**Pre-analysis plan**

**Quality of antenatal care and newborn health: findings from a cohort study in Ethiopia, Kenya, and South Africa**

**Background**

Previous studies and systematic reviews have assessed associations between antenatal care (ANC) and neonatal mortality. [1-3] Most studies examined the effect of at least one ANC visit or the number of ANC visits on newborn outcomes. A systematic review and meta-analysis investigating the effect of ANC on neonatal mortality found that at least one ANC visit with a skilled provider during pregnancy could reduce the risk of neonatal mortality by 39% in sub-Saharan African countries where the studies took place. [1] These analyses may have been limited. A Cochrane review analyzed the effects of specific antenatal care interventions (such as nutrition interventions, malaria prevention, and midwives-led models of care) on fetal loss. [4] Most evidence has been based on retrospective cross-section surveys. There evidence on associations between the quality of ANC and perinatal survival and newborn health remains limited.

**Data source**

This paper will use data from the eCohort study a longitudinal prospective survey on health system quality for maternal and newborn health. Pregnant women were enrolled during their first ANC visit and followed through pregnancy and delivery. The study took place in two sites in each country: one predominantly urban and one rural. Women were recruited in public and private health facilities in Ethiopia and Kenya and in public primary care facilities only in South Africa.

**Objectives**

The present paper will assess associations between the quality of ANC throughout pregnancy and newborn health and survival.

**Key variables**

**Confounders**

First, we will describe the characteristics of women who were followed until delivery in each country (**table 1**). We will report their sociodemographic status, baseline health conditions, including having any chronic illnesses or obstetric risk factors. These will include educational status, marital status, health literacy, wealth tertile (based on asset variables measured at baseline). Health status will include self-reported health, experience of danger signs at baseline, presence of any pregnancy risk factors and known multiple pregnancy at baseline. Pregnancy risk factors will include any self-reported chronic illness, anemia (<11g/dL, undernutrition (MUAC <23cm or BMI<18.5), obesity BMI>=30, age under 19 or over 35, or history of prior obstetric complications). Women will be classified as having no risk factor, at least one, at least two or three or more risk factors.

We will then present the birth outcomes, including late miscarriages, stillbirths, live births, early neonatal death, and late neonatal death (**table 2**).

***Primary outcomes***

The primary analysis will assess associations between the quality of ANC and three newborn health outcomes.

1. Late pregnancy losses (including fetal loss after 13 weeks of gestation and stillbirths )
2. Low birth weight infants (LBW), among live births[[1]](#footnote-1)
3. Perinatal mortality (stillbirth (fetal loss >=28 weeks of gestation) + early neonatal death (in the first 7 days after birth)

***Sensitivity analysis 1***

Gestational age at baseline (first ANC visit) was based on either the date of last menstrual period (LMP) reported by the pregnant woman or if LMP was also unknown, by the self-reported number of weeks pregnant. Given uncertainty in gestational ages at baseline, **analyses 1 and 3** will be repeated after excluding women with self-reported of number of weeks pregnant.

***Sensitivity analysis 2***

Birth weight was based on actual birth weight in kilograms (where LBW is defined as birth weight <2.5kg) reported by the mother. If actual weight was unknown, women were asked to report the baby’s size at birth (very large, larger than average, average, smaller than average and very small). We will repeat **analysis 2** in the subset for which birthweight was measured.

***Primary independent variables***

We will describe ANC utilization and create an index for the quality of ANC visits (**table 3**).

* **ANC utilization**
  + At least 4 ANC visits
  + At least 8 ANC visits
* **Quality of ANC (including first ANC and follow-up ANC visits)**
* Physical examinations
  + At least 4 blood pressure measurement (1 pt)
  + At least 4 weight measurement (1 pt)
  + Height: at ANC1 (1 pt)
  + Mid-upper arm circumference (MUAC): at ANC1 (1 pt)
* Diagnostic tests
  + At least 3 blood tests (1 pt)
  + At least 3 urine tests (1 pt)
  + At least 1 ultrasound (or at least 1 ultrasound before 3rd trimester[[2]](#footnote-2) ) (1 pt)
* History taking and screening
  + Date of last menstrual period at ANC1 (1 pt)
  + Depression screening at ANC1 (1 pt)
  + Danger signs screening at ANC1 (1 pt)
  + Previous pregnancies discussed at ANC1 (1 pt)
* Counseling
  + Nutrition at ANC1 (1 pt)
  + Exercise at ANC1 (1 pt)
  + Estimated due date given at ANC1 (1 pt)
  + Told to return to ANC visit at ANC1 (1 pt)
  + Birth preparedness at least twice in pregnancy[[3]](#footnote-3) (1 pt)
  + Signs of pregnancy complications to look at for at least twice in pregnancy2 (1 pt)
* Treatment and prevention
  + Iron and folic acid pills
    - Receiving at ANC1 (1 pt)
    - Reporting taking IFA during at least 75% of phone surveys during pregnancy (1 pt)
  + Calcium supplement
    - Reporting receiving calcium at least once in 3rd trimester (1 pt)
  + Deworming medication
    - Reporting receiving deworming at least once at any point after the 1st trimester (1 pt)
  + Tetanus toxoid vaccination at ANC1 (1 pt)
  + Insecticide treated bed net at ANC1 (in malaria endemic sites only) (1 pt)

**Statistical analysis**

We will use separate regression models to assess associations with the three primary outcomes: late pregnancy losses, LBW infants, and perinatal deaths. All models will be adjusted for a series of potential confounders including demographic characteristics, health status, and presence of risk factors at baseline (described above).

Models 1, 2 and 3 will assess associations between number of ANC visits and, respectively, late pregnancy losses, LBW, perinatal deaths. Number of visits will be categorized as only 1, 2-3, and 4+ visits.

Models 4, 5 and 6 will assess associations between the ANC quality score and, respectively, late pregnancy losses, LBW, perinatal deaths.

Models will include data pooled from all three countries and will include fixed effects for countries. Models will also include random effects for site (urban vs. rural) and robust standard errors.

**References**

1. Tekelab, T., et al., *The impact of antenatal care on neonatal mortality in sub-Saharan Africa: A systematic review and meta-analysis.* PLoS One, 2019. **14**(9): p. e0222566.

2. Wondemagegn, A.T., et al., *The effect of antenatal care follow-up on neonatal health outcomes: a systematic review and meta-analysis.* Public Health Rev, 2018. **39**: p. 33.

3. Berhe, T., et al., *Does quality of antenatal care influence antepartum stillbirth in Hossana City, South Ethiopia?* PLOS Glob Public Health, 2023. **3**(1): p. e0001468.

4. Ota, E., et al., *Antenatal interventions for preventing stillbirth, fetal loss and perinatal death: an overview of Cochrane systematic reviews.* Cochrane Database Syst Rev, 2020. **12**(12): p. Cd009599.

1. Birth weight was only assessed for babies still alive at the time of the survey. Therefore, this analysis will exclude neonatal deaths. [↑](#footnote-ref-1)
2. If this can be accurately assessed given gestational age uncertainty. [↑](#footnote-ref-2)
3. At least twice in pregnancy implies that the counselling should be done twice, in the beginning and toward the end of pregnancy. [↑](#footnote-ref-3)