

Estimating Low Birthweight Prevalence and Stillbirth Rate Among HIV Pregnant Women: A  
Secondary, Health Facility-Based Cross-Sectional Study in Manica Province, Mozambique.

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A thesis

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Abstract

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**Background:** Despite remarkable progress on increasing access to antiretroviral therapy (ART), HIV infection in pregnant women is still a global concern, leading to poor maternal and child health outcomes. Estimating low birthweight prevalence and stillbirth rate among HIV-infected mothers, and understanding contextual factors associated with these pregnancy outcomes, is critical to improve child survival. This study aims to close the gap on district-level estimates of low birth weight prevalence and stillbirth rate in central Mozambique.

**Methods:** We conducted a cross-sectional exploratory analysis by combining secondary registry and health facility survey data from 36 health facilities and 2,254 HIV-infected mothers in Manica province, Mozambique. We performed a binomial test and logistic regression models

with robust standard errors to estimate the corrected prevalence of low birth weight, small for gestational age and stillbirth rate, and associated risk factors. Crude and adjusted odds ratios were provided for assessed risk factors.

**Results:** Overall, the corrected prevalence of low birth weight, small for gestational age and stillbirth rate were 13.2% (95% CI: 11.8%, 14.7%), 9.3% (95% CI: 8.10%, 10.54%), and 17.0 per 1,000 births (95% CI: 12.5, 23.6), respectively. Substantial within-province variation existed, with low birth weight ranging from 8.9% in Chimoio to 24.2% in Sussundenga districts. Gestational age below thirty-seven weeks (OR: 1.65; 95% CI: 1.29, 2.10) and failure to initiate antiretroviral therapy during pregnancy (OR: 3.52, 95% CI: 1.26, 9.82) were significantly associated with increased risk of low birth weight and stillbirth, respectively.

**Conclusion:** Low birth weight and stillbirths continue to be concerning issues in the study setting. Therefore, efforts to improve the quality of care, particularly in antenatal care services and maternity wards, are suggested to further reduce low birthweight prevalence and stillbirth rate in Manica Province.

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## Acronyms

**ART** – antiretroviral therapy

**ARVs** – antiretrovirals

**CI** – confidence interval

**HIV/AIDS** – human immunodeficiency virus infection / acquired immune deficiency syndrome

**HF** – health facility

**LBW** – low birth weight

**LMIC** – low and middle-income countries

**MoH** – Ministry of health

**OR** – Odds ratio

**PMTCT** – prevention of mother-to-child transmission

**SAIA-SCALE** – Scaling up the System Analysis and Improvement Approach for prevention of mother to child transmission of HIV

**SARA** – Service availability and readiness assessment

**SBR** – stillbirth rate

**SISMA** – health information system monitoring and evaluation

**SRB** – sex at birth ratio

**WHO** – World Health Organization

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My deepest gratitude to my husband and sons, whose love and support are with me in whatever I pursue.

Finally, I thank all the people who contributed to this academic achievement.

## Dedication

I dedicate this thesis to my wonderful sons, Denilson Fernandes and Ivans Fernandes, who were my daily source of inspiration, true love, and emotional support. To my husband, Quinhas Fernandes for unending inspiration and support, and my parents.

## Background.

Globally, HIV remains a significant public health concern. Despite the remarkable achievements with expanding access to antiretroviral therapy (ART), HIV-AIDS remains a leading cause of death and disability. In 2019, worldwide, over 690,000 deaths were recorded among the 38 million people living with HIV.<sup>1</sup> Furthermore, in 2019, it was estimated that over 1.7 million people of all ages were newly HIV infected, with Eastern and Southern Africa representing 45.5% of the total cases.<sup>1,2</sup> Young women aged 15-24 years are particularly vulnerable, being twice as likely to have HIV than men in the same age group.<sup>3,4</sup> In sub-Saharan Africa, current projections estimate that five out of six new HIV infections in adolescents will be among girls aged 15-19 years.<sup>3</sup> Despite the concerning figures, as more people access ART (26 million people in 2020), AIDS-related deaths are consistently decreasing, with an estimated 39% decline between 2010 and 2019.<sup>1</sup> Mozambique, with 2.1 million people living with HIV and an estimated prevalence among adults of 13.2% in 2015, ranks second highest among the most affected countries in sub-Saharan Africa. The annual incidence rate for HIV is 5 per 1,000 person-year of exposure, being higher among women (6 per 1,000 PYR) than men (4 per 1,000 PYR), translating to 130,000 and 120,000 thousand new infections across all ages and among adults aged 15-49, respectively.<sup>1,2</sup>

HIV is a permanent threat to pregnant women and newborns. HIV infection in pregnant women can aggravate a serious but neglected issue – stillbirths (defined as an infant that has died in the womb, with a birth weight of 1,000 grams or more and an assumed equivalence of 28 weeks of gestation - WHO).<sup>5</sup> By 2015, globally, 2.6 million stillbirths were occurring annually, of which 1.3 million occurred during the labor period. Three-quarters of the stillbirths are

concentrated in sub-Saharan Africa, and 60% in rural areas, where access to health care is still a concern.<sup>5,6</sup> In Mozambique, the stillbirth rate is estimated at 10.7 per 1000 births.<sup>6</sup> HIV appears to be an important contributor to stillbirths. Results from a meta-analysis incorporating 31 studies suggested a 3.9-fold increase in odds of stillbirth among HIV-infected women compared with HIV-uninfected women.<sup>7</sup> In Mozambique, one of the few studies addressing this issue (conducted in one district referral hospital-Manhiça), found a 1.78-fold increased risk of stillbirth among HIV-infected pregnant women.<sup>8</sup> Understanding how this risk varies between and within provinces is essential as it may provide an opportunity to identify potentially modifiable contextual factors associated with an increased stillbirth risk.

Beyond leading to mother-to-child HIV transmission, exposure to HIV during pregnancy increases the risk of premature birth and low birth weight (LBW).<sup>9-11</sup> Previous studies in sub-Saharan Africa examining the association between HIV infection and LBW reported an increased risk of LBW among neonates born from HIV-infected mothers.<sup>9-12</sup> Studies on this topic have described maternal-related factors that influence the relationship between the mother's HIV status and the LBW, including the timing of HIV diagnosis, the disease stage at the time of diagnosis, the total period under ART, and existing clinical conditions such as tuberculosis, anemia, nutrition, and malaria during the pregnancy.<sup>10</sup> The degree to which these factors interact with each other and/or confound the association between maternal HIV infection and LBW is still uncertain. For example, one of the few studies conducted in Mozambique described no relationship between maternal HIV status and birth weight, contrasting with other studies in sub-Saharan Africa.<sup>10,13,14</sup> Further research to examine the role of maternal factors such as

chronic infections and ART treatment on LBW among HIV-infected women is needed and may contribute to improving the knowledge about the association between HIV and LBW.

