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**Research Project**

**Systematic Screening of Lower Genital Tract Infections in Low-Risk  
Pregnant Women for Gestational and Neonatal Outcomes: a Randomized  
Controlled Trial**

**Botucatu, 17th May 2026**

## **ABSTRACT**

**Introduction:** The investigation of systematic screening for asymptomatic genital infections in low-risk pregnant women is justified by the relevance of these conditions in determining adverse neonatal outcomes, such as prematurity, low birth weight, and perinatal morbidity and mortality. Despite its importance, previous studies have shown inconsistent results, largely due to methodological limitations related to sample size, lack of standardized treatment protocols, and insufficient follow-up of pregnant women. There is also divergence among national and international guidelines, which vary between universal and selective recommendations, highlighting gaps in the standardization of clinical practices.

**Objectives:** To investigate the effectiveness of implementing screening guidelines for asymptomatic genital infections in low-risk pregnant women in preventing adverse gestational and neonatal outcomes. The specific objectives are: to identify the most prevalent infections in this group; to evaluate the relationship between treatment and the incidence of complications; to compare outcomes between populations following systematic protocols and those that do not; and to propose recommendations for clinical practice and health policies based on a critical review of the literature and the results obtained.

**Methods:** This is a randomized controlled trial that will recruit 250 low-risk pregnant women, followed from the first trimester until delivery. Participants will be randomized into two groups: an intervention group, undergoing systematic screening with protocol-guided treatment, and a control group, managed according to current standard care practices, following the municipality's protocol for screening and treatment of genital infections. Primary outcomes include preterm birth, premature rupture of membranes, low birth weight, intra-amniotic infection, puerperal infection, neonatal infection, and fetal and neonatal mortality. Statistical analysis will follow the intention-to-treat principle, and differences in outcomes between groups will be estimated.

**Expected Results:** This study is expected to provide robust estimates on whether systematic screening reduces (or does not reduce) maternal and neonatal complications. The randomized controlled trial will be prospectively registered prior to the enrollment of the first participant, in accordance with current ethical standards.

**Keywords:** screening; lower genital tract infections; low-risk pregnancy; neonatal and gestational outcomes

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## ***Introduction***

The promotion of maternal and child health is a priority in global public health policies, encompassing strategic goals such as the Millennium Development Goals<sup>1</sup>. Among the various indicators reflecting a population's quality of life, infant mortality remains one of the most significant. In Brazil, despite a progressive decline in infant mortality rates over recent decades, the situation remains concerning and reveals marked regional and socioeconomic inequalities<sup>2,3</sup>.

The persistence of preventable deaths, particularly among vulnerable populations, underscores the need to strengthen preventive strategies and expand access to high-quality prenatal care. These early deaths are often attributed to a combination of biological and social factors, as well as deficiencies within healthcare systems. In particular, perinatal mortality—defined as fetal and early neonatal deaths with a birth weight of at least 500 grams or a gestational age of 22 weeks—has been recognized as one of the most appropriate indicators for assessing the quality of obstetric and neonatal care<sup>2</sup>.

Preventing adverse outcomes during pregnancy, particularly by reducing preterm birth and congenital infections, represents one of the most effective approaches to improving maternal and child health indicators. Understanding preventable causes of neonatal mortality and adopting more effective prenatal screening practices are essential strategies to achieve sustainable public health gains<sup>2</sup>. Among the less apparent causes of gestational complications are asymptomatic genital infections. Studies indicate that approximately 70% of preterm births occur spontaneously, and many of these cases may be associated with subclinical infections<sup>5</sup>.

