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THE ASSOCIATION BETWEEN INTERMITTENT PREVENTIVE TREATMENT UPTAKE AND ANAEMIA AMONGST PREGNANT WOMEN IN ZAMBIA IN 2018: A SPATIAL ANALYSIS

BY

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DECLARATION

I, Charlotte Mulaga Chishiba, hereby declare that except where specific reference is made to the work of others, the contents of this research report are original and have not been submitted in whole or in part for consideration for any other degree or qualification in this, or any other University. This research report is the result of my work and includes nothing which is the outcome of work done in collaboration, except where specifically indicated in the text.

_____C.Chishiba_____

(Signature of candidate)

28th September 2023

DEDICATION

I would like to dedicate this work to the special people in my life who have been a source of unwavering support and encouragement. Firstly, to my beloved son, Chimwemwe Jacob Chishiba, who constantly reminds me of the importance of perseverance and hard work. Your unconditional love and support have been my inspiration throughout this journey.

To my husband, Orleans Chishiba, thank you for being my rock and for always believing in me. Your encouragement and understanding have been a constant source of strength, and I am forever grateful to have you as my partner in life.

To my mother and father, thank you for your prayers, guidance, and unconditional love. Your steadfast guidance has been instrumental in helping me achieve my goals, and I am deeply thankful or your love and sacrifice.

I have come this far because of the unwavering support and encouragement from these special people in my life. I dedicate this work to them with deep gratitude and appreciation.

ABSTRACT

Background: This study investigated the association between Intermittent Preventive Treatment with Sulphadoxine Pyrimethamine (IPTp-SP) uptake and anaemia among Zambian pregnant women aged 15-49 in 2018. Despite WHO's endorsement of IPTp-SP to combat malaria-related anaemia, its prevalence continued to rise, significantly impacting maternal health.

Methodology: Using Zambia Demographic Health Survey 2018 data, 665 pregnant women receiving IPTp-SP were analysed for haemoglobin levels, determining anaemia through blood tests. Statistical methods included survey-adjusted proportions, means, bivariate analysis, multiple linear regression, and multi-level ordinal logistic models with spatial random effects. Spatial analyses used ArcMap for coverage analysis, ordinary least squares, and geographically weighted regression maps (GWR) techniques in R and Stata.

Results: Optimal IPTp-SP doses resulted in 36.98% anaemia prevalence (124/369), and suboptimal doses led to 42.85% (112/296). Factors associated with anaemia included household size, rich wealth index, high parity, and employment during pregnancy. Associations between IPTp-SP uptake and anaemia were identified: household size (four to six: AOR= 0.53; 95% CI 0.34 to 0.80; seven or more: AOR=0.57; 95% CI 0.35 to 0.91), adequate antenatal visits (AOR= 0.68; 95% CI 0.48 to 0.97), and rich wealth index (AOR= 0.68; 95% CI 0.34 to 0.98). Spatial analysis revealed anaemia hotspots in Southern, Luapula, and Eastern provinces, with iron supplements and household size identified as influential factors.

Conclusion: Despite IPTp-SP use, overall anaemia prevalence was 40%, with the highest rates in Southern, Luapula, and Western provinces. Targeted strategies focusing on improving iron tablet access, antenatal care attendance, and utilising spatial maps are crucial for mitigating adverse anaemia outcomes in these regions.

Keywords: Intermittent Preventive Treatment Uptake, Anaemia, Pregnant Women and Spatial Analysis

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OPERATIONAL DEFINITIONS

Anaemia	Refers to a medical condition characterised by a deficiency in the number of red blood cells or the amount of haemoglobin present within them, which falls below the typical range (less than 11g/dl) observed in healthy individuals (1).
Suboptimal uptake of IPTp-SP	Taking 2 doses or fewer doses of IPTp-SP(2).
Optimal uptake of IPTp-SP	Taking 3 or more doses of IPTp-SP (2).
Adequate antenatal visits	This was defined as 4 or more antenatal visits (3).
Inadequate antenatal visits	This was defined as less than 4 antenatal visits (3).

LIST OF ABBREVIATIONS AND ACRONYMS

ANC	-	Antenatal care
AIC	-	Akaike information criterion
AOR	-	Adjusted odds ratio
CAR	-	Conditional autoregressive
CSPro	-	Census and survey processing system
CQ	-	Chloroquine
DRC	-	Democratic Republic of Congo
GIS	-	Geographic information system
GWR	-	Geographically weighted regression
GPS	-	Geographic coordinate system
Hb	-	Haemoglobin
HIV/AIDS	-	Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome
IPTp	-	Intermittent Preventive Treatment
OLS	-	Ordinary least squares
SAR	-	Simultaneous autoregressive
SES	-	Socioeconomic status
SP	-	Sulphadoxine-pyrimethamine
WHO	-	World Health Organization
ZDHS	-	Zambia Demographic Health Survey

CHAPTER 1.0: INTRODUCTION

Chapter One provides an overview of the study, including the background, literature review, problem statement, research rationale, and objectives. The background examines malaria's impact on pregnancy, emphasizing its importance in public health research. The literature review explores anaemia, IPTp-SP utilisation, and predictors among pregnant women. The problem statement articulates the scale of the issue, highlighting gaps observed in the uptake of IPTp-SP and the prevalence of anaemia among pregnant women. The research rationale underscores the importance of understanding the impact of IPTp-SP on anaemia, given the potential adverse effects associated with anaemia. The study aimed to investigate the relationship between IPTp-SP uptake and anaemia, and its spatial distribution in pregnant women aged 15-49 in all 10 provinces in Zambia 2018.

1.1 Background

Anaemia during pregnancy is defined by decreased levels of haemoglobin in the blood, leading to reduced oxygen supply to the tissues and organs of both the mother and the foetus (4). Globally, anaemia affects an estimate 1.62 billion women (25% of the populace), of which 56 million are pregnant women (5). Additionally, it was estimated that 25% of all pregnant women have iron deficiency anaemia every year (5). The burden of anaemia amongst pregnant women increases the risk of maternal mortality and morbidity. Anaemia could also predispose to sepsis and other serious perinatal outcomes including low birth weight, preterm delivery, infants born with perinatal complications, and stunted growth (6). Malaria is one of the major causes of anaemia (7). However, other factors may also play a role. These factors include deficiencies in essential nutrients like iron, folate, and vitamin A, as well as genetic conditions such as sickle cell disease. Additionally, infections like Human Immunodeficiency Virus and Acquired Immunodeficiency Syndrome (HIV/AIDS) and parasitic infections, such as hookworm and

plasmodium, have been identified as potential causes of anaemia during pregnancy (8,9). Malaria in pregnancy can be prevented with medications and insecticide-treated nets (8). The World Health Organization (WHO) recommended intermittent preventive treatment (IPTp), explicitly with at least three doses of sulfadoxine-pyrimethamine (SP) (2). Nonetheless, the uptake of IPTp-SP is low in some developing countries (10).

In Africa, especially in the Sub-Saharan region, malaria-associated anaemia among pregnant women remains a public health burden and contributes to several complications such as low birth weight, preterm delivery, infants born with perinatal complications, and stunted growth (10). Approximately, over 200 million people are affected by malaria each year, out of which a quarter are pregnant women (11). Between the years 2000 and 2005, most African countries adopted measures to prevent malaria and its sequel (2,12). These included the use of IPTp-SP, early diagnosis and proper case management, and the use of insecticide-treated nets (7). Despite the implementation of these measures, malaria-associated anaemia remains a burden in pregnant women in most African countries including Zambia (13).

In Zambia, malaria is endemic in most parts of the country and has a seasonal variation with the highest prevalence in the rainy season (14–16). In 2018, more than five million cases of malaria, with an estimated case fatality rate of 23 per 100,000 were reported (15). In addition, due to the increased burden of malaria, pregnant women are at high risk of malaria-associated anaemia each year (17). Nevertheless, data from the Zambia Demographic Health Survey (ZDHS) reveal that the optimal uptake of IPTp-SP, defined as taking at least three doses, remains below the recommended threshold of 80%, standing at just 59% (18). This increases the risk of getting malaria during pregnancy which can cause malaria-related anaemia. Furthermore, the effect of IPTp-SP on the burden of malaria-associated anaemia in pregnancy is not well documented in Zambia's 10 provinces. This study is therefore aimed at understanding the association and spatial distribution of IPTp-SP uptake and malaria-related anaemia in pregnant women.

1.2 Literature Review

The purpose of this literature review is to provide a comprehensive and critical overview of the existing literature on anaemia in pregnancy and its association with IPTp-SP uptake among pregnant women aged 15-49 years in Zambia. The literature review will cover four main themes: firstly, the epidemiology and aetiology of anaemia in pregnancy; secondly the rationale and mechanism of IPTp-SP for preventing malaria and anaemia in pregnancy; thirdly the effectiveness and challenges of IPTp-SP implementation in Zambia and other countries with similar malaria transmission patterns; and lastly the spatial distribution and determinants of anaemia among pregnant women in Zambia. The literature review will also identify the gaps and limitations in the current knowledge and practice regarding anaemia in pregnancy and IPTp-SP uptake, as well as how this study aims to address them.

1.2.1 The aetiology and epidemiology of anaemia in pregnancy

Anaemia in pregnancy is a condition characterised by low haemoglobin levels in the blood, which can impair oxygen delivery to the tissues and organs of both the mother and the foetus (4). Anaemia in pregnancy can have serious adverse effects on maternal and foetal health outcomes, such as the increased risk of maternal mortality and morbidity, low birth weight, preterm delivery, foetal growth restriction and perinatal mortality (19). Anaemia in pregnancy can be caused by various factors, such as nutritional deficiencies, infections, genetic disorders, and chronic diseases. One of the most common infectious causes of anaemia in pregnancy is malaria, especially in regions where malaria transmission is high or unstable (20,21). Malaria infection during pregnancy can result in placental malaria, which can damage the placenta and reduce its ability to transfer nutrients and oxygen to the foetus (22). Malaria infection can also cause haemolysis, which is the destruction of red blood cells, leading to reduced haemoglobin levels and anaemia (7).

In a 2022 global systematic review and meta-analysis, the prevalence of anaemia in pregnant women was reported to be 37% (23). This review encompassed 52 studies, which collectively involved a total of over one million pregnant women (1,244,747 in total) (23). A systematic review and meta-analysis were conducted in Sub-Saharan Africa in 2021. They selected 25 studies, involving approximately 15,061 pregnant women. Among these women, 35.6% had anaemia (24). This finding indicates that anaemia remains a significant public health concern. To address this issue effectively, it is crucial to develop comprehensive intervention strategies that incorporate health and nutrition education, including interventions like iron and folic acid supplementation, antenatal care, and malaria control (24,25).

1.2.2 Utilisation of IPTp-SP in pregnancy and prevalence of anaemia

Sulfadoxine-pyrimethamine (SP) also commonly referred to as Fansidar is the medicine that is used to prevent malaria in pregnancy. Malaria in pregnancy has been known to cause anaemia and increase the risk of both maternal and neonatal deaths (26). The WHO recommended the use of IPTp-SP in the second trimester of pregnancy and that each dose be given a month apart until a woman delivers (2). Zambia has adopted the use of IPTp-SP as a preventive treatment for malaria in pregnancy with the use of at least four doses during pregnancy (27).

Several studies that explore the use of IPTp-SP for prevention of severe anaemia among pregnant women in malaria-endemic regions were conducted in other African countries however no known recent study was conducted in Zambia (28–30). A proxy retrospective cohort study which was conducted in Zambia, in 2011, to evaluate IPTp-SP uptake among pregnant women who were HIV-negative in Mansa showed that there were benefits with optimal doses (three or more) of IPTp that led to better health outcomes. Each dose was found to be protective against malaria and in turn improved the outcome, birth weight and

haemoglobin (Hb) levels. However, this study did not provide much detail on maternal anaemia which is also an important factor affecting pregnant women in malaria-endemic regions (31).

The uptake of IPTp-SP has been reported to help in the prevention of malaria in pregnancy and subsequent reduction in anaemia (28,29). A systematic review which was conducted in 2002 in Sub-Saharan Africa, showed that optimal doses of IPTp-SP reduced the risks of low birth weight (LBW), and maternal anaemia and improved pregnancy outcomes (10). The review however did not focus on the association of SP on anaemia. A randomised controlled trial done by Shulman in Kenya in 1999, where some women were allocated IPTp-SP and others the placebo, showed that IPTp-SP offered some protection against severe anaemia caused by malaria (32). This further supports that the optimal dosage of IPTp-SP offers more protection against maternal anaemia. Another study that showed a comparable result was a study done in Malawi in the year 2000, in which the women who took at least two doses of IPTp-SP got some protection against maternal anaemia and improved Hb levels by an average of 3g/dl (33). Although anaemia is multifactorial, most of the improved Hb levels were attributed to the uptake of IPTp-SP. Similar results were reported in a cross sectional study done in Ghana in 2011 where women who took IPTp-SP had a higher Hb than those who did not (28). In the same study, it was reported that severe anaemia was more common in the women that did not take IPTp-SP than those who took it. Therefore, a low rate of anaemia was found in women taking IPTp-SP. On the contrary, a randomised control trial done in Burkina Faso in 2008 on increased coverage and dosage of IPTp-SP found no significant difference in maternal anaemia and low birth weight between women that took IPTp-SP and those who did not take IPTp-SP (34). This was attributed to the fact that most women received less than two doses of IPTp-SP which diluted the impact of the intervention. Thus, more community awareness of the benefits of IPTp-SP was recommended.

A randomised control trial done in Mali in 2005 compared the use of hemoprophylaxis with Chloroquine (CQ) and SP to see which was more efficacious in the prevention of malaria (35). The study findings showed that two doses of SP were more efficacious in the prevention of maternal anaemia than a weekly dose of CQ as women had better Hb levels. These findings were consistent with another randomised controlled trial that showed that SP is more efficacious than CQ (29).

1.2.3 Predictors of IPTp-SP uptake and anaemia in pregnant women

1.2.3.1 Predictors of IPTp-SP uptake

Two significant challenges in maternal and child health encompass anaemia and intermittent preventative treatment with SP (28). Studies have revealed different predictors of IPTp-SP uptake and anaemia in pregnant women. In a cross sectional study conducted in Nigeria in 2009, the presence of a qualified healthcare professional(s) on-site, adequate medication availability, and access to information were found to be highly correlated with optimal coverage of IPTp-SP uptake (36). Similarly, a cross sectional study in Uganda in 2016 revealed that regular exposure to health-related media at least once a week was a significant predictor of IPTp-SP uptake (37).

Studies conducted in sub-Saharan Africa have identified key factors that influence the uptake of IPTp-SP. Specifically, a study done by Darteh and co-workers found that women with higher income, occupation, and education were more likely to take IPTp-SP (38). Additionally, two other studies have reported a positive link between higher levels of education and increased uptake of IPTp-SP (39,40).

The optimal uptake of IPTp-SP has been reported to be influenced by the timing and quality of antenatal care (ANC). In particular, studies have shown that initiating ANC in the first trimester

is substantially associated with optimal SP uptake (30,41). The timing of ANC initiation is a critical determinant of the number of SP doses a woman takes during pregnancy. Furthermore, a study conducted in Ghana demonstrated that good-quality ANC significantly predicts IPTp-SP coverage (42). Additionally, distance to health facilities has been identified as another important predictor of uptake, with women living closer to health facilities having more antenatal visits and a higher likelihood of increased IPTp-SP uptake (43,44). These findings highlighted the importance of timely and high-quality ANC and improved accessibility to health facilities in achieving optimal IPTp-SP coverage.

In some studies, socio-economic status has emerged as a significant social demographic determinant of the uptake of SP. Specifically, women belonging to the middle to richest wealth index have demonstrated a higher uptake of SP compared to their counterparts from poorer backgrounds (45,46). This trend can be attributed to the observed tendency of empowered women to seek and utilize better health interventions than women from impoverished backgrounds (46). Maternal age and parity have also been reported as significant predictors of IPTp-SP uptake. Specifically, women aged 30 years or older were found to have a higher uptake of SP compared to younger women (12). Furthermore, women who had three or more children had a lower IPTp-SP uptake than those who had one or two children(47). Other significant predictors of IPTp-SP reported are region and geographical location (12).