Low birth weight is defined by the World Health Organization (WHO) as weight at birth less than 2,500 grams regardless of gestational age.<sup>15</sup> In 2015, it was estimated that over 20 million newborns (15% of total births) were low weight at birth, with Asia and Africa accounting for over three-quarters of LBW cases.<sup>16</sup> At the current pace, achieving the 2025 nutrition target (defined in the 65th World Health Assembly, 2012) to reduce LBW by 30.0% is unlikely since the annual rate of reduction has not exceeded 1% between 2010 and 2015 (a minimal reduction rate of 3.0% *per annum* is required to achieve the goal).<sup>17</sup> Despite a 2.0% reduction in LBW between 2010 and 2015, the prevalence of LBW in Mozambique still high, estimated at 13.8% (sub-Saharan Africa range: 10.0%-15.7%), with a higher prevalence among neonates born to mothers below 20 years of age.<sup>17,18</sup> Nationally, there is no substantial difference between urban and rural areas (13.9% vs. 14.1%).<sup>19</sup> Estimating LBW prevalence accurately is challenging given the administrative data quality issues. Most LMIC still rely on mechanical scales, particularly in rural areas; therefore, newborn weights are commonly reported in multiples of 50 or 100 grams, resulting in measurement errors and misclassification of the LBW cases. For example, a child born with 2,460 grams, the weight would be rounded to 2,500 grams, therefore be classified as normal weight.<sup>20,21</sup>

This study aims to estimate the prevalence of LBW, small for gestational age (SGA) and the stillbirth rate among HIV-infected pregnant women and their children delivering in 36 health centers in Manica province – Mozambique between January and December 2017. Furthermore, the study assesses risk factors associated with LBW, SGA, and stillbirth among the study

population. The study data are from a baseline survey as part of an evaluation framework for a stepped-wedge cluster randomized trial (SAIA-SCALE) primarily focused on strengthening the prevention of mother-to-child HIV transmission (PMTCT) services in Manica province, Mozambique.<sup>22</sup>

## **Goals and Aims**

This study's overall goal is to describe fetal and newborn outcomes (LBW, SGA, and stillbirths) among HIV-infected mothers with facility delivery in a sample of 36 health facilities in Manica Province -Mozambique. The specific objectives include: 1) to estimate adverse birth outcomes (LBW, SGA and stillbirth rate per 1,000 births) among newborns born to HIV -infected mothers with facility deliveries; and 2) to explore maternal and facility-level factors associated with adverse birth outcomes (LBW, SGA, and stillbirth)

## **Conceptual Framework**

Multiple risk factors may lead to LBW through varied pathways. Overall, among HIV-infected pregnant women, tuberculosis, anemia, and other chronic conditions may contribute to poor maternal health status during pregnancy, which may interfere with weight gain and lead to inadequate intrauterine growth. However, factors such as ART initiation during pregnancy may have an opposite impact, leading to better health status during the pregnancy and, therefore, increased likelihood of normal infant weight at birth. Other factors such as parity, gestational age, smoking, and an antecedent of prematurity may directly interfere with intrauterine growth.<sup>15</sup> Regardless of the pathways, the most proximal condition to LBW is an intrauterine growth restriction. Together with other underlying cultural and socio-economic determinants,

all these factors contribute to an increased risk of LBW among infants born to HIV-infected pregnant women. On the other side, stillbirths appear to be driven mainly by complications during the labor period and third-trimester pregnancy (Figure 1).<sup>23</sup>

## Methods

**Study design:** We conducted a secondary, descriptive cross-sectional analysis using maternity registry data from 32 primary care facilities in Manica province between January and December 2017. The study included all HIV-infected mothers who gave birth to a live singleton with gestational age between 28 to 42 weeks.

**Setting:** Manica is one of the four provinces in central Mozambique, bordering Gaza, Inhambane, Sofala, Tete, and the neighboring country Zimbabwe. Manica has 12 districts, 118 primary-level health facilities, and approximately two million inhabitants.<sup>24</sup> In the primary study that this analysis is nested within (SAIA-SCALE), 36 health facilities were purposively selected to include the three highest volume (based on the volume of antenatal care visits in the year prior to study initiation) health facilities in each of the 12 districts. Three health facilities were excluded from this analysis due to lack of observations and one that had only one participant during the study period. All study health facilities are from the public sector and implement the Option B+ strategy to prevent mother-to-child HIV transmission (initiation of life-long ART after initial diagnosis regardless of CD4 counts).

**Data sources:** This study used secondary data from the SAIA-SCALE trial.<sup>22</sup> The baseline data were abstracted from photographs of maternity registries which record patient-level data from maternity ward admission to discharge. Descriptive health facility characteristics and human resources were collected on-site using standardized forms adapted from the World

Health Organization Service Availability and Readiness Assessment (SARA) tool. A trained study assistant collected and entered facility-level characteristics data into REDCap for data storage, transfer and quality control. We used Ministry of Health service delivery data from the health information system (SIS-MA; based on the DHIS2 platform) to estimate service workload. We also used the 2018 SARA data to cross-check and validate the health facility classification data. All the datasets were merged at the health facility level using unique identifiers.

**Study Outcomes:** We defined three **primary outcomes**: low birth weight, small for gestational age, and stillbirth rate. i) Low birthweight: For the study purpose, we adopted the WHO definition of weight at birth less than 2,500 grams regardless of the gestational age. The variable was dichotomized at a newborn weight of 2,500. To minimize LBW misclassification, we corrected birthweight value by randomly assigning birth weights recorded between 2,450 grams and 2,549 grams to multiples of 5 instead of the original multiples of 50. ii) Small for gestational age: SGA was defined as a corrected birth weight below the 10<sup>th</sup> percentile of weight for gestational age. The variable was dichotomized at a birthweight cutoff below 10<sup>th</sup> percentile, using the INTERGROWTH-21<sup>st</sup> standards/references curves.<sup>25</sup> iii) Stillbirth rate: Stillbirth was defined as the number of stillbirths per 1,000 births. WHO defines stillbirth as a baby born after 28 weeks of gestation with no vital signs.

**Covariates:** We grouped study covariates into three categories, including maternal characteristics (number of previous deliveries, gestational age at delivery, and ART initiation during pregnancy), newborn characteristics (sex at birth), and health facility characteristics (health facility type, number of MCH nurses working at ANC and maternity units, and MCH

nurses' workload at ANC and maternity defined as xxxx). These variables were selected based on review of the literature and their availability for this analysis.