Bacterial vaginosis (BV), classically described as vaginal dysbiosis, is a common condition affecting approximately one-third of women worldwide, with even higher prevalence among pregnant women<sup>4</sup>. In the United States, BV prevalence ranges from 5.8% to 19.3%, with higher rates observed in certain racial and ethnic groups<sup>4</sup>. Despite its high prevalence, BV is frequently asymptomatic, which hinders timely diagnosis and the implementation of preventive interventions. During pregnancy, BV has been associated with adverse obstetric outcomes, including preterm birth, early miscarriage, puerperal endometritis, and low birth weight<sup>4</sup>. The presence of coinfections further increases the risk of obstetric complications<sup>8</sup>. Sexually transmitted infections caused by *Trichomonas vaginalis* and *Chlamydia trachomatis*, which are also frequently asymptomatic, have a high inflammatory potential, potentially affecting the upper genital tract and compromising the integrity of fetal membranes.

Evidence suggests that vaginal dysbiosis facilitates bacterial ascension to the fetal membranes and amniotic fluid, promoting inflammatory processes that may trigger preterm premature rupture of membranes and preterm labor<sup>6</sup>. Although the underlying mechanisms are

not yet fully understood, the association between asymptomatic genital infections and adverse neonatal outcomes is well established in the literature<sup>16, 17, 18</sup>. The absence of clinical manifestations reinforces the need for systematic screening strategies integrated into prenatal care.

Despite evidence regarding the impact of asymptomatic genital infections during pregnancy<sup>16, 17, 18</sup>, systematic screening practices are not universally implemented, particularly among women classified as low-risk<sup>7</sup>. Traditionally, prenatal screening protocols focus on women with known risk factors, overlooking those who, even without prior risk indicators, may develop infections that compromise fetal health. The literature indicates that risk factors for bacterial vaginosis during pregnancy are inconsistent, underreported, and often neglected<sup>6</sup>.

The lack of clear policies addressing the screening of asymptomatic genital infections in low-risk pregnant women may contribute to the persistence of high rates of preterm birth and preventable neonatal complications.

Considering that preventive care is a cornerstone of modern medicine, evaluating the role of timely screening for lower genital tract infections may help consolidate routine prenatal care strategies<sup>6</sup>. The implementation of specific guidelines targeting this population could lead not only to improved gestational outcomes but also to a positive impact on the cost effectiveness of healthcare systems by reducing the need for interventions associated with potentially preventable complications.

Given the relevance of this issue and the gaps identified in current clinical practices, it is essential to promote research that evaluates the effectiveness of systematic screening and supports the development of more comprehensive protocols capable of addressing the needs of all pregnant women.

## **Study Rationale**

The importance of systematic treatment of asymptomatic genital infections in low-risk pregnant women is highlighted within a context in which maternal and child health remains a priority in public health policies<sup>1, 2, 3</sup>. Asymptomatic genital infections may not only affect maternal well-being but also lead to severe consequences for the newborn, including prematurity, low birth weight, and other complications that may impair child development<sup>6, 10</sup>. In many countries, neonatal mortality and morbidity rates remain alarmingly high, particularly among vulnerable populations<sup>11</sup>. The implementation of screening guidelines may promote a preventive

approach that would not only minimize the risks associated with these infections but also reduce the need for more complex and costly treatments resulting from adverse outcomes.

Despite this, major randomized controlled trials evaluating asymptomatic bacterial vaginosis (BV) in pregnant women have not demonstrated consistent positive effects on obstetric and neonatal outcomes. The study by Carey et al. found no benefit of a single 2 g dose of metronidazole<sup>12</sup>; the PREMET Study even reported an increased rate of preterm birth in the treated group<sup>13</sup>; Vermeulen and Bruinse observed higher rates of prematurity (<34 weeks) and neonatal infectious morbidity with the use of vaginal clindamycin<sup>14</sup>; and the large-scale PREMEVA Trial showed no reduction in late miscarriage or very preterm birth with oral clindamycin<sup>15</sup>.