1.2.3.2 Predictors of Anaemia

Iron deficiency, often caused by dietary factors, is one of the predictors of anaemia. Previous studies have suggested that dietary diversity and meal frequency may be associated with anaemia (48,49). However, the causal relationship between these factors and anaemia remains unclear. On the contrary, two studies in Ethiopia found no significant association between dietary diversity and anaemia in pregnancy (50,51). One possible approach to address iron

deficiency is through supplementation, which is often prescribed to pregnant women. Studies have shown that iron supplementation can lead to improved Hb levels compared to non-supplemented women (6,48,52). However, two studies in Ethiopia have yielded contradictory results, with no significant association found between iron supplementation and anaemia (50,53). The observed discrepancies may be attributed to geographical and socio-demographic variations across the study populations (52).

Various studies have reported household size as a significant predictor of anaemia. Specifically, a household size of four members or more is significantly associated with anaemia (6,51,53). Additionally, age has been identified as another predictor of anaemia in women. A study reported a significant association between anaemia in pregnancy and women aged 36 to 45 years (51). However, other studies have found weak or no association between age and anaemia (19,50).

Parasitic infections, particularly those caused by malaria and hookworm, have been reported to be significant predictors of anaemia. Studies conducted in Ghana and Ethiopia revealed that malaria parasite infection had a significant association with anaemia (54,55). However, studies conducted in low malaria endemic regions, in Zambia and Ethiopia showed no significant association between malaria and anaemia (19,50). On the other hand, hookworm infection was found to be significantly associated with anaemia, especially in pregnant women (56). In a similar study where hookworm parasites were not tested, no significant association was observed between deworming medication and anaemia (50).

Social economic status (SES) significantly affects anaemia in pregnancy. Anaemia during pregnancy is more likely to occur in women from lower SES origins than in those from higher backgrounds (19,25). A study found that women with a low income had a higher incidence of

anaemia, which was attributed to poor dietary habits and a high cost of living (53). Additionally, research has shown that higher levels of education among women are associated with a reduced risk of developing anaemia during pregnancy compared to those with lower education levels (48,50).

1.2.4 GIS, spatial distribution in Malaria IPTp-SP and anaemia

Spatial analysis in epidemiological modelling is motivated by the understanding that individuals residing in the same household or in proximity often encounter similar exposures, which can have shared influences on observed outcomes. This concept highlights the intrinsic potential of Geographical Information System (GIS) technology in health research. GIS enables the direct examination of spatial variation in disease and its correlation with environmental factors and healthcare systems (57,58). GIS can significantly contribute to epidemiological studies through the use of empirical disease modelling methodologies, particularly in regions with a growing disease burden like Africa. Mapping regional and temporal variations in disease risk becomes crucial in formulating control measures and delivering targeted treatments (57).

Autocorrelation, a statistical property commonly observed in ecological variables across geographic space, manifests as patches or gradients (59). In simpler terms, autocorrelation refers to the tendency of nearby geographic locations to exhibit similar values for a given variable. This means that areas in proximity are likely to have similar values, whether high or low, for a specific variable.

In the context of anaemia research in Zambia, existing spatial analysis studies have predominantly focused on children rather than pregnant women (54,60). Anaemia and IPTp-SP uptake have been examined, but the influence of geographical factors has not been adequately addressed. To date, no studies in Zambia have explored the spatial distribution of anaemia among pregnant women and its relationship with their areas of residence. Assessing geographical differentials in anaemia prevalence is crucial to address the regional variations.

Malaria is endemic to Zambia and is found in all its 10 provinces. Malaria tends to be seasonal and is less prevalent in the cold and dry seasons but more in the rainy season (61). The malaria burden in Zambia is also regional and most of the regions that have high rainfall have been reported to have the highest prevalence of malaria such as North-western, Northern, Muchinga, and Luapula provinces. Areas in the central part of the country which include the Copperbelt, Eastern, Western and Central provinces range from low to moderate burden of malaria, and the areas (Southern, Lusaka, and some parts of Western provinces) that experience low rainfall have a low burden of malaria (61). Another study in Zambia in 2015 (62) that determined spatial patterns of the incidence of malaria in the Chongwe district, reported that there were more clusters in the rainy season than in the dry season which corresponded with the pattern of malaria. Figure 1 shows the distribution of malaria in Zambia.

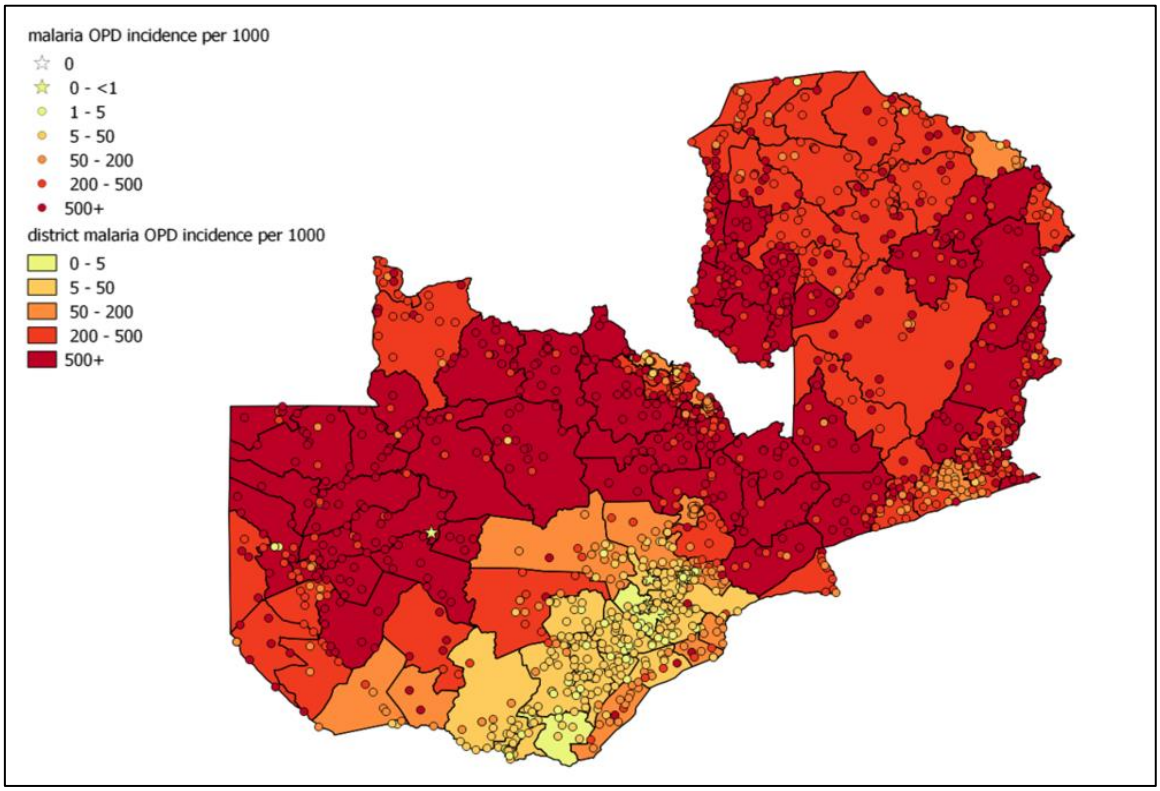

Figure 1 Map of Zambia's distribution of Malaria

Source: *https://www.nmec.org.zm/malaria-overivew*

In Ethiopia, studies conducted on the spatial distribution of anaemia revealed the presence of

notable spatial autocorrelation among clusters. These findings suggest that there were noteworthy geographical variations in the prevalence rates of anaemia across the region (63,64). These studies reported that malaria was not a significant factor in individuals who were anaemic and living in high malaria endemic regions. This highlights that anaemia is multifactorial. Another study that covered most of sub-Saharan Africa also showed that different geographical regions had different anaemia prevalence and other demographic factors affected the anaemia levels such as country, age group and malaria endemicity (65,66). There were no indications of spatial coverage for IPTp-SP uptake reported in the studies.

1.3 Problem statement

Malaria remains one of the top causes of death in Zambia, and contributes largely to maternal mortality and morbidity, mainly due to complications such as anaemia. Severe anaemia in pregnancy has been associated with decreased amniotic fluid volume, foetal cerebral vasodilatation and non-consoling foetal pulse designs (67). Furthermore, there is an increased risk of preterm delivery, unconstrained early termination, low birth weight and foetal demise (68). Despite the implementation of IPTp-SP in Zambia as a prevention strategy for anaemia in pregnancy, maternal mortality is still high because of anaemia. There is limited evidence of recent research to show the impact of anaemia and the association of IPTp-SP with anaemia prevalence in pregnancy and its spatial distribution (67).

1.4 Study Justification

According to the 2021 national strategic plan, the Zambian Ministry of Health plans to eliminate malaria by 95% in line with the WHO strategy for elimination of malaria 2016-2030 (69). One of the strategies they listed was the distribution of IPTp -SP at antenatal clinics to reduce malaria infections in pregnancy, thereby also reducing the prevalence of anaemia. However, there is limited evidence on the association between IPTp-SP uptake and malaria- related anaemia in

pregnant women in Zambia and its spatial distribution. Hence, this study will provide invaluable insights for decision-makers, enabling them to formulate targeted interventions and implement effective measures to combat anaemia in pregnancy, including strategies aimed at enhancing the utilisation of IPTp-SP. Furthermore, spatial methods generate maps at the regional level which will help in revealing the distribution of malaria, anaemia, and the uptake of IPTp through hot and cold spot analysis thereby allowing the development of evidence-based implementation strategies and policies.

1.5 Research Question

What is the association and spatial distribution of IPTp-SP uptake and anaemia in pregnant women aged 15 – 49 years in Zambia in 2018?

1.6 General objective (Aim)

This study aimed to determine the association and spatial distribution of IPTp-SP uptake and anaemia among pregnant women aged 15 – 49 years in Zambia in 2018.

1.7 Specific Objectives

1. To investigate the spatial prevalence of anaemia among pregnant women aged 15-49 years (who took or who were exposed) to IPTp-SP in Zambia in 2018.
2. To determine the association between IPTp-SP doses and the prevalence of anaemia amongst pregnant women aged 15 – 49 years in Zambia in 2018.
3. To determine the predictors of anaemia amongst pregnant women aged 15-49 years in Zambia in 2018, adjusting for spatial random effects.

1.8 Conceptual framework

The conceptual framework describes key factors affecting anaemia prevalence among Zambian pregnant women aged 15-49 based on the literature review. Central to this framework is the association between IPTp-SP exposure and anaemia, highlighting the interconnectedness of factors like age, region, and other variables influencing both IPTp-SP uptake and anaemia.

Diet plays a pivotal role, directly impacting anaemia levels. Adequate nutrition reduces anaemia risk; pregnant women with balanced diets exhibit lower anaemia rates. Iron supplementation positively correlates with higher haemoglobin (Hb) levels, benefiting those who receive it compared to non-recipients. Parasitic infections, notably hookworm and malaria, detrimentally impact Hb levels.

Household size and socioeconomic status influence both IPTp-SP uptake and anaemia. Larger households correlate with higher IPTp-SP uptake but are associated with lower Hb levels in pregnant women. Conversely, smaller households exhibit higher Hb levels but lower IPTp-SP uptake among pregnant women.

Other factors contributing to IPTp-SP uptake include wealth quantiles (rich and middle), education level, regular media exposure, parity (less than three children), early initiation of antenatal care (ANC), and age (particularly, women aged 30 or older).

Malaria endemicity influences IPTp-SP uptake, with higher endemic areas impacting Hb levels based on malaria severity. Women taking IPTp-SP experience milder malaria symptoms than non-users, affecting Hb levels positively. In this study, malaria was not measured among pregnant women.

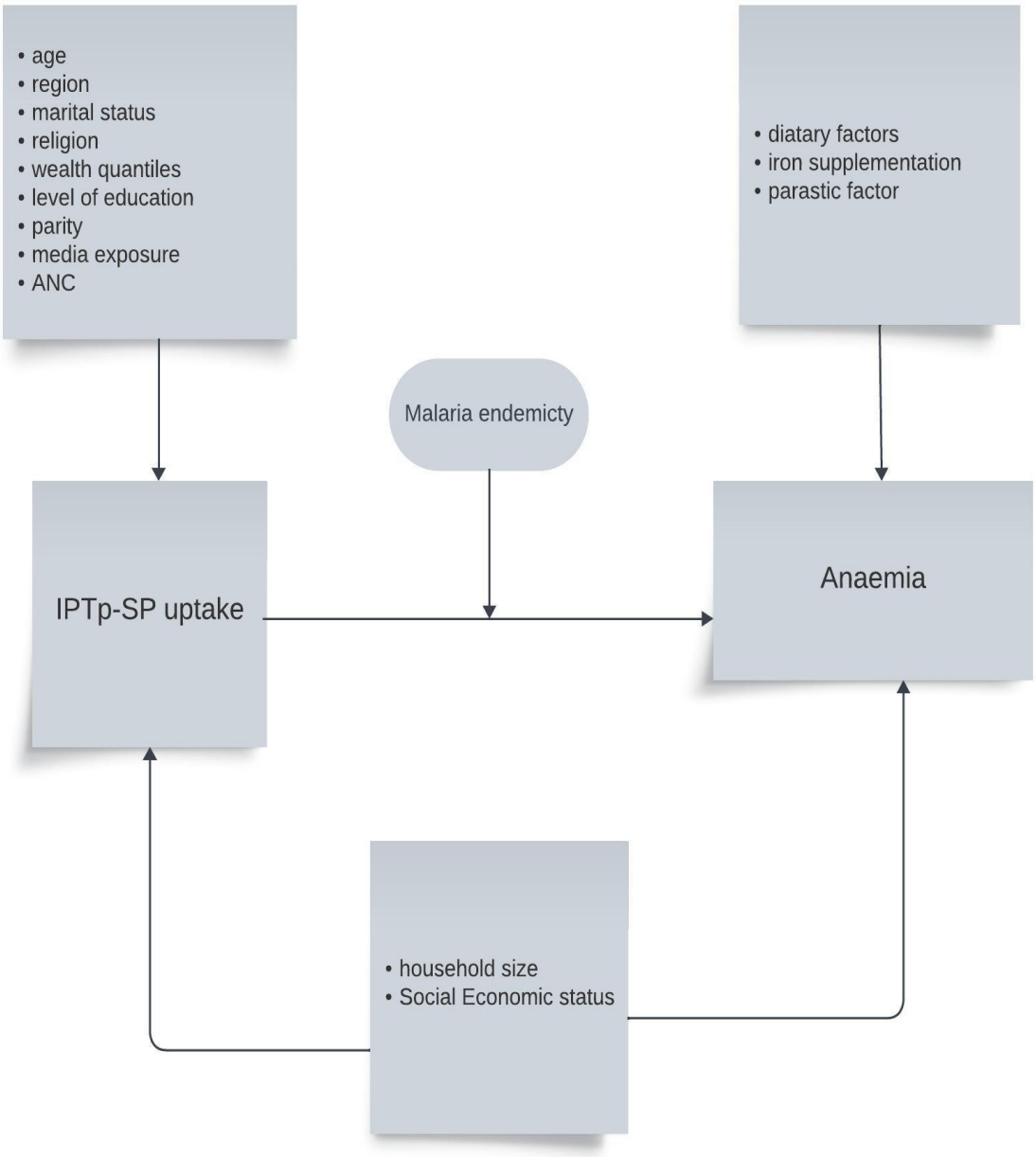

Figure 2: Conceptual Framework to relate Anaemia and IPTp-SP Uptake

CHAPTER 2.0 METHODOLOGY

2.1 Introduction

This chapter describes in detail the study setting of both the primary study and the secondary study as well as the data sources, data collection and statistical methods used to determine the association and spatial distribution of IPTp-SP uptake and anaemia in pregnant women.

2.2 Primary Study

2.2.1 Survey data source

Data was obtained from the Zambia Demographic Health Survey (ZDHS) which was conducted in 2018. This was a nationwide survey that included all women aged 15-49 and men aged 15-59 years. This data was obtained at the household level nation-wide in both rural and urban areas.

2.2.2 Survey study site

The ZDHS was conducted in Zambia which is a landlocked country located in the southern part of Africa (as shown in Figure 4). The climate is tropical or subtropical depending on the altitude. Zambia boarders with Namibia, Botswana, Angola, Congo DRC, Tanzania, and Malawi. The survey study site included all 10 provinces in Zambia (as shown in Figure 3: A Map of Zambia Showing the 10 Provinces) Malaria transmission is higher in rural areas when compared to urban areas and more transmissions occur in the rainy season (18). The surveys

are presentational of the whole national population.