Maternal characteristics were parameterized as follows. i) Parity was defined as the number of deliveries that the women had prior to the most recent pregnancy. The variable was categorized into five categories: nullipara (first delivery; reference group), second and third deliveries, multipara (4<sup>th</sup> and 5<sup>th</sup> deliveries), and grand multipara (6<sup>th</sup> or more deliveries). ii) ART initiation captured whether the women initiated ART during the pregnancy and was dichotomized into a binary form (with newly initiating ART as the reference group). iii) Gestational age at delivery was recoded into three categories: 28-36 complete weeks, 37-41 complete weeks (reference), and 42 or more complete weeks of gestation.

Newborn Characteristics: Newborn sex describes the sex assigned at birth, categorized as male (reference) and female.

Health facility characteristics: Health facilities classification was based on the Ministry of Health guidelines (decree 127, 2002 – Table A) and the Ministry of Health 2018 Service Availability and Readiness Assessment (SARA). i) Health facility location was coded as urban if located in a municipality or classified as district hospital or urban HF; otherwise, it was considered rural. ii) Health facility type was categorized as a district hospital, urban HF, and rural HF. iii) Number of maternal and child health nurses at antenatal care and maternities services describes the absolute number of nurses counted during in-person data collection. iv) MCH nurse workload was defined as the average number of first ANC visits per MCH nurse per day and the average number of deliveries per nurse per day, respectively. The average number of

ANC visits and maternity deliveries was calculated using service utilization data from the same time period that registry data covered (June- August/2018).

**Analysis:** Tables and plots were developed to assess data completion, potential outliers, and deviation from normality; we used this initial exploratory analysis to refine the model parametrization. We computed the mean and standard deviation for continuous variables and frequencies and percentages for categorical variables and generated descriptive statistics for all variables used to describe maternal and child clinical characteristics. Employing a binomial regression and accounting for clustering at the health facility level, we estimated the LBW and the corrected LBW prevalence, stratified by district and health facility location. Using the same model, we estimated the stillbirth rate per 1,000 births. We performed a logistic regression with generalized linear models (glm with link logit & robust standard errors) for each exploratory variable (crude analysis) to explore mother, child, and facility-level factors associated with LBW and SGA, followed by an adjusted model. The crude and adjusted odds ratios (and respective 95% CI) for the corrected LBW and SGA were reported. All the analysis was performed in R version 4.0.3.<sup>26</sup>

## **Results**

### **Descriptive Statistics**

The sample initially included 36 health facilities and 2,459 mothers; however, four maternities were excluded due to a lack of data on births to an HIV-infected woman during the study period. A total of 150 mothers were excluded for at least one of the following reasons: i) HIV negative test; ii) unknown HIV status; iii) gestational age below 28 weeks, and iv) baby with a birth weight below 1,000 or over 5,000 grams. Furthermore, three mothers were excluded due

to a lack of information on the district or health facility provenance. We remained with a total of 2,306 mother-infant pairs, which served as the final sample to estimate the stillbirth rate. An additional 52 mothers were excluded from the LBW and SGA analysis because the pregnancy outcome was a stillbirth. Therefore, the final sample used to estimate the LBW and SGA prevalence and associated risk factors included 2,254 mother-infant pairs (Figure 2).

Of the 2,254 HIV-infected mothers sampled, more than half (55%) were from three districts: Chimoio 734 (32.6%), Manica 349 (15.5%), and Gondola 281 (12.5%). Out of the 2,254 live newborns, 1,145 (50.8%) were male, and the estimated ratio of males to females was 1.03 (95% CI: 0.95, 1.12). Of the sampled mothers, n (57.3%) had a gestational age between 37 and 41 weeks, and over 90% were on ART. Study facilities had between one and six MCH nurses working at ANC services, and four to seven nurses working at maternity wards. Each of the MCH nurses assisted on average between three and four first ANC visits and one to three deliveries per day. About 45% (n) of the facilities had nutritionists, mostly concentrated in urban areas. Except for gestational age, the sample was balanced across groups defined by LBW. For SGA, only ART and newborn sex were balanced (Table 1 & 2).

**LBW Prevalence:** The overall estimated LBW prevalence was 8.7% (95% CI: 7.6%, 9.9%). This prevalence increased to 13.2% (95% CI: 11.8%, 14.7%) after correcting birthweights. There was substantial heterogeneity across districts, with Gondola (10.3%) and Manica (9.0%) districts having the lowest corrected LBW prevalence; The highest corrected LBW prevalence was observed in Sussundenga (24.2%) and Guro (22.4%). Furthermore, the corrected LBW prevalence in rural areas was 16.1% (95% CI:13.5%, 19.1%) compared to 11.9% (95% CI: 10.4%, 13,7%) observed in urban areas (Figure 3).

**SGA Prevalence:** We estimated an overall SGA prevalence of 9.4% (95% CI: 8.2%, 10.7%). This prevalence had a negligible change (9.27% (95% CI: 8.10%, 10.54%)) when birthweight for gestational age was corrected. We also found increased variability across districts with Mussorize (5.7%) and Chimoio (6.4%) districts reporting the lowest prevalence, and Sussundenga and Macate reporting the highest prevalence (estimated at 22.5% and 14.6%, respectively). Contrary to observed LBW patterns, the corrected SGA prevalence was similar in rural areas (9.8%; 95% CI: 7.7%, 12.3%) and urban areas (9.0%; 95% CI: 9.0%, 10.5%) (Figure 4).

### Model-based results

**Risk factors for LBW.** Newborns born to mothers with gestational age between 28 and 36 weeks had a 1.7-fold higher odds of having a LBW infant when compared to newborns born from mothers with full-term gestation (95% CI: 1.33, 2.17), after adjusting for health facility type and the number of nutritionists. Model-based crude results suggest that pregnant women on ART had an 11% (OR=0.89, 95% CI: 0.57, 1.40) lower odds of delivering a baby with LBW compared to HIV-infected pregnant women not on ART. This association was attenuated to 9% lower odds (OR = 0.91, 95% CI: 0.58, 1.44) after adjusting for health facility location and ANC workload. Using nullipara (no previous pregnancy) as the reference group, the adjusted odds of LBW was 38% lower for second births (OR=0.62, 95% CI: 0.38, 1.00) and 17% lower for those with six or more previous births (OR=0.83, 95% CI: 0.46, 1.51). The odds of LBW was also reduced in male infants (19% lower compared with females) and newborns at urban health facilities (28% lower than rural facilities). Except for gestational age, none of the other adjusted ORs were statistically significant (Table 3 and Figure 5).

