Was eye ointment given to the baby 1
44

- 45 Yes
46 No
47 Don't know
48

49 Was eye ointment given to the baby 2
50

- 51 Yes
52 No
53 Don't know
54

55 Was eye ointment given to the baby 3
56

- 57 Yes
58 No
59 Don't know
60

Please specify to how many babies and which one

1 Was the baby/babies admitted to hospital following delivery

- 2
3 Yes
4 No
5

6 Please specify the details about the reason for admission, number of babies admitted and which babies

7
8
9
10
11
12 Does baby 1 have any of the following symptoms?

- 13
14 Cough
15 Runny nose
16 Eye discharge
17 Sneezing
18 None
19

20 Does baby 2 have any of the following symptoms?

- 21
22 Cough
23 Runny nose
24 Eye discharge
25 Sneezing
26 None
27

28 Does baby 3 have any of the following symptoms

- 29
30 Cough
31 Runny nose
32 Eye discharge
33 Sneezing
34 None
35

36 Is the baby/babies receiving any treatment at the moment

- 37
38 Yes
39 No
40

41 Please specify

42 Feeding methods

- 43
44
45
46
47
48 Breastfeeding
49 Formula feeding
50 Mixed
51
52
53
54
55
56
57
58
59
60

Delivery details of Mother

Is the baby present with the biological mother

- Yes
 No

Please specify

Are you currently taking any treatment

- Yes
 No

Please specify

Have you had sexual intercourse since delivery of your baby?

- Yes
 No

Do you have any of the following symptoms?

- Discharge
 Pain when urinating
 None

Please specify

You have completed all the questions associated with this visit. You will now start with the process of specimen collection. You will need to collect the following specimens:

From the mother you will need to collect 3 vaginal swabs:

- Vaginal Swab 1 for STI testing (Storage)
- Vaginal Swab 2 for Microbiome (Storage)
- Vaginal Swab 3 for Profiling (Storage)

From the baby you need to collect:

- Nasopharyngeal swab
- Conjunctival

Select "Proceed" to capture the information associated with these specimens

Proceed

For peer review only - <http://bmjopen.bmj.com/site/about/guidelines.xhtml>

1 Please confirm the barcode for the vaginal swab collected for STI testing

2
3 [baseline_arm_1][participant_pin]-PNV1

5 Please confirm the barcode for the vaginal swab collected for Microbiome

7 [baseline_arm_1][participant_pin]-PNV3

10 Please confirm the Barcode for the Vaginal Swab collected for Profiling

12 [baseline_arm_1][participant_pin]-PNV2

14 Please confirm the Barcode for the Nasopharyngeal swab (right nose) baby 1

16 [baseline_arm_1][participant_pin]-PNB1N1

18 Please confirm the Barcode for the Nasopharyngeal swab (left nose) baby 1

20 [baseline_arm_1][participant_pin]-PNB1N2

23 Please confirm the barcode for the Nasopharyngeal swab (right nose) baby 2

24 [baseline_arm_1][participant_pin]-PNB2N1

27 Please confirm the barcode for the Nasopharyngeal swab (left nose) baby 2

28 [baseline_arm_1][participant_pin]-PNB2N2

31 Please confirm the barcode for the Nasopharyngeal swab (right nose) baby 3

33 [baseline_arm_1][participant_pin]-PNB3N1

35 Please confirm the barcode for the Nasopharyngeal swab (left nose) baby 3

37 [baseline_arm_1][participant_pin]-PNB3N2

39 Please confirm the Barcode for the Nasopharyngeal swab for STI testing baby 1

41 [baseline_arm_1][participant_pin]-PNB1N1

44 Please confirm the barcode for the Conjunctival swab (right eye) baby 1

45 [baseline_arm_1][participant_pin]-PNB1C1

48 Please confirm the barcode for the Conjunctival swab (left eye) baby 1

49 [baseline_arm_1][participant_pin]-PNB1C2

52 Please confirm the barcode for the Conjunctival swab (right eye) baby 2

54 [baseline_arm_1][participant_pin]-PNB2C1

56 Please confirm the barcode for the Conjunctival swab (left eye) baby 2

58 [baseline_arm_1][participant_pin]-PNB2C2

60

1 Please confirm the barcode for the Conjunctival swab (right eye) baby 3

2
3 [baseline_arm_1][participant_pin]-PNB3C1

4
5 Please confirm the barcode for the Conjunctival swab (left eye) baby 3

6
7 [baseline_arm_1][participant_pin]-PNB3C2

8
9 Please specify the vaginal pH

10
11
12
13 _____

14
15 Please select which pH strips are used to measure vaginal pH

16
17 CardinalHealth pH Indicator Strips (range 3.6-6.1)

18 pH Indicator Strips pH 0-14

19 Natureland vaginal pH test (range 3.5-6.5)

20
21 Did you give the participant the study voucher?

