

ASSESSMENT OF BIRTH OUTCOMES IN ESWATINI AFTER TRANSITION TO DOLUTEGRAVIR-BASED TREATMENT

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Acronyms

ANC	Antenatal care
APMR	ART Patient Monitoring and Reporting
APR	Antiretroviral Pregnancy Registry
ART	Antiretroviral therapy
ARV	Antiretroviral
CMIS	Client management information system
DTG	Dolutegravir
EFV	Efavirenz
EGPAF	Elizabeth Glaser Pediatric AIDS Foundation
EHHRRB	Eswatini Health and Human Research Review Board
IPD	Inpatient Department
IRB	Institutional Review Board
LMP	Last menstrual period
MOH	Ministry of Health
NNRTI	Non-nucleoside reverse-transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase
NTD	Neural tube defect
OPD	Outpatient Department
PI	Protease inhibitor
PIN	Personal identity number
PMTCT	Prevention of Mother-to-Child Transmission
PrEP	Pre-exposure prophylaxis
SID	Strategic Information Department
SRHU	Sexual Reproductive Health Unit
WHO	World Health Organization

Protocol Summary

Dolutegravir (DTG) is a second-generation integrase inhibitor that has demonstrated improved virologic efficacy and tolerance compared to efavirenz (EFV)-based first-line ART. Initial data in May 2018 from the Tsepamo study in Botswana had suggested a potential ~9-fold increase in risk of neural tube defects (NTD) among infants delivered to women receiving DTG at the time they became pregnant. However, in the most recent analysis through March 2022, NTD prevalence had stabilized at a low level, 0.11% (10 NTD in 9,460 exposures to DTG at conception); this is now the same as the NTD prevalence of 0.11% with non-DTG ART at conception (25 NTD in /23,664 births) and is compared to 0.07% in women without HIV infection (108 NTD in 170,723 births). Based on previous data from this study in 2020, demonstrating an earlier decrease in NTD prevalence, and updated risk-benefit analyses demonstrating that the benefits of DTG significantly outweigh the potential risks, the World Health Organization recommends DTG as a preferred first-line drug for treatment, but also indicates continued surveillance is needed to more definitively confirm or refute the NTD signal among women of reproductive potential.

To contribute to the evidence base on birth defects among women on DTG at conception and to support the national birth surveillance system that can be used to determine the rate of birth defects in the general population and evaluate outcomes of emergent therapies, we will be conducting an observational study at five high volume hospitals in Eswatini, in which birth defect and other data will be collected at the time of delivery for all women. The overall aim of this study is to evaluate the birth outcomes of HIV-positive women who are receiving DTG or other ARV drug regimens. The primary research objectives are to: 1) determine the proportion of neural tube defects among live and stillborn infants delivered by HIV-positive women on DTG at conception; 2) determine the proportion of neural tube defects among live and stillborn infants delivered by HIV-negative women; and 3) determine the proportion of neural tube defects among live and stillborn infants delivered by HIV-positive women on non-DTG ART at conception.

Data collection over an approximate 24-month period will involve two main components. The first is birth surveillance designed to capture the deliveries of all women presenting to study hospitals, including HIV-positive women with DTG exposure both before and during pregnancy or on another or no ART regimen and HIV-negative women as well as any stillbirths. Mothers' pregnancy history, birth outcomes, and HIV and ART information (as applicable) will be collected from existing clinic registers, reporting forms and databases. Secondly, more detailed information on health history, risk factors, and descriptions of birth defects and classification by clinical staff, will be collected through interviews and photographs with consenting mothers whose children have been identified by clinical staff to have major external birth defects at the time of delivery, or in the event of a medical abortion following the identification of a serious fetal birth defect

through ultrasonography. This information will be sent to an external pediatric specialist for a final confirmatory diagnosis.

NTD will be the primary study outcome. Key secondary outcome variables include other major and surface birth defects and other pregnancy outcomes that could be associated with ARV exposure, such as preterm delivery, low birthweight and stillbirths. The primary analysis will be descriptive, to determine the proportion of NTD among infants delivered by HIV-positive women on DTG at conception and HIV-negative women. Exploratory statistical investigations may be performed for birth defects or other outcomes among women living with HIV receiving DTG at conception, women living with HIV receiving non-DTG ART at conception, and women without HIV infection. If assumptions are met for NTD prevalence and the expected number of deliveries, one year of surveillance from these hospitals could provide the sample size needed to rule-out a relatively rare event like an NTD: approximately 10,000 women on DTG at conception.

Results will be disseminated by EGPAF to the Eswatini MOH at regional and national levels and other key stakeholders in-country as well as to a global audience to share information critical to our understanding of birth defects and other birth outcomes, among women on DTG at conception and in the general population.

Background & Scientific Rationale

Ensuring people living with HIV are on optimal ART regimens is a critical component to reaching the UNAIDS 95-95-95 goals by 2030 [1]. Dolutegravir (DTG) is a second-generation integrase inhibitor that has demonstrated improved virologic efficacy and tolerance compared to efavirenz (EFV)-based first-line ART [2, 3]. DTG has a high barrier to resistance, and in the face of growing transmitted and acquired drug resistance, especially to non-nucleoside reverse-transcriptase inhibitors (NNRTIs) like EFV, DTG offers strong first-line therapy [4, 5]. DTG has also been shown to be effective and safe when used for second-line therapy in combination with an optimized nucleoside reverse transcriptase (NRTI) backbone in individuals with virologic failure on NNRTI or protease inhibitor (PI)-based first-line regimens [6-8]. Two randomized clinical trials in pregnant women starting ART after the first trimester have demonstrated that DTG ART more rapidly decreased viral load than EFV ART, with a significantly larger proportion of women having undetectable viral load at delivery with DTG than EFV ART [9, 10].

However, in May 2018, investigators from the Tsepamo study, a multi-site surveillance of birth outcomes for HIV-positive and HIV-negative women at hospitals in Botswana reported a potential signal for neural tube defects (NTD) with use of DTG ART at conception [11]. Four NTD were identified in 426 (0.94%) women receiving DTG at the time they became pregnant. This was significantly greater than all other comparison groups, including women on non-DTG ART regimens at the time of conception, 14 NTD/11,300 deliveries, prevalence 0.12%; starting DTG during pregnancy, 0 NTD/2,812 deliveries; and HIV-negative women, 61 NTD/66,057 deliveries, prevalence 0.09%. The study expanded from eight to 18 sites, covering 72% of all births in Botswana. Repeat analysis of data through March 2019 demonstrated a decrease in NTD prevalence with receipt of DTG at conception to 0.30% (five NTD among 1,683 deliveries) [12]. While the prevalence of NTD declined from the initial report, the NTD prevalence remained significantly higher than observed with non-DTG ART at conception (0.10%), EFV at conception (0.04%), or DTG started during pregnancy (0.04%), or in HIV-uninfected women (0.08%). Additionally, the Botswana Ministry of Health and Wellness expanded surveillance of birth outcomes at 22 selected non-Tsepamo health facilities, expanding coverage to 92% of all births in Botswana when combined with Tsepamo sites [13]. From October 2018 through March 2019, at the MOH sites, one NTD was identified among 152 women receiving DTG at conception (prevalence 0.66%) compared to no NTD among 381 HIV-positive women receiving non-DTG ART at conception and two among 2,328 HIV-uninfected women (0.09%).

A more recent analysis of the Tsepamo study including data through April 2020 was presented at the International AIDS Conference in July 2020. The prevalence of NTD with DTG at conception further decreased to 0.19% (seven NTD/3,591 deliveries), remaining stable at this rate from September 2019 through April 2020 [14]. In comparison, NTD prevalence with non-DTG ART

at conception was 0.11% (21 NTD/19,361 deliveries), with the prevalence difference between DTG vs non-DTG at conception no longer statistically significantly different (prevalence difference 0.09%, 95% CI -0.03, 0.30%). The prevalence difference with DTG at conception did remain significantly higher than EFV at conception (eight NTD/10,958 deliveries, 0.07%, prevalence difference 0.12%), DTG started during pregnancy (two NTD/4,581 deliveries, 0.04%, prevalence difference 0.15%), and HIV-uninfected women (87 NTD/119,630 deliveries, 0.07%, prevalence difference 0.12%). Finally, the most recent results from the Tsepamo study, including data through March 2022 was presented at the International AIDS Conference in July 2022. NTD prevalence had stabilized at a low level, 0.11% (10 NTD in 9,460 exposures to DTG at conception); this is now the same as the NTD prevalence of 0.11% with non-DTG ART at conception (25 NTD in /23,664 births) and is compared to 0.07% in women without HIV infection (108 NTD in 170,723 births). The prevalence of NTD in infants born to women on DTG at conception does not substantially differ from other exposure groups; prevalence difference between DTG versus non-DTG at conception (0.00%, 95% CI -0.07, 0.10) and versus HIV-uninfected women (0.04%, 95% CI -0.01, 0.13).¹

Outside of the Botswana studies, one other NTD has been reported in the January 2020 Antiretroviral Pregnancy Registry (APR) out of 382 women receiving DTG at the time of conception (prevalence 0.26%) [15]. However, most reports in the APR come from higher income countries, most with national food folate fortification, which has been shown to be associated with a decline in population prevalence of NTD [16, 17]. In Brazil, a retrospective chart review of all women with pregnancies and possible DTG exposure included in the national antiretroviral therapy database was conducted; the results found no NTDs during the study period in women conceiving on either DTG (n=382) or EFV (n=1,045) as a comparator [18]. However, two NTD were reported post-hoc in women conceiving on DTG, bringing the estimated NTD prevalence with DTG at conception to 0.18% [18, 19]. Brazil has national food folate fortification, and this NTD prevalence with DTG at conception is higher than the population NTD prevalence estimate of 0.06% [20].

Thus, the available data suggest that if DTG at conception is associated with an increased risk of NTD, this risk is likely a ~2 to 3-fold increase over the overall population rates, and not the ~9-fold increase suggested by the initial Tsepamo data in May 2018. To provide perspective on the prevalence increase observed with non-genetic factors associated with an increased risk of NTD, maternal diabetes is associated with a 2 to 10-fold increase in NTD, maternal obesity a 1.5 to 3.5-fold increase, maternal hyperthermia a 2-fold increase, low maternal red blood cell folate levels a 4-fold increase, and receipt of valproate around the time of conception a 10-fold increase [21, 22].

¹Zash R et al. Update on neural tube defects with antiretroviral exposure in the Tsepamo study, Botswana. 24th International AIDS Conference, Montreal, abstract PELBB02, 2022.

Based on the decreased NTD prevalence in the updated Tsepamo study and updated risk-benefit analyses demonstrating that the benefits of DTG significantly outweigh the potential risks [5, 23, 24], the World Health Organization (WHO) recommends DTG as a preferred first-line drug for treatment as well as a preferred second-line drug in combination with an optimized NRTI backbone in individuals failing NNRTI or protease inhibitor –based therapy [25]. The 2019 guidelines note that women should be provided with information about benefits and risks to make an informed choice regarding the use of DTG or other ART, and that continued surveillance is needed to more definitively confirm or refute the NTD signal.

Eswatini is an optimal context in which to conduct birth surveillance and generate additional data in sub-Saharan Africa in a country without folate food fortification. The adult HIV prevalence is one of the highest in the world at 27% and is 35% among pregnant women [26, 27]. The facility delivery rate is 87.7% [28]. This relatively small country has 12 public hospitals, allowing for focused efforts in facility-level capacity building and data system strengthening in a subset of high volume hospitals to allow for robust data collection of birth outcomes in the country. Eswatini began transition of HIV-positive adolescents and adults, including women of reproductive potential, to DTG-based first- and second-line ART in April 2019. DTG introduction was gradual, particularly among women in this group, in an effort to first use existing EFV stock. However, transition is expected to ramp up in 2021 and thus, preconception DTG exposures will occur during the next couple years in Eswatini, making it an ideal country to institute further birth outcome surveillance to provide additional reliable data from Africa to refute or confirm the existing NTD association.