**SGA risk factors.** Newborns born to mothers with gestational age between 28 and 36 weeks of gestation had 81% (95% CI: 71%, 88%) lower odds of being SGA when compared to those born to mothers with full-term gestation. For women with post-term gestation, the odds of having a child weight less than 2,500g was 5.6 times higher (95% CI: 2.75, 11.27), after adjusting for health facility type and the number of nutritionists. The odds of having a SGA newborn was 5% (OR = 0.95, 95%: 0.55,1.63) lower when ART was initiated during pregnancy, 8% (OR=0.92; 95% CI: 0.69, 1.23) lower for male newborns, and 20% (OR: 0.80; 95% CI:0.52, 1.22) lower in urban health facilities. Similar to LBW, no adjusted OR was significant, except for gestational age (Figure 6).

**Stillbirth Rate.** On average, 17.0 per 1,000 births were born with no vital signs (95% CI: 12.5 to 23.6). This rate ranged from 38.4/1,000 births in Macossa district to 6.8/1,000 births in Machaze district. Guro and Macate did not register any stillbirths during the study period. After adjusting for facility location, parity, gestational age, and workload, the odds of stillbirth was 3.52-fold higher (95% CI: 1.26, 9.82) among HIV-infected pregnant women who were not on ART at the time of delivery.

## Discussion

In this exploratory analysis of birth outcomes among HIV-infected mothers in central Mozambique, the LBW prevalence was found to be 13%, which is high but consistent with the national 14% average and is within the range reported in other sub-Saharan Africa countries. Notably, the potential misclassification of birthweight estimates was found to underestimate LBW prevalence by 4.5 percentage points, suggesting that guidelines and equipment (including electronic scales) are needed to accurately measure birth weight in maternity wards. Small for

gestational age prevalence did not vary after correction, which is likely due to SGA including birthweight adjustments for specific gestational ages. However, the magnitude of risk of SGA observed in among women with gestational age equal or above 42 weeks is likely overestimated due to inaccurate estimates of gestational age. Indeed, some studies have suggested errors in determining accurately the gestational age, but the higher prevalence of SGA in this group compared to term pregnancies is unusual.<sup>27,28</sup>

Not surprisingly, and consistent with other studies, we did find that gestational age is the most relevant predictor of LBW. Indeed, two important processes, the gestation duration and the intrauterine growth rate have a solid causal relationship with LBW.<sup>15</sup> Even though other predictors were not significantly associated with LBW, the direction of association and the magnitude provide important information to guide program efforts. The increased risk of LBW in rural areas highlights a chronic problem of social disparities between urban and rural areas, including access to education, water, sanitation, food, healthcare, and other social determinants of health. The role of food availability on LBW prevalence in this setting deserves further scrutiny. The two districts with the highest LBW prevalence (Sussundenga and Guro) have different agricultural productivity profiles, with Sussundenga being a highly productive agricultural zone while Guro is cyclically prone to food insecurity. Social, cultural and economic aspects may play a role in the daily diet in this setting, suggesting that follow-up qualitative studies may help clarify the complexity of this issue.<sup>29</sup> Furthermore, within districts, disparities may correlate with community-level services availability, including the presence of community health workers or other community-based groups providing nutrition education. Currently,

several studies have demonstrated the role of community health workers in improving maternal and child health outcomes, particularly among vulnerable population in LMIC.<sup>30,31</sup>

Our findings indicate a concerning scenario regarding stillbirth. The stillbirth rate in this setting is almost two-fold higher than the national average, and significantly increases with failure to initiate ART during pregnancy. The literature around stillbirth rate among women with HIV is inconclusive, but the effect seems to vary by ART regimen used. In Mozambique, one of the few studies on this topic demonstrated a significant reduction in miscarriage and stillbirth rates (from 26% to 5%) among HIV-infected mothers on triple therapy with ART, which is consistent with our results.<sup>32,33</sup> Therefore, these study results are relevant to inform future research in this area. The issue of stillbirths is complex and correlates to the quality of care. The current state of the literature suggests that at least 40% of stillbirths are intrapartum. Unfortunately, in this study, we could not assess whether stillbirth occurred during or before the labor period due to a lack of data. We only observed 38 stillbirths in the study period, of which two were macerated, indicating that quality of care in the last trimester of pregnancy or during labor at maternity wards may persist. This topic deserves special attention going forward.

This study had notable limitations. First, it lacks patient-level sociodemographic, obstetric, and clinical variables such as duration of time on ART, which would have enriched our analysis of patient-level risk factors for adverse pregnancy outcomes. In addition, we were unable to link individual-level data across ANC and maternity services (as initially intended) due to inconsistencies with unique patient identifiers; therefore, we were unable to analyze potential risk factors from the ANC period. Second, because only three facilities were selected per district and only HIV-infected women were included in the sample, many (particularly small) clinics and

HIV-uninfected women were not included, which limits generalizability of study results. Despite these limitations, the study has important strengths. First, we were able to include a large sample using routine registry and survey-based data to estimate LBW and SGA prevalence, as well as stillbirth rate, across a large number of health facilities. Second, the analytical approach is robust, designed to describe facility-level heterogeneity, correct LBW and SGA estimates, and highlight critical issues of stillbirth classification. Third, we have addressed an important topic that is often neglected.

## **Conclusion**

Given the limitations in study design and data sources, these results should be interpreted with caution. Limitations notwithstanding, LBW prevalence is high in central Mozambique, with preventable deleterious long-term outcomes for LBW children. Notably, province-level aggregate estimates obscure substantial disparities between districts. Our analysis indicates that women delivering during the pre-term period are more likely to have babies with LBW. More importantly, we found that ART initiation in ANC services is associated with reduced odds of having a stillbirth. In the light of these findings, efforts to continue improving quality of care, particularly in ANC services and maternity wards, are needed to further reduce LBW prevalence and the stillbirth rate in Manica Province.