22
23 Yes

24 No

25
26 You have completed capturing the Post-Natal information. Please make sure to check that you have completed all
27 the fields.

28
29
30 Please give the participant 6 weeks immunization visit date as per schedule.

31
32
33 Please select "Complete" then "Save and Exit".

34
35
36 **Notes**

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40 Additional notes

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Post-Natal specimens Results

Date

Staff name

You are about to capture the results of the specimens collected during the post natal visit

Please select "Proceed" to continue

Proceed

Receive Date

Test date (Mother)

STI results from the mother

	Positive	Negative
CT	<input type="radio"/>	<input type="radio"/>
NG	<input type="radio"/>	<input type="radio"/>
TV	<input type="radio"/>	<input type="radio"/>

STI result, mother_calc

Test date (Baby)

STI Results from Baby 1

	Positive	Negative
CT (Right Nose)	<input type="radio"/>	<input type="radio"/>
NG (Right Nose)	<input type="radio"/>	<input type="radio"/>
TV (Right Nose)	<input type="radio"/>	<input type="radio"/>
CT (Left Nose)	<input type="radio"/>	<input type="radio"/>
NG (Left Nose)	<input type="radio"/>	<input type="radio"/>
TV (Left Nose)	<input type="radio"/>	<input type="radio"/>

1	CT (Right Eye)	<input type="radio"/>	<input type="radio"/>
2	NG (Right Eye)	<input type="radio"/>	<input type="radio"/>
3			
4	TV (Right Eye)	<input type="radio"/>	<input type="radio"/>
5	CT (Left Eye)	<input type="radio"/>	<input type="radio"/>
6	NG (Left Eye)	<input type="radio"/>	<input type="radio"/>
7			
8	TV (Left Eye)	<input type="radio"/>	<input type="radio"/>
9			

STI Results from Baby 2

	Positive	Negative
12		
13	<input type="radio"/>	<input type="radio"/>
14	<input type="radio"/>	<input type="radio"/>
15		
16	<input type="radio"/>	<input type="radio"/>
17	<input type="radio"/>	<input type="radio"/>
18	<input type="radio"/>	<input type="radio"/>
19	<input type="radio"/>	<input type="radio"/>
20	<input type="radio"/>	<input type="radio"/>
21	<input type="radio"/>	<input type="radio"/>
22	<input type="radio"/>	<input type="radio"/>
23	<input type="radio"/>	<input type="radio"/>
24	<input type="radio"/>	<input type="radio"/>
25	<input type="radio"/>	<input type="radio"/>
26	<input type="radio"/>	<input type="radio"/>
27	<input type="radio"/>	<input type="radio"/>
28	<input type="radio"/>	<input type="radio"/>
29	<input type="radio"/>	<input type="radio"/>

STI Results from Baby 3

	Positive	Negative
32		
33	<input type="radio"/>	<input type="radio"/>
34	<input type="radio"/>	<input type="radio"/>
35	<input type="radio"/>	<input type="radio"/>
36	<input type="radio"/>	<input type="radio"/>
37	<input type="radio"/>	<input type="radio"/>
38	<input type="radio"/>	<input type="radio"/>
39	<input type="radio"/>	<input type="radio"/>
40	<input type="radio"/>	<input type="radio"/>
41	<input type="radio"/>	<input type="radio"/>
42	<input type="radio"/>	<input type="radio"/>
43	<input type="radio"/>	<input type="radio"/>
44	<input type="radio"/>	<input type="radio"/>
45	<input type="radio"/>	<input type="radio"/>
46	<input type="radio"/>	<input type="radio"/>
47	<input type="radio"/>	<input type="radio"/>
48	<input type="radio"/>	<input type="radio"/>
49	<input type="radio"/>	<input type="radio"/>