EGPAF has been supporting the Kingdom of Eswatini since 2003 to prevent mother-to-child HIV transmission (PMTCT) and to provide HIV and AIDS care and treatment services to HIV-positive children and adults. Currently, EGPAF supports 65 health facilities in Hhohho and Shiselweni regions of Eswatini with PMTCT, HIV prevention (voluntary medical male circumcision, pre-exposure prophylaxis [PrEP]), HIV testing and counseling, ART and tuberculosis services. Together with the Ministry of Health (MOH) and other implementing partners, EGPAF has been leading efforts to strengthen birth outcomes monitoring, which will help ensure this surveillance study is well integrated into national health programming.

With planned broad transition of programs to DTG-based ART for first- and second-line treatment, it will be important to have in place sentinel surveillance to evaluate birth outcomes in women who become pregnant while receiving DTG or any new drug regimen. Through this effort, EGPAF will enhance the existing surveillance program through sentinel surveillance conducted as part of the study in five high-volume public hospitals. The system will allow for the collection of data on preconception DTG exposures and birth defects by capturing deliveries from all HIV-positive and HIV-negative women, primarily using existing facility sources. This surveillance will strengthen and improve upon efforts by the Eswatini MOH to introduce national routine pregnancy outcome and infant monitoring, helping to ensure the sustainability of such a system to evaluate new drugs

and interventions as they come to market, such as long-acting antiretrovirals for HIV treatment and prevention. Furthermore, there are currently no population-based estimates of birth defects in Eswatini. In addition to its utility in providing the comparative group for evaluating the effects of DTG exposure, these data will be useful for the country as a whole in describing the general burden of birth defects.

Study Objectives

The overall aim of this study is to evaluate the birth outcomes of HIV-positive women who are receiving DTG or other ARV drug regimens. The following primary research objectives will be addressed in selected hospitals in Eswatini:

1. To determine the proportion of neural tube defects among live and stillborn infants delivered by HIV-positive women on DTG at conception.
2. To determine the proportion of neural tube defects among live and stillborn infants delivered by HIV-negative women.
3. To determine the proportion of neural tube defects among live and stillborn infants delivered by HIV-positive women on non-DTG ART at conception.

The secondary research objectives are described below.

1. To determine the general prevalence of major external birth defects among all live and stillborn infants regardless of maternal HIV or ART status.
2. To describe pregnancy outcomes (e.g., all major and surface birth defects, preterm delivery, low birthweight, miscarriages) among women by HIV status, by ART regimen, by timing of exposure to DTG (pre- or post-conception), and other factors such as maternal age at delivery and gravida.

Study Design & Methods

Study Design Summary

This is an observational study at sentinel sites to evaluate the birth outcomes of women receiving the standard of care for ART treatment and the outcomes of HIV-negative women, with data collected at one time point for all women, at the time of delivery. Collecting data on all women who deliver at these sentinel sites with detailed information on any newborns with identifiable

birth defects will be critical to our understanding of birth outcomes and any birth defects. This will be achieved by conducting birth outcomes surveillance, with data collection planned on all deliveries during an approximate 24-month period. The target population includes all HIV-positive women with DTG exposure both before and during pregnancy, HIV-positive women on another or no ART regimen, and HIV-negative women delivering at selected hospitals. Detailed information will be collected through chart abstraction for all women, and through interviews and photographs with consenting mothers whose children have been identified to have major external birth defects.

NTD will be the primary study outcome. Key secondary outcome variables include other major and surface birth defects and other pregnancy outcomes that could be associated with ARV exposure, such as preterm delivery, low birthweight and stillbirths. The primary analysis will be descriptive, to determine the proportion of NTD among infants delivered by HIV-positive women on DTG at conception, HIV-negative women, and any available women not on DTG. Exploratory statistical investigations and modeling may be performed for birth defects or other outcomes among the groups described in secondary objective #2 provided there are sufficient sub-group numbers to do so. This will also depend on the extent of DTG transition at the time of data collection, particularly for comparisons of HIV-positive women on non-DTG regimens and those initiating DTG during pregnancy.

Site Selection

The study will be conducted in high-volume public hospitals (Table 1) across all four regions of Eswatini. Five out of the 12 hospitals in the country with the highest number of deliveries in 2020 were selected purposively. In January 2020 to December 2020, there were 20,501 deliveries in the selected hospitals and 6,393 deliveries among HIV-positive women who were on ART in antenatal care (ANC) [29]. Of the HIV-positive women on ART in ANC, 85% were on ART at the first visit, resulting in an estimated 5,434 women on ART at the time of conception in these five hospitals for the one-year period [26]. Assuming uptake of DTG will range from 65% to 90% for the women enrolled during the study period and that the delivery numbers for HIV positive women will be similar to previous programmatic numbers, this is estimated to yield 3,145 deliveries of women on DTG at conception. If assumptions are met or exceeded for NTD prevalence and the expected number of deliveries after one year of surveillance from these hospitals, approximately two years of enrollment could provide the sample size needed to rule-out a relatively rare event like an NTD (see Table 2).

Table 1. Study hospitals and number of deliveries, January to December 2020

No	Region	Hospital	# of deliveries	# of HIV positive women	# of HIV positive women on ART	Estimated # of women on DTG at conception*

1	Hhohho	Mbabane Government Hospital	5,579	1,768	1,767	872
2	Manzini	Raleigh Fitkin Memorial Hospital	5,534	1,979	1,978	961
3	Manzini	Mankayane Government Hospital	2,516	7,14	712	378
4	Lubombo	Good Shepherd Hospital	3,659	1,104	1,097	531
5	Shiselweni	Hlathikhulu Hospital	3213	828	825	403
	Total		20,501	6,393	6,379	3,145

*Based on assumptions and previous programmatic estimates

Study Population

For capture of routine pregnancy information, the study population is defined as all women delivering infants at selected hospitals in Eswatini, including women delivering stillborn infants and those who would have miscarriages or medical abortions due to identified congenital defects. A subset of this population will be recruited for additional data collection. Inclusion criteria for this subset are: (1) a birth defect as identified by a midwife or other clinician at the study hospital and (2) willing to provide informed consent. For the additional data collection component, women of any age will be considered eligible. Adolescents less than 18 years of age, defined as emancipated minors due to their pregnancy/motherhood status, will be asked to provide informed consent for themselves.

Sample Size Calculation

The sample size target will be based on updated Tsepamo study findings from 2022, which found an NTD prevalence of 0.11% (10/9,460 deliveries) compared to earlier data from 2019 which found a prevalence of 0.30% (5/1,683 deliveries) among women receiving DTG ART at conception [12]. When the sample size is between 7,500-10,000 for the exposure group of interest, a two-sided Wilson score-based 95% confidence interval for a single proportion will have a precision of 0.00083-0.00098 for an expected NTD prevalence of 0.11% among deliveries to women with DTG at conception exposure with a probability of at least 95% (Table 2)[30]. Sample sizes based on the prevalence for the other two groups using the latest Tsepamo study findings are also presented (0.07% for HIV-negative women and 0.11% for HIV-positive women not on DTG). As we expect the enrollment number for HIV-negative women to be higher than the other groups and the number of HIV-positive women on non-DTG regimens at conception to be low as DTG transition efforts mature, precision estimates are presented according to these expectations. Larger sample sizes will increase the power and decrease the type I error in the statistical models used to address secondary objective 2; therefore, we will enroll everyone during the study period. Sample sizes are provided in the table below based on varying proportions and precision.

Table 2. Sample sizes based on assumed proportions (0.0007, 0.0011) and precision ranges

Proportion	Precision (Half-Width)	Sample Size (N)	Probability
HIV-negative	0.0013	3800	0.946
0.0007	0.0014	3600	0.957
	0.0015	3400	0.966
	0.0016	3200	0.973
	0.00083	10000	0.968
HIV-positive on DTG at conception	0.00085	9500	0.962
	0.00087	9000	0.955
	0.00090	8500	0.946
	0.0011	8000	0.965
	0.00098	7500	0.958
	0.0029	1500	0.974
HIV-positive on non-DTG at conception	0.0032	1400	0.980
	0.0034	1300	0.985
	0.0035	1200	0.955
	0.0011	1100	0.965
	0.0036		

As there is some uncertainty with respect to the number of deliveries that will be observed among women receiving DTG ART at conception, enrollment numbers will be reviewed monthly for progress towards the study sample size to assess the likely trajectory for achieving the target sample size. All deliveries will be captured to help ensure we are positioned to detect an association between DTG preconception exposure and NTD, if one exists, and to be able to describe the prevalence of NTD in the general population.

Study Procedures

Enrolment:

Data collection will involve two main components: 1) birth surveillance designed to capture the deliveries of all women presenting to the five study hospitals and 2) interviews with women and photographs taken of their newborns with possible defects identified at birth. For each delivery, midwives or data collectors will complete a paper-based version of the study enrollment log (or master linking document) by writing in the date of admission, date of delivery, unique patient identifiers (e.g., Personal Identity Number [PIN], ANC and ART as applicable), ANC health facility name and the woman's name and her phone number, which are necessary to locate and link women's information in the registers and other sources (e.g., CMIS, APMR) and confirm her contact information in the case of duplicated/multiple records. To ensure that delivery data are captured in real-time (including weekends and overnight), facility-based nurse midwives will assist at the first point of data collection, particularly during off-work hours, when feasible. Per routine practice, nurse midwives will examine the infant for external birth defects; examinations of stillborns will be conducted if feasible. For each woman's entry on the log, the outcome of this examination will be documented, to capture whether or not a major external birth defect was identified. A generic term (e.g., 'determination') and an accompanying numeric response code will be used so those outside the study would not know the meaning of the code, to avoid capturing

any sensitive information in this log. This would then help to determine the next data collection step for each woman: recruit, consent, and interview to capture more detailed information on her health history and risk factors if there is a birth defect; if not, the data clerk will proceed with data abstraction. Additional procedures for each of these two steps are described below.

Chart abstraction:

Trained data collectors will be stationed at each study hospital and will be primarily responsible for data collection of still- and live-born deliveries at maternity, and any miscarriages or medical abortions due to identified congenital defects of women presenting to the facilities (Gynecology/outpatient department [OPD]/inpatient department [IPD]) to the extent possible. Each day, data collectors will review the enrollment logs completed by midwives and cross-reference those forms with the clinic registers to verify that all deliveries have been captured. They will abstract basic information about the mother, child, pregnancy and delivery using registers, patient handheld cards, and other paper-based or electronic sources, such as the national client management information system (CMIS) and the ART Patient Monitoring and Reporting (APMR), to the extent necessary, and enter into a study record using an electronic form loaded onto an electronic device. Since routine information will be collected from the existing records, and does not include any primary data collection with participants, the activity presents no more than minimal risk of harm to participants and a waiver of consent is requested.

The main study data sources used in hospitals will be the maternity and perinatal registers and the ANC card. Data, which are not available in the hospital registers or the ANC card, will be accessed in the following way:

- Data from women's electronic database entries will be extracted and integrated into their study records. This will be done by data collectors at hospitals using the onsite databases or by study staff accessing them offsite (e.g., at the EGPAF national office). For the latter, this is likely to occur when additional data collection support is needed or when the older version of an electronic database like CMIS, APMR, or the health management information system (HMIS) needs to be accessed, for example, when women received care at an ART clinic that has not yet been updated to the current electronic data capture system. Variables include PrEP regimen and start and stop dates for women who were HIV negative at the time and for women with HIV, ARV drugs taken at current regimen (as applicable) and date of last menstrual period (LMP) for women presenting to the gynecological ward or other department with miscarriages or for recommended medical abortions and for women presenting to maternity if it has not already been captured by midwives.