However, these studies present significant methodological limitations, including the use of medications and/or dosing regimens not standardized as first-line therapy, lack of test-of-cure assessment, limited follow-up, and potential sampling biases. These limitations suggest that the absence of observed benefit may be related to inadequate screening and treatment protocols, underscoring the need for updated investigations that incorporate integrated interventions, appropriate monitoring, and clearly defined clinical outcomes.

Currently, screening for genital infections during prenatal care still shows considerable variation across national and international guidelines. In Brazil, the Ministry of Health recommends universal screening for syphilis, HIV, and hepatitis B and C at the first prenatal visit, as a mandatory and widely implemented measure<sup>16</sup>. The Brazilian Federation of Gynecology and Obstetrics (FEBRASGO), in turn, emphasizes that the absence of symptoms does not exclude the possibility of vaginal infection, recommending that screening also be considered in asymptomatic pregnant women<sup>16</sup>.

In contrast, guidelines such as those from the Centers for Disease Control and Prevention (CDC) in the United States recommend screening for chlamydia and gonorrhea only in pregnant women under 25 years of age or in those with defined risk factors, rather than universally<sup>19</sup>. Additionally, screening for other sexually transmitted infections in pregnant women remains inconsistent and often dependent on individual risk assessment and local protocols, and asymptomatic pregnant women without increased risk are generally not included in these recommendations<sup>19</sup>. The International Society for the Study of Vulvovaginal Disease (ISSVD) also does not recommend screening for bacterial vaginosis in asymptomatic women, except in high-risk populations, and acknowledges the lack of specific protocols for low-risk asymptomatic pregnant women<sup>20</sup>.

There is, therefore, a clear need to deepen the understanding of the clinical and social implications of asymptomatic genital infections during pregnancy, particularly among low-risk women. Further research on this topic may provide a more comprehensive understanding of optimal screening and treatment practices, while also contributing to the education and training of future healthcare professionals.

This study is grounded in the principles of preventive medicine. By providing evidence on the effectiveness of systematic treatment of asymptomatic genital infections in low-risk pregnant women, it may support the development of clinical protocols and guidelines, promoting a more informed and evidence-based medical practice. Furthermore, by addressing the relationship between genital infections and neonatal and gestational outcomes, this work highlights the importance of health education for both pregnant women and healthcare professionals, fostering a more critical and sensitive approach to maternal health needs.

## **Objetives**

To investigate the effectiveness of implementing systematic screening for asymptomatic genital infections in low-risk pregnant women in preventing adverse gestational and neonatal outcomes.

### ***Specific Objectives***

- To identify the prevalence of asymptomatic genital infections among low-risk pregnant women;
- To evaluate the association between the treatment of asymptomatic genital infections and the reduction in the incidence of adverse gestational and neonatal outcomes;
- To compare the rates of gestational and neonatal outcomes in populations that follow screening guidelines for asymptomatic genital infections with those that do not;
- To propose recommendations for clinical practice and health policies based on a review of the literature on screening for asymptomatic genital infections and their impact on neonatal outcomes.

## **Methods**

This is an academic study conducted as part of a Master's dissertation, linked to the Graduate Program in Pathology at São Paulo State University "Júlio de Mesquita Filho" (UNESP). The methodological design consists of a randomized controlled trial aimed at evaluating the effectiveness of implementing screening and treatment guidelines for asymptomatic genital infections in preventing adverse gestational and neonatal outcomes among low-risk pregnant women.

### ***Study Setting and Population***

The study will be conducted in Uruguaiana, a municipality located in southern Brazil, including low-risk pregnant women referred by the Family Health Strategy (FHS) to a reference Women's Health Unit. Participants will be followed from the first trimester of pregnancy until delivery.

## ***Sample Size Calculation***

The primary outcome will be the occurrence of spontaneous preterm birth. Based on the literature and local data, a proportion of 40% preterm birth is assumed in the group with bacterial vaginosis (BV) diagnosed early in pregnancy, compared to 10% in the group without BV (eubiosis). A two-sided test was adopted, with a type I error rate ( $\alpha$ ) of 1% and statistical power ( $1-\beta$ ) of 90%, with a 1:1 allocation ratio between groups.