Result of birth PCR for baby 1

- Positive
- Negative
- Indeterminate
- Not yet available

1 Result of birth PCR for baby 2

- 2
- 3 Positive
- 4 Negative
- 5 Indeterminate
- 6 Not yet available
- 7

8 Result of birth PCR for baby 3

- 9
- 10 Positive
- 11 Negative
- 12 Indeterminate
- 13 Not yet available
- 14
- 15

16

17 **Notes**

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22 Notes

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6-Week Immunization Visit Activities

Staff name

Today's date

Time

Did the mother present within the specified dates below:

Start Date: [predelivery_checki_arm_1][sixweek_remind_schedpd]

Actual Date: [predelivery_checki_arm_1][sixw_im_schedpd]

End Date: [predelivery_checki_arm_1][sixw_im_close_schedpd]

Yes

No

You are about to administer the questions associated with 6-weeks immunization visit.

Please select "Proceed"

Proceed

How many babies were delivered?

1

2

3

Was baby 1 admitted to hospital since the last study visit

Yes

No

Was baby 2 admitted to hospital following delivery

Yes

No

Was baby 3 admitted to hospital following delivery

Yes

No

Please specify

1 Does baby 1 have any of the following symptoms?
2

- 3 Cough
4 Runny nose
5 Eye discharge
6 Sneezing
7 None
8

9 Does baby 2 have any of the following symptoms?
10

- 11 Cough
12 Runny nose
13 Eye discharge
14 Sneezing
15 None
16

17 Does baby 3 have any of the following symptoms?
18

- 19 Cough
20 Runny nose
21 Eye discharge
22 Sneezing
23 None
24

25 Are any of the babies receiving any treatment at the moment
26
27
28
29
30

31 Feeding methods
32

- 33 Breastfeeding
34 Formula feeding
35 Mixed
36

37 Have you or the baby been to the clinic since the last visit with us?
38

- 39 Yes
40 No
41

42 What was the purpose of your visit?
43

- 44 ANC Visit
45 HIV/ART
46 STI Treatment
47 Other
48
49

50 Summary notes from the visit
51
52
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1 Do you know your current HIV status?
2

- 3 HIV negative (tested today by clinical staff)
4 HIV positive on ART
5 Known HIV positive, not on ART
6 Newly diagnosed HIV positive (tested today by clinical staff)
7 Don't know (never tested)
8 Don't know (no yet tested today)
9

10 Please conduct a HIV Rapid test and capture the result below
11

- 12 Positive
13 Negative
14

15 Please conduct a confirmatory HIV Rapid test and capture the result below
16

- 17 Positive
18 Negative
19

20 HIV PCR result of baby 1
21

- 22 Positive
23 Negative
24 No result
25

26 Please record barcode for blood and HIV PCR
27

28 _____
29
30
31

32 HIV PCR result of baby 2
33

- 34 Positive
35 Negative
36 No result
37

38 Please record barcode for blood and HIV PCR
39

40 _____
41
42

43 HIV PCR result of baby 3
44

- 45 Positive
46 Negative
47 No result
48

49 Please record barcode for blood and HIV PCR
50

51 _____
52
53

54 NOTE

55 You have collected all specimens associated with this visit. Once you select the "Proceed" option below you will be
56

57 CT: [post_natal_arm_1][sti_result_ct]
58

59 NG: [post_natal_arm_1][sti_result_ng]
60

TV: [post_natal_arm_1][sti_result_tv]

Proceed

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1 STI result, mother_calc
2
3
4
5

6 Does the participant report any medication allergies?
7

- 8 Yes
9 No
10
-

11 Please contact the study clinician before giving any treatment. Please specify discussed medication allergies and
12 treatment plan with the study clinician
13
14
15
16
17

18 The following treatment has been provided
19

- 20 Azithromycin 1g stat dose
21 Azithromycin 2g stat dose
22 Ceftriaxone 250mg IM injection
23 Ceftriaxone 1g IM injection
24 Metronidazole 400mg bd x 1 week
25 Metronidazole 2g stat dose
26 Clotrimazole pessary and/or cream
27 Trimethoprim/sulfamethoxazole 400/80 mg 2 tbl. bds for 5 days (bactrim)
28
-

29 Date treatment given
30
31
32
33

34 Partner notification provided
35

- 36 Yes, 1
37 Yes, multiple
38 No
39
-

40 Please explain why the partner notification note was not provided?
41
42
43
44
45
46

47 The mother tested positive for an STI at the Post Natal visit. You need to collect a Nasal Pharyngeal swab for baby 1.
48 Did you manage to collect this specimen?
49