As part of completion of the enrollment log for women presenting to maternity, midwives or data collectors will capture the women's LMP from her handheld ANC card (if she has brought her card and this information is documented in her card), as this is critical to determining primary

outcomes, and other information as needed (see Table 3). Receipt of PrEP in pregnancy will also be captured on the log, and a 'yes' response will prompt data collectors or the larger study team to extract regimen and start and stop dates from electronic sources as needed and as described above for the women's study record.

Information about miscarriages (or spontaneous abortions, defined as < 28 weeks gestation), will also be captured to the extent possible, but will be dependent on women's self-report and presentation to the gynecological ward. Similarly, information about medically induced abortions will also be collected as feasible (described further below). Data collectors will make regular, frequent visits to the ward or other departments co-located at the same hospital as the maternity to check for any miscarriages (which may be found in the gynecological inpatient and outpatient registers or improvised registers) or medical abortions. Clinic staff may also notify study team members of women potentially meeting study criteria outside of the maternity ward. Similar information will be abstracted for women with miscarriages and abortions (to the extent it is available) and live or still births.

Interviews with women

A woman who delivers an infant with an identified major external birth defect will be referred by clinic staff and recruited for enrollment into a separate study component. Because women who have abortions will only be recruited for the study if the pregnancy was terminated due to the presence of a birth defect detected by imaging, attempts will also be made to interview them. If this is not feasible, for instance if the woman has already been discharged or the midwife is unavailable, her information will be abstracted from existing records, similar to the procedure for miscarriages as described above, plus information on the identified congenital defect. These data may be collected retrospectively (while still within the study period) or prospectively.

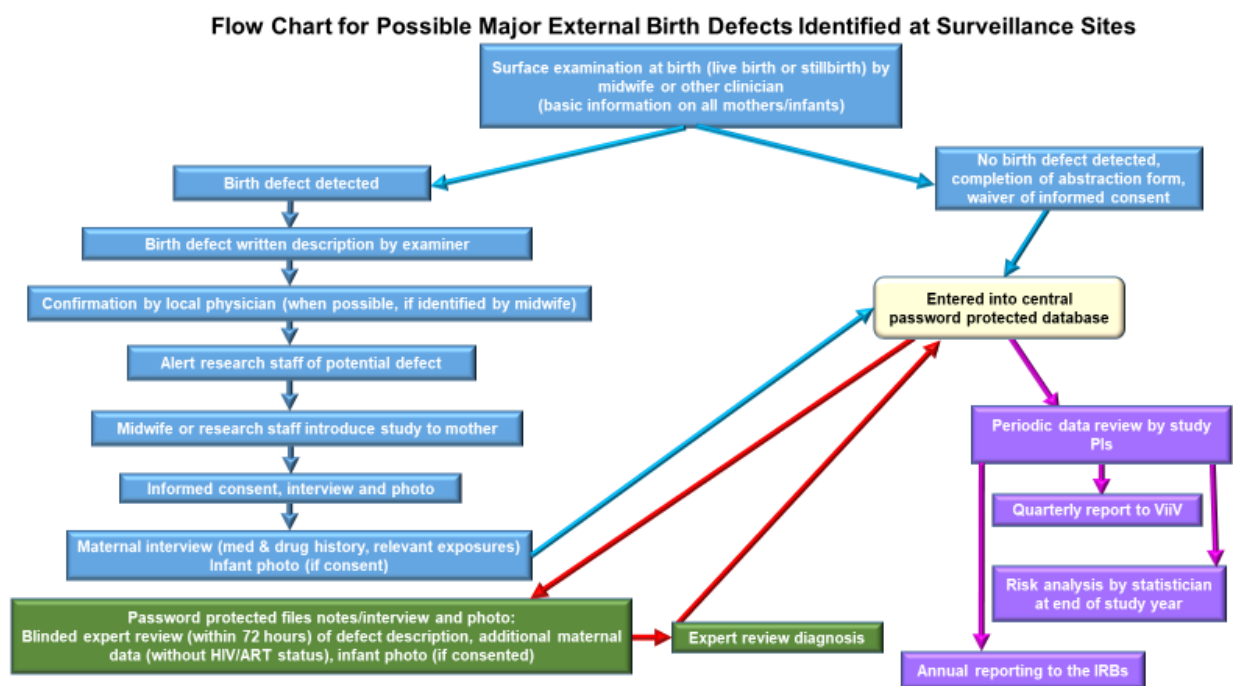
If she is willing to hear more about the study, she will undergo an informed consent process. Nurses and data collectors will be trained in the administration of informed consent, and either may perform this task. Women will be interviewed for more in-depth information on her HIV testing and ART history, other medical history of selected conditions (e.g., diabetes, malaria, TB) and potential teratogenic exposures. Data will be verified from the women's handheld patient cards and other medical records as available. Accompanying photographs of the infant will also be taken (with consent) from multiple perspectives to provide a complete picture of the defect.

As routine practice, doctors based at the maternities should examine any infant identified by the nurse midwife as having an external defect and consult on the diagnosis. As part of surveillance, existing EGPAF mentors and the study team will support efforts to standardize and strengthen this practice. The interview responses, which will include relevant details of the major structural abnormality through closed and open-ended questions, and photographs (if available), will be sent to an external expert/specialist, for a final confirmatory diagnosis by the study coordinator or other study team member. This expert will have training in medical genetics or a similar field and have

experience with these types of reviews for other studies or registries. The specialist will review the information (first stripped of HIV and ART status) and diagnosis made by the site level clinical team. It will not include the woman’s name, contact information or the hospital name; she will be identified by her study identification number only. Healthcare workers will receive feedback on the diagnoses made by the specialist. If the diagnosis by the specialist differs from the diagnosis made by the clinical staff, healthcare workers in study sites may contact the mother (with permission and phone number obtained at the time of the interview) to inform her of the final diagnosis and provide any further information or referrals as needed and appropriate.

Below is a figure that summarizes the flow of information for possible birth defects identified at surveillance sites, including reporting to the donor (ViiV Healthcare) and to the institutional review boards (IRBs).

Figure 1. Flow Chart for Possible Major External Birth Defects Identified at Surveillance Site



Training

As part of the study, health providers (doctors, nurses) in each hospital maternity will receive training to further strengthen their skills in examination and identification of birth defects. The study coordinator will also provide support to midwives at maternities for surveillance activities. The study coordinator and investigators will conduct regular monitoring visits to the hospitals to provide mentorship on performing examinations to ensure birth defects are accurately classified

and to review surveillance forms against facility records for quality assurance. In addition, mentorship and supportive supervision are already provided by implementing partners (including EGPAF) and by the MOH on a regular basis. Training and ongoing supportive supervision will be provided to nurse midwives and other providers at study hospitals to strengthen documentation practices, in addition to skills building for conducting examinations and identifying birth defects.

Study Variables and Definitions

For all deliveries/births, routine data will be captured on mother’s pregnancy history, birth outcomes, and HIV and ART information as applicable. Variables to be collected will include:

- Mother’s age, gravidity, parity, LMP, and HIV status
- Pregnancy outcomes: stillbirth (≥ 20 weeks), prematurity (< 37 weeks), delivery mode, infant birth weight, any major surface birth defects, including NTD, and neonatal death before discharge
- If HIV-positive: ART regimen at time of conception (ARVs, date initiated) and any changes through delivery (ARVs, start/stop dates).
- If HIV-negative: receipt of PrEP in pregnancy (start/stop dates), PrEP regimen

Table 3 below presents the variables to be collected through surveillance on all women and probable variable sources. They are subject to change, and will be ultimately determined by what is routinely collected under the program, as we are relying on existing data. Tool versions and instructions for completion may change over time and we will align our data collection accordingly.

Table 3. Illustrative variables to be collected for routine surveillance (all women), by likely source

Variables		Source(s)
Pregnancy and HIV history	Mother’s age	Maternity register, Perinatal register
	ANC facility	Maternity register, ANC card
	Last menstrual period	ANC card
	Gravidity	Maternity register
	Parity	Maternity register, Perinatal register
	HIV status and date of last test prior to L&D	Maternity register, Perinatal register
	HIV retesting (eligibility, testing date and result)	Maternity register
	HIV testing if not tested previously (testing date and result)	Maternity register
	Gestational age at first ANC	Perinatal register
Birth outcomes	Gestational age at delivery	Perinatal register
	Mode of delivery	Maternity register, Perinatal register
	Date of delivery	Maternity register, Perinatal register
	Stillbirth (FSB, MSB)	Maternity register, Perinatal register
	Sex of baby	Maternity register, Perinatal register

	Weight at birth	Maternity register, Perinatal register
	Single or multiple birth	Free form text in maternity register*
	Neonatal death before discharge: cause, baby age at death	Perinatal register
ART/PrEP	Current ART regimen and date started	CMIS, APMR, Perinatal register, handheld ART card
	ART regimen at time of conception (if different from above), start/stop dates	CMIS, APMR, handheld ART card
	Any other ART regimen taken during pregnancy (if applicable), start/stop dates	CMIS, AMR, handheld ART card
	Receipt of PrEP in pregnancy	ANC card
	Current PrEP use, regimen, start/stop dates	CMIS, ANC card, APMR
For women presenting to health facility with miscarriages and medically induced abortions**		
Pregnancy and HIV history	Mother's age	Gyn OPD/IPD registers, ANC card
	Last menstrual period	CMIS, ANC card
	Gravidity	Gyn/OPD/IPD registers, ANC card
	Parity	Gyn/OPD/IPD registers, ANC card
	Pregnancy condition	Gyn/OPD/IPD registers, ANC card
	HIV status	Gyn/OPD/IPD registers, ANC card, CMIS, APMR, handheld ART card
ART/PrEP	On ART	Gyn/OPD/IPD registers, ANC card, CMIS, APMR, handheld ART card
	Current ART regimen and date started	CMIS, APMR, ANC card, handheld ART card
	ART regimen at time of conception (if different from above), start/stop dates	CMIS, APMR, ANC card, handheld ART card
	Any other ART regimen taken during pregnancy (if applicable), start/stop dates	CMIS, APMR, ANC card, handheld ART card
	Current PrEP use, regimen start/stop dates	CMIS, APMR, ANC card
Birth defect (abortions only)	Birth defect and description	Ultrasound scan report

*Will capture to the extent that this is appropriately documented.

**Abortions due to identified congenital defects will only be captured under surveillance if it is not possible to conduct an interview

For the primary analysis, outcomes will be defined as follows:

HIV-positive status: women with a documented positive result in the perinatal and/or maternity register or other clinical source record.

HIV-negative status: women with the last HIV test result recorded during pregnancy or labor and delivery as negative.

DTG at conception: (for women on DTG-based regimens): determined using the date of initiation of DTG and date of LMP or gestational age at delivery (if LMP not available). Given the uncertainty around LMP and dates of conception, we are defining ART at conception as maternal ART that started up to 8 weeks after the calculated LMP date, which would be up to 6 weeks after the estimated date of conception. This will help to ensure we include the first 4 weeks of gestation, the defined period for neural tube closure.

NTD: definite (confirmed by photograph) or probable (diagnosed on the basis of a description but with no photograph) myelomeningocele, meningocele, encephalocele, anencephaly with or without craniorachischisis or iniencephaly.

Other birth defects: Using the parameters defined by the Tsepamo study, other abnormalities identified by routine surface examination before hospital discharge will be classified as major external structural malformations if they are deemed to be significant from a clinical, surgical or cosmetic standpoint [12]. Also as in Tsepamo, surface examinations will not include those of the inside of the mouth, auscultation of the heart, or testing for inguinal hernias, undescended testes, or hip dysplasia. Other diagnostics, such as imaging, may be used to make a birth defect determination for women who ultimately undergo a medically induced abortion as a result of a birth defect identified in utero. Ultrasounds are occasionally used at study hospitals at the request of patients or under certain circumstances, though chromosomal testing, mutation analysis and autopsy data will not be used.