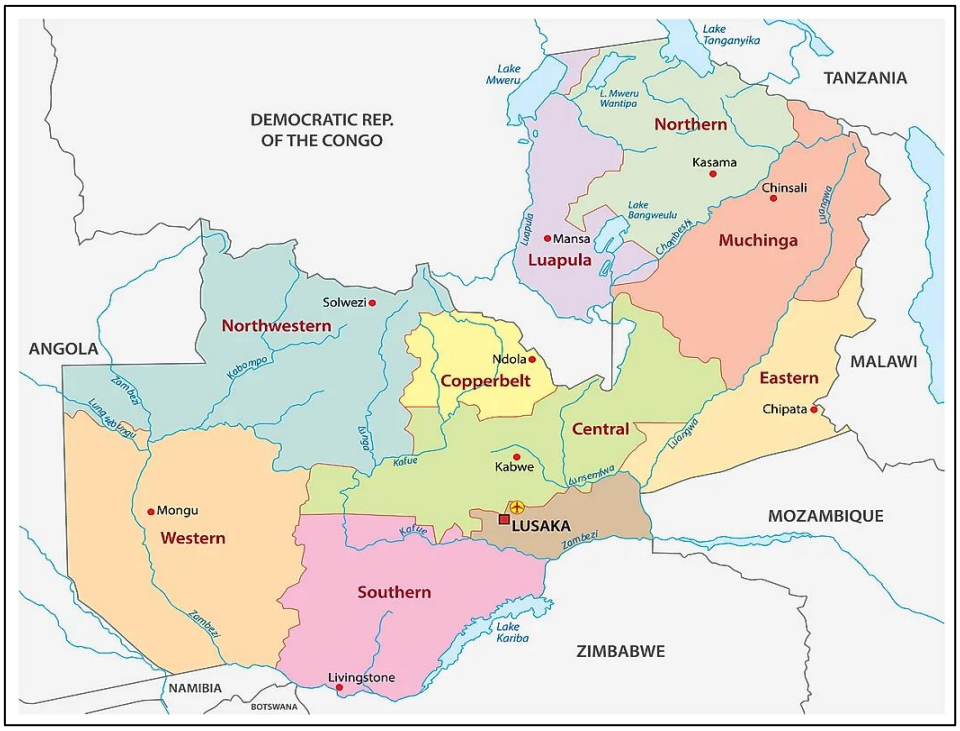

Figure 3: A Map of Zambia Showing the 10 Provinces

Source: https://www.worldatlas.com/maps/zambia

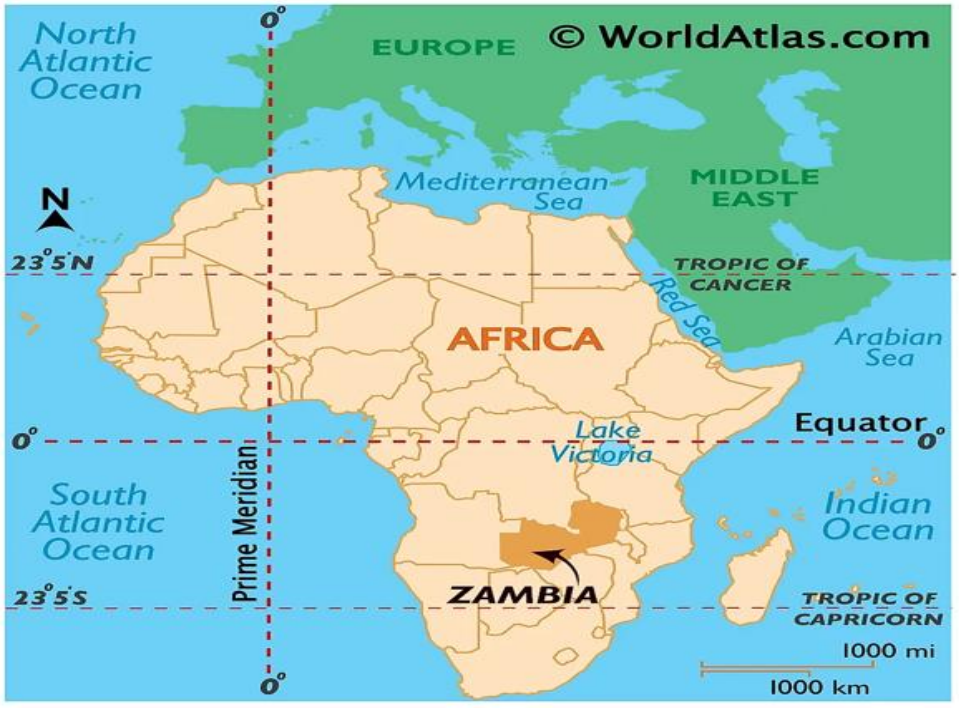

Figure 4: Map of Africa showing Zambia's location.

Source: https://www.worldatlas.com/maps/zambia

2.2.3 Primary study design and sampling method

This was a cross-sectional survey. The survey was conducted from 18th July 2018 to 24th January 2019. The stratified two-stage sample design was used for the 2018 ZDHS. Selecting sample locations (clusters) made up of enumeration areas (EAs) was the initial stage. Within each sampling stratum, EAs were chosen with a probability proportional to their size. 545 clusters in total were chosen. In the following phase, households were systematically sampled. Each of the chosen clusters underwent a household listing operation. Each cluster had an average of 133 households during the listing process, from which a predetermined number of 25 households were chosen using a systematic equal probability selection method to provide a sample size of 13,625 households. At the national, urban, rural, and provincial levels, the findings from this sample were representative (18).

2.2.4 Primary data collection

The data collection process involved the administration of four questionnaires - household, women's, men's, and biomarker assessments. These questionnaires were initially conducted in a paper format and later transferred to electronic tablets for data storage and analysis. The DHS Program's Model Surveys served as the basis for the questionnaires, which were modified to reflect Zambia-specific population and health challenges. Seven regional languages were added once the English versions of all the questions were completed: these were Bemba, Kaonde, Lozi, Lunda, Luvale, Nyanja, and Tonga. To ascertain the uptake (dosage) of IPTp-SP, specific questions were posed. Additionally, levels of anaemia were assessed through blood samples obtained through a finger prick and analysed using the portable HemoCue 201+ device (18).

2.2.5 Primary Data management

Data that was stored electronically was transferred to the ZamStats central office in Lusaka through a safe internet file streaming system, where they were kept on a password-protected

computer. Data editing was done by CSPro software which checked for inconsistence and to resolve these inconsistences field tables were generated which were sent to the field workers to recheck the quality of data. (18).

2.3 Secondary study design

2.3.1 Target population and study design

This study is a cross-sectional study using data collected from the ZDHS 2018. The study population are the women aged 15-49 who were pregnant in 2018.

2.3.2 Power computations

The power was calculated in Stata 17 (70) using the power command with the outcome variable being anaemia and the uptake of IPTp-SP as the main exposure variable. To account for the cluster design of the study, the design effect was used to get the effective sample size. The outcome variable is anaemia or no anaemia, and the exposure variable is uptake suboptimal (less than two doses), or optimal (three or more doses). The estimated sample size was 1,109. The proportion of women who took optimal IPTp-SP according to the literature was 59%. The proportion that took suboptimal IPTp-SP was 41%. Anaemia assumptions were 40% had anaemia and 31% did not have anaemia. Using two proportion commands in STATA power was calculated to be above 80% (appendix D).

2.3.3 Study participants

In the 2018 Demographic Health Survey, a total of 13,595 households were included in the sample. Of these, 12,943 were found to be occupied and 12,831 were successfully interviewed. Among the interviewed households, 14,189 women aged 15-49 were eligible for individual interviews, and 13,683 were interviewed. Of these, approximately 1,109 women were pregnant at the time of the survey. However, 36 pregnant women were excluded from the study because

they did not have the outcome variable, namely anaemia and 408 were excluded for missing information on IPTp-SP uptake. The process of sample selection is presented in Figure 5.

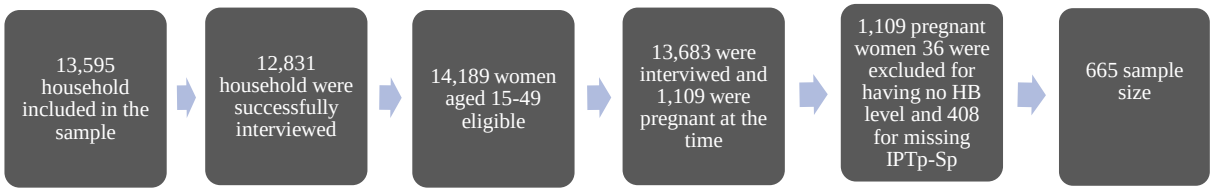

Figure 5: Sample selection process

2.3.4 Data Management and Analysis

2.3.4.1 Data Management

The dataset used in this study was obtained with the approval of measure DHS and is available on the DHS Program website (https://dhsprogram.com/data/). The dataset includes both individual and household survey data and is available in both Stata and shapefile formats for use in ArcGIS. To obtain the variables of interest, the individual dataset and the personal dataset were merged. Before analysis, missing variables related to the outcome were dropped, and new variables were created to facilitate analysis.

To ensure that the sample was representative of the entire population of the country, sample weighting was performed. This was necessary to account for the complex, multi-level weighted nature of the primary data, which was collected through a survey. By using sample weighting, the results of the analysis are more likely to reflect the true population characteristics.

2.3.5 Measurement of variables

The measurement variables were obtained from the questions asked in the DHS questionnaire. Which can be found on the following website: https://dhsprogram.com/pubs/pdf/DHSQ7/DHS7_Household_QRE_EN_16Mar2017_DHSQ7.pdf and the women's specific questionnaire

https://dhsprogram.com/pubs/pdf/DHSQ7/DHS7-Womans-QRE-EN-17Dec2018-DHSQ7.pdf

Measurements and variable definitions are found in table 1 below.

Table 1: List of study variables and their types of measurements.

Variable type	Variable name	Type of variable	Definitions
Outcome variable	Anaemia	Continuous/binary	Anaemia was treated both as a continuous and binary (interaction) Anaemia level of less than 11g/dl mean the woman has anaemia. Above 11g/dl means the woman does not have anaemia this is according to the WHO classification of anaemia. This was derived from the haemoglobin measurement that was taken during the survey using the portable HemoCue 201+ device.
Explanatory variables	IPTP-SP uptake	Binary	sub-optimal -If a woman took 2 or fewer doses and optimal -if she took three or more doses. This was derived from the survey question, how many times did you take SP/Fansidar during this pregnancy?
	Age	Categorical	This is a continuous variable that was categorised as follows 15-25, 26-35, and 36-49
	Parity	Categorical	This was a continuous variable that was categorized into 2 groups, 0-3 births and above 4
	Employment status	Binary	This was a multi- nominal variable that was categorised into working and not working
	Wealth quintile	Categorical	The wealth index in the DHS is a composite measure of a household's living standard. This is calculated from ownership of selected assets such as bicycles, materials used for construction and types of water access and sanitation facilities. Households were classified into five categories poorest, poor, moderate, richer, and richest. This was re-categorised into quintiles of poor, middle and rich
	Marital status	Categorical	This was categorised as married/ not married
	Household size	Categorical	This was a continuous variable that was categorized into 3 categories 1-3, 4-6, 7 and above
	Timing of antenatal	Categorical	This was a continuous variable that was categorised into trimesters 1st to 3rd trimester when the woman first started her antenatal visits
	Province	Multi-nominal	These were all the provinces where survey was conducted all the 10 Provinces in Zambia namely, Lusaka, Copperbelt, North-Western, Western, Luapula, Central, Northern, Muchinga, Eastern and Southern
	Educational level	Multi-nominal	This is categorized as higher, secondary, primary, no education this was derived from the question What was the highest level of school he attended: primary, secondary, or higher?

	Type of ANC	Multi-nominal	The place that the woman attended her antenatal whether government or private
	Drugs for intestinal parasites during pregnancy	Binary	The women who received deworming and the women who did not receive deworming yes/no
	Iron supplements	Binary	For the women who took iron folate and the women who did not take iron folate yes/no
	Exposure to media	Multi-nominal	This is categorised as news/radio/tv once a week, news/radio/tv less than once a week, news/radio/tv almost every day and no media access
	Number of antenatal visits	Categorical	This was a continuous variable that was categorized into two groups less than 4 visits inadequate, 4 and above adequate visits
	Sex of head of household	Binary	Male or female
	Residence	Binary	place of residence rural or urban

2.3.6 Data Analysis

Various methods were employed to analyse the survey data at a significance level of 0.05 and a 95% confidence interval. These methods included unadjusted univariate and bivariate analysis, survey design-adjusted Pearson and Student t-tests, and multi-variable and multi-level linear regression models. Non-random effects were initially checked at the individual level and random effects were assessed using multilevel linear regression and conditional autoregressive (CAR) models. To ensure the robustness of the estimates, all models fitted in Stata were replicated in R. Furthermore, a sensitivity analysis was conducted by fitting the various models. Notably, observations without outcome variables were excluded from the analysis, resulting in the exclusion of 36 observations that did not have their Hb levels and 408 that had missing information on IPTp-SP. Explanatory variables were assessed to determine how they affected the outcome variables and non-missing variables. Figure 6 provides a visual representation of the analysis strategy for each objective. More detailed explanations of these techniques are available in the upcoming sections of this chapter.

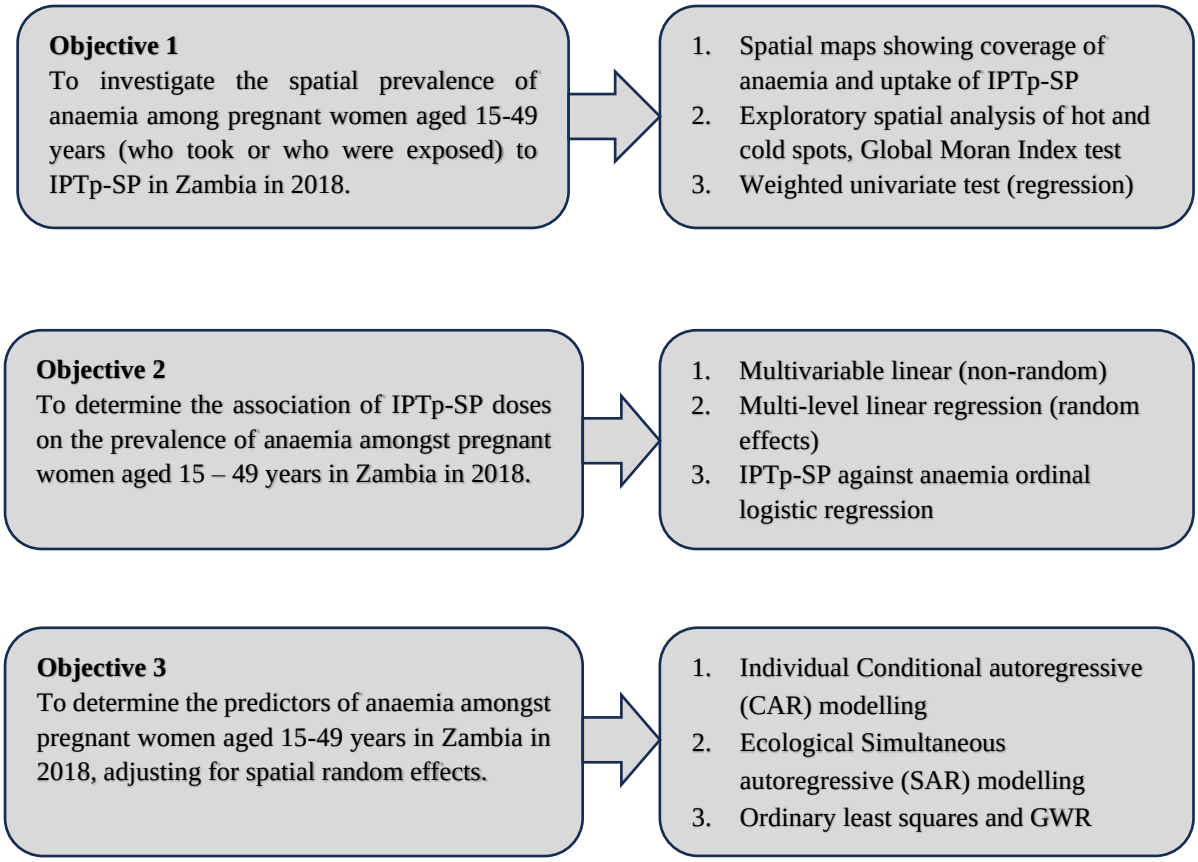

Figure 6: The diagrammatic presentation of the data analysis plan

2.3.6.1 Data Analysis for Objective 1:

To investigate the spatial prevalence of anaemia among pregnant women aged 15-49 years (who took or who were exposed) to IPTp-SP in Zambia in 2018.