- 50 Yes
51 No
52
-

53 Please confirm the PIN for the Nasal Pharyngeal swab for baby 1.
54

- 55 [baseline_arm_1][participant_pin]-NPB1
56
57
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1 The mother tested positive for an STI at the Post Natal visit. You need to collect a Nasal Pharyngeal swab for baby 2.
2 Did you manage to collect this specimen?
3

- 4 Yes
5 No
6

7 Please confirm the PIN for the Nasal Pharyngeal swab for baby 2 .
8

9 [baseline_arm_1][participant_pin]-NPB2
10

11
12 The mother tested positive for an STI at the Post Natal visit. You need to collect a Nasal Pharyngeal swab for baby 3.
13 Did you manage to collect this specimen?

- 14 Yes
15 No
16

17
18 Please confirm the PIN for the Nasal Pharyngeal swab for baby 3.
19

20 [baseline_arm_1][participant_pin]-NPB3
21

22 You have completed capturing the Post-Natal information. Please make sure to check that you have completed all
23 the fields.
24

25 Please select "Unverified" then "Save and Exit".
26
27

28 Notes

29 Additional notes
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Adverse Outcomes

Staff Name

Today's date

Start time

Was there an adverse birth outcome?

- Yes
- No

Was there a serious adverse event

- Yes
- No

Early loss of baby

What type of early loss?

- Miscarriage
- Ectopic
- Termination of pregnancy
- Still Born

Date

Ectopic pregnancy

Date of surgery

Termination pregnancy

Date

Reviewed by site PI

- Yes
- No

Date Reviewed

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Review Notes

Name of Reviewer

Remco Peters

You have completed capturing the adverse outcomes information. Please make sure to check that you have completed all the fields.

Please select "Complete" then "Save and Exit".

Notes

Additional notes

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Activities Associated with Visit

Staff Details

Staff Name

Today's Date

Start time

Presentation Outcome

Presentation outcome.

Did the participant present at the study site for this visit?

- Yes
 No

Activities Associated with ToC for Arm 1

You are about to facilitate activities associated with the 4-week ToC. You will need to execute the following:

1. Collect Specimens
2. Run a STI test
3. Conduct clinical history and behavioral questionnaire
4. Symptom screening if negative test
5. Treatment and partner referral if positive test

Proceed

Activities Associated with 32 Week Visit

You are about to facilitate activities associated with the 32 week visit. You will need to execute the following:

1. Collect Specimens
2. Run a STI test
3. Conduct clinical history and behavioral questionnaire
4. Symptom screening if negative test
5. Treatment and partner referral if positive test

Proceed

You are about to facilitate activities associated with the 32 week visit. You will need to execute the following:

1. Collect Specimens
2. Conduct clinical history and behavioral questionnaire
3. Symptom screening
4. Treatment and partner referral if positive screening

Proceed

Activities Associated with the First Postnatal Visit

You are about to facilitate activities associated with the the 1st post natal visit. You will need to execute the following:

1. Determine the presentation date (Only proceed when its 14 days after the delivery date)
2. Collect pregnancy and birth outcomes data (Discharge Summary and/or Road to Health Card)
3. Conduct mother and child clinical examination and history questionnaire
4. Specimen collection for mother and child

Proceed

Pregnancy and Birth Outcome Data

You are about to start with the pregnancy and birth outcome data capturing.

You can use the discharge summary and road to health as your data sources.

Select "Proceed" below to display the pregnancy and birth outcome details

Proceed

Delivery date

Mother and Baby Clinical Examination and History

You are done capturing the pregnancy and birth outcome data.

The next step is to capture the mother and baby clinical examination and history details.

Select "Proceed" below to display the questionnaire.

Proceed

Scheduling the 6 week Immunization Date

Schedule a 6 week immunization.

Use the below date assist to schedule the 6 week immunization date.

The below field must be equal to 42.

Use the date field above to ensure that the current field is equal to 42.

Collection of Vaginal Loops

You will need to collect a single vaginal loop that will be used to prepare two slides. Once collected you will need to prepare the slides for storage.

Proceed

Date of collection of vaginal loops

....