Data Management

Data will be entered directly into ODK-X database (from tablet or any other configured electronic devices) using existing paper-based and electronic clinical record sources. Data collectors will be primarily responsible for birth surveillance while data collectors and nurse midwives will be responsible for interviews with women and taking photographs. Both will work together to help ensure every woman meeting study eligibility criteria is captured. Everyone responsible for collecting data or supervising collection will be trained on protocol specific procedures, research ethics and data entry procedures into ODK-X. Branching and skip patterns as well as logic checks and reasonable ranges will be built into data collection tools to help assure data quality. In addition, data collected for the study may need to be triangulated using multiple clinic sources, patient handheld cards, and electronic databases for relevant variables; the study team may request providers help to reconcile inconsistencies across sources.

Experienced EGPAF data management staff will oversee data entry and maintain the study database. The database will be stored on a secure web-based server using the ODK-X platform,

which has built-in encryption capabilities. All electronic devices used in the study will be password protected and access to the ODK-X application will include another level of authentication.

Data will be synchronized with the secure cloud-based server maintained by EGPAF Global, ideally on a daily basis or later (e.g., weekly) when internet connectivity is intermittent. For data that may need to be extracted from electronic sources at the EGPAF Mbabane office, the data manager or other data staff will be able to update entries to the most up-to-date database and make other modifications as needed. The study database will be automatically backed up daily on OneDrive-based repository. The backups will synchronize automatically at multiple specified times during the day. In case of data loss in the primary database in country, these backups will be used for data recovery. The in-country data manager will be responsible for the daily operations of the database, including verifying that the data are synchronizing properly between point of data collection and the database. The global data manager will support the in-country team in terms of building additional validation controls as needed, verifying that the backups are synchronizing properly on the server and routine maintenance of the server. Access to the EGPAF server will be restricted to authorized study personnel.

Confidentiality Protections

There is a minimal risk of confidentiality breach. Clinic and other ID numbers, names and contact numbers will be collected to ensure our ability to link data for a complete study record and carry out quality assurance practices. In addition, by virtue of their presence in the clinic and data abstraction activities from existing clinic records, data collectors and other study team members as part of study monitoring, will view individual health information. However, identifying information will not be contained in the same dataset with study-related information from the abstraction and interviews; this information will only be identified by a unique study identification (ID) number.

At each hospital, the study team will maintain a master enrollment log that permits linking of the participant through their ID numbers, name and contact number used for health services delivery, to their unique study number. As described above, data collectors and midwives will be responsible for completing the log. Unique study ID numbers will be preprinted on the enrollment logs. This master log will be kept in a locked cabinet in a locked office with limited access at study sites. Data collectors will also enter selected information (PIN, clinic numbers, names, phone numbers, and study ID numbers) into an abbreviated electronic version of the log loaded onto the electronic device. Only selected members of the study team will have access to the paper and electronic master documents based on the need to facilitate data collection. The electronic version will have even greater restricted access and will be used primarily for quality assurance and to enter any updates to the records that can only be done through accessing national databases from a central (office) location; data collectors will only view/access the electronic log for their respective sites. In addition, all study team members will sign a data handling and confidentiality agreement and complete an online ethics course certification. Data will also be stored in password-protected

systems or devices, with prompts to change passwords on a regular basis. Finally, to the extent possible, data abstraction will occur in a private location of the health facility to minimize any risk of unauthorized viewing of medical records.

Separate enrollment logs will be maintained for women who participate in interviews and will include participant names, the unique study ID number assigned to them and the date consented and enrolled into the study. If they agree, the log will also include their phone number to be contacted in case additional follow-up information is deemed necessary to provide after the specialist's review. Participant names and contact information will not be on any study documents linked to their interview responses nor in the study database. To minimize the risk of someone inadvertently hearing women's responses, the study team will work with hospital managers to identify private areas for interviews, such as a separate consultation room.

The enrollment logs will be destroyed after completion of data analysis. Other paper-based study documents, namely the signed consent forms for women participating in interviews, will be retained for five years after completion of the study. After that time, the documents will be destroyed and the in-country PI or designee will document the destruction.

Information provided to the specialist on birth defects will be stripped of any identifiers and shared securely with appropriate safeguards in place (e.g., password-protection, secure link instead of email). They will have access to this information until the final study analyses are completed, then we will request the specialist to document the destruction/deletion of all related study materials.

Statistical Analysis Plan

Summary statistics will be calculated for all variables of interest to describe the sample. Specifically, means and standard deviations or medians and interquartile ranges (depending on the distribution of the data) as well as minima and maxima will be calculated for all continuous variables. Frequency counts and percentages will be reported for all categorical variables.

Primary Objectives 1, 2, and 3: The proportion of NTD among all live and stillborn infants delivered by (1) HIV-positive women on DTG at conception and (2) HIV-negative women will be calculated as the number of births with NTD divided by the total number of births for each group of women, and (3) HIV-positive women on non-DTG ART at conception. The 95% confidence intervals around these proportions will be calculated with the Wilson Score method, which is appropriate for small proportions close to zero. The difference in the proportions between the three groups will be estimated along with the corresponding 95% confidence interval based on the Newcombe method. These analyses will be conducted both with and without NTD identified through ultrasound for women who underwent medically induced abortions. Statistical inference will only be made if there is sufficient power to do so.

Secondary Objective 1: The general prevalence (proportion) of major external birth defects among all live and still born infants regardless of maternal HIV or ART status will be calculated as the number of births with major external birth defects divided by the total number of births to all women. The 95% confidence intervals around the prevalence of these birth defects will be calculated with the Wilson Score method.

Secondary Objective 2: Frequencies and proportions of pregnancy outcomes (e.g., all major and surface birth defects, preterm delivery, low birthweight) will be calculated along with 95% Wilson Score confidence intervals for subgroups of women based on HIV status, ART regimen, timing of exposure to DTG (pre- or post-conception), and timing of exposure to any other ART regimen. Estimates of differences in proportions among HIV-positive women will be considered as follows: (1) Women who started on DTG ART preconception and those who started on non-DTG regimen preconception; (2) women who started on DTG preconception and those who started on DTG during pregnancy; and (3) women who started on DTG preconception and those who started a non-DTG regimen during pregnancy. Finally, all HIV-positive women on any ART regimen will be compared to HIV-negative women. Differences in these proportions between the subgroups of women will be examined with simple (unadjusted) and multiple (adjusted) logistic regression or log-binomial models. Relative risk (risk ratios) will be reported along with their corresponding 95% confidence intervals. If reliable statistical estimates cannot be generated, due to a small number of cases, we will use Firth's penalized maximum likelihood approach. Adjusted models will control for factors such as maternal age at delivery and gravida. All potential covariates will be pre-defined in a separate data analysis plan.

Ethical Considerations

Informed Consent Procedures

Written informed consent will be obtained by midwives or study staff trained in consenting procedures prior to the collection of any primary study data. Before conducting an interview, they will explain the study to the participant using the informed consent form in their preferred language (siSwati or English). This will include the purpose of the study, the risks and benefits of participation and how risks will be mitigated. They will explain that participation is voluntary and it is their choice to participate in the study; participants will be assured that they may refuse to participate or refuse to answer any questions and it will not affect their receipt of any health services. The consent form will be read clearly to participants; literate participants or witnesses of illiterate participants will be asked to read along. Participants will have the opportunity to ask any questions regarding study procedures. Once the consent form has been read and the participant feels all their questions and/or concerns have been addressed, literate participants will be asked to sign and date the consent form in the appropriate signature block. For those who are illiterate, a

thumbprint will be used to indicate consent and a witness will observe the consent process, sign and date the form to certify that the participant has been read the consent on that day and voluntarily agreed to take part in the study. Participants will be offered a copy of the informed consent form, which includes study team's contact numbers, in case they have any additional questions about participation.

Women with deliveries who consent for the study will be asked if they agree to 1) participate in an interview, 2) have photographs taken of her child (children for multiple births) to help classify the birth defect, and 3) be followed up later if the specialist reviewing her case has a different diagnosis than the maternity or other pertinent information to share. However, women may still participate in the study if they only agree to #1 or #2; if they agree to one or both of these components, they may also still participate in the study, even if they do not consent to #3.

Risks and Benefits

This observational study has minimal risk, with the primary risk being a breach of confidentiality. Ways to address this and the risk of privacy breaches have been described above in a previous section. Secondly, women participating in interviews could also feel uncomfortable or upset by the questions on their previous health history, use of drugs or other therapies, or their HIV status, particularly as they are being questioned after learning of a major birth defect in their child or undergoing an abortion. The midwives and other study staff who may be involved in this study component will be trained in non-biased interview techniques and undergo role-playing in training sessions to hone this practice. Participants will also be assured that they do not have to answer any question that they do not feel comfortable responding to, and that they may leave the study at any time.

There will be no direct benefits to participants from taking part in this study. However, the information provided by participants will add make a valuable contribution to the international and national evidence base on birth defects and risk factors, which could help to improve pregnancy and birth outcomes in the future for other women and their children.

Request for Consent Waiver

Other than the primary data collected from women with probable or definite birth defects, surveillance data will be available through routine collection of clinical data during the provision of medical care. No additional information will be collected outside of what is routinely recorded in patient records during standard medical care. For this component, there will be no direct interaction with the patients by the data collectors or other study team members for the purposes of the study. Therefore, a waiver of informed consent is being requested for the following reasons according to the U.S. Code of Federal Regulations (CFR 46.116(f)):

1. The research presents no more than minimal risk of harm to subjects,
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects; and

3. The research could not practicably be carried out without the waiver or alteration (given the number of deliveries to captured as necessitated by this study design).

Serious Adverse Events Reporting

While they are not anticipated, any serious adverse event related to the study, and which the study team is made aware of, will be reported promptly to the IRBs and the donor in accordance with their respective procedures. Reporting of any birth defects and stillbirths among women on DTG will be reported to the donor per Figure 1 above. This information will be summarized in annual reports to the IRBs. Any suspected or confirmed breaches in confidentiality will also be reported to the IRBs and the study facility will be notified as appropriate.

Compensation for Participation

Study participants will not be paid to participate in the study, nor will they be provided with incentives.

Ethical Review

This protocol will be reviewed by the Eswatini Health and Human Research Review Board (EHHRRB) and an IRB in the US.

Limitations

As this study relies heavily on routinely collected data, the primary study limitation is possible incomplete recording by health providers and inaccuracies in the records. As described above, the study team will support nurse midwives and other providers at study hospitals to strengthen documentation practices to mitigate this risk. Study staff will perform routine quality assurance checks and resolve missing and inaccurate data entries to the extent possible through ongoing data cleaning and frequent site monitoring. Secondly, as this study takes place at hospitals only, we will not be able to capture the outcomes of home deliveries. However, the facility delivery rate in the country is about 88%. Similarly, women who experience miscarriages may not present to the clinic, so we will likely underrepresent this number. Finally, during the interviews with women, there may be a certain degree of social desirability or recall biases as they try to remember for instance the name and timing of a particular medication they took, especially after they have just learned of a birth defect in their newborn or fetus. Interviewers will be trained to employ tools such as calendars, reminders of memorable events like holidays and use photographs or descriptions of certain drugs to help stimulate one's memory. They will also be trained to ask questions and receive responses in a way that does not imply judgement.

Dissemination and Utilization

The Eswatini MOH will work closely with EGPAF to disseminate results at regional and national levels and other key stakeholders in-country through study-specific meetings and via existing platforms, such as technical working group and research advisory committee meetings. The MOH will be involved throughout the study preparation and implementation stages, through MOH investigators (from the Sexual Reproductive Health Unit), Health Research and Innovations Unit, and Epidemiology and Disease Control Unit to help ensure that data serve the country’s needs for birth surveillance and that results can inform the birth surveillance network for Eswatini going forward. At regional and global levels, findings from this study will be shared across other EGPAF programs and with the donor. Abstract(s) will be submitted for consideration at national and international meetings and manuscript(s) will be submitted to an international peer-reviewed journal.