We analysed objective 1 by applying survey weights to account for the complex sampling design, ensuring that the estimates accurately represented the target population. Data cleaning, variable creation, and analysis were performed using Stata 17. Descriptive analysis involved computing frequencies, percentages, means, and standard deviations.

In order to compare mean haemoglobin levels across different categorical variables, we utilised the Stata command "svy mean," which is equivalent to conducting a one-way analysis of variance and Student's t-test.

Spatial analysis in this study involved the utilisation of different software tools. Specifically, we employed the Geoda V.1.8.10 website(https://geoda.software.informer.com/1.8/) and ArcGIS V.10.8.1 (71) for conducting spatial analyses. The base files for Zambia's administrative regions were obtained from the DIVA-GIS website (https://www.diva-gis.org/gdata). To link the occurrence of anaemia and uptake of IPTp-SP to their corresponding geospatial locations (survey cluster values), we merged the DHS data with the geographic poisoning system (GPS) dataset using STATA 17 (70). Subsequently, we imported these values into ArcMap software for calculating anaemia and uptake of IPTp-SP proportions at the cluster, zonal, and regional levels.

The prevalence of anaemia and the uptake of IPTp-SP were visually represented through maps generated in ArcMap, displaying the spatial distribution of these variables.

2.3.6.2 Data Analysis for Objective 2

To determine the association of IPTp-SP doses uptake on the prevalence of anaemia amongst pregnant women aged 15 – 49 years in Zambia in 2018.

To investigate the potential association of anaemia, we fitted a bivariate linear model. Next, we ran stepwise with a cut off 0.25 keeping age and IPTp-SP uptake in the model. The variables that were selected in the backward stepwise were included in the multivariable linear regression model. The final model included IPTp-SP, age, province, wealth index, woman's occupation, media exposure, household size, parity, woman's education level and type of antenatal care. To account for the clustering sampling frame of the data, we used multilevel linear regression models and fitted random and fixed effects.

To further analyse IPTp-SP uptake, we employed a methodology that involved the creation of an interaction variable between anaemia and IPTp-SP uptake. The interaction variable was used

to explore the relationship between these two variables in four categories: suboptimal anaemia, suboptimal with no anaemia, optimal anaemia, and optimal with no anaemia.

To investigate the potential association between the interaction variable for anaemia against IPTp-SP uptake and several covariates, we fitted a bivariate logistic model. Next, we included the covariates that showed significant or marginally significant at a cut-off of 0.20 in a weighted analysis into a multi-level ordinal logistic model. The final model included age, household size, wealth index, iron tablets, antenatal visits, and province as predictors of IPTp-SP uptake and anaemia.

2.3.6.3 Data Analysis for Objective 3

To determine the predictors of anaemia amongst pregnant women aged 15-49 years in Zambia in 2018, adjusting for spatial random effects.

To assess the extent and intensity of spatial presence, we employed spatial autocorrelation analysis. Specifically, the global Moran's Index was utilised to examine spatial autocorrelation. Therefore, to analyse this objective, three approaches were used. Firstly, a Conditional Autoregressive (CAR) model was fitted using the variables from the final linear model obtained in objective 2 using R. The model was fitted at the district level and the province variable was excluded because it was accounted for in the spatial analysis (see appendix C for CAR code). Secondly, a Simultaneous Autoregressive (SAR) model was fitted in Stata. This was to analyse data at an ecological level (SAR models consider patterns in the response variable that are related to nearby places rather than anticipated by explanatory variables). Only variables that were significant and marginally significant in the multi-level linear regression were fitted. The data was combined with the shapefile by using the collapse command at the district level. Three SAR models were fitted. The first was the spatial lag of the dependent variable, the second was the spatial lag of the independent variable, the third was the spatial model with the spatially autoregressive errors and finally all three kinds of spatial lag terms (equation 1)

$Y=pWY + X\beta + WX\gamma + \varepsilon$ *Equation 1: Independent lad SAR model*

Where:

Y= dependent variable

P= spatial autoregressive parameter

X= independent variable

W= raw normalised adjacency

β= coefficients

ε= unobservable error term

The model with the least AICs with a significant Wald test of spatial terms was considered the best model after which prediction maps were run.

To delve deeper into spatial relationships and gain a comprehensive understanding of the underlying factors, as well as predict outcomes based on this knowledge, the study employed two regression techniques: Ordinary Least Squares (OLS) and Geographically Weighted Regression (GWR). By employing GWR, we were able to account for variations in the relationships being modelled across the study area. This approach effectively considers the spatial variability in both model parameters and errors (equation 2).

$Y=\beta 0 + \beta 1X1 + \beta 2X2 + \beta nXn + \varepsilon$ *Equation 2: GWR model*

Where:

Y=dependent variable

β= coefficients

X= explanatory variables

ε= residual error

2.4 Ethical Considerations

Informed consent was obtained from all interview respondents at the primary level of data collection. Before using the data, we sought permission from the DHS program team (refer to

Appendix B for details). We also obtained ethical approval from the University of the Witwatersrand Research Ethics Committee (Medical) with ethics certificate number M221182, and a copy of the ethics clearance certificate can be found in Appendix A1.

CHAPTER 3.0: RESULTS

This chapter presents the findings of the research objectives outlined in Chapter 2. The results are organized: descriptive statistics, regression analysis models, and spatial maps. The descriptive statistics section provides a summary of the data collected. The regression analysis models section presents the statistical relationship between the dependent and independent variables and the spatial maps section presents visual representations of the data to help identify spatial patterns and relationships between variables. Figure 7 below shows a diagrammatic representation of the results.

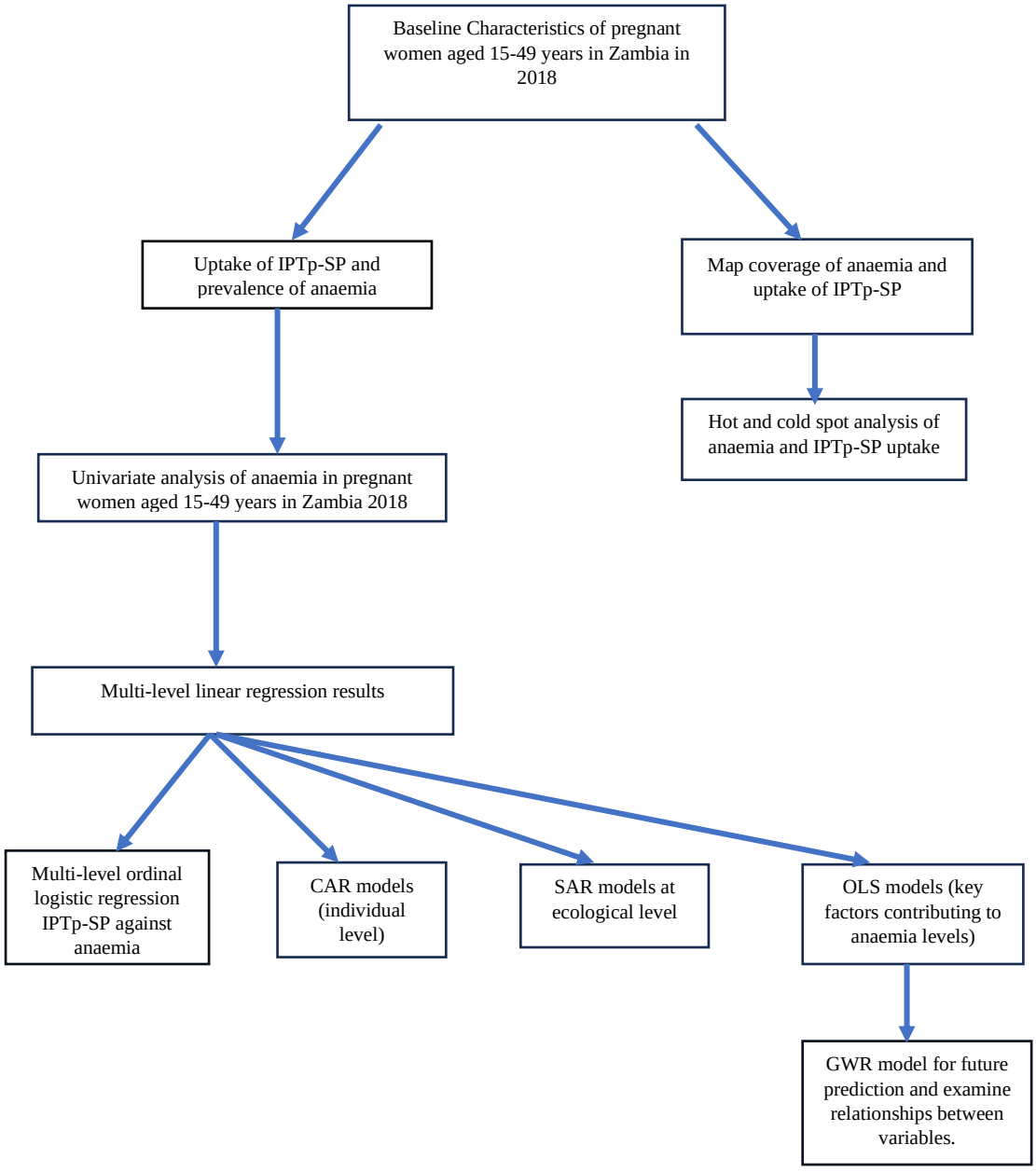

Figure 7: Diagrammatic representation of results.

3.1 Baseline characteristics of anaemia amongst pregnant women aged 15-49 years in Zambia in 2018

The study included 665 women who had their Hb levels measured (shown in Table 2 and

Table *3*). Among them, 46.82% took suboptimal doses of IPTp-SP while approximately 53.18% took optimal doses. The average Hb level was higher in women who took optimal doses (mean=11.40g/dl, SD=1.51) than those who had suboptimal doses (mean=11.29g/dl, SD=1.64). Most women were in the age group 26-35 years (49.44%). The mean Hb levels were similar across the groups, except for women aged 36-49 years who had a lower mean Hb of 10.97g/dl (SD=1.81). Most households (over 80%) were headed by males, and more than 50% of women had some level of education. More than 80 % of the women were married. The mean Hb levels were comparable among all provinces, except for the Southern province which had a significantly lower mean of 10.90g/dl (SD=1.12). Almost all women (approximately 95%) had taken iron tablets. Among those who had adequate antenatal visits, more than 60% had adequate visits.

Table 2: Baseline characteristics of anaemia (weighted) of pregnant women aged 15 - 49 years in Zambia in 2018.

Variables	Total population		Hb level (g/dl)		*p-value*
	n	%	Mean	SD	
Age (Years)					0.820
15-25	342	49.44	11.37	1.48	
26-35	274	39.65	11.43	1.63	
36-49	75	10.91	10.97	1.81	
Sex of Head of Household					0.790
Male	587	84.92	11.34	1.60	
Female	104	15.08	11.39	1.45	
Residence					0.330
Urban	213	30.80	11.27	1.48	
Rural	478	69.20	11.39	1.61	
Education Level					0.440
No Education	76	11.01	11.36	1.75	
Primary	366	53.01	11.30	1.64	
Secondary	212	30.73	11.41	1.49	
Higher	36	5.25	11.53	1.16	
Wealth Index					0.041*
Poor	236	34.11	11.35	1.68	
Middle	226	32.67	11.29	1.53	
Rich	230	33.22	11.41	1.49	
Parity					0.600
0 – 3 Children	475	69	11.43	1.54	
≥ 4 Children	216	31	11.17	1.66	
Woman Occupation					0.098
Not Working	359	51.97	11.29	1.64	
Working	332	48.03	11.41	1.51	
Marital Status					0.990
Not Married	80	11.51	11.29	1.68	
Married	611	88.49	11.36	1.57	
Household Size					0.019*

1 – 3	179	25.90	11.00	1.36
4 – 6	311	45.04	11.48	1.55
≥ 7	201	29.06	11.46	1.77

Key: Hb = Haemoglobin, SD = Standard deviation. *Statistically significant at *p-value* less than 0.05 (<5%).

Table 3: Baseline characteristics of anaemia (weighted) of pregnant women aged 15 - 49 years in Zambia in 2018.

Variables	Total population		Hb level (g/dl)		*p-value*
	n	%	Mean	SD	
IPTp-SP					0.260
Sub-optimal	324	46.82	11.29	1.51	
Optimal	368	53.18	11.40	1.64	
Province					0.400
Central	59	8.49	11.92	1.93	
Copperbelt	64	9.31	11.12	1.68	
Eastern	113	16.37	11.33	1.34	
Luapula	64	9.26	11.34	1.89	
Lusaka	101	14.59	11.48	1.31	
Muchinga	40	5.80	11.81	2.20	
North-Western	32	4.58	11.57	1.91	
Northern	64	9.19	11.39	1.48	
Southern	110	15.95	10.90	1.12	
Western	45	6.47	11.18	1.49	
Media Exposure					0.960
No Media Access	317	45.92	11.24	1.61	
News/Radio/Tv Less Than Once a Week	67	9.73	11.49	1.47	
At Least Once A Week	106	15.27	11.71	1.63	
News/Radio/Tv/Almost Everyday	201	29.08	11.29	1.50	
Slept Under Bednet					0.720
No Net	338	48.88	11.37	1.47	
Slept Under Bednet	353	51.12	11.33	1.68	
Timing Of First Antenatal Visits					0.530
No Visits	13	1.89	11.39	2.24	
First Trimester	221	32.02	11.59	1.62	
Second Trimester	433	62.67	11.24	1.52	
Third Trimester	24	3.43	11.11	1.52	
Iron Tablets					0.390
No	29	4.18	11.14	2.36	
Yes	662	95.82	11.36	1.54	
Type Of Antenatal					0.650
No ANC	25	3.56	11.43	2.41	
Government Facilities	649	93.83	11.36	1.55	
Private Facilities	18	2.61	10.91	1.15	
Intestinal Drugs					0.700
No	184	26.55	11.42	1.55	
Yes	508	73.45	11.33	1.59	
Antenatal Visits					0.270
Inadequate	257	37.11	11.30	1.50	
Adequate	435	62.89	11.38	1.63	

Key: ANC = Antenatal care, Hb = Haemoglobin, SD = Standard deviation. *Statistically significant at *p-value* less than 0.05 (<5%).

3.2 Prevalence and uptake of IPTp-SP anaemia in relation to dosage

Table 4 presents the prevalence of anaemia among pregnant women aged 15-49 years, categorized by their reported use of IPTp-SP. Anaemia was defined as a haemoglobin level below 11 g/dl, while no anaemia was defined as a haemoglobin level of 11 g/dl or higher. The table indicates that among those who reported using IPTp-SP, 39.93% had anaemia, while 60.07% did not. Notably, there was a decrease in the prevalence of anaemia with increased uptake of IPTp-SP, with 42.85% of those with suboptimal uptake and 36.98% of those with optimal uptake experiencing anaemia. However, it is worth mentioning that the observed p-values did not reach statistical significance.

Table 4: Prevalence and uptake of IPTp-SP anaemia in relation to dosage

Variable	Anaemia n (%)		Pearson chi	*p-value*
	No anaemia 429 (60.27%)	Anaemia 236 (39.73%)		
Reported use of IPTp-SP				
Did not take	35 (62.58%)	21 (37.42%)	0.108	0.742
Took SP	394 (60.07%)	215 (39.93%)		
Dosage of SP				
Sub-optimal	184 (57.15%)	112 (42.85%)	1.286	0.257
Optimal	245 (63.02%)	124 (36.98%)		

3.3 Global Moran Index

The results revealed significant clustering in the distribution of anaemia, indicating the need for additional spatial analysis to explain this phenomenon further. The outcome was anaemia, which yielded a Moran Index of 0.100 and a significant level or *p-value* of 0.006.