Confirm the pin associated with the first vaginal loop that will be used for

[baseline_arm_1][participant_pin]-FL1

Confirm the PIN associated with the second vaginal loop that will be used for

[baseline_arm_1][participant_pin]-FL2

Storage of Loops

You have collected both slides. Before commencing with the rest of the specimens, please make sure to do the following:

1. Slides are individually packed in their own package
2. Record PIN on outside of package
3. Complete the lab CRF with matching PINs and test instructions

Proceed

Vaginal Swab Collection

You will now collect 3 vaginal swabs. They will be used as follows:

1. STI testing (1st Specimen)
2. Profiling (2nd Specimen)
3. Microbiome (3rd Specimen)

Proceed

....

Date of specimen collection for vaginal swabs

Confirm the PIN associated with the first vaginal swab

[baseline_arm_1][participant_pin]-FV1

.....

Confirm the PIN associated with the second vaginal swab

[baseline_arm_1][participant_pin]-FV2

Confirm the PIN associated with the third vaginal swab

[baseline_arm_1][participant_pin]-FV3

Nasopharyngeal Swab Collection

You are about to collect the Nasopharyngeal swab on the Baby.

Collect the specimen and confirm the PIN below.

[baseline_arm_1][participant_pin]-NS1

GeneXpert Testing for the First Specimen

You will now start with the testing of the first vaginal swab specimen.

Follow the below steps:

1. Ensure that the GeneXpert Machine is switched-on. Perform a quikc qulaity check on the machine.
2. Load the specimen and run the machine.
3. Conduct Clinical History and Behavioural Questionnaire

Select "Start Test" when ready to run the test.

Start Test

Clinical History and Behavioural Questionnaire

You have started running the STI test.

Conduct clinical history and behavioural questionnaire. Select "Proceed" to display the questionnaire

Proceed

How often have you had sex since the last time we saw you?

- 0
- 1 to 5 times a week
- More than 5 times a week

STI Results

	Positive	Negative
NG	<input type="radio"/>	<input type="radio"/>
TV	<input type="radio"/>	<input type="radio"/>
CT	<input type="radio"/>	<input type="radio"/>

1 The participant tested positive for an STI.

2
3 The next step is to administer treatment with the participant.

4
5 Select "Proceed" to display treatment options.

6
7 Proceed

8
9
10

11
12 The next step is to screen the patient for STI symptoms

13
14 Is the participant symptomatic?

15 Yes

16 No

17
18
19 The participant screened positive for at least a single STI symptom

20
21 The next step is to administer treatment with the participant.

22
23 Select "Proceed" to display treatment options.

24
25 Proceed

26 27 **Treatment and Partner Notification**

28
29 Select the treatment regimen you administered to the participant

30
31 Azithromycin

32 Doxycyclin

33 Ceftriaxone

34 Metronidazole

35
36 Did you administer partner notification treatment?

37
38 Yes

39 No

40 41 42 **Storage Processes**

43
44 You have collected all required specimens.

45
46 You can now prepare the specimens for storage, follow the below steps:

47 1. Ensure that each specimen has a complete Lab CRF

48 2. Pack the Lab CRFs in the specimen container

49 3. Ensure that the Lab CRF is complete and specimens are stored according to the storage requirements.

50
51 Select "Confirm" after perform the above specimen procedures.

52
53 Confirm

1 **Notes**

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3 Additional notes
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Close-out

Staff member _____

Date _____

Participant ID: [baseline_arm_1][participant_pin_verify]

TERMINATION DETAILS

Date of termination _____

Study Time-Point

- BASELINE
- TOC
- 32 WEEKS
- POST-NATAL VISIT

Reason for termination

- End of study (study completed)
- death (participant)
- Participant refused further participation
- Participant unable to adhere to visit schedule
- Participant relocated, no follow-up planned
- Investigator decision
- unable to contact the participant
- Participant not eligible for enrollment
- Invalid ID due to duplicate screening/enrollment
- Other
- Early study closure
- End of study (adverse outcome)

Specify refusal reason/ Investigator reason _____

Other, Specify _____

.....
General Comments _____

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Ad-Hoc

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Staff name

Please capture date of visit

Please summarize the purpose of the visit

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Safety Protocol

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Today's date

Time

Staff

Safety Protocol Issue

- Social Harm
- Protocol Violation
- Unanticipated Problem

Date Reported

Notes

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STI Data Qc And Filing

SECTION A: STAFF DETAILS

Staff Member Name _____

Date _____

SECTION B: QUALITY ASSURANCE

Forms Received from the Field

- BQ Consent form
- Study Note
- Proof of Reimbursement
- Enrolment Log
- Expert Baseline: CT/NG
- Expert Baseline: TV
- Expert Postnatal: CT/NG
- Expert Postnatal: TV
- NHLS: CD4 Count
- NHLS: Syphilis Test
- NHLS: Viral Load
- NHLS: Baby HIV PCR
- OTHER
(Select all that you received)

Other - Specify the other form(s) received _____

QUALITY ASSURANCE: Phase 2A

Get all the participant's enrolment source documents and perform a comprehensive QC on all the source documents. After the QC is done, mark each document as "checked, properly completed" if you have no query opened on the source document.