The results will inform the ongoing national surveillance program, through the provision of feedback on the quality and completeness of key indicators that could be considered for any national tool refinements and the surveillance process itself (e.g., data collection, clinic flow, etc.). As relevant, data on DTG-based ART and other regimens will also be shared with the Eswatini National AIDS Program to contribute to future discussions on national ART guideline updates for women of child-bearing age.

Estimated Study Timeline

Below is an estimated study timeline, starting from the time of receipt of IRB approval. Once approval of the protocol package has been obtained from Eswatini and US IRBs, the study duration is estimated to be 30 months, with approximately one month to develop standard operating procedures, train midwives and other study staff and prepare facilities, 24 months for data collection and approximately five months following data collection to clean, analyze and disseminate the final data. Interim data analysis, writing and dissemination activities will also be conducted while data collection is ongoing.

ACTIVITY	QUARTER (Q)									
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10
Study training and site preparation	X									
Data collection	X	X	X	X	X	X	X	X	X	
Data cleaning and analysis					X				X	
Write-up of findings					X	X			X	X
Dissemination						X				X

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Participant PTID:

Eswatini Birth Outcomes Study

Assessment of Birth Outcomes in Eswatini after Transition to Dolutegravir-Based Treatment

Chart Abstraction Form for live births, stillbirths and miscarriages

MATERNITY NAME		MBABANE GOVERNMENT HOSPITAL <input type="checkbox"/> 1 RALEIGH FITKIN MEMORIAL HOSPITAL <input type="checkbox"/> 2 GOOD SHEPHERD HOSPITAL <input type="checkbox"/> 3 HLATIKHULU HOSPITAL <input type="checkbox"/> 4 MANKAYANE GOVERNMENT HOSPITAL <input type="checkbox"/> 5
DATA COLLECTOR'S NAME/ID:	DAY / MONTH / YEAR OF ABSTRACTION:	
NAME: _____	____ / ____ / 20____	
ID: _____		
DATA COLLECTION POINT:		
	MATERNITY <input type="checkbox"/>	
	OPD/GYNECOLOGY <input type="checkbox"/>	

#	Variables	Response Options	Directions
Pregnancy and HIV history, Source: registers			
1.	Date of admission (dd/mm/yyyy)	____ / ____ / _____	
2.	Mother's age	_____ years <input type="checkbox"/> 1 Unknown/not documented <input type="checkbox"/> 87	
3.	Gravidity	___ # of pregnancies <input type="checkbox"/> 1 Unknown/ not documented <input type="checkbox"/> 87	
4.	Parity	___ # of births <input type="checkbox"/> 1 Unknown/not documented <input type="checkbox"/> 87	
5.	Last menstrual period (LMP)	_____	
6.	Gestational age at L&D booking <i>Not applicable for miscarriages/ medical induced abortions</i>	_____ weeks, _____ days <input type="checkbox"/> 1 Don't know/not documented <input type="checkbox"/> 87 N/A <input type="checkbox"/> 99	
7.	HIV status at L&D/admission	HIV positive <input type="checkbox"/> 1 HIV negative <input type="checkbox"/> 2 Never tested for HIV <input type="checkbox"/> 4 Unknown/not documented <input type="checkbox"/> 87	

8.	Tested for HIV at L&D (<i>indicate yes if there is a date of HIV test entered</i>) <i>Not applicable for miscarriages/medically induced abortions</i>	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Unknown/not documented <input type="checkbox"/> 87 N/A <input type="checkbox"/> 99	SKIP TO Q SKIP TO Q SKIP TO Q
9.	HIV test result at L&D <i>Not applicable for miscarriages</i>	HIV positive <input type="checkbox"/> 1 HIV negative <input type="checkbox"/> 2 Inconclusive <input type="checkbox"/> 3 N/A <input type="checkbox"/> 99	
10.	Date of most recent HIV test prior to L&D (<i>dd/mm/yyyy</i>) <i>Not applicable for miscarriages</i>	___/___/____ <input type="checkbox"/> 1 Unknown/not documented <input type="checkbox"/> 87 N/A <input type="checkbox"/> 99	
Birth outcomes, Source: registers			
11.	Birth outcome	Live birth <input type="checkbox"/> 1 Stillbirth <input type="checkbox"/> 2 Miscarriage <input type="checkbox"/> 3 Medically induced abortion <input type="checkbox"/> 4	<i>If miscarriage or abortion, go to Q22</i>
12.	Single or multiple birth <i>Not applicable for miscarriages/medically induced abortions</i>	Single <input type="checkbox"/> 1 Twin <input type="checkbox"/> 2 Triplet <input type="checkbox"/> 3 N/A <input type="checkbox"/> 99	For options 2 and 3, form will return to Q12 to ask for each subsequent child while retaining the same maternal information
13.	Gestational age at delivery	_____ weeks, _____ days <input type="checkbox"/> 1 Unknown/not documented <input type="checkbox"/> 87	
14.	Mode of delivery	Normal vaginal delivery (NVD) <input type="checkbox"/> 1 Assisted vaginal delivery (AVD) <input type="checkbox"/> 2 Elective C-section (ELCS) <input type="checkbox"/> 3 Emergency C-section (EMCS) <input type="checkbox"/> 4	
15.	Date of delivery (<i>dd/mm/yyyy</i>)	___/___/____ <input type="checkbox"/> 1	
16.	If stillbirth	FSB (fresh) <input type="checkbox"/> 1 MSB (macerated) <input type="checkbox"/> 2 N/A – live birth <input type="checkbox"/> 99	
17.	Sex of baby	Male <input type="checkbox"/> 1 Female <input type="checkbox"/> 2 Ambiguous <input type="checkbox"/> 3	
18.	Weight at birth	___ grams <input type="checkbox"/> 1 Unknown/not documented <input type="checkbox"/> 87	
19.	Neonatal death before discharge	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2	SKIP TO Q
20.	Causes of infant death	_____ <input type="checkbox"/> 1	

		Unknown/not documented <input type="checkbox"/> 87	
21.	Infant age at death	_____ hours <input type="checkbox"/> 1 Unknown/not documented <input type="checkbox"/> 87	<i>For all responses go to Q25</i>
22.	If miscarriage or abortion, date of miscarriage/abortion (dd/mm/yyyy)	Same as date of admission <input type="checkbox"/> 1 Different from admission date: ___/___/____ <input type="checkbox"/> 2 Unknown/not documented <input type="checkbox"/> 87	
23.	Gestational age at time of miscarriage/abortion	___ # of births <input type="checkbox"/> 1 Unknown/not documented <input type="checkbox"/> 87	
24.	Pregnancy condition	_____	
25.	Was a birth defect identified?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Unknown/not documented <input type="checkbox"/> 87 N/A <input type="checkbox"/> 99	
26.	Comments: Please use this section to indicate any additional relevant information found in source documents, including maternal complications (e.g., preeclampsia, diabetes, etc.) or child's condition (e.g., birth defect, jaundice, prematurity). <i>Applies to all infants/birth outcomes.</i>	_____ _____ _____ _____ _____	
Antiretroviral Therapy (ART), Sources: registers, electronic database			
27.	ART regimen	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2	<i>SKIP to Q</i>
28.	First two drugs ('NRTI backbone') listed in the CURRENT ART regimen:	ABC/3TC <input type="checkbox"/> 1 AZT/3TC <input type="checkbox"/> 2 TDF/3TC <input type="checkbox"/> 3 Other, specify: _____ <input type="checkbox"/> 88 Unknown/not documented <input type="checkbox"/> 87	
29.	Third drug listed in the CURRENT ART regimen:	NVP <input type="checkbox"/> 1 EFV <input type="checkbox"/> 2 ATV/r <input type="checkbox"/> 3 LPV/r <input type="checkbox"/> 4 DTG <input type="checkbox"/> 5 DRV <input type="checkbox"/> 6 Other, specify: _____ <input type="checkbox"/> 88 Unknown/not documented <input type="checkbox"/> 87	
30.	Date started CURRENT ART regimen	Known <input type="checkbox"/> 1 Date: ___/___/____ (dd/mm/yyyy) Unknown/not documented <input type="checkbox"/> 87	

31.	If unknown, when was current regimen started?	During pregnancy <input type="checkbox"/> 1 Before pregnancy <input type="checkbox"/> 2 Unknown/not documented <input type="checkbox"/> 87	
32.	Changes in ART regimen in the past 12 months (<i>from date of admission</i>)	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2	SKIP to Q
33.	Number of changes in ART regimen in past 12 months	One <input type="checkbox"/> 1 Two <input type="checkbox"/> 2 Three <input type="checkbox"/> 3	
FIRST change in ART regimen in the last 12 months from date of admission. Must be different from CURRENT regimen. Source: electronic database			
34.	First two drugs ('NRTI backbone') listed in the CURRENT ART regimen:	ABC/3TC <input type="checkbox"/> 1 AZT/3TC <input type="checkbox"/> 2 TDF/3TC <input type="checkbox"/> 3 Other, specify: _____ <input type="checkbox"/> 88 Unknown/not documented <input type="checkbox"/> 87	
35.	Third drug listed in the CURRENT ART regimen:	NVP <input type="checkbox"/> 1 EFV <input type="checkbox"/> 2 ATV/r <input type="checkbox"/> 3 LPV/r <input type="checkbox"/> 4 DTG <input type="checkbox"/> 5 DRV <input type="checkbox"/> 6 Other, specify: _____ <input type="checkbox"/> 88 Unknown/not documented <input type="checkbox"/> 87	
36.	ART regimen start date (<i>dd/mm/yyyy</i>)	Known <input type="checkbox"/> 1 Date: ___ / ___ / _____ Unknown/not documented <input type="checkbox"/> 87	
37.	ART regimen stop date (<i>dd/mm/yyyy</i>)	Known <input type="checkbox"/> 1 Date: ___ / ___ / _____ Unknown/not documented <input type="checkbox"/> 87	
38.	Reason for stopping	Side effects <input type="checkbox"/> 1 Treatment failure <input type="checkbox"/> 2 Drug interactions (e.g., TB treatment) <input type="checkbox"/> 3 Pregnancy <input type="checkbox"/> 4 Change in treatment protocol <input type="checkbox"/> 5 Other, specify: _____ <input type="checkbox"/> 88 Unknown/not documented <input type="checkbox"/> 87	
SECOND change in ART Regimen in the last 12 months from date of admission. Must be different from CURRENT regimen. Source: electronic database			
39.	First two drugs ('NRTI backbone') listed in the CURRENT ART regimen:	ABC/3TC <input type="checkbox"/> 1 AZT/3TC <input type="checkbox"/> 2 TDF/3TC <input type="checkbox"/> 3 Other, specify: _____ <input type="checkbox"/> 88 Unknown/not documented <input type="checkbox"/> 87	
40.	Third drug listed in the CURRENT ART regimen:	NVP <input type="checkbox"/> 1 EFV <input type="checkbox"/> 2 ATV/r <input type="checkbox"/> 3 LPV/r <input type="checkbox"/> 4 DTG <input type="checkbox"/> 5	