3.3.1 Prevalence of anaemia and IPTp-SP coverage amongst pregnant women in Zambia in 2018

Figure 8 shows the unadjusted prevalence of anaemia and IPTp-SP uptake at the district level in Zambia. Districts such as Kazungula, Livingstone, Kalomo, Choma, Namwala, and others

showed low uptake of IPTp-SP. A high uptake of IPTp-SP was observed in Chililabombwe, Chingola, Kalulushi, Mwinilunga, and other districts. A low prevalence of anaemia was observed in Kawambwa, Mporokoso, Mungwi, and other districts. A high prevalence of anaemia was seen in Mkushi, Chongwe, Kalomo, Choma, Mumbwa, and other districts. After reviewing the map, it became evident that certain regions exhibiting high IPTp-SP uptake, such as Chongwe, Mkushi, Nchelenge, Chiengi, and Kabompo, also displayed prevalence of anaemia.

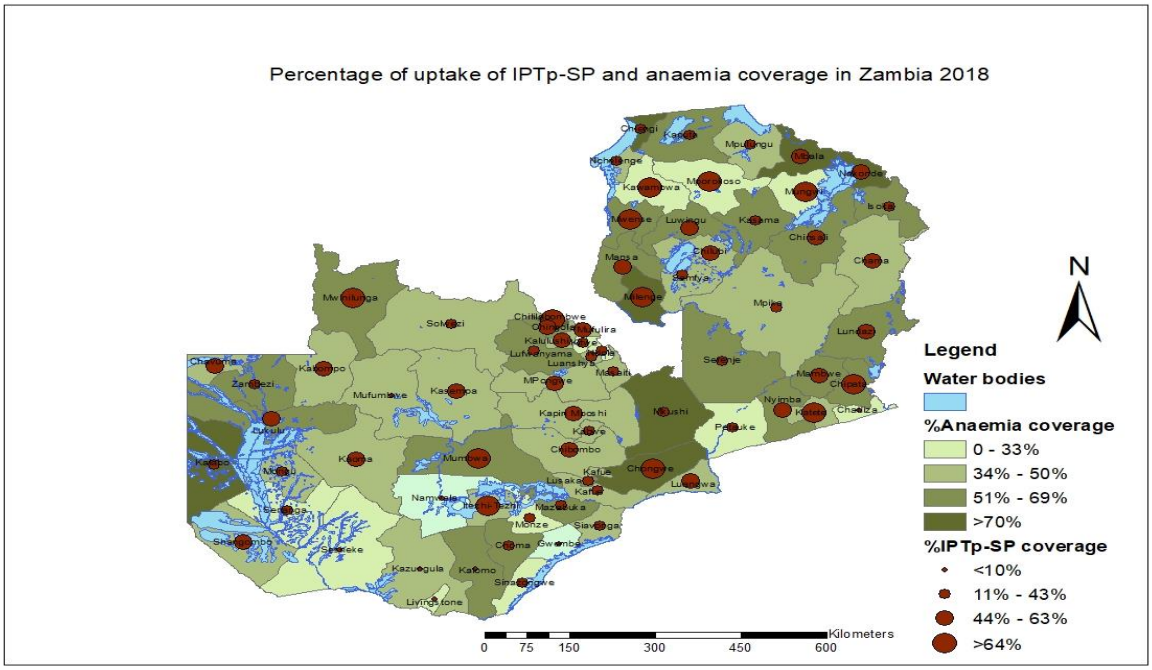

Figure 8: Map of Zambia showing the distribution of prevalence of anaemia and IPTp-SP

Figure 9 below shows the hot and cold spots of anaemia and IPTp-SP uptake in Zambia among pregnant women in 2018 at 90%, 95%, and 99% confidence. The cold spots for anaemia are Chililabombwe, Chingola, Mufulira, Kitwe, and Kalulushi. The hot spots for anaemia shown in the map are Mazabuka, Chongwe, and Serenje, including parts of Chipata and Mambwe districts. For IPTp-SP coverage, cold spots were observed in Kalomo, Choma, Sinazongwe, and Livingstone. The hot spots were Chipata, Lundazi, Mambwe, Chadiza, Nyimba, Katete,

and Chibombo districts. The districts of Chipata, Mambwe, and Chibombo emerged as simultaneous hotspots for both anaemia (low Hb levels) and low IPTp-SP uptake.

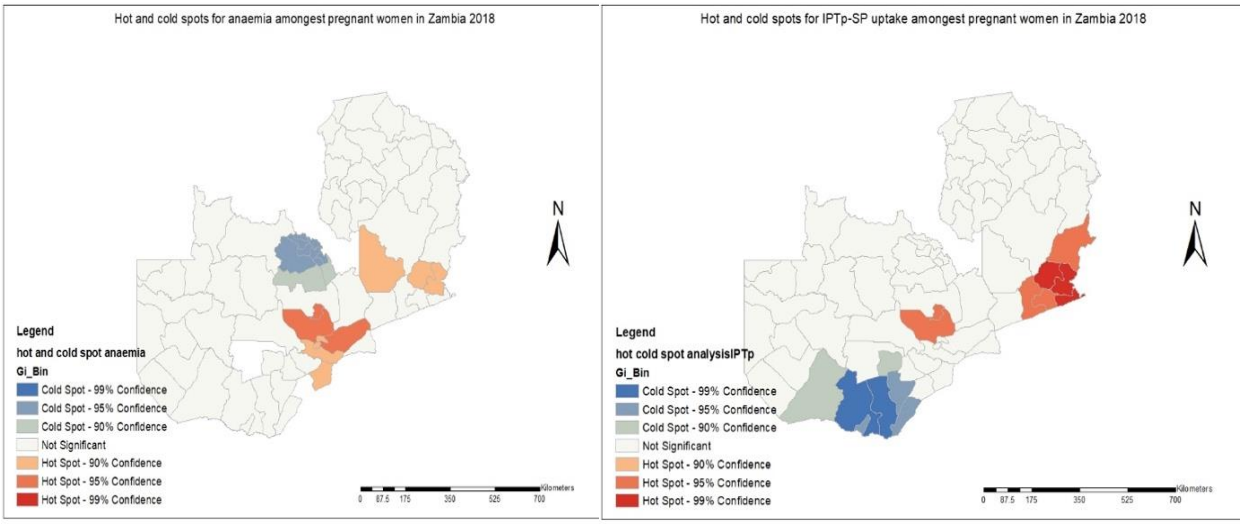

Figure 9: Map of Zambia showing the hot and cold spot of anaemia and IPTp-SP uptake.

3.4 Univariate linear regression results for anaemia among pregnant women aged 15-49 years in Zambia in 2018.

Univariate linear regression on the association of IPTp-SP uptake on anaemia showed that province, household size, exposure to media at least once a week were significant predictors of anaemia prevalence. From the univariate regression even though IPTp-SP was not significant with anaemia, it showed that women with optimal uptake had a higher Hb than women who had suboptimal uptake of IPTp-SP. Anaemia levels were lower in Eastern, Southern and Western province compared to other provinces. Household size with four to six individuals had higher Hb levels compared to the other categories even though a household with seven or more individuals was marginally significant. Women that had media exposure at least once a week had higher Hb levels than women who did not have access to media [Coeff=0.48, 95%CI (0.80 to 8.7), p=0.019]. The rest of the variables were not significantly associated with anaemia. These results are shown in Table 5 and Table 6.

Table 5: Univariate linear regression of anaemia in pregnant women aged 15-49 years in Zambia in 2018.

Variable	Coefficient	95% CI	*p-value*
Age (years)			
15-25	Ref		
26-35	0.05	(-0.32-0.43)	0.773
36-49	-0.40	(-1.04-0.23)	0.212
Sex of head of household			
Male	Ref		
Female	0.42	(-0.35-0.43)	0.835
Residence			
Urban	Ref		
Rural	0.12	(-0.38-0.62)	0.629
Women highest education level			
No education	Ref		
Primary	-0.07	(-0.54-0.40)	0.778
Secondary	0.04	(-0.54-0.63)	0.881
Higher	0.17	(-0.50-0.84)	0.616
Wealth index			
Poor	Ref		
Middle	-0.05	(-0.38-0.28)	0.751
Rich	0.06	(-0.38-0.51)	0.781
Parity			
0 – 3	Ref		
≥ 4	-2.68	(-0.62-0.08)	0.134
Women's occupation			
Not working	Ref		
Working	0.12	(-0.25-0.49)	0.530
Marital status			
Not married	Ref		
Married	0.06	(-0.44-0.56)	0.802
Household size			
1 – 3	Ref		
4 – 6	0.48	0.01-0.95	0.044*
≥ 7	0.46	(-0.03-0.94)	0.067

*Statistically significant at *p-value* less than 0.05 (<5%).

Table 6: Univariate linear regression of anaemia in pregnant women aged 15-49 years in Zambia in 2018.

Variable	Coefficient	95% CI	*p value*
IPTp-SP			
Sub-optimal	Ref		
Optimal	0.12	(-0.21-4.38)	0.481
Province			
Central	Ref		
Copperbelt	-0.79	(-1.61-0.03)	0.058
Eastern	-0.58	(-1.14-0.03)	0.040*
Luapula	-0.58	(-1.20-0.04)	0.065
Lusaka	-0.43	(-1.20-0.23)	0.198
Muchinga	-0.10	(-0.84-0.63)	0.779
North-western	-0.34	(-1.00-0.32)	0.310
Northern	-0.52	(-1.13-0.08)	0.088
Southern	-1.01	(-1.74-0.29)	0.007*
Western	-0.73	(-1.30-0.16)	0.012*
Exposure to media			
No media	Ref		
News/radio/tv less than once a week	0.26	(-0.12-0.64)	0.178
At least once a week	0.48	0.08-0.878	0.019*
News/radio/tv almost every day	0.06	(-0.30-0.41)	0.753
Slept under bednet			
No net	Ref		
Slept under bednet	-0.04	(-0.43-0.35)	0.825
Timing of first antenatal visits			
No visits	Ref		
First trimester	0.19	(-1.25-1.64)	0.793
Second trimester	-0.15	(-1.58-1.27)	0.832
Third trimester	-0.29	(-1.84-1.26)	0.717
Iron tablets			
No	Ref		
Yes	0.22	(-0.70-1.13)	0.644
Type of ANC			
No ANC	Ref		
Government facilities	-0.07	(-1.05-0.90)	0.884
Private facilities	-0.53	(-2.12-1.07)	0.517
Intestinal Drugs			
No	Ref		
Yes	-0.09	(-0.42-0.23)	0.582
Antenatal visits			
Inadequate	Ref		
Adequate	0.09	(-0.27-0.44)	0.629

*Statistically significant at *p-value* less than 0.05 (<5%). Ref=reference at 0

3.5 Multi-level Linear Regression Results of Anaemia and its predictors

Stepwise regression was used to determine which variables are selected for the multi-variable analysis at a cut-off of 0.25 locking in age and IPTp-SP. Using Stata, both non-random and random effects were fitted, table 7 below shows the results. The multilevel model (random effects) accounted for the clustering to get correct estimates of confidence intervals, significant test and standard errors, and hence multi-level model results will be used in the discussion.

Compared to other provinces, Southern, Western and Luapula had lower Hb levels [Coeff=-0.60, 95%CI (-1.18 to 0.03), p= 0.039), [Coeff=-0.80, 95%CI (-1.38 to 0.23), p= 0.006] and [Coeff=-0.55, 95%CI (-1.07 to 0.03) p=0.040] and Copperbelt, Eastern were marginally significant. Hb levels were higher in women whose households had more individuals. Households with more than three individuals had increased Hb levels than households with less than three individuals. Women who were in the rich wealth index had higher Hb levels than women who were in the poor wealth index category [Coeff=0.42, 95% CI 0.04 to 0.81, p=0.031]. Women who had more than three children had lower Hb levels than women who had less than three children [Coeff=-0.35, 95%CI (-0.71 to 0.00), p=0.051] this was marginally significant. Pregnant women who were working had higher Hb levels than women who were not working [Coeff=0.30, 95%CI (0.06 to 0.54), p=0.015]. Adjusting for these factors women that took optimal IPTp-SP had 0.07g/dl higher Hb level that the women that took suboptimal IPTp-SP, but this was not statistically significant [Coeff=0.07, 95%CI (-0.18 to 0.31), p=0.593].

Table 7: Multi-level random effects linear regression on anaemia for pregnant women aged 15-49 years in Zambia in 2018.

Variables	Non-Random effects			Random effects		
	Coefficient	95%CI	*p value*	Coefficient	95%CI	*p-value*
IPTp-SP						
Sub-optimal	Ref			Ref		
Optimal	0.01	(-0.25-0.27)	0.938	0.07	(-0.18-0.31)	0.593
Age (years)						
15-25 years	Ref			Ref		
26-35 years	-0.07	(-0.49-0.34)	0.729	0.02	(-0.29-0.33)	0.901
36-49 years	-0.40	(-1.27-0.47)	0.364	-0.03	(-0.51-0.46)	0.915
Province						
Central	Ref			Ref		
Copperbelt	-0.84	(-1.60-0.09)	0.029*	-0.56	(-1.14-0.02)	0.058
Eastern	-0.58	(-1.14-0.02)	0.042*	-0.46	(-0.96-0.05)	0.078
Luapula	-0.58	(-1.20-0.03)	0.066	-0.55	(-1.07-0.03)	0.040*
Lusaka	-0.44	(-1.14-0.26)	0.220	-4.22	(-0.98-0.14)	0.139
Muchinga	-0.02	(-0.74-0.71)	0.959	-0.02	(-0.59-0.55)	0.947
North-western	-0.34	(-1.05-0.36)	0.342	-0.28	(-0.89-0.33)	0.372
Northern	-0.55	(-1.15-0.05)	0.073	-0.39	(-0.93-0.15)	0.153
Southern	-0.96	(-1.62-0.30)	0.005*	-0.60	(-1.18-0.03)	0.039*
Western	-0.85	(-1.43-0.26)	0.005*	-0.80	(-1.38-0.23)	0.006*
Women's highest education level						
No education	Ref			Ref		
Primary	-0.07	(-0.52-0.37)	0.751	-0.06	(-0.43-0.32)	0.771
Secondary	0.05	(-0.44-0.44)	0.829	0.04	(-0.40-0.49)	0.858
Higher	0.06	(-0.93-1.05)	0.909	-0.53	(-1.32-0.25)	0.183
Household size						
1 – 3	Ref			Ref		
4 – 6	0.62	0.23-1.02	0.002*	0.45	0.13-0.76	0.005*
≥ 7	0.72	0.30-1.13	0.001*	0.50	0.14-0.85	0.006*
Exposure to media						
No media	Ref			Ref		
News/radio/tv less than once a week	0.15	(-0.26-0.56)	0.473	0.07	(-0.32-0.46)	0.734
At least once a week	0.27	(-0.15-0.68)	0.213	0.12	(-0.23-0.47)	0.508
News/radio/tv almost every day	-0.05	(-0.53-0.42)	0.827	-0.15	(-0.49-0.19)	0.385
Wealth index						
Poor	Ref			Ref		
Middle	-0.05	(-0.36-0.26)	0.755	-0.10	(-0.38-0.19)	0.507
Rich	0.12	(-0.33-0.57)	0.589	0.42	0.04-0.81	0.031*
Parity						
0 – 3	Ref			Ref		
≥ 4	-0.35	(-0.86-0.15)	0.171	-0.35	(-0.71-0.00)	0.051
Type of ANC						
No ANC	Ref			Ref		
Government facilities	0.07	(-0.80-0.94)	0.871	-0.01	(-0.60-0.58)	0.974
Private facilities	-0.16	(-1.34-1.01)	0.784	0.86	(-0.30-2.03)	0.147
Woman's occupation						
Not working	Ref			Ref		
Working	0.23	(-0.06-0.51)	0.114	0.30	0.06-0.54	0.015*

*Statistically significant at *p-value* less than 0.05 (<5%) ref=reference at 0.

3.6 Association between IPTp-SP uptake and anaemia

Baseline characteristics (Table 8) revealed that a higher proportion of women aged 15-25 years had optimal IPTp-SP uptake and no anaemia (31.61%). In contrast, the Southern province had a higher prevalence of sub-optimal IPTp-SP uptake and anaemia (44.60%), with very few women having optimal uptake and no anaemia. It was also observed that women from households with four to six individuals had higher uptake of IPTp-SP with no anaemia

(38.09%), followed by those with seven or more individuals (34.43%). Additionally, a greater proportion of women with adequate antenatal care (37.78%) had optimal IPTp-SP uptake and no anaemia compared to those with inadequate care (26.30%). Finally, it was found that women in the poor wealth index category were more likely to have sub-optimal IPTp-SP doses and no anaemia, while women in the middle and rich categories were more likely to have optimal uptake and no anaemia.