IN CASES WHERE A QUERY IS OPENED. PLEASE CONTACT THE RESPONSIBLE DATA COLLECTOR IMMEDIATELY!

Please note that you also accept receipt of all source documents by checking them below.

	Checked, Properly Completed	Not completed, Returned to the RA
Consent Form	<input type="radio"/>	<input type="radio"/>
Study Note	<input type="radio"/>	<input type="radio"/>
Proof of Reimbursement	<input type="radio"/>	<input type="radio"/>
Enrolment Log	<input type="radio"/>	<input type="radio"/>
Expert Baseline: CT/NG	<input type="radio"/>	<input type="radio"/>

1	Expert Baseline: TV	<input type="radio"/>	<input type="radio"/>
2	Expert Postnatal: CT/NG	<input type="radio"/>	<input type="radio"/>
3			
4	Expert Postnatal: TV	<input type="radio"/>	<input type="radio"/>
5	NHLS: CD4 Count	<input type="radio"/>	<input type="radio"/>
6	NHLS: Syphilis Test	<input type="radio"/>	<input type="radio"/>
7	NHLS: Viral Load	<input type="radio"/>	<input type="radio"/>
8	NHLS: Baby HIV PCR	<input type="radio"/>	<input type="radio"/>
9			
10			
11	[forms_received_oth]	<input type="radio"/>	<input type="radio"/>
12			

13
14 Skip

17 Electronic Data QC

18
19 **You are supposed to go through each electronic data tool and ensure the following:**

- 20
21
22 **1. Each Tracking Field has a data point.**
23
24 **2. The data is consistent**
25
26 **3. The data is verified with source documents**

27
28 **After doing the above inspection. You marked the forms as complete and locked the form.**

29
30
31 **Once all the forms are checked and properly completed.**

	Checked and Completed Properly	Query Opened
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.....

Date of QC _____

COMMENTS

Comments _____

SAVING INSTRUCTION

MARK THIS FORM AS COMPLET ONCE VERIFIED AND LOCK IT.

SELECT SAVE AND EXIT FORM.

Proceed to QC other source documents.

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Scheduling 2

Scheduling of Dates Associated with [randomization].

NOTE

You are about to schedule dates associated with [randomization] participants.

Please select "Proceed".

Proceed

Scheduling of Dates Associated

NOTE:

You are about to schedule dates associated with microbiome participants.

Please select "proceed"

Proceed

Scheduling Dates for 3-Week ToC

NOTE: The participant tested positive and therefore we need to schedule a date, exactly 3-weeks from today to conduct a test-of-cure.

Scheduling the 3-week ToC

NOTE:

Please schedule a date, 3 weeks from today treatment given. Please use the calculator assistance to ensure that you schedule a date exactly 21 days from today.

Calculator Assist

The number here must be equal to 21

ERROR

The field does not equal to 21, please change it

Have you handed the TOC date to the participant?

Yes
 No

Scheduling Dates Associated with ToC Reminder

1 Schedule date for REMINDER of 3-week ToC visit
2
3
4 _____
5

6 Calculator Assist for scheduling ToC reminder date
7

8 The reminder phone call will be made 18 days following the treatment date. The number of days need to equal to 18.
9
10
11 _____
12

13 ERROR

14 You did not enter the date correctly. The number should equal to 18. Please redo the date.
15
16

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19 Scheduling Dates Associated with 3-Week ToC Missed Visit Date
20
21
22

23
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25 NOTE:

26 You have successfully scheduled the reminder date.

27
28 Please select "proceed" to schedule the missed visit date for the 3 week ToC visit.