The sample size was estimated using the formula for comparison of two independent proportions, resulting in 60 pregnant women per group. Anticipating a 20% loss to follow-up, the planned sample size is 75 participants per group (total = 150). Spontaneous abortions and fetal deaths will not be treated as losses but will instead be analyzed as secondary outcomes, preserving the validity of the primary analysis. Based on an estimated prevalence of bacterial vaginosis (BV) of approximately 30% among pregnant women receiving care in the municipal health system of Uruguaiana (RS), it is estimated that approximately 250 pregnant women will need to be screened to achieve the target sample size of 150 participants (75 per group), including both women with and without BV.

The sample size calculation was verified using the normal approximation for two independent proportions and will be reported in accordance with CONSORT guidelines<sup>25</sup> for randomized clinical trials (including parameters, assumptions, and hypotheses).

## ***Eligibility Criteria***

Low-risk pregnant women (without comorbidities associated with medically indicated preterm birth) admitted to the Women's Health service during the first trimester of pregnancy will be included in the study. There will be no specific exclusion criteria; all pregnant women who meet the inclusion criteria and agree to participate will be enrolled.

## ***Randomization, Allocation Concealment, and Study Groups***

The participant randomization scheme will be generated using an electronic spreadsheet in Microsoft Excel®, configured to produce a random allocation sequence between the Intervention and Control groups. The process will be conducted by a nursing technician exclusively designated for this role, who will assign participants according to the chronological order of arrival of low-risk pregnant women at the Women's Health service.

The physician responsible for clinical care will have no prior access to the allocation sequence; group assignment will be revealed only at the time of the consultation, after the

participant has been enrolled in the study. This procedure is intended to ensure allocation concealment and to minimize potential selection and performance biases. The randomization sequence and allocation list will be stored in a password-protected file, accessible only to the designated nursing technician.

### ***Data Collection Procedures***

Eligible pregnant women will be identified within the Primary Health Care setting, specifically through the Family Health Strategy (FHS) units of the municipality. The initial approach will be conducted by the FHS nurse responsible for patient intake and initiation of prenatal care.

During the first prenatal visit, pregnant women in the first trimester who meet the low-risk criteria—defined as the absence of comorbidities associated with medically indicated preterm birth—will be identified. Following eligibility assessment, each woman will be individually invited to participate in the study after receiving a clear and accessible explanation of the study objectives, procedures, and the voluntary nature of participation.

Women who express interest in participating will be referred to the municipal Women's Health referral service, where the study will be formally presented by the principal investigator or a trained member of the research team. Written informed consent will then be obtained. Only after completion of this process will participants be enrolled in the study and undergo randomization.

Women who decline participation will continue to receive standard prenatal care according to routine municipal health service protocols, with no impact on the care provided. Data collection will commence only after group allocation (intervention or control) has been established. All study-related procedures will be conducted in the obstetric consultation room at the municipal Women's Health referral service, in accordance with a standardized protocol defined a priori by the research team.

Data will be obtained from three primary sources: clinical interviews, collection of vaginal and endocervical biological samples, and review of maternal and neonatal medical records.

The clinical interview and biological sample collection will be performed during a single visit at the referral service, following informed consent and allocation. This visit will last approximately 20 minutes, encompassing both the interview and gynecological examination procedures.

The clinical interview will capture maternal sociodemographic and obstetric characteristics, as well as relevant clinical information for pregnancy follow-up. All data will be

recorded using study-specific electronic case report forms (eCRFs) designed for the systematic capture of clinical, laboratory, and obstetric data.

Vaginal samples for microbiological analysis will be systematically collected at all prenatal visits conducted at the Women's Health referral service. Samples will be subjected to Gram staining and classified according to the criteria predefined in the study protocol.