Table 8: The Optimal versus Suboptimal Characteristics of Women with and those without Anaemia

Variables	optimal- no anaemia	suboptimal- no anaemia	optimal-anaemia	suboptimal- anaemia
Age (years)				
15-25	108 (31.61%)	95 (27.86%)	66 (19.31%)	72 (21.21%)
26-35	100 (36.34%)	69 (25.31%)	57 (20.65%)	49 (17.71%)
36-49	24 (31.91%)	20 (26.99)	13 (17.70%)	18 (23.40%)
Province				
Central				
Luapula	21 (32.66%)	18 (28.36%)	15 (22.68%)	10 (16.29%)
Southern	10 (9.35%)	32 (29.42%)	18 (16.64%)	49 (44.60%)
Western	16 (36.11%)	13 (28.55%)	7 (15.69%)	9 (19.66%)
Household size				
1 – 3	44 (24.54%)	40 (22.07%)	44 (24.45%)	52 (28.93%)
4 – 6	119 (38.09%)	86 (27.48%)	54 (17.18%)	54 (17.25%)
$\geq$ 7	69 (34.43%)	60 (29.80%)	39 (19.26%)	33 (16.51%)
Iron Tablets				
No	1 (4.6%)	15 (50.4%)	3 (8.73%)	10 (36.27%)
Yes	230 (34.78%)	170 (25.72%)	133 (20.14%)	128 (19.35%)
Antenatal visits				
Inadequate	67 (26.30%)	86 (33.37%)	40 (15.74%)	63 (24.58%)
Adequate	164 (37.78%)	99 (22.85%)	96 (21.98%)	76 (17.39%)
Wealth Index				
Poor	73 (30.75%)	77 (32.48%)	44 (18.61%)	43 (18.16%)
Middle	75 (33.12%)	52 (23.03%)	45 (19.78%)	54 (24.07%)
Rich	84 (36.75%)	56 (24.54%)	47 (20.64%)	42 (18.07%)

3.6.1 Multilevel logistic regression on IPTp-SP and anaemia

Table 9 shows the results of the ordinal logistic regression. The Southern province showed 5.06 times greater odds of falling into the higher category encompassing optimal or suboptimal IPTp-SP uptake with anaemia compared to the Central province (95% CI 2.25 to 11.43). Luapula and Western provinces were marginally significant after adjusting for confounders with AOR of 2.02 and 2.14 respectively (95% CI 0.97 to 4.22 and 0.96 to 4.74). Participants from larger households, comprising four to six and those with seven or more members, showed a significant association with having optimal or suboptimal IPTp-SP uptake without anaemia, with 0.53 (95% CI 0.35 to 0.80) and 0.57 (95%CI 0.35 to 0.91) times respectively, compared

to those in smaller households of one to three members after adjusting for confounding factors. Furthermore, women who took iron tablets showed 0.42 times higher odds of having optimal or suboptimal IPTp-SP uptake with no anaemia compared to women who did not take iron tablets. The latter was marginally significant (95% CI 0.17 to 1.03, p=0.059), after adjusting for confounding factors. Women who had adequate antenatal visits showed 0.68 times of having optimal IPTp-SP uptake with no anaemia compared to those who had inadequate antenatal visits, with an (95% CI 0.48 to 0.97, p=0.034) after adjusting for confounders. Finally, it was found that women in the rich wealth index category showed 0.58 (95% CI 0.34 to 0.98, p=0.044) times of having optimal or suboptimal IPTp-SP uptake with no anaemia compared to women in the poor and middle category.

Table 9: Multilevel logistic regression on uptake of IPTp-SP against anaemia

Variables	AOR	95%CI	*p-value*
Age (years)			
15-25	1 ref		
26-35	1.23	0.86-1.75	0.255
36-49	1.05	0.60-1.83	0.864
Province			
Central	1 ref		
Luapula	2.02	0.97-4.22	0.061
Southern	5.06	2.25-11.43	<0.001*
Western	2.14	0.96-4.74	0.062
Household size			
1 – 3	1 ref		
4 – 6	0.53	0.34-0.80	0.003*
≥ 7	0.57	0.35-0.91	0.019*
Iron Tablets			
No	1 ref		
Yes	0.42	0.17-1.03	0.059
Antenatal visits			
Inadequate	1 ref		
Adequate	0.68	0.48-0.97	0.034*
Wealth Index			
Poor	1 ref		
Middle	0.98	0.67-1.45	0.929
Rich	0.58	0.34-0.98	0.044*

*Statistically significant at p-value less than 0.05 (<5%).

3.7 Predictors of anaemia after adjusting for spatial random effects

3.7.1 Conditional Autoregressive model: Individual level analysis

Conditional Autoregressive models were fitted using the same variables that were significant in the multi-level analysis. Province was excluded from the model because it was accounted for in the spatial modelling. Table 10 shows the summary of the fixed effects model after adjusting for random effects. The model showed that a household size of four to six individuals was a significant predictor of anaemia, with a coefficient of 1.42 (95% Bayesian credible interval BCI 1.02 to 2.00), adjusting for spatial correlation and keeping other variables constant. Woman's occupation was also a significant predictor of anaemia, with a coefficient of 1.44 (95% BCI 1.09 to 1.58), adjusting for spatial correlation and keeping other variables constant. The facility that a woman attended for antenatal care was also a significant predictor, with a coefficient of 1.45 (95% BCI 1.07 to1.96), adjusting for spatial correlation and keeping all other variables constant. The maps in Figures 10 to 12 show the structured and the unstructured random effects maps. The structured maps show a sizeable difference in the anaemia level, with low levels reported in Southern parts, particularly districts in the Southern province. The unstructured random effects are mostly not significant, but they help show a fair variation over and above the structured effects. They indicate lower Hb levels in some districts in Luapula province and no anaemia in parts of Lusaka province. The total effect, controlling for both unstructured and structured effects, shows that districts in the Southern province have lower levels of Hb and are more anaemic. Some districts in Luapula, the districts in Lusaka province, and some parts of Muchinga also show that they are not anaemic

Table 10: Conditional Autoregressive model: Individual level analysis for predictors of anaemia after adjusting for spatial random effects.

Variables	Coefficient	95% CI of the Coefficient
IPTp-SP		
Suboptimal	ref	
Optimal	1.16	0.83 – 1.63
Age (years)		
15-25	ref	
26-35	0.92	0.64 – 1.30
36-49	0.87	0.51 – 1.52
Household size		
1 – 3	ref	
4 – 6	1.42	1.02 – 2.00
≥ 7	1.31	0.92 – 1.87
Wealth Index		
Poor	ref	
Middle	0.90	0.65 – 1.23
Rich	1.20	0.78 – 1.86
Woman Occupation		
Not working	ref	
Working	1.44	1.09 – 1.88
Parity		
0 – 3	ref	
≥ 4	1.00	0.64 – 1.52
Media Exposure		
No media	ref	
News/radio/tv less than once a week	0.95	0.61 – 1.46
At least once a week	0.89	0.61 – 1.29
News/radio/tv almost every day	0.95	0.65 – 1.38
Type of antenatal		
No ANC	ref	
Government facilities	1.45	1.07 – 1.96
Private facilities	3.33	0.64 – 23.8
Woman education		
No education	ref	
Primary	0.65	0.40 – 1.02
Secondary	0.82	0.47 – 1.39
Higher	0.73	0.31 – 1.67
Intercept	1.13	0.60 – 2.16

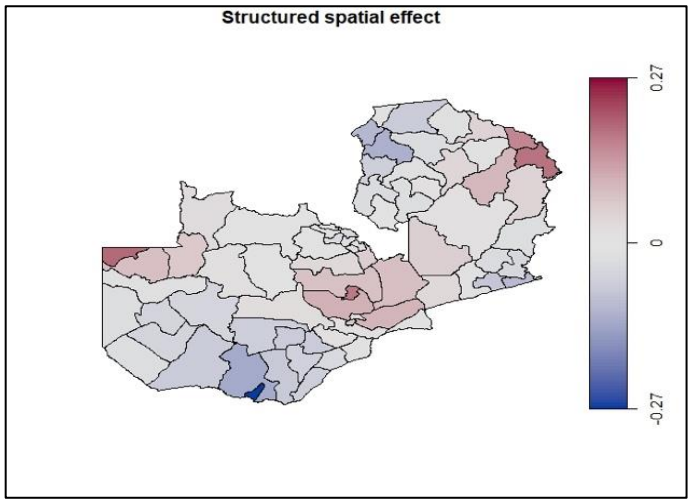

Figure 10: Map of Zambia showing the structured spatial effects.

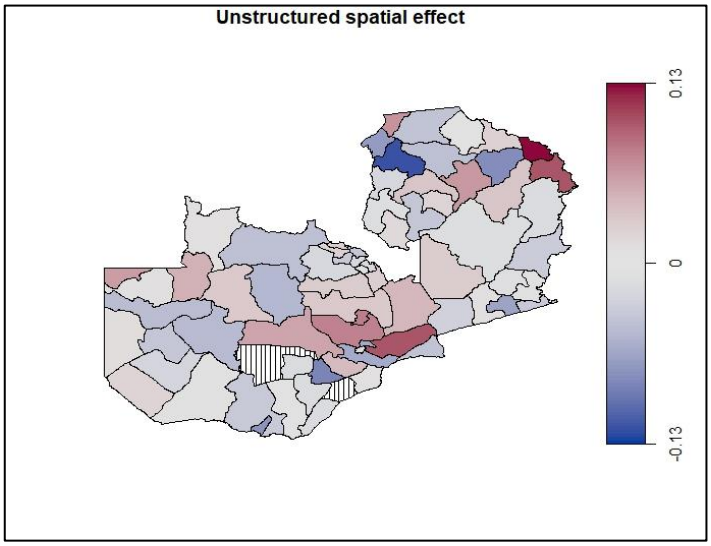

Figure 11: Map of Zambia showing the unstructured spatial effects.

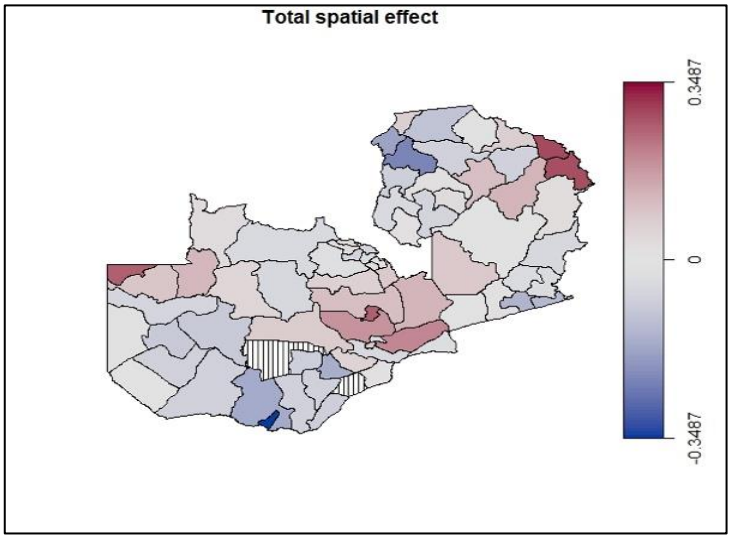

Figure 12: Map of Zambia showing the total spatial effects.

3.7.2 Analysis at Ecological Level: Simultaneous Autoregressive Modelling

Table 11 shows the results of the SAR model for anaemia. Uptake of IPTp-SP had a positive relationship with anaemia, although the *p-value* was not significant. With an increase in the uptake of IPTp-SP, there was a corresponding elevation in Hb levels across all districts. This increase led to a reduction in the prevalence of anaemia in neighbouring districts, a phenomenon referred to as indirect spillover effects. Age had a negative relationship with Hb levels: as age increased the Hb levels were lower. This negative trend was influenced by spatial lag, resulting in indirect effects. This lag coefficient consistently held a negative value for all districts, even though the associated p-value did not demonstrate statistical significance. Parity also had a negative relationship with Hb levels: as parity increased the Hb levels were lower in all districts. The model is summarized by equation 3.

$$Y=15.90 + 0.09X_1 - 0.12X_2 + 0.23X_3 + 1.27WY + \epsilon$$

Equation 3: Dependent lag SAR model for anaemia

Equation table SAR for anaemia model

Where:

Y= the dependent variable

X_{1-x}= the independent variables

W= row normalised adjacency matrix

15.90= intercept

1.27= coefficient of spatial component (spatial term)

ϵ= unobservable error term

Table 11: Analysis at Ecological level: Simultaneous Autoregressive Modelling

Variable	Direct Impact	*p-value*	Indirect impact	*p-value*	total impact	*p-value*
IPTp-SP	0.16	0.940	0.22	0.896	0.38	0.919
Age	-0.11	0.970	-1.05	0.904	-1.46	0.941
Household size	0.23	0.959	1.12	0.904	1.73	0.935
Wealth index	0.07	0.954	0.11	0.907	0.18	0.933
Parity	-0.35	0.966	-0.78	0.899	-1.13	0.937
Woman occupation	0.32	0.964	0.65	0.909	0.98	0.939
Intercept	15.9	0.018				
Spatial term	1.27	<0.001				

Figure 13 below shows two maps; the full information means map and the residual error map. The full mean information map shows the predicted mean of the dependent variable conditional on the independent variables and any spatial lags of the independent variables. The map shows areas that have low Hb levels (anaemia) in the Southern province (Kazungula, Namwala, Choma, Monze). Western province (Senanga, Mongu, Koama), Copperbelt (parts of Chingola, Kitwe). Eastern province (parts of Chipata). The residual map shows residual errors and autoregressive errors.

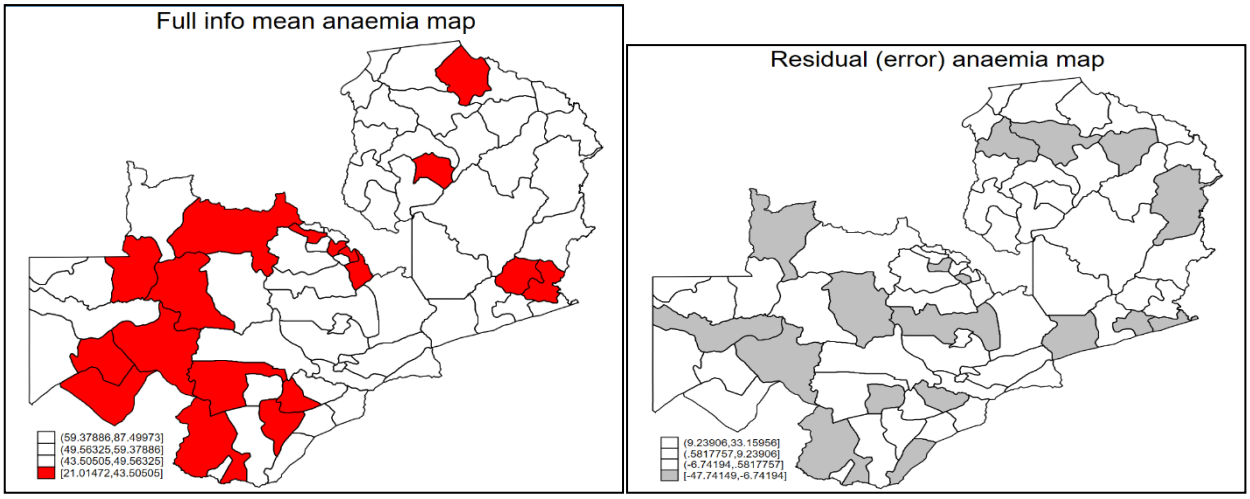

Figure 13: Two maps of Zambia showing the mean anaemia and residual error anaemia.

3.7.3 Analysis using ordinary least squares (OLS) and geographically weighted regression (GWR).

The table 12 below shows that only iron tablets were statistically significant predictors of anaemia p=0.004. Household size was marginally significant p=0.080. The rest of the variables were not significant. The Variance Inflation Factor (VIF) for the variables was not greater than 7.5 meaning that they were no multicollinearity in the model.