29
30 Proceed
31

32 Schedule the date for the MISSED VISIT of the ToC visit.
33

34 This date should be 3 weeks after the date on which the participant received their test result.
35
36 _____
37
38

39 Calculator Assist for scheduling 3-week ToC Missed Visit
40

41 The participant's time period allowed for attending a ToC will start 3 weeks after they received their result and will
42 close 3 weeks after the date they received their result.
43

44 The number here must show 35
45
46
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49
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51 _____
52

53 ERROR

54 You did not enter the date correctly. The number should equal to 35. Please redo the date.
55

56 NOTE:

57 You have successfully scheduled the 3-week ToC close date

58
59 Please select "proceed" to start scheduling the next visit dates

60 Proceed

1 Dates Associated with reminder for the 28 Week call

2

3

4

5 NOTE:

6 You are about to schedule dates for the call reminder at 28 weeks.

8 Please select "Proceed".

10 Proceed

12 Note:

13 Schedule the date for the 28 week call. We will contact each participant to ask the date for their 30 weeks clinic visit

14 is.

15

16

17

18 _____

20 Calculation assist for scheduling the 32-week reminder date.

21 This number must equal to 196

22

23

24 _____

26 Days to call reminder

27

28

29 _____

32 ERROR

33 The number you have entered does not match 196. Please select a different date so that the number equals to 196.

35 Scheduling the Dates Associated with the 32 Week Gestational Visit

36

37

38

39 NOTE

40 You are about the start scheduling dates associated with the 32 week visit. You will need to schedule the following

41 associated dates:

42

- 43 1. Week 32 date
 - 44 2. Week 32 reminder date
 - 45 3. Week 32 missed visit date
- 46

47 Select "Proceed" to start scheduling

49 Proceed

51 Schedule the date for the 32 week gestational age, visit

52

53

54 Note to RA: please make sure that this date does not fall on Friday, weekend, and public holidays.

55

56

57 _____

59 Days Difference (the difference between 32 weeks & Gestational age)

60

1 Calculate assist for 32 week visit

2
3 The number here must equal to [gest_week_calc]

4
5
6
7
8 _____
9
10 Match

11 _____
12
13 The date you have entered does not meet the 93 day criteria. Does the intended or original date fall on a Friday
14 weekend or public holiday?

15
16 Yes

17 No

18
19
20 ERROR

21 The numbers you have entered does not match. Please select a different date so that the numbers match.

22
23 Dates Associated with reminder for the 32 Week Gestational Age Visit

24
25
26
27 NOTE:

28 You have successfully scheduled the 32 week date.

29
30 We will need to contact the participant at least 7 days before the scheduled visit to remind them.

31
32 Select "Proceed" to schedule the reminder date for the 32 week visit.

33
34 Proceed

35
36 Note:

37 Schedule the date for the 32 week reminder. We will contact each participant starting 7 days prior to their 32-week
38 gestation date. That means the date scheduled here should be 7 days earlier then the scheduled date for the
39 32-week visit.

40
41
42 _____
43
44 Calculation assist for scheduling the 32-week reminder date.

45
46 This number must equal to 7

47
48
49 _____
50
51 ERROR

52 The number you have entered does not match 7. Please select a different date so that the number equals to 7

Dates associated with the 32 week gestational age missed visit**NOTE:**

You have successfully scheduled the 32 week reminder date.

Select "Proceed" to schedule the 32 week missed visit date.

Proceed

Schedule the date for the 32 week missed visit date.

Note: Participants will have 3 weeks (21 days) to present for their 32 week visit date after which the visit will be closed out.

Calculation Assist for scheduling the 32-Week missed visit date.

This number must equal to 21

ERROR

The number you have entered does not match 21. Please select a different date so that the number equals to 21

Estimated Delivery Date

You are about to schedule the Estimated Delivery Date.

Please select "proceed"

Proceed

Estimated Delivery Date

Days difference between estimated date of delivery and gestational age

1 Calculation Assist for scheduling the Estimated Date for Delivery date.

2
3 This number must equal to [edod_calc]
4
5
6
7

8 Match
9
10

11
12 ERROR

13 The number you have entered does not match. Please select a different date so that the numbers match
14

15 You have completed all the scheduling dates.

16
17 Please check that all dates entered comply with the "calculation assistance". Once this has been done you can select
18 "Complete" and "Save & Exit"
19
20

21
22 **NOTES**
23

24 Notes box
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Data Quality

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Name

Time

For peer review only

Updated Estimated Delivery Date

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Please specify the updated delivery date

For peer review only