## Figures

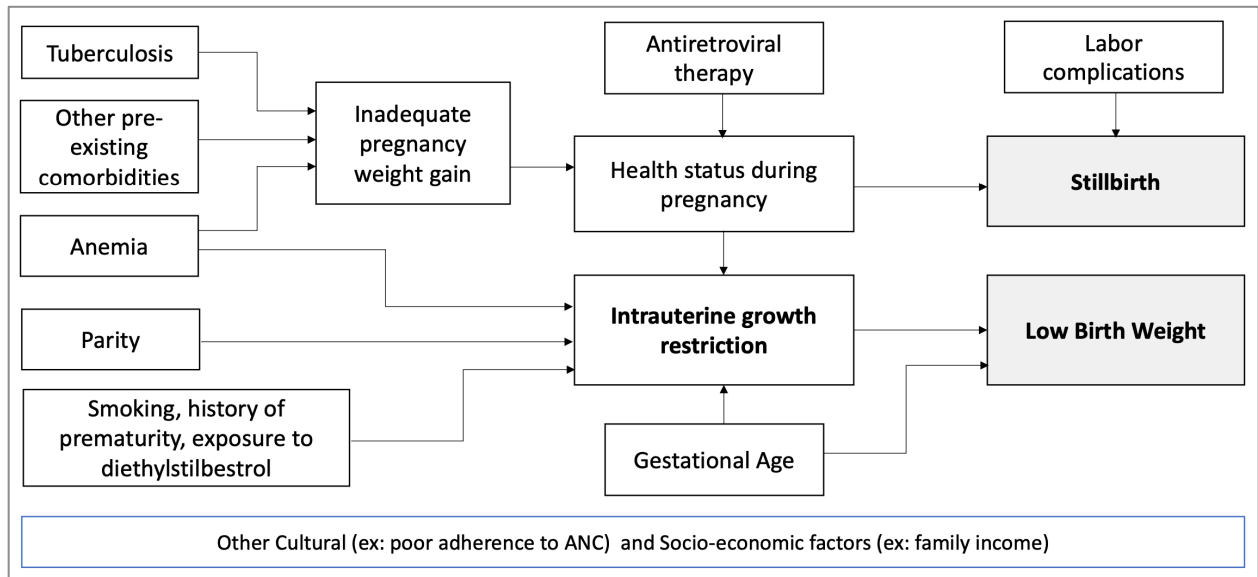


Figure 1: Conceptual Framework. Adapted from Amer Imdad, Zulfiqar Bhutta. 2013<sup>34</sup>