Table 12: OLS regression model

Variable	Coefficient	*p-value*	VIF
Age	0.01	0.961	3.14
Wealth index	-0.03	0.629	2.98
Woman occupation	-0.07	0.555	1.42
Access media	0.05	0.266	1.68
Parity	-0.16	0.391	2.83
Household size	0.17	0.080	3.48
Iron tablets	0.56	0.004	4.07
Woman education	-0.01	0.914	2.71
Type of ANC	-0.24	0.236	3.32
IPTp-SP uptake	0.17	0.148	1.37
Intercept	0.35	0.924	

A GWR model was employed, only variables that were significant and marginally significant in the OLS model were used to examine the relationships between anaemia and two variables: iron tablets and household size. The coefficients derived from the model were subsequently mapped to visualize these relationships. Figure 14 and 15 illustrates the spatial patterns of the predictive strength associated with the variables. The areas highlighted in red indicate locations where household size is a strong predictor of anaemia, encompassing Luapula, Northern, and Muchinga provinces, as well as certain parts of Copperbelt (Chililabombwe and Chingola districts). Conversely, the blue areas represent regions where household size demonstrates weaker predictive power. Regarding iron tablets, Lusaka, Southern, and parts of Western province exhibit a strong predictive relationship between anaemia and the consumption of iron tablets (equation 4).

$Y=\beta_0+ \beta_1X_1 + \beta_2X_2 \ldots.+ \varepsilon$ *Equation 4: For GWR model*

Where:

Y= anaemia

β= Coefficients (0.35+ β_1(household size) + β_2(iron tablets)

ε= residual error

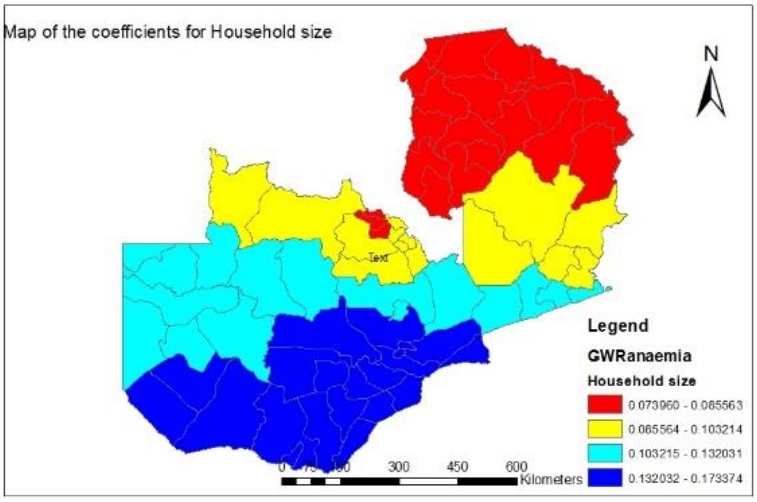

Figure 14: Map of Zambia showing the coefficients for household size

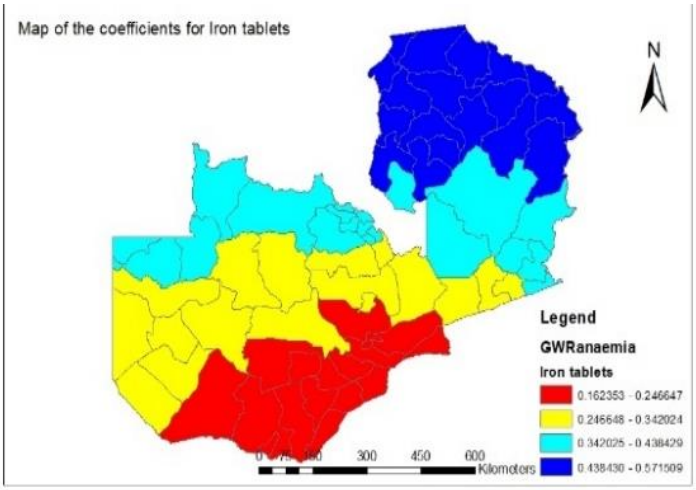

Figure 15: Map of Zambia showing the coefficients for iron tablets.

CHAPTER 4.0: DISCUSSION AND CONCLUSION

4.1 Introduction to the Discussion

In this study, the investigation focused on examining the association between IPTp-SP uptake and anaemia among women aged 15-49 in Zambia in 2018, while also exploring the spatial distribution of these factors. By combining IPTp-SP uptake and anaemia prevalence, the aim to identify the key factors that influence both conditions using spatial and non-spatial models. The discussion of the current study findings is presented according to each specific objective.

4.1.1 Sociodemographic factors associated with anaemia.

The results of this study demonstrate a significant association between anaemia and certain demographic factors. Specifically, pregnant women in the Southern, Western, and Luapula provinces exhibited lower levels of haemoglobin compared to Central province. This difference was found to be statistically significant. The underlying reasons for this variation could be attributed to factors such as food preferences, cultural practices regarding dietary choices during pregnancy (72). These findings align with evidence from a study conducted in Ethiopia (63), which also observed varying levels of Hb across different geographic regions. The disparities in haemoglobin levels were attributed to differences in diets, access to healthcare services, and the presence of infectious diseases prevalent in each region.

In this study, it was found that employed women exhibited higher levels of Hb compared to unemployed women. This difference can be attributed to the fact that higher income levels enable women to access better diets and healthcare facilities. Several studies (56,73,74) have indicated that lower income levels adversely impact Hb levels, as women with limited financial resources cannot afford a diverse range of nutritious foods. However, it is worth noting that a study conducted in Lusaka, Zambia (19), revealed contrasting results. In this case, the employment status of women was not found to be associated with anaemia. This deviation from

the previous findings can be explained by the fact that most women in urban households in Lusaka had the means to meet their dietary requirements.

In this study, an association was found between household size and anaemia. However, despite this association, no significant difference in Hb levels was observed based on household size. Furthermore, the prevalence of anaemia was not negatively impacted by larger households. Therefore, the findings suggest that while household size is associated with anaemia, it does not have a significant effect on Hb levels or the overall prevalence of anaemia. This could be attributed to the resilience of some families with larger household sizes, as they are still able to provide for their needs. A socio economic study conducted in Kabwe showed that despite the challenges, individuals were capable of supporting their families (75). These findings contradict previous studies that suggested higher household sizes are associated with a higher prevalence of anaemia, primarily due to financial constraints faced by the household in these countries (51,53,76,77).

The current study revealed a potential effect of parity, specifically the number of children, on anaemia levels. Women with more than four children exhibited lower Hb levels compared to those with fewer than four children, although this association was only marginally significant. These findings align with prior studies that have reported an association between parity and anaemia, supporting the notion that higher parity may be associated with an increased risk of anaemia (51,64). This finding could potentially be attributed to the relationship between the number of childbirths experienced by women and the subsequent increase in blood loss, ultimately leading to lower Hb levels within the bloodstream (78). Likewise, previous pregnancies can lead to a depletion of maternal iron reserves as a result of the heightened nutritional requirements during pregnancy and postpartum blood loss (79). However, it is important to note that these findings differ from some other studies in Zambia and Ethiopia,

which did not find a significant association between anaemia and parity as both were done in urban areas as compared to this study that covered both urban and rural (19,53). Furthermore, anaemia in this study was not associated with place of residence, age, educational attainment, the place a woman attended antenatal care and media exposure. Though this was not consistent with other studies that found these to be significant (48,50,54,64,80). Perhaps this could be attributed to the difference in sample size and geographical variations.

Despite age not being statistically significant it was still observed that the women in the oldest age group (36-49 years) had lower Hb levels. These findings are consistent with the findings from two studies done in Ethiopia (50,51) and a study done in Zambia which found a weak association between age and anaemia (19).

4.1.2 IPTp-SP uptake and anaemia

The use of IPTp-SP has been known to be efficacious in prevention against malaria in pregnancy (12,32). In this study, the prevalence of anaemia among pregnant women that took IPTp-SP was 39.93% in 2018. In 2019 the World Bank estimated the prevalence of anaemia to be 39.3% in pregnant women in Zambia (81). A study conducted in Lusaka province Zambia by Lubeya and co-workers (19) revealed the prevalence of anaemia in pregnant women to be around 36.2% in 2017. IPTp-SP in Zambia was first adopted in 2002 with two doses as optimal (17), which then increased dosage to three or more in 2012 (2). Regarding the trends with anaemia levels, it shows that anaemia is multi-factorial and IPTp-SP is not the only intervention that improves anaemia levels.

In this study there was presence of anaemia in both women who took and those who did not take IPTp-SP. Among women who took the optimal dosage, approximately three-fifths (63.02%) did not have anaemia, although these results were not statistically significant. A Ghanaian study (11) reported that 58.4% of women who did not take IPTp-SP were anaemic,

compared to 22.8% of users of IPTp-SP. The study attributed this discrepancy to the usage of IPTp-SP among women. Additionally, a randomised controlled study by Shulman and co-workers in Kenya (29) demonstrated that IPTp-SP protected pregnant women from malaria and reduced the incidence of severe anaemia compared to a placebo. The study also indicated an improvement in Hb levels among pregnant women who took IPTp-SP. However, the study findings indicate that IPTp-SP had no significant effect on anaemia. One possible explanation for this result is the limitation of the study design, which relied on cross-sectional data collected at the household level. The study was unable to verify the administration and consumption of the drug through cross-referencing with health records, which may have affected the accuracy of the findings. This finding is consistent with a study conducted by Agyeman and co-workers (82), which revealed that while IPTp-SP is effective in reducing malaria, it does not have a significant impact on the Hb levels of pregnant women. These results contradict numerous other studies that have shown improvements in Hb levels among women who took the optimal dosage of IPTp-SP (11,12,32,83,84).

To further examine the factors associated with IPTp-SP uptake, the study analysed the interaction between IPTp-SP uptake and anaemia. The findings revealed that several factors were significantly associated with IPTp-SP uptake, including province, household size, iron tablets, antenatal visits, and wealth index. The findings indicated that women who took iron tablets were more likely to have a lower prevalence of anaemia, this association was marginally significant. The observed results are consistent with the understanding that iron is essential for the synthesis of haemoglobin which result in improved Hb levels (85). These results are consistent with another Zambian study that showed that taking iron tablets improved Hb levels (86). A study conducted in Ghana also found that increased uptake of folic acid during pregnancy reduced the prevalence of anaemia (77). On the contrary, other studies have observed

that iron tablets did not significantly reduce the prevalence of anaemia, as pregnant women with anaemia also reported iron tablet usage (53,74).

Furthermore, the study findings demonstrated that adequate antenatal visits were associated with a reduced prevalence of anaemia. This could be because ANC provides an opportunity for exposure to prophylaxis, increased screening, and treatment of anaemia. Pregnant women who had more than four antenatal visits had higher haemoglobin levels compared to those with fewer visits. These findings align with other studies that have reported a decreased prevalence of anaemia among women who utilised antenatal visits (73,77,86).

4.1.3 Spatial Distribution of Anaemia

In this study, variations in Hb levels across different provinces in Zambia were observed. Specifically, the Southern, Luapula, and Western Provinces exhibited lower Hb levels compared to the other provinces. Conversely, higher Hb levels were observed in Muchinga, Lusaka, and North-western provinces, with particular emphasis on the Chavuma district in North-western Province. However, the current study findings showed some inconsistencies in the prevalence of anaemia and malaria distribution. The results further suggested that Southern, Lusaka, and parts of the Central Provinces have low malaria prevalence rates. Conversely, certain regions within these low malaria prevalence areas, such as Southern Province (19,87), exhibited low Hb levels. On the other hand, provinces with high malaria transmission rates, including North-western, Copperbelt, Muchinga, parts of Western, Luapula, and parts of Eastern, showed higher Hb levels (15,31). These observations indicate that anaemia is a complex condition influenced by multiple factors, and malaria alone cannot account for all cases. This finding is consistent with a previous study conducted in Lusaka, which found no significant association between anaemia and malaria in a low transmission province like Lusaka (19). These findings, contribute to the understanding that anaemia's aetiology is multifactorial,

and it is important to consider various factors beyond malaria when investigating and addressing anaemia prevalence in different regions.

4.1.4 Predictors of Anaemia Using Spatial Analysis

By incorporating adjustments for spatial random effects in the CAR models, the study identified several strong predictors of anaemia, including household size, the woman's occupation, and the facility where she attends her antenatal care. These predictors align with findings from other studies that have also linked them to anaemia (6,51,53). In a comprehensive analysis, known as the total effects model, the study gained a more nuanced understanding of the spatial effects of anaemia. Notably, Kazungula and Livingstone districts in the Southern Province exhibited the lowest levels of Hb, which could be attributed to their susceptibility to flooding, resulting in socio-economic disruptions and infectious disease outbreaks (88).

Furthermore, the ecological SAR model, after accounting for spatial random effects, demonstrated that anaemia is region-specific, and the influencing factors vary across different regions hence there were no significant spill-over effects. This finding aligns with previous research highlighting the geographical variations in anaemia prevalence which can be attributed to a range of factors, including socioeconomic factors, access to healthcare, and nutritional disparities. These elements can contribute to differences in anaemia rates across different regions or areas. (54,63,64). Findings from the GWR provide valuable insights into the localized relationships between the examined variables and anaemia prevalence. By uncovering these spatial variations, the GWR model enhances the study understanding of the contextual factors influencing anaemia. Such information can guide targeted interventions and policy decisions tailored to the specific needs of each region. The areas that have low iron uptake need attention because they could lead to severe complications for pregnant women, children, and those at high risk. Therefore, there is a need for the government to utilise community-lead

approaches to sensitize the community on the importance of taking iron supplements during pregnancy. They can also ensure that the facilities have an adequate of supply of iron tablets. Household size can be complex, but policymakers can make sure that adequate policies that ensure women's access to contraception are implemented. These include removing barriers such as age of consent for women allowing women younger than 18 to have access to contraception.

4.2 Strengths and limitations

The strengths and limitations of this study are discussed in four categories: Exposure and outcome variables classification; generalisability of result findings; confounding adjustment and validity of the data analysis. The following paragraphs present a sequential discussion of these.

4.2.1 Exposure and outcome variables classification

One major strength in the study variables is that the study collected individual-level data, including household family size, wealth index, and woman's Hb levels. Additionally, variables at the ecological level, such as province, district, and cluster, were also considered. This comprehensive data allowed for robust statistical inference and analysis, enabling a deeper understanding of the factors under investigation. Nevertheless, there are some limitations. One notable limitation of the study was the absence of important covariates, such as the woman's nutritional information and pre-pregnancy Hb levels, as well as the presence of sickle cell anaemia. These missing variables could have provided additional insights and a more comprehensive understanding of the factors influencing the outcomes under investigation. Another constraint of the study stemmed from potential recall bias among the participating women, specifically regarding the accurate reporting of the number of IPTp-SP doses they had

received during pregnancy. This recall bias may have introduced some degree of uncertainty or error in the data, which should be considered when interpreting the findings.

4.2.2 Generalisability of result findings

The study utilised data from the ZDHS, a nationally representative study, enhancing the generalisability of the findings to pregnant women aged 15-49 years across all provinces in Zambia. Moreover, the study benefited from a large sample size, providing robust statistical power for making meaningful inferences. By revealing geographical differentials in anaemia levels among pregnant women, the study's findings align with comparable research conducted in Africa (63–65). The insights gained from this study can inform future interventional studies aiming to address the impact of IPTp-SP uptake on anaemia, guiding the development of effective strategies.

4.2.3 Confounding Adjustment

To address confounding variables, the study employed multiple regression analysis while adjusting for spatial random effects. One key strength of using GWR models was the ability to account for confounding and multicollinearity, allowing us to identify factors directly impacting anaemia and evaluate the influence of IPTp-SP on pregnant women's Hb levels. However, it is important to acknowledge a limitation of the study design, namely the cross-sectional design, which prevented us from incorporating time-varying covariates. This limitation restricted the ability to measure Hb levels at different stages of pregnancy and assess the impact of IPTp-SP across these stages.

4.2.4 Validity of data analysis

To ensure the validity of the results, the study employed rigorous statistical analysis techniques. Initially, a linear regression model was utilised, followed by the implementation of multi-level analysis to adjust for clustering, considering the two-stage survey design of the data collection

process. The study incorporated spatial analysis techniques, utilising CAR, and SAR models. This approach provided insights into the spatial patterns and correlations within the data, enhancing the study's ability to understand the geographical aspects of the phenomenon being studied. As a result, The study observed narrower confidence intervals in comparison to the non-spatial counterpart. Thus, considering that spatial random effects lead to further enhancements in both the model and parameter estimation, surpassing the capabilities of traditional statistical models. Moreover, the study employed predictive inference techniques, utilising OLS and GWR models within ArcMap. This allowed for the exploration and prediction of outcomes, offering valuable insights into the potential future trends and variations in the studied variables.