Endocervical samples will be collected once per trimester, totaling three collections throughout pregnancy, for the detection of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Mycoplasma genitalium*, and *Trichomonas vaginalis* using real-time polymerase chain reaction (PCR). Specimen collection will include a speculum examination using a sterile, non-lubricated Collins bivalve vaginal speculum.

Vaginal samples will be obtained using a sterile swab for Gram-stained smear preparation, and endocervical specimens will be collected using a cytobrush for subsequent DNA extraction. All procedures will be performed by trained personnel in an appropriate clinical setting, in accordance with biosafety standards and ensuring participant comfort.

Blood tests included in the study will be limited to those routinely performed during prenatal care, in accordance with current Brazilian Ministry of Health guidelines. No additional blood samples will be collected exclusively for research purposes.

Vaginal smears will be prepared and stained by the research team within the healthcare facility. Microscopic evaluation will be performed using Gram staining, and classification will follow the Nugent criteria, along with the methods described by Dong, Cibley & Cibley (1991), and Ison & Hay. Slides will then be labeled, stored under appropriate conditions, and subsequently sent to the Laboratory of Immunopathology of the Maternal–Fetal Interface at the Experimental Research Unit of São Paulo State University (UNESP) for reanalysis and quality control. Diagnostic reliability will be assessed through concordance between local and reference laboratory readings.

Endocervical samples will be collected in a specific transport buffer and forwarded for molecular analysis using the Allplex™ CT/NG/MG/TV Assay (Seegene). Briefly, nucleic acids will be extracted using the EXTRACTA® DNA/RNA de Patógenos – MPTA MDx kit (Loccus), followed by real-time PCR for the simultaneous detection of *C. trachomatis*, *N. gonorrhoeae*, *M. genitalium*, and *T. vaginalis*.

Samples positive for *M. genitalium* will undergo additional analysis for mutations in the 23S rRNA gene associated with macrolide resistance. All diagnosed vaginal and cervical infections will be treated in accordance with current clinical guidelines, including those from the Centers for Disease Control and Prevention (CDC) and the International Society for the Study of Vulvovaginal Disease (ISSVD), as detailed in Table 1.

**Table 1. Treatment Regimens for Infections in the Intervention Group**

Detected Infection	First-line treatment	Second-line treatment
Vulvovaginal candidiasis	Miconazole 2% vaginal cream for 14 days	Clotrimazole 1% vaginal cream for 12 days
Bacterial vaginosis	Metronidazole vaginal gel 7.5 mg/g, 5 g intravaginally once daily for 7 days	Clindamycin 2% vaginal gel, 5 g intravaginally once daily for 7 days
Aerobic vaginitis	Clindamycin 2% vaginal gel, 5 g intravaginally once daily for 14 days	Amoxicillin–clavulanate 500 mg/125 mg orally every 8 hours for 7–10 days
<i>C. trachomatis</i>	Azithromycin 1 g orally in a single dose	Amoxicillin 500 mg orally every 8 hours for 7 days
<i>N. gonorrhoeae</i>	Ceftriaxone 500 mg intramuscularly in a single dose	Gentamicin 240 mg intramuscularly in a single dose plus azithromycin 2 g orally in a single dose
<i>M. genitalium</i>	Moxifloxacin 400 mg orally once daily for 14 days	Spectinomycin 2g intramuscularly in a single dose
<i>T. vaginalis</i>	Metronidazole 500 mg orally every 12 hours for 5–7 days	

Participants in the control group will receive standard care according to the current municipal clinical protocol. Screening for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* will be performed exclusively during the first trimester and restricted to pregnant women younger than 30 years, using the Cobas® 4800 system. The management of vulvovaginal infections will be based on clinical criteria. Participants will be followed at quarterly intervals solely for data collection. Treatment will follow the standard municipal protocol, in accordance with Brazilian Ministry of Health guidelines.