		DRV <input type="checkbox"/> 6 Other, specify: _____ <input type="checkbox"/> 88 Unknown/not documented <input type="checkbox"/> 87	
41.	ART regimen start date (dd/mm/yyyy)	Known <input type="checkbox"/> 1 Date: ___ / ___ / ___ Unknown/not documented <input type="checkbox"/> 87	
42.	ART regimen stop date (dd/mm/yyyy)	Known <input type="checkbox"/> 1 Date: ___ / ___ / ___ Unknown/not documented <input type="checkbox"/> 87	
43.	Reason for stopping	Side effects <input type="checkbox"/> 1 Treatment failure <input type="checkbox"/> 2 Drug interactions (e.g., TB treatment) <input type="checkbox"/> 3 Pregnancy <input type="checkbox"/> 4 Change in treatment protocol <input type="checkbox"/> 5 Other, specify: _____ <input type="checkbox"/> 88 Unknown/not documented <input type="checkbox"/> 87	
THIRD change in ART Regimen in the last 12 months from date of admission. Must be different from CURRENT regimen. Source: electronic database			
44.	First two drugs ('NRTI backbone') listed in the CURRENT ART regimen:	ABC/3TC <input type="checkbox"/> 1 AZT/3TC <input type="checkbox"/> 2 TDF/3TC <input type="checkbox"/> 3 Other, specify: _____ <input type="checkbox"/> 88 Unknown/not documented <input type="checkbox"/> 87	
45.	Third drug listed in the CURRENT ART regimen:	NVP <input type="checkbox"/> 1 EFV <input type="checkbox"/> 2 ATV/r <input type="checkbox"/> 3 LPV/r <input type="checkbox"/> 4 DTG <input type="checkbox"/> 5 DRV' <input type="checkbox"/> 6 Other, specify: _____ <input type="checkbox"/> 88 Unknown/not documented <input type="checkbox"/> 87	
46.	ART regimen start date (dd/mm/yyyy)	Known <input type="checkbox"/> 1 Date: ___ / ___ / ___ Unknown/not documented <input type="checkbox"/> 87	
47.	ART regimen stop date (dd/mm/yyyy)	Known <input type="checkbox"/> 1 Date: ___ / ___ / ___ Unknown/not documented <input type="checkbox"/> 87	
48.	Reason for stopping	Side effects <input type="checkbox"/> 1 Treatment failure <input type="checkbox"/> 2 Drug interactions (e.g., TB treatment) <input type="checkbox"/> 3 Pregnancy <input type="checkbox"/> 4 Change in treatment protocol <input type="checkbox"/> 5 Other, specify: _____ <input type="checkbox"/> 88 Unknown/not documented <input type="checkbox"/> 87	
Pre-exposure Prophylaxis (PrEP), Source: electronic database			
49.	Receipt of PrEP in pregnancy (indicated from log)	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Unknown/not documented <input type="checkbox"/> 87	END
50.	PrEP regimen	TDF + 3TC <input type="checkbox"/> 1	

		Cabotegravir (injection) <input type="checkbox"/> 2 Dapivirine <input type="checkbox"/> 3 Unknown/not documented <input type="checkbox"/> 87	
51.	Date started PrEP (dd/mm/yyyy)	Known <input type="checkbox"/> 1 Date: ___/___/_____ Unknown/not documented <input type="checkbox"/> 87	
52.	Date stopped PrEP (dd/mm/yyyy)	Known <input type="checkbox"/> 1 Date: ___/___/_____ Unknown/not documented <input type="checkbox"/> 87	
53.	Select yes if abortion	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2	<p>Select 'Yes' if it's an abortion and the woman is available for an interview. If yes, conduct entire interview.</p> <p>Select "No" if it is an abortion and women is not available for an interview. If "No", skip to PART V: BIRTH DEFECT QUESTIONS on the women interview form.</p>

Assessment of Birth Outcomes in Eswatini following Transition to Dolutegravir-based Treatment**Women Interview Form for Suspected Birth Defects**

MATERNITY NAME		MBABANE GOVERNMENT HOSPITAL <input type="checkbox"/> 1 RALEIGH FITKIN MEMORIAL HOSPITAL <input type="checkbox"/> 2 GOOD SHEPHERD HOSPITAL <input type="checkbox"/> 3 HLATIKHULU HOSPITAL <input type="checkbox"/> 4 MANKAYANE GOVERNMENT HOSPITAL <input type="checkbox"/> 5
INTERVIEWER'S NAME/ID:	DAY / MONTH / YEAR OF INTERVIEW:	
NAME: _____	____ / ____ / <u>20</u> ____	
ID: _____		
INDICATE IF;	LIVE/STILLBIRTH, START FROM PART 1 MEDICAL ABORTION, WOMEN AVAILABLE, START FROM PART 1 MEDICAL ABORTION, WOMEN NOT AVAILABLE GO TO PART V:	

PART I. MATERNAL CHARACTERISTICS AND HEALTH HISTORY

Instructions: I will start with questions about your pregnancy history. I will ask you questions but also verify in your records as we go along.

1.1	Nationality	Eswatini <input type="checkbox"/> 1 Other, specify: _____ <input type="checkbox"/> 88
1.2	Date of last menstrual period (dd/mm/yyyy)	From records: ___/___/___ <input type="checkbox"/> 1 Estimated: ___/___/___ <input type="checkbox"/> 2
1.3	Gestational age at booking	_____ weeks, _____ days <input type="checkbox"/> 1 Don't know/not documented <input type="checkbox"/> 87
1.4	Mother's weight at first ANC	_____ Kgs <input type="checkbox"/> 1 Don't know <input type="checkbox"/> 87
1.5	Mother's most recent weight	At last ANC _____ Kgs <input type="checkbox"/> 1 At delivery _____ Kgs <input type="checkbox"/> 2 Don't know at both ANC and delivery <input type="checkbox"/> 87
1.6	Mother's height at ANC	_____ Cm <input type="checkbox"/> 1 Don't know <input type="checkbox"/> 87
1.7	Gravida	_____ # of pregnancies <input type="checkbox"/> 1 Don't know <input type="checkbox"/> 87

1.8	Parity	___ # of births <input type="checkbox"/> 1 Don't know <input type="checkbox"/> 87	
1.9	Have you had any previous preterm deliveries (about < 37 weeks gestation)?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87 N/A <input type="checkbox"/> 99	
1.10	Have you had any previous stillborn children?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87 N/A <input type="checkbox"/> 99	
1.11	How many birth defects have you had in your previous pregnancies?	None <input type="checkbox"/> 1 Number: ___ <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87 N/A <input type="checkbox"/> 99	
1.12	If yes, please specify birth defect(s) or describe (if name unknown)	_____	

HIV-RELATED HISTORY

1.13	When was your most recent HIV test done?	Before pregnancy <input type="checkbox"/> 1 During pregnancy, before delivery <input type="checkbox"/> 2 At labor and delivery <input type="checkbox"/> 3 After delivery, before hospital discharge <input type="checkbox"/> 4 Don't know <input type="checkbox"/> 87	
1.14	What is your HIV status?	HIV positive <input type="checkbox"/> 1 HIV negative <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87 Never tested for HIV <input type="checkbox"/> 4	SKIP TO Q SKIP TO Q SKIP TO Q
1.15	When was your first positive HIV test?	___/___/___ (dd/mm/yyyy) <input type="checkbox"/> 1 Don't know <input type="checkbox"/> 87	
1.16	When was your most recent HIV negative test?	___/___/___ (dd/mm/yyyy) <input type="checkbox"/> 1 Don't know <input type="checkbox"/> 87	
1.17	When did you initiate ART?	___/___/___ (dd/mm/yyyy) <input type="checkbox"/> 1 Don't know <input type="checkbox"/> 87 N/A – never on ART <input type="checkbox"/> 99	

PART II. HIV-RELATED DRUG USE

Instructions (to say to participant): For this and subsequent questions, we are interested in learning more about what health conditions you have and what medicines you took before and after pregnancy. I will start with asking about HIV medicines, for treatment or prophylaxis. Then, I will ask about any medical conditions and other medicines, selected behaviors and any pregnancy complications. Finally, I will talk to you about the baby and birth and information on the suspected birth defect.

For interviewers, please note: <i>Before pregnancy</i> refers to the time from the month before pregnancy based on LMP or best estimate. This section should be skipped for HIV negative women.			
2.1	Is there documentation of ANY ARVs initiated or continued during this pregnancy?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2	SKIP TO Q
2.2	Is there documentation of ARVs at the time of conception?	Yes, ART <input type="checkbox"/> 1 Yes, PrEP <input type="checkbox"/> 2 No <input type="checkbox"/> 3 Don't know/not documented <input type="checkbox"/> 87	If '2' Skip to Q2.32
2.3	Initial regimen prescribed or continued during pregnancy	TDF+3TC <input type="checkbox"/> 1 TDF+3TC+EFV <input type="checkbox"/> 2 TDF+3TC+DTG <input type="checkbox"/> 3 AZT+3TC+DTG <input type="checkbox"/> 4 AZT+3TC+EFV <input type="checkbox"/> 5 Other, specify: _____ <input type="checkbox"/> 88	
2.4	Start date of initial regimen: <i>dd/mm/yyyy</i>	___ / ___ / _____	
2.5	Indicate if any part of the date is estimated (<i>can select more than one if a 'Yes' response is selected</i>)	No <input type="checkbox"/> 1 Yes, day <input type="checkbox"/> 2 Yes, month <input type="checkbox"/> 3 Yes, year <input type="checkbox"/> 4	
2.6	Is there documentation of change of ARVs to a new regimen during pregnancy?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2	SKIP TO Q
2.7	How many times were ARVs changed during pregnancy?	One <input type="checkbox"/> 1 Two <input type="checkbox"/> 2 Three <input type="checkbox"/> 3	
2.8	Date of first change of ARV regimen: <i>dd/mm/yyyy</i>	___ / ___ / _____	
2.9	Indicate if any part of the date is estimated (<i>can select more than one if a 'Yes' response is selected</i>).	No <input type="checkbox"/> 1 Yes, day <input type="checkbox"/> 2 Yes, month <input type="checkbox"/> 3 Yes, year <input type="checkbox"/> 4	
2.10	Reason for first change of ARV regimen?	Side effects <input type="checkbox"/> 1 Treatment failure <input type="checkbox"/> 2 Drug interactions (e.g., TB treatment) <input type="checkbox"/> 3 Pregnancy <input type="checkbox"/> 4 Change in treatment protocol <input type="checkbox"/> 5 Other, specify: _____ <input type="checkbox"/> 88 Don't know/not documented <input type="checkbox"/> 87	
2.11	Second ARV regimen in pregnancy?	TDF+3TC+EFV <input type="checkbox"/> 1 TDF+3TC+DTG <input type="checkbox"/> 2 AZT+3TC+DTG <input type="checkbox"/> 3 AZT+3TC+EFV <input type="checkbox"/> 4 Other, specify: _____ <input type="checkbox"/> 88	

2.12	Date of second change of ARV regimen: <i>dd/mm/yyyy</i>	___ / ___ / _____	
2.13	Indicate if any part of the date is estimated (<i>can select more than one if a 'Yes' response is selected</i>)	No <input type="checkbox"/> 1 Yes, day <input type="checkbox"/> 2 Yes, month <input type="checkbox"/> 3 Yes, year <input type="checkbox"/> 4	
2.14	Reason for second change of ARV regimen?	Side effects <input type="checkbox"/> 1 Treatment failure <input type="checkbox"/> 2 Drug interactions (e.g., TB treatment) <input type="checkbox"/> 3 Pregnancy <input type="checkbox"/> 4 Change in treatment protocol <input type="checkbox"/> 5 Other, specify: _____ <input type="checkbox"/> 88 Don't know/not documented <input type="checkbox"/> 87	
2.15	Third ARV regimen in pregnancy?	TDF+3TC+EFV <input type="checkbox"/> 1 TDF+3TC+DTG <input type="checkbox"/> 2 AZT+3TC+DTG <input type="checkbox"/> 3 AZT+3TC+EFV <input type="checkbox"/> 4 Other, specify: _____ <input type="checkbox"/> 88	
2.16	Date of third change of ARV regimen: <i>dd/mm/yyyy</i>	___ / ___ / _____	
2.17	Indicate if any part of the date is estimated (<i>can select more than one if a 'Yes' response is selected</i>)	No <input type="checkbox"/> 1 Yes, day <input type="checkbox"/> 2 Yes, month <input type="checkbox"/> 3 Yes, year <input type="checkbox"/> 4	
2.18	Reason for third change of ARV regimen?	Side effects <input type="checkbox"/> 1 Treatment failure <input type="checkbox"/> 2 Drug interactions (e.g., TB treatment) <input type="checkbox"/> 3 Pregnancy <input type="checkbox"/> 4 Change in treatment protocol <input type="checkbox"/> 5 Other, specify: _____ <input type="checkbox"/> 88 Don't know/not documented <input type="checkbox"/> 87	
2.19	Fourth ARV regimen in pregnancy?	TDF+3TC+EFV <input type="checkbox"/> 1 TDF+3TC+DTG <input type="checkbox"/> 2 AZT+3TC+DTG <input type="checkbox"/> 3 AZT+3TC+EFV <input type="checkbox"/> 4 Other, specify: _____ <input type="checkbox"/> 88	
2.20	Date of fourth change of ARV regimen: <i>dd/mm/yyyy</i>	___ / ___ / _____	
2.21	Indicate if any part of the date is estimated (<i>can select more than one if a 'Yes' response is selected</i>)	No <input type="checkbox"/> 1 Yes, day <input type="checkbox"/> 2 Yes, month <input type="checkbox"/> 3 Yes, year <input type="checkbox"/> 4	
2.22	During the time of your last menstrual period, did you miss any days taking your ARVS?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87	