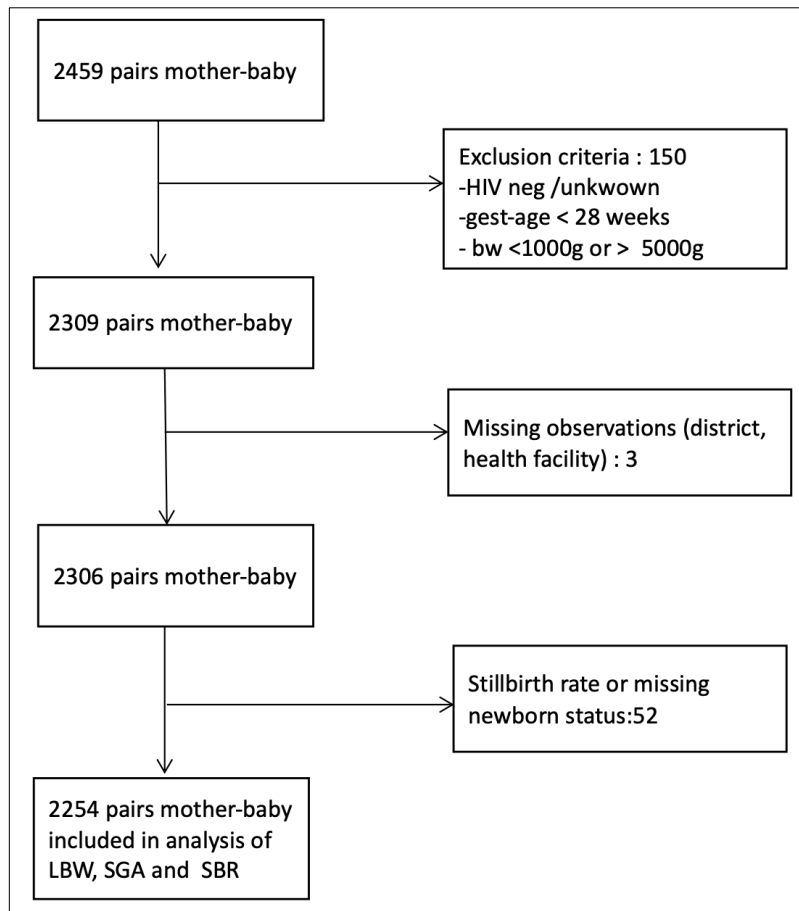


Figure 2: Cohort of Mother-Infant Pairs Included in the Study

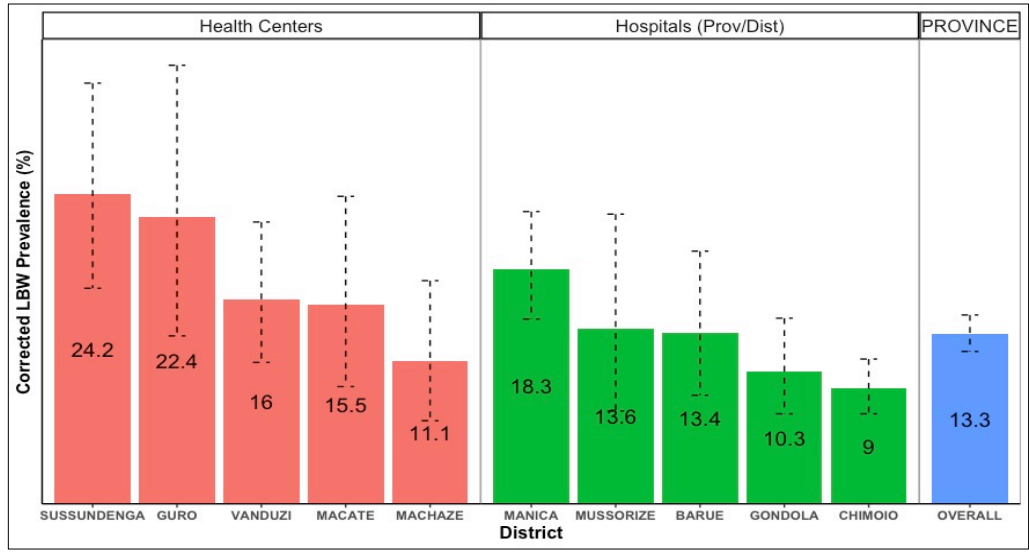


Figure 3: Prevalence of LBW by District

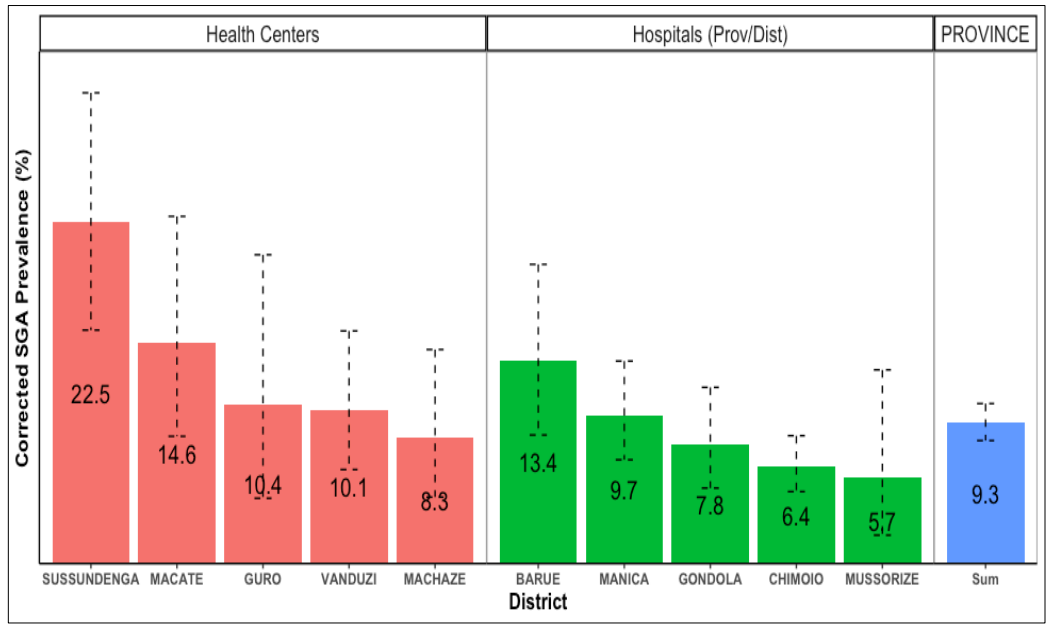


Figure 4: Prevalence of SGA by District

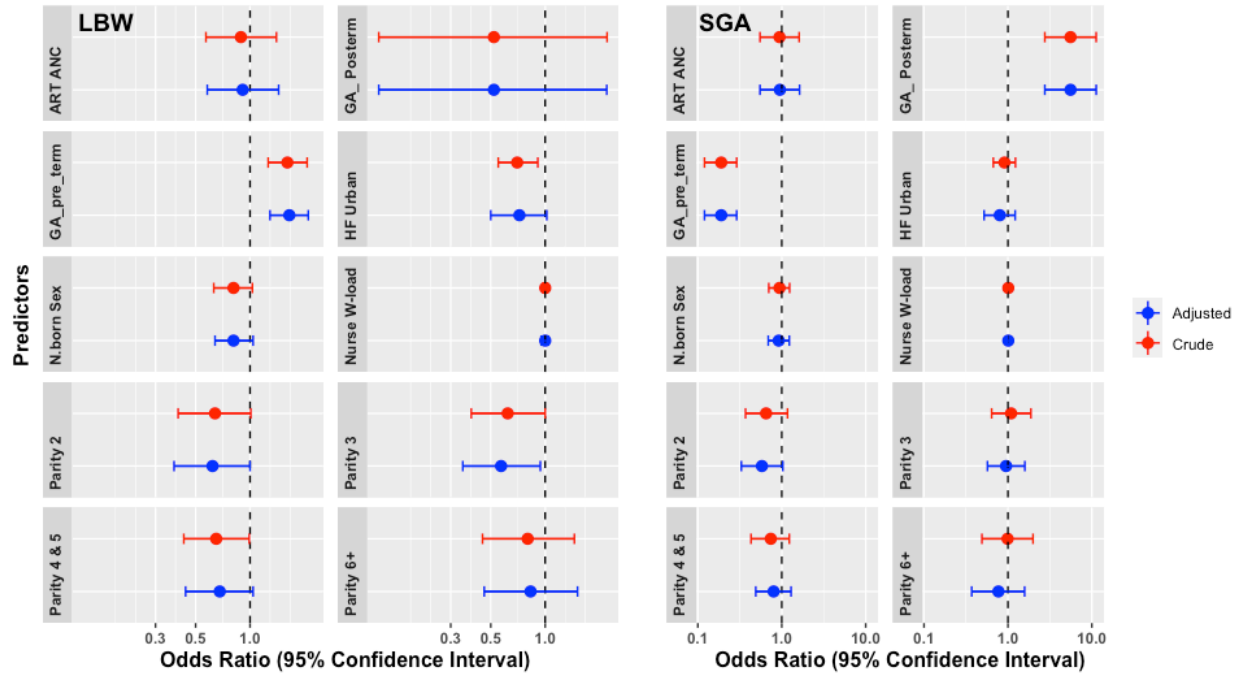


Figure 5: Factors Associated with LBW and SGA

## Tables

Table 1: Participant Characteristics by LBW and SGA

	Overall	LBW		SGA	
	(n=2254) N (% n)	BW>2,500g (n=1955) N (% n)	BW<2,500g (n=299) N (% n)	BW/GA >10th perc (n=2045) N (% n)	BW/GA <10th perc (n=209) N (% n)
<b>Total live births</b>					
<b>Parity (%)</b>					
Nullipara	223 (12.5)	184 (11.8)	39 (17.0)	200 (12.3)	23 (14.6)
2nd delivery	387 (21.7)	341 (21.9)	46 (20.0)	360 (22.1)	27 (17.2)
3rd delivery	358 (20.1)	316 (20.3)	42 (18.3)	318 (19.5)	40 (25.5)
4th & 5th delivery	680 (38.1)	597 (38.4)	83 (36.1)	627 (38.5)	53 (33.8)
>=6 delivery	137 (7.7)	117 (7.5)	20 (8.7)	123 (7.6)	14 (8.9)
<b>Gestational age (%)</b>					
28-36weeks	930 (41.3)	775 (39.6)	155 (51.8)	904 (44.2)	26 (12.4)
37-41weeks	1291 (57.3)	1149 (58.8)	142 (47.5)	1123 (54.9)	168 (80.4)
>=42 weeks	33 (1.5)	31 (1.6)	2 (0.7)	18 (0.9)	15 (7.2)
<b>ART during pregnancy (%)</b>					
Yes	1872 (91.7)	1631 (91.8)	241 (90.9)	1705 (91.8)	167 (91.3)
<b>Newborn sex</b>					
Male	1145 (50.8)	1007 (51.5)	138 (46.2)	1042 (51.0)	103 (49.3)