**Table 2. Treatment Regimens for Infections in the Control Group**

Detected Infection	First-line treatment	Second-line treatment
Vulvovaginal candidiasis	Miconazole 2% vaginal cream for 14 days	Clotrimazole 1% vaginal cream for 12 days

Bacterial vaginosis	Metronidazole 500 mg orally every 12 hours for 5–7 days	Clindamycin 300 mg orally every 12 hours for 7 days
<i>C. trachomatis</i>	Azithromycin 1 g orally in a single dose	
<i>N. gonorrhoeae</i>	Ceftriaxone 500 mg intramuscularly in a single dose	
<i>T. vaginalis</i>	Metronidazole 500 mg orally every 12 hours for 5–7 days	

Neonatal data and final outcomes will be obtained through review of hospital medical records after delivery, at the reference maternity hospital. Collected variables will include mode of delivery, maternal postpartum complications, and maternal length of hospital stay, as well as neonatal outcomes, including rooming-in or admission to the neonatal intensive care unit (NICU), length of neonatal hospitalization, preterm birth, premature rupture of membranes, low birth weight, neonatal infection, fetal death, and neonatal mortality.

Participants younger than 18 years will be eligible only with the presence and authorization of a legal guardian. In such cases, written informed consent will be obtained from the guardian, and assent will be obtained from the minor participant.

With regard to transportation to the Women’s Health referral service, costs will be borne by the participant, as referral to this service is already part of the routine care pathway within the municipal public health system and occurs independently of study participation. However, for eligible participants who lack transportation, biological sample collection and obstetric consultations will be conducted at their originating Family Health Strategy (FHS) unit.

In these cases, dedicated schedules will be organized within the FHS units, allowing the obstetrician member of the research team to provide care directly at the primary care facility. This approach will be applied to participants in both the intervention and control groups, ensuring equity in follow-up, access to study procedures, and continuity of prenatal care without compromising standard clinical management.

Participants will be followed from enrollment in the first trimester until delivery. All data will be stored in an anonymized electronic database with restricted access to authorized research personnel, ensuring data confidentiality and security.

### ***Biological Sample Collection***

At the time of allocation to the intervention group, participants will undergo a speculum examination using a sterile, non-lubricated Collins bivalve vaginal speculum. Vaginal samples will be collected using a sterile swab, and endocervical secretions will be obtained using a cytobrush for subsequent DNA extraction and molecular detection of *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Mycoplasma genitalium*, and *Trichomonas vaginalis*:

1. Inspection of the external genitalia for the detection of vulvar, perineal, and perianal lesions;
2. Insertion of a non-lubricated Collins bivalve vaginal speculum for inspection of the vaginal walls and cervix;
3. Measurement of vaginal pH using indicator strips (range: 4.0–7.0; Merck, Darmstadt, Germany);
4. Collection of vaginal fluid from the mid-vaginal wall using a sterile swab for preparation of slides to be stained by the Gram method;
5. Performance of the amine (whiff) test using 10% potassium hydroxide;
6. Collection of endocervical secretions using a cytobrush for the investigation of endocervicitis;
7. Collection of cervical cytology (Pap smear), when indicated.

### ***Study Risks***

Participants may benefit from closer clinical monitoring throughout pregnancy, including systematic evaluation of vaginal and endocervical infections and timely identification of potential complications. Early diagnosis and appropriate management of these conditions may contribute to improved maternal and neonatal outcomes.

In addition, participants may benefit from access to specialized obstetric care provided by trained professionals involved in the study. At a broader level, this study is expected to generate relevant scientific evidence regarding the role of vaginal and endocervical infections in pregnancy outcomes, which may contribute to improvements in prenatal care protocols and public health strategies.

This study will be conducted in accordance with the principles of the Declaration of Helsinki and applicable national regulations. The study protocol has been approved by the Research Ethics Committee (Comitê de Ética em Pesquisa – CEP) under the Brazilian National Research Ethics Commission (CONEP) system.