2.23	<p>Is there documentation of termination or defaulting of ARVs during pregnancy? (stopping ARVs and not starting onto a new regimen prior to delivery)</p> <p><i>Yes responses include women not on ARVs at time of delivery but previously on ARVs in pregnancy</i></p>	<p>Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2</p>	SKIP TO Q
2.24	Date of ARV termination/defaulting date: dd/mm/yyyy	___/___/_____	
2.25	Indicate if any part of the date is estimated (can select more than one if a 'Yes' response is selected).	<p>No <input type="checkbox"/> 1 Yes, day <input type="checkbox"/> 2 Yes, month <input type="checkbox"/> 3 Yes, year <input type="checkbox"/> 4</p>	
2.26	Comments (please provide any ARV related clarifications or explanations for a disruption of ARVs >1 week).	<p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p>	
2.27	Did you take any other medicine (including traditional medicine) or therapy?	<p>Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2</p>	SKIP TO Q
2.28	If yes, first medicine/therapy:	_____	
2.29	First medicine/therapy: When did you take it? (<i>multiple responses permitted in some cases</i>)	<p>Up to a month before pregnancy <input type="checkbox"/> 1 In 1st trimester <input type="checkbox"/> 2 In 2nd trimester <input type="checkbox"/> 3 In 3rd trimester <input type="checkbox"/> 4 Don't know if before or during pregnancy <input type="checkbox"/> 5 During pregnancy, but don't know trimester <input type="checkbox"/> 6</p>	
2.30	If yes, second medicine/therapy:	<p>_____</p> <p>No second therapy <input type="checkbox"/> 99</p>	SKIP TO Q
2.31	Second medicine/therapy: When did you take it? (<i>multiple responses permitted in some cases</i>)	<p>Up to a month before pregnancy <input type="checkbox"/> 1 In 1st trimester <input type="checkbox"/> 2 In 2nd trimester <input type="checkbox"/> 3 In 3rd trimester <input type="checkbox"/> 4 Don't know if before or during pregnancy <input type="checkbox"/> 5 During pregnancy, but don't know trimester <input type="checkbox"/> 6</p>	

2.32	If on PrEP, PrEP regimen	TDF+3TC <input type="checkbox"/> 1 Cabotegravir (injection) <input type="checkbox"/> 2 Dapivirine <input type="checkbox"/> 3 Unknown/not documented <input type="checkbox"/> 87
2.34	Date started PrEP (dd/mm/yyyy)	Known <input type="checkbox"/> 1 Date: ___ / ___ / ___ Unknown/not documented <input type="checkbox"/> 87
2.35	Date stopped PrEP (dd/mm/yyyy)	Known <input type="checkbox"/> 1 Date: ___ / ___ / ___ Unknown/not documented <input type="checkbox"/> 87

PART III. RISK FACTORS

MICRONUTRIENTS

	Micronutrient Use	No	Yes, but unknown timing	Yes, Before pregnancy	Yes, 1 st trimester	Yes, 2 nd trimester	Yes, 3 rd trimester
3.1	FOLIC ACID	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.2	MULTIVITAMIN	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.3	FERROUS SULFATE (IRON)	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

DIABETES

3.4	Do you currently have diabetes?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87
3.5	Did you have diabetes before this pregnancy?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87
3.6	If yes to 3.4, what medicines for your diabetes did you take very early in this pregnancy between your first and third month of pregnancy? (Response should exclude traditional medicines)	None <input type="checkbox"/> 1 Injections <input type="checkbox"/> 2 Tablets <input type="checkbox"/> 3
3.7	If yes to 3.4, were you able to keep your sugar in control during this pregnancy?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87

CONVULSIONS (EPILEPSY)

3.8	Have you ever had convulsions?			Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87	SKIP TO Q SKIP TO Q		
3.9	Did you have convulsions just before you got pregnant?			Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87			
3.10	Did you have any convulsions during this pregnancy?			Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87			
	Medicines used for convulsions (Epilepsy)	No	Yes, but unknown timing	Yes, Before pregnancy	Yes, 1st trimester	Yes, 2nd trimester	Yes, 3rd trimester
3.11	VALPROIC ACID (DEPAKENE)	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.12	PHENYTOIN (DILANTIN)	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.13	FELBAMATE (FELBATOL)	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.14	CARBAMAZEPINE (TEGRETOL)	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.15	PHENOBARBITAL (LUMINAL)	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.16	OTHER MEDICINE, SPECIFY: _____	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

MALARIA

3.17	Did you have malaria during this pregnancy?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87	SKIP TO Q SKIP TO Q
3.18	Did you take any medicines or remedies for malaria during this pregnancy?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87	SKIP TO Q SKIP TO Q

	Medicines used for Malaria	No	Yes, but unknown timing	Yes, Before pregnancy	Yes, 1 st trimester	Yes, 2 nd trimester	Yes, 3 rd trimester
3.19	COARTEM (ARTEMETHER/ LUMAFANTRINE)	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.20	DUOCOTEXIN (DIHYDROARTEMISININ/ PIPERAQUINE)	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.21	FANSIDAR	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.22	QUININE	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.23	UNKNOWN MEDICINE	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.24	OTHER MEDICINE, SPECIFY: _____	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

TUBERCULOSIS

3.25	Did you have tuberculosis during this pregnancy?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87						SKIP TO Q SKIP TO Q
3.26	Did you take any medications or remedies for tuberculosis during this pregnancy?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87						SKIP TO Q SKIP TO Q
	Medicines used for TB	No	Yes, but unknown timing	Yes, Before pregnancy	Yes, 1 st trimester	Yes, 2 nd trimester	Yes, 3 rd trimester	
3.27	INH	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3.28	RIFAMPIN	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

	Medicines used for TB	No	Yes, but unknown timing	Yes, Before pregnancy	Yes, 1 st trimester	Yes, 2 nd trimester	Yes, 3 rd trimester
3.29	PYRAZINAMIDE (PZA)	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.30	ETHAMBUTOL	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.31	STREPTOMYCIN	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.32	UNKNOWN MEDICINE	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.33	OTHER MEDICINE, SPECIFY: _____	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

FEVER

3.34	Did you have any fevers, including those due to malaria, TB, flu with difficulty breathing/bad cough, pneumonia, or other illness?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87					
3.35	Did you have fevers around the time you got pregnant?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87					SKIP TO Q SKIP TO Q
3.36	Did you take any medicines or remedies for the fever?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87					SKIP TO Q SKIP TO Q
	Medicines used for Fever	No	Yes, but unknown timing	Yes, Before pregnancy	Yes, 1 st trimester	Yes, 2 nd trimester	Yes, 3 rd trimester
3.37	ASPIRIN	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.38	PARACETAMOL (PANADOL)	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.39	IBUPROFEN (BRUFEN)	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

	Medicines used for Fever	No	Yes, but unknown timing	Yes, Before pregnancy	Yes, 1 st trimester	Yes, 2 nd trimester	Yes, 3 rd trimester
3.40	DICLOFENAC	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.41	OTHER MEDICINE, SPECIFY: _____	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

ANTIBIOTIC USE

3.42	Did you take antibiotics for anything other than fever during this pregnancy?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87	SKIP TO Q SKIP TO Q
3.43	If yes, for what condition?	Specify: _____ <input type="checkbox"/> 1 Don't know <input type="checkbox"/> 87	

	Antibiotics	No	Yes, but unknown timing	Yes, Before pregnancy	Yes, 1 st trimester	Yes, 2 nd trimester	Yes, 3 rd trimester
3.44	CIPROFLOXACIN	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.45	CEFTRIAZONE	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.46	ERYTHROMYCIN	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.47	AMOXICILLIN	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.48	DOXYCYCLINE	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.49	PENICILLIN	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.50	CLOXACILLIN	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

	Antibiotics	No	Yes, but unknown timing	Yes, Before pregnancy	Yes, 1 st trimester	Yes, 2 nd trimester	Yes, 3 rd trimester
3.51	FLUCONAZOLE	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.52	COTRIMOXAZOLE	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.53	OTHER, SPECIFY: _____	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

ANY OTHER DRUG/THERAPY USE

Please use the space below to document any other drugs or therapies that were taken before pregnancy (= time from the month before pregnancy based on LMP or best estimate) or during pregnancy.							
	Other	No	Yes, but unknown timing	Yes, Before pregnancy	Yes, 1 st trimester	Yes, 2 nd trimester	Yes, 3 rd trimester
3.54	_____	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3.55	_____	<input type="checkbox"/>	Don't know if before or during pregnancy <input type="checkbox"/> 1 During pregnancy, but don't know trimester <input type="checkbox"/> 2	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

TRADITIONAL MEDICINE

3.56	Did you take any traditional medicine right before pregnancy or at any time during pregnancy?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87	<i>SKIP TO Q</i> <i>SKIP TO Q</i>
3.57	If yes, what condition did you take it for? <i>Select all that apply. The next two questions will be asked for each condition indicated here.</i>	Diabetes <input type="checkbox"/> 1 Convulsions (Epilepsy) <input type="checkbox"/> 2 Malaria <input type="checkbox"/> 3 TB <input type="checkbox"/> 4 Fever <input type="checkbox"/> 5 Other, specify: _____ <input type="checkbox"/> 88 Don't know <input type="checkbox"/> 87	
3.58	Indicate the name or main ingredient of the medicine.	Specify: _____ <input type="checkbox"/> 1 Don't know <input type="checkbox"/> 87	
3.59	When did you take it?	During first trimester <input type="checkbox"/> 1 During second trimester <input type="checkbox"/> 2 During third trimester <input type="checkbox"/> 3 Before pregnancy <input type="checkbox"/> 4 During pregnancy, but don't know trimester <input type="checkbox"/> 5	May have multiple responses to 1-5; if select 6,

		Don't know if before or during pregnancy <input type="checkbox"/> 6	should be only response
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BEHAVIORAL RISK FACTORS

3.60	How often did you consume alcohol during pregnancy?	Never <input type="checkbox"/> 1 Occasionally <input type="checkbox"/> 2 Sometimes <input type="checkbox"/> 3 Frequently <input type="checkbox"/> 4	
3.61	How often did you smoke cigarettes or use other tobacco products during pregnancy?	Never <input type="checkbox"/> 1 Occasionally <input type="checkbox"/> 2 Sometimes <input type="checkbox"/> 3 Frequently <input type="checkbox"/> 4	