Table 2: Facility Characteristics

	Overall	Rural	Urban
	(n=32) N (% n)	(n=23) N (% n)	(n=9) N (% n)
<b>Total health facilities</b>			
ANC MCH nurses [median (IQR)]	3.0 (1.0-6.0)	2.0 (1.0-6.0)	3.0 (2.0-7.0)
Maternity MCH nurses [median (IQR)]	4.0 (4.0 -7.0)	4.0 (2.0-5.0)	5.0 (4.0-7.0)
ANC workload [median (IQR)]	3.9 (1.9-6.6)	2.9 (1.5-5.6)	3.9 (1.9-6.6)
Maternity workload [median (IQR)]	1.4 (1.1 -2.26)	1.2 (1.1- 2.0)	1.8 (1.1- 2.2)
Mother2mother group (%)			
Yes	27 (84.4)	18 (78.3)	9 (100.0)
Nutritionists (%)			
Yes	13 (44.8)	6 (28.6)	7 (87.5)

Table 3: Crude and Adjusted Odds Ratios for LBW and SGA

	LBW		SGA	
	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
<b>ART during pregnancy</b>				
No	Ref	Ref	Ref	Ref
Yes	0.89 (0.57, 1.40)	0.91 (0.58, 1.44) <sup>a, b</sup>	0.94 (0.55, 1.61)	0.95 (0.55, 1.63) <sup>a, b</sup>
<b>Newborn sex</b>				
Female	Ref	Ref	Ref	Ref
Male	0.81 (0.63, 1.03)	0.81 (0.64, 1.04) <sup>d</sup>	0.94 (0.70, 1.24)	0.92 (0.69, 1.23) <sup>a, b</sup>
<b>ANC workload</b>	1.00 (0.97, 1.03)	1.00 (0.95, 1.04) <sup>a, c, e</sup>	1.01 (0.98, 1.05)	1.01 (0.98, 1.05) <sup>a, c, e</sup>
<b>Parity</b>				
Nullipara	Ref	Ref	Ref	Ref
2nd deliv	0.64 (0.40, 1.01)	0.62 (0.38, 1.00) <sup>c, f</sup>	0.65 (0.37, 1.17)	0.58 (0.33, 1.03) <sup>c, f</sup>
3rd deliv	0.62 (0.39, 1.00)	0.57 (0.35, 0.94)	1.09 (0.64, 1.88)	0.95 (0.57, 1.59)
4th & 5th deliv	0.65 (0.43, 0.99)	0.68 (0.44, 1.04)	0.74 (0.43, 1.23)	0.80 (0.49, 1.29)
>=6 deliv	0.80 (0.45, 1.45)	0.83 (0.46, 1.51)	0.99 (0.49, 1.99)	0.77 (0.37, 1.58)
<b>Gestational Age</b>				
37-41 weeks	Ref	Ref	Ref	Ref
28-36 weeks	1.61 (1.26, 2.07)	1.65 (1.29, 2.10) <sup>a, b</sup>	0.19 (0.12, 0.29)	0.19 (0.12, 0.29) <sup>a, b</sup>
>=42 weeks	0.52 (0.12, 2.20)	0.52 (0.12, 2.19)	5.57 (2.75, 11.26)	5.57 (2.75, 11.27)
<b>HF Location</b>				
Rural	Ref	Ref	Ref	Ref
Urban	0.70 (0.55, 0.91)	0.72 (0.50, 1.02) <sup>b, c</sup>	0.91 (0.67, 1.23)	0.80 (0.52, 1.22) <sup>b, c</sup>
<b>Nutritionists</b>				
None	Ref	Ref	Ref	Ref
One	1.26 (0.90, 1.75)	1.33 (0.95, 1.87)	1.30 (0.88, 1.93)	1.31 (0.88, 1.96)
Two	0.74 (0.54, 1.02)	0.87 (0.56, 1.02) <sup>a</sup>	0.85 (0.58, 1.23)	0.86 (0.57, 1.30) <sup>a</sup>

Hf location<sup>a</sup>, ANC workload<sup>b</sup>, Nutritionists<sup>c</sup>, Gestational age<sup>d</sup>, ART during pregnancy<sup>e</sup>, Newborn sex<sup>f</sup>

## References

1. UNAIDS. Global Hiv Statistics 2020. *End AIDS epidemic*. 2020;(June):1-3.
2. UNAIDS. AIDSinfo. 2019.
3. Birdthistle I, Tanton C, Tomita A, et al. Recent levels and trends in HIV incidence rates among adolescent girls and young women in ten high-prevalence African countries: a systematic review and meta-analysis. *Lancet Glob Heal*. 2019;7(11):e1521-e1540. doi:10.1016/S2214-109X(19)30410-3
4. Hegdahl HK, Fylkesnes KM, Sandøy IF. Sex differences in HIV prevalence persist over time: Evidence from 18 countries in Sub-Saharan Africa. *PLoS One*. 2016;11(2):1-17. doi:10.1371/journal.pone.0148502
5. Lawn JE, Blencowe H, Waiswa P, et al. Stillbirths: rates, risk factors, and acceleration towards 2030. *Lancet*. 2016;387(10018):587-603.
6. Blencowe H, Cousens S, Jassir FB, et al. National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis. *Lancet Glob Heal*. 2016;4(2):e98-e108.
7. Brocklehurst P, French R. The association between maternal HIV infection and perinatal outcome: a systematic review of the literature and meta-analysis. *BJOG An Int J Obstet Gynaecol*. 1998;105(8):836-848.
8. García-Basteiro AL, Quintó L, Macete E, et al. Infant mortality and morbidity associated with preterm and small-for-gestational-age births in Southern Mozambique: A retrospective cohort study. *PLoS One*. 2017;12(2):e0172533.
9. Chen JY, Ribaudo HJ, Souda S, et al. Highly active antiretroviral therapy and adverse birth outcomes among HIV-infected women in Botswana. *J Infect Dis*. 2012;206(11):1695-1705. doi:10.1093/infdis/jis553
10. Biodun N Olagbuji , Michael Chudi Ezeanochie, Adedapo B Ande VOO. Obstetric and perinatal outcome in HIV positive women receiving HAART in urban Nigeria. *Arch Gynecol Obs*. (;281(6):991-4.).
11. Dreyfuss ML, Msamanga GI, Spiegelman D, et al. Determinants of low birth weight among HIV-infected pregnant women in Tanzania. *Am J Clin Nutr*. 2001;74(6):814-826. doi:10.1093/ajcn/74.6.814
12. Zeleke BM, Zelalem M, Mohammed N. Incidence and correlates of low birth weight at a referral hospital in northwest ethiopia. *Pan Afr Med J*. 2012;12(1):1-8. doi:10.11604/pamj.2012.12.4.1284
13. González R, Rupérez M, Sevene E, et al. Effects of HIV infection on maternal and neonatal health in southern Mozambique: A prospective cohort study after a decade of antiretroviral drugs roll out. *PLoS One*. 2017;12(6):1-17. doi:10.1371/journal.pone.0178134
14. Wedi COO, Kirtley S, Sally Hopewell Dp, Corrigan R, Kennedy SH, Hemelaar J. Perinatal outcomes associated with maternal HIV infection: a systematic review and meta-analysis. *Lancet HIV*. 2016;3: e33–e48.
15. Kramer MS. Determinants of low birth weight: methodological assessment and meta-analysis. *Bull World Health Organ*. 1987;65(5):663.