4.3 Conclusion and Recommendations

The overall prevalence of anaemia in this study was 40%. Additionally, women who were employed exhibited better Hb levels than non-working women, and household size was found to have a significant positive association with Hb levels. Furthermore, pregnant women who took iron tablets showed higher Hb levels compared to those who did not. Adequate attendance of antenatal visits during pregnancy was also associated with a higher likelihood of better Hb levels. There were significant disparities in anaemia levels among the provinces. Analysis of the maps indicated that the Southern province had the lowest recorded Hb levels, followed by the Western, Luapula, and Eastern provinces. These variations in anaemia levels can be attributed to individual-level factors such as wealth index, with women from poor or middle-income backgrounds being more susceptible to anaemia compared to those from wealthier backgrounds. Considering the multifaceted nature of anaemia, it is evident that tailored approaches such as improving iron uptake is crucial to addressing anaemia levels. Therefore, the Ministry of Health can implement policies aimed at prioritizing and promoting iron supplementation to address this issue in the affected provinces. At the facility level, healthcare

providers should continue to educate and encourage women to take their prescribed iron tablets. In addition, engaging with community structures such as community health workers, health worker volunteers, and youth-friendly spaces can help raise awareness and disseminate messages about the significance of iron tablet consumption at the community level.

Household size has been identified as a significant future predictor of anaemia from the GWR model. Therefore, it is crucial to prioritize messaging campaigns that emphasize family planning and highlight the importance of maintaining a family size that can be adequately supported in these areas. By adopting such an approach, policymakers can tailor their strategies to address the specific needs of each province effectively.

Incorporating spatial analysis into future investigations of temporal trends will bolster the existing evidence and emphasize the significance of this methodology. Additionally, comparative studies examining anaemia in pregnant women alongside other factors like diet will contribute valuable insights for policy development. Furthermore, employing a mixed-method approach encompassing both qualitative and quantitative research will provide a comprehensive understanding of the various factors influencing anaemia in pregnant women.

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APPENDICES

Appendix A1 Ethics

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Miss Charlotte Mulaga

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M221182

NAME: (Principal Investigator)	Miss Charlotte Mulaga
DEPARTMENT:	Epidemiology and Biostatistics
PROJECT TITLE:	*The effect of intermittent preventive treatment uptake on Anemia amongst pregnant women in Zambia in 2018: A spatial analysis*
DATE CONSIDERED:	Ad hoc
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof E. Musenge
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	09/12/2022

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions.Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report.** The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **November** and will therefore be due in the month of **November** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

C.Mulaga — Principal Investigator Signature

09/12/2022 — Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix A2 Plagiarism declaration

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

FACULTY OF HEALTH SCIENCES

PLAGIARISM DECLARATION TO BE SIGNED BY ALL HIGHER DEGREE STUDENTS

SENATE PLAGIARISM POLICY: APPENDIX ONE

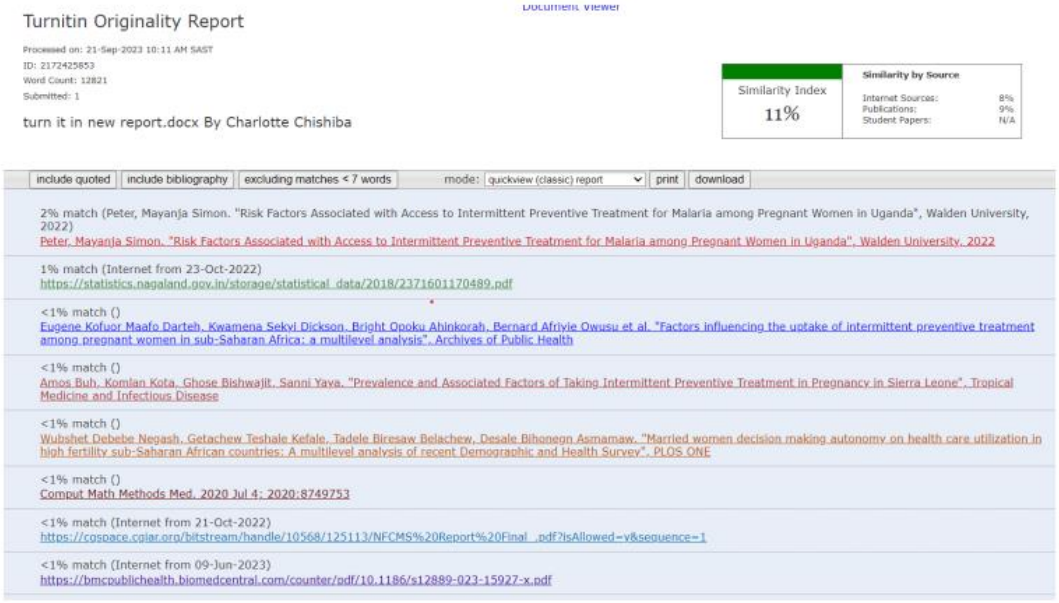
I Charlotte Chishiba (Student number: 2606351) am a student registered for the degree of MSc Epidemiology Implementation Science in the academic year 2023.

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature: C.Chishiba Date: 20/09/2023

Appendix A3 Turnitin report



Turnitin Originality Report

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Amos Buh, Komlan Kota, Ghose Bishwajit, Sanni Yaya. "Prevalence and Associated Factors of Taking Intermittent Preventive Treatment in Pregnancy in Sierra Leone", Tropical Medicine and Infectious Disease

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Comput Math Methods Med. 2020 Jul 4; 2020:8749753

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https://bmcpublichealth.biomedcentral.com/counter/pdf/10.1186/s12889-023-15927-x.pdf

Supervisor 1 signature:

Supervisor 2 signature

Appendix B Authorisation letter DHS

Jun 21, 2022

Charlotte Chishiba
University of the Witswaterands
Zambia
Request Date: 06/20/2022

Dear Charlotte Chishiba:

This is to confirm that you are approved to use the following SPA Datasets for your registered research paper titled: "Uptake of Intermittent preventive treatment with sulfodoxine- prymethamine against malaria and anemia a spatial analysis":

Kenya, Malawi, Zambia

To access the datasets, please login at: https://www.dhsprogram.com/data/dataset_admin/login_main.cfm. The user name is the registered email address, and the password is the one selected during registration.

The IRB-approved procedures for DHS public-use datasets do not in any way allow respondents, households, or sample communities to be identified. There are no names of individuals or household addresses in the data files. The geographic identifiers only go down to the regional level (where regions are typically very large geographical areas encompassing several states/provinces). Each enumeration area (Primary Sampling Unit) has a PSU number in the data file, but the PSU numbers do not have any labels to indicate their names or locations. In surveys that collect GIS coordinates in the field, the coordinates are only for the enumeration area (EA) as a whole, and not for individual households, and the measured coordinates are randomly displaced within a large geographic area so that specific enumeration areas cannot be identified.

The DHS Data may be used only for the purpose of statistical reporting and analysis, and only for your registered research. To use the data for another purpose, a new research project must be registered. All DHS data should be treated as confidential, and no effort should be made to identify any household or individual respondent interviewed in the survey. Also, be aware that re-distribution of any DHS micro-level data, either directly or within any tool/dashboard, is not permitted. Please reference the complete terms of use at: https://dhsprogram.com/Data/terms-of-use.cfm.

The data must not be passed on to other researchers without the written consent of DHS. However, if you have coresearchers registered in your account for this research paper, you are authorized to share the data with them. All data users are required to submit an electronic copy (pdf) of any reports/publications resulting from using the DHS data files to: references@dhsprogram.com.

Sincerely,

Bridgette Wellington

Bridgette Wellington
Data Archivist
The Demographic and Health Surveys (DHS) Program

530 Gaither Road, Suite 500, Rockville, MD 20850 USA +1.301.407.6500 +1.301.407.6501 fax icf.com

Appendix C CAR model

```
setwd ("C:/Users/charlotte chishiba/Desktop/Resaerch stata/data")

library(haven)

Data1 <- read_stata("arc2cleaned.dta")

View(Data1)

##read in a shapefile

setwd ("C:/Users/charlotte chishiba/Desktop/Resaerch stata/ZMB_adm")

zamadm2 <- st_read("ZMB_adm2.shp")

# Plot spatial data with sf

plot(zamadm2)

# Create a custom ggplot2 plot of spatial data

ggplot() +

geom_sf(data = zamadm2, aes(fill = ID_2)) +

scale_fill_gradient(low = "blue", high = "red") +

theme_void()

install.packages("BayesX")

####changing to bnd from sf

library(BayesX)

library(sf)

zamadm2_bnd <- sf2bnd(zamadm2)

zamadm2_bnd <- shp2bnd(shpname="ZMB_adm2", regionnames="ID_2")

plot(zamadm2,border = "red", axes = TRUE, las = 1)

library(ggplot2)

zagra <- bnd2gra(zamadm2_bnd)

imodel <- bayesx(anaemia_hemo ~ as.factor(IPTp_SP) + as.factor(age)+
as.factor(household_size) + as.factor(wealth_tertiles)+ as.factor(woman_occupation)
```

```
+as.factor(parity) + as.factor(access_media) + as.factor(type_of_anc) +
as.factor(woman_edulevel)+

sx(id_2, bs = "mrf", map = zagra) +

sx(id_2, bs = "re"), family = "binomial", method = "MCMC",

iterations = 50000, burnin = 2000, step = 10, weights = NULL,

subset = NULL, offset = NULL, na.action = NULL, seed = 12345,

predict = TRUE, data = Data1)

summary(imodel)

# getting odds ratio

exp(coef(imodel))

## odds ratios at 95% CI

exp(cbind(OR = coef(imodel), confint(imodel)))

###plot structured spatial effect

plot(imodel, term = "sx(id_2):mrf", map =zamadm2_bnd, main = "Structured spatial effect")

###plot unstructured spatial effect

plot(imodel, term = "sx(id_2):re", map = zamadm2_bnd, main = "Unstructured spatial effect")

#####total spatial effect

plot(imodel, term = "sx(id_2):total", map = zamadm2_bnd,

main = "Total spatial effect", digits = 4)
```

Appendix D Power calculation
Power calculation Formula

Outcome Variable: Anaemia, No Anaemia

Exposure : Uptake (2 or less doses), optimal (3 or more doses)

H0: Those that took IPTp had no anaemia

Estimates sample size =1109

Proportion of women who took IPTp=59% we will use optimal uptake from the literature

Proportion who suboptimal IPTp=41%

N1 = 59% * 1109 = 654

N2 = 41% * 1109= 456

The prevalence of anaemia in Zambia is around 38%

Assumptions

Anaemia in pregnant women that took IPTp= 40%

Anaemia in women who did not take IPTp= 31%

Using STATA to find

```
. power twoproportions 0.40 0.31, n1(654) n2(456)

Estimated power for a two-sample proportions test
Pearson's chi-squared test
H0: p2 = p1  versus  Ha: p2 != p1

Study parameters:

        alpha =    0.0500
            N =     1,110
           N1 =       654
           N2 =       456
        N2/N1 =    0.6972
        delta =   -0.0900  (difference)
           p1 =    0.4000
           p2 =    0.3100

Estimated power:

        power =    0.8695
```

Appendix E Stata Analysis

```
***Weighted data ******************************
egen strata=group(province residence)
gen sampwt=hv005/1000000
gen psu=clus_no
svyset psu [pw=sampwt],strata(strata)


 set more off
 set showbaselevels all

****Descriptive analysis
****Unweighted p values
svy linearized: tab IPTp_SP, count col percent obs
svy linearized: tab age , count col percent obs
svy linearized: tab v151 , count col percent obs
svy linearized: tab province , count col percent obs
svy linearized: tab residence , count col percent obs
svy linearized: tab woman_edulevel, count col percent obs
svy linearized: tab household_size, count col percent obs
svy linearized: tab access_media, count col percent obs
svy linearized: tab wealth_tertiles, count col percent obs
svy linearized: tab slept_bednet2 , count col percent obs
svy linearized: tab parity, count col percent obs
svy linearized: tab antenatal, count col percent obs
svy linearized: tab iron_tablets, count col percent obs
svy linearized: tab type_of_anc, count col percent obs
svy linearized: tab intestinal_taken, count col percent obs
svy linearized: tab woman_occupation, count col percent obs
svy linearized: tab marital_status2 , count col percent obs
svy linearized: tab antenatal_visits, count col percent obs
```

```
svy: mean Hb, over(IPTp_SP) coeflegend
estat sd
svy: mean Hb, over(age) coeflegend
estat sd
svy: mean Hb, over(v151) coeflegend
estat sd
svy: mean Hb, over(province) coeflegend
estat sd
svy: mean Hb, over(residence) coeflegend
estat sd
svy: mean Hb, over(woman_edulevel) coeflegend
estat sd
svy: mean Hb, over( household_size) coeflegend
estat sd
svy: mean Hb, over(access_media) coeflegend
estat sd
svy: mean Hb, over( wealth_tertiles) coeflegend
estat sd
svy: mean Hb, over( slept_bednet2) coeflegend
estat sd
svy: mean Hb, over( parity) coeflegend
estat sd
svy: mean Hb, over( antenatal) coeflegend
estat sd
svy: mean Hb, over( iron_tablets) coeflegend
estat sd
svy: mean Hb, over( type_of_anc) coeflegend
estat sd
```

```
svy: mean Hb, over( intestinal_taken) coeflegend
```

```
estat sd

svy: mean Hb, over( woman_occupation) coeflegend

estat sd

svy: mean Hb, over( marital_status2) coeflegend

estat sd

svy: mean Hb, over( marital_status2) coeflegend

estat sd

test _b[c.hemoglobin_level@0bn.marital_status2] =
_b[c.hemoglobin_level@1.marital_status2]

svy: mean Hb, over( antenatal_visits) coeflegend

estat sd

test _b[c.hemoglobin_level@0bn.antenatal_visits] =
_b[c.hemoglobin_level@1.antenatal_visits]

*****test for normality on hemoglobin_level

pnorm Hb if IPTp_SP==1

pnorm Hb if IPTp_SP==0

sdtest Hb, by (IPTp_SP)

***UNIVARITE ANALYSIS

*****SAVY SET DATA

svy: regress Hb i.IPTp_SP

testparm i.IPTp_SP

svy: regress Hb i.age

testparm i.age

svy: regress Hb i.v151

testparm i.v151

svy: regress Hb i. province

testparm i. province


svy: regress Hb i.residence

testparm i.residence

svy: regress Hb i.woman_edulevel

testparm i.woman_edulevel
```

svy: regress Hb i.household_size

testparm i.household_size

svy: regress Hb i.access_media

testparm i.access_media

svy: regress Hb i.wealth_tertiles

testparm i.wealth_tertiles

svy: regress Hb i.slept_bednet2

testparm i.slept_bednet2

svy: regress Hb i.parity

testparm i.parity

svy: regress Hb i.antenatal

testparm i.antenatal

svy: regress Hb i.iron_tablets

testparm i.iron_tablets

svy: regress Hb i.type_of_anc

testparm i.type_of_anc

svy: regress Hb i.intestinal_taken

testparm i.intestinal_taken

svy: regress Hb i.woman_occupation

testparm i.woman_occupation

svy: regress Hb i.marital_status2

testparm i.marital_status2

svy: regress Hb i.antenatal_visits

testparm i.antenatal_visits

sw, pe(0.20) lockterm1: regress Hb (i.IPTp_SP i.age) i.v151 i.province i.residence i.woman_edulevel i.household_size i.access_media i.wealth_tertiles i.slept_bednet2 i.parity i.antenatal i.iron_tablets i.type_of_anc i.intestinal_taken i.woman_occupation i.marital_status2 antenatal_visits

svy: regress Hb i.IPTp_SP i.age i.wealth_tertiles i.province i.household_size i.woman_occupation i.access_media i.parity i.type_of_anc i.woman_edulevel

****Checking for multicolinearity

display "tolerance = " 1-e(r2) " VIF = " 1/(1-e(r2))

estat gof

***multi-level

xtset clus_no

****multi-level analysis for random effects

xtreg Hb i.IPTp_SP i.age i.wealth_tertiles i.province i.household_size i.woman_occupation i.access_media i.parity i.type_of_anc i.woman_edulevel, mle