PREGNANCY COMPLICATIONS AND COVID-19

3.62	Maternal diagnoses/complications during pregnancy (<i>select all that apply</i>)	None <input type="checkbox"/> 1 Pre-eclampsia <input type="checkbox"/> 2 Hypertension <input type="checkbox"/> 3 Diabetes mellitus <input type="checkbox"/> 4 Excess weight gain, obesity <input type="checkbox"/> 5 Syphilis <input type="checkbox"/> 6 High blood pressure <input type="checkbox"/> 7 Other, specify: _____ <input type="checkbox"/> 88	
3.63	Hemoglobin at ANC	Hgb at first ANC: _____ <input type="checkbox"/> 1 Hgb at other ANC visit (if 1 st not available): _____ <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87	
3.64	Were you diagnosed with COVID-19 during this pregnancy?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2	SKIP TO Q
3.65	If yes, how was it diagnosed?	COVID-19 test done <input type="checkbox"/> 1 Diagnosis based on symptoms only <input type="checkbox"/> 2 Other, specify: _____ <input type="checkbox"/> 88	
3.66	If yes, what trimester were you diagnosed?	First <input type="checkbox"/> 1 Second <input type="checkbox"/> 2 Third <input type="checkbox"/> 3 Don't know <input type="checkbox"/> 87	

PART IV. INFANT AND DELIVERY OUTCOMES

	<i>Instructions: I will now ask you questions about the birth (and child if NOT still born). As before, I will ask you questions while also verifying in your records.</i>		
4.1	Gestational age at delivery (or at time of medical induced abortion)	_____ weeks, _____ days <input type="checkbox"/> 1 Don't know/not documented <input type="checkbox"/> 87	

4.2	Single or multiple birth	Single <input type="checkbox"/> 1 Twin <input type="checkbox"/> 2 Triplet <input type="checkbox"/> 3	<i>Qs should repeat for second and third births</i>
4.3	Date of birth or abortion (dd/mm/yyyy)	___/___/_____	
4.4	Type of birth	Liveborn <input type="checkbox"/> 1 Stillborn <input type="checkbox"/> 2 Medically Induced Abortion <input type="checkbox"/> 3	
4.5	Birth weight	___ grams <input type="checkbox"/> 1 Don't know <input type="checkbox"/> 87	
4.6	Child sex	Male <input type="checkbox"/> 1 Female <input type="checkbox"/> 2 Ambiguous <input type="checkbox"/> 3	<i>For abortion and stillbirth, Q should be answered, then skip to Q4.11</i>
4.7	Length	___ cm <input type="checkbox"/> 1 Don't know <input type="checkbox"/> 87	
4.8	Head circumference	___ cm <input type="checkbox"/> 1 Don't know <input type="checkbox"/> 87	
4.9	Apgar score	_____ <input type="checkbox"/> 1 Don't know <input type="checkbox"/> 87	
4.10	Newborn complications	Jaundice <input type="checkbox"/> 1 Hypoglycemia <input type="checkbox"/> 2 Resuscitation <input type="checkbox"/> 3 Other, specify: _____ <input type="checkbox"/> 88	
4.11	Date birth defect identified (dd/mm/yyyy)	___/___/_____	

PART V. BIRTH DEFECT QUESTIONS

5.1	One or more abnormalities identified:	First infant born <input type="checkbox"/> 1 Second infant born <input type="checkbox"/> 2 Third infant born <input type="checkbox"/> 3	<i>Skip pattern to go to the affected child(ren)</i>
5.2	Is the abnormality an extra digit?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2	<i>SKIP TO Q</i>
5.3	Where are the extra digits? (select all that apply)	Left hand <input type="checkbox"/> 1 Right hand <input type="checkbox"/> 2 Left foot <input type="checkbox"/> 3 Right foot <input type="checkbox"/> 4 Don't know <input type="checkbox"/> 87	

5.4	Where on the left hand is the extra digit located?	Near the fifth digit (pinky finger) <input type="checkbox"/> 1 Near the thumb <input type="checkbox"/> 2 Other place, specify: _____ <input type="checkbox"/> 88	
5.5	Does the extra digit appear as:	A fully formed extra digit (seems to look like a finger and have bone in it) <input type="checkbox"/> 1 Soft, without a bone (sometimes hanging by a stalk) <input type="checkbox"/> 2	
5.6	Where on the right hand is the extra digit located?	Near the fifth digit (pinky finger) <input type="checkbox"/> 1 Near the thumb <input type="checkbox"/> 2 Other place, specify: _____ <input type="checkbox"/> 88	
5.7	Does the extra digit appear as:	A fully formed extra digit (seems to look like a finger and have bone in it) <input type="checkbox"/> 1 Soft, without a bone (sometimes hanging by a stalk) <input type="checkbox"/> 2	
5.8	Where on the left foot is the extra digit located?	Near the fifth digit (pinky toe) <input type="checkbox"/> 1 Near the big toe <input type="checkbox"/> 2 Other place, specify: _____ <input type="checkbox"/> 88	
5.9	Does the extra digit appear as:	A fully formed extra digit (seems to look like a finger and have bone in it) <input type="checkbox"/> 1 Soft, without a bone (sometimes hanging by a stalk) <input type="checkbox"/> 2	
5.10	Where on the right foot is the extra digit located?	Near the fifth digit (pinky toe) <input type="checkbox"/> 1 Near the big toe <input type="checkbox"/> 2 Other place, specify: _____ <input type="checkbox"/> 88	
5.11	Does the extra digit appear as:	A fully formed extra digit (seems to look like a finger and have bone in it) <input type="checkbox"/> 1 Soft, without a bone (sometimes hanging by a stalk) <input type="checkbox"/> 2	
5.12	Please provide any other details on this abnormality that are not captured above.	Description: _____ _____ _____ _____ _____ _____ _____	
5.13	Is the head and neck exam NORMAL? (includes skull, fontanelles, eyes, ears, nose, jaw)	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87	SKIP TO Q

5.14	If no, please describe abnormality: (please include as much detail as possible) <i>If not known, explain why:</i>	Description: _____ _____ _____ _____ _____ _____ _____	
5.15	Is there evidence of hydrocephalus (swollen head)?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87	
5.16	Is there a defect in the skull?	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87	
5.17	If there is a defect in the skull, is it:	Completely covered by skin <input type="checkbox"/> 1 Partly covered by skin <input type="checkbox"/> 2 Covered by a thin sac/membrane <input type="checkbox"/> 3 Not covered by skin (brain tissue visible) <input type="checkbox"/> 4 Don't know <input type="checkbox"/> 87	
5.18	Is the mouth, lip and palate exam NORMAL? (cleft lip or palate)	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87	SKIP TO Q
5.19	If no, please describe abnormality: (please include as much detail as possible) <i>If not known, explain why:</i>	Description: _____ _____ _____ _____ _____ _____ _____	
5.20	Is the chest exam NORMAL? (shape and respiratory movements)	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87	SKIP TO Q
5.21	If no, please describe abnormality: (please include as much detail as possible) <i>If not known, explain why:</i>	Description: _____ _____ _____ _____ _____ _____ _____	
5.22	Are the abdominal and anal exam NORMAL? (masses/anal closure defect)	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87	SKIP TO Q

5.23	<p>If no, please describe abnormality: (please include as much detail as possible)</p> <p><i>If not known, explain why:</i></p>	<p>Description: _____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p>	
5.24	<p>Are the arms and legs NORMAL? (length, shape, missing parts)</p>	<p>Yes <input type="checkbox"/> 1</p> <p>No <input type="checkbox"/> 2</p> <p>Don't know <input type="checkbox"/> 87</p>	<p>SKIP TO Q</p>
5.25	<p>If no, please describe abnormality: (please include as much detail as possible)</p> <p><i>If not known, explain why:</i></p>	<p>Description: _____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p>	
5.26	<p>Are the fingers and toes NORMAL? (including nails, number, dangling fused, shape or parts missing, abnormally large or small)</p>	<p>Yes <input type="checkbox"/> 1</p> <p>No <input type="checkbox"/> 2</p> <p>Don't know <input type="checkbox"/> 87</p>	<p>SKIP TO Q</p>
5.27	<p>If no, please describe abnormality: (please include as much detail as possible)</p> <p><i>If not known, explain why:</i></p>	<p>Description: _____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p>	
5.28	<p>Is the Spine exam NORMAL? (lumps or cysts or bulging in the back including the neck, thorax or lumbar area)</p>	<p>Yes <input type="checkbox"/> 1</p> <p>No <input type="checkbox"/> 2</p> <p>Don't know <input type="checkbox"/> 87</p>	<p>SKIP TO Q</p>
5.29	<p>If no, please describe abnormality: (please include as much detail as possible)</p> <p><i>If unknown, explain why:</i></p>	<p>Description: _____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p>	

5.30	Where in the spine is the defect located? (Select all that apply)	Cervical <input type="checkbox"/> 1 Thoracic <input type="checkbox"/> 2 Lumbosacral <input type="checkbox"/> 3 Don't know <input type="checkbox"/> 87	
5.31	Is the spinal defect:	Covered in hair and NOT bulging out <input type="checkbox"/> 1 Covered in hair and bulging out <input type="checkbox"/> 2 Bulging out and completely covered with skin <input type="checkbox"/> 3 Bulging out and partly covered with skin <input type="checkbox"/> 4 Bulging out and covered with only a sac/thin membrane <input type="checkbox"/> 5 Open-can see the spine/spinal cord <input type="checkbox"/> 6 Don't know <input type="checkbox"/> 87	
5.32	Are the hips and genitalia NORMAL? (including urethra, testes, penile shaft, vagina, labia)	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87	SKIP TO Q
5.33	If no, please describe abnormality: (please include as much detail as possible) <i>If not known, explain why:</i>	Description: _____ _____ _____ _____ _____ _____ _____ _____ _____	
5.34	Is the skin exam NORMAL? (pale, blue, birth marks, or any large very red areas)	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 Don't know <input type="checkbox"/> 87	SKIP TO Q
5.35	If no, please describe abnormality: (please include as much detail as possible) <i>If not known, explain why:</i>	Description: _____ _____ _____ _____ _____ _____ _____ _____ _____	
5.36	Describe any other abnormality, unusual finding or make any comment about abnormality	Description: _____ _____ _____ _____ _____ _____ _____ _____ _____	

5.37	Please indicate the preliminary diagnosis for this child.	<p>Central nervous system: Anencephaly <input type="checkbox"/> 1 Encephalocele <input type="checkbox"/> 2 Microcephaly <input type="checkbox"/> 3 Myelomeningocele/Spina bifida, open defect <input type="checkbox"/> 4 Myelomeningocele/Spina bifida, closed defect <input type="checkbox"/> 5 Hydrocephalus <input type="checkbox"/> 6 Craniorachischisis <input type="checkbox"/> 7</p> <p>Eye and ear malformations: Anophthalmia <input type="checkbox"/> 8 Microphthalmia <input type="checkbox"/> 9 Anotia <input type="checkbox"/> 10 Microtia <input type="checkbox"/> 11</p> <p>Orofacial clefts: Cleft lip <input type="checkbox"/> 12 Cleft palate <input type="checkbox"/> 13 Cleft lip and palate <input type="checkbox"/> 14</p> <p>Malformations of digestive system and genital organs Imperforate anus <input type="checkbox"/> 15 Hypospadias <input type="checkbox"/> 16</p> <p>Musculoskeletal: Talipes equinovarus / Clubfoot <input type="checkbox"/> 17 Reduction defects of the limb(s) <input type="checkbox"/> 18 Exomphalos (omphalocele) <input type="checkbox"/> 19 Gastroschisis <input type="checkbox"/> 20 Polydactyly <input type="checkbox"/> 21</p> <p>Other, specify: _____ <input type="checkbox"/> 88</p>	
5.38	Confirm that a doctor has reviewed and approved of the responses in section 5.	Yes <input type="checkbox"/> 1 No <input type="checkbox"/> 2 If no, why? _____	
5.39	Providers completing or providing input on this form (list all that apply)	Doctor name: _____ Midwife name: _____ Other: _____	

	A	B	C	D	E	F	G	H	I	J	K	L
1	Eswatini Birth Outcomes Study											
2	Birth Defects Specialist Evaluation Form, Version 2.0, 17 November 2021											
3	Date Sent	PTID	Preliminary (Interview) diagnosis	If other, specify	Interview Description (optional)	Instance (photo file) if available	Reviewer Defect Description	Organ system	If other, specify	Organ System/Preferred Term	Final defect determination	Comments
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