16. World Health Organization (WHO). Low Birth Weight Policy Brief. *South Asia*. 2014;28:66.
17. WHO & U. Low birthweight estimates. *World Heal Organ*. 2019;4(3):3-9.
18. Instituto Nacional de Estatística. Inquérito Demográfico e de Saúde. 2013.
19. He Z, Bishwajit G, Yaya S, Cheng Z, Zou D, Zhou Y. Prevalence of low birth weight and its association with maternal body weight status in selected countries in Africa: A cross-sectional study. *BMJ Open*. 2018;8(8):1-8. doi:10.1136/bmjopen-2017-020410
20. Channon AAR, Padmadas SS, McDonald JW. Measuring birth weight in developing countries: does the method of reporting in retrospective surveys matter? *Matern Child Health J*. 2011;15(1):12-18.
21. Edouard L, Senthilselvan A. Observer error and birthweight: Digit preference in recording. *Public Health*. 1997;111(2):77-79. doi:10.1016/S0033-3506(97)90004-4
22. Sherr K, Gimbel S, Rustagi A, et al. Systems analysis and improvement to optimize pMTCT (SAIA): a cluster randomized trial. *Implement Sci*. 2014;9(1):1-14.
23. Aminu M, Unkels R, Mdegela M, Utz B, Adaji S, Van Den Broek N. Causes of and factors associated with stillbirth in low-and middle-income countries: a systematic literature review. *BJOG An Int J Obstet Gynaecol*. 2014;121:141-153.
24. INE. IV Recenseamento Geral da População e Habitação, 2017 Resultados Definitivos – Moçambique. *Inst Nac Estatística, Maputo-Moçambique*. 2019:16-21.
25. Intergrowth-21. Intergrowth-21st newborn biometry standards/ references. The Global Service Network.
26. R Core Team. R: A Language and Environment for Statistical Computing. 2018.
27. Caughey AB, Snegovskikh V V., Norwitz ER. Postterm pregnancy: How can we improve outcomes? *Obstet Gynecol Surv*. 2008;63(11):715-724. doi:10.1097/OGX.0b013e318186a9c7
28. Clausson B, Cnattingius S, Axelsson O. Outcomes of post-term births: the role of fetal growth restriction and malformations. *Obstet Gynecol*. 1999;94(5):758-762.
29. SETSAN. Análise de Políticas Nacionais Impacto dos sistemas agrícolas e alimentares na Nutrição. 2013:136.
30. Perry HB, Zulliger R, Rogers MM. Community health workers in low-, middle-, and high-income countries: an overview of their history, recent evolution, and current effectiveness. *Annu Rev Public Health*. 2014;35:399-421.
31. Gogia S, Sachdev HPS. Home-based neonatal care by community health workers for preventing mortality in neonates in low-and middle-income countries: a systematic review. *J Perinatol*. 2016;36(1):S55-S73.
32. Tshivuila-Matala COO, Honeyman S, Nesbitt C, Kirtley S, Kennedy SH, Hemelaar J. Adverse perinatal outcomes associated with antiretroviral therapy regimens: systematic review and network meta-analysis. *Aids*. 2020;34(11):1643-1656.
33. Marazzi MC, Palombi L, Nielsen-Saines K, et al. Extended antenatal use of triple antiretroviral therapy for prevention of mother-to-child transmission of HIV-1 correlates with favorable pregnancy outcomes. *Aids*. 2011;25(13):1611-1618.
34. Imdad A, Bhutta ZA. Nutritional management of the low birth weight/preterm infant in community settings: A perspective from the developing world. *J Pediatr*. 2013;162(3 SUPPL.):S107-S114. doi:10.1016/j.jpeds.2012.11.060

## Appendix Tables

Table A: Ministry of Health Classification of Health Facilities

	Location	Catchment area	Human Resources	Maternity
District hospital	Municipality	50.000-250.000	32- 42 (5MCH nurses)	-
Urban HF type A	Municipality	40.000-100.000	27- 40 (4MCH nurses)	-
Urban HF type B	Municipality	18.000-48.000	14 (2MCH)	-
Urban HF type C	Municipality	10.000-25.000	4 (1MCH nurses)	-
Rural HF type I	Village -Centre	16.000-35.000	13 to 16 (2MCH nurses)	8-10 beds
Rural HF type II	Village –rural	7.500-20.000	4 (1MCH nurse)	3 beds

Table B: Birth Outcomes by District

Total of births	Overall	Live born	Stillbirth	LBW	SGA
	n=2306 N(n%)	n=2254 N(n%)	n=38 N(n%)	n=299 N(n%)	n=209 N(n%)
<b>District</b>					
Barue	163 (7.1)	157 (7.0)	6 (15.8)	21 (7.0)	21 (10.0)
Chimoio	741 (32.1)	734 (32.6)	6 (15.8)	66 (22.1)	47 (22.5)
Gondola	286 (12.4)	281 (12.5)	5 (13.2)	29 (9.7)	22 (10.5)
Guro	70 (3.0)	67 (3.0)	0 (0.0)	15 (5.0)	7 (3.3)
Macate	105 (4.6)	103 (4.6)	0 (0.0)	16 (5.4)	15 (7.2)
Machaze	145 (6.3)	144 (6.4)	1 (2.6)	16 (5.4)	12 (5.7)
Macossa	26 (1.1)	23 (1.0)	1 (2.6)	1 (0.3)	0 (0.0)
Manica	356 (15.4)	349 (15.5)	7 (18.4)	64 (21.4)	34 (16.3)
Mussorize	92 (4.0)	88 (3.9)	2 (5.3)	12 (4.0)	5 (2.4)
Sussundenga	127 (5.5)	120 (5.3)	3 (7.9)	29 (9.7)	27 (12.9)
Vanduzi	195 (8.5)	188 (8.3)	7 (18.4)	30 (10.0)	19 (9.1)