All participants will provide written informed consent prior to enrollment. For participants younger than 18 years, written informed consent will be obtained from a legal guardian, and assent will be obtained from the minor participant.

- I. All data will be handled in accordance with the Brazilian General Data Protection Law (Lei nº 13.709/2018), ensuring confidentiality, anonymity, and secure storage of participant information.

### ***Outcomes***

The primary outcomes will be preterm birth and preterm premature rupture of membranes (PPROM). Secondary outcomes will include miscarriage, intra-amniotic infection, puerperal infection, neonatal infection, fetal death, and neonatal mortality. All clinical, laboratory, and obstetric data will be recorded using standardized forms and stored in an anonymized electronic database. Participants will be followed until delivery, with neonatal data collected directly from hospital medical records. Losses to follow-up, deliveries occurring outside the referral network, and other events that may compromise data completeness will be systematically monitored. Data will be analyzed according to the intention-to-treat principle, whereby participants will be analyzed in the groups to which they were originally assigned, regardless of adherence to the treatment protocols.

### ***Ethical Considerations***

Prior to study initiation, approval will be obtained from the Municipal Health Department and from the Santa Casa de Uruguaiana Hospital, formalized through a co-participation agreement following registration of the study in the Academic Project System (SAP) of the Federal University of Pampa (UNIPAMPA), and approval by the Research Ethics Committee (Comitê de Ética em Pesquisa – CEP). The study will be conducted in accordance with national regulatory standards for research involving human participants, as established by Resolution No. 466/2012. Participant anonymity and the confidentiality of identifiable data will be ensured in compliance with the Brazilian General Data Protection Law (Lei nº 13.709/2018). Prior to participant recruitment, the study will be prospectively registered in a publicly accessible clinical trials registry, such as ClinicalTrials.gov or the Brazilian Clinical Trials Registry (ReBEC).

### ***Statistical Analysis***

Statistical analyses will be performed using SPSS (IBM Corp., Armonk, NY, USA). Descriptive analyses will be conducted, with categorical variables presented as absolute and relative frequencies, and continuous variables summarized using measures of central tendency and dispersion, as appropriate. Between-group comparisons will be

performed using the chi-square test or Fisher's exact test for categorical variables, and the Student's *t*-test or Mann–Whitney *U* test for continuous variables, depending on the distribution of the data. Normality will be assessed using appropriate tests and graphical methods.

In addition, logistic regression models may be used to estimate the association between the intervention and neonatal outcomes, adjusting for potential confounding variables. Results will be reported as odds ratios (ORs) with 95% confidence intervals (CIs). A two-sided significance level of 0.05 will be adopted for all analyses. Missing data will be handled using multiple imputation methods

## 1. Study Schedule

<b>2026</b>	J A N	F E B	M A R	A P R	M A Y	J U N	J U L	A U G	S E P	O C T	N O V	D E C
Literature review	X	X	X	X	X							
Project evaluation	X	X	X	X	X	X						
Data collection								X	X	X	X	X
<b>2027</b>	J A N	F E B	M A R	A P R	M A Y	J U N	J U L	A U G	S E P	O C T	N O V	D E C
Data collection	X	X	X	X	X	X	X	X	X	X	X	X
Data analysis				X	X	X	X	X	X	X	X	X
Partial report (CEP)												X
<b>2028</b>	J A N	F E B	M A R	A P R	M A Y	J U N	J U L	A U G	S E P	O C T	N O V	D E C
Data collection	X	X	X	X	X	X	X					
Data analysis	X	X	X	X	X	X	X	X	X	X	X	X
<b>2029</b>	J A N	F E B	M A R	A P R	M A Y	J U N	J U L	A U G	S E P	O C T	N O V	D E C
Manuscript writing	X	X	X	X	X	X	X					

Revision					X	X	X	X	X	X		
Final report (CEP)											X	X
Submission											X	X

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